ANCO's ASCO20 Virtual Highlights

August 22, 2020

ANCO

Educating and Empowering the
Northern California Cancer Community

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Association of Northern California Oncologists (ANCO)

presents

ASCO20 Virtual Highlights

Saturday, August 22, 2020; 8AM-12:30PM

Agenda & Schedule

8:00AM OPENING REMARKS & INTRODUCTIONS
Daniel P. Mirda, MD, Program Moderator and *ANCO President*

8:05AM ASCO HIGHLIGHTS 2020: BREAST CANCER
Melinda Telli, MD, *Stanford University*

8:35AM ASCO HIGHLIGHTS 2020: GENITOURINARY CANCER
Primo N. "Lucky" Lara, MD, *University of California, Davis*

9:05AM ASCO HIGHLIGHTS 2020: GASTROINTESTINAL ONCOLOGY
Tyler Johnson, MD, *Stanford University*

9:35AM BREAK

10:00AM ASCO HIGHLIGHTS 2020: HEAD AND NECK CANCER
Jonathan Riess, MD, *University of California, Davis*

10:30AM ASCO HIGHLIGHTS 2020: LUNG CANCER
Caroline McCoach, MD, PhD *University of California, San Francisco*

11:00AM CANCER CARE DURING THE TIME of COVID-19
Moderator: **Robert Miller, MD**,**FACP, FASCO**, ASCO
Panelists: **Pelin Cinar, MD, MS**, *University of California, San Francisco*
Tatini Datta, MD *University of California, Davis*
Michael Zachary Koontz, MD, *Pacific Cancer Care*
Raymond Liu, MD, *The Permanente Medical Group*
Daniel Mirda, MD, *St. Joseph Health Medical Group*
Melinda Telli, MD, *Stanford University*

12:30PM ADJOURN

ASCO20 Virtual Highlights

Program Overview

ANCO's ASCO20 Virtual Highlights will summarize the major research and treatment advancements presented at this year's ASCO20 Virtual Meeting. The program will focus on breast, gastrointestinal, genitourinary, head and neck, and lung cancers, as well as a panel on cancer care during the time of COVID-19. The faculty will place these developments in context as to their immediate clinical utility.

Target Audience

ASCO20 Virtual Highlights has been designed to meet the educational needs of oncologists, oncology nurses, oncology pharmacists, and other health care professionals involved in the care of people with cancer.

Educational Objective

At the conclusion of this educational activity, participants should be able to:

Review, summarize, and interpret new advances and implement changes in the treatment of breast, genitourinary, gastrointestinal, head and neck, and lung cancers and cancer care during the time of COVID-19 as presented at the ASCO20 Virtual Meeting.

Program Planning Committee

The Physician Course Director for ANCO's ASCO20 Virtual Highlights is Daniel Mirda, MD, Annadel Medical Group. Dr. Mirda was assisted by the ANCO Board of Directors (A. Dimitrios Colevas, MD, Tatini Datta, MD, Bradley C. Ekstrand, MD, David Gandara, MD, Matthew Gubens, MD, Tyler Paul Johnson, MD, Michael Zachary Koontz, MD, Raymond Liu, MD, Joel Neal, MD, Stephanie Ossowski, MD, and Thach-Giao Truong, MD) and other Institutional Member and Group Member contacts in the selection of the faculty for ANCO's ASCO20 Virtual Highlights.

Program Faculty

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Associate Professor of Medicine in the Division of Medical Oncology
Stanford University

Speaker Disclosure of Relevant Financial Relationships

Pelin Cinar, MD, MS, disclosed that she does not have any relevant financial relationships with commercial interests.

Tatini Datta, MD, disclosed that she does not have any relevant financial relationships with commercial interests.

Tyler Johnson, MD, disclosed that he does not have any relevant financial relationships with commercial interests.

Michael Zachary Koontz, MD, disclosed that he does not have any relevant financial relationships with commercial interests.

Primo N. Lara, Jr., MD, disclosed that he does not have any relevant financial relationships with commercial interests.

Raymond Liu, MD, disclosed that he has received research funds from Genentech.

Caroline McCoach, MD, PhD, disclosed that she has received research funds from Novartis and Revolution Medicine.

Robert S. Miller, MD, FACP, FASCO, disclosed that he does not have any relevant financial relationships with commercial interests.

Daniel Mirda, MD, disclosed that he does not have any relevant financial relationships with commercial interests.

Jonathan Riess, MD, disclosed that he has received advisors fees from Medtronic ; consultant fees from EcoR1 , and research funds from AstraZeneca, Medtronic, Merck, Novartis, Revolution Medicine, and Spectrum.

Melinda L. Telli, MD, disclosed that she is an advisor: AbbVie, Celgene, Daiichi Sankyo, Genentech, G1 Therapeutics, Immunomedics, Lilly, Merck, Pfizer; and has Contracted Research (To her institution): AbbVie, AstraZeneca, Bayer, Calithera, EMD Serono, Genentech, Merck, OncoSec, Pfizer, PharmaMar, Tesaro, Vertex

Acknowledgement of Commercial Support

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Major Support

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Additional Support

Alexion Pharmaceuticals • Bristol-Myers Squibb Oncology • Caris Life Sciences • Deciphera • Eisai • Exact Sciences • Exelixis •Genentech• GlaxoSmithKline• Guardant Health• Kite, A Gilead Company • Merck• • Pharmacyclics • Seattle Genetics• Sun Pharma

ASCO HIGHLIGHTS 2020: BREAST CANCER

Melinda Telli, MD,
Stanford University

Presentation
Abstracts
Abbreviated Bio/CV

ASCO Update: Breast Cancer

Melinda Telli, M.D.
Associate Professor of Medicine
Stanford University School of Medicine
Director, Breast Cancer Program
Stanford Cancer Institute

August 22, 2020

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Disclosures

- Advisor: AbbVie, Celgene, Daiichi Sankyo, Genentech, G1 Therapeutics, Immunomedics, Lilly, Merck, Pfizer
- Contracted Research (To my institution): AbbVie, AstraZeneca, Bayer, Calithera, EMD Serono, Genentech, Merck, OncoSec, Pfizer, PharmaMar, Tesaro, Vertex

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Breast Cancer Abstracts

Presenter	Title
Khan	A randomized phase III trial of the value of early local therapy for the intact primary tumor in patients with metastatic breast cancer: ECOG-ACRIN 2018
Cortes	KEYNOTE-355: Randomized, double-blind, phase 3 study of pembrolizumab + chemotherapy versus placebo + chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer
Lin	Tucatinib vs. placebo added to trastuzumab and capecitabine for patients with previously treated HER2+ metastatic breast cancer with brain metastases (HER2CLIMB)

Role of early local therapy in de novo MBC?

Role of PD-1 addition in 1st line metastatic TNBC?

Role of tucatinib in HER2+ MBC?

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ECOG-ACRIN
cancer research group
Reshaping the future of patient care

A Randomized Phase III Trial of the Value of Early Local Therapy for the Intact Primary Tumor in Patients with Metastatic Breast Cancer: ECOG-ACRIN 2108

Seema A. Khan, Fengmin Zhao, Lawrence J. Solin, Brian Leyland-Jones, Lori J. Goldstein, David Cella, Mark Basik, Mehra Golshan, Thomas Julian, Barbara A. Pockaj, Christine A. Lee, Wajeeha Razaq, Joseph A. Sparano, Gildy V. Babiera, Irene A. Dy, Sarika Jain, Paula Silverman, Carla S. Fisher, Amye J. Tevaarwerk, Lynne I. Wagner, George W. Sledge .

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PRESENTED BY: Seema A. Khan MD

http://clicktoeditURL.com 1

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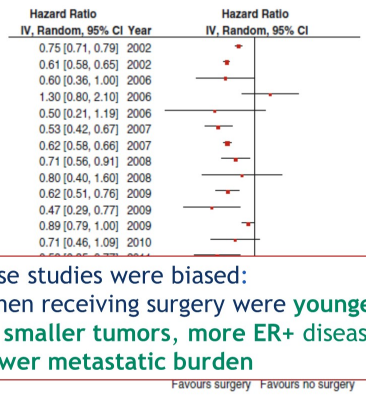
Background

- About 6% of newly diagnosed breast cancer patients present with Stage IV disease and an intact primary tumor (IPT).
- Locoregional treatment (LRT) for the IPT is hypothesized to improve survival based on retrospective analyses.



These studies were biased:
women receiving surgery were **younger**, had **smaller tumors**, **more ER+** disease, and a **lower metastatic burden**

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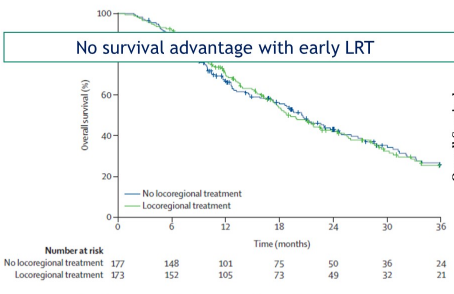
Completed randomized trials testing the value of LRT in *de novo* Stage IV breast cancer have provided conflicting data

Tata memorial Hospital, Mumbai, India

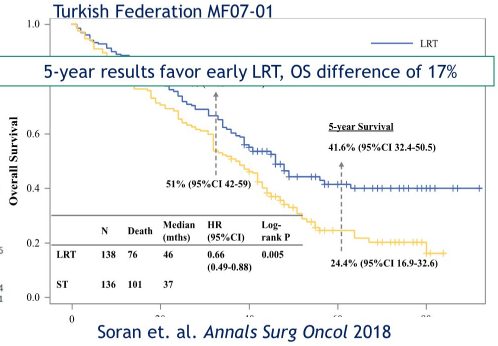
No survival advantage with early LRT



Badwe et. al. *Lancet Oncol* 2017

Turkish Federation MF07-01

5-year results favor early LRT, OS difference of 17%



Soran et. al. *Annals Surg Oncol* 2018

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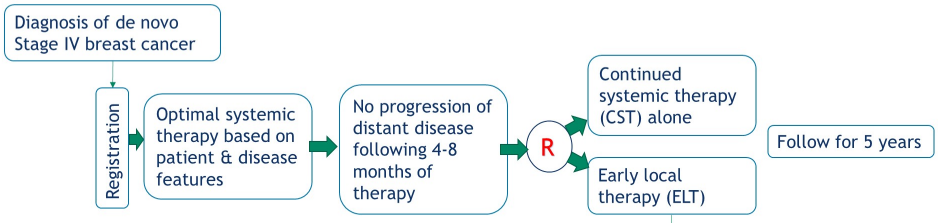
Design of E2108

Opened in 2011, last patient enrolled in 2015.



Statistical design amended in 2013 due to slow accrual.
With **368 enrolled, 258 randomized** and total information of 152 deaths, we would have 85% power to detect a **19% difference in the 3-year OS rates**

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Endpoints

Primary

- Overall survival

Secondary

- Time to locoregional progression
- Health-related quality of life
- Absolute value of circulating tumor cell burden
- Collection of biological samples

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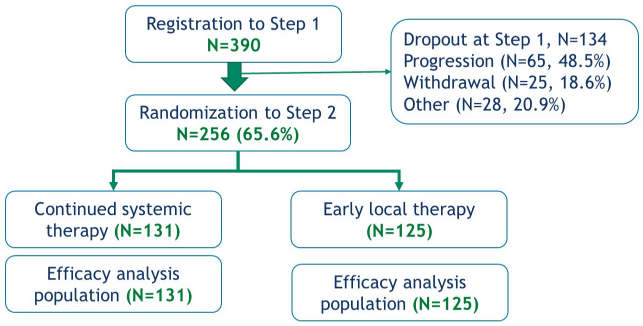
Consort diagram



- Overall cross-over rate between arms was 14% while the planned cross-over rate was 15%.

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Results: participant characteristics.

	Registered (N=390)	Not randomized (N=134)	Randomized (N=256)	P
Median Age in years (range)		57 (29-84)	56 (25-86)	0.54
Race/ethnicity	% of 390	% of 134	% of 256	
European	77.3	104 (80.6)	200 (82.3)	0.51
African	15.8	24 (18.6)	38 (15.6)	
Latina	8.4	9 (7.2)	24 (10.3)	0.33
Postmenopausal	249/390	68.7%	63.9%	0.45
Breast cancer subtype	% of 393	% of 134	% of 256	0.07
HR positive & HER2 negative	54.2	58.5	59.6	
Triple negative	10.2	15.4	8.2	
HER2 positive	28.8	26.2	32.2	

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Results: distant disease patterns and initial systemic therapy used.

	Registered (N=390)	Not randomized (N=134)	Randomized (N=256)	P
Metastatic sites	% of 390	% of 134	% of 256	
Bone only	31.5	27.1	37.9	0.51
Visceral only	26.4	32.3	24.2	
Bone & visceral	27.2	40.6	40.9	0.33
	% of 373	% of 126	% of 247	
Initial systemic therapy				0.93
Only endocrine therapy	27.2	31.7	31.2	
Chemotherapy ± HER2-directed agent*	54.2	54.8	53.8	
Both endocrine and chemotherapy	13.7	13.5	15.0	
*HER-2 directed therapy was used in 103/113 patients with HER-2 positive tumors				

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Results: primary tumor characteristics.

	Drop-out during Initial systemic therapy N=134	Randomized to Step 2 Distant disease stable or responding N=256	
Primary tumor	% of 134	% of 256	
T1-3, N0-1	50.4	52.0	
T4 and/or N2-3	49.6	48.0	
Primary tumor palpable	87.2	86.1	0.763
Direct invasion into skin	23.3	11.6	0.003
Skin nodules present	13.5	6.4	0.019
Attached to fascia	24.2	17.9	0.358
No skin involvement or pain	59.1	66.1	0.173

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Results: characteristics of randomized participants, by arm.

	Continued systemic therapy (N=126)	Early local therapy (N=121)
Median Age in years (range)	56 (25-86)	55 (30-81)
	% of 126	% of 121
Race/ethnicity		
European	82.0	82.0
African	15.3	16
Latina	12	8.6
Single organ system involved	60.3	52.1
Breast cancer subtype		
HR positive & HER2 negative	57	59.0
Triple negative	9.1	7.8
HER2 positive	33.9	33.0

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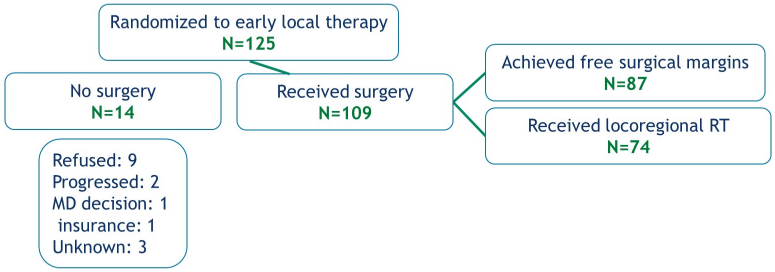
Delivery of locoregional therapy in early local therapy arm



- In the systemic therapy arm, 25 women received surgery: 13 in the year following randomization and 12 at a later time.

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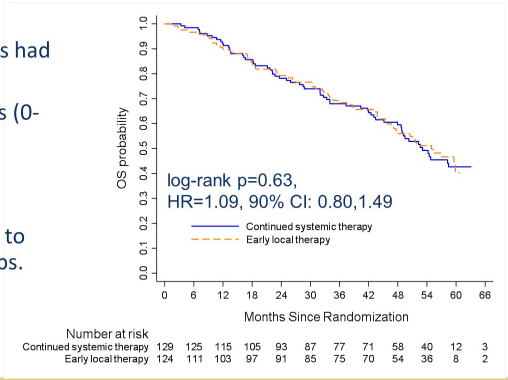
Results: overall survival

- As of December 10, 2019, 121 patients had died (80% of full information).
- Median follow-up time was 53 months (0-91)
- Median survival was 54 months
- Stratified log rank test and Cox proportional hazard model were used to compare OS between treatment groups.



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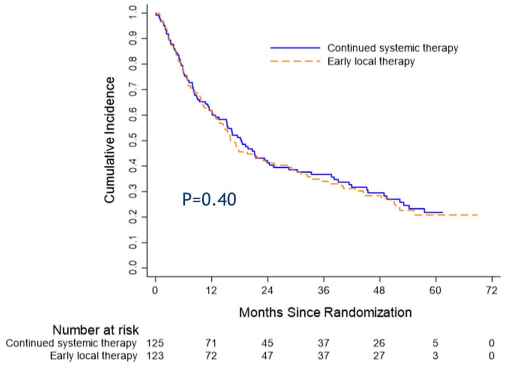
Results: progression-free survival

- As of the data cutoff date, 178 patients had disease progression or death
- 89 patients on each arm
- Kaplan-Meier estimates of PFS were compared by treatment arm using a stratified log-rank test



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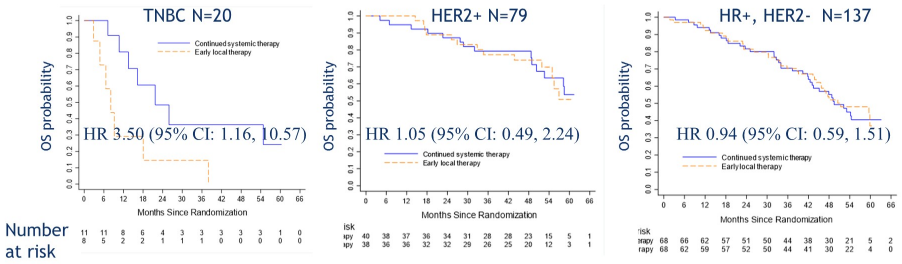
Results: overall survival by tumor subtype



- For 20 women with TNBC, survival was worse in the early local therapy arm.

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Locoregional progression.

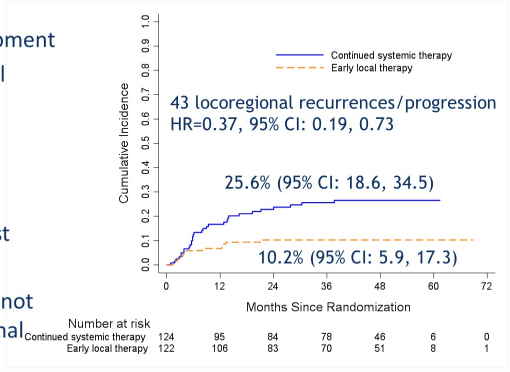
Definitions

Continued systemic therapy arm: Development of symptoms leading to a decision for local therapy.

Early local therapy arm

1) Regional nodal progression
2) Chest wall disease or invasive in-breast recurrence;

The occurrence of distant progression did not preclude the reporting of later local-regional recurrence/progression



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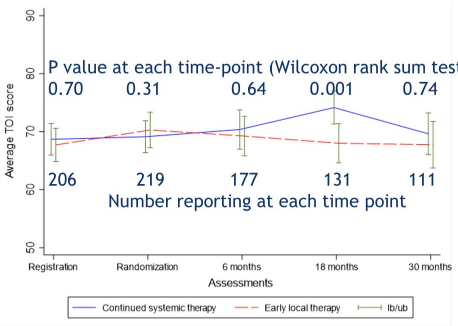
Results: health-related quality of life.

- FACT-B TOI was the primary HRQoL endpoint
- Measured by the prorated aggregate score of the 24 items from the FACT-B
- FACT-B TOI was significantly lower in patients receiving early local therapy at 18 months post randomization
- No significant difference was found between arms at other assessment time points



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Conclusions

- Early local therapy does not improve survival in patients with de novo metastatic breast cancer and an intact primary tumor.
- Although we saw a 2.5-fold higher risk of local disease progression without LRT, the use of LRT for the primary site did not lead to improved HRQOL.
- Based on available data, LRT for the primary tumor should not be offered to women with Stage IV breast cancer with the expectation of a survival benefit.
- When systemic disease is well-controlled with systemic therapy but the primary site is progressing, LRT may be considered.
- Results from JCOG-1017 are pending.

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KEYNOTE-355: Randomized, Double-Blind, Phase 3 Study of Pembrolizumab + Chemotherapy versus Placebo + Chemotherapy for Previously Untreated Locally Recurrent Inoperable or Metastatic Triple-Negative Breast Cancer

Javier Cortes[1], David W. Cescon[2], Hope S. Rugo[3], Zbigniew Nowecki[4], Seock-Ah Im[5], Mastura Md Yusof[6], Carlos Gallardo[7], Oleg Lipatov[8], Carlos H. Barrios[9], Esther Holgado[1], Hiroji Iwata[10], Norikazu Masuda[11], Marco Torregroza Otero[12], Erhan Gokmen[13], Sherene Loi[14], Zifang Guo[15], Jing Zhao[15], Gursel Aktan[15], Vassiliki Karantza[15], Peter Schmid[16]

[1]IOB Institute of Oncology, Quiron Group; VaII d'Hebron Institute of Oncology (VHIO), Madrid & Barcelona, Spain; [2]Princess Margaret Cancer Centre, Toronto, Ontario, Canada; [3]University of California San Francisco Comprehensive Cancer Center, San Francisco, CA, USA; [4]Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw, Poland; [5]Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul, Korea; [6]Pantai Hospital, Kuala Lumpur, Malaysia; [7]Arturo Lopez Perez Foundation, Santiago, Chile; [8]Republican Clinical Oncology Dispensary, Republic of Bashkortostan, Russian Federation; [9]Oncology Research Unit, HSL, PUCRS, Porto Alegre, Brazil; [10]Aichi Cancer Center Hospital, Nagoya, Japan; [11]National Hospital Organization, Osaka National Hospital, Osaka, Japan; [12]Oncomedica S.A., Monteria, Colombia; [13]Ege University Medical Faculty, Izmir, Turkey; [14]Peter McCallum Cancer Centre, Melbourne, Australia; [15]Merck & Co., Inc., Kenilworth, NJ, USA; [16]Barts Cancer Institute, Centre for Experimental Cancer Medicine, London, UK

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Pembrolizumab Monotherapy in mTNBC

- Pembrolizumab monotherapy showed durable antitumor activity and manageable safety in patients with mTNBC[1-4]
  - Improved clinical responses observed in patients with higher PD-L1 expression[4]
  - Responses to pembrolizumab monotherapy were more durable than those to chemotherapy[4]

Study	Population	N	ORR	Median DOR, mo (range)	Median PFS, mo (95% CI)	6-mo PFS	12-mo OS
KEYNOTE-012[1]	Heavily pretreated PD-L1–positive[a]	27	18.5%	NR (3.4 – 10.8+)	1.9 (1.7 – 5.5)	24.4%	43.1%
KEYNOTE-086A[2]	Previously treated PD-L1–unselected	170	5.3%	NR (1.2+ – 21.5+)	2.0 (1.9 – 2.0)	14.9%	39.8%
KEYNOTE-086B[3]	Previously untreated PD-L1–positive[b]	84	21.4%	10.4 (4.2 – 19.2+)	2.1 (2.0 – 2.2)	27.0%	61.7%
KEYNOTE-119[4]	Previously treated PD-L1–unselected	312	9.6%	12.2 (2.2 – 32.5+)	2.1 (2.0 – 2.1)	14.7%	42.8%

mTNBC = metastatic triple-negative breast cancer; ORR = objective response rate; DOR = duration of response; mo = month; PFS = progression-free survival; OS = overall survival; NR = not reached.
[a]Expression in stroma or ≥1% of tumor cells by immunohistochemistry and the 22C3 antihuman PD-1 antibody (Merck & Co., Kenilworth, NJ). [b]Assessed at a central laboratory using the PD-L1 IHC 22C3 pharmDx assay defined as the combined positive score (CPS), the number of PD-L1–positive cells (tumor cells, lymphocytes, macrophages) divided by total number of tumor cells × 100; PD-L1–positive = CPS ≥1.
1. Nanda R et al. *J Clin Oncol* 2016;34:2460-7. 2. Adams S et al. *Ann Oncol* 2019;30:397-404. 3. Adams S et al. *Ann Oncol* 2019;30:405-11. 4. Cortes J et al. *Ann Oncol* 2019; 30(suppl 5):v851-v934.

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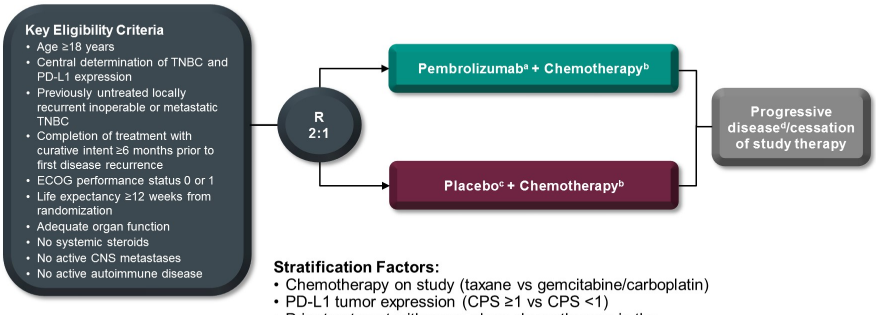
KEYNOTE-355 Study Design (NCT02819518)



Stratification Factors:
- Chemotherapy on study (taxane vs gemcitabine/carboplatin)
- PD-L1 tumor expression (CPS ≥1 vs CPS <1)
- Prior treatment with same class chemotherapy in the neoadjuvant or adjuvant setting (yes vs no)

[a]Pembrolizumab 200 mg intravenous (IV) every 3 weeks (Q3W)
[b]Chemotherapy dosing regimens are as follows:
Nab-paclitaxel 100 mg/m^2 IV on days 1, 8, and 15 every 28 days
Paclitaxel 90 mg/m^2 IV on days 1, 8, and 15 every 28 days
Gemcitabine 1000 mg/m^2/carboplatin AUC 2 on days 1 and 8 every 21 days

[c]Normal saline
[d]Treatment may be continued until confirmation of progressive disease
CNS=central nervous system; ECOG=Eastern Cooperative Oncology Group; PD-L1=programmed death ligand 1; R=randomized; TNBC=triple-negative breast cancer

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Study Endpoints

- Primary Endpoints
  - PFS[a] in patients with PD-L1–positive tumors[b] (CPS ≥10 and CPS ≥1) and in the ITT population
  - OS[c] in patients with PD-L1–positive tumors[b] (CPS ≥10 and CPS ≥1) and in the ITT population
- Secondary Endpoints
  - ORR[a,c]
  - DOR[a,c]
  - DCR[a,c]
  - Safety in all treated patients

PFS = progression-free survival; OS = overall survival; ORR = objective response rate; DOR = duration of response; DCR = disease control rate (CR+PR+SD ≥24 wks).
[a]Based on RECIST v 1.1 assessed by a central imaging vendor; [b]PD-L1 assessed at a central laboratory using the PD-L1 IHC 22C3 pharmDx assay and measured using the combined positive score (CPS; number of PD-L1–positive tumor cells, lymphocytes, and macrophages divided by total number of tumor cells x 100);[c]To be presented at a later date.

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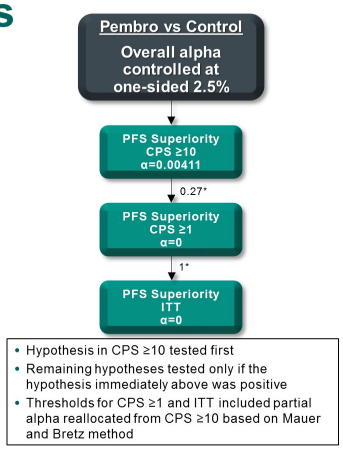
Statistical Considerations

- Overall alpha controlled at one-sided 0.025, split among PFS (0.005),OS (0.018), and ORR (0.002)
- PFS was tested using a hierarchical strategy
- Prespecified analysis plan allows alpha from successful hypotheses to be passed to other hypotheses
- Final PFS assessment performed at second interim analysis:
  - Data cutoff date: December 11, 2019



PFS = progression-free survival; OS = overall survival; ORR = objective response rate. PD-L1 assessed at a central laboratory using the PD-L1 IHC 22C3 pharmDx assay and measured using the combined positive score (CPS; number of PD-L1–positive tumor cells, lymphocytes, and macrophages divided by total number of tumor cells x 100).
*The weights for alpha reallocation from each hypothesis to the others are represented by the numbers along the lines connecting hypotheses.

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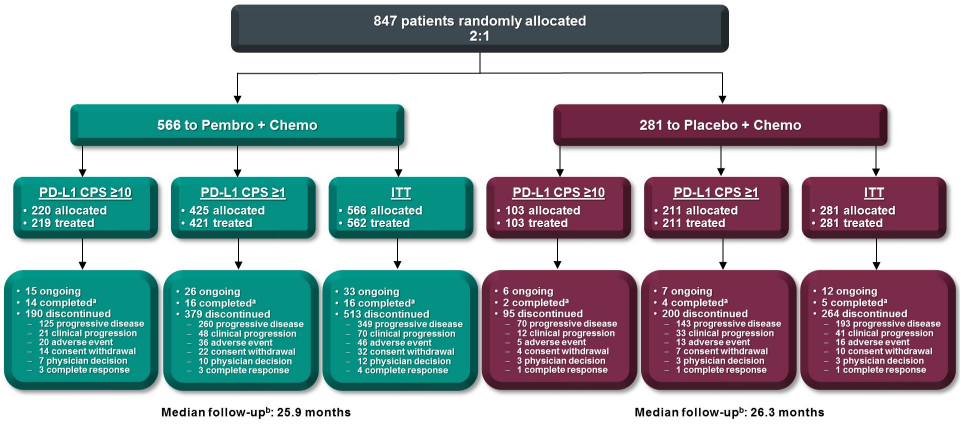
Treatment Disposition of All Randomized Patients



[a]Includes all patients who received 35 administrations of pembrolizumab or placebo and discontinued from chemotherapy; [b]Defined as the time from randomization to the database cutoff date of December 11, 2019.

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Baseline Characteristics, ITT

Characteristic, n (%)	All Subjects, N = 847	
	Pembro + Chemo N = 566	Placebo + Chemo N = 281
Age, median (range), yrs	53 (25-85)	53 (22-77)
ECOG PS 1	232 (41.0)	108 (38.4)
PD-L1–positive CPS ≥1	425 (75.1)	211 (75.1)
PD-L1–positive CPS ≥10	220 (38.9)	103 (36.7)
Chemotherapy on study		
Taxane	255 (45.1)	127 (45.2)
Gemcitabine/Carboplatin	311 (54.9)	154 (54.8)
Prior same-class chemotherapy		
Yes	124 (21.9)	62 (22.1)
No	442 (78.1)	219 (77.9)
Disease-free interval		
de novo metastasis	167 (29.5)	84 (29.9)
<12 months	126 (22.3)	50 (17.8)
≥12 months	270 (47.7)	147 (52.3)

Data cutoff date: December 11, 2019.

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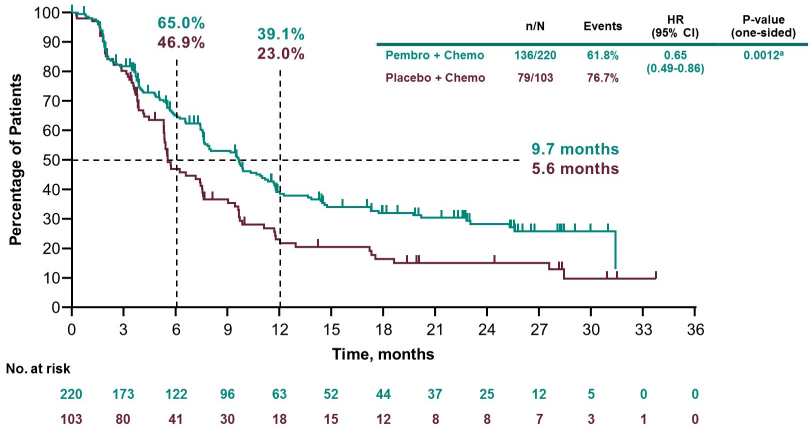
Progression-Free Survival: PD-L1 CPS ≥10



	n/N	Events	HR (95% CI)	P-value (one-sided)
Pembro + Chemo	136/220	61.8%	0.65 (0.49-0.86)	0.0012[a]
Placebo + Chemo	79/103	76.7%		

[a]Prespecified *P* value boundary of 0.00411 met.
Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Data cutoff December 11, 2019.

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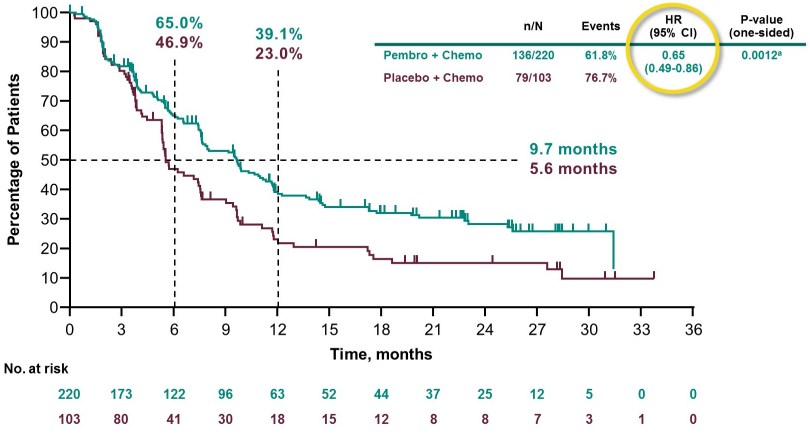
Progression-Free Survival: PD-L1 CPS ≥10



	n/N	Events	HR (95% CI)	P-value (one-sided)
Pembro + Chemo	136/220	61.8%	0.65 (0.49-0.86)	0.0012[a]
Placebo + Chemo	79/103	76.7%		

[a]Prespecified *P* value boundary of 0.00411 met.
Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Data cutoff December 11, 2019.

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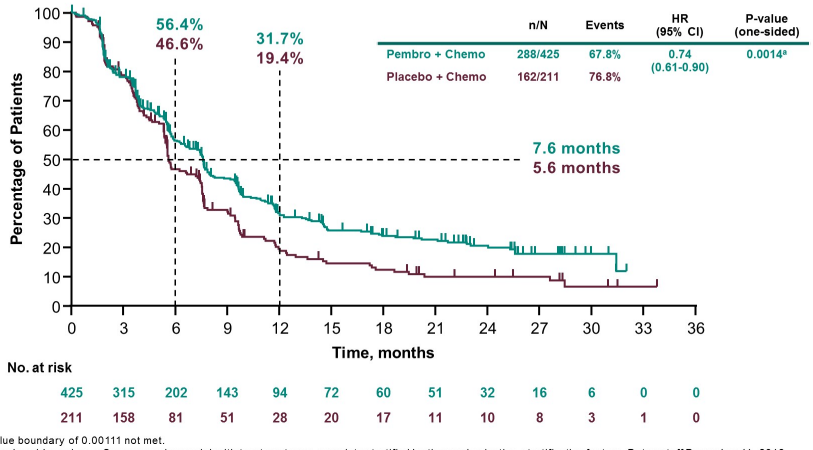
Progression-Free Survival: PD-L1 CPS ≥1



	n/N	Events	HR (95% CI)	P-value (one-sided)
Pembro + Chemo	288/425	67.8%	0.74 (0.61-0.90)	0.0014[a]
Placebo + Chemo	162/211	76.8%		

[a]Prespecified *P* value boundary of 0.00111 not met.
Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Data cutoff December 11, 2019.

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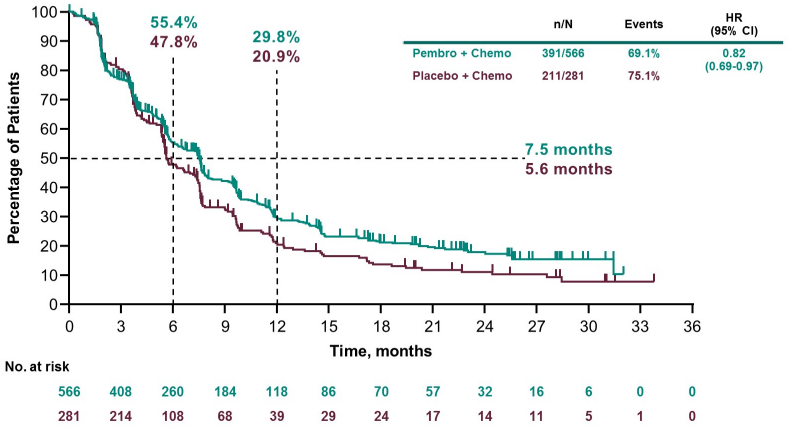
Progression-Free Survival: ITT



	n/N	Events	HR (95% CI)
Pembro + Chemo	391/566	69.1%	0.82 (0.69-0.97)
Placebo + Chemo	211/281	75.1%	

Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Statistical significance was not tested due to the prespecified hierarchical testing strategy. Data cutoff December 11, 2019.

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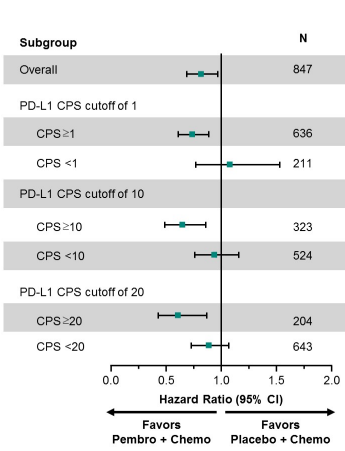
Progression-Free Survival in PD-L1 CPS Subgroups



Subgroup	N	Median PFS (mo) Pembro + Chemo	Median PFS (mo) Placebo + Chemo	Hazard Ratio for Progression or Death (95% CI)
Overall	847	7.5	5.6	0.82 (0.69 to 0.97)
PD-L1 CPS cutoff of 1				
CPS ≥1	636	7.6	5.6	0.74 (0.61 to 0.89)
CPS <1	211	6.3	6.2	1.08 (0.77 to 1.53)
PD-L1 CPS cutoff of 10				
CPS ≥10	323	9.7	5.6	0.65 (0.49 to 0.86)
CPS <10	524	5.8	5.7	0.94 (0.76 to 1.16)
PD-L1 CPS cutoff of 20				
CPS ≥20	204	9.5	5.4	0.61 (0.43 to 0.87)
CPS <20	643	6.6	5.8	0.89 (0.73 to 1.07)

PFS in the CPS ≥1 and CPS ≥10 populations were primary endpoints; PFS in the CPS ≥20 population was an exploratory endpoint. Data cutoff December 11, 2019.

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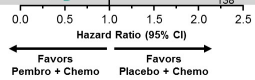
Progression-Free Survival in Subgroups: PD-L1 CPS ≥10

Subgroup	N	Median PFS (mo) Pembro + Chemo	Median PFS (mo) Placebo + Chemo	Hazard Ratio for Progression or Death (95% CI)
Overall	323	9.7	5.6	0.65 (0.49 to 0.86)
Age (years)				
<65	257	9.5	5.5	0.63 (0.46 to 0.87)
≥65	66	10.7	7.6	0.67 (0.37 to 1.23)
Geographic region				
N America/EU/ANZ	212	9.6	5.7	0.69 (0.49 to 0.97)
Asia	56	17.3	5.6	0.45 (0.22 to 0.91)
Rest of world	55	7.6	6.2	0.65 (0.40 to 1.56)
ECOG PS				
0	196	9.8	7.5	0.74 (0.51 to 1.07)
1	127	7.6	3.9	0.50 (0.33 to 0.78)
On-study chemotherapy				
Taxane	143	9.9	5.4	0.51 (0.33 to 0.78)
Gemcitabine/Carboplatin	180	8.0	7.2	0.77 (0.53 to 1.11)
Prior same class chemotherapy				
Yes	65	7.5	5.4	0.60 (0.32 to 1.15)
No	258	9.9	5.7	0.66 (0.48 to 0.90)
Prior neoadjuvant/adjuvant chemotherapy				
Yes	193	7.9	5.7	0.78 (0.55 to 1.12)
No	130	11.0	5.4	0.47 (0.30 to 0.74)
Disease-free interval				
de novo metastasis	103	9.7	5.3	0.48 (0.29 to 0.79)
<12 months	66	7.5	7.2	1.00 (0.51 to 1.95)
≥12 months	153	9.9	6.6	0.64 (0.43 to 0.95)
Number of metastatic sites				
<3	184	11.8	9.0	0.68 (0.46 to 1.00)
≥3	138	7.6	4.5	0.52 (0.34 to 0.78)



Data cutoff December 11, 2019.

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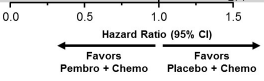
Progression-Free Survival in Subgroups: PD-L1 CPS ≥1

Subgroup	N	Median PFS (mo) Pembro + Chemo	Median PFS (mo) Placebo + Chemo	Hazard Ratio for Progression or Death (95% CI)
Overall	636	7.6	5.6	0.74 (0.61 to 0.90)
Age (years)				
<65	505	7.5	5.6	0.75 (0.61 to 0.93)
≥65	131	8.2	6.6	0.69 (0.45 to 1.07)
Geographic region				
N America/EU/ANZ	411	7.6	5.7	0.77 (0.61 to 0.98)
Asia	117	7.7	5.6	0.56 (0.36 to 0.89)
Rest of world	108	6.6	5.4	0.84 (0.52 to 1.36)
ECOG PS				
0	387	7.7	6.7	0.78 (0.61 to 1.00)
1	248	6.6	5.4	0.63 (0.46 to 0.87)
On-study chemotherapy				
Taxane	288	7.6	5.1	0.60 (0.45 to 0.81)
Gemcitabine/Carboplatin	348	7.5	7.5	0.86 (0.66 to 1.11)
Prior same class chemotherapy				
Yes	136	7.5	5.4	0.57 (0.37 to 0.86)
No	500	7.6	6.6	0.79 (0.64 to 0.99)
Prior neoadjuvant/adjuvant chemotherapy				
Yes	392	6.8	5.7	0.85 (0.67 to 1.09)
No	244	8.0	5.5	0.57 (0.41 to 0.78)
Disease-free interval				
de novo metastasis	200	7.6	5.6	0.66 (0.46 to 0.94)
<12 months	129	5.8	5.4	0.76 (0.49 to 1.17)
≥12 months	304	7.7	6.6	0.75 (0.57 to 0.99)
Number of metastatic sites				
<3	362	9.2	6.7	0.71 (0.54 to 0.92)
≥3	271	6.2	5.3	0.70 (0.52 to 0.94)



Data cutoff December 11, 2019.

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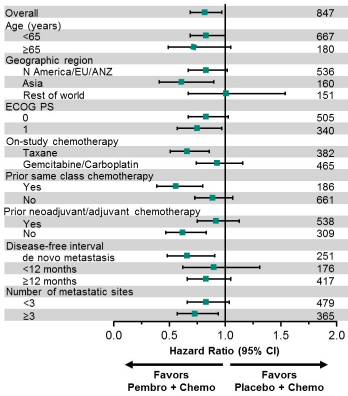
Progression-Free Survival in Subgroups: ITT

Subgroup	N	Median PFS (mo) Pembro + Chemo	Median PFS (mo) Placebo + Chemo	Hazard Ratio for Progression or Death (95% CI)
Overall	847	7.5	5.6	0.82 (0.69 to 0.97)
Age (years)				
<65	667	7.3	5.6	0.83 (0.69 to 1.00)
≥65	180	9.2	6.2	0.72 (0.49 to 1.05)
Geographic region				
N America/EU/ANZ	536	7.5	5.7	0.83 (0.67 to 1.02)
Asia	160	8.8	6.7	0.61 (0.41 to 0.90)
Rest of world	151	5.8	5.4	1.01 (0.67 to 1.54)
ECOG PS				
0	505	7.6	6.6	0.83 (0.67 to 1.03)
1	340	6.8	5.5	0.75 (0.57 to 0.97)
On-study chemotherapy				
Taxane	382	7.6	5.3	0.66 (0.51 to 0.86)
Gemcitabine/Carboplatin	465	7.4	7.4	0.93 (0.74 to 1.16)
Prior same class chemotherapy				
Yes	186	7.5	5.4	0.56 (0.39 to 0.80)
No	661	7.6	6.6	0.89 (0.73 to 1.07)
Prior neoadjuvant/adjuvant chemotherapy				
Yes	538	6.3	5.7	0.92 (0.75 to 1.13)
No	309	8.0	5.5	0.62 (0.47 to 0.83)
Disease-free interval				
de novo metastasis	251	7.7	5.5	0.66 (0.48 to 0.91)
<12 months	176	5.6	5.6	0.90 (0.62 to 1.31)
≥12 months	417	7.6	6.6	0.83 (0.66 to 1.05)
Number of metastatic sites				
<3	479	8.0	7.2	0.83 (0.66 to 1.04)
≥3	365	5.9	5.3	0.73 (0.57 to 0.94)



Data cutoff December 11, 2019.

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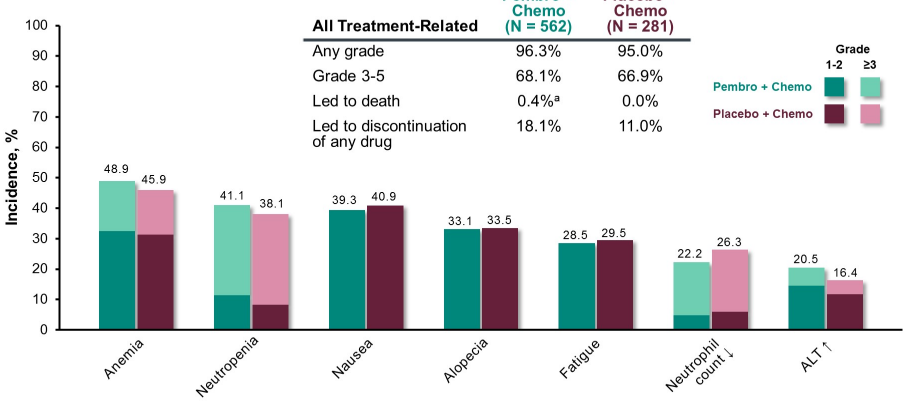
Treatment-Related AEs

All Treatment-Related	Pembro + Chemo (N = 562)	Placebo + Chemo (N = 281)
Any grade	96.3%	95.0%
Grade 3-5	68.1%	66.9%
Led to death	0.4%[a]	0.0%
Led to discontinuation of any drug	18.1%	11.0%



Treatment-Related AEs with Incidence ≥20% in Either Treatment Group

[a]1 patient from acute kidney injury and 1 patient from pneumonia. Data cutoff date: December 11, 2019.

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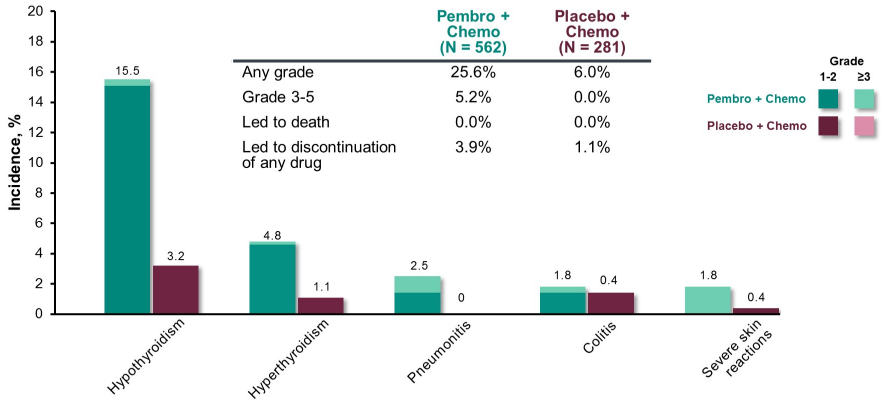
Immune-Mediated AEs



	Pembro + Chemo (N = 562)	Placebo + Chemo (N = 281)
Any grade	25.6%	6.0%
Grade 3-5	5.2%	0.0%
Led to death	0.0%	0.0%
Led to discontinuation of any drug	3.9%	1.1%

Immune-Mediated AEs with Incidence ≥10 Patients in Either Treatment Group[a]

[a]Based on a list of terms prespecified by the sponsor and included regardless of attribution to study treatment or immune relatedness by the investigator; related terms included. Data cutoff date: December 11, 2019.

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Summary

- Pembrolizumab + chemotherapy resulted in a statistically significant and clinically meaningful improvement in PFS versus chemotherapy alone for the first-line treatment of PD-L1–positive (CPS ≥10) mTNBC
- A trend towards improved efficacy with PD-L1 enrichment was observed in patients treated with pembrolizumab + chemotherapy
- Improvement in PFS was observed across patient subgroups
- Safety was consistent with the known profiles of each regimen
- These findings suggest a role for the addition of pembrolizumab to standard chemotherapy for the first-line treatment of mTNBC

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Tucatinib vs Placebo Added to Trastuzumab and Capecitabine for Patients with Previously Treated HER2+ Metastatic Breast Cancer with Brain Metastases (HER2CLIMB)

Nancy U. Lin, Rashmi K. Murthy, Carey Anders, Virginia Borges, Sara Hurvitz, Sherene Loi, Vandana Abramson, Philippe L. Bedard, Mafalda Oliveira, Amelia Zelnak, Michael DiGiovanna, Thomas Bachelot, A. Jo Chien, Ruth O'Regan, Andrew Wardley, Volkmar Mueller, Lisa Carey, Suzanne McGoldrick, Grace An, Eric P. Winer

PRESENTED AT: 2020ASCO ANNUAL MEETING #ASCO20

PRESENTED BY: Nancy Lin, nlin@partners.org

Presented By Nancy Lin at TBD

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Background

- Up to half of patients with HER2+ metastatic breast cancer may develop brain metastases and effective and tolerable treatment options are needed.[1-4]
- Tucatinib is an oral TKI, recently approved by the FDA, that is highly selective for the kinase domain of HER2 with minimal inhibition of EGFR.[5-6]

HER2CLIMB Randomized, Double-blind, Pivotal Trial

Key Eligibility Criteria
- HER2+ metastatic breast cancer
- Prior treatment with trastuzumab, pertuzumab, and T-DM1
- ECOG performance status 0 or 1
- Brain MRI at baseline

*Stratification factors: presence of brain metastases (yes/no), ECOG status (0 or 1), and region (US or Canada or rest of world)

R* (2:1)

N=410: **Tucatinib** 300 mg PO BID + **Trastuzumab** 6 mg/kg Q3W, loading dose 8 mg/kg C1D1 + **Capecitabine** 1000 mg/m² PO BID Days 1-14; *21-day cycle*

N=202: **Placebo** + **Trastuzumab** 6 mg/kg Q3W, loading dose 8 mg/kg C1D1 + **Capecitabine** 1000 mg/m² PO BID Days 1-14; *21-day cycle*

https://clinicaltrials.gov/ct2/show/NCT02614794

1. Bendell JC, et al. Cancer 2003;97:2972-7.
2. Brufsky AM, et al. Clin Cancer Res 2011;17:4834-43.
3. Leyland-Jones B. J Clin Oncol 2009;27:5278-86.
4. Olson EM, et al. Breast 2013;22:525-31.
5. Moulder SL, et al. Clin Cancer Res 2017;23:3529-36.
6. Pheneger T, et al. Cancer Research 2009;69:1795.

TKI: tyrosine kinase inhibitor

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PRESENTED BY: Nancy Lin, nlin@partners.org

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HER2CLIMB Primary Analysis Results

- The HER2CLIMB trial met all primary and alpha-controlled secondary endpoints at the first interim analysis.
- Importantly, the secondary endpoint of PFS in patients with brain metastases was met.

PFS by BICR N=480*	Overall Survival N=612	PFS by BICR in patients with brain metastases N=291
Risk of progression or death was reduced by **46%**	Risk of death was reduced by **34%**	Risk of progression or death was reduced by **52%**
95% CI: 0.42 to 0.71, P<0.001	95% CI, 0.50 to 0.88, P=0.005	95% CI, 0.34 to 0.69, P<0.001

PFS: progression-free survival; BICR: blinded independent central review
*The primary endpoint of PFS was assessed in the first 480 patients enrolled.

Murthy RK, et al. *N Engl J Med* 2020;382:597-609.

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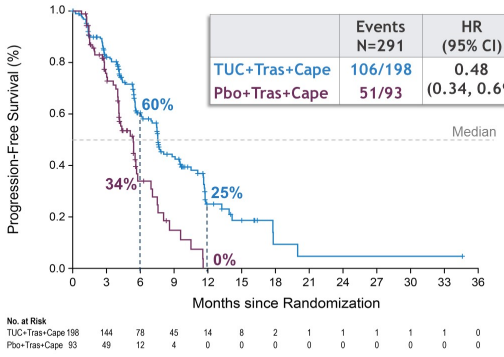
Progression-Free Survival* in Patients with Brain Metastases

Alpha-controlled secondary endpoint in the HER2CLIMB trial



	Events N=291	HR (95% CI)	P Value
TUC+Tras+Cape	106/198	0.48 (0.34, 0.69)	<0.00001
Pbo+Tras+Cape	51/93		

Risk of progression or death in patients with brain metastases was reduced by 52% in the total population

One-year PFS (95% CI):	
TUC+Tras+Cape 25% (17, 34)	Pbo+Tras+Cape 0%
Median PFS (95% CI):	
TUC+Tras+Cape 7.6 months (6.2, 9.5)	Pbo+Tras+Cape 5.4 months (4.1, 5.7)

Prespecified efficacy boundary for PFS-brain metastases (P=0.0080) was met at the first interim analysis.
Data cut off: Sep 4, 2019

*PFS, defined as time from randomization to documented disease progression (assessed by blinded independent central review) or death from any cause. Analysis does not include patients with dural lesions only.

Murthy RK, et al. *N Engl J Med* 2020;382:597-609.

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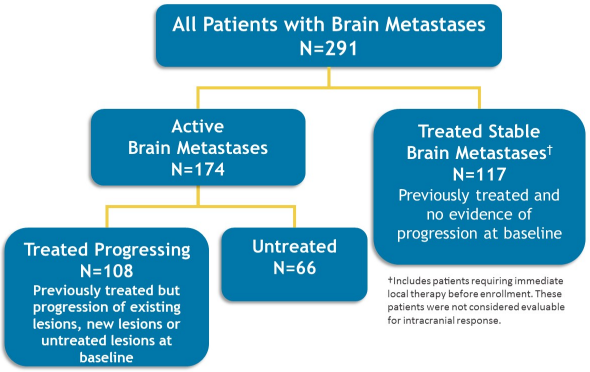
HER2CLIMB Analysis of Patients with Brain Metastases

- Brain MRI at baseline for all patients
- Brain MRI for brain metastases patients every 6 weeks in first 24 weeks, every 9 weeks thereafter
- Eligible brain metastases patients:
  - Not requiring immediate local therapy
  - Requiring local therapy during screening could be eligible after washout*



*These patients were included in the Treated Stable group for analysis.

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Exploratory Analyses of Intracranial Efficacy and Survival

- Response and progression according to RECIST 1.1 for brain lesions only
- Analyses based on investigator assessment
- All patients with brain metastases
  - CNS-PFS: time from randomization to disease progression in the brain or death
  - OS: overall survival
- Patients with measurable intracranial (IC) disease
  - ORR-IC: confirmed intracranial objective response
  - DOR-IC: duration of intracranial response
- Patients who received CNS-directed local therapy and continued study treatment after isolated CNS progression*
  - Time from randomization to second progression or death
  - Time from first isolated CNS progression to second progression or death

*Note: First CNS progression was captured as a PFS event in the primary analysis. CNS: central nervous system.

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Baseline Characteristics of HER2CLIMB Patients with Brain Metastases

		TUC+Tras+Cape (N=198)	Pbo+Tras+Cape (N=93)
Age (years), median (range)		53 (22, 75)	52 (25, 75)
Female, n (%)		197 (99.5)	92 (98.9)
ECOG PS, n (%)	0	92 (46.5)	38 (40.9)
	1	106 (53.5)	55 (59.1)
Histology, n (%)	ER and/or PR positive	107 (54.0)	59 (63.4)
	ER and PR negative	88 (44.4)	34 (36.6)
Metastatic (any location) at initial diagnosis, n (%)		77 (38.9)	39 (41.9)
Non-CNS metastatic disease		192 (97.0)	90 (96.8)
Prior local therapy for brain metastases	Prior radiotherapy	140 (70.7)	64 (68.8)
	Whole brain radiation	77 (38.9)	45 (48.4)
	Targeted radiation	92 (46.5)	32 (34.4)
	Prior surgery	33 (16.7)	13 (14.0)

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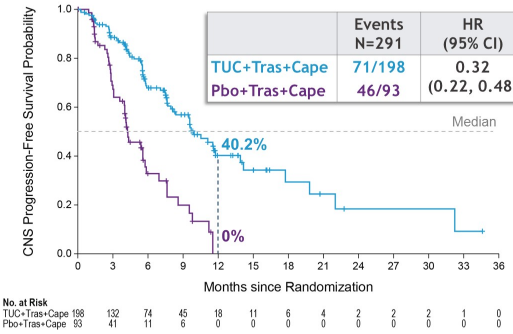
CNS-PFS Benefit in Patients with Brain Metastases



	Events N=291	HR (95% CI)	P Value
TUC+Tras+Cape	71/198	0.32 (0.22, 0.48)	<0.00001
Pbo+Tras+Cape	46/93		

Risk of CNS progression or death was reduced by 68% in patients with brain metastases

One-year CNS-PFS (95% CI):	
TUC+Tras+Cape 40.2% (29.5, 50.6)	Pbo+Tras+Cape 0%
Median CNS-PFS (95% CI):	
TUC+Tras+Cape 9.9 months (8.0, 13.9)	Pbo+Tras+Cape 4.2 months (3.6, 5.7)

CNS-PFS: time from randomization to disease progression in the brain or death by investigator assessment.
HR: hazard ratio computed from Cox proportional hazards model using stratification factors (ECOG performance status: 0/1, and Region of world: North America/Rest of World) at randomization. All P values are nominal.

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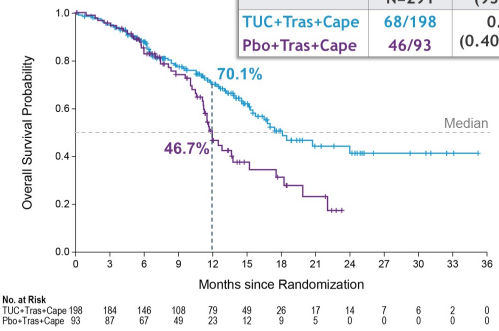
OS Benefit in Patients with Brain Metastases



	Events N=291	HR (95% CI)	P Value
TUC+Tras+Cape	68/198	0.58 (0.40, 0.85)	0.005
Pbo+Tras+Cape	46/93		

Risk of death was reduced by 42% in patients with brain metastases

One-year OS (95% CI):	
TUC+Tras+Cape 70.1% (62.1, 76.7)	Pbo+Tras+Cape 46.7% (33.9, 58.4)
Median OS (95% CI):	
18.1 months (15.5, NE)	12.0 months (11.2, 15.2)

NE: not estimable

HR: hazard ratio computed from Cox proportional hazards model using stratification factors (ECOG performance status: 0/1, and Region of world: North America/Rest of World) at randomization. All P values are nominal.

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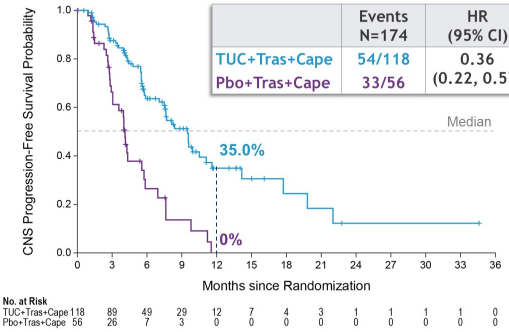
CNS-PFS Benefit in Patients with Active Brain Metastases



	Events N=174	HR (95% CI)	P Value
TUC+Tras+Cape	54/118	0.36 (0.22, 0.57)	<0.0001
Pbo+Tras+Cape	33/56		

Risk of CNS progression or death was reduced by 64% in patients with active brain metastases

One-year CNS-PFS (95% CI):	
TUC+Tras+Cape 35.0% (23.2, 47.0)	Pbo+Tras+Cape 0%
Median CNS-PFS (95% CI):	
9.5 months (7.5, 11.1)	4.1 months (2.9, 5.6)

CNS-PFS: time from randomization to disease progression in the brain or death by investigator assessment
HR: hazard ratio computed from Cox proportional hazards model using stratification factors (ECOG performance status: 0/1, and Region of world: North America/Rest of World) at randomization. All P values are nominal.

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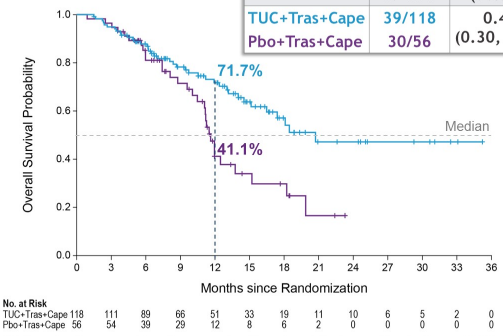
OS Benefit in Patients with Active Brain Metastases



	Events N=174	HR (95% CI)	P Value
TUC+Tras+Cape	39/118	0.49 (0.30, 0.80)	0.004
Pbo+Tras+Cape	30/56		

Risk of death was reduced by 51% in patients with active brain metastases

One-year OS (95% CI):	
TUC+Tras+Cape 71.7% (61.4, 79.7)	Pbo+Tras+Cape 41.1% (25.5, 56.1)
Median OS (95% CI):	
20.7 months (15.1, NE)	11.6 months (10.5, 13.8)

NE: not estimable

HR: hazard ratio computed from Cox proportional hazards model using stratification factors (ECOG performance status: 0/1, and Region of world: North America/Rest of World) at randomization. All P values are nominal.

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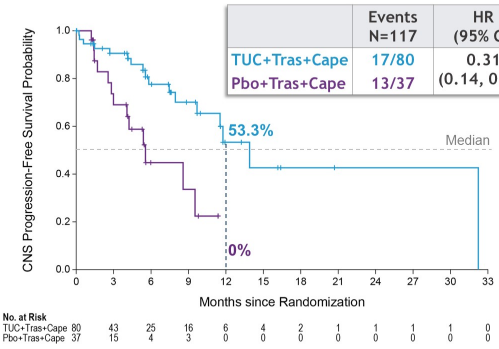
CNS-PFS Benefit in Patients with Stable Brain Metastases



	Events N=117	HR (95% CI)	P Value
TUC+Tras+Cape	17/80	0.31 (0.14, 0.67)	0.002
Pbo+Tras+Cape	13/37		

Risk of CNS progression or death was reduced by 69% in patients with stable brain metastases

One-year CNS-PFS (95% CI):	
TUC+Tras+Cape 53.3% (31.4, 71.0)	Pbo+Tras+Cape 0%
Median CNS-PFS (95% CI):	
13.9 months (9.7, 32.2)	5.6 months (3.0, 9.5)

CNS-PFS: time from randomization to disease progression in the brain or death by investigator assessment
HR: hazard ratio computed from Cox proportional hazards model using stratification factors (ECOG performance status: 0/1, and Region of world: North America/Rest of World) at randomization. All P values are nominal.

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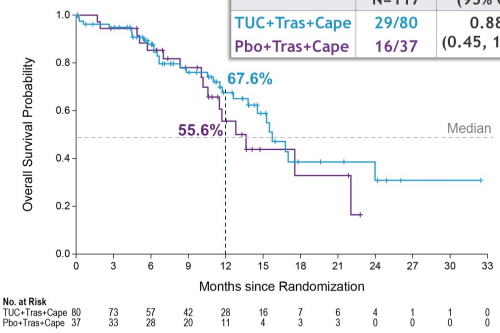
OS in Patients with Stable Brain Metastases

	Events N=117	HR (95% CI)	P Value
TUC+Tras+Cape	29/80	0.88 (0.45, 1.70)	0.70
Pbo+Tras+Cape	16/37		



Risk of death was reduced by 12% in patients with stable brain metastases

One-year OS (95% CI):	
TUC+Tras+Cape 67.6% (53.8, 78.0)	Pbo+Tras+Cape 55.6% (34.1, 72.6)
Median OS (95% CI):	
15.7 months (13.8, NE)	13.6 months (10.2, 22.0)

HR: hazard ratio computed from Cox proportional hazards model using stratification factors (ECOG performance status: 0/1, and Region of world: North America/Rest of World) at randomization. All P values are nominal.

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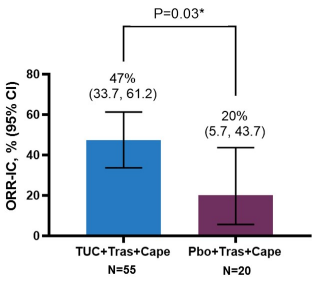
Intracranial Response Rate (ORR-IC) in Patients with Active Brain Metastases and Measurable Intracranial Lesions at Baseline

Confirmed Objective Response Rate (RECIST 1.1)



*Stratified Cochran-Mantel-Haenszel P value

	TUC+Tras+Cape (N=55)	Pbo+Tras+Cape (N=20)
Best Overall Intracranial Response[a], n (%)		
Complete Response (CR)	3 (5.5)	1 (5.0)
Partial Response (PR)	23 (41.8)	3 (15.0)
Stable Disease (SD)	24 (43.6)	16 (80.0)
Progressive Disease (PD)	2 (3.6)	0
Not Available[b]	3 (5.5)	0
Subjects with Objective Response of Confirmed CR or PR, n	26	4
Duration of Intracranial Response (DOR-IC)[e] (95% CI)[f], months	6.8 (5.5, 16.4)	3.0 (3.0, 10.3)

(a) Confirmed Best overall response assessed per RECIST 1.1. (b) Subjects with no post-baseline response assessments. (c) Two-sided 95% exact confidence interval, computed using the Clopper-Pearson method (1934). (d Cochran-Mantel-Haenszel test controlling for stratification factors (ECOG performance status: 0/1, and Region of world: North America/Rest of World) at randomization. (e) As estimated using Kaplan-Meier methods. (f) Calculated using the complementary log-log transformation method (Collett, 1994).

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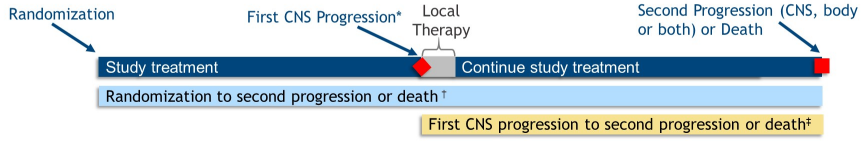
PFS in Patients with Isolated Progression in the Brain Who Continued with Assigned Study Treatment



	Median time from randomization to second progression or death	HR	Median time from first CNS progression to second progression or death	HR
TUC+Tras+Cap N=21	15.9 months (11.7, 28.2)	0.292 (0.11, 0.77) P=0.009	7.6 months (3.9, 11.3)	0.332 (0.13, 0.85) P=0.02
Pbo+Tras+Cap N=9	9.7 months (4.9, 12.0)		3.1 months (1.2, 4.1)	

*Note: First CNS progression was captured as a PFS event in the primary analysis.
†Time from randomization to second progression or death among patients who received local therapy and continued study treatment after isolated CNS progression.
‡Time from first isolated CNS progression to second progression or death among patients who received local therapy and continued study treatment after isolated CNS progression.

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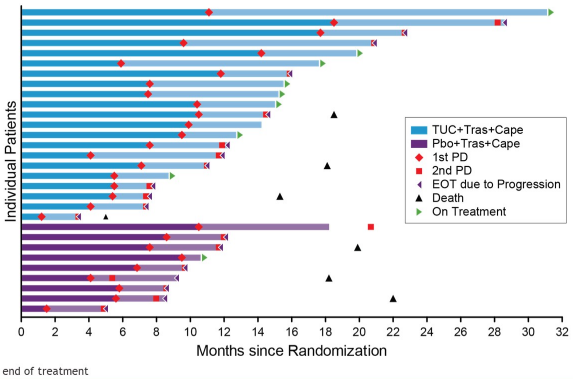
Duration on Treatment for Patients with Isolated Progression in the Brain Who Continued with Assigned Study Treatment



PD: progressive disease; EOT: end of treatment

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Conclusions

- The addition of tucatinib to trastuzumab and capecitabine doubled the intracranial response rate, reduced the risk of CNS progression or death by two-thirds, and reduced the risk of death by nearly half.
- The CNS-PFS results represent a delay in progression in the brain.
- Tucatinib is the first TKI to demonstrate prolongation of overall survival in patients HER2+ MBC with brain metastases in a randomized, controlled trial.
- These results together with the HER2CLIMB primary analysis demonstrate that this is an active regimen for intracranial and extracranial disease in patients with HER2+ MBC.

TKI: tyrosine kinase inhibitor

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Randomized phase II clinical trial of cisplatin/carboplatin and etoposide (CE) alone or in combination with nivolumab as frontline therapy for extensive-stage small cell lung cancer (ES-SCLC): ECOG-ACRIN EA5161.

Authors:
Ticiana Leal, Yating Wang, Afshin Dowlati, DeQuincy Andrew Lewis, Yuanbin Chen, Amit Ramesh Mohindra, Mohammad Razaq, Harish G. Ahuja, Jijun Liu, David M. King, Christopher Joseph Sumey, Suresh S. Ramalingam; University of Wisconsin Carbone Cancer Center, Madison, WI; ECOG-ACRIN Biostatistics Center, Boston, MA; Case Western Reserve University and University Hospitals Case Medical Center, Cleveland, OH; Randolph Cancer Ctr, Asheboro, NC; Car Print d Hematology Centers of Western Michigan, Grand Rapids, MI; Ramesh K Mohindra MD PC, Franklin, MI; University of Oklahoma Health Sciences Center, Oklahoma City, OK; Aspirus Reg Cancer Ctr, Wausau, WI; Illinois Cancer Care, Peoria, IL; Minnesota Onc, St Paul, MN; Univ of Colorado, Aurora, CO; Winship Cancer Institute, Emory University Hospital, Atlanta, GA

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Abstract Disclosures

Research Funding:
ECOG-ACRIN

Background:
Immune checkpoint inhibition is now given in combination with chemotherapy for first line (1L) therapy of extensive stage small cell lung cancer (ES-SCLC). We conducted a randomized phase II study of nivolumab (anti-PD1) in combination with platinum-etoposide (CE) as 1L treatment for patients with ES-SCLC (EA5161, NCT03382561).

Methods:
Patients with measurable (RECIST v1.1) ES-SCLC, ECOG performance status 0 or 1, who had not received prior systemic treatment for ES-SCLC were enrolled. Patients were randomized 1:1 to nivolumab 360 mg + CE every 21 days for 4

the PFS compared to CE with HR 0.65 (95% CI, 0.46, 0.91; p = 0.012); mPFS 5.5 versus 4.6 months, respectively. Secondary endpoint of OS was also improved with nivolumab + CE versus CE with HR 0.67 (95% CI, 0.46, 0.98; p = 0.038); mOS 11.3 versus 8.5 months. Among patients who initiated study therapy, nivolumab + CE significantly improved the PFS compared to CE with HR 0.68 (95% CI, 0.48, 1.00; p = 0.047); mPFS 5.5 versus 4.7 months, respectively; in this population, OS was also improved with nivolumab + CE versus CE with HR 0.73 (95% CI, 0.49, 1.11; p = 0.14); mOS 11.3 versus 9.3 months. The ORR was 52.29% versus 47.71%. The incidence of treatment-related grade 3/4 AEs was 77% versus 62% and AEs leading to discontinuation 6.21% versus 2.07%. Ten patients remain on maintenance nivolumab. Lethal adverse events independent of treatment were similar between the two arms (9 in arm A; 7 in arm B).

Conclusions:

The addition of nivolumab to CE as 1L treatment for ES-SCLC significantly improved PFS and OS. No new safety signals were observed. Clinical trial information: NCT03382561

KEYNOTE-355: Randomized, double-blind, phase III study of pembrolizumab + chemotherapy versus placebo + chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer.

Authors:
Javier Cortes, David W. Cescon, Hope S. Rugo, Zbigniew Nowecki, Seock-Ah Im, Mastura Md Yusof, Carlos Gallardo, Oleg Lipatov, Carlos Henrique Barrios, Esther Holgado, Hiroji Iwata, Norikazu Masuda, Marco Torregroza Otero, Erhan Gokmen, Sherene Loi, Zifang Guo, Jing Zhao, Gursel Aktan, Vassiliki Karantza, Peter Schmid; IOB Institute of Oncology, Quiron Group & Vall d´Hebron Institute of Oncology (VHIO), Madrid & Barcelona, Spain; Princess Margaret Cancer Centre, Toronto, ON, Canada; University of California San Francisco Comprehensive Cancer Center, San Francisco, CA; Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw, Poland; Seoul National University Hospital, Seoul, South Korea; Pantai Hospital, Kuala Lumpur, Malaysia; Arturo Lopez Perez Foundation, Santiago, Chile; Republican Clinical Oncology Dispensary of the Ministry of Public Health of Bashkortostan Republic, Ufa, Russian Federation; Centro de Hematologia e Oncologia, Porto Alegre, Brazil; Aichi Cancer Center Hospital, Nagoya, Japan; National Hospital Organization, Osaka National Hospital, Osaka, Japan; Oncomedica S.A., Monteria, Colombia; Ege University Medical Faculty, Izmir, Turkey; Peter MacCallum Cancer Institute, Melbourne, VIC, Australia; Merck & Co., Inc., Kenilworth, NJ; Barts Cancer Institute, Centre for Experimental Cancer Medicine, London, United Kingdom

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Abstract Disclosures

Research Funding:
Merck & Co., Inc.

Background:
Pembrolizumab (pembro) monotherapy showed promising antitumor activity and manageable safety in patients (pts) with metastatic TNBC in KEYNOTE-012, -086 and -119. KEYNOTE-355 (ClinicalTrials.gov, NCT02819518) compared

log-rank tests were used to assess treatment group differences. HR and 95% CIs were based on a stratified Cox regression model. AEs were monitored throughout the study and graded per NCI CTCAE v4.0.

Results:

As of Dec 11 2019, median follow-up was 17.5 mo for pembro + chemo (n=566) and 15.5 mo for chemo (n=281). Pembro + chemo significantly improved PFS vs chemo alone in pts with CPS ≥10 tumors (Table), meeting one of the protocol-defined primary objectives. Although the boundary for a statistically significant benefit of pembro + chemo in pts with CPS ≥1 tumors was not met and formal testing in ITT was not performed, the pembro treatment effect increased with PD-L1 enrichment (Table). OS follow-up is ongoing. Grade 3-5 treatment-related AE rates were 68.1% with pembro + chemo (2 deaths) vs 66.9% with chemo (0 deaths); rates of grade 3-4 immune-mediated AEs and infusion reactions were 5.5% vs 0%. Clinical trial information: NCT02819518.

Conclusion:

Pembro combined with several chemo partners showed a statistically significant and clinically meaningful improvement in PFS vs chemo alone in pts with previously untreated locally recurrent inoperable or metastatic TNBC whose tumors expressed PD-L1 (CPS ≥10). Pembro + chemo was generally well tolerated, with no new safety concerns.

Population	Treatment	Median PFS, mo	HR (95% CI)	*P*-value	*P*-value boundary
CPS ≥10	P + C (n=220) vs C (n=103)	9.7 vs 5.6	0.65 (0.49-0.86)	0.0012	0.00411
CPS ≥1	P + C (n=425) vs C (n=211)	7.6 vs 5.6	0.74 (0.61-0.90)	0.0014	0.00111
ITT	P + C (n=566) vs C (n=281)	7.5 vs 5.6	0.82 (0.69-0.97)	-	n/a

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Tucatinib versus placebo added to trastuzumab and capecitabine for patients with previously treated HER2+ metastatic breast cancer with brain metastases (HER2CLIMB).

Authors:
Nancy U. Lin, Rashmi Krishna Murthy, Carey K. Anders, Virginia F. Borges, Sara A. Hurvitz, Sherene Loi, Vandana G Abramson, Philippe L. Bedard, Mafalda Oliveira, Amelia Bruce Zelnak, Michael DiGiovanna, Thomas Bachelot, Amy Jo Chien, Ruth O'Regan, Andrew M. Wardley, Volkmar Müller, Lisa A. Carey, Suzanne M. McGoldrick, Grace An, Eric P. Winer; Dana-Farber Cancer Institute, Boston, MA; University of Texas MD Anderson Cancer Center, Houston, TX; Duke University Medical Center, Durham, NC; University of Colorado Comprehensive Cancer Center, Aurora, CO; David[illegible]n School of Medicine at UCLA, Los Angeles, CA; Peter MacCallum Cancer Institute, Melbourne, VIC, Australia; Vanderbilt-Ingram Cancer Center, Nashville, TN; Princess Margaret Cancer Centre, Toronto, ON, Canada; Hospital Universitari Vall d'Hebron, Barcelona, Spain; Winship Cancer Institute, Atlanta, GA; Yale Cancer Center, New Haven, CT; Centre Léon Bérard, Lyon, France; University of California San Francisco, San Francisco, CA; University of Wisconsin Carbone Cancer Center, Madison, WI; The Christie NHS Foundation Trust, Manchester Academic Health Science Centre & Division of Cancer Sciences, School of Medical Sciences, Faculty of Biology Medicine & Health, University of Manchester, Manchester, United Kingdom; Department of Gynecology, Hamburg-Eppendorf University Medical Center, Hamburg, Germany; University of North Carolina, Chapel Hill, NC; Seattle Children's Hospital, Seattle, WA; Seattle Genetics, Inc., Bothell, WA; Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA

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Abstract Disclosures

Research Funding:
Seattle Genetics

Background:
Tucatinib (TUC) is an investigational, highly selective HER2 kinase inhibitor. HER2CLIMB (NCT02614794) showed clinically meaningful and statistically significant improvements in overall survival (OS) and progression free survival (PFS) in all pts, prolongation of PFS in pts with brain metastases (BM), and objective response rate (ORR) when TUC was added to trastuzumab (T) and capecitabine (C). Primary methods and outcomes have been reported previously (Murthy NEJM 2019). We report the results of exploratory efficacy analyses in pts with BM.

Methods:
All pts with HER2+ metastatic breast cancer (MBC) enrolled in HER2CLIMB had a baseline brain MRI. Pts with BM were eligible and classified as untreated, treated stable, or treated and progressing. Pts were randomized 2:1 to receive TUC or placebo, in combination with T and C. Efficacy analyses in pts with BM at baseline were performed by applying RECIST 1.1 to the brain based on investigator evaluation. CNS-PFS (progression in the brain or death) and OS were evaluated in BM pts overall. Intracranial (IC) confirmed ORR (ORR-IC) and IC duration of response (DOR-IC) were evaluated in BM pts

with measurable IC disease. After isolated brain progression, pts could continue study therapy after local treatment until second progression, and time from randomization to second progression or death was evaluated.

Results:

Overall, 291 pts (48%) had BM at baseline: 198 (48%) in the TUC arm and 93 (46%) in the control arm. There was a 68% reduction in risk of CNS-PFS in the TUC arm (HR: 0.32; 95% CI: 0.22, 0.48; P < 0.0001). Median CNS-PFS was 9.9 mo in the TUC arm vs 4.2 mo in the control arm. Risk of death overall was reduced by 42% in the TUC arm (OS HR: 0.58; 95% CI: 0.40, 0.85; P = 0.005). Median OS was 18.1 mo vs 12.0 mo. ORR-IC was higher in the TUC arm (47.3%; 95% CI: 33.7, 61.2) vs the control arm (20.0%; 95% CI: 5.7, 43.7). Median DOR-IC was 6.8 mo (95% CI: 5.5, 16.4) vs 3.0 mo (95% CI: 3.0, 10.3). In pts with isolated brain progression who continued study therapy after local treatment (n = 30), risk of second progression or death was reduced by 67% (HR: 0.33; 95% CI: 0.11, 1.02), and median PFS from randomization was 15.9 mo vs 9.7 mo, favoring the TUC arm.

Conclusions:

In pts with heavily previously treated HER2+ MBC with BM, TUC in combination with T and C doubled the ORR-IC, reduced risk of IC progression or death by two thirds and reduced risk of death by nearly half. If approved, TUC in combination with T and C has the potential to become a new standard of care in pts with HER2+ MBC with and without BM. Clinical trial information: NCT02614794.

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CURRICULUM VITAE

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***Date of Preparation*:** May 8, 2020

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Education:

1992-1996	University of Pennsylvania B.A. in Biology with Distinction, Concentration in Molecular Biology
1998-2002	George Washington University School of Medicine Doctor of Medicine with Distinction

Professional Training & Employment:

06/25/2002 – 06/30/2003	Intern, Internal Medicine, Stanford University School of Medicine
07/01/2003 – 06/30/2005	Resident, Internal Medicine, Stanford University School of Medicine
07/01/2005 – 06/30/2008	Fellow, Medical Oncology, Stanford University School of Medicine
07/01/2008 – 11/30/2009	Instructor in Medicine, Stanford University School of Medicine
12/01/2009 – 07/31/2010	Acting Assistant Professor of Medicine, Stanford University School of Medicine, Division of Oncology
08/01/2010 –	Member, Stanford Cancer Institute
08/01/2010 – 12/31/2018	Assistant Professor of Medicine, Stanford University School of Medicine, Division of Oncology
01/01/2019 -	Associate Professor of Medicine, Stanford University School of Medicine, Division of Oncology

Awards & Honors:

1996	Magna cum laude, University of Pennsylvania
1999	Alex Horwitz First-Year Scholar Award for the highest percentage of credit hours graded at the Honors level, George Washington University School of Medicine
2000	Tauber Scholarship Recipient, George Washington University School of Medicine
2002	Alpha Omega Alpha Honor Society
2002	George Washington University Primary Care Award
2008	American Society of Clinical Oncology Merit Award
2008	Susan G. Komen for the Cure Postdoctoral Fellowship Award, Translational
2008	Medical Oncology Research Addressing Fellows' Challenges Scholarship Award
2009	National Institutes of Health Loan Repayment Program Award
2009	American Society of Clinical Oncology Young Investigator Award
2010	Stanford University Division of Oncology Teaching Award
2011	Stanford Cancer Institute New Investigator Award
2012	Stanford University Division of Oncology Teaching Award
2013	Stanford University Division of Oncology Teaching Award
2014	Stanford University Division of Oncology Teaching Award
2014	Triple Step Toward the Cure Champion Award
2015	Komen Scholar, Susan G. Komen for the Cure

2017	San Francisco Bay Area Top Doctor, Medical Oncology, Castle Connolly
2018	Hero Award, Triple Negative Breast Cancer Foundation Peace, Love & A Cure Gala
2018	San Francisco Bay Area Top Doctor, Medical Oncology, Castle Connolly
2019	San Francisco Bay Area Top Doctor, Medical Oncology, Castle Connolly
2019	Susan G. Komen Visionary Award, Susan G. Komen San Francisco Bay Area
2020	San Francisco Bay Area Top Doctor, Medical Oncology, Castle Connolly

Licensure & Certification:

2003	Medical License, Medical Board of California, A84689
2005, 2015	Certified, Internal Medicine, American Board of Internal Medicine
2008, 2018	Certified, Medical Oncology, American Board of Internal Medicine

University Administrative Service:

2008 - 2011	Data Safety & Monitoring Committee, Stanford Cancer Institute
2015 -2018	Stanford Breast Oncology Protocol Review Committee Co-Chair
2016 -	Stanford Cancer Institute, Scientific Review Committee
2016	Stanford Cancer Institute, Breast Cancer Transformation Committee
2016 -	Stanford Cancer Institute, Breast Cancer Patient Education Committee
2018 -	Leader, Breast Oncology Clinical Research Group, Stanford Cancer Institute
2020 -	Director, Breast Cancer Program, Stanford Cancer Institute
2020 -	Associate Director, Stanford Women's Cancer Center
2020 -	Leader, Breast Cancer Clinical Care Program

Service to Professional Organizations:

2009 -	Breast Cancer Core Committee, Eastern Cooperative Oncology Group
2010 - 2013	American Society of Clinical Oncology Scientific Program Committee, Triple-Negative Breast Cancer/Cytotoxics/Local Therapy Track
2010 - 2013	Breast Cancer Symposium Program Committee
2013 - 2014	American Society of Clinical Oncology Breast Cancer Maintenance of Certification Working Group
2014 - 2017	American Board of Internal Medicine Medical Oncology Self Evaluation Process (SEP) Committee
2014 -	Breast Cancer Guideline Panel, National Comprehensive Cancer Network (NCCN)
2015 -	American Society of Clinical Oncology Breast Cancer Adjuvant Chemotherapy and Targeted Therapy Guideline Adaptation Panel
2018 -	American Society of Clinical Oncology Breast Cancer Guideline Advisory Group

Service as Grant Reviewer:

2011	DOD/CDMRP 2011 Breast Cancer Research Program Scientist Reviewer
2014 -	Susan G. Komen for the Cure Grant Review Committee Member
2015 -	Stanford Cancer Institute Developmental Cancer Research Award Grant Reviewer
2017	Breast Cancer Now UK, Catalyst Programme Grant Reviewer
2018 -	AACR Breast Cancer Research Grants Scientific Review Committee

Other Experience and Professional Activities:

2008 -	Physician Volunteer, Bay Area Cancer Connections, Palo Alto, CA
2010 - 2015	Member, Scientific Advisory Board Triple-Step Toward the Cure
2011 -	Member, Facing Our Risk of Cancer Empowered (FORCE) Scientific Advisory Board
2017 -	Chair, Data Safety & Monitoring Committee, G1 Therapeutics Phase II Triple-Negative Breast Cancer Trial

ASCO HIGHLIGHTS 2020: GENITOURINARY CANCER

Primo N. "Lucky" Lara, MD
University of California, Davis

Presentation
Abstracts
Abbreviated Bio/CV

Best of Virtual ASCO 2020: *Genitourinary Oncology*

Primo N. Lara, Jr., M.D.
Professor of Medicine and Executive Associate Dean
University of California Davis School of Medicine

Director, UC Davis Comprehensive Cancer Center
Sacramento, CA

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NCI Designated Comprehensive Cancer Center

1

Maintenance avelumab + best supportive care (BSC) versus BSC alone after platinum-based first-line chemotherapy in advanced urothelial carcinoma: JAVELIN Bladder 100 phase III results

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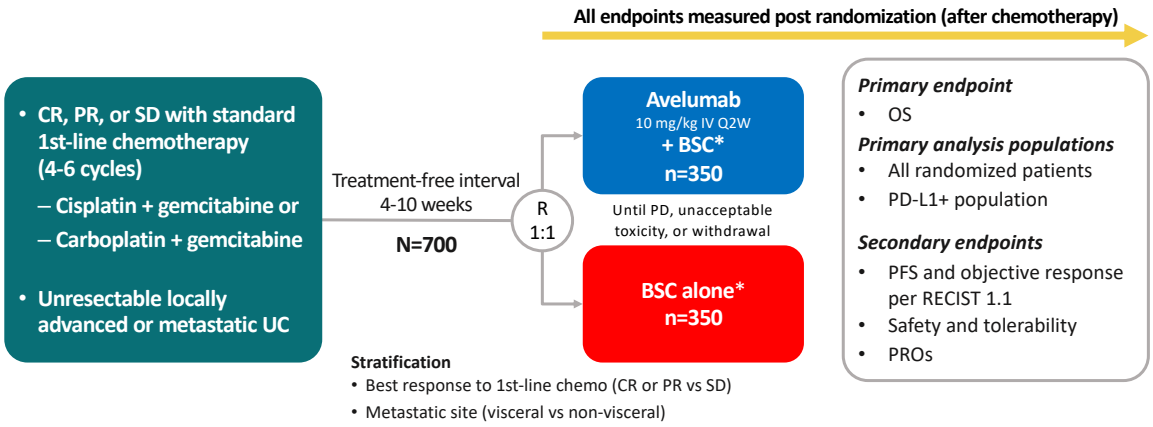
JAVELIN Bladder 100 study design (NCT02603432)



PD-L1+ status was defined as PD-L1 expression in ≥25% of tumor cells or in ≥25% or 100% of tumor-associated immune cells if the percentage of immune cells was >1% or ≤1%, respectively, using the Ventana SP263 assay; 358 patients (51%) had a PD-L1–positive tumor

BSC, best supportive care; **CR,** complete response; **IV,** intravenous; **PR**, partial response; **PRO**, patient reported outcome; **Q2W,** every 2 weeks; **R**, randomization; **RECIST 1.1,** Response Evaluation Criteria in Solid Tumors version 1.1; **SD**, stable disease

*BSC (eg, antibiotics, nutritional support, hydration, or pain management) was administered per local practice based on patient needs and clinical judgment; other systemic antitumor therapy was not permitted, but palliative local radiotherapy for isolated lesions was acceptable

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Select baseline characteristics

	Overall population (N=700)		PD-L1+ population (N=358)	
	Avelumab + BSC (N=350)	BSC alone (N=350)	Avelumab + BSC (N=189)	BSC alone (N=169)
Median age, years	68	69	70	70
Site of primary tumor, %				
Upper tract (renal pelvis, ureter)	30	23	23	21
Lower tract (bladder, urethra, prostate gland)	70	77	77	79
Site of baseline metastasis, %				
Visceral	55	55	47	47
Nonvisceral*	45	45	53	53
PD-L1 status, %†				
Positive	54	48	100	100
Negative	40	38	0	0
Unknown	6	14	0	0
1st-line chemotherapy regimen, %				
Gemcitabine + cisplatin	52	59	53	58
Gemcitabine + carboplatin	42	35	39	32
Gemcitabine + cisplatin/carboplatin‡	6	6	7	9
Not reported	0	1	0	1
Best response to 1st-line chemotherapy, %				
CR or PR	72	72	74	76
SD	28	28	26	24

*Nonvisceral includes patients with locally advanced disease or only nonvisceral disease, including bone metastasis
†PD-L1+ status was defined as PD-L1 expression in ≥25% of tumor cells or in ≥25% or 100% of tumor-associated immune cells if the percentage of immune cells was >1% or ≤1%, respectively (SP263 assay); among patients evaluable for PD-L1 status in the avelumab and control arms, 58% and 56% had a PD-L1+ tumor, respectively
‡Patients who switched platinum regimens while receiving 1st-line chemotherapy

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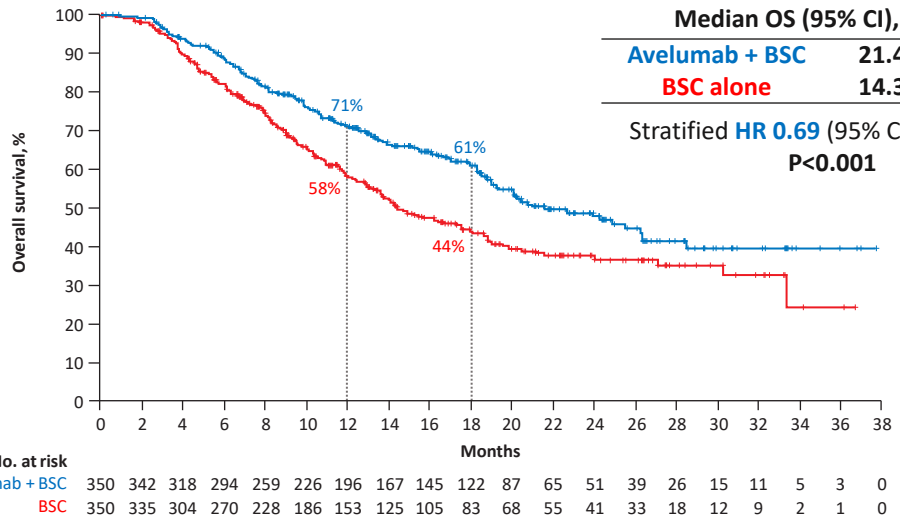
OS in the overall population



Median OS (95% CI), months	
Avelumab + BSC	**21.4** (18.9, 26.1)
BSC alone	**14.3** (12.9, 17.9)

Stratified **HR 0.69** (95% CI, 0.56, 0.86)
P<0.001

No. at risk																				
Avelumab + BSC	350	342	318	294	259	226	196	167	145	122	87	65	51	39	26	15	11	5	3	0
BSC	350	335	304	270	228	186	153	125	105	83	68	55	41	33	18	12	9	2	1	0

OS was measured post randomization (after chemotherapy); the OS analysis crossed the prespecified efficacy boundary based on the alpha-spending function (P<0.0053)

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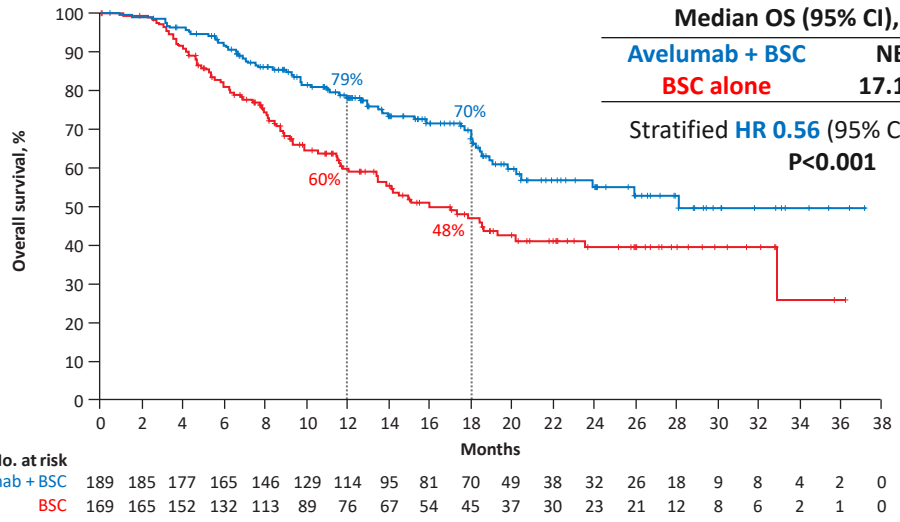
OS in the PD-L1+ population



Median OS (95% CI), months	
Avelumab + BSC	**NE** (20.3, NE)
BSC alone	**17.1** (13.5, 23.7)

Stratified **HR 0.56** (95% CI, 0.40, 0.79)
P<0.001

No. at risk																				
Avelumab + BSC	189	185	177	165	146	129	114	95	81	70	49	38	32	26	18	9	8	4	2	0
BSC	169	165	152	132	113	89	76	67	54	45	37	30	23	21	12	8	6	2	1	0

OS was measured post randomization (after chemotherapy); the OS analysis crossed the prespecified efficacy boundary based on the alpha-spending function (P<0.0014). **NE**, not estimable

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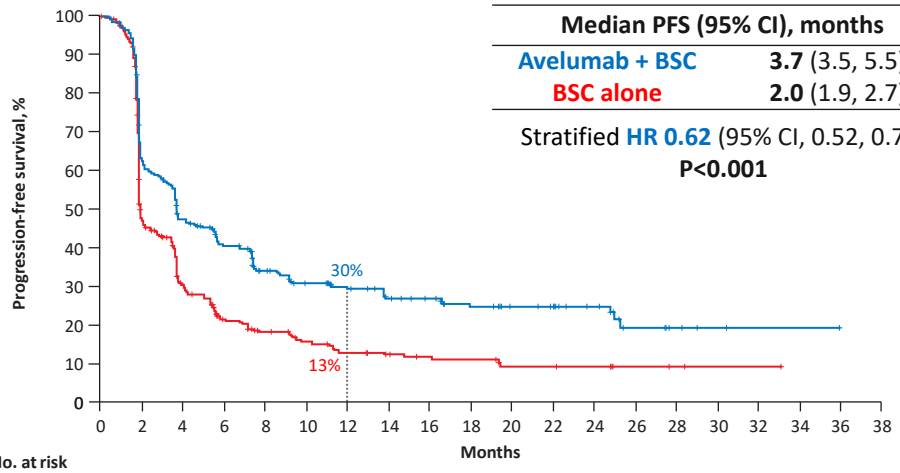
PFS by independent radiology review in the overall population



Median PFS (95% CI), months	
Avelumab + BSC	**3.7** (3.5, 5.5)
BSC alone	**2.0** (1.9, 2.7)

Stratified HR 0.62 (95% CI, 0.52, 0.75)
P<0.001

No. at risk																		
Avelumab + BSC	350	198	145	118	90	72	59	49	45	34	27	25	17	9	4	2	1	1	0
BSC	350	144	87	52	39	31	24	20	17	16	10	10	7	3	2	1	1	0	

PFS was measured post randomization (from end of chemotherapy)

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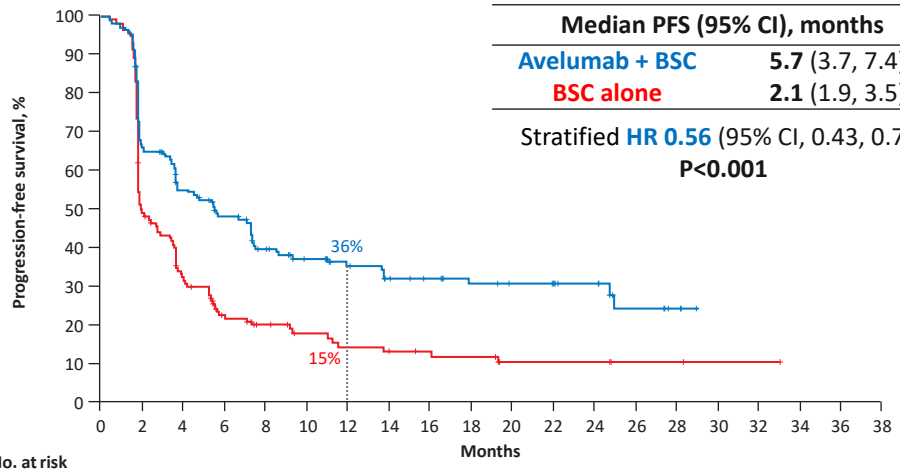
PFS by independent radiology review in the PD-L1+ population



Median PFS (95% CI), months	
Avelumab + BSC	**5.7** (3.7, 7.4)
BSC alone	**2.1** (1.9, 3.5)

Stratified HR 0.56 (95% CI, 0.43, 0.73)
P<0.001

No. at risk																	
Avelumab + BSC	189	114	89	73	55	45	35	29	26	20	17	17	12	7	2	0	
BSC	169	80	51	28	21	16	13	12	10	9	5	5	5	2	2	1	1	0

PFS was measured post randomization (from end of chemotherapy)

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Confirmed objective response

Response to maintenance therapy post randomization

	Overall population		PD-L1+ population	
	Avelumab + BSC (N=350)	BSC alone (N=350)	Avelumab + BSC (N=189)	BSC alone (N=169)
ORR, % (95% CI)	**9.7** (6.8, 13.3)	**1.4** (0.5, 3.3)	**13.8** (9.2, 19.5)	**1.2** (0.1, 4.2)
Stratified odds ratio (95% CI)	7.464 (2.824, 24.445)		12.699 (3.160, 114.115)	
Best overall response, %				
Complete response	6.0	0.9	9.5	0.6
Partial response	3.7	0.6	4.2	0.6
Stable disease	12.6	13.1	10.1	13.6
Non-CR/non-PD	18.9	12.9	20.1	13.0
Progressive disease	37.1	48.3	31.2	48.5
Not evaluable*	21.7	24.3	24.9	23.7
Disease control, %†	41.1	27.4	43.9	27.8

PD, progressive disease
Objective response was assessed by independent radiology review; in patients with a CR after chemotherapy, best overall response was not evaluable if no evidence of disease at baseline was maintained after randomization, or PD if disease progression occurred after randomization
*Reasons for not evaluable included no evidence of disease at baseline; no post-baseline assessments; SD <6 weeks after randomization; PD >12 weeks after randomization; new anticancer therapy started before first post-baseline assessment; or all post-baseline assessments have objective response of not evaluable
†Patients with a best overall response of CR, PR, SD, or non-CR/non-PD

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Subsequent anticancer therapy

	Overall population		Subgroup who discontinued study therapy due to PD	
	Avelumab + BSC (N=350)	BSC alone (N=350)	Avelumab + BSC (N=189)	BSC alone (N=263)
Discontinued and received subsequent drug therapy, %	**42.3**	**61.7**	**70.4**	**75.3**
PD-L1/PD-1 inhibitor	**6.3**	**43.7**	**9.0**	**52.9**
Fibroblast growth factor receptor inhibitor	2.6	2.3	4.8	3.0
Any other drug	40.0	34.0	67.2	41.8
Discontinued with no subsequent drug therapy, %	33.4	30.9	29.6	24.7
Study treatment ongoing, %	24.3	7.4	–	–

All percentages were calculated using the denominator of all patients in the treatment arm within each population; some patients received >1 category of subsequent therapy

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Treatment-emergent AEs (any causality)

	Avelumab + BSC (N=344)		BSC alone (N=345)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any TEAE, %	**98.0**	**47.4**	**77.7**	**25.2**
Fatigue	17.7	1.7	7.0	0.6
Pruritus	17.2	0.3	1.7	0
UTI	17.2	4.4	10.4	2.6
Diarrhea	16.6	0.6	4.9	0.3
Arthralgia	16.3	0.6	5.5	0
Asthenia	16.3	0	5.5	1.2
Constipation	16.3	0.6	9.0	0
Back pain	16.0	1.2	9.9	2.3
Nausea	15.7	0.3	6.4	0.6
Pyrexia	14.8	0.3	3.5	0
Decreased appetite	13.7	0.3	6.7	0.6
Cough	12.8	0.3	4.6	0
Vomiting	12.5	1.2	3.5	0.6
Hypothyroidism	11.6	0.3	0.6	0
Rash	11.6	0.3	1.2	0
Anemia	11.3	3.8	6.7	2.9
Hematuria	10.5	1.7	10.7	1.4
IRR	10.2	0.9	0	0

- TEAEs led to discontinuation of avelumab in 11.9%
- Death was attributed by the investigator to study treatment toxicity in 2 patients (0.6%) in the avelumab + BSC arm
  - Due to sepsis (in Cycle 10) and ischemic stroke (100 days after a single dose of avelumab)

Table shows TEAEs of any grade occurring in ≥10% or grade ≥3 TEAEs occurring in ≥5% in either arm

AE, adverse event; **IRR,** infusion-related reaction; **TEAE,** treatment-emergent adverse event; **UTI,** urinary tract infection
Safety was assessed in all patients who received ≥1 dose of avelumab in the avelumab arm, or who completed the cycle 1 day 1 visit in the BSC arm (N=689)

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Immune-related AEs

	Avelumab + BSC (N=344)	
	Any grade	Grade 3
Any irAE, %	**29.4**	**7.0**
Hypothyroidism	10.2	0.3
Rash	4.9	0.3
Hyperthyroidism	4.7	0
Rash maculopapular	2.3	0.3
Pruritis	2.0	0
Pneumonitis	1.5	0.3
Colitis	0.9	0.6
Increased ALT	0.9	0.9
Increased AST	0.6	0.6
Hyperglycemia	0.9	0.9
Myositis	0.6	0.6

- No grade 4/5 irAEs occurred
- High-dose corticosteroids (≥40 mg total daily prednisone or equivalent) were administered following irAE in 9.0% of avelumab-treated patients

Table shows irAEs of any grade occurring in ≥1% or grade ≥3 irAEs occurring in ≥0.5% in either arm

irAEs were identified according to a prespecified case definition
ALT, alanine aminotransferase; **AST**, aspartate aminotransferase; **irAE,** immune-related adverse event

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"My two cents": ASCO 2020 Metastatic Urothelial Cancer

- Avelumab maintenance in mUC patients with CR/PR/SD after 1st-line platinum-based therapy is now standard-of-care
  - Avelumab prolonged OS across all prespecified subgroups:
    - cisplatin-based or carboplatin-based chemotherapy, or response or SD with 1st-line induction chemotherapy
  - Approved by US FDA in June 2020

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IMvigor010: Primary Analysis From a Phase III Randomized Study of Adjuvant Atezolizumab vs Observation in High-Risk Muscle-Invasive Urothelial Carcinoma

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IMvigor010 Study Design

Key eligibility[a]
- **High-risk MIUC (bladder, renal pelvis, ureter)**
- **Radical cystectomy/nephroureterectomy with LN dissection** within ≤ 14 weeks
  - **ypT2-T4a or ypN+** for patients treated with **NAC**[b]
  - **pT3-T4a or pN+** for patients **not treated with NAC**[b]
- No postsurgical radiation or AC
- If no prior NAC given, patient had to be ineligible for, or declined, cisplatin-based AC
- ECOG PS 0-2
- **Tissue sample for PD-L1 testing**

R 1:1

Atezolizumab 1200 mg q3w *(16 cycles or 1 year)*

No crossover allowed

Observation[c] **q3w**

Disease recurrence/ survival follow-up

Tumor assessments: q12w for years 1-3, (q24w for years 4-5 and at year 6)

Stratification factors
- Number of LNs resected (< 10 vs ≥ 10)
- Prior NAC (Yes vs No)
- LN status (+ vs –)
- Tumor stage (≤ pT2 vs pT3/pT4)
- PD-L1 status[a] (IC0/1 vs IC2/3)

- **Primary endpoint:** DFS (ITT population)
- **Key secondary endpoint:** OS (ITT population)
- **Exploratory analyses:** Biomarkers including PD-L1 status
- **Safety**

AC, adjuvant chemotherapy; DFS, disease-free survival; ITT, intention to treat; LN, lymph node; MIUC, muscle-invasive UC. [a] Protocol amendments broadened eligibility to "all-comers" (initially, only PD-L1–selected patients were enrolled [IC2/3: PD-L1 expression on tumor-infiltrating immune cells (IC) ≥ 5% of tumor area [VENTANA SP142 IHC assay]) and to patients with MIUC (initially, only patients with muscle-invasive bladder cancer were enrolled). [b] Upper-tract UC staging: ypT2-4 or ypN+ (with NAC) and pT3-4 or pN+ (without NAC). [c] Alternating clinic visits and phone calls.

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Baseline Characteristics

	Atezolizumab (N = 406)	Observation (N = 403)
Median age, years (range)	67 (31-86)	66 (22-88)
Male, n (%)	**322 (79)**	**316 (78)**
ECOG PS, n (%)		
0	248 (61)	259 (64)
1	142 (35)	130 (32)
2	16 (4)	14 (4)
Primary tumor site, n (%)		
Bladder	**377 (93)**	**378 (94)**
Upper tract (ureter, renal pelvis)	29 (7)	25 (6)
Prior neoadjuvant chemotherapy, n (%)[a]	**196 (48)**	**189 (47)**
Pathologic tumor stage, n (%)[b]		
pT2N0	34 (8)	39 (10)
pT3N0	**124 (31)**	**119 (30)**
pT4N0	**32 (8)**	**33 (8)**
≤pT2-4 and pN+, n (%)[a]	**212 (52)**	**208 (52)**
PD-L1 IHC status, n (%)[c]		
IC0	57 (14)	66 (16)
IC1	152 (37)	138 (34)
IC2	147 (36)	144 (36)
IC3	50 (12)	55 (14)

Data cutoff: November 30, 2019. Median follow-up: 21.9 mo. [a] Per interactive voice/web response system (IxRS). [b] Per electronic case report form (eCRF). [c] Archival and/or fresh pre-treatment FFPE tumor tissue from all patients (surgical resection or lymph node dissection) were prospectively tested for PD-L1 status per a central laboratory and used as a stratification factor; 119 patients were enrolled using IC2/3 selection, and 690 patients were enrolled under an "all-comer" protocol.

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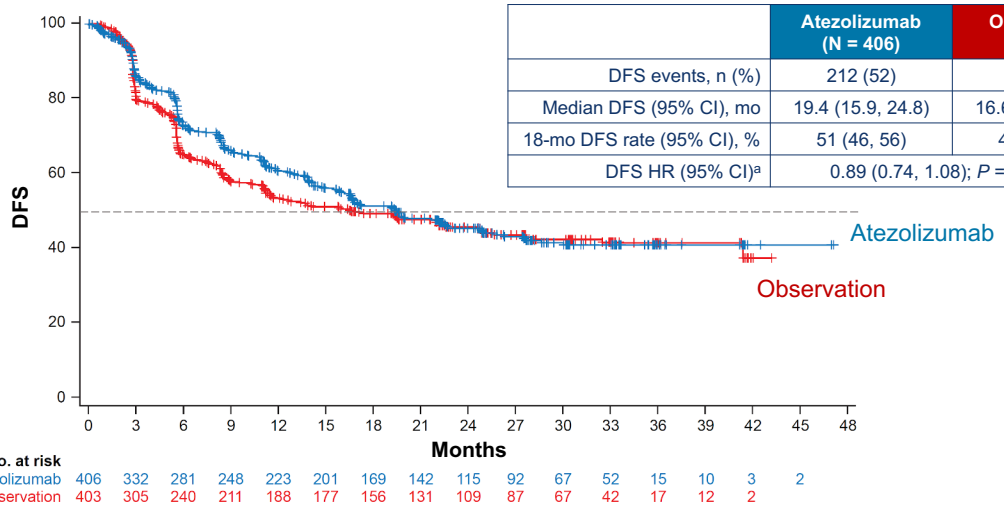
DFS in ITT Population



	Atezolizumab (N = 406)	Observation (N = 403)
DFS events, n (%)	212 (52)	208 (52)
Median DFS (95% CI), mo	19.4 (15.9, 24.8)	16.6 (11.2, 24.8)
18-mo DFS rate (95% CI), %	51 (46, 56)	49 (44, 54)
DFS HR (95% CI)[a]	0.89 (0.74, 1.08); *P* = 0.2446[b]	

No. at risk

Atezolizumab	406	332	281	248	223	201	169	142	115	92	67	52	15	10	3	2
Observation	403	305	240	211	188	177	156	131	109	87	67	42	17	12	2	

Data cutoff: November 30, 2019. Median follow-up: 21.9 mo. [a] Stratified by post-resection tumor stage, nodal status and PD-L1 status. [b] 2-sided.

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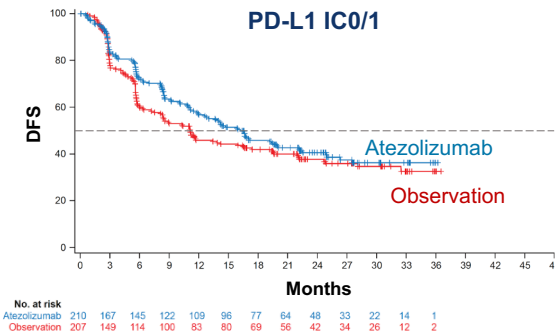
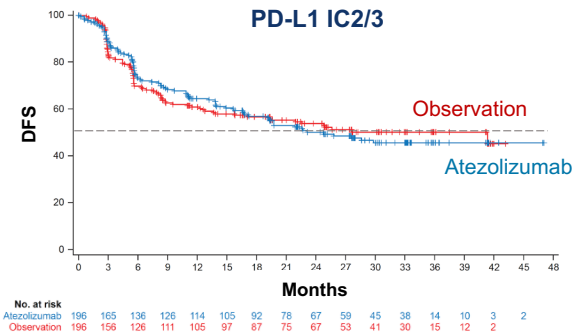
DFS by PD-L1 Status



No. at risk

Atezolizumab	210	167	145	122	109	96	77	64	48	33	22	14	1	
Observation	207	149	114	100	83	80	69	56	42	34	26	12	2	



No. at risk

Atezolizumab	196	165	136	126	114	105	92	78	67	59	45	38	14	10	3	2
Observation	196	156	126	111	105	97	87	75	67	53	41	30	15	12	2	

	Atezolizumab (n = 210)	Observation (n = 207)
DFS events, n (%)	118 (56)	120 (58)
HR (95% CI)[a]	0.81 (0.63, 1.05)	

Atezolizumab (n = 196)	Observation (n = 196)
94 (48)	88 (45)
1.01 (0.75, 1.35)	

Data cutoff: November 30, 2019. IC2/3, PD-L1–expressing IC on ≥ 5% of tumor area (VENTANA SP142 assay); IC0/1, < 5%. [a] Stratified by tumor stage and nodal status.

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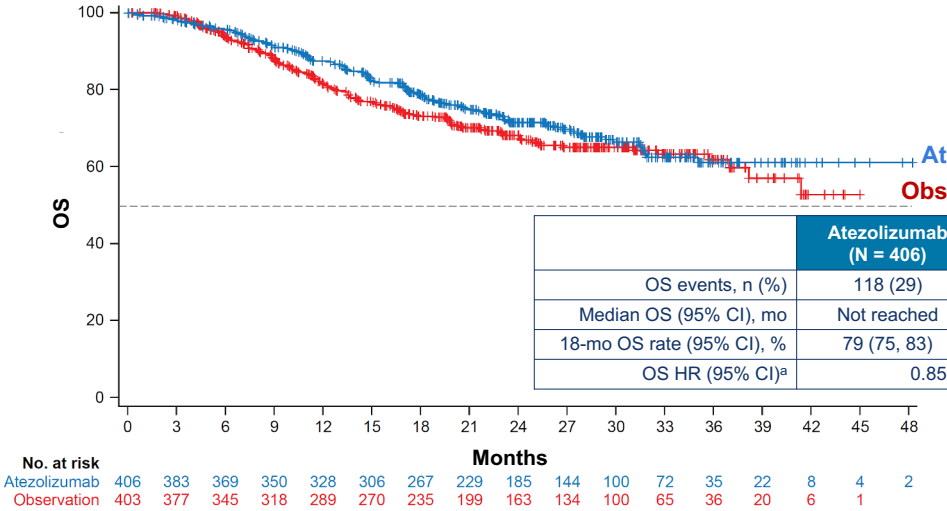
Interim OS Analysis in ITT Population



	Atezolizumab (N = 406)	Observation (N = 403)
OS events, n (%)	118 (29)	124 (31)
Median OS (95% CI), mo	Not reached	Not reached
18-mo OS rate (95% CI), %	79 (75, 83)	73 (69, 78)
OS HR (95% CI)[a]	0.85 (0.66, 1.09)	

Data cutoff: November 30, 2019. Median follow-up: 21.9 mo. Most common subsequent non-protocol therapies included immunotherapy (9% in atezolizumab arm vs 21% in observation arm), chemotherapy (27% vs 25%) and targeted therapy (5% vs 2%). [a] OS results are shown for descriptive purposes only. HR stratified by tumor stage, nodal status and PD-L1 status.

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"My two cents": ASCO 2020 Muscle Invasive Urothelial Cancer

- Adjuvant atezolizumab failed to improve outcomes in high risk muscle invasive UC
- Standard-of-care remains the same: neoadjuvant cisplatin-based chemotherapy followed by radical cystectomy

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mRCC Treatment Principles

1. Goal is CURE
   - … or prolongation of life
2. Immunotherapy offers best chance for cure
   - Combination IO-based therapy now frontline standard of care for most patients
3. Angiogenesis is active throughout ccRCC natural history
   - Allows for within-class sequential therapy

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Selected Pivotal Frontline RCC Trials

Pivotal Trial (Year Reported)	No.	Response Rate (%)	Median PFS (Mo)	Median OS (Mo)
Sunitinib vs. IFN-α (2007)	750	47 vs. 12	11 vs. 5	26.4 vs. 21.8
Pazopanib vs. sunitinib (2013)	1,110	31 vs. 25	8.4 vs. 9.5	28.4 vs. 29.3
Cabozantinib vs. sunitinib (poor/intermediate risk, 2017)	157	46 vs. 18	8.2 vs. 5.6	30 vs. 21.8
Temsirolimus vs. IFN-α (poor risk, 2007)	626	8.6 vs. 4.8	5.5 vs. 3.1	10.9 vs. 7.3
Nivolumab/ipilimumab vs. sunitinib (poor/intermediate risk, 2018)	1,070	41.6 vs. 26.5	11.5 vs. 8.4	NR vs. 26
Avelumab/axitinib vs. sunitinib (2019)	886	55 vs. 25.5	13.8 vs. 8.4	NR
Pembrolizumab/axitinib vs. sunitinib (2019)	840	59 vs. 36	15 vs. 11	NR

Tenold M & Lara P, et al. ASCO 2020 Educational Book 40187-196.

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Phase II Study of Nivolumab and Salvage Nivolumab + Ipilimumab in Treatment-Naïve Patients with Advanced Renal Cell Carcinoma (HCRN GU16-260)

Michael B. Atkins[1], Opeyemi A. Jegede[2], Naomi B. Haas[3], David F. McDermott[4], Mehmet A. Bilen[5], Charles G. Drake[6], Jeffrey A. Sosman[7], Robert Alter[8], Elizabeth R. Plimack[9], Brian Rini[10], Michael Hurwitz[11], David Peace[12], Sabina Signoretti[13], Catherine J. Wu[2], Paul J. Catalano[2], Hans Hammers[14]

[1]Georgetown-Lombardi Comprehensive Cancer Center, Washington, DC; [2]Dana Farber Cancer Institute, Boston, MA; [3]University of Pennsylvania Abramson Cancer Center, Philadelphia, PA; [4]Beth Israel Deaconess Medical Center, Boston, MA; [5]Winship Cancer Institute of Emory University, Atlanta GA; [6]Columbia Herbert Irving Comprehensive Cancer Center, New York, NY; [7]Northwestern Lurie Comprehensive Cancer Center, Chicago, IL; [8]John Theurer Cancer Center, Hackensack, NJ; [9]Fox Chase Cancer Center, Philadelphia, PA; [10]Cleveland Clinic Taussig Cancer Institute, Cleveland, OH (currently at Vanderbilt-Ingram Cancer Center, Nashville, TN); [11]Yale-Smilow Comprehensive Cancer Center, New Haven, CT; [12]University of Illinois Chicago, Chicago, IL; [13]Brigham and Women's Hospital Boston, MA, [14]University of Texas Southwestern Sammons Cancer Center, Dallas, TX.

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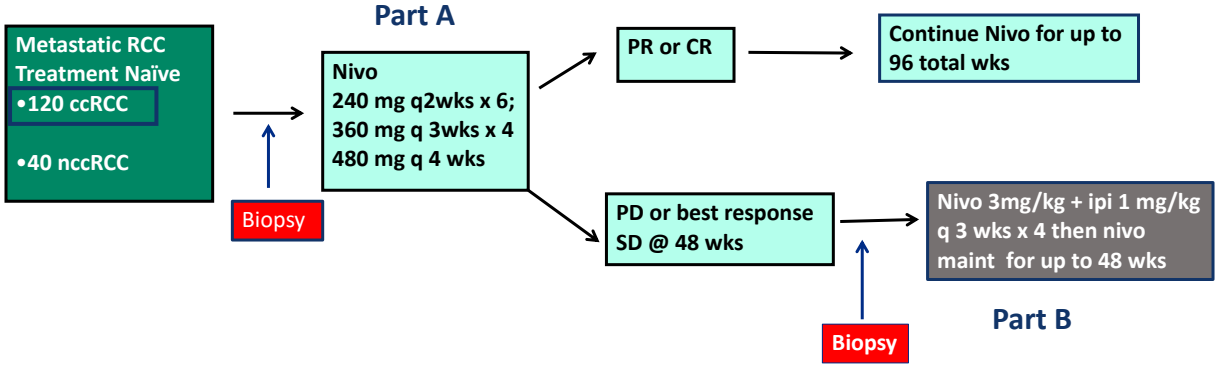
HCRN GU16-260: Study Design

IIT at 12 sites conducted through the HCRN GU Group
Support provided by BMS (CM209-669)



Extensive Biomarker studies in collaboration with the DFHCC Kidney Cancer SPORE
DOD Translational Partnership Grant (Atkins, Wu)

Scans q12 weeks; Confirm response and PD;
Measurements by RECIST 1.1
Mandatory biopsies

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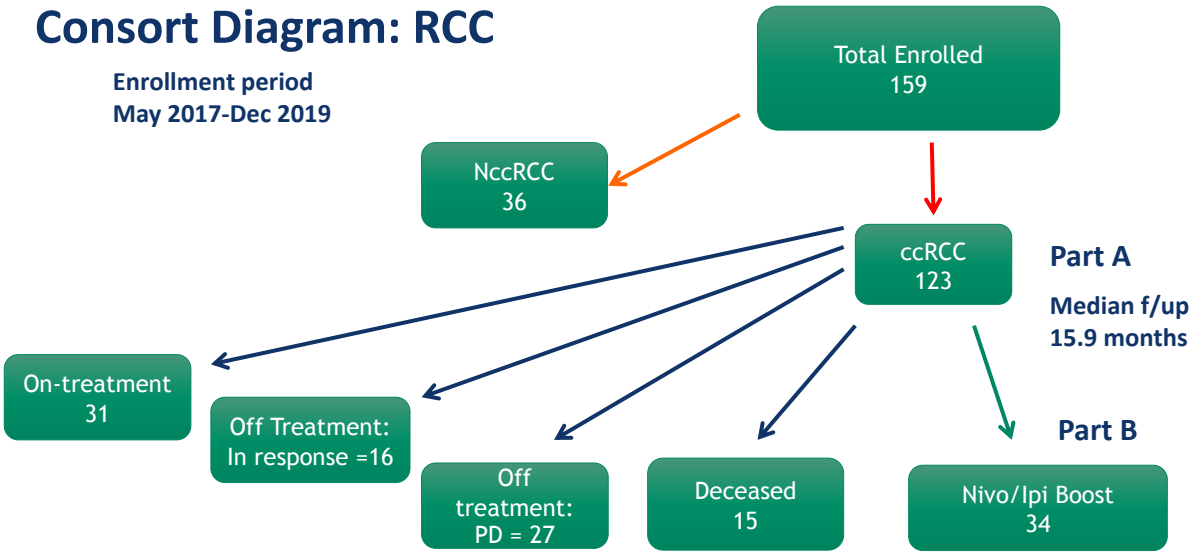
Consort Diagram: RCC

Enrollment period
May 2017-Dec 2019



Data Lock: April 17, 2020

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Objective Response Rates: Nivo Monotherapy: Part A

Best Response N (%)	IMDC Risk Category (N)			Total (N= 123) N (%)
	Favor (30) N (%)	Interm (80) N (%)	Poor (12) N (%)	
CR	4 (13.3)	3 (3.8)	0	7 (5.7)
PR*	11 (36.7)	17 (21.2)	3 (25)	32 (26.0)
SD	15 (50.0)	26 (32.5)	5 (42)	46 (37.4)
PD	0	34 (42.5)	4 (33)	38 (30.9)
ORR	15/30 (50)	20/80 (25)	3/12 (25)	39/123 (31.7)
(95% CI) %	(31.3,68.7)	(16.6, 35.1)		(23.6, 40.7)

*** 1 PR with missing IMDC Risk Category**

ORR: 39/123 = 31.7%
95% CI (23.6, 40.7%)

Sarcomatoid RCC ORR:
7/22 = 31.8% (all PRs)
95% CI (13.9, 54.9%)

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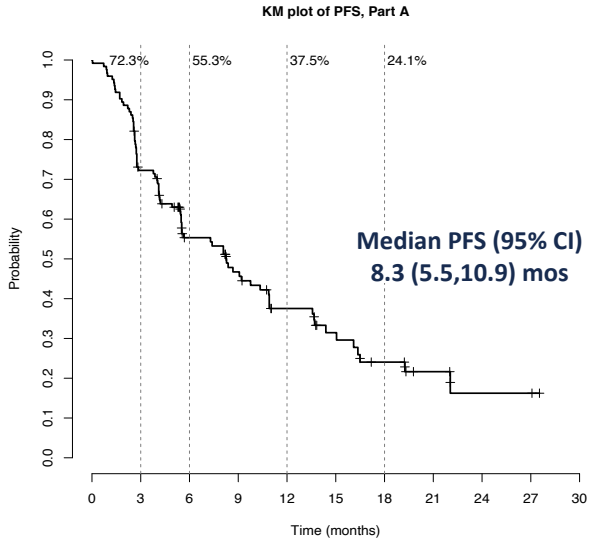
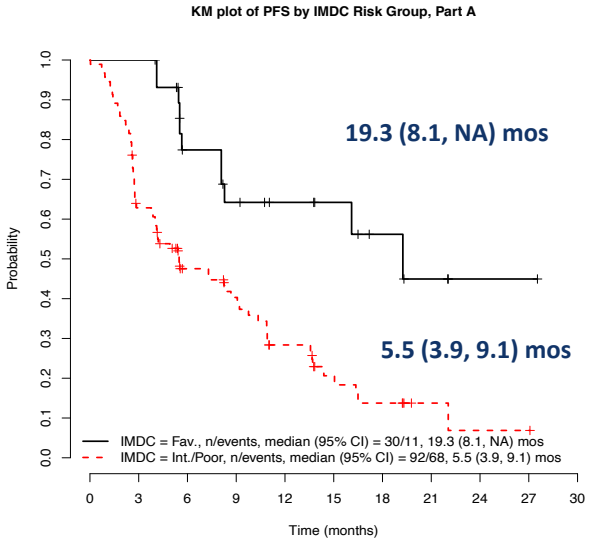
Progression Free Survival: Nivo Monotherapy (Part A)





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Disposition: Nivo/ipi Salvage (Part B)

- Potentially Eligible for Part B (65)
  - Progressive Disease (n=59)
  - Stable Disease at 48 wks (n=6)
- Not Enrolled: (31)
  - IrAE/AE in Part A (n=4)
  - Symptomatic PD/Alternative Systemic Rx/ Biopsy not possible (n=21)
  - Alternative Rx (surgery, RT) (n=6)
- Enrolled (34)
  - Evaluable (n=30)
  - Inevaluable (n=4) (PD, withdrew, ineligible x2)
  - 26 of 34 (76%) remain alive

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Objective Response Rates: Nivo/Ipi Salvage (Part B)

Best Response N (%)	IMDC Risk Category (N=30)			Total N (%)
	Favor (4)	Interm (24)	Poor (2)	
CR	0	0	0	0
PR	2 (50)	2 (8.3)	0	4 (13.3)
SD	1 (25)	6 (25)	0	7 (23.3)
PD	1 (25)	16 (66.7)	2 (100)	19 (63.3)

ORR: 4/30 = 13.3%
95% CI (3.8, 30.7)

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Treatment Emergent Toxicity: Nivo/ipi Salvage (Part B)

N=30	Grade 2: N (%)	Grade ≥ 3: N (%)
Fatigue	5 (17%)	2 (7%)
Colitis/Diarrhea	2 (7%)	4 (13%)
Endocrine	2 (7%)	1 (3%)
Hepatic	0	1 (3%)
Renal	0	2 (7%)
Lipase	6 (20%)	7 (23%)
Pulmonary	1 (3%)	1 (3%)
Myositis/myocarditis	2 (7%)	1 (3%)
Skin	5 (17%)	2 (7%)

Grade ≥ 3 Toxicity
12/30 = 40%

7 of 12 ↑Lipase

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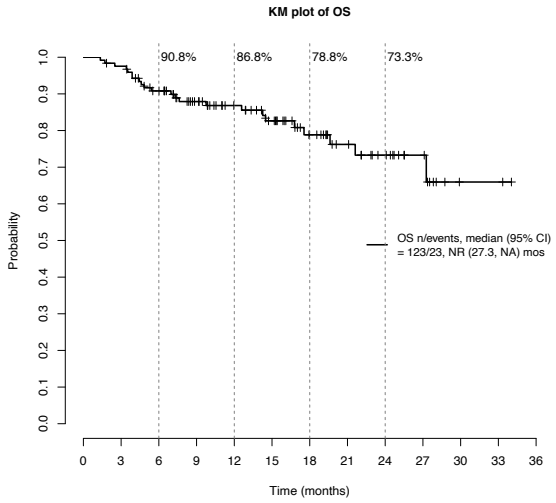
Overall Survival: ccRCC



100/123 = 81% of patients remain alive

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Pembrolizumab Plus Axitinib Versus Sunitinib as First-Line Therapy for Advanced Renal Cell Carcinoma: Updated Analysis of KEYNOTE-426

E. R. Plimack[1]; B. I. Rini[2]; V. Stus[3]; R. Gafanov[4]; T. Waddell[5]; D. Nosov[6]; F. Pouliot[7]; D. Soulières[8]; B. Melichar[9]; I. Vynnychenko[10]; S. J. Azevedo[11]; D. Borchiellini[12]; R. S. McDermott[13]; J. Bedke[14]; S. Tamada[15]; L. Yin[16]; M. Chen[16]; L. R. Molife[17]; M. B. Atkins[18]; T. Powles[19]

[1]Fox Chase Cancer Center, Philadelphia, PA, USA; [2]Clevland Clinic Taussig Cancer Institute, Cleveland, OH, USA (currently at Vanderbilt-Ingram Cancer Center, Nashville, TN, USA); [3]Dnipropetrovsk Medical Academy of Ministry of Health of Ukraine, Dnipro, Ukraine; [4]Russian Scientific Center of Roentgenoradiology, Moscow, Russia; [5]The Christie NHS Foundation Trust, Manchester, United Kingdom; [6]Central Clinical Hospital With Outpatient Clinic, Moscow, Russia; [7]CHU of Quebec and Laval University, Quebec City, QC, Canada; [8]Centre Hospitalier de l'Universitaire de Montréal, Montréal, QC, Canada; [9]Palacky University Medical School and Teaching Hospital, Olomouc, Czech Republic; [10]Sumy State University, Sumy Regional Oncology Center, Sumy, Ukraine; [11]Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil; [12]Centre Antoine Lacassagne, Université Côte d'Azur, Nice, France; [13]Adelaide and Meath Hospital and University College Dublin, Dublin, Ireland; [14]Eberhard-Karls University Tübingen, Tübingen, Germany; [15]Osaka City University Hospital, Osaka, Japan; [16]Merck & Co., Inc., Kenilworth, NJ, USA; [17]MSD UK, London, United Kingdom; [18]Georgetown Lombardi Comprehensive Cancer Center, Washington, DC, USA; [19]Barts Health NHS Trust and the Royal Free NHS Foundation Trust, Barts Cancer Institute, and Queen Mary University of London, London, United Kingdom

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KEYNOTE-426 Study Design

Key Eligibility Criteria
- Newly diagnosed or recurrent stage IV clear cell RCC
- No previous systemic treatment for advanced disease
- Measurable disease per RECIST v1.1

Stratification Factors
- IMDC risk group (favorable vs intermediate vs poor)
- Geographic region (North America vs Western Europe vs ROW)

R (1:1)
N = 861

n = 432 → Pembrolizumab 200 mg IV Q3W for up to 35 cycles + Axitinib 5 mg orally twice daily[a]

n = 429 → Sunitinib 50 mg orally once daily for first 4 weeks of each 6-week cycle[b]

End Points
- **Dual primary:** OS and PFS (RECIST v1.1, BICR) in ITT
- **Key secondary:** ORR (RECIST v1.1, BICR) in ITT
- **Other secondary**: DOR (RECIST v1.1), safety

[a]Axitinib dose could be increased to 7 mg, then 10 mg, twice daily if safety criteria were met; dose could be reduced to 3 mg, then 2 mg, twice daily to manage toxicity. [b]Sunitinib dose could be decreased to 37.5 mg, then 25 mg, once daily for the first 4 weeks of each 6-week cycle to manage toxicity. Data cutoff: January 6, 2020.

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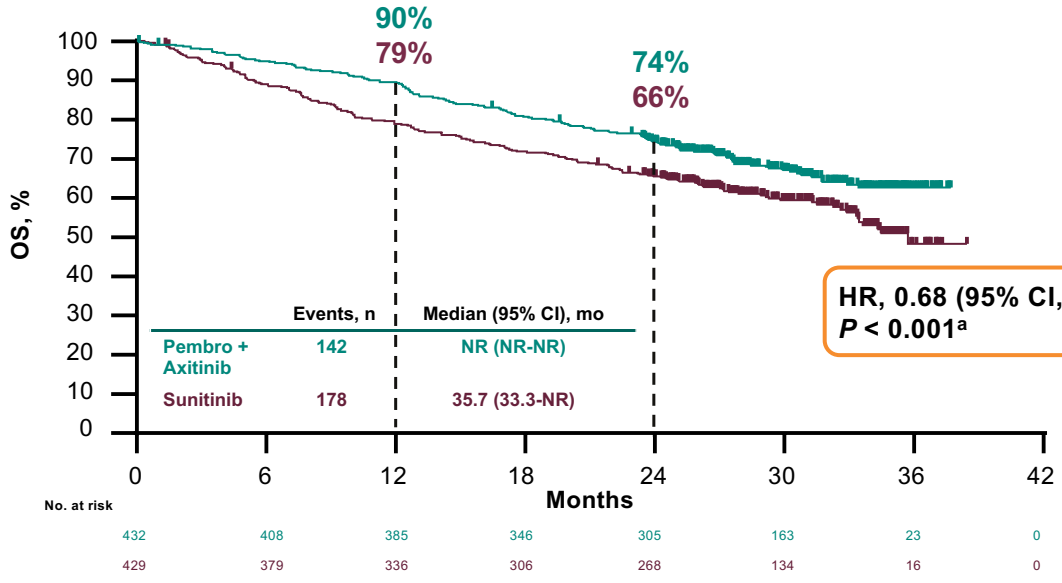
OS in the ITT Population



HR, 0.68 (95% CI, 0.55-0.85)
P < 0.001[a]

[a]Because superiority of pembrolizumab + axitinib was shown at the first interim analysis, no alpha was allocated to OS; only nominal *P* values are reported. Data cutoff: January 6, 2020.

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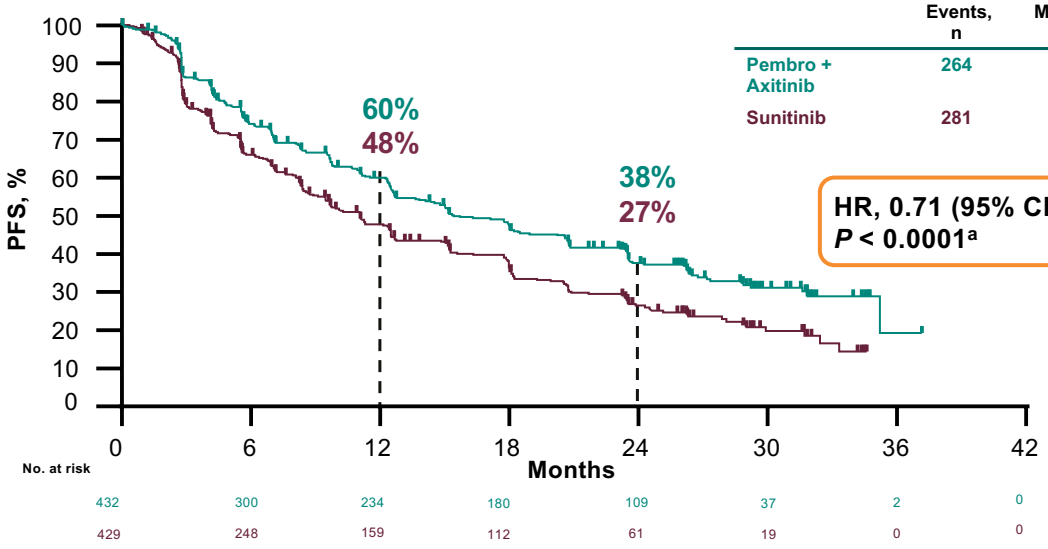
PFS in the ITT Population



	Events, n	Median (95% CI), mo
Pembro + Axitinib	264	15.4 (12.7-18.9)
Sunitinib	281	11.1 (9.1-12.5)

HR, 0.71 (95% CI, 0.60-0.84)
***P* < 0.0001[a]**

[a]Because superiority of pembrolizumab + axitinib was shown at the first interim analysis, no alpha was allocated to PFS; only nominal *P* values are reported. Data cutoff: January 6, 2020.

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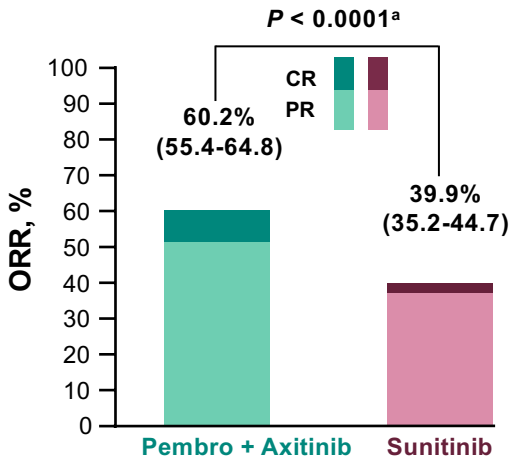
Confirmed Objective Response Rate
ITT Population



	Pembro + Axitinib n = 432	Sunitinib n = 429
Best response, n (%)		
CR	38 (8.8)	13 (3.0)
PR	222 (51.4)	158 (36.8)
SD	100 (23.1)	150 (35.0)
PD	49 (11.3)	74 (17.2)
NE[b]	16 (3.7)	28 (6.5)
NA[c]	7 (1.6)	6 (1.4)
Duration of response, median (range), mo	23.5 (1.4+ to 34.5+)	15.9 (2.3 to 31.8+)

[a]Because superiority of pembrolizumab + axitinib was shown at the first interim analysis, no alpha was allocated to confirmed objective response; only nominal *P* values are reported. [b]Postbaseline assessment available but not evaluable (ie, all postbaseline assessments with insufficient data for assessment of response per RECIST v1.1 or CR/PR/SD <6 weeks from randomization). [c]No postbaseline assessment available for response evaluation; + indicates an ongoing response at time of last disease assessment. Data cutoff: January 6, 2020.

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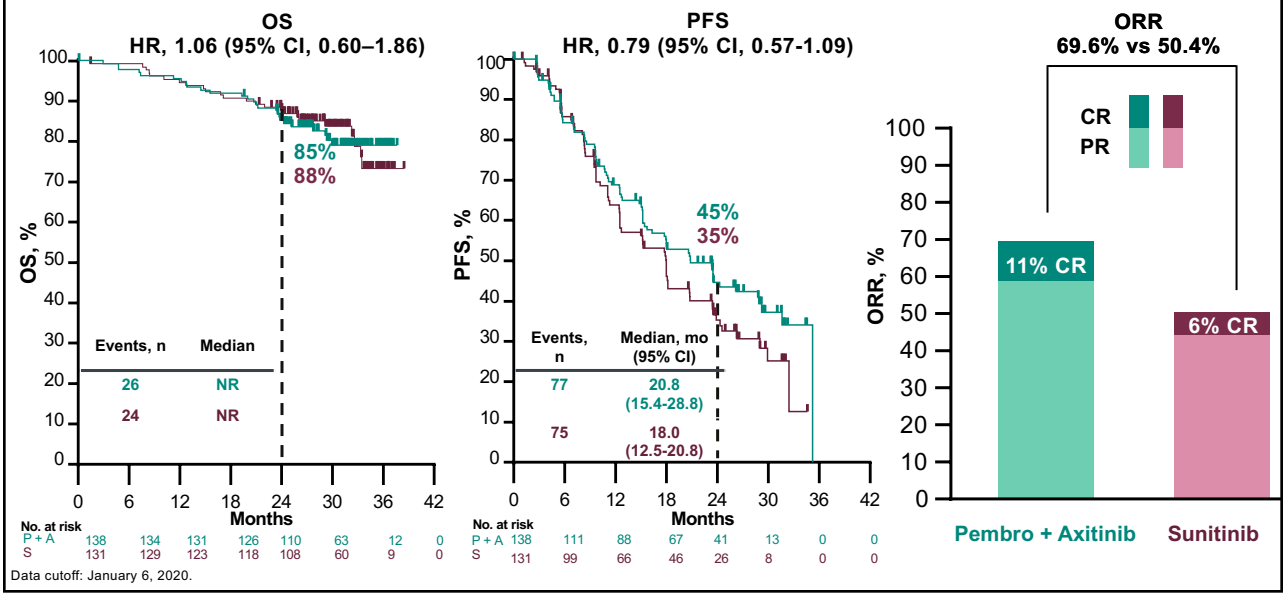
IMDC Favorable Risk: OS, PFS, and ORR



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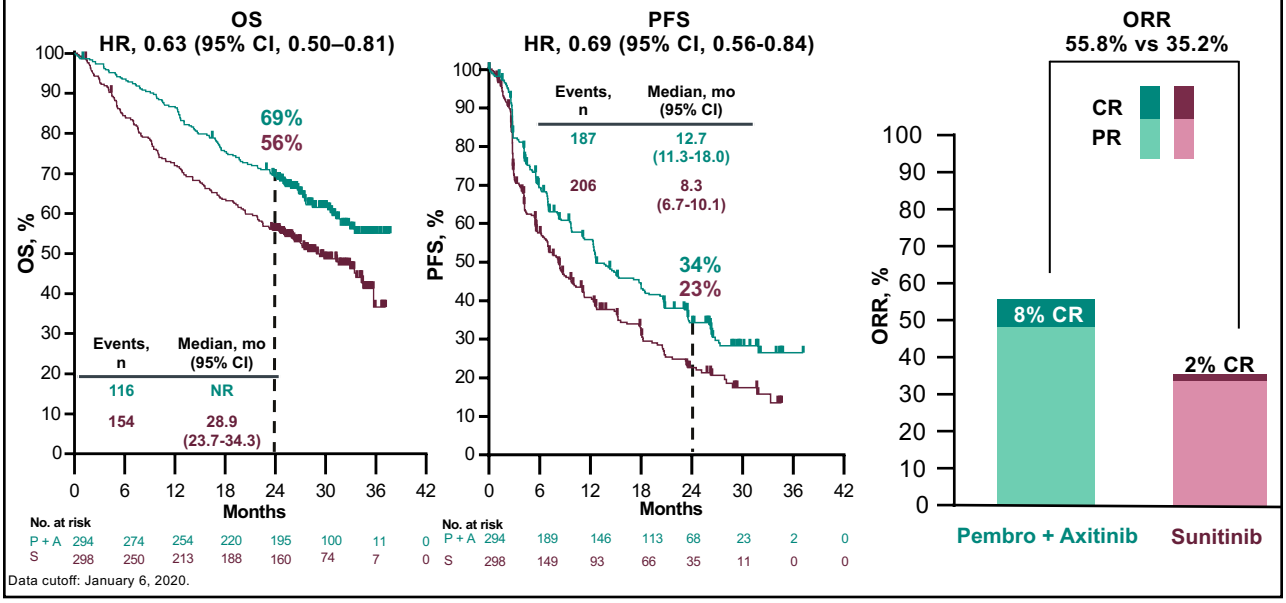
IMDC Intermediate/Poor Risk: OS, PFS, and ORR



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"My two cents": ASCO 2020 mRCC

- Pembrolizumab + axitinib confirmed as a standard of care (over sunitinib) in treatment-naïve mRCC
  - OS: HR, 0.68; *P* < 0.001; 24-month rate, 74% vs 66%
  - PFS: HR, 0.71; *P* < 0.0001; 24-month rate, 38% vs 27%
  - ORR: 60% vs 40%; *P* < 0.0001
  - CR rate: 9% vs 3%
- Single-agent nivolumab as frontline therapy in treatment naïve ccRCC yields:
  - ORR: 32%; 6% CR; Median DOR = 19.3 months
  - Median PFS = 8.3 months
  - Efficacy comparable to single agent Pembrolizumab in same setting
- Monotherapy with Nivo or Pembro may be an option for frontline patients not eligible for (or refuse) VEGFR-TKI containing combination therapy
- Nivo/Ipi salvage in Nivo non-responders is only modestly active (ORR = 13%)

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Diagnostic Performance of ^{18}F-DCFPyL-PET/CT and its Impact on Clinical Management of Patients with Biochemically Recurrent Prostate Cancer: Results from a Phase 3, Prospective, Multicenter Study (CONDOR)

Michael J. Morris*, Peter R. Carroll, Lawrence Saperstein, Frédéric Pouliot, David Josephson, Jeffrey Y.C. Wong, Austin R. Pantel, Steve Y. Cho, Kenneth Gage, Morand Piert, Andrei Iagaru, Janet H. Pollard, Vivien Wong, Jessica Donato Jensen, Nancy Stambler, Michael A. Gorin, Barry A. Siegel

Memorial Sloan Kettering Cancer Center, New York, NY; Dept. of Urology, University of California San Francisco, San Francisco, CA; Yale School of Medicine, New Haven, CT; Cancer Research Center, Centre Hospitalier Universitaire (CHU) de Québec-Université Laval, Quebec City, QC; Tower Urology, Los Angeles, CA; City of Hope, Duarte, CA; University of Pennsylvania, Philadelphia, PA; University of Wisconsin School of Medicine, Madison, WI; Moffitt Cancer Center, Tampa, FL; University of Michigan, Ann Arbor, MI; Stanford University, Stanford, CA; Carver College of Medicine - University of Iowa, Iowa City, IA; Progenics Pharmaceuticals, Inc., New York, NY; Department of Urology, Johns Hopkins University School of Medicine, Baltimore, MD; Siteman Cancer Center/Washington University, Saint Louis, MO

PRESENTED AT: 2020 ASCO ANNUAL MEETING #ASCO20

PRESENTED BY: Michael J. Morris, MD

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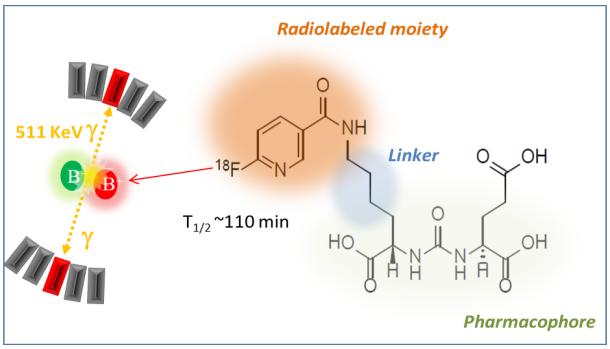
^{18}F-DCFPyL: A PSMA-targeted PET radiopharmaceutical

- **Lysine-linked, urea-based small molecule**
- **Targets the extracellular domain of PSMA**
- **High specific activity**
- **9 (±20%) mCi administered intravenously as bolus injection**
- **Imaging performed 1-2 hours following administration**



Chen et al. Clin Cancer Res 2011; laboratory of Martin G. Pomper, MD, PhD

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Eligibility Criteria

Select Inclusion Criteria

- Post-RP: PSA ≥0.2 ng/mL or
- Post-RT or cryotherapy: PSA ≥2 ng/mL above nadir
- Negative or equivocal imaging per institution's SOC work-up (including bone scan, CT, MRI, FDG PET, ^{18}F-fluciclovine or ^{11}C-choline PET)

Select Exclusion Criteria

- Ongoing treatment with any systemic therapy
- Treatment with ADT within 3 months prior to Day 1

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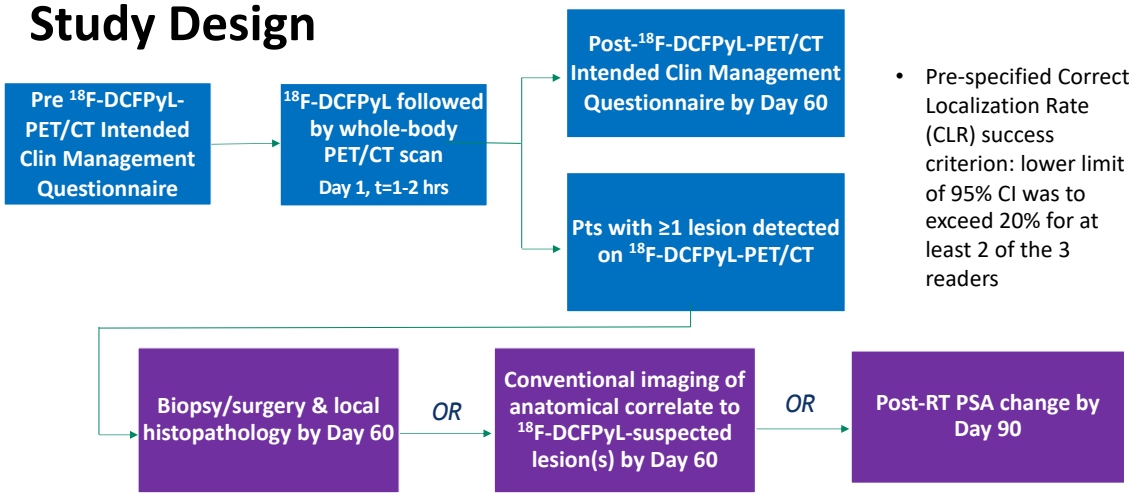
Study Design



- Pre-specified Correct Localization Rate (CLR) success criterion: lower limit of 95% CI was to exceed 20% for at least 2 of the 3 readers

Central imaging core lab
- **Three blinded, independent ^{18}F-DCFPyL-PET/CT readers**
- **Two separate truth panel readers**

14 sites in the US and Canada

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Select Baseline Characteristics, N=208

Patients Screened/Consented (N)	**217**
Patients dosed (N)	**208**
Age (years): Median (range)	**68 (43, 91)**
Months from Prostate Cancer Diagnosis: Median (range)	**71 (3, 356)**
Prior Prostate Cancer Therapies, N (%)	
RP only	103 (49.5)
RP and RT	74 (35.6)
RT only	31 (14.9)
At least 1 prior systemic therapy	58 (27.9)
Total Gleason Score, N (%)	
< 8	153 (73.6)
≥ 8	55 (26.4)

PSA: Median (range) ng/mL	**0.8 (0.17, 98.45)**
PSA Group (N=202), N (%)	
<2.0 ng/mL	**139 (68.8)**
<0.5 ng/mL	69 (34.2)
0.5 to <1.0 ng/mL	37 (18.3)
1.0 to <2.0 ng/mL	33 (16.3)
≥2.0 ng/mL	**63 (31.2)**
2.0 to <5.0 ng/mL	33 (16.3)
≥5.0 ng/mL	30 (14.9)

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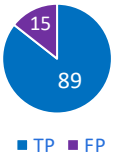
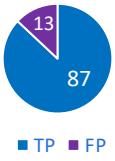
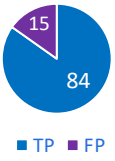
Diagnostic Performance of ^{18}F-DCFPyL PET/CT in Biochemical Recurrence: Correct Localization Rate

	All subjects (N=208)		
	Reader 1	Reader 2	Reader 3
Positive ^{18}F-DCFPyL Scan on Subject Level (Detection Rate)	137 (65.9%)	124 (59.6%)	123 (59.1%)
Unevaluable*	33	24	24
CLR (TP/(TP+FP))	89/104 85.6% (95% CI 78.8, 92.3) 	87/100 87.0% (95% CI 80.4, 93.6) 	84/99 84.8 (95% CI 77.8, 91.9) 

*SOT not submitted or false negative at the lesion level

- Correct Localization Rate met the primary endpoint, as the lower limit of the 95% CI far exceeded 20% by all 3 readers

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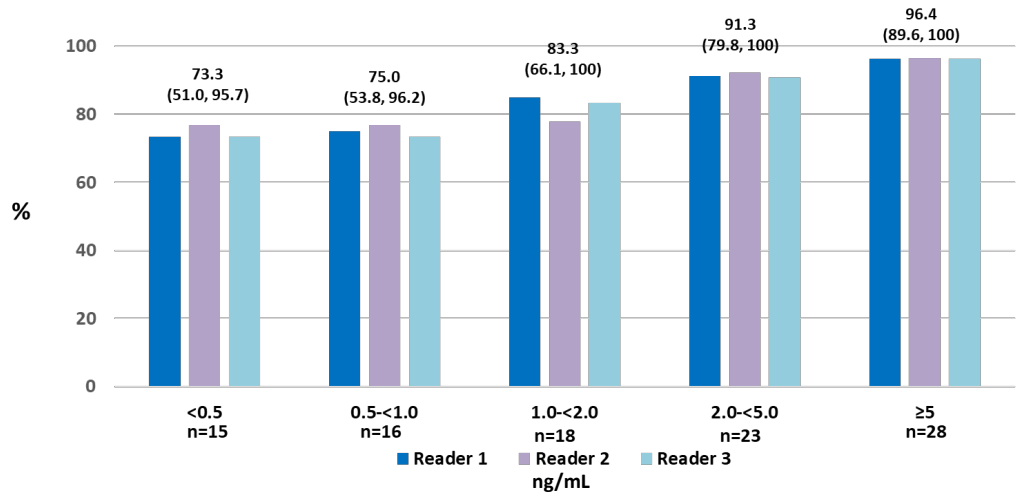
Correct Localization Rate by PSA



Median values for each group of three readers provided

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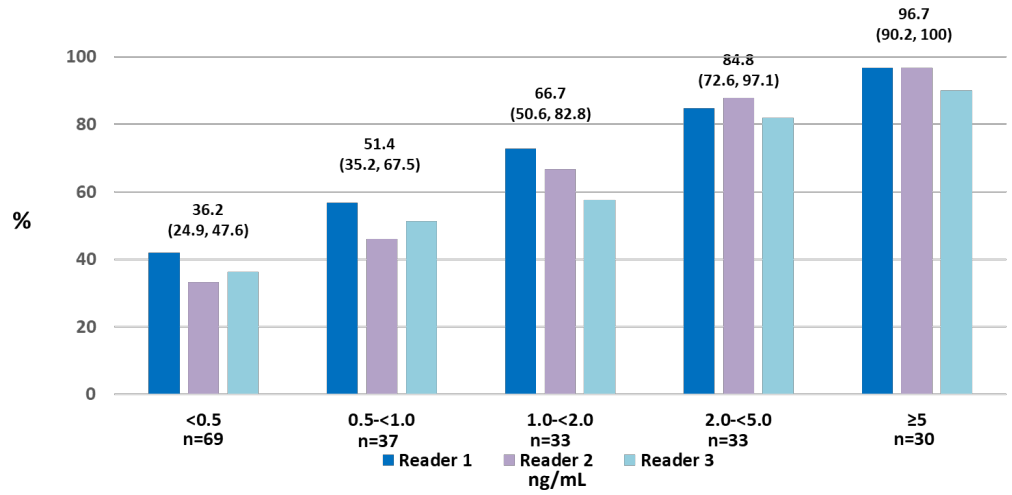
Detection Rate by PSA



Median values for each group of three readers provided

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Change of Management

- 63.9% of evaluable subjects had a change in intended management after ^{18}F-DCFPyL-PET/CT
  - 78.6% were attributable to positive and 21.4% to negative ^{18}F-DCFPyL-PET/CT scans
    - Noncurative systemic therapy to salvage local therapy (n = 43; 21.0%)
    - Salvage local therapy to systemic therapy (n = 58; 28.3%)
    - Observation to initiating therapy (n = 49; 23.9%)
    - Planned treatment to observation (n = 9; 4.4%)

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"My two cents"

- **^{18}F-DCFPyL-PET/CT**
  - Appears to complement conventional imaging in men with biochemically recurrent prostate cancer
  - Detects occult disease even at PSA values below 0.5
  - Has clinical utility in localized, biochemically recurrent, and metastatic prostate cancer

UCDAVIS COMPREHENSIVE CANCER CENTER

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Updated Overall Survival Results From PROSPER: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Enzalutamide in Men With Nonmetastatic Castration-Resistant Prostate Cancer

Cora N. Sternberg,[1] Karim Fizazi,[2] Fred Saad,[3] Neal D. Shore,[4] Ugo De Giorgi,[5] David F. Penson,[6] Ubirajara Ferreira,[7] Petro Ivashchenko,[8] Eleni Efstathiou,[9] Katarzyna Madziarska,[10] Michael Kolinsky,[11] Daniel I. G. Cubero,[12] Bettina Noerby,[13] Fabian Zohren,[14] Xun Lin,[14] Katharina Modelska,[15] Jennifer Sugg,[16] Joyce Steinberg,[16] Maha Hussain[17]

[1]Englander Institute for Precision Medicine, Weill Cornell Medicine, New York, NY, USA; [2]Gustave Roussy, Villejuif Cedex, France; [3]University of Montreal Hospital Center (CHUM), Montreal, QC, Canada; [4]Carolina Urologic Research Center, Myrtle Beach, SC, USA; [5]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy; [6]Vanderbilt University, Nashville, TN, USA; [7]State University of Campinas (Unicamp), Campinas, SP, Brazil; [8]Kyiv City Clinical Hospital #3, Kyiv, Ukraine; [9]MD Anderson Cancer Center, Houston, TX, USA; [10]Wroclaw Medical University, Wroclaw, Poland; [11]Cross Cancer Institute, University of Alberta, Edmonton, AB, Canada; [12]ABC Foundation School of Medicine, Santo André, Brazil; [13]Sygehus, Lillebælt, Vejle, Denmark; [14]Pfizer Inc., San Francisco, CA, USA; [15]Formerly of Pfizer Inc., San Francisco, CA, USA; [16]Astellas Pharma, Inc., Northbrook, IL, USA; [17]Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL, USA

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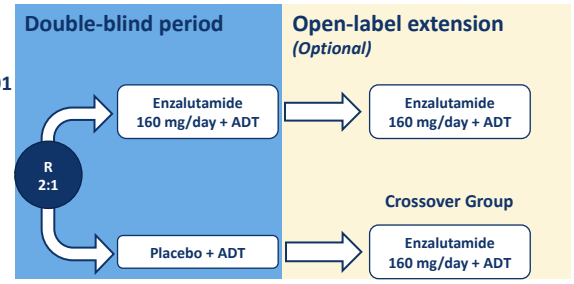
PROSPER Study Design

Key Eligibility Criteria
- nmCRPC (central review)
- Rising PSA despite castrate testosterone level (≤ 50 ng/dL)
- Baseline PSA ≥ 2 ng/mL
- PSA doubling time ≤ 10 months

Stratification
- PSA doubling time (< 6 mo vs 6-10 mo)
- Baseline use of bone-targeting agent (Y/N)

N = 1401



Primary endpoint
- MFS (defined as time from randomization to radiographic progression or death within 112 days of treatment discontinuation without evidence of radiographic progression)

Secondary endpoints
- OS
- Time to PSA progression
- Safety
- PSA response
- Quality of life

ADT, androgen deprivation therapy; MFS, metastasis-free survival; nmCRPC, nonmetastatic castration-resistant prostate cancer; OS, overall survival; PSA, prostate-specific antigen; R, randomization.

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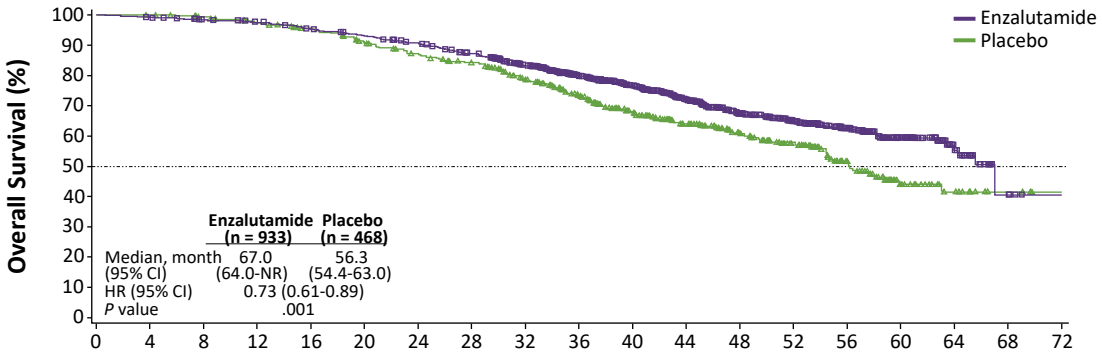
PROSPER Final Overall Survival Analysis

Enzalutamide was associated with a statistically significant 27% reduction in the risk of death



Patients at risk																			
Enzalutamide	933	926	910	897	874	850	822	782	700	608	517	424	327	244	169	89	33	4	0
Placebo	468	467	459	444	428	404	381	363	321	274	219	177	140	106	64	30	16	3	0

CI, confidence interval; HR, hazard ratio; NR, not reached.

52

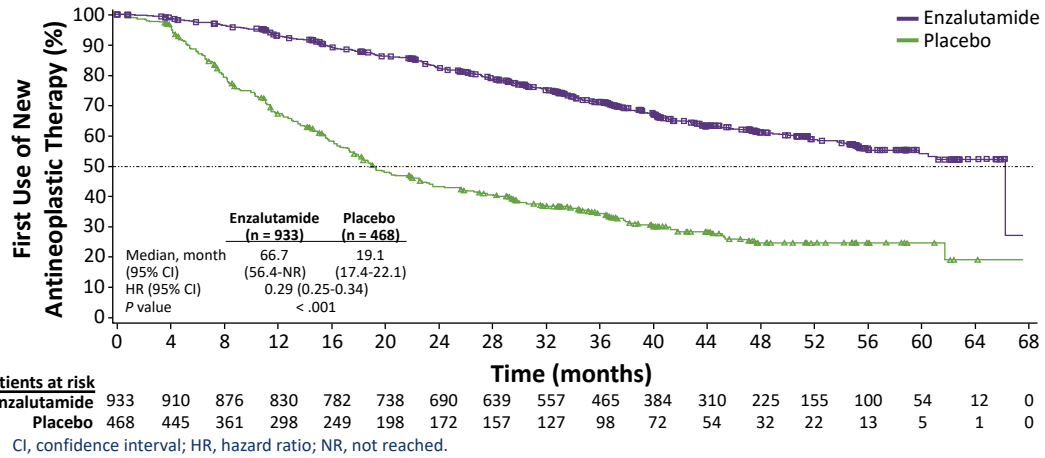
PROSPER Subsequent Antineoplastic Therapy

	Enzalutamide Group (n = 930)	Placebo Group (n = 465)
Patients taking ≥ 1 antineoplastic therapy after treatment discontinuation*	**33%**	**65%**
Subsequent therapies used by ≥ 5% of patients in any treatment group†		
Abiraterone acetate	49%	59%
Docetaxel	60%	47%
Enzalutamide‡	14%	36%
Cabazitaxel	15%	16%
Bicalutamide	9%	14%

*Percentages based on the total number of patients in each treatment group.
†Percentages based on the number of patients who received ≥ 1 antineoplastic therapy after treatment discontinuation.
‡Does not include the 87 patients who were randomized to placebo and received enzalutamide in the open-label extension.

53

PROSPER Time to First Use of Subsequent Antineoplastic Therapy



CI, confidence interval; HR, hazard ratio; NR, not reached.

54

PROSPER Safety

		Enzalutamide + ADT (n = 930)		Placebo + ADT (n = 465)
Median duration of treatment, mo (range)		**33.9 (0.2-68.8)**		**14.2 (0.1-51.3)**
Any adverse event	94%	34 per 100 patient-years	82%	60 per 100 patient-years
Within the first 3 months	65%	—	52%	—
Within the first 6 months	76%	—	64%	—
Any grade ≥ 3 adverse event	48%	17 per 100 patient-years	27%	20 per 100 patient-years
Within the first 3 months	10%	—	5%	—
Within the first 6 months	15%	—	12%	—
Any serious adverse event	40%	14 per 100 patient-years	22%	16 per 100 patient-years
Any adverse event leading to discontinuation	17%	6 per 100 patient-years	9%	6 per 100 patient-years
Any adverse event leading to death	5%	2 per 100 patient-years	1%	< 1 per 100 patient-years

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Overall Survival (OS) Results of Phase III ARAMIS Study of Darolutamide (DARO) Added to Androgen Deprivation Therapy (ADT) for Non-metastatic Castration-Resistant Prostate Cancer (nmCRPC)

Karim Fizazi,[1] Neal D. Shore,[2] Teuvo Tammela,[3] Albertas Ulys,[4] Egils Vjaters,[5] Sergey Polyakov,[6] Mindaugas Jievaltas,[7] Murilo Luz,[8] Boris Alekseev,[9] Iris Kuss,[10] Marie-Aude Le Berre,[10] Oana Petrenciuc,[11] Amir Snapir,[12†] Toni Sarapohja,[12] Matthew Raymond Smith[13]

[1]Institut Gustave Roussy and University of Paris-Saclay, Villejuif, France; [2]Carolina Urologic Research Center, Myrtle Beach, SC, USA; [3]Tampere University Hospital, Tampere, Finland; [4]National Cancer Institute, Vilnius, Lithuania; [5]Stradins Clinical University Hospital, Riga, Latvia; [6]N.N. Alexandrov National Cancer Centre of Belarus, Minsk, Belarus; [7]Lithuanian University of Health Sciences, Medical Academy, Kaunas, Lithuania; [8]Hospital Erasto Gaertner, Curitiba, Brazil; [9]National Medical Research Radiological Center, Ministry of Health of the Russian Federation, Moscow, Russia; [10]Bayer AG, Berlin, Germany; [11]Bayer HealthCare Pharmaceuticals, Inc., Whippany, NJ, USA; [12]Orion Corporation Orion Pharma, Espoo, Finland [†]; [13]Massachusetts General Hospital Cancer Center, Boston, MA, USA

[†]Present affiliation: PCI Biotech, Oslo, Norway

ARAMIS (NCT02200614) was sponsored by Orion Corporation Orion Pharma and Bayer AG

56

ARAMIS: Double-Blind, Placebo-Controlled, Phase III Trial to Evaluate Darolutamide vs Placebo in nmCRPC

- **Darolutamide is a structurally distinct ARI with low BBB penetration and low potential for DDIs[1–4]**

Patients
- Men with nmCRPC
- PSADT ≤10 months

Stratification
- PSADT (≤6 months vs >6 months)
- Osteoclast-targeted therapy (yes vs no)

Randomization 2:1

N=1509

Darolutamide 600 mg BID + ADT n=955

Placebo BID + ADT n=554

Primary analysis: MFS — Sep 3, 2018

Unblinding† — Final analysis: OS — Nov 15, 2019

†170 patients randomized to placebo crossed over to darolutamide treatment after unblinding

1 Primary endpoint met at primary analysis (significance level 0.05)[5]
- MFS median 40.4 months darolutamide vs 18.4 months placebo
- HR 0.41 (95% CI 0.34–0.50); *P*<0.0001

Safety[5]
- Favorable safety profile
- No increased incidence of most ARI-associated AEs with darolutamide

2 Secondary endpoints assessed for significance at final analysis (hierarchical testing; final α=0.0498)
- OS
- Time to pain progression
- Time to first cytotoxic chemotherapy
- Time to first SSE

1. Moilanen AM, et al. *Sci Rep*. 2015;5:12007. 2. Williams S, et al. *J Clin Oncol*. 2020;38(suppl 6):abstr 326. 3. Zurth C, et al. *J Clin Oncol*. 2019;37(7_suppl):156. 4. Shore N, et al. *Targ Oncol*. 2019;14:527–539. 5. Fizazi K, et al. *N Engl J Med*. 2019;380:1235–1246.
ADT, androgen deprivation therapy; AE, adverse event; ARI, androgen receptor inhibitor; BBB, blood–brain barrier; BID, twice daily; CI, confidence interval; DDI, drug–drug interaction; HR, hazard ratio; MFS, metastasis-free survival; nmCRPC, non-metastatic castration-resistant prostate cancer; OS, overall survival; PSADT, prostate-specific antigen doubling time; SSE, symptomatic skeletal event.

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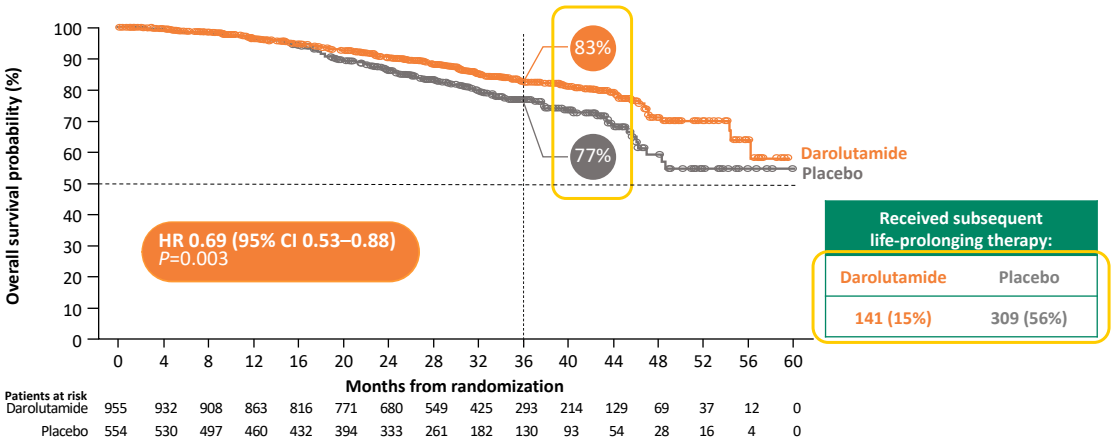
ARAMIS Overall Survival: 31% Reduction in Risk of Death

Survival benefit evident despite many placebo group patients receiving subsequent life-prolonging therapy



Received subsequent life-prolonging therapy:

Darolutamide	Placebo
141 (15%)	309 (56%)

At data cut-off for final analysis (November 15, 2019), median follow-up was 29.1 months. Median treatment duration was 25.8 months for patients randomized to darolutamide (double-blind and open-label periods), 11.0 months for crossover patients receiving darolutamide (open-label period), and 11.6 months for the patients receiving placebo during the double-blind period.
Three-year survival rates are indicated on the Kaplan-Meier curve by a vertical dotted line. CI, confidence interval; HR, hazard ratio.

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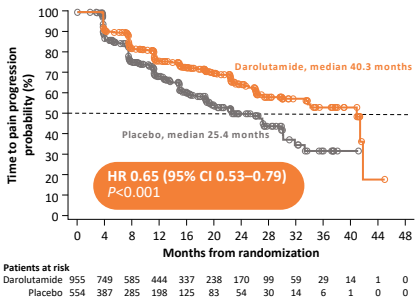
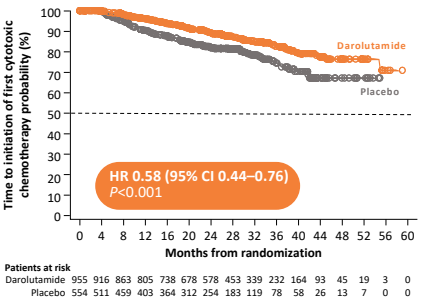
ARAMIS: All Secondary Endpoints Significantly in Favor of Darolutamide vs Placebo

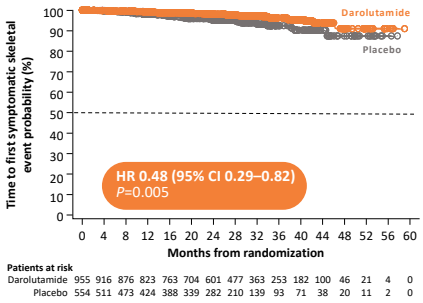
Time to pain progression†



Time to first cytotoxic chemotherapy



Time to first SSE



†Time to pain progression was evaluated using data from the primary analysis cut-off date of September 3, 2018.
All analyses for the placebo group include the 170 patients who crossed over to darolutamide treatment during the open-label study period.
CI, confidence interval; HR, hazard ratio; SSE, symptomatic skeletal event.

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"My two cents": Non-Metastatic CRPC

- In patients with nmCRPC, newer generation AR-targeted therapies significantly reduce risk of death compared to placebo
  - Apalutamide (HR 0.78; 22% reduction; p=0.01)
  - Enzalutamide (HR 0.73; 27% reduction; p=0.001)
  - Darolutamide (HR 0.69; 31% reduction; p=0.003)
- Adverse events appeared to be manageable
- Caveat: Non-metastatic CRPC population is rapidly shrinking as more sensitive imaging technology accelerates

UC DAVIS COMPREHENSIVE CANCER CENTER

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Maintenance avelumab + best supportive care (BSC) versus BSC alone after platinum-based first-line (1L) chemotherapy in advanced urothelial carcinoma (UC): JAVELIN Bladder 100 phase III interim analysis.

Authors:
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Abstract Disclosures

Research Funding:
This study was funded by Pfizer as part of an alliance between Pfizer and Merck KGaA, Darmstadt, Germany.

Background:
Platinum-based chemotherapy is an active 1L regimen for advanced UC; however, progression-free survival (PFS) and overall survival (OS) are generally short because of chemotherapy resistance. This randomized, phase 3 trial (JAVELIN Bladder 100; NCT02603432) evaluated avelumab (anti–PD-L1) as maintenance therapy following response or stable disease with 1L platinum-based chemotherapy in patients with advanced UC.

Methods:

IMvigor010: Primary analysis from a phase III randomized study of adjuvant atezolizumab (atezo) versus observation (obs) in high-risk muscle-invasive urothelial carcinoma (MIUC).

Authors:
Maha H. A. Hussain, Thomas Powles, Peter Albers, Daniel Castellano, Siamak Daneshmand, Juergen Gschwend, Hiroyuki Nishiyama, Stephane Oudard, Darren Tayama, Nicole N. Davarpanah, Viraj Degaonkar, Yi Shi, Sanjeev Mariathasan, Petros Grivas, Peter H. O'Donnell, Jonathan E. Rosenberg, Daniel M. Geynisman, Jean H. Hoffman-Censits, Daniel Peter Petrylak, Joaquim Bellmunt; Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL; Barts Cancer Institute, Queen Mary University of London, London, United Kingdom; Department of Urology, Heinrich-H University, Düsseldorf, Germany; Hospital Universitario 12 de Octubre, Madrid, Spain; USC Norris Comprehensive Cancer Center, Los Angeles, CA; Department of Urology, Technical University of Munich, Munich, Germany; University of Tsukuba, Tsukuba, Japan; Georges Pompidou Hospital, Paris, France; Genentech, South San Francisco, CA; Genentech, Inc., South San Francisco, CA; Genentech, San Francisco, CA; University of Washington, Seattle, WA; University of Chicago Comprehensive Cancer Center, Chicago, IL; Memorial Sloan Kettering Cancer, New York, NY; Fox Chase Cancer Center, Philadelphia, PA; Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD; Smilow Cancer Center, Yale University, New Haven, CT; Beth Israel Deaconess Medical Center, Boston, MA

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Abstract Disclosures

Research Funding:
F. Hoffmann-La Roche Ltd

Background:
Radical surgery ± cisplatin-based neoadjuvant chemo (NAC) is the mainstay treatment (tx) for MIUC, with no conclusive level 1 evidence for adjuvant chemo (AC). Here we present the primary analysis from IMvigor010, a global, open-label, multicenter, randomized trial of adjuvant atezo (anti–PD-L1; approved in metastatic UC [mUC] settings) in pts with MIUC at high risk of recurrence following primary resection.

Methods:
Pts with MIUC (bladder, upper tract [UT]), ECOG PS 0-2 and resected tissue for PD-L1 testing on immune cells (IC; VENTANA SP142 assay) were enrolled ≤ 14 wks after radical cystectomy/nephroureterectomy with lymph node (LN) dissection. Pathologic stage: 1) ypT2-4a or ypN+ if pts had NAC or 2) pT3-4a or pN+ if pts did not have NAC. No postsurgical radiation or AC was allowed; if no NAC was given, pts must have been ineligible for or declined cisplatin-based AC. Pts were randomized 1:1 to atezo 1200 mg IV q3w or obs for 16 cycles or 1 y (stratification factors: no. of LNs resected, pathologic nodal status, pathologic tumor stage, PD-L1 status, prior NAC). Disease-free survival (DFS) was the primary endpoint (EP). Final DFS, first interim overall survival (OS; secondary EP) and safety are reported.

Results:

The ITT population included 809 pts (median follow-up, 21.9 mo). In the atezo and obs arms, respectively, 48% and 47% had NAC; 7% and 6% had UTUC as primary disease; 48% each had LN+ disease. DFS and OS are in Table. Baseline prognostic/clinical factors did not influence DFS tx benefit; stratified HR was 0.81 (95% CI: 0.63, 1.05) in IC0/1 pts (PD-L1 < 5%; n = 417) and 1.01 (0.75, 1.35) in IC2/3 pts (PD-L1 ≥ 5%; n = 392). 16% of atezo-treated pts had a tx-related G3-4 AE. Skin and gastrointestinal toxicities most commonly led to tx discontinuation.

Conclusions:

IMvigor010, the first phase 3 adjuvant study of a checkpoint inhibitor in MIUC, did not meet its primary EP of DFS. More tx discontinuation due to AEs was seen vs mUC studies. Safety was generally consistent with previous studies. Clinical trial information: NCT02450331.

IMvigor010 primary analysis	Atezo (N = 406)	Obs (N = 403)
Final DFS		
No. of Events (%)	212 (52)	208 (52)
Median (95% CI), mo	19.4 (15.9, 24.8)	16.6 (11.2, 24.8)
HR (95% CI)[a]	0.89 (0.74, 1.08); *P* = 0.2446[b]	
First interim OS		
No. of Events (%)	118 (29)	124 (31)
Median (95% CI), mo	NR	NR
HR (95% CI)[a]	0.85 (0.66, 1.09); *P* = 0.1951[c]	

NR, not reached. Data cut off: Nov 30, 2019. [a] Stratified by nodal status, post-resection tumor stage, PD-L1 status. [b] 2-sided *P* value. [c] DFS, then OS tested hierarchically. OS *P* value for descriptive purposes.

Eligible patients with unresectable locally advanced or metastatic UC without disease progression after 4-6 cycles of gemcitabine with either cisplatin or carboplatin were randomized 1:1 to receive maintenance avelumab (10 mg/kg IV every 2 weeks) + best supportive care (BSC) or BSC alone, stratified by best response to 1L chemotherapy (complete/partial response vs stable disease) and by visceral vs nonvisceral disease when initiating 1L chemotherapy. The primary endpoint was OS, assessed from randomization in 2 primary populations: all randomized patients and patients with PD-L1+ tumors (Ventana SP263 assay). Secondary endpoints included PFS, objective response, and safety.

Results:

700 patients were randomly assigned to maintenance avelumab + BSC (n=350) or BSC alone (n=350) and were followed for a median of 19.6 and 19.2 months, respectively. Overall, 358 (51%) had PD-L1+ tumors. Avelumab + BSC significantly prolonged OS vs BSC alone in all randomized patients (hazard ratio [HR] 0.69; 95% CI 0.56, 0.86; 1-sided p=0.0005); median OS with avelumab + BSC vs BSC alone was 21.4 vs 14.3 months, respectively. Avelumab + BSC also significantly prolonged OS vs BSC alone in patients with PD-L1+ tumors (HR 0.56; 95% CI 0.40, 0.79; 1-sided p=0.0003); median OS was not reached vs 17.1 months, respectively. An OS benefit was also observed across all prespecified subgroups. The HR for PFS based on blinded independent central review with avelumab + BSC vs BSC alone was 0.62 (95% CI 0.52, 0.75) in all randomized patients and 0.56 (95% CI 0.43, 0.73) in patients with PD-L1+ tumors. In treated patients in the avelumab + BSC (n=344) vs BSC alone (n=345) arms, respectively, all-causality adverse events (AEs) were reported at any grade in 98.0% vs 77.7% and at grade ≥3 in 47.4% vs 25.2%, and the most frequent grade ≥3 AEs were urinary tract infection (4.4% vs 2.6%), anemia (3.8% vs 2.9%), hematuria (1.7% vs 1.4%), fatigue (1.7% vs 0.6%), and back pain (1.7% vs 2.3%).

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Conclusions:

JAVELIN Bladder 100 met its primary objective, demonstrating significantly prolonged OS with 1L maintenance avelumab + BSC vs BSC alone in advanced UC in all randomized patients and patients with PD-L1+ tumors. Efficacy benefits were seen across all prespecified subgroups, and the safety profile of avelumab was consistent with previous studies of monotherapy. Clinical trial information: NCT02603432.

Phase II study of nivolumab and salvage nivolumab + ipilimumab in treatment-naïve patients (pts) with advanced renal cell carcinoma (RCC) (HCRN GU16-260).

Authors:
Michael B. Atkins, Opeyemi Jegede, Naomi B. Haas, David F. McDermott, Mehmet Asim Bilen, Charles G. Drake, Jeffrey Alan Sosman, Robert S. Alter, Elizabeth R. Plimack, Brian I. Rini, Michael E. Hurwitz, David J. Peace, Sabina Signoretti, Catherine J. Wu, Paul J. Catalano, Hans J. Hammers; Georgetown Lombardi Comprehensive Cancer Center, Washington, DC; Dana Farber Cancer Institute, Boston, MA; Penn Medicine Abramson Cancer Center, Philadelphia, PA; Beth Israel Deaconess Medical Center, Dana-Farber/Harvard Cancer Center, Boston, MA; Department of Hematology and M Oncology, Emory University School of Medicine, Atlanta, GA; Herbert Irving Comprehensive Cancer Center, New York, NY; Vanderbilt University Ingram Cancer Center, Nashville, TN; Northern New Jersey Cancer Center, Englewood, NJ; Fox Chase Cancer Center, Philadelphia, PA; Cleveland Clinic Taussig Cancer Institute, Cleveland, OH; Yale School of Medicine, New Haven, CT; University of Illinois at Chicago, Chicago, IL; Department of Pathology, Brigham and Women's Hospital, Boston, MA; Dana-Farber Cancer Institute, Boston, MA; Harold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Dallas, TX

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Abstract Disclosures

Research Funding:
Bristol Meyers Squibb

Background:
Nivolumab (nivo) is FDA approved for pts with VEGFR TKI-resistant RCC and the nivo + ipilimumab (nivo/ipi) combination is FDA approved for treatment naïve pts with IMDC intermediate and poor risk RCC. Little information is available on the efficacy and toxicity of nivo monotherapy in treatment naïve RCC or the efficacy of nivo/ipi salvage therapy in pts with tumors resistant to initial nivo monotherapy.

Methods:
Eligible pts with treatment naïve RCC received nivo 240mg IV q2 wk x 6 doses followed by 360mg IV q3 wk x 4 doses followed by 480 mg q4 wk until progressive disease (PD), toxicity, or completion of 96 wks of treatment (Part A). Pts with PD prior to or stable disease (SD) at 48 wks (pSD) were potentially eligible to receive salvage nivo (3mg/kg) /ipi (1 mg/kg) q3 wk x 4 doses followed by q4 wk nivo maintenance for up to 48 wks (Part B). All pts were required to submit tissue from a metastatic lesion obtained within 12 months (mo) prior to study entry and prior to Part B. Pathology specimens will be analyzed by immunohistochemistry, quantitative immunofluorescence, WES and RNAseq with results linked to clinical outcome.

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♦
pnlara@ucdavis.edu
June 2020

Summary of Qualifications

Academic medical oncologist with expertise in genitourinary and thoracic malignancies

Extensive experience in cancer clinical trial design, development, and conduct, with emphasis on novel antineoplastics and biologics (developmental therapeutics)

Leader, team player, mentor, and consensus builder

Board Certifications

Diplomate, Internal Medicine, American Board of Internal Medicine, November 1996 – 2016

Diplomate, Medical Oncology, ABIM, November 1999 – present

Medical Licensure

Medical Board of California, Physician and Surgeon certification, October 25, 1995 to present

State of Illinois, 1993-96

Academic Appointments

Director, University of California Davis Comprehensive Cancer Center (a National Cancer Institute-designated Comprehensive Cancer Center), April 1, 2018-present

Executive Associate Dean for Cancer Programs, UC Davis School of Medicine, April 1, 2018-present

Codman-Radke Endowed Chair for Cancer Research, April 1, 2018-present

Acting Director, University of California Davis Comprehensive Cancer Center, July 1, 2016-March 31, 2018

Associate Dean for Cancer Programs, UC Davis School of Medicine, 7/206-3/2018

Professor of Medicine (Step 8.5), Division of Hematology-Oncology, Department of Internal Medicine, University of California Davis School of Medicine, July 2006 – present

Associate Director for Translational Research, University of California Davis Comprehensive Cancer Center, November 2008 – 2016

Associate Professor of Medicine, Division of Hematology-Oncology, Department of Internal Medicine, University of California Davis, July 2002 – June 2006

Assistant Professor of Medicine, Division of Hematology-Oncology, Department of Internal Medicine, University of California Davis, July 1999 – June 2002

Staff Physician, Urgent Care, Department of Medicine, Kaiser Permanente Medical Center, South Sacramento, 1997-1999

Visiting Post-Doctoral Scholar, University of California Davis Cancer Center, 1996-1999

Instructor (Adjunct), Rush Medical College, Rush University, Chicago, IL July 1993 – June 1996

Medical Training and Education

Fellowship, Hematology-Oncology, University of California Davis School of Medicine, UCD Cancer Center, Sacramento, CA, July 1996 to June 1999

Residency, Internal Medicine, Rush Presbyterian-St. Luke's Medical Center, Chicago, IL, July 1994 to June 1996

Internship, Internal Medicine, Rush Presbyterian-St. Luke's Medical Center, Chicago, IL, July 1993 to June 1994

Rotating Internship, University of the Philippines-Philippine General Hospital, Manila, May 1991 to April 1992

Doctor of Medicine, College of Medicine, University of the Philippines, Manila, June 1987 to May 1992 (includes mandatory rotating internship as above)

Bachelor of Science in Biology, *Magna Cum Laude*, University of the Philippines College of Science, Quezon City, June 1983 to April 1987

Formal Executive and Leadership Training

"Negotiation and Leadership"; Program on Negotiation, Harvard Law School, May 2015

Results:

123 pts with clear cell(cc) RCC were enrolled between 5/2017 and 12/2019 at 12 participating HCRN sites. Median age 65 (range 32-86 years); 72% male. IMDC favorable 30 (25%), intermediate 79 (65%) and poor risk 12 (10%). 22 (18%) had a component of sarcomatoid histology (SARC). 117 pts are currently evaluable for response. RECIST defined ORR was: 34 (29.3%)[CR 5 (4.3%), PR 29 (24.8%)], SD 47 (40.2%), PD 36 (30.7%). ORR by irRECIST was 35%. ORR by IMDC was: favorable 12/29 (41.4%), intermediate/poor 22/87 (25.3%) and for SARC 6/22 (27.3%). Median DOR is 13.8 (10.9, NA) mo. Median PFS is 7.4 (5.5, 10.9) mo. 110 pts remain alive. 60 pts (54 PD, 6 pSD) to date were potentially eligible for salvage nivo/ipi (Part B), but 28 did not enroll due to symptomatic PD (17), grade 3-4 toxicity on nivo (8), other (3). 27 of 32 Part B pts are currently evaluable for efficacy and 30 for toxicity. Best response to nivo/ipi was PR (11%), SD (30%), PD (59%). ORR by irRECIST was 19%. Grade 3-5 Treatment-related AEs (TrAE) were seen in 35/123 (28)% on nivo with 1 death due to respiratory failure. Grade 3-4 TrAE were seen in 10/30 (33%) on nivo/ipi with 0 deaths. Correlative studies are pending.

Conclusions:

Nivo monotherapy is active in treatment naïve ccRCC across all IMDC groups. Toxicity is consistent with prior nivo studies. Salvage treatment with nivo/ipi after nivo monotherapy was feasible in 53% of pts with PD/pSD, with 11% responding. Clinical trial information: NCT03117309.

Print

ASCO HIGHLIGHTS 2020: GASTROINTESTINAL ONCOLOGY

Tyler Johnson, MD

Stanford University

Presentation
Abstracts
Abbreviated Bio/CV

ASCO 2020: GI Updates

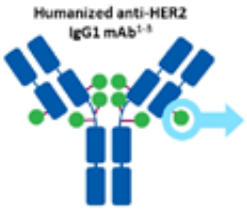
Tyler Johnson
Stanford University Medical Center
Clinical Assistant Professor

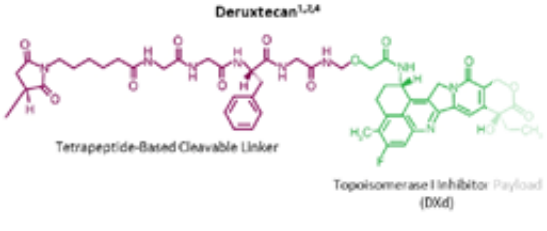
1

T-DXd is a Novel ADC Designed to Deliver an Antitumor Effect

T-DXd is an ADC with 3 components:

- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker



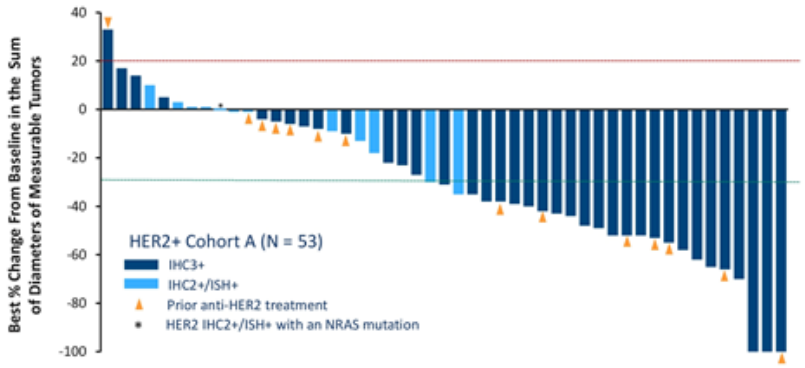


Payload mechanism of action: topoisomerase I inhibitor
High potency of payload
High drug to antibody ratio = 8
Payload with short systemic half-life
Stable linker-payload
Tumor-selective cleavable linker
Membrane-permeable payload

The clinical relevance of these features is under investigation.
ADC, antibody-drug conjugate.
1. Nakada T, et al. *Chem Pharm Bull* (Tokyo). 2019;67(3):173-185. 2. Ogitani Y, et al. *Clin Cancer Res*. 2016;22(20):5097-5108. 3. Trail PA, et al. *Pharmacol Ther*. 2018;181:126-142. 4. Ogitani Y, et al. *Cancer Sci*. 2016;107(7):1039-1046.

2

Best Change in Tumor Size



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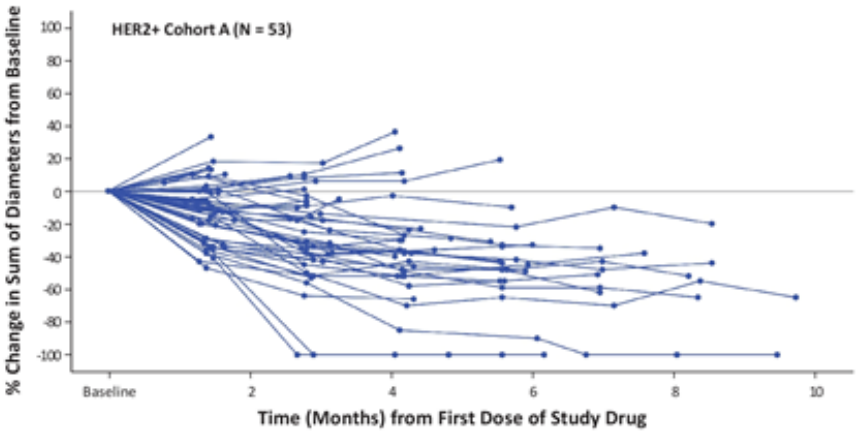


4

DESTINY-CRC01

AEs of Special Interest: Interstitial Lung Disease

	All Patients (N = 78)					
Preferred Term, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade/ Total
Interstitial Lung Disease	0	2 (2.6)	1 (1.3)	0	2 (2.6)	5 (6.4)

Among the 5 total events:

- Median time to investigator-reported onset was 80 days (range, 22-132)
- 5 of 5 patients with grade ≥ 2 ILD received corticosteroids
- 2 patients recovered, 1 did not recover (later died due to disease progression), and 2 died
- In the 2 fatal cases, onset was from 40-126 days, both received steroids as part of treatment, and death occurred 6-18 days after diagnosis

Protocol recommendations: Monitor for symptoms. Hold T-DXd and start steroids as soon as ILD is suspected

Drug related; ILD was determined by an Independent ILD Adjudication Committee based on 44 preferred terms.
One additional grade 5 ILD case in Cohort B was reported after the data cutoff. This case was adjudicated after data cutoff as drug-related ILD.

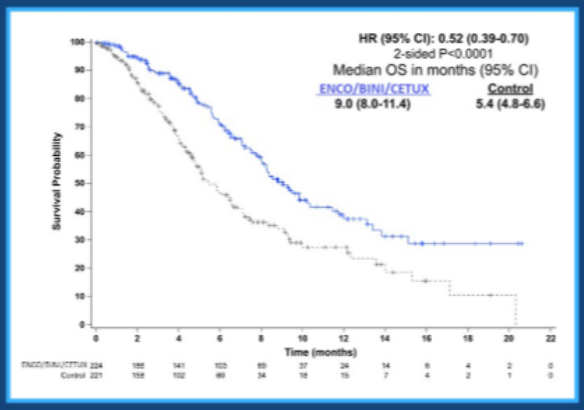
5

Her2 matters in CRC.

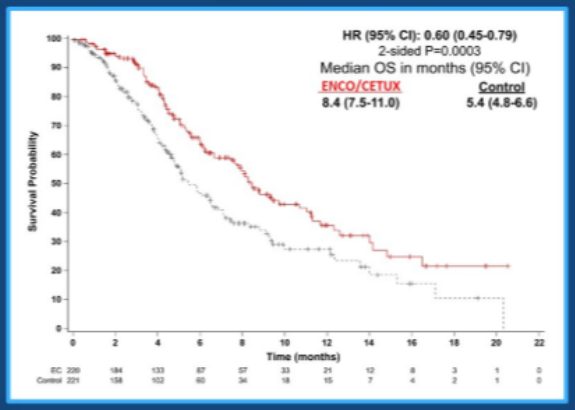
6

Primary Analysis: Overall Survival and Objective Response Rate

ENCO/BINI/CETUX vs Control*



ENCO/CETUX vs Control*



Objective Response Rate (First 331 Randomized Patients)

Confirmed Response by blinded central review	ENCO/BINI/CETUX N=111	ENCO/CETUX N=113	Control N=107
Objective Response Rate	**26%**	**20%**	**2%**
95% (CI)	(18%, 35%)	(13%, 29%)	(<1%, 7%)
p-value vs. Control	<0.0001	<0.0001	

* survival analysis conducted in all randomized patients.

Kopetz et al. N Engl J Med 2019; 381:1632.

7

BRAFm V600E matters in CRC.

8

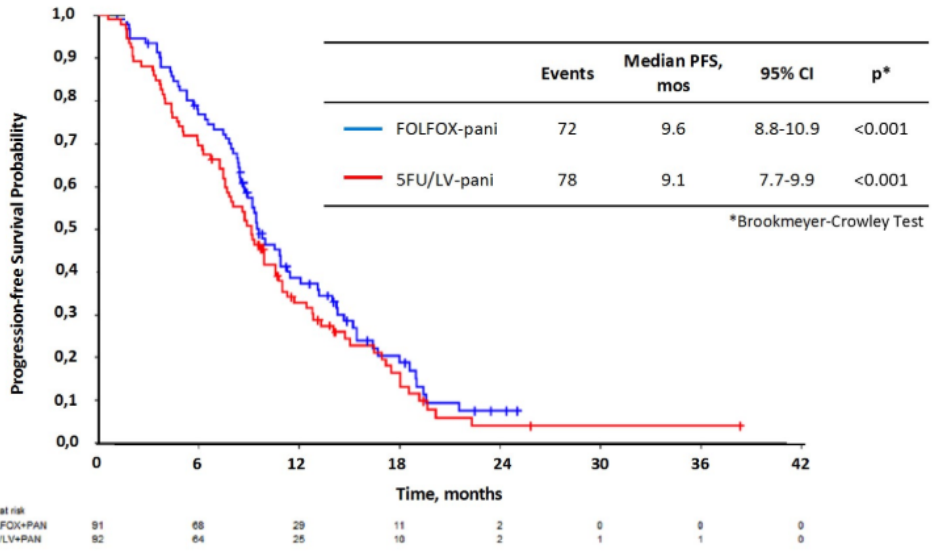
Main eligibility criteria

- ✓ Initially unresectable mCRC not previously treated with chemotherapy for metastatic disease
- ✓ Availability of tumor sample (primary and/or metastatic sites) for molecular testing
- ✓ Age ≥ 70 years
- ✓ ECOG PS 1 or 2 for patients aged 70 to 75 years; ECOG PS 0 or 1 for patients aged > 75 years
- ✓ RAS and BRAF status wild-type of primary colorectal cancer or related metastasis, centrally assessed
- ✓ Geriatric assessment by means of G8 screening tool and CRASH score
- ✓ Adequate bone marrow, liver, renal, cardiac functions

9

Primary Endpoint: Progression-free Survival

Median follow up: 20.5 mos (Data Cutoff: 04 Feb 2020)



	Events	Median PFS, mos	95% CI	p*
FOLFOX-pani	72	9.6	8.8-10.9	<0.001
5FU/LV-pani	78	9.1	7.7-9.9	<0.001

*Brookmeyer-Crowley Test

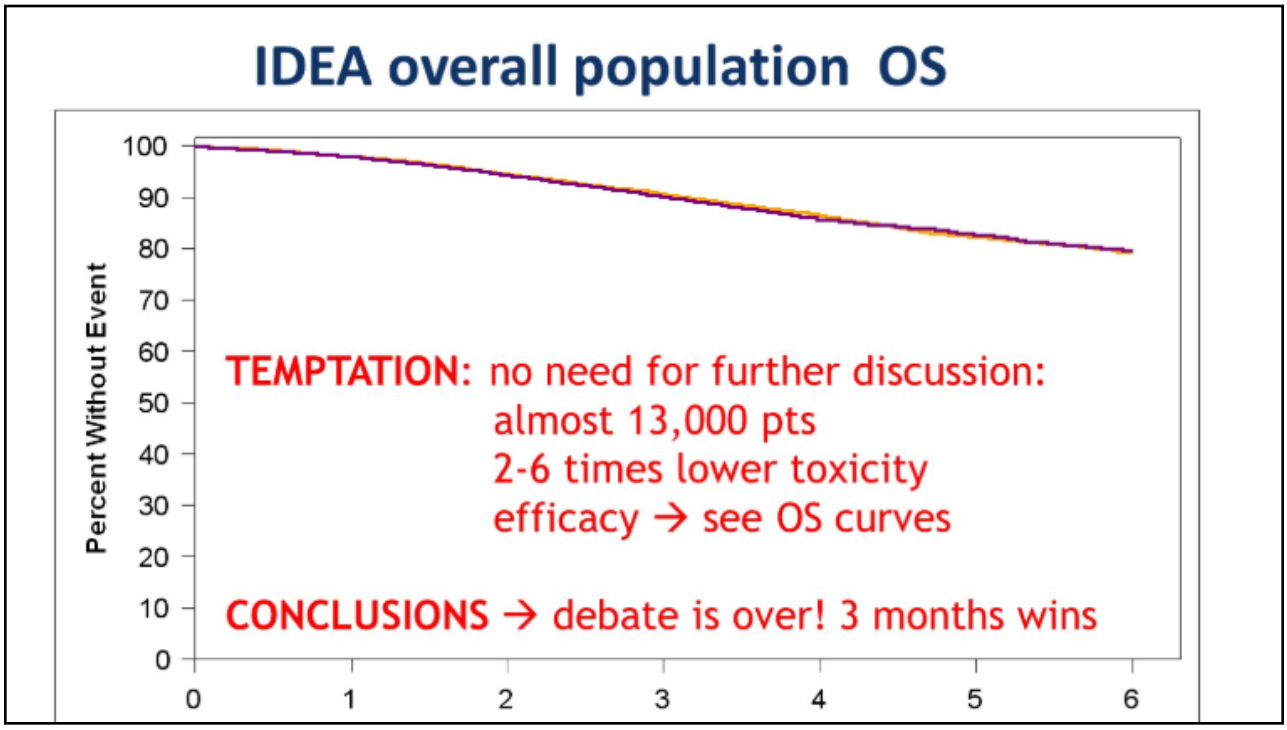
10

Attenuated chemotherapy is appropriate in elderly CRC.

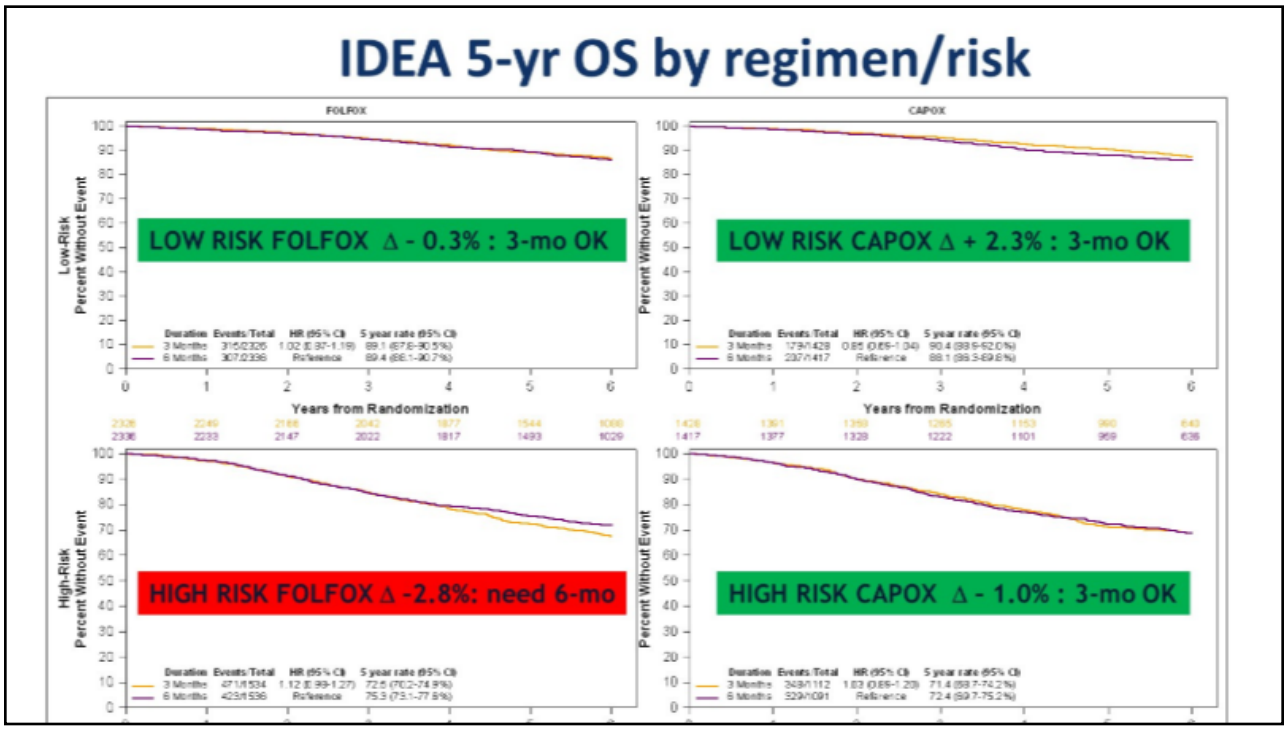
11

Celecoxib did not improve outcomes when added to adjuvant therapy for CRC.

12


IDEA overall population OS
Percent Without Event
100
90
80
70
60
50
40
30
20
10
0
0
1
2
3
4
5
6
TEMPTATION: no need for further discussion:
almost 13,000 pts
2-6 times lower toxicity
efficacy → see OS curves
CONCLUSIONS → debate is over! 3 months wins

13

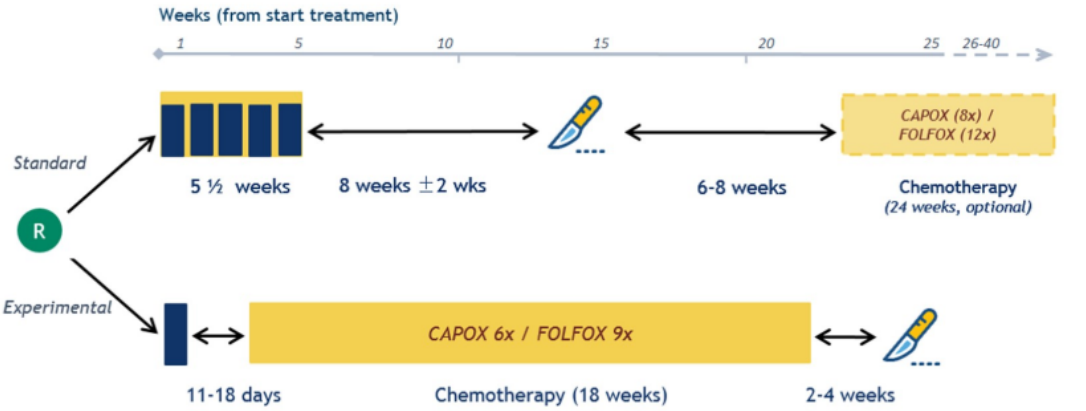

IDEA 5-yr OS by regimen/risk
FOLFOX
CAPOX
Low-Risk
Percent Without Event
High-Risk
Percent Without Event
Years from Randomization
LOW RISK FOLFOX Δ - 0.3% : 3-mo OK
LOW RISK CAPOX Δ + 2.3% : 3-mo OK
HIGH RISK FOLFOX Δ -2.8%: need 6-mo
HIGH RISK CAPOX Δ - 1.0% : 3-mo OK

14

3 m XELOX is the new 6 m FOLFOX.*

15

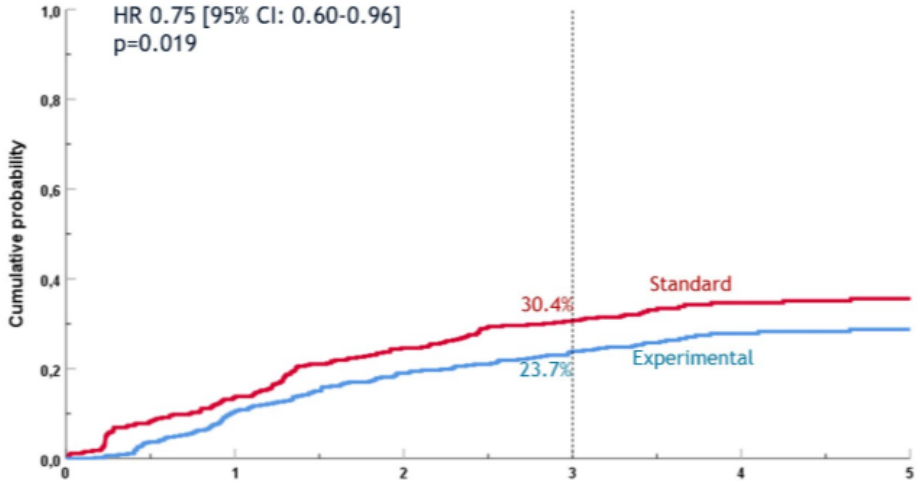
Study design



Standard: week 1-6: 28x1.8 Gy or 25x2 Gy at working days combined with capecitabine b.i.d. 825 mg/m² (twice daily) day 1-33-38.
Experimental: week 1: 5x5 Gy, week 3-20: 6x CAPOX (capecitabine b.i.d.1000 mg/m² (twice daily) day 1-14 every 3 weeks orally, oxaliplatin 130 mg/m² day 1 every 3 weeks iv or alternatively 9x FOLFOX4 (folinic acid, fluorouracil and oxaliplatin all iv every 2 weeks)

16

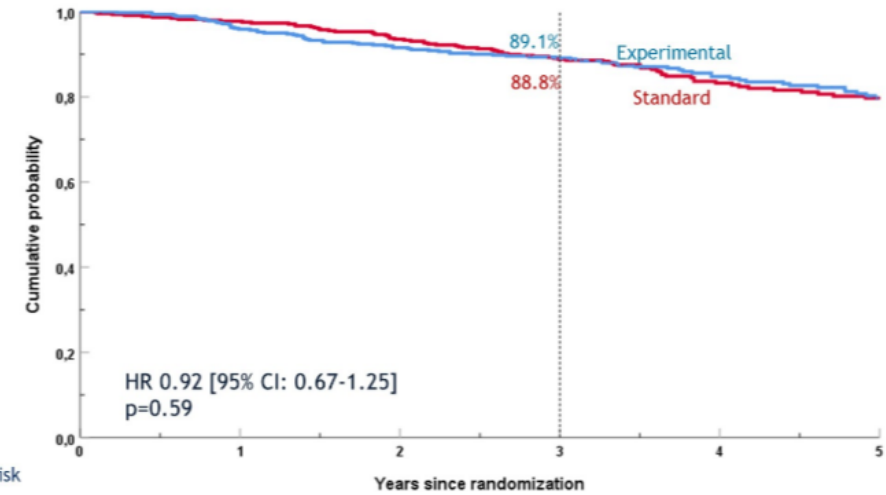
Disease-related Treatment Failure



No. at Risk						
Standard	450	385	334	300	152	127
Experimental	462	410	367	338	168	135

17

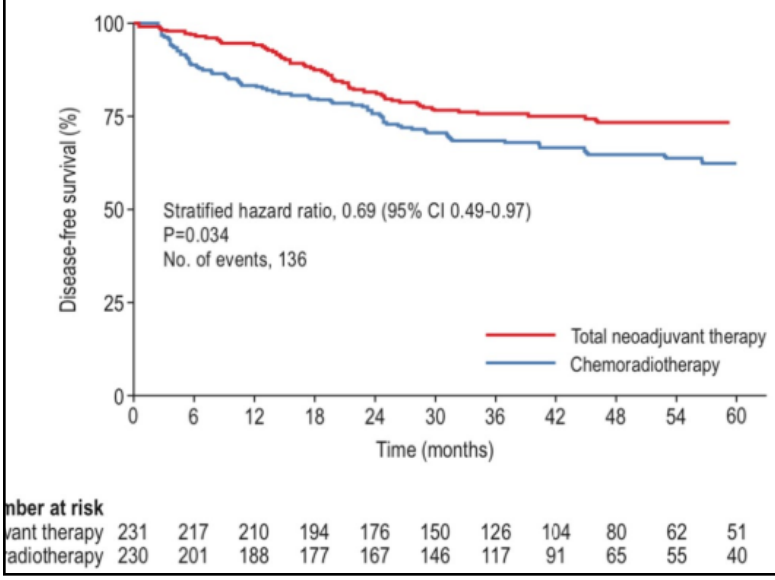
Overall Survival



No. at Risk						
Standard	450	438	418	391	204	163
Experimental	462	442	421	402	205	159

18

Disease-Free Survival



mber at risk

vant therapy	231	217	210	194	176	150	126	104	80	62	51
adiotherapy	230	201	188	177	167	146	117	91	65	55	40

3-yrs DFS rate:

- **75.7% [95%CI: 69.4-80.8] for the TNT group**
- **68.5% [95%CI: 61.9-74.2] for the CRT group**

HR: 0.69; p=0.034

19

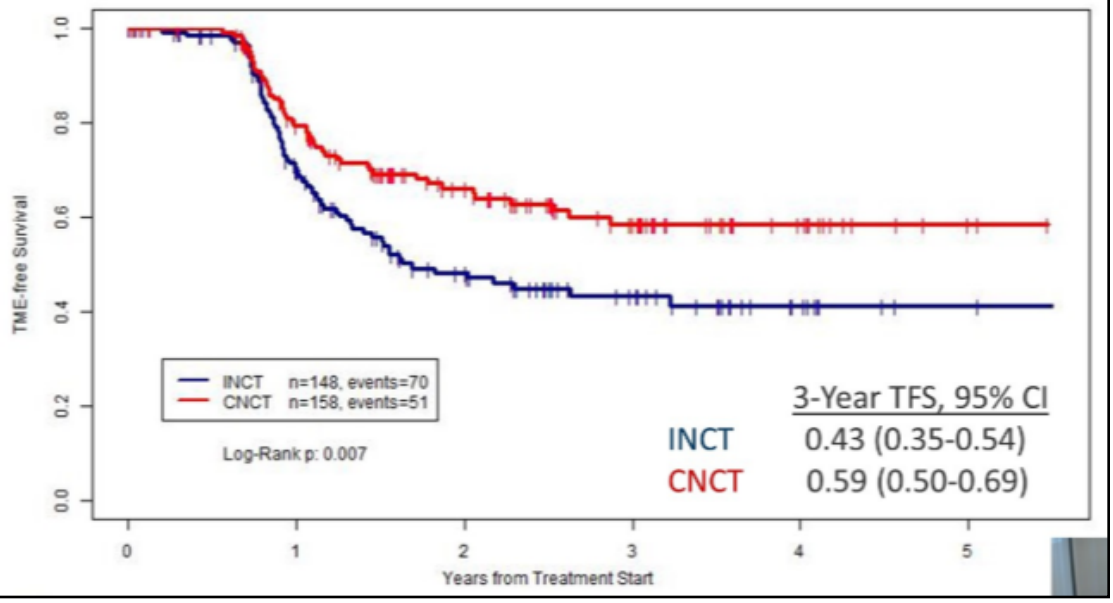
Consider some version of TNT.

20

OPRA

21

Results: TME-Free by Treatment Group

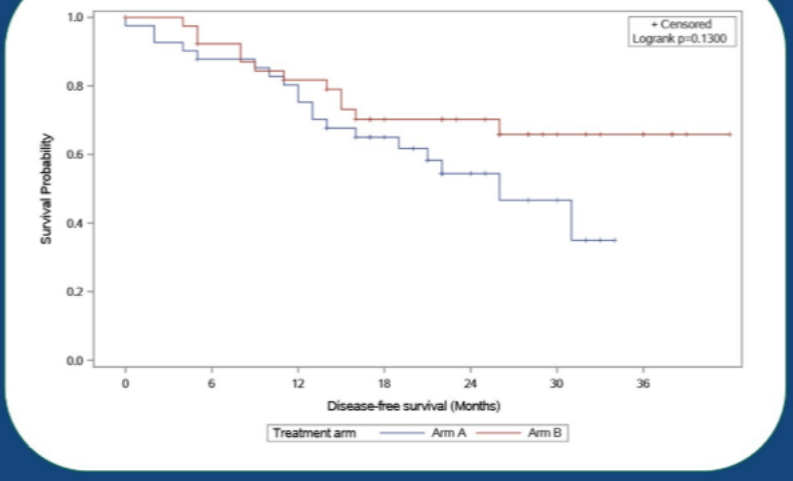


22

Consider W&W, but probably still as part of a trial.

23

Disease-free Survival (DFS)



	FLOT	FLOT / T + P
mDFS *	26 months [13 - n.r.]	not reache

HR (95% CI) for Arm B vs. Arm A: 0.576 (0.278 - 1.139), p = 0.14

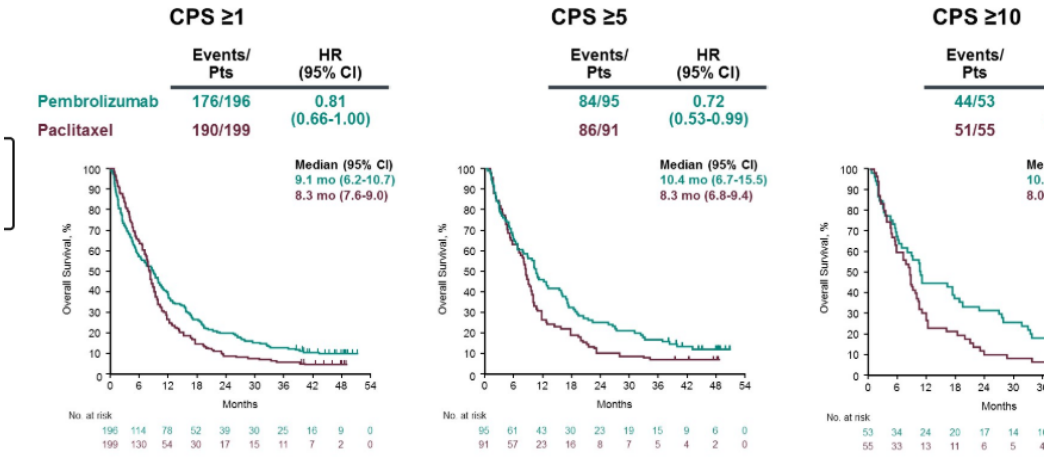
*Median Follow-up 22 months

24

Addition of anti-HER2 therapy to periop FLOT is intriguing.

25

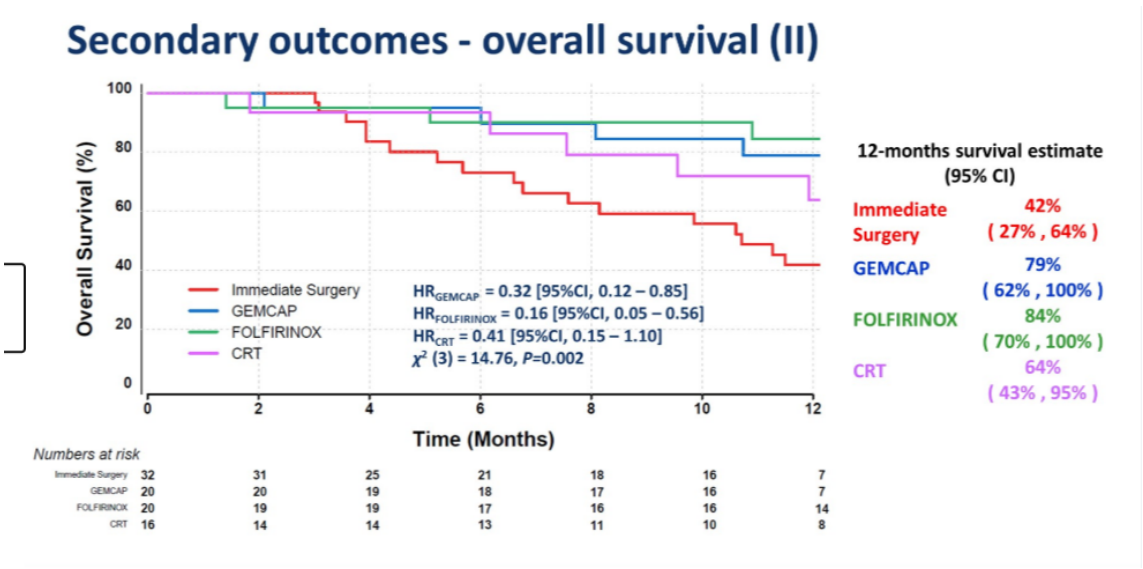
Overall Survival by CPS



26

In PDL-1 + pts, esp if CPS>10, consider immunotherapy in gastric cancer.

27

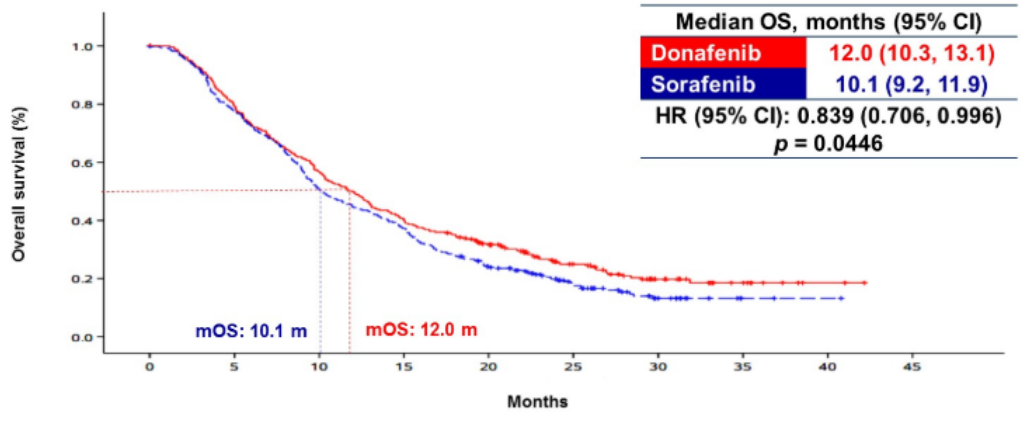


28

Consider periop chemotherapy in PDAC.

29

Donafenib was associated with a significantly longer overall survival than sorafenib (ITT); superiority was also demonstrated



Donafenib	334	264	189	134	95	54	25	10	2	0
Sorafenib	334	259	170	124	75	39	15	2	1	0

CI, confidence interval; FAS, full analysis set; HR, hazard ratio; OS, overall survival

30

A phase II, multicenter, open-label study of trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing metastatic colorectal cancer (mCRC): DESTINY-CRC01.

Authors:
Salvatore Siena, Maria Di Bartolomeo, Kanwal Pratap Singh Raghav, Toshiki Masuishi, Fotios Loupakis, Hisato Kawakami, Kensei Yamaguchi, Tomohiro Nishina, Marwan Fakih, Elena Elez, Javier Rodriguez, Fortunato Ciardiello, Kapil Saxena, Eriko Yamamoto, Emarjola Bako, Yasuyuki Okuda, Javad Shahidi, Axel Grothey, Takayuki Yoshino; Department of Oncology and Hemato-Oncology, Università degli Studi di Milano and Niguarda Cancer Center, Grande Ospedale Metropolitano Niguarda, Milan, Italy; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; MD Anderson Cancer Center, Houston, TX; Aichi Cancer Center Hospital, Aichi, Japan; Oncology Institute Veneto IOV-IRCCS, Padua, Italy; Kindai University Hospital, Osaka, Japan; The Cancer Institute Hospital of JFCR, Tokyo, Japan; National Hospital Organization Shikoku Cancer Center, Matsuyama, Japan; City of Hope Medical Center, Philadelphia, PA; Hospital Universitari Vall d'Hebron, Barcelona, Spain; Department of Medical Oncology, Gastrointestinal Oncology Unit, Clínica Universidad de Navarra, University of Navarra, Navarra, Spain; Università degli studi della Campania L.Vanvitelli, Caserta, Italy; Daiichi Sankyo Inc., Basking Ridge, NJ; Daiichi Sankyo, Co, Ltd, Tokyo, Japan; Daiichi Sankyo, Inc., Basking Ridge, NJ; Daiichi Sankyo, Co., Ltd, Tokyo, Japan; West Cancer Center, Germantown, TN; National Cancer Center Hospital East, Kashiwa, Japan

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Abstract Disclosures

Research Funding:
Daiichi Sankyo Co., Ltd.

Background:
T-DXd is an antibody-drug conjugate composed of an anti-HER2 antibody, cleavable tetrapeptide-based linker, and topoisomerase I inhibitor payload. Early studies have shown promising activity in advanced HER2-expressing tumors. DESTINY-CRC01 (DS8201-A-J203; NCT03384940) is a phase 2, open-label, multicenter study of T-DXd in pts with HER2-expressing mCRC.

Methods:
Pts with centrally confirmed HER2-expressing, *RAS*–wild type mCRC that progressed on ≥ 2 prior regimens received T-DXd 6.4 mg/kg every 3 weeks (q3w) in 3 cohorts (A: HER2 IHC 3+ or IHC 2+/ISH+; B: IHC 2+/ISH−; C: IHC 1+). The primary endpoint was confirmed objective response rate (ORR) by independent central review in cohort A; secondary endpoints included, disease control rate (DCR; CR + PR + SD), duration of response (DOR), progression-free survival (PFS), overall survival (OS), and ORR in cohorts B and C.

Encorafenib plus cetuximab with or without binimetinib for *BRAF* V600E metastatic colorectal cancer: Updated survival results from a randomized, three-arm, phase III study versus choice of either irinotecan or FOLFIRI plus cetuximab (BEACON CRC).

Authors:
Scott Kopetz, Axel Grothey, Eric Van Cutsem, Rona Yaeger, Harpreet Singh Wasan, Takayuki Yoshino, Jayesh Desai, Fortunato Ciardiello, Fotios Loupakis, Yong Sang Hong, Neeltje Steeghs, Tormod Kyrre Guren, Hendrik-Tobias Arkenau, Pilar Garcia-Alfonso, Ashwin Gollerkeri, Kati Maharry, Janna Christy-Bittel, Josep Tabernero; The University of Texas MD Anderson Cancer Center, Houston, TX; West Cancer Center, Germantown, TN; University Hospitals Gasthuisberg Leuven, KU Leuven, Leuven, Belgium; Memorial Sloan Kettering Cancer Center, New York, NY; Hammersmith Hospital, Im College Health Care Trust, London, United Kingdom; National Cancer Center Hospital East, Kashiwa, Japan; Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; University of Campania, Naples, Italy; Istituto Toscano Tumori, Pisa, Italy; Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; Netherlands Cancer Institute, Amsterdam, Netherlands; Department of Oncology, Oslo University Hospital, Oslo, Norway; Sarah Cannon Research Institute UK Limited, London, United Kingdom; Hospital General Universitario Gregorio Marañón, Madrid, Spain; Pfizer Inc, Cambridge, MA; Pfizer Inc., Boulder, CO; Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain

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Abstract Disclosures

Research Funding:
Pfizer Inc.

Background:
BEACON CRC is a randomized, phase 3 study which evaluated the triplet of encorafenib (ENCO) + binimetinib (BINI) + cetuximab (CETUX) and the doublet of ENCO + CETUX vs. investigator's choice of irinotecan + CETUX or FOLFIRI + CETUX in patients (pts) with *BRAF*V600E metastatic colorectal cancer (mCRC) whose disease had progressed after 1-2 prior regimens in the metastatic setting. Primary endpoints were overall survival (OS) and objective response rate (ORR; by blinded central review) for triplet vs control. In a previous interim analysis, triplet and doublet improved OS and ORR versus standard of care. Here we report on an updated analysis.

Methods:
Updated analysis includes 6 months of additional follow-up and response data for all randomized pts. The study is ongoing.

Results:

Pts received triplet (n=224), doublet (n=220), or control (n=221). Median OS was 9.3 months (95% confidence interval [CI]:8.2, 10.8) for triplet and 5.9 months (95% CI:5.1-7.1) for control (hazard ratio [HR] (95% CI): 0.60 (0.47-0.75)). Median OS for doublet was 9.3 months (95% CI: 8.0-11.3) (HR vs. control: 0.61 (0.48-0.77). Confirmed ORR was 26.8% (95% CI: 21.1%-33.1%) for triplet, 19.5% (95% CI: 14.5%-25.4%) for doublet, and 1.8% (95% CI: 0.5%-4.6%) for control. Retrospective subgroup analyses suggested some pts may benefit more from triplet than doublet therapy (Table). Both triplet and doublet showed improved OS compared to control in all subgroups. Adverse events were consistent with prior analysis, with grade ≥3 adverse events in 65.8%, 57.4%, and 64.2% for triplet, doublet and control, respectively.

Conclusions:

The updated analysis of the BEACON CRC study confirmed that encorafenib + cetuximab with or without binimetinib improved OS and ORR in previously treated pts with *BRAF* V600E mCRC compared with standard chemotherapy. Clinical trial information: NCT02928224.

OS in select subgroups, triplet vs. doublet.

		Events/Patients	Triplet vs Doublet Medians (months)	HR (95% CI)*
All Patients		265/444	9.3 vs 9.3	0.95 (0.74-1.21)
CRP	**High**	139/174	6.5 vs 5.1	0.76 (0.54, 1.06)
	Normal	120/261	13.8 vs 14.0	1.09 (0.76, 1.56)
ECOG PS	**1**	153/216	8.1 vs 6.1	0.81 (0.59, 1.11)
	0	112/228	10.4 vs 13.9	1.28 (0.88, 1.86)
No. of organs	**3+**	141/214	8.5 vs 6.7	0.69 (0.49, 0.96)
	<=2	124/230	10.0 vs 12.3	1.34 (0.94, 1.91)
Tumor Status	**Partially/Not Resected**	123/188	8.5 vs 8.3	0.80 (0.56, 1.14)
	Resected	142/256	9.5 vs 12.3	1.20 (0.86, 1.68)

*HR<1 favors triplet; HR>1 favors doublet

First-line FOLFOX plus panitumumab versus 5FU plus panitumumab in RAS-BRAF wild-type metastatic colorectal cancer elderly patients: The PANDA study.

Authors:
Sara Lonardi, Marta Schirripa, Federica Buggin, Lorenzo Antonuzzo, Barbara Merelli, Giorgia Boscolo, Saverio Cinieri, Samantha Di Donato, Riccardo Lobefaro, Roberto Moretto, Vincenzo Formica, Alessandro Passardi, Vincenzo Ricci, Nicoletta Pella, Mario Scartozzi, Fable Zustovich, Vittorina Zagonel, Matteo Fassan, Luca Boni, Fotios Loupakis, Gono Group; Veneto Institute of Oncology (IOV)-IRCCS, Padua, Italy; Department of Oncology, Oncology 1, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy; Medical Oncology, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy; Oncology Unit, ASST Papa Giovanni XXIII, Bergamo, Italy; Medical Specialties Department, Oncology and Oncologic Hemato ULSS 3 Serenissima, Milan, Italy; Department of Oncology, Medical Oncology, "Antonio Perrino" Hospital, Brindisi, Italy; Medical Oncology Department, Nuovo Ospedale-Santo Stefano, Prato, Italy; Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Department of Translational Research and New Technologies in Medicine and Surgery, Unit of Medical Oncology 2, Azienda Ospedaliera Universitaria Pisana, Pisa, Italy; Medical Oncology Unit, Tor Vergata University, Rome, Italy; Department of Medical Oncology, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy; Medical Oncology, A.O. S. Croce and Carle Teaching Hospital, Cuneo, Italy; Department of Oncology - ASUI Udine University Hospital, Udine, Italy; Medical Oncology Department, University Hospital, University of Cagliari, Cagliari, Italy; Medical Oncology Unit, Azienda ULSS 1, Belluno, Italy; Oncologia Medica 1, Istituto Oncologico Veneto IRCCS Padova, Padua, Italy; Department of Medicine (DIMED), Pathology Unit, University of Padua, Padua, Italy; Clinical Trial Coordinating Center, AOU Careggi, Florence, Italy

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Abstract Disclosures

Research Funding:
GONO Group, Pharmaceutical/Biotech Company

Background:
Data on first-line treatment efficacy in elderly patients are limited. Many analyses adopt a questionable cut-off of 65 years and specific evidence with anti-EGFRs is low. FOLFOX-panitumumab (pan) is an option for RAS wild-type (wt) untreated mCRC patients. Guidelines recommend considering fluoropyrimidine monotherapy as an option for elderly patients, but no randomized studies have ever explored the role of the combination with an anti-EGFR.

Methods:
This is a prospective, open-label, multicenter phase II randomized trial. Unresectable and previously untreated *RAS-BRAF* wt mCRC patients aged ≥70 were randomized to receive FOLFOX-pan (arm A), or 5FU/LV-pan (arm B) for up to 12 cycles followed by pan maintenance until PD. The primary EP was PFS in both arms. Stratification criteria were age (≤75 vs > 75 years), ECOG PS (0–1 vs 2) and geriatric assessment with G8 Score (≤14 vs > 14). In each treatment arm, the null

hypothesis for median PFS was set at ≤6 months. Assuming an expected median PFS time ≥9.5 months with both experimental regimens, a sample size of 90 patients in each arm granted to the study a power of 90%, with a type I error rate equal to 5% (1-sided Brookmeyer-Crowley test) for rejecting the null hypothesis. No formal comparison between the two arms was planned.

Results:

From Jul 2016 to Apr 2019 a total of 394 patients were screened, 211 were deemed eligible for inclusion and 185 were randomized (92 arm A and 93 arm B). Main pts' characteristics were (arm A/B): males 66%/61%; median age 77/77y; PS≥1 49%/55%; right colon 23%/21%; G8 > 14 31%/30%. At a median follow up of 20.5 mos, 135 (arm A/B: 64/71) PD events were collected. Median PFS was 9.6 (95% CI 8.8-10.9) in arm A with FOLFOX-pan and 9.1 (95% CI 7.7-9.9) in arm B with 5FU/LV-pan. Response rates were (arm A/B): 65%/57%. Grade 3-4 toxicities were (arm A/B): neutropenia 9.8%/1.1%; diarrhea 16.3%/1.1%; stomatitis 9.8%/4.4%; neurotoxicity 3.3%/0%; fatigue 6.5%/4.4%; skin rash 25%/24.2%, hypomagnesemia 3.3%/7.7%.

Conclusions:

Large prospective randomized studies in molecularly selected elderly mCRC are feasible with multicenter collaborative efforts. Primary EP was met in both treatment arms. 5FU/LV plus panitumumab for up to 12 cycles followed by panitumumab maintenance until PD might be a reasonable option in elderly mCRC patients with RAS/BRAF wt tumors deserving further investigations in phase III trials. Clinical trial information: NCT02904031.

Print

Celecoxib in addition to standard adjuvant therapy with 5-fluorouracil, leucovorin, oxaliplatin (FOLFOX) in stage III colon cancer: Results from CALGB/SWOG 80702.

Authors:
Jeffrey A. Meyerhardt, Qian Shi, Charles S. Fuchs, Donna Niedzwiecki, Tyler J. Zemla, Priya Kumthekar, Katherine A Guthrie, Felix Couture, J. Phillip Kuebler, Johanna C. Bendell, Pankaj Kumar, DeQuincy Andrew Lewis, Benjamin R. Tan, Monica M. Bertagnolli, Axel Grothey, Howard S. Hochster, Richard M. Goldberg, Alan P. Venook, Charles David Blanke, Anthony Frank Shields; Dana-Farber Cancer Institute, Boston, MA; Alliance Statistics and Data Center, Mayo Clinic, Rochester, MN; Yale Cancer Center, Smilow Cancer Hospital, Yale School of Medicine, New Haven, CT; Department of Biostatistics and Bioinformatics, Duke University Medical Center, Durham, NC; Department of Health Sciences Re[Print], Mayo Clinic, Rochester, MN; Northwestern Memorial Hospital, Chicago, IL; Fred Hutchinson Cancer Research Center, and SWOG Statistics and Data Management Center, Seattle, WA; Centre Hospitalier Universitaire de Québec, Quebec City, QC, Canada; Columbus Oncology Associates, Columbus, OH; Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; Illinois CancerCare, Peoria, IL; Randolph Cancer Ctr, Asheboro, NC; Washington University School of Medicine, St. Louis, MO; Dana-Farber Cancer Institute/Brigham and Women's Hospital/Harvard Medical School, Boston, MA; West Cancer Center, Germantown, TN; Rutgers Cancer Institute, New Brunswick, NJ; West Virginia University Cancer Institute, Morgantown, WV; University of California San Francisco, San Francisco, CA; Oregon Health and Science University, Portland, OR; Karmanos Cancer Institute, Wayne State University, Detroit, MI

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Abstract Disclosures

Research Funding:
U.S. National Institutes of Health, Pharmaceutical/Biotech Company

Background:
Aspirin and cyclooxygenase-2 (COX-2) inhibitors have been associated with a reduced risk of colorectal polyps and cancer in observational and randomized studies. CALGB/SWOG 80702 tested the effect of celecoxib, a COX-2 inhibitor, on reducing the risk of recurrence in stage III CC.

Methods:
CALGB/SWOG 80702 is a 2x2 randomized controlled phase III trial of 3 v 6 months of adjuvant FOLFOX (data previously reported as part of the IDEA collaboration) with concurrent celecoxib (400 mg daily) v placebo x 3 yrs for patients (pts) with resected stage III CC. The primary endpoint of the trial is disease-free survival (DFS), defined as time from randomization to recurrence or death from any cause. The trial was designed to provide 91% power to detect a hazard ratio (HR) of 0.79 in favor of celecoxib with 2-sided alpha = 0.05 (775 events required); due to slowing accumulation of events 4 years after complete accrual, power was lowered to 85% with same HR and alpha assumptions (696 events required). The DSMB released data on February 24, 2020 at median f/u of 5.6 yrs with 689 DFS events.

Results:

Between June 2010 and November 2015, 2,526 pts were consented and randomized to the trial. Treatment arms were well balanced by patient and tumor prognostic features, as well as low-dose aspirin use. Baseline characteristics included 45% female, 18% non-White, 8% Hispanic, 15% T4, 26% N2. 3-yr DFS for celecoxib was 76.3% v 73.3% for placebo (HR 0.89 [95% CI 0.77-1.04]; P = 0.14). 5-yr overall survival (OS) was 83.9% for celecoxib v 81.7% for placebo (HR 0.87 [95% CI 0.72-1.05]; P = 0.14). When considering the 4 treatment arms separately, 3-yr DFS was 77.0% for 12 cycles FOLFOX + celecoxib, 74.9% for 12 cycles FOLFOX + placebo, 75.5% for 6 cycles FOLFOX + celecoxib, and 71.9% for 6 cycles FOLFOX + placebo (log rank P = 0.22; P interaction = 0.64). There were no significant differences in grade 3-4 toxicity with celecoxib v placebo. Compliance with protocol celecoxib treatment, defined as 3 yrs of therapy completion or recurrence/death while on treatment, was 58.1% pts on celecoxib and 60.2% pts on placebo.

Conclusions:

The addition of celecoxib to standard chemotherapy did not significantly improve DFS or OS. Clinical trial information: NCT01150045.

Overall survival (OS) and long-term disease-free survival (DFS) of three versus six months of adjuvant (adj) oxaliplatin and fluoropyrimidine-based therapy for patients (pts) with stage III colon cancer (CC): Final results from the IDEA (International Duration Evaluation of Adj chemotherapy) collaboration.

Authors:
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Research Funding:
U.S. National Institutes of Health, Other Government Agency

Background:
In overall population, IDEA pooled analysis did not demonstrate non-inferiority (NI) regarding 3y DFS in pts with stage III CC receiving 3m vs. 6m of adj FOLFOX/CAPOX. However, in pts treated with CAPOX (especially in low-risk pts), 3m of therapy was as effective as 6m. Results of OS and 5y DFS are reported.

Methods:
OS was defined as time from enrollment to death due to all causes. OS NI margin was conservatively set to be Hazard Ratio (HR) = 1.11, which is equivalent to: the maximum acceptable loss of OS efficacy, by shortening treatment to 3m, was half of the OS efficacy gained in MOSAIC trial (i.e., 2.26% absolute reduction in 5y OS rate). Pre-planned sub-group

analyses included by regimen and risk group for both OS and 5y DFS. NI was to be declared if the one-sided false discovery rate adjusted (FDRa) NI p-value < 0.025.

Results:

With an overall median survival follow-up of 72 m (range per study, 62 to 84 m), 2584 deaths and 3777 DFS events among 12,835 pts from six trials were observed. Across 6 studies, 39.5% of pts received CAPOX (rate by study, 0% to 75.1%). Overall, the 5y OS rate was 82.4% (3m) and 82.8% (6m), with estimated OS HR of 1.02 (95% confidence interval [CI], 0.95-1.11; FDRa NI p, 0.058) and absolute 5-y OS rate difference of -0.4% (95% CI, -2.1 to 1.3%). Overall, the 5y DFS rate was 69.1% (3m) and 70.8% (6m), with estimated DFS HR of 1.08 (95%CI, 1.01-1.15, FDRa NI p, 0.22). HRs (95% CI) within subgroups see table.

Conclusions:

5y OS rate reported in IDEA trials was higher than historical rates, regardless of duration of therapy. While overall survival in IDEA did not meet prior statistical assumptions for NI in overall population, the 0.4% difference in 5y OS should be placed in clinical context. OS and 5y DFS results continue to support the use of 3m adjuvant CAPOX for the vast majority of stage III colon cancer pts. This conclusion is strengthened by the substantial reduction of toxicities, inconveniencies and cost associated with shorter treatment duration. Clinical trial information: NCT01150045; 2009-010384-16; NCT00749450; ISRCTN59757862; 2007-003957-10; UMIN000008543; 2007-000354.

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	OS	Long-term DFS
CAPOX	0.96 (0.85, 1.08)	0.98 (0.88, 1.08)
FOLFOX	1.07 (0.97, 1.18)	1.16 (1.06, 1.26)
Low Risk (T1-3 N1)	0.95 (0.84, 1.08)	1.04 (0.94, 1.14)
High Risk (T4 or N2)	1.08 (0.98, 1.19)	1.12 (1.03, 1.22)

Short-course radiotherapy followed by chemotherapy before TME in locally advanced rectal cancer: The randomized RAPIDO trial.

Authors:
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Abstract Disclosures

Research Funding:
Dutch Cancer Foundation, Swedish Cancer Society, Swedish Research Council, Spanish Ministry of Economy and Competitiveness, Spanish Clinical Research Network and European Regional Development Fund.

Background:
Local control in locally advanced rectal cancer (LARC) has improved. However, systemic relapses remain high even with postoperative chemotherapy, possibly due to low compliance. Short-course radiotherapy (SCRT) followed by delayed surgery with, in the waiting period, chemotherapy, may lead to better compliance, downstaging and fewer distant metastases. The main objective of the international multicenter phase III RAPIDO trial is to decrease Disease-related Treatment Failure (DrTF), defined as locoregional failure, distant metastasis, a new primary colon tumor or treatment-related death, by reducing the risk of systemic relapse without compromising local control.

Methods:

MRI-diagnosed LARC patients with either cT4a/b, extramural vascular invasion, cN2, involved mesorectal fascia or enlarged lateral lymph nodes considered to be metastatic were randomly assigned to SCRT (5x5 Gy) with subsequent six cycles of CAPOX or nine cycles of FOLFOX4 followed by total mesorectal excision (TME) (experimental arm) or, capecitabine-based chemoradiotherapy (25-28 x 2.0-1.8 Gy) followed by TME and optional, predefined by hospital policy, postoperative eight cycles of CAPOX or twelve cycles of FOLFOX4 (standard arm).

Results:

Between June 2011 and June 2016, 920 patients were randomized. Pathological complete response rates were 27.7% vs 13.8% (OR 2.40 [1.70 – 3.39]; $p< 0.001$) in the experimental and standard arms, respectively. At three years, cumulative probability of DrTF was 23.7% in the experimental arm and 30.4% in the standard arm (HR 0.76 [0.60 – 0.96]; $p = 0.02$). Probability at three years of distant metastasis and locoregional failure were, in the experimental and standard arms, 19.8% vs 26.6% (HR 0.69 [0.53 – 0.89]; $p = 0.004$) and 8.7% vs 6.0% (HR 1.45 [0.93 – 2.25]; $p = 0.10$), respectively. No differences in DrTF between hospitals with or without policy for postoperative chemotherapy were found (p = 0.37). Overall health ($p = 0.192$), quality of life ($p = 0.125$) and low anterior resection syndrome score ($p = 0.136$) were comparable between the two treatment arms.

Conclusions:

A lower rate of DrTF, as a result of a lower rate of distant metastases, in high-risk LARC patients can be achieved with preoperative short-course radiotherapy, followed by chemotherapy and TME than by conventional chemoradiotherapy. In addition, the high pCR rate, achieved with the experimental treatment regimen can contribute to organ preser. This treatment can be considered as a new standard of care. Clinical trial information: NCT01558921.

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Preliminary results of the organ preservation of rectal adenocarcinoma (OPRA) trial.

Authors:
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Research Funding:
U.S. National Institutes of Health

Background:
Organ preservation (OP) with a watch and wait strategy (WW) and total neoadjuvant therapy (TNT) are new treatment paradigms for patients with locally advanced rectal cancer. The safety and efficacy of WW and of TNT have not been studied prospectively.

Methods:
Patients with MRI stage II and III rectal adenocarcinoma were randomized to 4 months of FOLFOX or CAPEOX before (Induction) or after (Consolidation) fluorouracil or capecitabine based chemoradiotherapy (CRT). Patients were re-staged 8-12 weeks after finishing TNT with digital rectal exam, flexible sigmoidoscopy and MRI. Patients with complete or near-complete clinical response were offered WW. Those with incomplete response had total mesorectal excision. The trial was designed so that each arm served as its own single-stage study that discriminates between 3-year disease-free survival (DFS) rates of 75% (historical null) and 85%, with 86% power, and a two-sided type I error of 5%. Secondary objectives included comparing DFS, OP, and distant metastasis-free survival (DMFS) rates between the two arms using the log-rank test.

Results:
Of 324 patients enrolled, 307 (152 I, 155 C) are currently evaluable for the time-to-event analysis as of 2/1/2020. Median follow-up is 2.1 years; 52 DFS events were observed. Patient demographics and tumor characteristics were generally balanced across the two arms. Full compliance with systemic chemotherapy was 82% and 81% for the I- and C-arms, respectively. The median radiation dose was 5400 cGy for both arms. Table shows 3-y DFS, DMFS, and OP rates.

Conclusions:

A WW strategy for patients with locally advanced rectal cancer that achieve a clinical complete response to TNT results in organ preservation for a high proportion of patients without compromising survival. Up-front CRT followed by consolidation chemotherapy resulted in a numerically higher WW rate compared to induction chemotherapy followed by CRT. Clinical trial information: NCT02008656.

3-year rates with 95% CI.

	Induction		Consolidation		p*
DFS	78%	(70%,87%)	77%	(69%,86%)	0.90
DMFS	81%	(74%,90%)	83%	(76%,91%)	0.86
OP	43%	(35%,54%)	58%	(49%,69%)	0.01

*log-rank test

Perioperative trastuzumab and pertuzumab in combination with FLOT versus FLOT alone for HER2-positive resectable esophagogastric adenocarcinoma: Final results of the PETRARCA multicenter randomized phase II trial of the AIO.

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Abstract Disclosures

Research Funding:
Roche

Background:
Perioperative FLOT is a standard of care for resectable, esophagogastric adenocarcinoma (EGA). This trial evaluates the addition of trastuzumab (tras) and pertuzumab (per) to FLOT for HER2-positive resectable patients (pts).

Methods:

PETRARCA is a prospective, multicenter, randomized, investigator initiated trial planned as a phase II/III investigation. We report the phase II part of this trial. Pts with HER2+ resectable EGA (≥ cT2 or cN+) were enrolled. Pts were randomized 1:1 to 4 pre- and post-operative cycles of FLOT (Docetaxel 50 mg/m²; Oxaliplatin 85 mg/m²; Leucovorin 200 mg/m²; 5-FU 2600 mg/m², q2w) (Arm A) or the same regimen with tras 8/6 mg/kg and per 840 mg q3w, followed by 9 cycles tras/per (arm B). Primary endpoint for the phase II part was the rate of pathological complete remission (pCR). Main secondary endpoints were DFS, OS and safety.

Results:

The trial closed prematurely and did not proceed to phase III. In total, 81 pts were randomized (A, 41; B, 40). Baseline characteristics were balanced (overall, male 79%; median age 60; cT3/T4 86%; cN+ 85%; GEJ 75%). 93% in arm A and 90% in arm B completed pre-OP treatment as planned. More pts had at least one dose modification in arm B (A, 44%; B, 70%). The pCR rate was significantly improved with tras/per (A, 12%; B, 35%; p = 0.02). Likewise, the rate of pathological lymph node negativity was higher with tras/per (A, 39%; B, 68%). R0-resection rate (A, 90%; B, 93%) and surgical morbidity (A: 43%; B, 44%) were comparable. Moreover, in-house mortality was equal in both arms (overall 2.5%). Median DFS was 26 months in arm A and not yet reached in arm B (HR 0.58, p = 0.14). After a median follow-up of 22 months median OS was not yet reached. DFS and OS rates [with 95% CI] at 24 months were 54% [38-71%] and 77% [63-90%] in arm A and 70% [55-85%] and 84% [72-96%] in arm B, respectively. In terms of toxicity more ≥ grade 3 adverse events were reported with tras/per (75% vs. 85%), especially diarrhea (5% vs. 41%) and leukopenia (13% vs 23%).

Conclusions:

The addition of tras/per to perioperative FLOT significantly improved pCR and nodal negativity rates in pts with Her2+ resectable esophagogastric adenocarcinoma at the price of higher rates of diarrhea and leukopenia. Clinical trial information: NCT02581462.

Pembrolizumab versus paclitaxel for previously treated patients with PD-L1–positive advanced gastric or gastroesophageal junction cancer (GC): Update from the phase III KEYNOTE-061 trial.

Authors:
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Abstract Disclosures

Research Funding:
Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA

Background:
KEYNOTE-061 (NCT02370498) is a global phase 3 study of pembrolizumab vs paclitaxel as second-line therapy for GC. At the time of primary analysis (data cutoff: Oct 26, 2017), in patients with PD-L1–positive status (combined positive score [CPS] ≥1), pembrolizumab did not significantly prolong overall survival (OS) vs paclitaxel (9.1 months vs 8.3 months) but did elicit a longer duration of response (DOR) and a favorable safety profile vs paclitaxel. We present results of KEYNOTE-061 in patients with CPS ≥1, ≥5, and ≥10 after 2 additional years of follow-up (cutoff: Oct 7, 2019).

Methods:
Adult patients with GC that progressed after platinum + fluoropyrimidine chemotherapy were randomly assigned 1:1 to pembrolizumab 200 mg Q3W for up to 35 cycles (~2 y) or standard-dose paclitaxel. OS and progression-free survival (PFS) in the CPS ≥1 population were the primary end points. Comparisons were made using stratified log-rank tests.

Results:

At the time of this analysis, 366/395 patients with CPS ≥1 had died (92.6%). Pembrolizumab prolonged OS vs paclitaxel in PD-L1–positive patients (Table). No significant differences appeared between groups in PFS (Table). Objective response rate (ORR) was higher for pembrolizumab in the CPS ≥10 group, and DOR was longer with pembrolizumab using all CPS cutoffs (Table). There were fewer drug-related adverse events (AEs) with pembrolizumab than paclitaxel in the overall population (53% vs 84%).

Conclusions:

This long-term analysis found that second-line pembrolizumab prolonged OS among patients with PD-L1–positive GC and led to fewer drug-related AEs vs paclitaxel. Clinical trial information: NCT02370498.

Efficacy Outcomes.

	Pembrolizumab CPS ≥1 n = 196	Paclitaxel CPS ≥1 n = 199	Pembrolizumab CPS ≥5 n = 95	Paclitaxel CPS ≥5 n = 91	Pembrolizumab CPS ≥10 n = 53	Paclitaxel CPS ≥10 n = 55
OS, deaths, n (%)	176 (89.8)	190 (95.5)	84 (88.4)	86 (94.5)	44 (83.0)	51 (92.7)
OS, months, median (95% CI)	9.1 (6.2-10.7)	8.3 (7.6-9.0)	10.4 (6.7-15.5)	8.3 (6.8-9.4)	10.4 (5.9-18.3)	8.0 (5.1-9.9)
HR (95% CI)	0.81 (0.66-1.00)	—	0.72 (0.53-0.99)	—	0.69 (0.46-1.05)	
P	0.03	—	0.02	—	0.04	—
PFS, months, median (95% CI)	1.5 (1.4-2.0)	4.1 (3.2-4.3)	1.6 (1.4-2.8)	4.0 (2.8-4.4)	2.7 (1.4-4.3)	4.0 (2.7-4.4)
HR (95% CI)	1.25 (1.02-1.54)	—	0.98 (0.71-1.34)	—	0.79 (0.51-1.21)	—
ORR, % (n)	16.3 (32)	13.6 (27)	20.0 (19)	14.3 (13)	24.5 (13)	9.1 (5)
DOR, months, (range)	19.1 (1.4+ to 47.1+)	5.2 (1.3+ to 16.8)	32.7 (4.1 to 47.1+)	4.8 (1.3+ to 15.3)	NR (4.1 to 47.1+)	6.9 (2.6 to 6.9)

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SWOG S1505: Results of perioperative chemotherapy (peri-op CTx) with mfolfirinox versus gemcitabine/nab-paclitaxel (Gem/nabP) for resectable pancreatic ductal adenocarcinoma (PDA).

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Abstract Disclosures

Research Funding:
U.S. National Institutes of Health

Background:
Clinical outcomes after curative treatment of resectable PDA remain suboptimal. To assess the potential of early control of systemic disease with multiagent peri-op CTx, we conducted a prospective trial in the National Clinical Trials Network.

Methods:
S1505 was a randomized phase II trial of peri-op CTx (12 weeks pre-, 12 weeks post-op) with either mFOLFIRINOX (Arm 1) or Gem/nabP (Arm 2). Eligibility required confirmed tissue diagnosis of PDA, ECOG PS 0 or 1, and resectable disease per Intergroup criteria. Primary outcome was 2-year overall survival (OS), using a "pick the winner" design; for 100 eligible patients (pts), accrual up to 150 pts was planned to account for cases deemed ineligible at central radiology review. We previously presented data on eligibility (ASCO 2019 abstr 4137). Here we present the final efficacy and toxicity results for the eligible pts.

Results:
From 2015 to 2018, 147 pts were enrolled; there were 102 eligible pts; 55 in Arm 1; 47 in Arm 2. For Arms 1 and 2 respectively: median age, 66 (44-76) and 64 (46-76) years; males, 36 (65%) and 24 (51%); and ECOG PS 0, 34 (62%) and 31 (66%) pts. Treatment details are shown in Table. For Arm 1 and Arm 2, respectively: Two-year OS was 41.6% and

48.8%; median OS was 22.4 months and 23.6 months. Neither arm's 2-year OS estimate was statistically significantly higher than the *a priori* threshold of 40% (p=0.42 in Arm 1 and p=0.12 in Arm 2). Median disease-free survival (DFS) after resection was 10.9 months in Arm 1 and 14.2 months in Arm 2 (p=0.87).

Conclusions:

We have demonstrated: 1) two-year OS of 41.6% (median 22.4 months) with mFOLFIRINOX and 48.8% (median 23.6 months) with Gem/nabP for all eligible pts starting treatment for resectable PDA; 2) post-resection DFS of 10.9 months and 14.2 months, respectively; 3) adequate safety and high resectability rates with peri-op CTx; 4) little evidence that either regimen improves OS compared with the historical standard. Clinical trial information: NCT02562716.

Outcomes by Treatment Arm for Eligible Patients (N=102).

	Arm 1 (mFOLFIRINOX; N=55)	Arm 2 (Gem/nabP; N=47)
Started pre-op CTx	53 (96%)	45 (96%)
Completed pre-op CTx	46 (84%)	40 (85%)
Surgical resection	40 (73%)	33 (70%)
Complete or major pathologic response*	10 (25%)	14 (42%)
Started post-op CTx	33 (60%)	28 (60%)
Completed all treatment	27 (49%)	19 (40%)
Diarrhea^	15%	7%
Neutropenia^	19%	38%
Peripheral neuropathy^	9%	7%

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*Denominator is those who underwent resection (40 and 33 for Arm 1 and 2, resepectively). ^Only grade 3 or higher

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B.A. Brigham Young University, *Magna Cum Laude* (American Studies; 2005**).**

M.D. University of Pennsylvania (now Perelman) School of Medicine **(**2009**).**

Post-graduate Training

Internal Medicine Residency: Stanford University (2009-2012)

Chief Resident: Stanford University (2012-2013)

Hematology/Oncology Fellowship: Stanford University (2013-2016)

Academic awards

- **National Merit Scholar** 1999
- **BYU Heritage Scholar** (four year full-tuition scholarship) 1999-2005
- **BYU invited convocation speaker** 2005
- **Penn FOCUS fellowship** research grant recipient 2008
- **Stanford Rathmann Medical Education Fellowship** 2017
- **Stanford Department of Medicine Teaching Award** 2018
- **ASCO Education Scholar** 2019

Leadership Roles

- **Stanford Internal Medicine Chief Resident:** Helped lead all aspects of the Stanford internal medicine residency program. 2012-2013
- **Stanford Oncology Inpatient Service Director:** I supervise educational initiatives on that service and administer matters between the inpatient oncology service, the hospital, and the internal medicine training program. 2016-present

- **Senior Associate Program Director, Stanford Oncology Fellowship Program:** I help lead all aspects of the Stanford oncology fellowship program. I have re-built the oncology training curriculum nearly from scratch. I have designed and brought into being a "boot camp" for new fellows. 2017-present
- **Editor-in-Chief, HemOncReview.com**: I have helped create from inception to publication one of the internet's largest hematology/oncology question banks.
- **Board of Directors for Association of Northern California Oncologists (ANCO):** My contributions to the board have included re-orienting the association's mission to better align our activities with our distinct regional footprint. In particular, I spear-headed the creation of both a regional oncology job board and the design of a regional trial aggregator that will eventually allow patients and doctors in Northern California to search trials at all interested sites. 2017-present

Medical Education Experience

- **Supervising Resident (2010-2012):** I was widely recognized for excellence in teaching and clinical care and was invited to serve as chief resident largely as a result of these efforts. 2010-2012
- **Morning Report (2012-2013)**: As a chief resident, I taught morning reports 2-4 times per week over the course of one academic year. Consistently received exceptional feedback. 2012-2013
- **Internal Medicine Intern Communication Skills Curriculum (2013-2014):** Designed and implemented a randomized, controlled, cross-over trial to test the impact of a novel curriculum meant to enhance communication skills of internal medicine interns. Results were not statistically significant. 2013-2014
- **E4C full faculty member (2017-present):** E4C faculty members teach most aspects of the medical curriculum at Stanford. I began teaching as an "associate" as a senior fellow and now receive 0.25 FTE as a "full-time" faculty member. As such, I mentor 5 medical students per year, participating in virtually every clinical aspect of their training as well as serving as a sounding board for their concerns and problems. 2015-present

Results:

At data cutoff (Aug 9, 2019), 78 pts (A, 53; B, 7; C, 18) had received T-DXd. Median age was 58.5 y (range, 27-79 y), 52.6% of pts were male, and 89.7% had left colon or rectum cancer; median number of prior regimens was 4 (range, 2-11); all pts had prior irinotecan. Median treatment duration was 3.5 mo (95% CI, 2.1-4.3 mo; cohort A, 4.8 mo [95% CI, 3.9-5.8 mo]); 38.5% of pts remained on T-DXd treatment. The confirmed ORR was 45.3% (24/53 pts; 95% CI, 31.6%-59.6%) in cohort A, including 1 CR and 23 PRs; median DOR was not reached (95% CI, 4.2 mo-NE). The ORR in pts with prior anti-HER2 treatment was 43.8% (7/16 pts; 95% CI, 19.8%-70.1%). The DCR was 83.0% (44/53 pts; 95% CI, 70.2%-91.9%); median PFS was 6.9 mo (95% CI, 4.1 mo-NE); median OS was not reached. No responses were observed in cohorts B or C. Grade ≥ 3 treatment-emergent adverse events (TEAEs) occurred in 61.5% of pts (48/78); the most common (≥10%) were decreased neutrophil count (21.8%) and anemia (14.1%). Seven pts (9.0%) had TEAEs leading to drug discontinuation. Five pts (6.4%) had interstitial lung disease (ILD) adjudicated by an independent committee as related to T-DXd (2 grade 2; 1 grade 3; 2 grade 5 [the only drug-related deaths]).

Conclusions:

Overall, T-DXd 6.4 mg/kg q3w demonstrated remarkable activity in pts with HER2-expressing mCRC refractory to standard therapies, with a safety profile consistent with previous results. ILD is an important risk and requires careful recognition and intervention. Clinical trial information: NCT03384940.

Print

ASCO HIGHLIGHTS 2020: HEAD AND NECK CANCER

Jonathan Riess, MD
University of California, Davis

Presentation
Abstracts
Abbreviated Bio/CV

ASCO 2020 Virtual Highlights: Head and Neck Cancer

Jonathan W. Riess, M.D. M.S.
Associate Professor of Medicine
University of California Davis School of Medicine
UC Davis Comprehensive Cancer Center

UCDAVIS COMPREHENSIVE CANCER CENTER

NCI CCC
A Comprehensive Cancer Center Designated by the National Cancer Institute

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Disclosures

Honoraria/Consulting: Novartis, Blueprint Medicine, Medtronic, Boehringer Ingelheim

Research Funding (To Institution): Merck, Novartis, Spectrum, AstraZeneca, Revolution Medicines

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Abstracts for Discussion

- Abstract 6502: Phase II/III trial of post-operative chemoradiotherapy comparing 3-weekly cisplatin with weekly cisplatin in high-risk patients with squamous cell carcinoma of head and neck (JCOG1008). Dr. Kiyota et al.
- Abstract 6505: KEYNOTE-048: Progression after the next line of therapy following pembrolizumab (P) or P plus chemotherapy (P+C) vs EXTREME (E) as first-line (1L) therapy for recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). Dr. Harrington et al.
- Abstract 6503: Randomized phase II study of axitinib versus observation in patients with recurred or metastatic adenoid cystic carcinoma. Dr. Keam et al.

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JCOG
Japan Clinical Oncology Group

Phase II/III Trial of Post-operative Chemoradiotherapy Comparing 3-Weekly Cisplatin with Weekly Cisplatin in High-risk Patients with Squamous Cell Carcinoma of the Head and Neck (JCOG1008)

Naomi Kiyota, Makoto Tahara, Hirofumi Fujii, Tomoko Yamazaki, Hiroki Mitani, Shigemichi Iwae, Yasushi Fujimoto, Yusuke Onozawa, Nobuhiro Hanai, Takenori Ogawa, Hiroki Hara, Nobuya Monden, Eiji Shimura, Shujiro Minami, Takashi Fujii, Kaoru Tanaka, Takeshi Kodaira, Junki Mizusawa, Kenichi Nakamura, Ryuichi Hayashi

Head and Neck Cancer Study Group of the Japan Clinical Oncology Group (JCOG-HNCSG)

Japan Registry of Clinical Trials Registry Number: jRCTs031180135

PRESENTED BY: Naomi Kiyota, MD, PhD, Kobe University Hospital, Japan, E-mail: nkiyota@med.kobe-u.ac.jp

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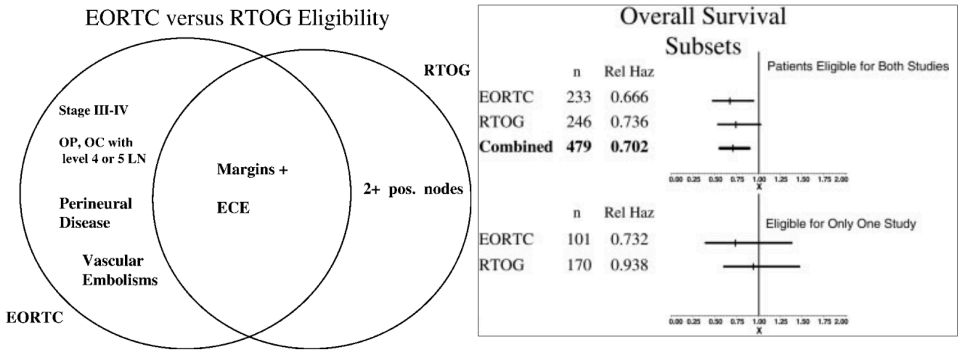
EORTC 22931 / RTOG 9501 Combined Analysis
Bernier et al., Head Neck 2005



Cisplatin 100 mg/m2 q3weeks x 3 + 66 Gy RT. 40% do not get 3rd cycle and toxic.

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- Standard cisplatin 100 mg/m2 q3weeks x 3
- Tata Memorial Hospital Study – weekly cisplatin + RT at 30 mg/m2 plus RT failed to confirm non-inferiority Majority oral cavity tumors (87.3%).
- Primary endpoint: 2-year locoregional control (53.5% vs. 73.1% (HR 1.76 (95% CI 1.11-2.79). Worse survival outcomes though better tolerability.
- Major weakness: Standard weekly cisplatin dose is 40 mg/m2

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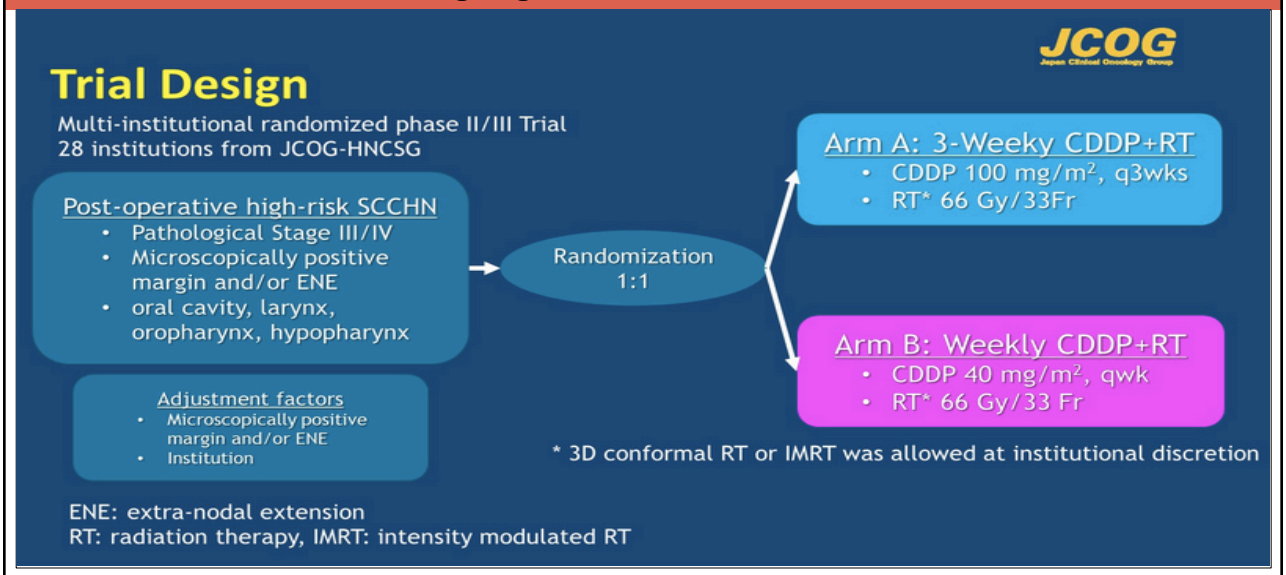

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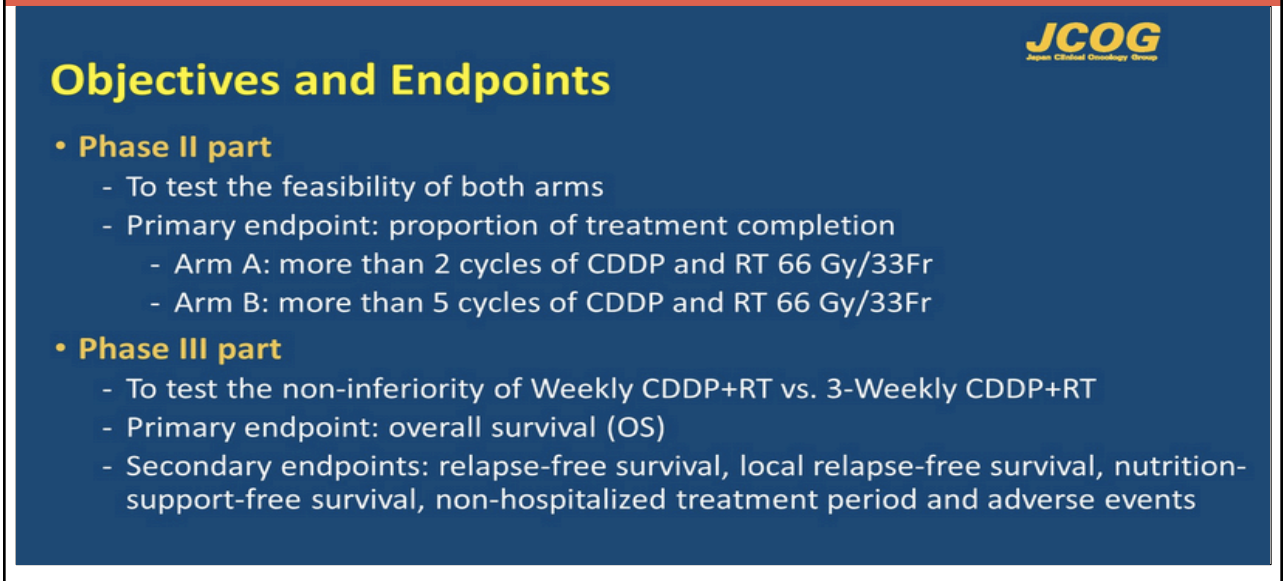

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Key Eligibility Criteria

JCOG Japan Clinical Oncology Group

1. Histologically proven squamous cell carcinoma
2. Primary site: oral cavity, larynx, oropharynx and hypopharynx
3. Pathological Stage III, IVA or IVB (UICC 7th edition)
4. High-risk factors for recurrence
   microscopic positive margin and/or extra-nodal extension
5. Within 56 days from curative surgery
6. Age 20 – 75 years
7. ECOG PS 0-1
8. No prior chemotherapy, radiation therapy, and hormone therapy
9. Written informed consent

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Interim Analyses

JCOG Japan Clinical Oncology Group

- **Phase II part: 1st interim analysis**
  - DSMC allowed to continue Phase III part because of confirmation of feasibility of both arms on 7/Sep/2015
- **Phase III part: 1st and 2nd interim analyses**
  - 1st interim analysis was planned when half of the sample size was registered
    - DSMC allowed further enrollment on 18/Mar/2017
  - 2nd interim analysis was planned after accrual completion
    - DSMC recommended terminating the trial early and publishing the results because the statistical boundary for non-inferiority of OS had met the pre-specified stopping criteria on 14/Dec/2019

DSMC: Data and Safety Monitoring Committee

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Statistical Considerations

- **Phase II part**
  - Proportion of treatment completion in both arms
  - H_0: 50%, H_A: 80%
  - One-sided alpha of 0.025 and power of 0.9 in each arm
  - Target sample size: 33 patients in each, total 66 patients
- **Phase III part**
  - Assumed 5y OS: Arm A 49%, Arm B 52%
  - Non-inferiority margin 10% (correspond to hazard ratio (HR) of 1.32)
  - One-sided alpha of 0.05 and power of 0.75
  - Target sample size of 260 patients in 5 years

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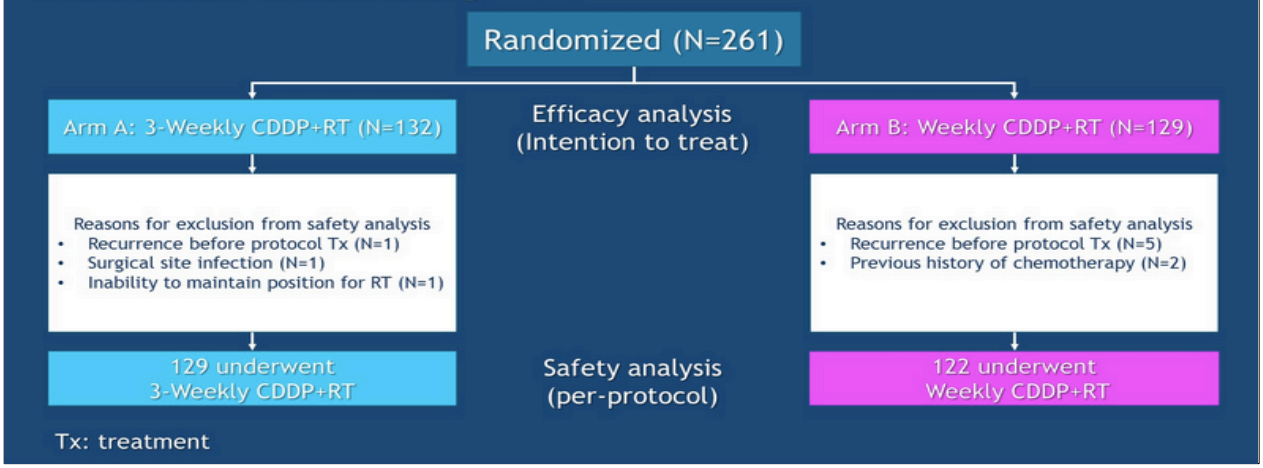
CONSORT Flow Diagram



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Patient Characteristics (1)

JCOG Japan Clinical Oncology Group

Characteristic		Arm A: 3-Weekly CDDP+RT (N=132)	Arm B: Weekly CDDP+RT (N=129)
Age	Median (range)	62 (26-75)	61 (20-75)
Sex	Female	22	19
	Male	110	110
ECOG-PS	0	92	94
	1	40	35
Primary site	Oral cavity	61	60
	Larynx	12	11
	Oropharynx	14	21
	Hypopharynx	45	37

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Patient Characteristics (2)

JCOG Japan Clinical Oncology Group

Characteristic		Arm A: 3-Weekly CDDP+RT (N=132)	Arm B: Weekly CDDP+RT (N=129)
High-risk factors*	Positive margin	43	42
	Extra-nodal extension	112	109
Pathological T	T1	13	7
	T2	26	40
	T3	25	23
	T4	68	59
Pathological N	N0	9	6
	N1	10	15
	N2	107	104
	N3	5	2
	Nx	1	2

*overlapped

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Treatment Delivery and Compliance

JCOG Japan Clinical Oncology Group

Parameter		Arm A: 3-Weekly CDDP+RT (N=132)	Arm B: Weekly CDDP+RT (N=129)
Total RT dose (Gy)	Median (IQR)	66 (66-66)	66 (66-66)
Duration of RT (days)	Median (IQR)	49 (47-51)	49 (46-50)
Interval from surgery to RT initiation (days)	Median (IQR)	49 (42-56)	50 (43-56)
Cycles of CDDP	Median (IQR)	3 (3-3)	6 (5-7)
Cumulative dose of CDDP (mg/m^2)	Median (IQR)	280 (250-299)	239 (199-277)

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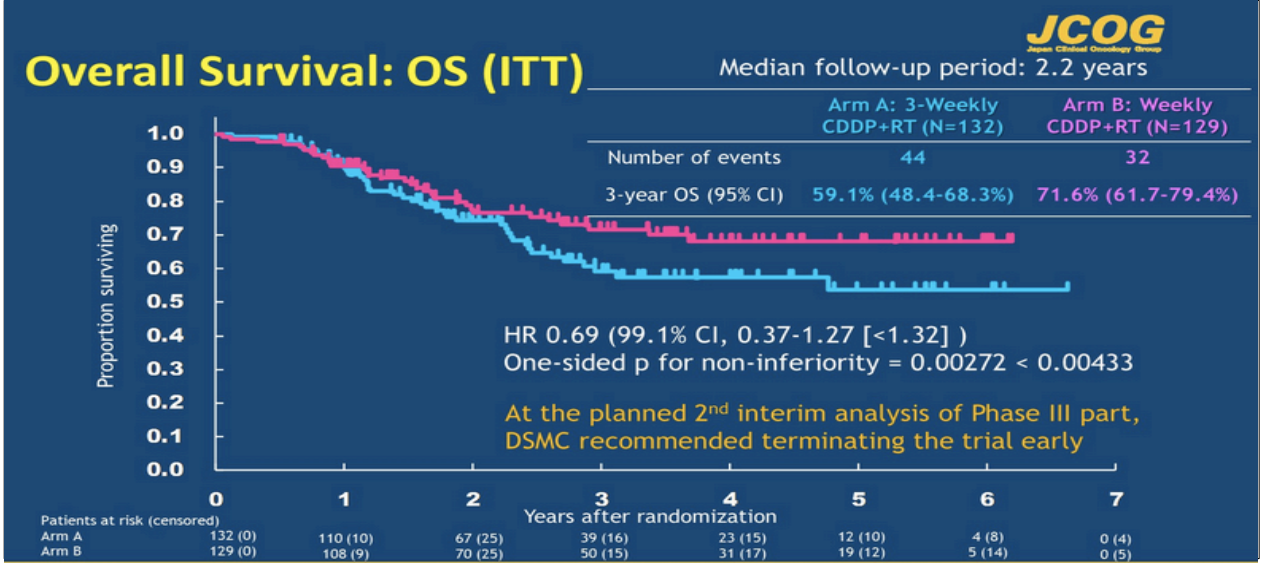
Overall Survival: OS (ITT)

JCOG Japan Clinical Oncology Group

Median follow-up period: 2.2 years



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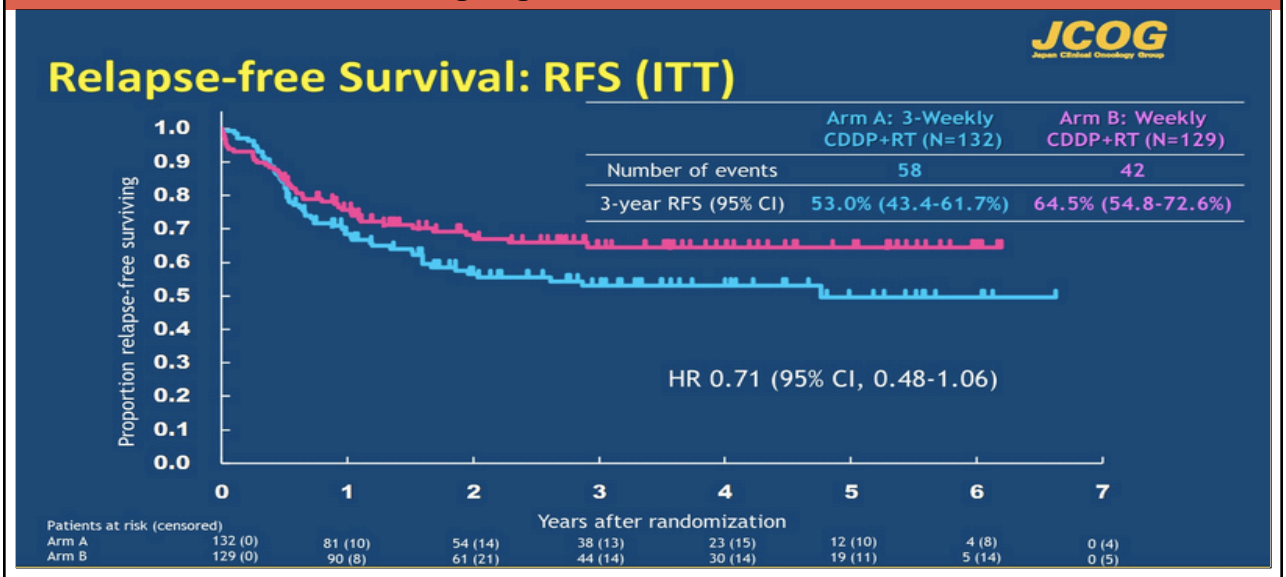

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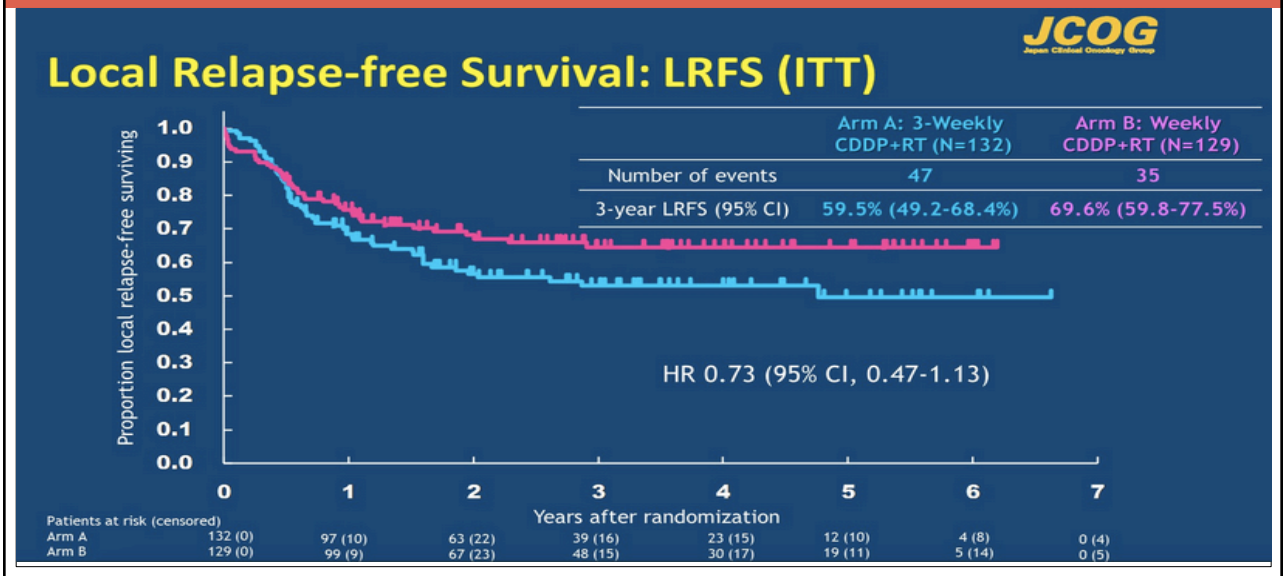

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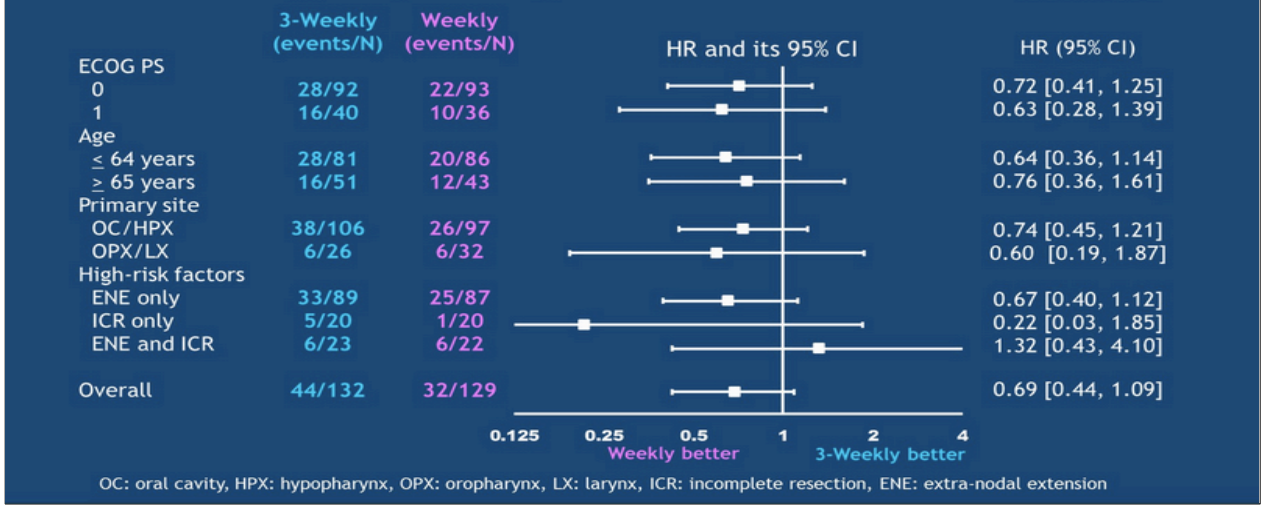
Planned Subgroup Analysis for OS

JCOG



OC: oral cavity, HPX: hypopharynx, OPX: oropharynx, LX: larynx, ICR: incomplete resection, ENE: extra-nodal extension

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JCOG

Acute Hematological Toxicities

Hematological	Arm A: 3-Weekly CDDP+RT (N=129)		Arm B: Weekly CDDP+RT (N=122)	
	Any grade	Grade 3-4 (%)	Any grade	Grade 3-4
Total	129 (100%)	79 (61.2%)	122 (100%)	79 (64.8%)
Leukopenia	123 (95.3%)	71 (55.0%)	114 (93.4%)	75 (61.5%)
Neutropenia	118 (91.5%)	63 (48.8%)	106 (86.9%)	43 (35.3%)
Anemia	129 (100%)	18 (14.0%)	122 (100%)	16 (13.1%)
Thrombocytopenia	85 (65.9%)	3 (2.3%)	102 (83.6%)	4 (3.3%)
Febrile neutropenia	7 (5.4%)	7 (5.4%)	5 (4.1%)	5 (4.1%)

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Acute Hematological Toxicities

JCOG Japan Clinical Oncology Group

Hematological	Arm A: 3-Weekly CDDP+RT (N=129)		Arm B: Weekly CDDP+RT (N=122)	
	Any grade	Grade 3-4 (%)	Any grade	Grade 3-4
Total	129 (100%)	79 (61.2%)	122 (100%)	79 (64.8%)
Leukopenia	123 (95.3%)	71 (55.0%)	114 (93.4%)	75 (61.5%)
Neutropenia	118 (91.5%)	63 (48.8%)	106 (86.9%)	43 (35.3%)
Anemia	129 (100%)	18 (14.0%)	122 (100%)	16 (13.1%)
Thrombocytopenia	85 (65.9%)	3 (2.3%)	102 (83.6%)	4 (3.3%)
Febrile neutropenia	7 (5.4%)	7 (5.4%)	5 (4.1%)	5 (4.1%)

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Acute Non-hematological Toxicities*

JCOG Japan Clinical Oncology Group

Non-hematological	Arm A: 3-Weekly CDDP+RT (N=129)		Arm B: Weekly CDDP+RT (N=122)	
	Any grade	Grade3-4(%)	Any grade	Grade3-4
Mucositis	118 (91.5%)	30 (23.3%)	113 (92.6%)	34 (27.9%)
Dysphagia	75 (58.1%)	24 (18.6%)	59 (48.4%)	14 (11.5%)
Dermatitis	118 (91.4%)	19 (14.7%)	112 (91.8%)	14 (11.5%)
Nausea	87 (67.4%)	17 (13.2%)	57 (46.7%)	6 (4.9%)
Infection	25 (19.4%)	15 (11.6%)	18 (14.8%)	8 (6.6%)
Hyponatremia	119 (92.2%)	13 (10.1%)	100 (82.0%)	13 (10.7%)
Renal impairment	51 (39.5%)	0 (0%)	36 (29.5%)	0 (0.0%)
Hearing impairment	22 (17.1%)	5 (3.9%)	9 (7.4%)	2 (1.6%)
Peripheral neuropathy	7 (5.4%)	0 (0.0%)	2 (1.6%)	0 (0.0%)

- *Grade 3 or more toxicities which occurred in ≥10% patients or toxicities of special interest

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Summary

- Phase II/III study of Weekly CDDP+RT vs. 3-Weekly CDDP+RT
  - Met its primary endpoint of non-inferiority in OS
    - HR 0.69 (99.1% CI, 0.37-1.27 [<1.32])
    - One-sided p for non-inferiority = 0.00272 < 0.00433
  - Better relapse-free survival for Weekly CDDP+RT
    - HR 0.71 (95% CI, 0.48-1.06)
  - Better local relapse-free survival for Weekly CDDP+RT
    - HR 0.73 (95% CI, 0.48-1.13)
  - Favorable safety profile for Weekly CDDP+RT
    - Decreased incidence of acute toxicities of neutropenia, dysphagia, nausea, infection, hyponatremia, renal impairment and hearing impairment

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My Take

- Weekly cisplatin 40 mg/m2 non-inferior to bolus cisplatin in terms of overall survival
- Improved RFS and LRFS with weekly cisplatin (95% CI slightly crossed 1).
- Favorable toxicity profile.
- Non-inferior **does not mean** superior
- Nevertheless, feel better about weekly cisplatin 40 mg/m2
- Radiosensitization question (is weekly better)
- Updated results needed
- What about in definitive chemoradiation setting?
- Is Japanese population same as US?

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KEYNOTE-048: Progression After the Next Line of Therapy Following Pembrolizumab or Pembrolizumab Plus Chemotherapy vs EXTREME as First-Line Therapy for Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma

Kevin Harrington,[1] Danny Rischin,[2] Richard Greil,[3] Denis Soulieres,[4] Makoto Tahara,[5] Gilberto Castro,[6] Amanda Psyrri,[7] Neus Baste,[8] Prakash C. Neupane,[9] Åse Bratland,[10] Thorsten Fuereder,[11] Brett G. M. Hughes,[12] Ricard Mesia Sr.,[13] Nuttapong Ngamphaiboon,[14] Tamara Rordorf,[15] Wan Zamaniah Wan Ishak,[16] Yayan Zhang,[17] Burak Gumuscu,[17] Ramona F. Swaby,[17] Barbara Burtness[18]

[1]The Institute of Cancer Research/The Royal Marsden NHS Foundation Trust National Institute of Health Research Biomedical Research Centre, London, UK; [2]Peter MacCallum Cancer Centre, Melbourne, Australia; [3]Paracelsus Medical University, Salzburg Cancer Research Institute, and Cancer Cluster Salzburg, Salzburg, Austria; [4]Centre Hospitalier de l'Université de Montréal, Montréal, QC, Canada; [5]National Cancer Center Hospital East, Kashiwa, Japan; [6]Instituto do Cancer do Estado de Sao Paulo, Sao Paulo, Brazil; [7]National Kapodistrian University of Athens, Attikon University Hospital, Athens, Greece; [8]Vall d'Hebron University Hospital, Barcelona, Spain; [9]University of Kansas Medical Center, Kansas City, KS, USA; [10]Oslo University Hospital, Oslo, Norway; [11]Medical University of Vienna, Vienna, Austria; [12]Royal Brisbane and Women's Hospital and University of Queensland, Brisbane, Australia; [13]Catalan Institute of Oncology, Hospitalet de Llobregat, Barcelona, Spain; [14]Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; [15]University Hospital, Zurich, Switzerland; [16]University of Malaya, Kuala Lumpur, Malaysia; [17]Merck & Co., Inc., Kenilworth, NJ, USA; [18]Yale School of Medicine and Yale Cancer Center, New Haven, CT, USA

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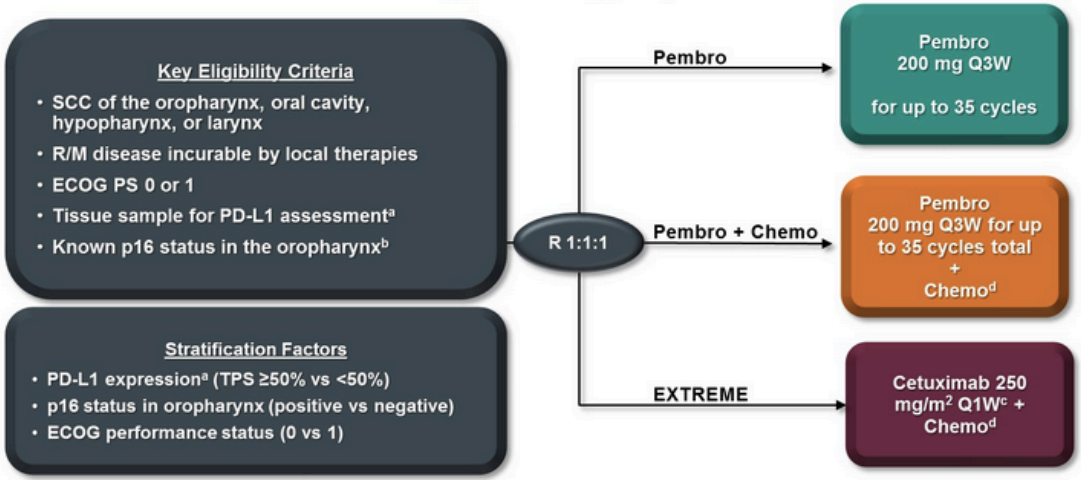
KEYNOTE-048 Study Design (NCT02358031)



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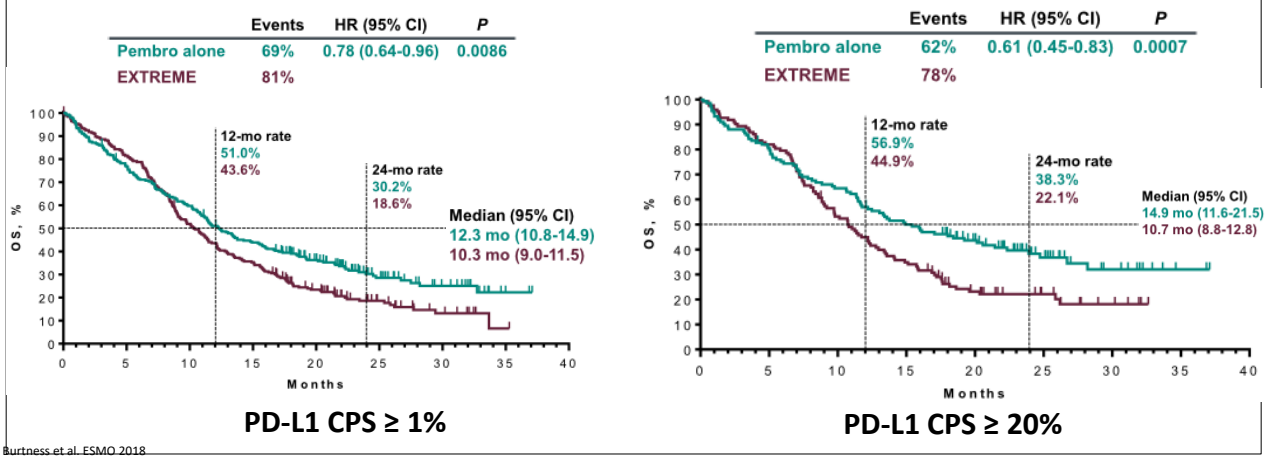
KEYNOTE-048: Pembrolizumab +/- Chemotherapy in Newly diagnosed R/M HNSCC



Burtness et al. ESMO 2018

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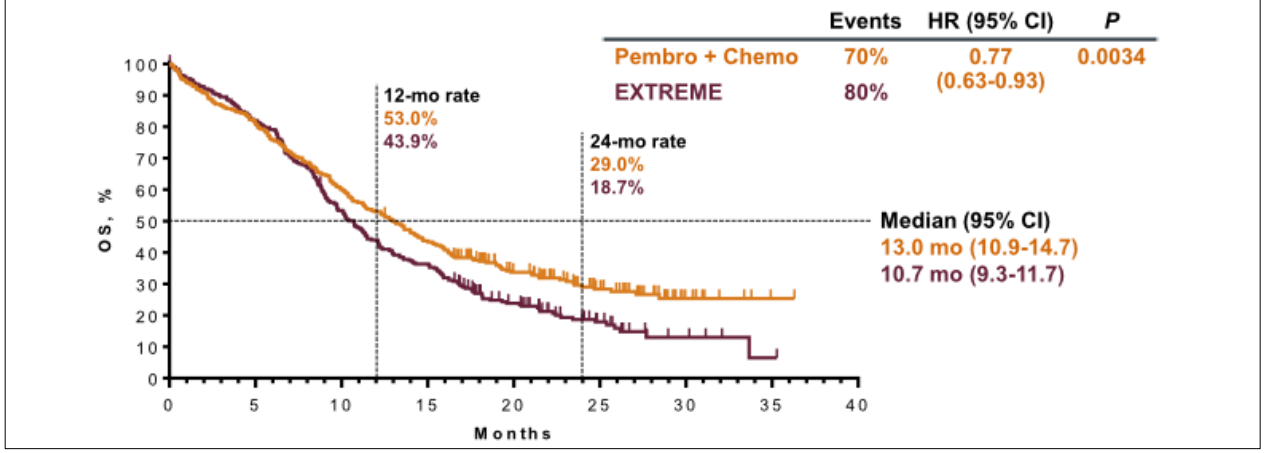
KEYNOTE-048: Pembrolizumab +/- Chemotherapy in Newly diagnosed R/M HNSCC



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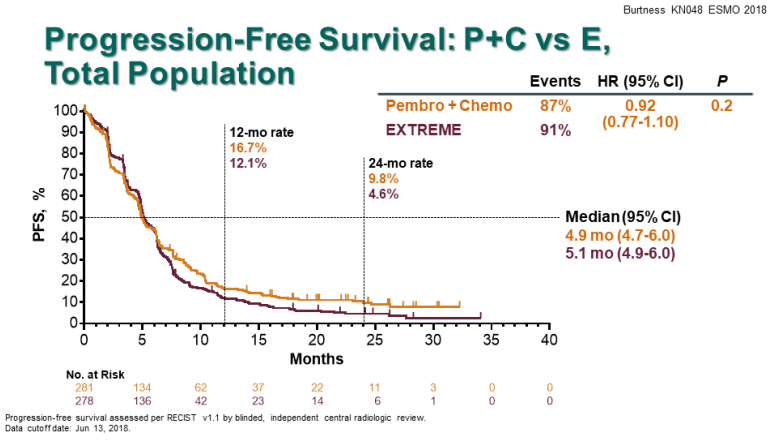
KEYNOTE-048: Pembrolizumab +/- Chemotherapy in Newly diagnosed R/M HNSCC



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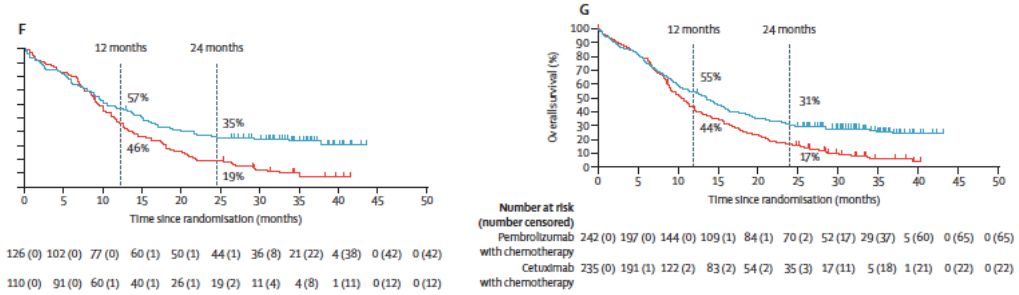
KEYNOTE-048: Pembrolizumab +/- Chemotherapy in Newly diagnosed R/M HNSCC



PD-L1 CPS ≥ 20% **PD-L1 CPS ≥ 1%**

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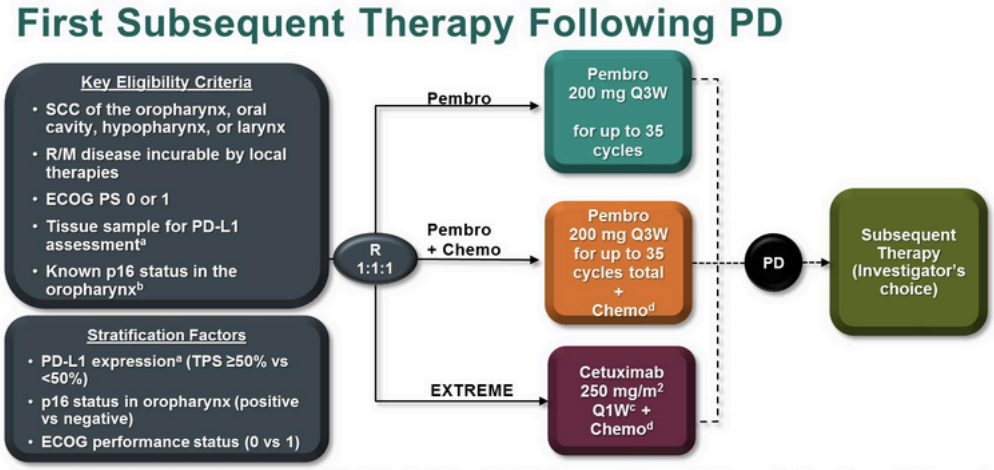

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Assessments and Statistical Analysis

- PFS2: time from randomization to objective tumor progression on next-line therapy or death from any cause
  - Exploratory outcome assessed in patients receiving subsequent therapy after 1L therapy

Patients who did not receive 2L therapy or who stopped 2L therapy without PD and did not start 3L therapy	Patients who stopped 2L therapy with PD	Patients who stopped 2L therapy without PD and started 3L therapy
Counted as an event at the time of death if the patient died Censored at the time of last known survival if the patient was alive	Counted as an event at the time of PD	Counted as an event at the start of 3L therapy

  - Estimated using the Kaplan-Meier method
  - HR and 95% CIs based on a Cox regression model with Efron's method of handling ties with treatment as a covariate
    - Stratified by ECOG PS, HPV status, and PD-L1 for CPS ≥1 and total populations
    - Stratified by ECOG PS and HPV status for CPS ≥20 population

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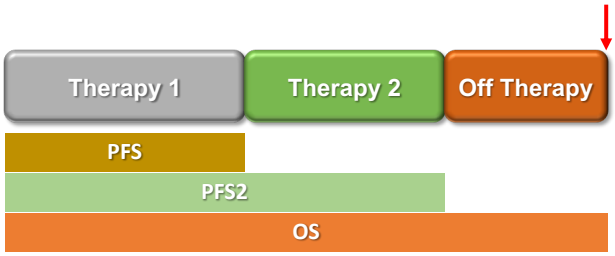
Progression Free Survival2 - PFS2

As first defined by the EMA in 2012[1]: time from randomization to objective tumor progression on next-line treatment or death from any cause, whichever occurs first



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Why Use PFS2

- When
- To ass
- To ass
- To ass
- To ass
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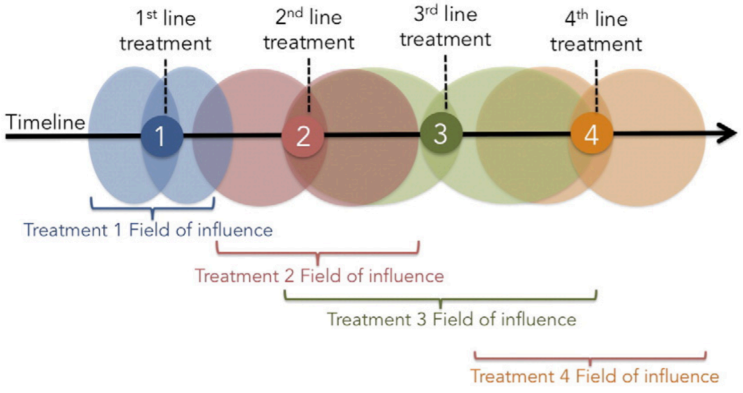
Action-at-a-distance: The effect of sequential clinical treatments on each other



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EMA Recommendations

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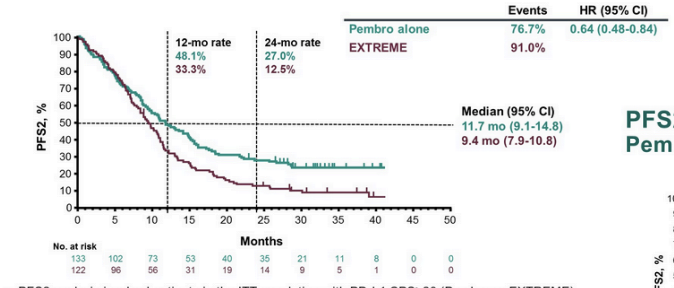
ANCO's ASCO20 Virtual Highlights

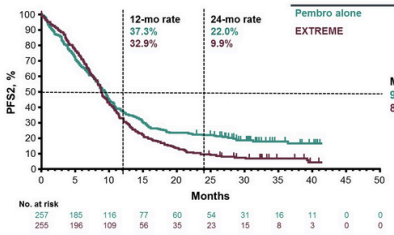
PFS2: Initially Randomized, Pembro vs EXTREME, CPS ≥20 Population



	Events	HR (95% CI)
Pembro alone	76.7%	0.64 (0.48-0.84)
EXTREME	91.0%	

- PFS2 analysis involved patients in the ITT population with PD-L1 CPS≥20 (Pembro vs EXTREME)

PFS2: Initially Randomized, Pembro vs EXTREME, CPS ≥1 Population



	Events	HR (95% CI)
Pembro alone	80.9%	0.80 (0.66-0.96)
EXTREME	92.5%	

- PFS2 analysis involved patients in the ITT population with PD-L1 CPS≥1 (Pembro vs EXTREME)

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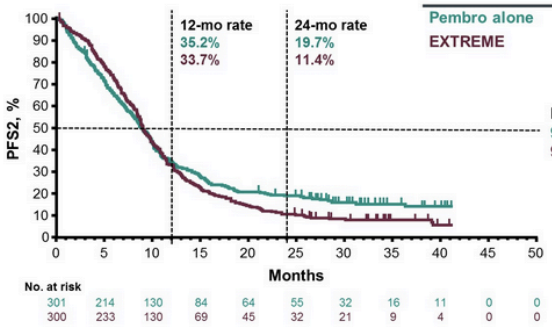
PFS2: Initially Randomized, Pembro vs EXTREME, Total Population



	Events	HR (95% CI)
Pembro alone	82.7%	0.90 (0.75-1.07)
EXTREME	91.0%	

- PFS2 analysis involved patients in the ITT population (Pembro vs EXTREME)

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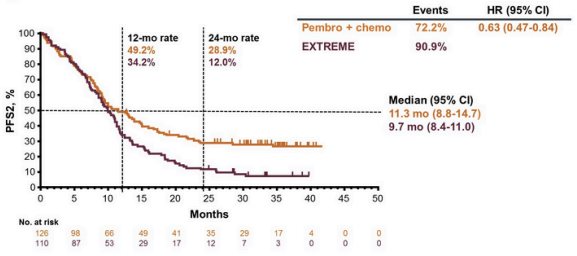
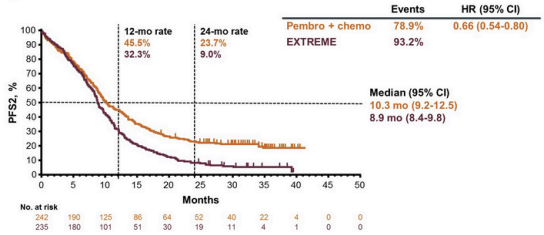
PFS2: Initially Randomized, Pembro + Chemotherapy vs EXTREME, CPS ≥20 Population



- PFS2 analysis involved patients in the ITT population with PD-L1 CPS≥20 (Pembro + Chemotherapy vs EXTREME)

PFS2: Initially Randomized, Pembro + Chemotherapy vs EXTREME, CPS ≥1 Population



- PFS2 analysis involved patients in the ITT population with PD-L1 CPS≥1 (Pembro + Chemotherapy vs EXTREME)

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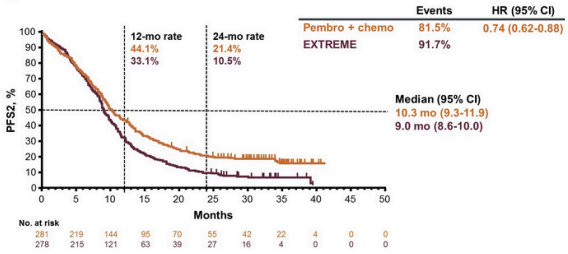
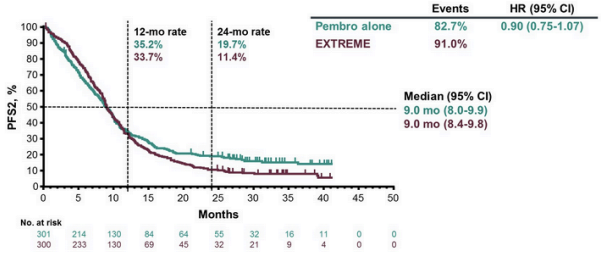
PFS2: Initially Randomized, Pembro + Chemotherapy vs EXTREME, Total Population



- PFS2 analysis involved patients in the ITT population (Pembro + Chemotherapy vs EXTREME)

PFS2: Initially Randomized, Pembro vs EXTREME, Total Population



- PFS2 analysis involved patients in the ITT population (Pembro vs EXTREME)

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First Subsequent Therapy

n (%)	Pembro Monotherapy n = 301	Pembro + Chemotherapy n = 281	EXTREME n = 300
Any new anticancer treatment[a]	148 (49.2)	115 (40.9)	159 (53.0)
Chemotherapy	135 (44.9)	88 (31.3)	102 (34.0)
EGFR inhibitor	59 (19.6)	37 (13.2)	19 (6.3)
Immune checkpoint inhibitor	6 (2.0)	12 (4.3)	50 (16.7)
Other immunotherapy	1 (0.3)	0 (0.0)	6 (2.0)
Kinase inhibitor	1 (0.3)	7 (2.5)	1 (0.3)
Other	2 (0.7)	1 (0.4)	2 (0.7)

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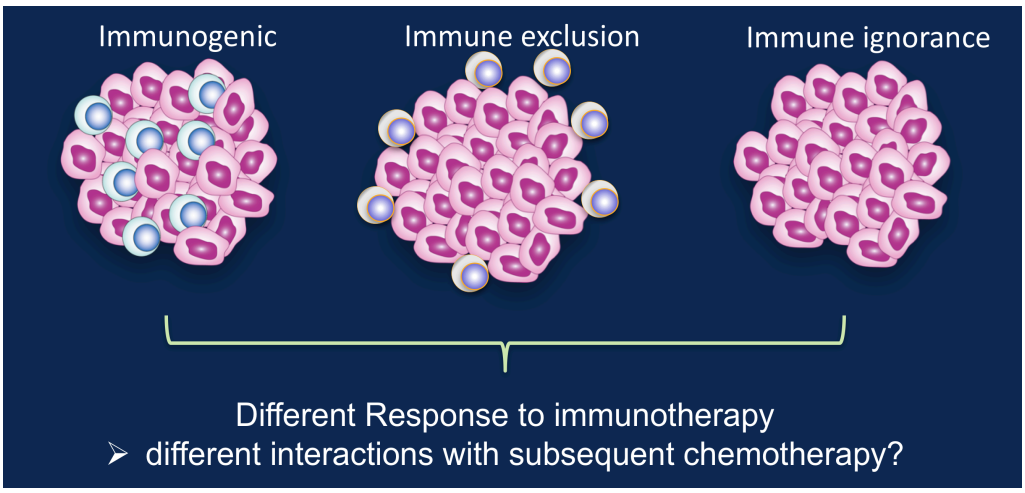

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Summary and Conclusions

- Pembro monotherapy vs EXTREME
  - PFS2 was longer for pembro arm in patients with PD-L1 CPS ≥20 and CPS ≥1
  - PFS2 was similar between arms for the total population
- Pembro + chemotherapy vs EXTREME
  - PFS2 was longer for pembro + chemotherapy arm in patients with PD-L1 CPS ≥20, CPS ≥1 and the total population
- These data further support use of pembro and pembro + chemotherapy as 1L treatment of R/M HNSCC

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My Take

- Agree - these data further support pembro or pembro + chemo for 1L treatment of R/M HNSCC.
- Some selection bias in subsequent treatments may influence outcomes
- Stratify by CPS score (≥20%, ≥1% and negative CPS) regarding pembro vs. chemo-pembro.
- PFS2 may underlie OS benefit where initial PFS benefit not realized despite OS benefit.

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ANCO's ASCO20 Virtual Highlights

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Randomized phase II study of axitinib versus observation in patients with recurred or metastatic adenoid cystic carcinoma

Bhumsuk Keam[1], Eun Joo Kang[2], Myung-Ju Ahn[3], Chan-Young Ock[1], Keun-Wook Lee[4], Jung Hye Kwon[5], Yaewon Yang[6], Yoon Hee Choi[7], Min Kyoung Kim[8], Jun Ho Ji[9], Tak Yun[10], Byung-Ho Nam[11], Sung-Bae Kim[12]

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Background

- Adenoid Cystic Tumors are rare salivary gland malignancies
- Generally chemotherapy refractory with low response rates (taxanes ORR=0%).
- Minimal activity of immune checkpoint blockade
- Occasionally express ER, PR, AR that where hormonal therapies (i.e. ADT) can be used.

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- Role of anti-angiogenic agents in R/M ACC

agents	Target	Primary Endpoint	N	RR (PR)	SD	mPFS (mo)	mOS (mo)	ref
Lenvatinib	VEGFR, PDGFR, KIT,RET,FGFR	ORR	33	15.6%	75%	17.5	NR	1
Axitinib	VEGFR, PDGFR, KIT	ORR	33	9.1%	75.8%	5.7	-	2
Sorafenib	VEGFR, PDGFR, KIT,RET,RAF	PFS at 12 months	23	11%	68%	11.3	19.6	3
Sorafenib	VEGFR, PDGFR, KIT,RET,RAF	ORR	19	11%	59%	8.9	26.4	4
Sunitinib	VEGFR, PDGFR, KIT	ORR	14	0%	78.6%	7.2	18.7	5
Dovitinib	FGFR, VEGFR, PDGFR	ORR	35	6%	94%	8.2	20.6	6
Dovitinib	FGFR, VEGFR, PDGFR	4m PFS rate	32	3.1%	93.8%	6.0	NR	7

1.Tchekmedyian V et al, J Clin Oncol. 2019;37(18):1529-1537. 2. Ho AL et al, Ann Oncol. 2016;27(10):1902-8. 3 Thomson DJ et al Head Neck. 2015;37(2):182-7. 4. Locati LD et al, Eur J Cancer. 2016;69:158-165. 5.Chau NG et al, Ann Oncol. 2012;23(6):1562-70. 6.Dillon PM et al, Clin Cancer Res. 2017;23(15):7. 7.Keam B et al, Cancer. 2015;121(15):2612-77.

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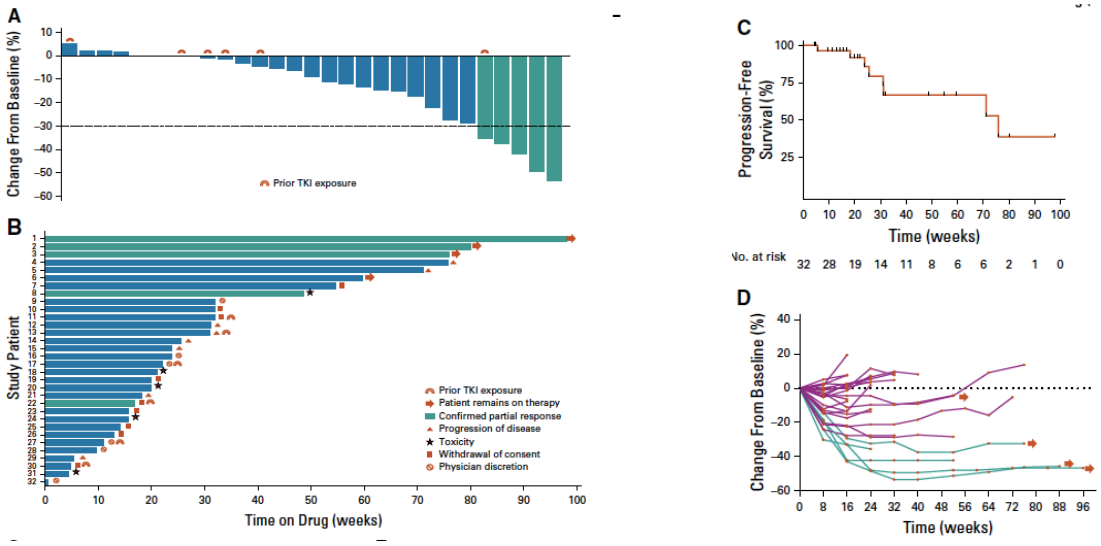

Lenvatinib in R/M Adenoid Cystic Carcinoma – 15.6% ORR, mPFS = 17.3 months

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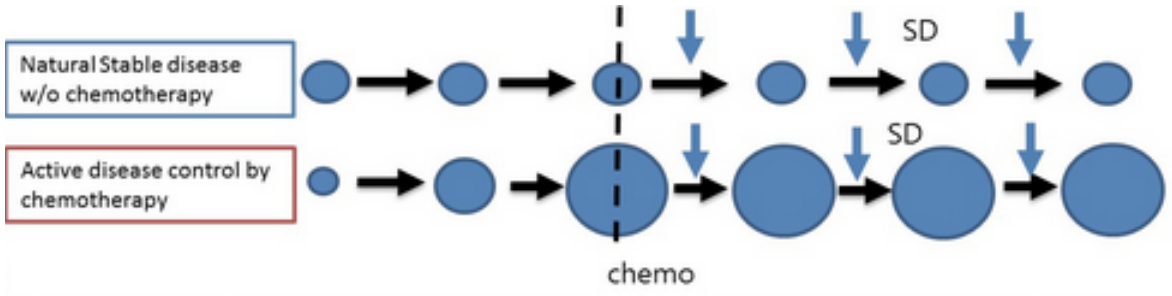

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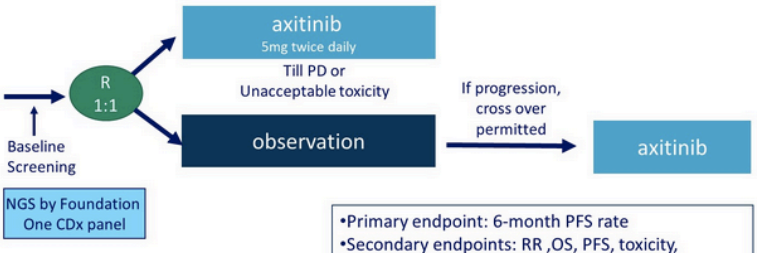
Study Design

- Multi-center of Korea Cancer Study Group was participated (KCSG HN16-08)
- Prospective, open-label, randomized phase II trial (NCT02859012)

Key inclusion criteria
•Recurred/ metastatic / unresectable ACC

•Disease progression within 9 months prior informed consents

•ECOG PS 0-1
•Age ≥ 20
•Measurable lesion
•Prior chemotherapy is allowed (any chemo line)



•Primary endpoint: 6-month PFS rate
•Secondary endpoints: RR ,OS, PFS, toxicity, exploring predictive genomic alteration
•N= 60 (30per each arm)

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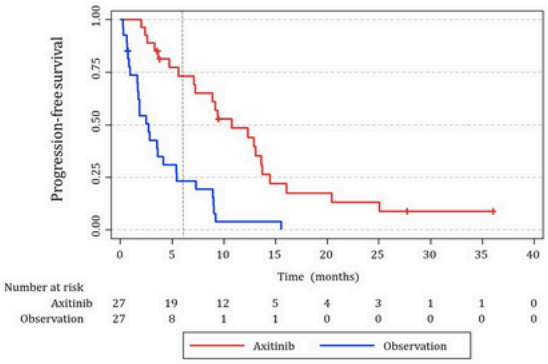
Progression-free survival



	Axitinib (N=27)	Observation (N=27)
6-month PFS rate, % (95% CI)	73% (52-86%)	23% (9-41%)
Median PFS, months (95% CI)	10.8 (7.1-13.6)	2.8 (1.7-4.2)
Hazard Ratio (95% CI)	0.25 (0.14-0.48) p<0.0001	

ORR=0.0%

OS - NR vs. 27.2 months

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Most frequently observed AEs

Adverse Events	Axitinib(N=30), N(%)			Observation arm (N=30) , N(%)		
	Grade 1-2	Grade3-4	Total	Grade 1-2	Grade3-4	Total
Stomatitis/mucositis	13(43.3)	0(0.0)	13(43.3)	1(3.3)	0(0.0)	1(3.3)
Anorexia	10(33.3)	1(3.3)	11(36.7)	0(0.0)	0(0.0)	0(0.0)
Fatigue	7(23.3)	4(13.3)	11(36.7)	2(6.7)	0(0.0)	2(6.7)
Hypertension	7(23.3)	7(23.3)	14(46.7)	0(0.0)	0(0.0)	0(0.0)
Proteinuria	10(33.3)	0(0.0)	10(33.3)	0(0.0)	0(0.0)	0(0)
Hand-foot syndrome (PPE)	5(16.7)	0(0.0)	5(16.7)	0(0.0)	0(0.0)	0(0.0)
Diarrhea	4(13.3)	3(10.0)	7(23.3)	0(0.0)	0(0.0)	0(0.0)
Dyspepsia	4(13.3)	1(3.3)	5(16.7)	4(13.3)	0(0.0)	4(13.3)
Weight loss	6(20.0)	1(3.3)	7(23.3)	0(0.0)	0(0.0)	0(0.0)
Aspartate aminotransferase (AST) increased	2(6.7)	1(3.3)	3(10.0)	1(3.3)	0(0.0)	1(3.3)
Dyspnea	4(13.3)	1(3.3)	5(16.7)	0(0.0)	0(0.0)	0(0.0)
Headache	4(13.3)	0(0.0)	4(13.3)	2(6.7)	0(0.0)	2(6.7)
QT prolongation	0(0.0)	1(3.3)	1(3.3)	0(0.0)	0(0.0)	0(0.0)
Constipation	4(13.3)	0(0.0)	4(13.3)	2(6.7)	0(0.0)	2(6.7)
Nausea	3(10.0)	0(0.0)	3(10.0)	1(3.3)	0(0.0)	1(3.3)
Skin rash(maculopapular)	2(6.7)	0(0.0)	2(6.7)	0(0.0)	0(0.0)	0(0.0)

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My Take

- **First randomized trial in R/M Adenoid Cystic Carcinoma**
- **Lack of response but some tumor shrinkage and improved 6-month PFS**
- **Multikinase TKIs with anti-angiogenic activity do appear to have some activity in these tumors**
- **Consideration of Clinical Trials Based Upon Risks/Benefits**

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Phase II/III trial of post-operative chemoradiotherapy comparing 3-weekly cisplatin with weekly cisplatin in high-risk patients with squamous cell carcinoma of head and neck (JCOG1008).

Authors:
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Abstract Disclosures

Research Funding:
National Cancer Center Research and Development Fund, Japan Agency for Medical Research and Develpmet Fund

Background:
The standard treatment for post-operative high-risk patients (pts) with locally advanced squamous cell carcinoma of the head and neck (LA-SCCHN) is chemoradiotherapy with 3-weekly cisplatin (CDDP) (100 mg/m^2, q3wk, 66 Gy/33Fr; 3-weekly CDDP+RT). However, one concern with 3-weekly CDDP+RT is insufficient CDDP compliance due to high-dose-related toxicities. Weekly CDDP+RT (40 mg/m^2, qwk, 66 Gy/33Fr; weekly CDDP+RT) is an alternative regimen with better compliance. Here, we conducted a phase II/III trial of weekly CDDP+RT in post-operative high-risk LA-SCCHN.

Methods:
This is a multi-institutional randomized phase II/III trial to confirm the non-inferiority of weekly CDDP+RT (Arm B) compared with 3-weekly CDDP+RT (Arm A). The trial enrolled pts aged 20-75 years with post-operative high-risk features

(microscopically positive margin and/or extranodal extension) and ECOG-PS 0-1. Pts were randomized in a 1:1 ratio to Arm A or Arm B. Primary endpoint of phase II was the proportion of treatment completion and that of phase III was overall survival (OS). A non-inferiority margin of hazard ratio (HR) was set at 1.32.

Results:

Between Oct 2012 and Dec 2018, 261 pts were enrolled (Arm A 132 pts, Arm B 129 pts). At the planned second interim analysis in phase III with 76/161 events, the Data and Safety Monitoring Committee recommended terminating the trial and publishing the results because the statistical boundary for OS non-inferiority had met the pre-specified stop criteria. With a median follow-up of 2.2 years in all randomized pts, 3-year OS was 59.1% in Arm A and 71.6% in Arm B with a HR of 0.69 (99.1% CI, 0.374-1.273 [< 1.32], one-sided p for non-inferiority = 0.00272 < 0.00433). 3-year RFS was 53.0% in Arm A and 64.5% in Arm B with a HR of 0.71 (95% CI, 0.48-1.06). Regarding acute adverse events, neutropenia (≥ grade 3), increased creatinine (≥ grade 2), hearing impairment (≥ grade 2) and mucositis (≥ grade 2) occurred in 48.8%, 8.5%, 7.8% and 55.0% in Arm A and 35.3%, 5.7%, 2.5% and 59.0% in Arm B, respectively. For compliance, median total dose of CDDP was 280 mg/m^2 (IQR, 250-299) in Arm A and 239 mg/m^2 (IQR, 199-277) in Arm B. Total radiation dose was 66 Gy (IQR, 66-66) in both arms. Proportion of treatment completion was 93.2% in Arm A and 86.8% in Arm B.

Conclusions:

Weekly CDDP+RT is non-inferior to 3-weekly CDDP+RT for post-operative high-risk LA-SCCHN pts and has a favorable toxicity profile. Weekly CDDP+RT should be considered the new standard treatment option for these pts. Clinical information: 000009125.

Print

KEYNOTE-048: Progression after the next line of therapy following pembrolizumab (P) or P plus chemotherapy (P+C) vs EXTREME (E) as first-line (1L) therapy for recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC).

Authors:
Kevin Joseph Harrington, Danny Rischin, Richard Greil, Denis Soulieres, Makoto Tahara, Gilberto Castro, Amanda Psyrri, Neus Baste, Prakash C. Neupane, Åse Bratland, Thorsten Fuereder, Brett Gordon Maxwell Hughes, Ricard Mesia, Nuttapong Ngamphaiboon, Tamara Rordorf, Wan Zamaniah Wan Ishak, Yayan Zhang, Burak Gumuscu, Ramona F. Swaby, Barbara Burtness; The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust Nation Institute of Health Research Biomedical Research Centre, London, United Kingdom; Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; Paracelsus Medical University, Salzburg Cancer Research Institute, and Cancer Cluster Salzburg, Salzburg, Austria; Centre Hospitalier de l'Université de Montréal, Montréal, QC, Canada; National Cancer Center Hospital East, Kashiwa, Japan; Instituto do Cancer do Estado de São Paulo, São Paulo, Brazil; National Kapodistrian University of Athens, Attikon University Hospital, Athens, Greece; Vall d'Hebron University Hospital, Barcelona, Spain; University of Kansas Medical Center, Kansas City, KS; Oslo University Hospital, Oslo, Norway; Medical University of Vienna, Vienna, Austria; Royal Brisbane & Women's Hospital and University of Queensland, Brisbane, QLD, Australia; Catalan Institute of Oncology, Hospitalet de Llobregat, Barcelona, Spain; Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; University Hospital, Zurich, Switzerland; University Malaya, Kuala Lumpur, Malaysia; Merck & Co., Inc., Kenilworth, NJ; Yale School of Medicine and Yale Cancer Center, New Haven, CT

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Abstract Disclosures

Research Funding:
Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA

Background:
1L P vs E improved OS in PD-L1 CPS ≥20 and CPS ≥1 populations, and led to noninferior OS in the total population, with favorable safety; 1L P+C vs E had superior OS in CPS ≥20, CPS ≥1, and total populations with comparable safety in the phase 3 KEYNOTE-048 study (NCT02358031) in patients with R/M HNSCC. Neither P vs E nor P+C vs E improved PFS in the PD-L1 CPS ≥20, CPS ≥1, or total populations. Here, we present the progression after the next line of therapy (PFS2) to assess the effect of 1L P or P+C and subsequent anticancer therapy on patient outcomes.

Methods:
Patients with locally incurable R/M HNSCC and no prior systemic therapy in the R/M setting were randomly assigned 1:1:1 to P, P+C, or E. PFS2 was defined as time from randomization to objective tumor progression on next-line therapy or death from any cause. PFS2 was estimated using the Kaplan-Meier method as an exploratory outcome confined to

those receiving subsequent therapy after 1L P. HR and 95% CIs were based on a Cox regression model with Efron's method of tie handling with treatment as a covariate (stratified by ECOG performance status [PS], HPV status, and PD-L1 for CPS ≥1 and total populations; by ECOG PS and HPV status for CPS ≥20 population). Data cutoff: Feb 25, 2019.

Results:

Of 882 (301 [P]; 281 [P+C]; 300 [E]) treated patients,422 (P: 148 [49.2%]; P+C: 115 [40.9%]; E: 159 [53.0%]) received subsequent anticancer therapy after 1L P, most commonly C (P: 135 [44.9%]; P+C: 88 [31.3%]; E: 102 [34.0%]); EGFR inhibitor (P: 59 [19.6%]; P+C: 37 [13.2%]; E: 19 [6.3%]); and immune checkpoint inhibitor (P: 6 [2.0%]; P+C: 12 [4.3%]; E: 50 [16.7%]); patients may have received more than one type of subsequent therapy. Median PFS2 is reported in Table.

Conclusions:

In patients with R/M HNSCC, longer median PFS2 was observed in the CPS ≥20 and CPS ≥1 populations for P vs E, and in the CPS ≥20, CPS ≥1, and total populations for P+C vs E. These data further support use of 1L P or P+C in patients with R/M HNSCC. Clinical trial information: NCT02358031.

Population	Treatment	Median PFS2, month	HR (95% CI)	24-mo PFS2 rate, %
CPS ≥20	P (n=133) vs E (n=122)	11.7 vs 9.4	0.64 (0.48-0.84)	27.0 vs 12.5
CPS ≥1	P (n=257) vs E (n=255)	9.4 vs 8.8	0.80 (0.66-0.96)	22.0 vs 9.3
Total	P (n=301) vs E (n=300)	9.0 vs 9.0	0.90 (0.75-1.07)	19.7 vs 11.4
CPS ≥20	P+C (n=126) vs E (n=110)	11.3 vs. 9.7	0.63 (0.47-0.84)	28.9 vs 12.0
CPS ≥1	P+C (n=242) vs E (n=235)	10.3 vs 8.9	0.66 (0.54-0.80)	23.7 vs 9.0
Total	P+C (n=281) vs E (n=278)	10.3 vs 9.0	0.74 (0.62-0.88)	21.4 vs 10.5

Print

Randomized phase II study of axitinib versus observation in patients with recurred or metastatic adenoid cystic carcinoma.

Authors:
Bhumsuk Keam, Eun Joo Kang, Myung-Ju Ahn, Chan-Young Ock, Keun Wook Lee, Jung Hye Kwon, Yaewon Yang, Yoon Hee Choi, Min Kyoung Kim, Jun Ho Ji, Tak Yun, Byung-Ho Nam, Sung-Bae Kim; Seoul National University Hospital, Seoul, South Korea; Division of Medical Oncology, Department of Internal Medicine, Korea University Guro Hospital, Korea University College of Medicine, Seoul, South Korea; Division of Hematology-Oncology, Department of Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; Department of Inter Medicine, Seoul National University Hospital, Seoul, South Korea; Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, South Korea; Department of Internal Medicine, Kangdong Sacred Heart Hospital, Hallym University College of Medicine, Seoul, South Korea; Department of Internal Medicine, Chungbuk Univeristy Hospital, Chungbuk University College of Medicine, Cheongju, South Korea; Department of Internal Medicine, Dongnam Institute of Radiological and Medical Sciences, Busan, South Korea; Department of Internal Medicine, Yeungnam University Hospital, Yeungnam University College of Medicine, Daegu, South Korea; Division of Hematology-Oncology, Department of Internal Medicine, Samsung Changwon Hospital, Sungkyunkwan University School of Medicine, Changwon, South Korea; Rare Cancers Clinic, Center for Specific Organs Cancer, National Cancer Center, Goyang-Si, Gyeonggi-Do, South Korea; HERINGS, The Institute of Advanced Clinical and Biomedical Research, Seoul, South Korea; Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

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Abstract Disclosures

Research Funding:
Adenoid cystic carcinoma research foundation

Background:
Adenoid cystic carcinoma (ACC) does not respond to cytotoxic chemotherapy. Several anti-angiogenic agents were evaluated in single arm phase II trials. However, the role of chemotherapy is still controversial, because of natural stable disease course without chemotherapy and lack of randomized trial. We firstly conducted a randomized trial to evaluate the efficacy of axitinib compared to observation.

Methods:
In this multicenter, prospective phase II trial, we enrolled recurred, metastatic ACC patients who progressed within 9 months. Patients were randomly assigned either axitinib (5mg twice daily) or observation arm with 1:1 ratio. Crossover to the axitinib arm was permitted for patients in the observation arm who had disease progression. The primary

endpoint was 6-month progression-free survival (PFS) rate. The secondary endpoints included objective response rate (ORR), overall survival (OS), PFS, duration of response and adverse events.

Results:

A total of 60 patients randomly allocated to axitinib (N=30) and observation arm (N=30) and response evaluation was conducted in 57 patients. With a median follow-up of 25.4 months, the 6-month PFS rate was 73.2% (95% confidence interval [CI], 54.8 to 88.1%) in the axitinib arm and 23.2% (95% CI, 9.3 to 41.1%) in the observation arm (hazard ratio, 0.19; 95% CI, 0.08 to 0.45; *P*< 0.001). Median PFS was 10.8 months in axitinib arm and 2.8 months in observation arm (*P*< 0.001). The ORR was 3.3% (95% CI, 0.1 to 17.2%) in the axitinib arm, and 0% (95% CI, 0 to 12.8%) in the observation arm. The disease control rate was 100% (95% CI, 88.4 to 100%) in the axitinib arm and 51.9% (95% CI, 32.0 to 71.3%) in the observation arm. After crossover, ORR of axitinib in the observation arm was 11.1% (95% CI, 2.4 to 29.2%). Median OS was not reached in axitinib arm, 28.5 months in observation arm (*P* = 0.688). The most frequently reported adverse events of axitinib were grade 1 or 2 oral mucositis and fatigue. Detailed data of adverse events and mutational profile data will be presented.

Conclusions:

In this first randomized trial in patients with recurred or metastatic ACC, axitinib significantly increased 6-month PFS rate compared to observation. Clinical trial information: NCT02859012.

Print

Curriculum Vitae

Jonathan Wesley Riess, M.D., M.S.

Personal Information

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Fax:	(916) 734-7946
Email:	jwriess@ucdavis.edu

Education

Education and Training

1996-2000	Swarthmore College, Swarthmore, PA, B.A., Psychobiology, Graduated with Honors
2000-2006	Robert Wood Johnson Medical School, Camden, NJ, M.D., Medicine
2006-2009	University of California San Francisco, San Francisco, CA, Residency, Internal Medicine
2009-2011	Stanford University School of Medicine, Stanford, CA, Fellowship, Hematology/Oncology
2011-2013	Stanford University School of Medicine, Stanford, CA, M.S., Epidemiology: Clinical Intensive Course in Clinical Research: Study Design and Performance
2013-2013	EORTC-ASCO-AACR, Brussels, Belgium, Molecular Markers of Medicine Tutorial
2016-2016	SWOG (Southwest Oncology Group) Hope Foundation, Bar Harbor, ME, Integrative Translational Science Center Workshop

Employment

Employment History

06/2013-06/2019	UC Davis, School of Medicine, Sacramento, CA, Assistant Professor
07/2019-Present	UC Davis School of Medicine, Sacramento, CA, Associate Professor

Extending Knowledge

Broadcast, Print or Electronic Media

1. Non-Small Cell Lung Cancer: Clinical and Economic Considerations in Targeting Therapy Based on Molecular Profiling, Website, December 12, 2013, The American Journal of Managed Care (AJMC.com).
2. Should We Do Broad Sequencing of All Lung Tumors?, Website, June 2, 2014, Global Resource for Advancing Cancer Education (GRACE).
3. PD-L1 Expression in Thymic Malignancies, Website, August 7, 2014, OncLive.
4. DDR2 Mutations in Squamous Cell Lung Cancer, Other, August 20, 2014, Grace: http://cancergrace.org/lung/2014/08/20/iaslc_riess_squamous_lc_ddr2_mutations/.
5. FGFR and Its Role in Treating Squamous Cell Lung Cancer, Other, August 29, 2014, Grace: http://cancergrace.org/lung/2014/08/29/iaslc_riess_fgfr_role_squamous_lc/.
6. Treating Leptomeningeal Carcinomatosis in Lung Cancer, Other, September 05, 2014, Grace: http://cancergrace.org/lung/2014/09/05/iaslc_riess_treating_leptomeningeal_carcinomatosis/.
7. Lung Cancer Living Room, Other, October 20, 2015, Addario Foundation: https://www.youtube.com/watch?v=deAdmRRmTcs.
8. Interview: "Immunotherapy Advances in Lung Cancer", Television Interview, June 2016, Fox News.
9. "ROS1 Fusions in Lung Cancer", Video, September 13, 2016, OncLive: http://cancergrace.org/lung/tag/squamous-cell-lung-cancer/.
10. Lung Cancer Living Room - Best of ASCO 2017, Website, 7/9/2017, Addario Foundation.
11. Invited Commentary: "In Search of an Oncogene Driver for Squamous Lung Cancer", Other, March 30, 2018, JAMA.

Workshops, Conferences, Presentations and Short Courses

1. Erlotinib and MK2206, Invited Speaker, International Association for the Study of Lung Cancer Targeted Therapies of Lung Cancer Meeting, Santa Monica, CA, February 19, 2013.
2. Non-Small Cell Lung Cancer: Clinical and Economic Considerations in Targeting Therapy Based on Molecular Profiling, Invited Speaker, Physicians, pharmacists, and other healthcare professionals, December 12, 2013.
3. Shifting Paradigms in Non-Small Cell Lung Cancer: Personalized Medicine and Immunotherapy, Invited Speaker, Internal Medicine Grand Rounds, University of California Davis, Sacramento, CA, February 22, 2014.
4. Changing Paradigms in the Treatment of Non-Small Cell Lung Cancer, Invited Speaker, Department of Internal Medicine Grand Rounds (UC Davis Faculty, Fellows, and Residents), Sacramento, CA, February 27, 2014.
5. "Thoracic Oncology Cases", Presenter, Multidisciplinary Management of Cancers CME Conference, Stanford Cancer Institute, Stanford, CA, March 7, 2014.
6. "Importance of Clinical Trials and Their Essence for Improving Patient Outcomes", Invited Speaker, Addario Lung Cancer Foundation Lung Cancer Living Room (Patient Group), San Carlos, CA, October 20, 2015.
7. "Thoracic Tumor Board Cases", Presenter, Multidisciplinary Management of Cancers CME Conference, Silverado Resort and Spa, Napa, CA, March 18, 2016.
8. Panelist: “Head and Neck Oncology Cases”, Invited Speaker, Multidisciplinary Management of Cancers CME conference, ANCO (Association of Northern California Oncologists), Silverado Resort and Spa Napa, CA, March 17-19, 2017.

9. Int Med Grand Rounds: "Complications of Immune Checkpoint Blockade: The New Great Masquerader", Invited Speaker, Dept faculty, fellows, residents, Sacramento, January 11, 2018, 31 Attendees.
10. Parp Inhibitors: New Insights, Invited Speaker, International Lung Cancer Congress, Huntington Beach, CA, July 26-28, 2018.
11. Poster Presentations Discussion, Invited Speaker, International Lung Cancer Congress, Huntington Beach, CA, July 26-28, 2018.

Grants and Contracts

Grants Active

08/01/2015 - 07/31/2020	Grant #201502309, $903,326, Other - Young Investigator, Targeting KRAS Mutant Lung Cancers, David Gandara (subaward PI) (Principal Investigator), Mass. General Hospital (SU2C Dream Team Subaward)
07/01/2018 - 06/30/2020	Grant #2P30CA093373 (supplement), $120,000, Other - Principal Awardee, NCI Cancer Clinical Investigator Team Leadership Award (CCITLA), Primo Lara, MD (Principal Investigator), NIH/NCI, Percentage Effort=15%

Grants Completed

08/01/2013 - 07/31/2016	Grant #5 K12 CA 138464, $499,010, Other - K12 Scholar, Paul Calabresi Career Development Award for Clinical Oncology (K12) at UC Davis, Primo Lara (Principal Investigator), NIH/NCI
01/01/2014 - 12/31/2016	Grant #IRG9512516-0, $30,000, Principal Investigator, American Cancer Society IRG, American Cancer Society
07/01/2015 - 09/30/2016	Grant #FL16RJ1, $25,000, Principal Investigator, A Pilot Study of Multiplex Immunofluorescence to Optimize Hsp90 Client Oncoprotein Knockdown in EGFR-mutant Non-Small Cell Lung Cancer (NSCLC), UC Davis Academic Senate, Interdisciplinary Research Grants
04/01/2015 - 03/31/2017	Grant #OP Fund 36743, $15,000, Principal Investigator, Award# 36743, Christine Landgraf Memorial Award
03/01/2015 - 10/31/2018	Grant #OP Fund 21A69, $166,155.00, Principal Investigator, Award #8682 SC (201500288), UCSF Addario Foundation Subcontract

Honors & Awards

2003	Robert Wood Johnson Summer Research Fellowship
2006	Alpha Omega Alpha
2006	Stanley S. Bergen Medal of Excellence. Robert Wood Johnson School of Medicine

ASCO HIGHLIGHTS 2020: LUNG CANCER

Caroline McCoach, MD, PhD
University of California, San Francisco

Presentation
Abstracts
Abbreviated Bio/CV

ANCO's ASCO20 Virtual Highlights

Caroline McCoach MD PhD
Assistant Professor of Thoracic Oncology
University of California, San Francisco
August 22, 2020

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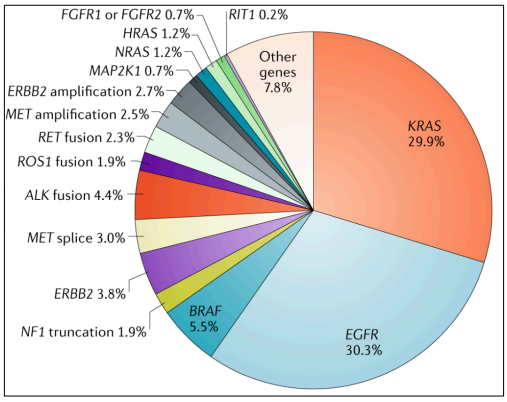
Molecular Subtypes



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Skoulidis, F., Heymach, J.V. *Nat Rev Cancer* **19,** 495–509 (2019).

2

ADAURA

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3

Osimertinib as adjuvant therapy in patients with stage IB–IIIA EGFR mutation positive NSCLC after complete tumor resection: ADAURA

Roy S. Herbst[1], Masahiro Tsuboi[2], Thomas John[3], Christian Grohe[4], Margarita Majem[5], Jonathan W. Goldman[6], Sang-We Kim[7], Dominika Marmol[8], Yuri Rukazenkov[8], Yi-Long Wu[9]

[1] Medical Oncology, Yale School of Medicine and Yale Cancer Center, New Haven, CT, USA; [2] Department of Thoracic Surgery and Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [3] Department of Medical Oncology, Austin Health, Melbourne, Australia; [4] Klinik für Pneumologie - Evangelische Lungenklinik Berlin Buch, Berlin, Germany; [5] Medical Oncology Services, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [6] David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, USA; [7] Department of Oncology, Asan Medical Center, Seoul, South Korea; [8] Oncology Research & Development, AstraZeneca, Cambridge, United Kingdom; [9] Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital and Guangdong Academy of Medical Sciences, Guangzhou, China

PRESENTED AT: 2020 ASCO ANNUAL MEETING #ASCO20

PRESENTED BY: Roy S. Herbst

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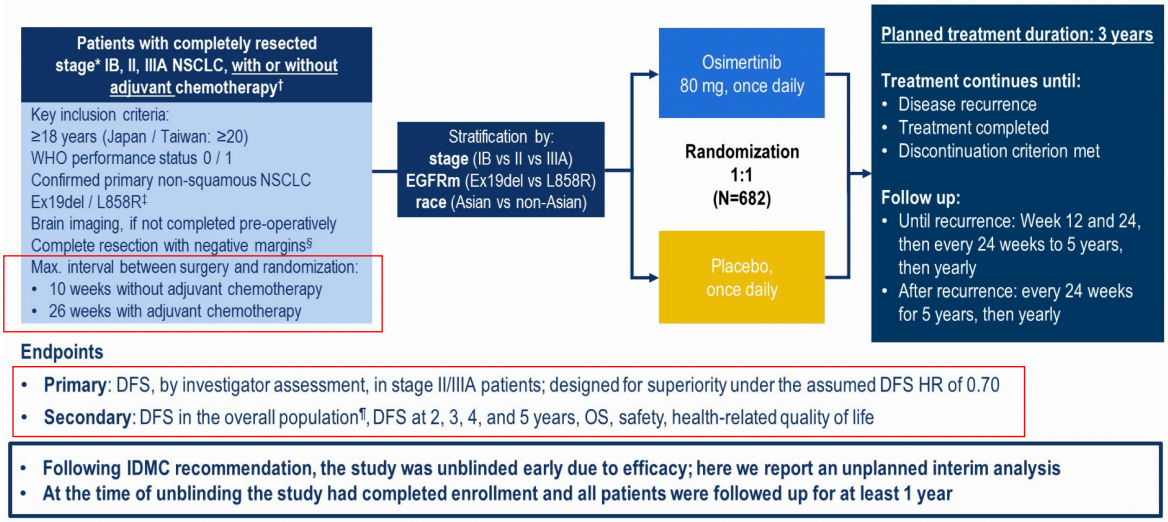
ADAURA Phase III double-blind study design



Endpoints

- **Primary**: DFS, by investigator assessment, in stage II/IIIA patients; designed for superiority under the assumed DFS HR of 0.70
- **Secondary**: DFS in the overall population¶, DFS at 2, 3, 4, and 5 years, OS, safety, health-related quality of life

- **Following IDMC recommendation, the study was unblinded early due to efficacy; here we report an unplanned interim analysis**
- **At the time of unblinding the study had completed enrollment and all patients were followed up for at least 1 year**

Herbst RS et al. ASCO 2020 Abstract LBA5

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ADAURA – Adjuvant osimertinib in patients with stage IB-IIIA EGFR positive NSCLC

Baseline characteristics in the overall population (stage IB/II/IIIA)

Characteristic, %	Osimertinib (n=339)	Placebo (n=343)
Sex: male / female	32 / 68	28 / 72
Age, median (range), years	64 (30–86)	62 (31–82)
Smoking status: smoker* / non-smoker	32 / 68	25 / 75
Race: Asian / non-Asian	64 / 36	64 / 36
WHO performance status: 0 / 1	64 / 36	64 / 36
AJCC staging at diagnosis (7th edition): IB / II / IIIA	31 / 35 / 34	31 / 34 / 35
Histology: adenocarcinoma / other†	95 / 5	96 / 4
EGFR mutation at randomization‡: Ex19del / L858R	55 / 45	56 / 44
Adjuvant chemotherapy: yes / no	55 / 45	56 / 44

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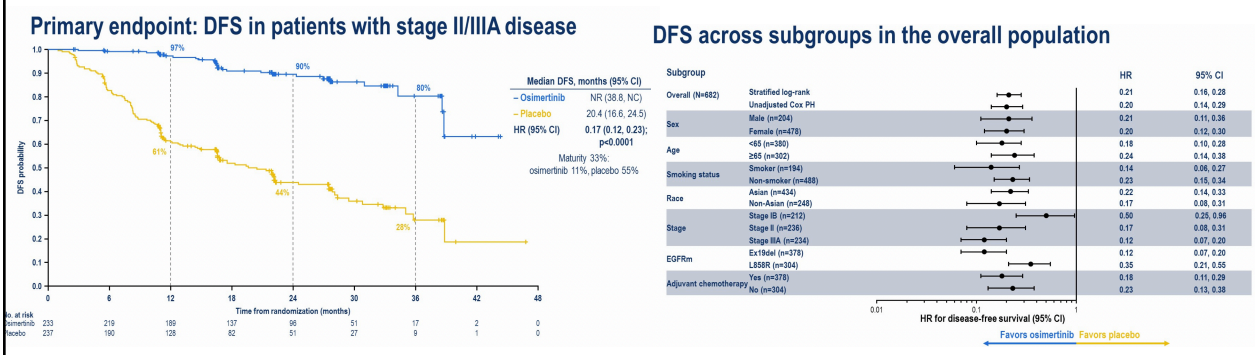
ADAURA – Adjuvant osimertinib in patients with stage IB-IIIA EGFR positive NSCLC



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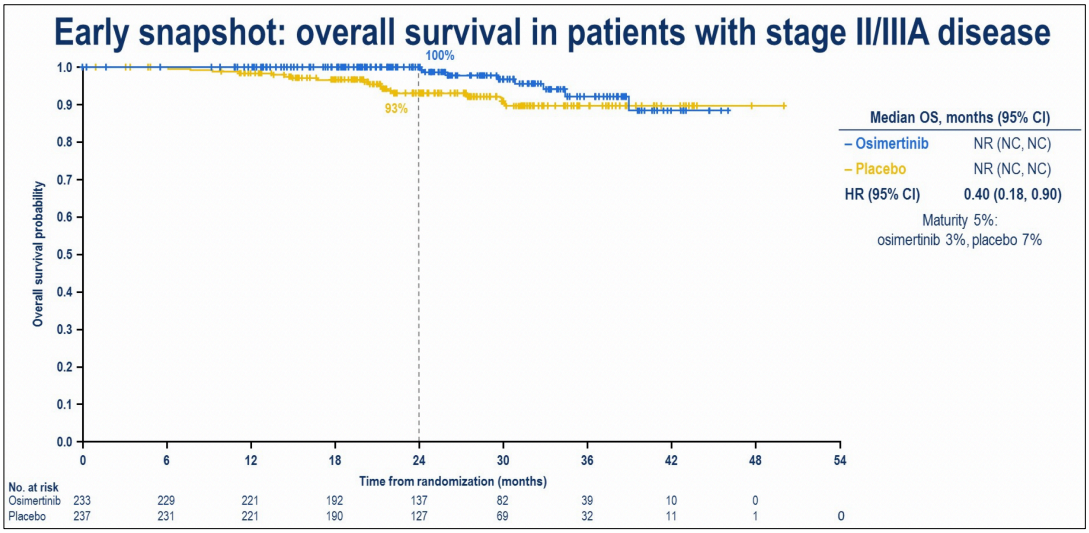
7

ADAURA – Adjuvant osimertinib in patients with stage IB-IIIA EGFR positive NSCLC



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ADAURA – Adjuvant osimertinib in patients with stage IB-IIIA EGFR positive NSCLC

Safety summary

AE, any cause*, n (%)	Osimertinib (n=336)	Placebo (n=343)
Any AE	327 (97)	306 (89)
Any AE Grade ≥3	68 (20)	48 (14)
Any AE leading to death	0	1 (<1)
Any serious AE	54 (16)	44 (13)
Any AE leading to discontinuation	38 (11)	15 (4)
Any AE leading to dose reduction	25 (7)	2 (1)
AE, possibly causally related†, n (%)		
Any AE	303 (90)	190 (55)
Any AE Grade ≥3	32 (10)	9 (3)
Any AE leading to death	0	0
Any serious AE	9 (3)	2 (1)

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CTONG1104/ADJUVANT: Adjuvant gefitinib vs chemotherapy for resected N1-N2 *EGFR*m NSCLC—Final overall survival

Inclusion criteria (n=220)
- ≥18 years
- ECOG PS 0–1
- Completely resected pathological stage II–IIIA (N1–N2) NSCLC
- EGFR activating mutation (exon 19 deletions or exon 21 L858R)

R 1:1

Stratified by:
- EGFR mutation
- N stage

Gefitinib 250 mg/day for 24 months or until PD or unacceptable toxicity

Vinolrelbine (25 mg/m^2 Days 1 and 8) **+ cisplatin** (75 mg/m^2 Day 1) Q3W for up to 4 cycles

Disease-free survival

Pathology stage, n (%)	Gefitinib	Vinolrelbine + cisplatin
IIA (N1)	33 (29.7)	33 (29.7)
IIB	4 (3.6)	4 (3.6)
IIIA	72 (64.9)	71 (64.0)

Efficacy assessment
- Every 12 weeks for 3 years
- Every 6 months after 3 years

Endpoints
- **Primary endpoint:** DFS
- **Secondary endpoints:** 3- and 5-year DFS rate, OS, 5-year OS rate, safety, HRQoL (FACT-L, LCSS, TOI), exploratory biomarker analyses

Wu Y-L, et al. ASCO 2020. Abstract 9005.

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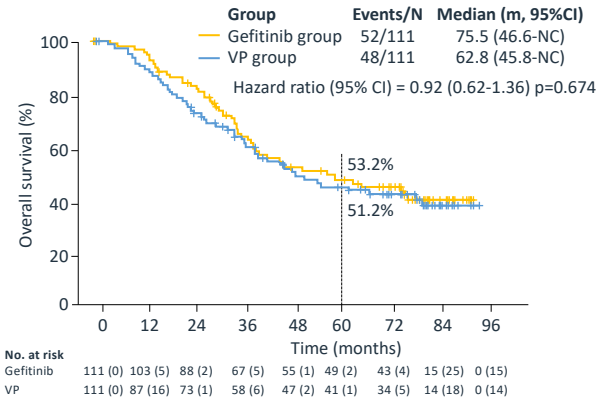
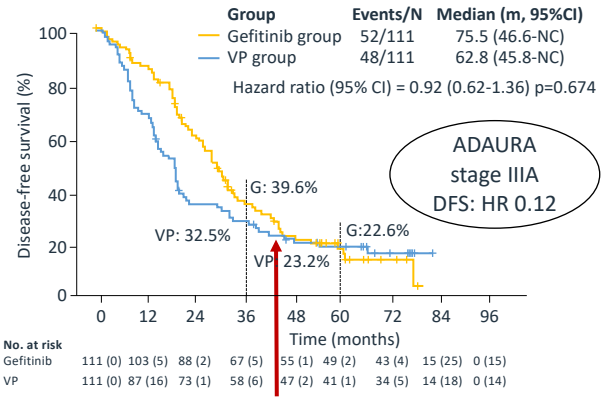
CTONG1104/ADJUVANT: Overall survival and disease-free survival

Overall survival (ITT population)



Disease-free survival (ITT population)



➢ Does duration of adjuvant therapy matter?

Loss of benefit at about 1 year after stopping the two years adjuvant therapy

Wu Y-L, et al. ASCO 2020. Abstract 9005.

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Adjuvant TKI Conclusions

- Adjuvant osimertinib demonstrates a significant improvement in disease free survival in patients with stage IB/II and IIIA EGFRm NSCLC
- The trial closed early due to anticipated efficacy resulting in unblinding, thus we may never know true OS benefit
- DFS benefit was present regardless of whether patients received adjuvant therapy or not
- Subgroup of patients who were likely cured with surgery +/- adjuvant chemotherapy who still received osimertinib
- Questions remain about the OS and the cost of this treatment but likely to become SOC and be translated to other molecular subtypes.

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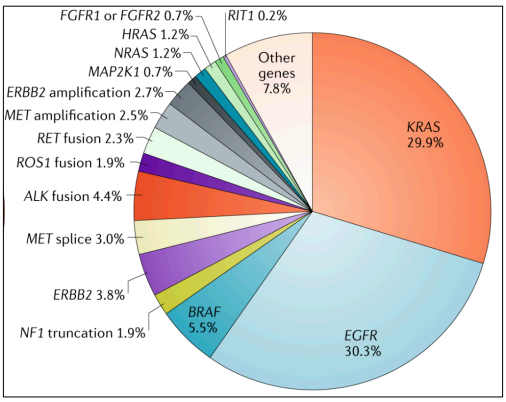
HER2 Exon 20



Skoulidis, F., Heymach, J.V. *Nat Rev Cancer* **19,** 495–509 (2019).

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Trastuzumab Deruxtecan (T-DXd; DS-8201) in Patients With HER2-Mutated Metastatic Non-Small Cell Lung Cancer: Interim Results of DESTINY-Lung01

Egbert F. Smit, Kazuhiko Nakagawa, Misako Nagasaka, Enriqueta Felip, Yasushi Goto, Bob T. Li, Jose M. Pacheco, Haruyasu Murakami, Fabrice Barlesi, Andreas Saltos, Maurice Perol, Hibiki Udagawa, Kapil Saxena, Ryota Shiga, Ferdinand Guevara, Suddhasatta Acharyya, Javad Shahidi, David Planchard, Pasi A. Jänne

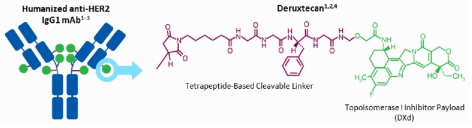
On behalf of the DESTINY-Lung01 investigators

PRESENTED AT: 2020 ASCO ANNUAL MEETING #ASCO20

PRESENTED BY: Prof Egbert F. Smit, Netherlands Cancer Institute, e.smit@nki.nl

T-DXd is an ADC with 3 components:

- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker



Smit EF et al. ASCO 2020 Abstract 9504c

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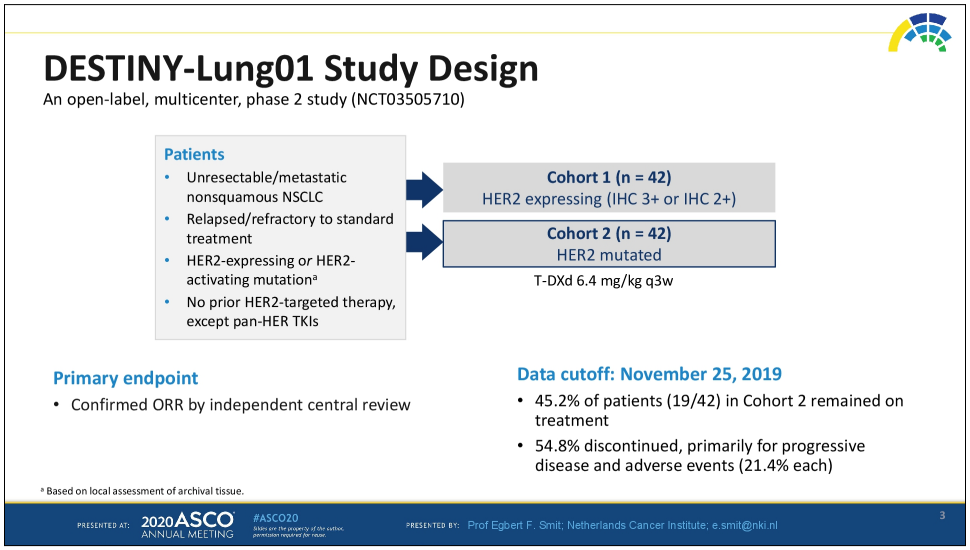

Smit EF et al. ASCO 2020 Abstract 9504

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DESTINY-Lung01

	Patients (N = 42)
Age, median (range), years	63.0 (34-83)
< 65 years, %	59.5
Female, %	64.3
Region, % Asia / North America / Europe	35.7 / 31.0 / 33.3
ECOG performance status 0 / 1, %	23.8 / 76.2
HER2 mutation, %	
Kinase domain	90.5
Extracellular domain	4.8
Not reported	4.8
Presence of CNS metastases, %	45.2

Prior Treatment, %	Patients (N = 42)
Platinum-based therapy	90.5
Anti–PD-1 or –PD-L1 inhibitor	54.8
Docetaxel	19.0

Smit EF et al. ASCO 2020 Abstract 9504

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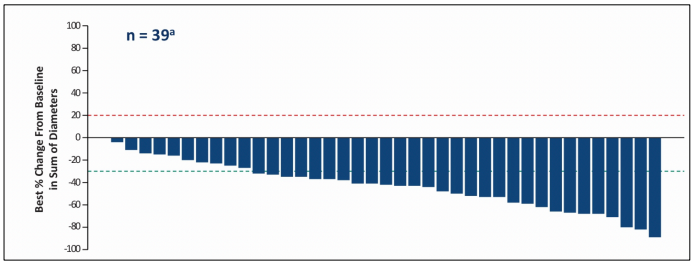
DESTINY-Lung01

Best Change in Tumor Size



Efficacy Results

	Patients (N = 42)
Confirmed ORR by ICR	**61.9% (n = 26)** (95% CI, 45.6%-76.4%)
CR	2.4% (n = 1)
PR	59.5% (n = 25)
SD	28.6% (n = 12)
PD	4.8% (n = 2)
Not evaluable	4.8% (n = 2)
Disease control rate	90.5% (95% CI, 77.4%-97.3%)
Duration of response, median	Not reached (95% CI, 5.3 months-NE)
PFS, median	14.0 mo (95% CI, 6.4-14.0 months)

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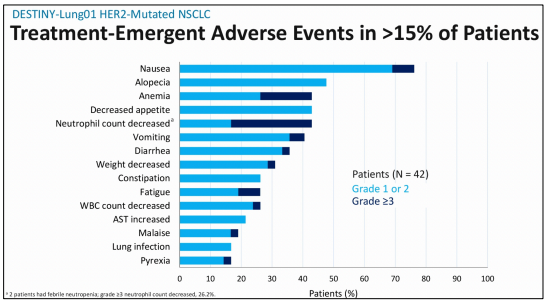
DESTINY-Lung01



	All Patients (N = 42)					
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade/ Total
Interstitial lung disease	0[a]	5 (11.9)	0	0	0	5 (11.9)

- Median time to onset of investigator-reported ILD was at 86 days (range, 41-255 days)
- 4 patients had drug withdrawn and 1 had drug interrupted
- All patients received steroid treatment
- 2 patients recovered, 1 recovered with sequelae, 1 was recovering, and 1 had not recovered by data-cutoff
- No grade 5 ILD was observed in this cohort

Smit EF et al. ASCO 2020 Abstract 9504

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Targeting Her2 mutations in NSCLC

Trial	Dose	ORR	PFS	Reference
Destiny- Lung01	6.4mg/kg	62%	14 m	ASCO 2020
Trastuzumab + Pertuzumab (n=14) MyPathway study	8mg/kg(L)->6mg/kg Q3w 840mg(L)->420mg Q3w	21%	-	Hainsworth JCO2018
Pyrotinib (n=60)	400mg daily	30%	6.9m	Zhou C, et al. JCO 2020
Afatinib (n=13) NICHE study	40mg daily	7.7%	15.9 weeks	Dziadziuszko R, et al JTO 2019
Ado-Trastuzumab/ T-DM1 (n=18)	3.6mg/kg	44%	5 m	Li B., JCO 2019

Smith EF et al. ASCO 2020 Abstract 9504

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DESTINY-Lung01 HER2-Mutated NSCLC

Conclusions

- T-DXd demonstrated clinical activity in this interim analysis with a high ORR and durable responses in patients with HER2-mutated NSCLC
  - ORR, 61.9% (95% CI, 45.6%-76.4%)
  - Median DOR not reached
  - Estimated median PFS, 14.0 months
- The safety profile in the HER2-mutated cohort was generally consistent with what was previously reported[1-5]
  - Low-grade gastrointestinal and hematologic AEs were most common
  - Drug-related ILD events observed in this patient population were low grade, and there were no deaths. However, ILD remains an important identified risk for patients treated with T-DXd and requires careful monitoring and management
- These data demonstrate the potential of T-DXd as a new treatment option for patients with HER2-mutated NSCLC
- Enrollment in this HER2-mutated cohort was expanded with an additional 50 patients to better characterize the risk-benefit ratio of T-DXd in patients with HER2-mutated NSCLC

1. Tsurutani J, et al. *Cancer Discov.* 2020; Mar [epub ahead of print]; 2. Tamura K et al. *Lancet Oncol.* 2019;20(6):816-826; 3. Modi S, et al. *N Engl J Med.* 2020;382(7):610-621; 4. Modi S, et al. *J Clin Oncol.* Feb [epub ahead of print]; 5. Shitara K, et al. *Lancet Oncol.* 2019;20(6):827-836.

Smit EF et al. ASCO 2020 Abstract 9504

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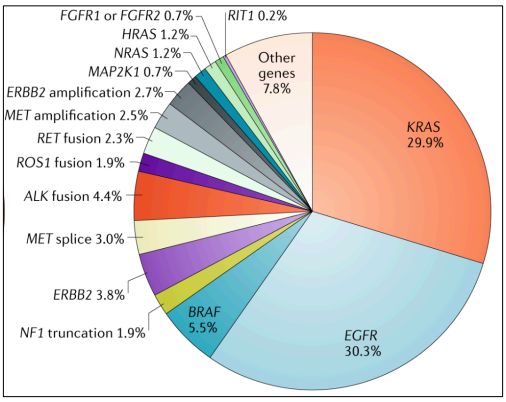
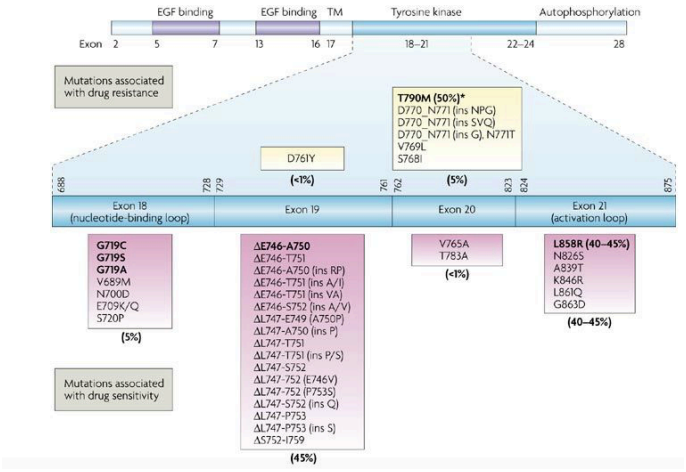
EGFR Exon 20



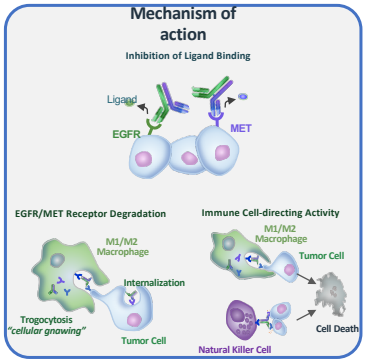
Skoulidis, F., Heymach, J.V. *Nat Rev Cancer* **19,** 495–509 (2019).

EGFR EXON 20 INSERTIONS IN NON-SMALL CELL LUNG CANCER



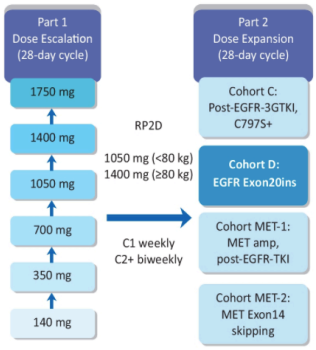
Sharma et al *Nature Reviews Cancer* **volume 7**, pages 169–181 (2007)

CHRYSALIS: Amivantamab (JNJ-61186372),
an anti-EGFR-MET bispecific antibody, in *EGFR* MUTANT (exon 20 insertion) NSCLC



Key Objectives
- Part 1: Establish RP2D(s)
- Part 2: Safety and preliminary efficacy at RP2D(s)
- PK and immunogenicity

Key Eligibility Criteria
- Metastatic/unresectable NSCLC
- Progressed on prior therapy or ineligible for or refused current therapies
- ECOG PS ≤1
- Evaluable (Part 1) or measurable disease (Part 2)
- Activating EGFR or MET mutations or amplifications and progressed on previous SOC (Part 2)
- Previously definitively treated brain metastases allowed



Park K, et al. ASCO 2020. Abstract 9512.

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Demographics

Table 1. Demographics and Disease Characteristics of Response-Evaluable Patients

	Total (N=39)		Total (N=39)
Median age, years (range)	61 (40–78)	**Median time from initial diagnosis, months (range)**	12 (1–56)
Male / Female, n (%)	19 (49) / 20 (51)	**Adenocarcinoma, n (%)**	39 (100)
Race, n (%)		**Exon20ins mutation, n (%)**	39 (100)
Asian	25 (64)	**Median prior lines, n (range)**	1 (0–7)
Black	1 (3)	**Prior systemic therapies, n (%)**	33 (85)
White	11 (28)	Platinum-based chemotherapy	29 (74)
Not reported	2 (5)	Immuno-oncology therapy[a]	13 (33)
ECOG PS, n (%)		EGFR TKI	9 (23)
0	14 (36)	Bevacizumab	4 (10)
1	24 (62)	**No prior therapy, n (%)**	6 (15)
2	1 (3)		

[a]nivolumab, atezolizumab, pembrolizumab, durvalumab; ECOG PS=Eastern Cooperative Oncology Group performance status; EGFR=epidermal growth factor receptor; TKI=tyrosine kinase inhibitor

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Adverse Events

Table 2. Adverse Events in Patients Treated at the RP2D (Safety Population)	
Adverse Events in the Safety Population, n (%)	**Total (N=50)**
Any AE	48 (96)
Serious AE	14 (28)
Grade ≥3 AE	18 (36)
AEs leading to death (all unrelated to amivantamab)	4 (8)
AEs leading to discontinuation	3 (6)
AEs leading to dose reduction	5 (10)
AEs leading to dose interruption[a]	15 (30)
All-grade AEs (≥15%), n (%)	
Rash[b]	36 (72)
Infusion related reaction	30 (60)
Paronychia	17 (34)
Constipation	13 (26)
Hypoalbuminemia	11 (22)
Dyspnea	10 (20)
Fatigue	9 (18)
Back pain	8 (16)
Stomatitis	8 (16)

[a]Excludes infusion related reactions, [b]Includes dermatitis acneiform, rash, rash generalized, rash maculo-papular, rash pustular, rash papular, erythema, generalized erythema, rash erythematous, macule, perineal rash, rash pruritic, dermatitis; AE=adverse event; RP2D=recommended phase 2 dose

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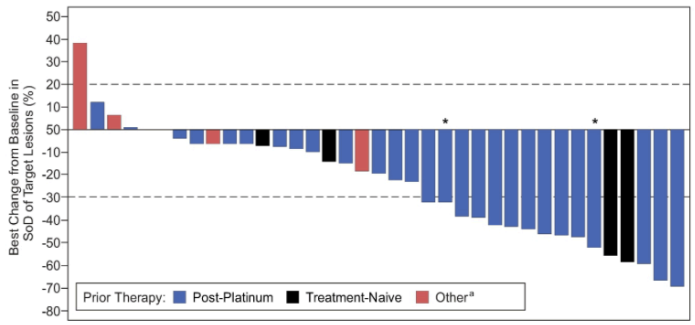
CHRYSALIS: Response to amivantamab

Figure 2. Best Percentage Change from Baseline in Sum of Target Lesion Diameters



*Unconfirmed partial response. [a]2 patients treated with EGFR TKIs, 1 with bevacizumab plus radiation therapy, 1 with adjuvant immuno-oncology chemotherapy. 2 patients did not have post-baseline disease assessments and are not included in the plot. SoD=sum of diameters

	Total	Post-platinum
Overall response rate[a], % (95% CI)	36 (21–53)	41 (24–61)
Clinical benefit rate[b], % (95% CI)	67 (50–81)	72 (53–87)

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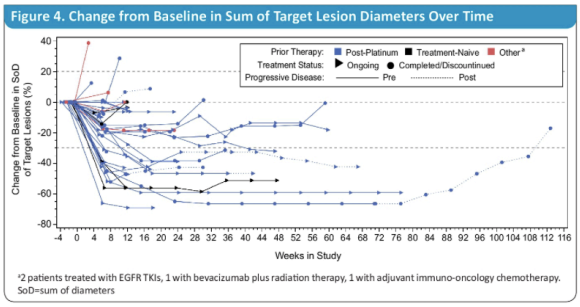
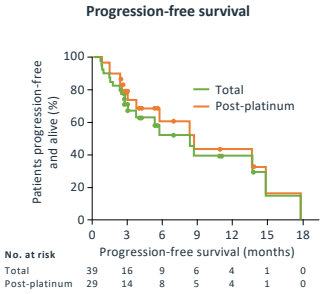
CHRYSALIS: Durable responses and progression-free survival with amivantamab





- Amivantamab is a dual EGFR-MET antibody with a unique MOA
- It is active in Exon 20 ins NSCLC, with ORR=36% & some long DOR
- The drug is relatively well tolerated
- FDA breakthrough designation granted

Park K, et al. ASCO 2020. Abstract 9512.

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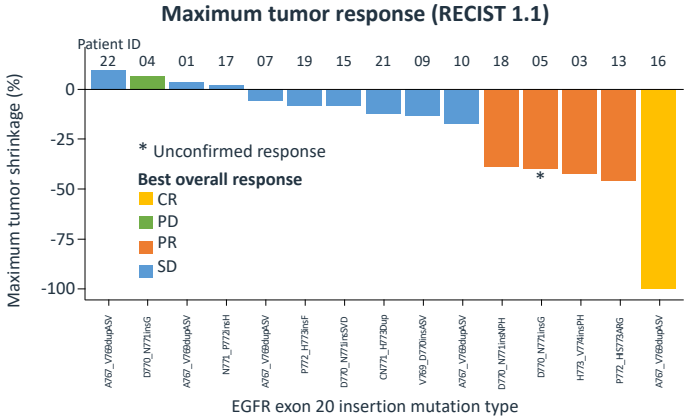
ECOG-ACRIN 5162: Phase 2 study of osimertinib 160 mg in advanced NSCLC with EGFR exon 20 insertions



Overall Efficacy
- Confirmed ORR: 24% (4/17)
- DCR: 82% (14/17)
- mPFS: 9.6 mo (95% CI, 4.1–10.7)
- mDOR: NA (95% CI, 4.7–NA)

Piotrowska Z, et al. ASCO 2020. Abstract 9513.

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Indirect comparison of TAK-788 vs real-world data outcomes in refractory non-small cell lung cancer (NSCLC) with *EGFR* exon 20 insertions - 9580

- Mobocertinib (TAK-788), a novel EGFR TKI, is currently in clinical development for NSCLC with *EGFR* exon 20 insertions
  - A single-arm phase 1/2 study (NCT02716116) is ongoing; in preliminary analyses, mobocertinib has shown evidence of antitumor activity in previously treated patients with NSCLC and *EGFR* exon 20 insertions treated with 160 mg qd (median progression-free survival [PFS], 7.3 months; confirmed objective response rate [ORR] 43%), with a manageable safety profile[4]
  - Mobocertinib was recently granted Breakthrough Therapy Designation by the US Food and Drug Administration for the treatment of patients with metastatic NSCLC with *EGFR* exon 20 insertions whose disease progressed on or after platinum-based chemotherapy

Table 3. ORR: Comparison of Mobocertinib vs RWD

	Mobocertinib n=28	RWD n=71	
		Unweighted	Weighted
Event, n	12	10	
ORR, % (95% CI)	43 (24.5, 62.8)	14 (7.0, 24.4)	13 (0.4, 25.1)
Rate Difference, % (95% CI)		28.8 (8.74, 48.8)	30.1 (8.02, 52.23)
OR (95% CI) *P* value		4.58 (1.68, 12.48) 0.0030	5.14[a] (1.35, 19.65) 0.0167
OR, covariate adjusted[b] (95% CI) *P* value			5.346 (1.740, 16.422) 0.0034

[a] Logistic regression model with inverse probability of treatment weighting (IPTW); [b] Multivariate model adjusting for the same set of matching variables as covariates in the logistic regression model
OR, odds ratio

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Conclusions

- Several new FDA approved targeted agents, thus critical to do NGS with broad panel for patients both to ensure identifying all treatment options, to preserve tissue and identify future clinical trial options
- Promising therapies for patients with traditionally difficult to target alterations (EGFR and HER2 exon 20)
- ADAURA provides compelling evidence for use of targeted therapy in the adjuvant setting which requires shared decision making with patients given that there remain many unanswered questions

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Osimertinib as adjuvant therapy in patients (pts) with stage IB–IIIA EGFR mutation positive (EGFRm) NSCLC after complete tumor resection: ADAURA.

Authors:
Roy S. Herbst, Masahiro Tsuboi, Thomas John, Christian Grohé, Margarita Majem, Jonathan Wade Goldman, Sang-We Kim, Dominika Marmol, Yuri Rukazenkov, Yi-Long Wu; Medical Oncology, Yale School of Medicine and Yale Cancer Center, New Haven, CT; Department of Thoracic Surgery and Oncology, National Cancer Center Hospital East, Chiba, Japan; Department of Medical Oncology, Austin Health, Heidelberg, Australia; Klinik für Pneumologie - Evangelische Lungenklinik Berlin Buch, Berlin, Germany; Department of Medical Oncology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA; Department of Oncology, Asan Medical Center, Seoul, Korea, Republic of (South); Late Oncology Statistics, AstraZeneca, Cambridge, United Kingdom; Oncology Research & Development, AstraZeneca, Cambridge, United Kingdom; Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, School of Medicine, South China University of Technology, Guangzhou, China

Abstract Disclosures

Research Funding:
AstraZeneca

Background:
Osimertinib is a 3rd-generation, CNS-active, EGFR-TKI with superior efficacy to comparator EGFR-TKI (gefitinib/erlotinib) in treatment-naïve EGFRm advanced NSCLC. Approx. 30% of pts with NSCLC present with early stage (I–IIIA) disease; surgery is the primary treatment. Adjuvant chemotherapy is standard of care in pts with resected stage II–III NSCLC and select stage IB pts; however, recurrence rates are high and other therapies are needed. ADAURA (NCT02511106) is a Ph III, double-blind, randomized study assessing the efficacy and safety of osimertinib vs placebo (PBO) in pts with stage IB–IIIA EGFRm NSCLC after complete tumor resection and adjuvant chemotherapy, when indicated. Following Independent Data Monitoring Committee recommendation, the trial was unblinded early due to efficacy; we report an unplanned interim analysis.

Methods:
Eligible pts: ≥18 years (Japan/Taiwan: ≥20), WHO PS 0/1, primary non-squamous stage IB/II/IIIA NSCLC, confirmed EGFRm (ex19del/L858R), complete resection of primary NSCLC with full recovery from surgery; postoperative chemotherapy was allowed. Pts were randomized 1:1 to osimertinib 80 mg once daily orally or PBO to receive treatment for up to 3 years and stratified by stage (IB/II/IIIA), mutation type (ex19del/L858R), and race (Asian/non-Asian). Primary endpoint: disease-free survival (DFS) by investigator in stage II–IIIA pts. Secondary endpoints: overall survival (OS) and safety. Data cutoff (DCO): 17 Jan 2020.

Results:

Globally, 682 pts were randomized to treatment: osimertinib n=339, PBO n=343. Baseline characteristics were balanced across arms (osimertinib/PBO): stage IB 31/31%, stage II/IIIA 69/69%, female 68/72%, ex19del 55/56%, L858R 45/44%. In stage II–IIIA pts, DFS hazard ratio (HR) was 0.17 (95% CI 0.12, 0.23); p<0.0001 (156/470 events); 2-year DFS rate was 90% with osimertinib vs 44% with PBO. In the overall population, DFS HR was 0.21 (0.16, 0.28); p<0.0001 (196/682 events); 2-year DFS rate was 89% with osimertinib vs 53% with PBO. OS was immature (4% maturity) with 29/682 deaths (osimertinib n=9, PBO n=20) at DCO. The safety profile was consistent with the known safety profile of osimertinib.

Conclusions:

Adjuvant osimertinib is the 1st targeted agent in a global trial to show a statistically significant and clinically meaningful improvement in DFS in pts with stage IB/II/IIIA EGFRm NSCLC after complete tumor resection and adjuvant chemotherapy, when indicated. Adjuvant osimertinib provides an effective new treatment strategy for these pts. Clinical trial information: NCT02511106.

Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-mutated metastatic non-small cell lung cancer (NSCLC): Interim results of DESTINY-Lung01.

Authors:
Egbert F. Smit, Kazuhiko Nakagawa, Misako Nagasaka, Enriqueta Felip, Yasushi Goto, Bob T. Li, Jose Maria Pacheco, Haruyasu Murakami, Fabrice Barlesi, Andreas Nicholas Saltos, Maurice Perol, Hibiki Udagawa, Kapil Saxena, Ryota Shiga, Ferdinand M. Guevara, Suddhasatta Acharyya, Javad Shahidi, David Planchard, Pasi A. Janne; Netherlands Cancer Institute, Amsterdam, Netherlands; Kindai University Hospital, Osaka, Japan; Karmanos Cancer Institute, Detroit, MI; Hospital Universitari Vall d'Hebron, Barcelona, Spain; National Cancer Center Hospital, Tokyo, Japan; Memorial Sl Kettering Cancer Center, New York, NY; University of Colorado, Aurora, CO; Shizuoka Cancer Center, Shizuoka, Japan; Aix Marseille University, CNRS, INSERM, CRCM, Assistance Publique–Hôpitaux de Marseille, Marseille, France; Moffitt Cancer Center, Tampa, FL; Centre Léon Bérard, Lyon, France; National Cancer Center East, Chiba, Japan; Daiichi Sankyo Inc., Basking Ridge, NJ; Institut Gustave Roussy, Thoracic Team, Villejuif, France; Dana-Farber Cancer Institute and the Belfer Center for Applied Cancer Science, Boston, MA

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Abstract Disclosures

Research Funding:
Daiichi Sankyo, Inc.

Background:
T-DXd is an antibody-drug conjugate composed of an anti-HER2 antibody, cleavable tetrapeptide-based linker, and topoisomerase I inhibitor payload. In a phase I trial, patients (pts) with HER2-mutated NSCLC who received T-DXd had a confirmed objective response rate (ORR) of 72.7% (8/11) (Tsurutani et al, WCLC 2018). DESTINY-Lung01 (NCT03505710) is an ongoing, multicenter, phase II study of T-DXd in pts with non-squamous NSCLC overexpressing HER2 or containing a HER2-activating mutation. We report data for the cohort with HER2 mutations after a median follow-up of 8.0 mo (range, 1.4-14.2 mo).

Methods:
Pts were treated with T-DXd 6.4 mg/kg every 3 weeks. The primary endpoint was confirmed ORR (complete response [CR] + partial response [PR]) by ICR. Additional endpoints were disease control rate (DCR; CR + PR + stable disease), duration of response (DOR), progression-free survival (PFS), and safety.

Results:
At data cutoff (25 Nov 2019), 42 pts (64.3% female) had received T-DXd. Median age was 63.0 years (range, 34-83 years; < 65 y, 59.5%); 45.2% had central nervous system metastases; ECOG performance status was 0 in 23.8% of pts and 1 in

76.2%. HER2 mutations were predominantly in the kinase domain (90.5%). Most pts (90.5%) had prior platinum-based chemotherapy and 54.8% had anti–PD-1 or –PD-L1 treatment; median number of prior treatment lines was 2 (range, 1-6). Median treatment duration was 7.75 mo (range, 0.7-14.3 mo); 45.2% of pts remained on treatment. Confirmed ORR by ICR among the 42 pts was 61.9% (95% CI, 45.6%-76.4%); median DOR was not reached at data cutoff; 16 of 26 responders remained on treatment at data cutoff; DCR was 90.5% (95% CI, 77.4%-97.3%); estimated median PFS was 14.0 mo (95% CI, 6.4-14.0 mo). All pts (42/42) had treatment-emergent adverse events (TEAEs); 64.3% were grade ≥ 3 (52.4% drug-related), including decreased neutrophil count (26.2%) and anemia (16.7%). There were 5 cases (11.9%) of drug-related interstitial lung disease (ILD) as adjudicated by an independent committee (all grade 2, no grade ≥ 3) and 1 case of grade 1 ILD is pending adjudication. TEAEs led to dose interruption in 25 pts (59.5%), dose reduction in 16 pts (38.1%), and treatment discontinuation in 10 pts (23.8%).

Conclusions:

T-DXd demonstrated promising clinical activity with high ORR and durable responses in pts with HER2-mutated NSCLC. The safety profile was generally consistent with previously reported studies. Clinical trial information: NCT03505710.

ECOG-ACRIN 5162: A phase II study of osimertinib 160 mg in NSCLC with EGFR exon 20 insertions.

Authors:
Zofia Piotrowska, Yating Wang, Lecia V. Sequist, Suresh S. Ramalingam; Massachusetts General Hospital Cancer Center, Boston, MA; ECOG-ACRIN Biostatistics Center, Boston, MA; Massachusetts General Hospital, Boston, MA; Winship Cancer Institute, Emory University Hospital, Atlanta, GA

Research Funding:
U.S. National Institutes of Health

Background:
EGFR exon 20 insertions (ins20), which comprise 4-10% of EGFR-mutant NSCLC, are generally refractory to first- and second-generation EGFR TKIs. While the clinical activity of the third-generation EGFR TKI osimertinib against EGFR ins20 is unknown, preclinical studies suggest its favorable therapeutic window may allow for inhibition of EGFR isn20 at clinically-achievable doses (Hirano, Oncotarget 2015). We report the results of EA5162, a single-arm, phase II study of osimertinib 160 mg in NSCLC pts with EGFR ins20 (NCT03191149).

Methods:
Pts with advanced NSCLC with an EGFR ins20 mutation identified by any local, CLIA-certified tissue assay were treated with osimertinib 160 mg daily until progression, intolerable toxicity or withdrawal. At least one prior line of therapy was required; stable, asymptomatic brain metastases were allowed. The primary endpoint was objective response rate (ORR). Secondary endpoints included safety, progression-free survival (PFS) and overall survival. The estimated sample size was 19 patients.

Results:
21 pts were enrolled between 4/2018 and 7/2019 (median age 65; 15 female, 6 male; median 2 prior therapies); 1 patient did not meet eligibility criteria due to laboratory studies obtained 1 day out of window. As of 1/21/20, 6 pts remain on treatment. Among the 20 eligible pts, the best response was PR in 4 pts and CR in one pt, for a confirmed ORR of 25%; 12 (60%) pts had SD. The median PFS was 9.7 months (95% CI, 4.07, NA), median duration of response (DOR) was 5.7 months (95% CI, 4.73, NA.) Grade > 3 treatment-related adverse events (TRAE) observed in > 1 pt included anemia (n=2), fatigue (n=2), prolonged QT interval (n=2.) One pt had grade 4 respiratory failure, there were no grade 5 TRAEs. One pt discontinued study treatment due to grade 3 anemia.

Conclusions:

Osimertinib 160mg daily is well-tolerated and showed clinical activity in EGFR ins20-mutant NSCLC with a response rate of 25%, disease control rate of 85%, and mPFS of 9.7 months. The adverse events with osimertinib 160 mg QD in this cohort were consistent with other reports of this regimen; grade 3 rash and diarrhea were not observed. Clinical trial information: NCT03191149.

Prepared: June 21, 2020

University of California, San Francisco

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EDUCATION

1998 - 2005	Stanford University	PhD	Biochemistry	Dr. Patrick Brown
2005 - 2009	University of Colorado School of Medicine	MD		
2009 - 2010	University of California, Davis		Internal Medicine Internship	
2010 - 2012	University of California, Davis		Internal Medicine Residency	
2012 - 2013	University of California, Davis		Internal Medicine Chief Residency	
2013 - 2014	University of California, Davis		Medical Oncology- Clinical Research Fellowship	Dr Karen Kelly
2014 - 2017	University of Colorado School of Medicine		Hematology/ Oncology Fellowship	Dr Robert Doebele

LICENSES, CERTIFICATION

10/2010	California State Medical License A114380
8/2013	Board Certification (Internal Medicine)
11/2017	Board Certification (Medical Oncology)

PRINCIPAL POSITIONS HELD

10/2017 - present	University of California, San Francisco	HS Assistant Clinical Professor	Internal Medicine

HONORS AND AWARDS

2006	Student Cancer Research Award	University of Colorado School of Medicine

2013	Internal Medicine Trainee Research Award	University of California, Davis
2016	Career Enhancement Award	University of Colorado Lung Cancer SPORE
2017	Career Enhancement Award Renewal	University of Colorado Lung Cancer SPORE
2019	UCSF Cancer League Award "Determination of the Molecular Basis of Tumor Cell and Immune Microenvironment Differences Predictive of Treatment Response in Non-Small Cell Lung Cancer"	University of California, San Francisco

KEYWORDS/AREAS OF INTEREST

Lung Cancer
Lung Adenocarcinoma
Lung Squamous Cell Carcinoma
Acquired Resistance
Targeted Therapy
Immunotherapy
ALK, ROS1, EGFR, MET, BRAF, SHP2
Activating Mutation
Oncogenes

PROFESSIONAL ACTIVITIES

MEMBERSHIPS

2013 - present American Society of Clinical Oncology

2015 - present International Association for the Study of Lung Cancer

SERVICE TO PROFESSIONAL PUBLICATIONS

2019 - present ad hoc reviewer Journal of Clinical Oncology

2017 - present ad hoc reviewer Journal of Thoracic Oncology

2017 - present ad hoc reviewer Clinical Cancer Research

2017 - present ad hoc reviewer Journal of Clinical Oncology Precision Oncology

2017 - present ad hoc reviewer Clinical Lung Cancer

2017 - present ad hoc reviewer Cancer Research and Treatment Communications

2017 - present ad hoc reviewer British Journal of Cancer