Society for Immunotherapy of Cancer

Advances in Cancer Immunotherapy™ Webinar: Clinical Updates

From ESMO Virtual Congress 2020

Thursday, January 7, 2021

12:00-1:00 p.m. ET

Webinar Agenda

12:00-12:05 p.m. ET Overview: Welcome and Introductions

12:05-12:40 p.m. ET Presentations

12:40-12:55 p.m. ET Question and Answer Session

12:55-1:00 p.m. ET Closing Remarks

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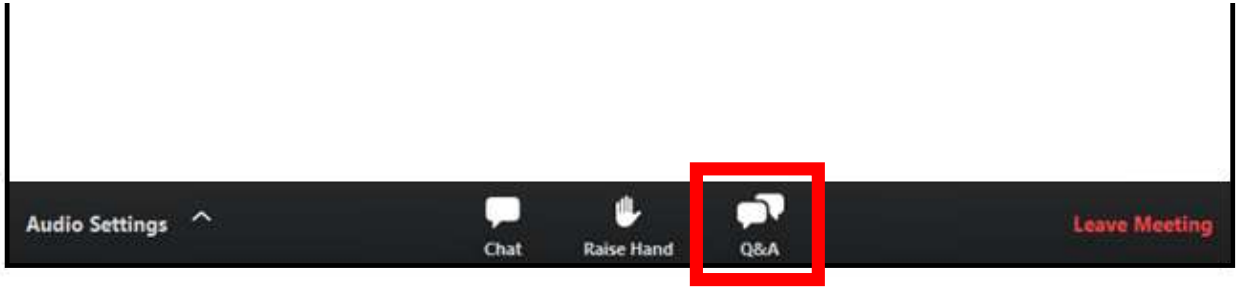
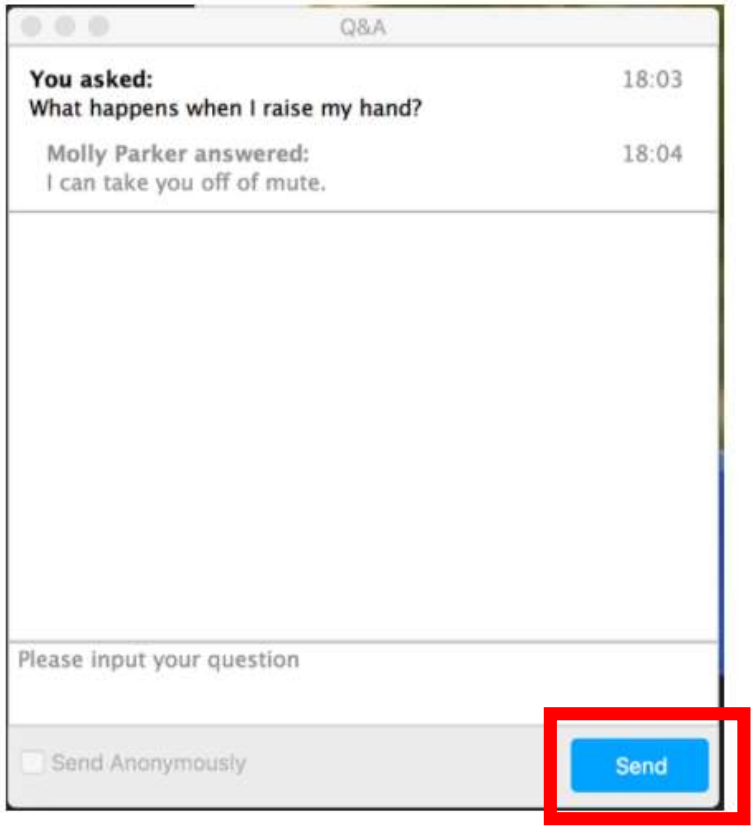
How to Submit Questions

- Click the “Q&A” icon located on at the bottom of your Zoom control panel
- Type your question in the Q&A box, then click “Send”
- Questions will be answered in the Question & Answer session at the end of the webinar (as time permits)





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Webinar Faculty

Lillian Siu, MD – Princess Margaret Cancer Center

Toni Choueiri, MD – Dana-Farber Cancer Institute

Sumanta Pal, MD – City of Hope

Jeffery Weber, MD, PhD – NYU Langone Medical Center

Learning objectives

Upon completion of this webinar, participants will be able to:

- Describe advances in immune checkpoint inhibitor therapies for highly immunotherapy-responsive cancers including melanoma and renal cell carcinoma
- Outline novel immunotherapeutic strategies and implications for future cancer care
- Explain the rationale behind and implications of current combination immunotherapy studies

EE [2]1

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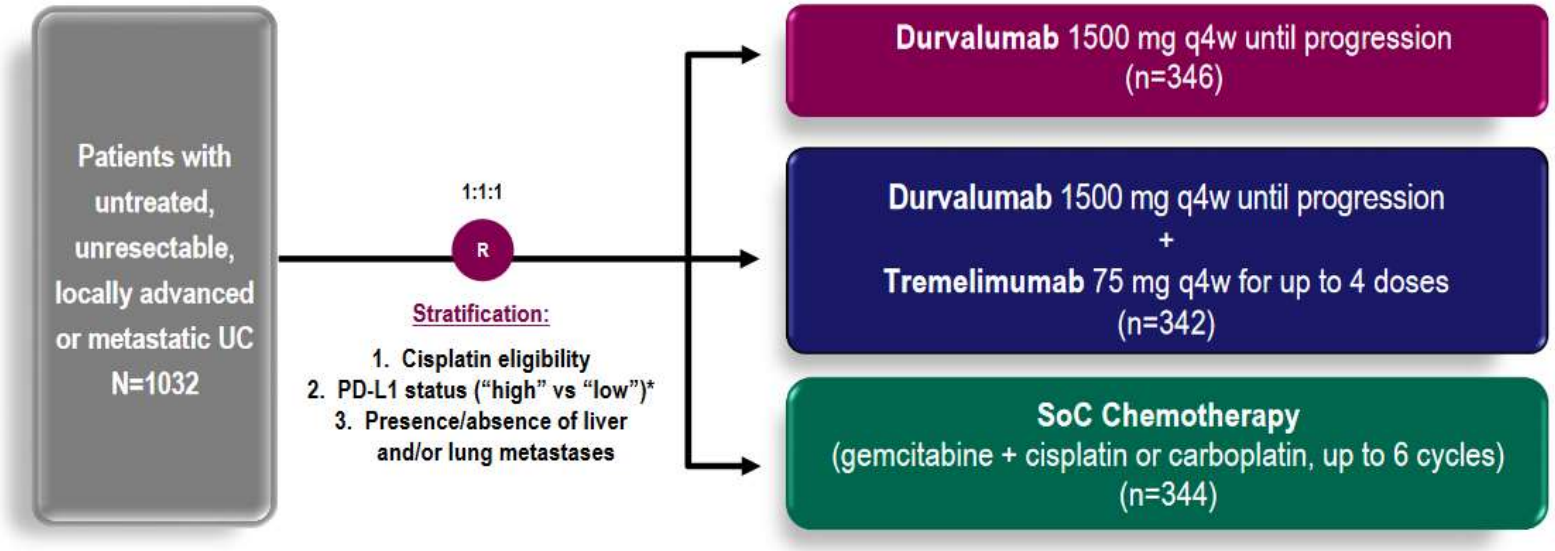
Webinar outline

- Genitourinary cancers
- Melanoma
- Head and neck cancer
- Gastrointestinal cancer
- Novel agents

A phase 3, randomized, open-label study of first-line durvalumab with or without tremelimumab in patients with unresectable, locally advanced or metastatic urothelial carcinoma (DANUBE)

Thomas Powles, Michiel S. van der Heijden, Daniel Castellano, Yohann Loriot, Matthew D. Galsky, Daniel P. Petrylak, Osamu Ogawa, Se Hoon Park, Andrea Necchi, Jae-Lyun Lee, Ugo De Giorgi, Martin Bögemann, Aristotelis Bamias, André P. Fay, Ignacio Duran, Natasha Angra, Ashok K. Gupta, Philip He, Wendy Levin, Joaquim Bellmunt

Study design



CO-PRIMARY ENDPOINTS

- OS (D vs SoC in PD-L1 high)
- OS (D+T vs SoC in all comers)

SELECT SECONDARY ENDPOINTS

- OS (D vs SoC in all comers)
- OS (D+T vs SoC in PD-L1 high)
- PFS, ORR, and DoR

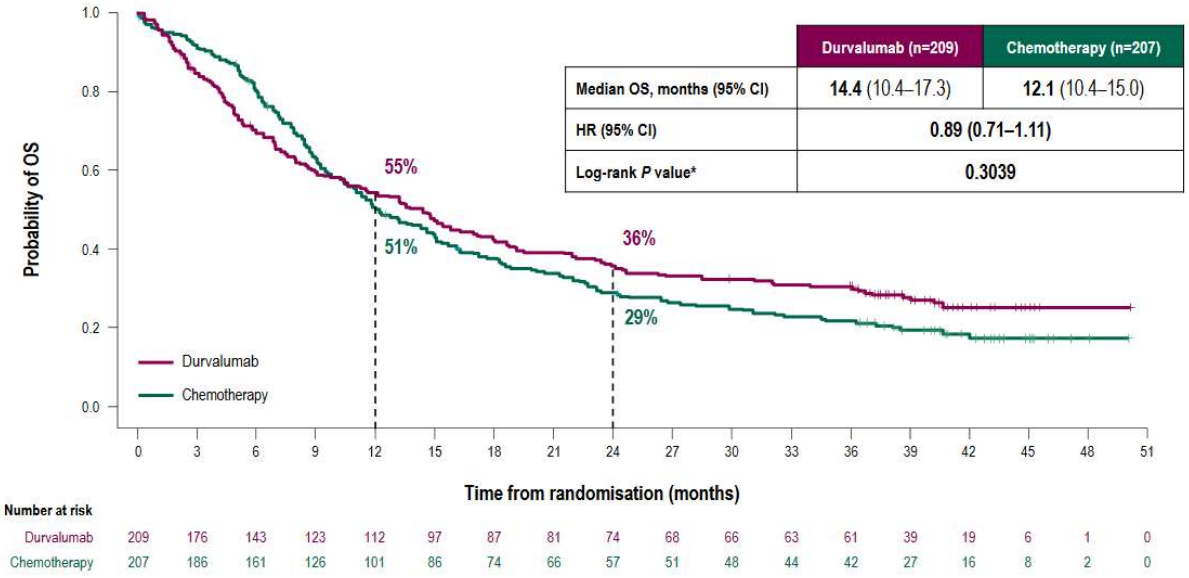
Data cutoff date (final analysis): January 27, 2020

Minimum follow-up from date last patient randomised: 34 months

Median follow-up for survival: 41.2 months for all patients

Powles, ESMO 2020.

Co-primary endpoint – OS in PD-L1-high population

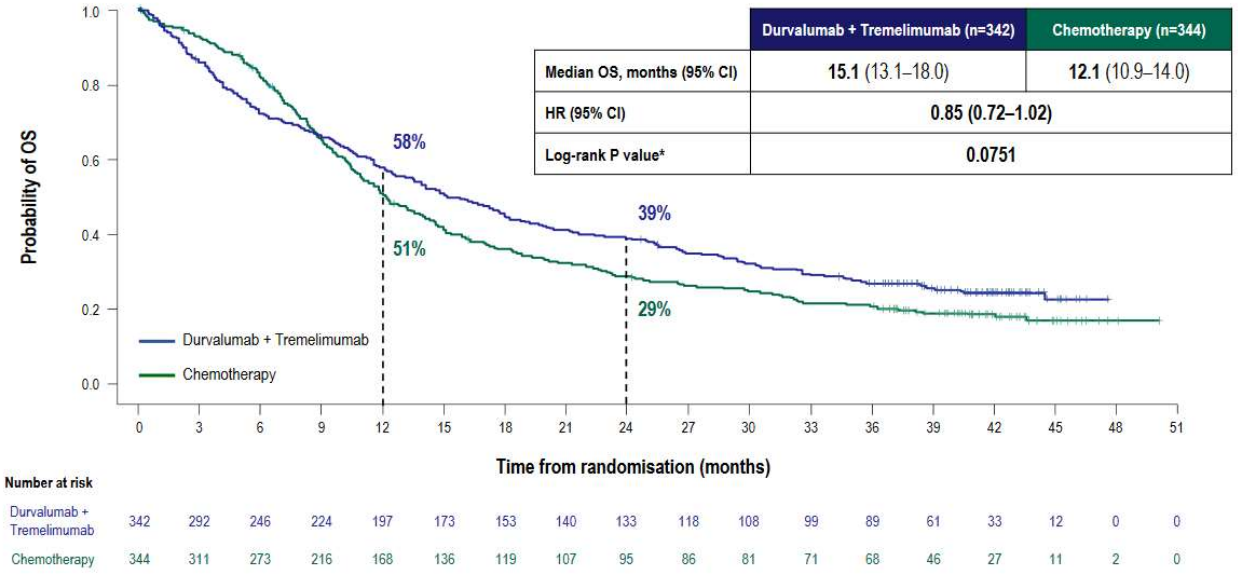


	Durvalumab (n=209)	Chemotherapy (n=207)
Median OS, months (95% CI)	**14.4** (10.4–17.3)	**12.1** (10.4–15.0)
HR (95% CI)	0.89 (0.71–1.11)	
Log-rank *P* value*	0.3039	

	PD-L1–High Population		
Co-primary #1 population Co-primary #2 population	Durvalumab n=209	Durvalumab + Tremelimumab n=205	Chemotherapy n=207
Objective response rate*	28%	47%	48%
Cisplatin eligible	29% (34/117)	47% (54/115)	50% (56/113)
Cisplatin ineligible	26% (24/92)	47% (42/90)	47% (44/94)
Best objective response*			
Complete response	10%	12%	7%
Partial response	18%	35%	41%
Stable disease ≥8 weeks	21%	18%	23%
Progressive disease	51%	34%	20%
Median duration of response*, months (95% CI)	18.5 (7.6–NE)	10.0 (7.4–18.7)	5.8 (5.1–7.0)

Powles, ESMO 2020.

Co-primary endpoint – OS in ITT



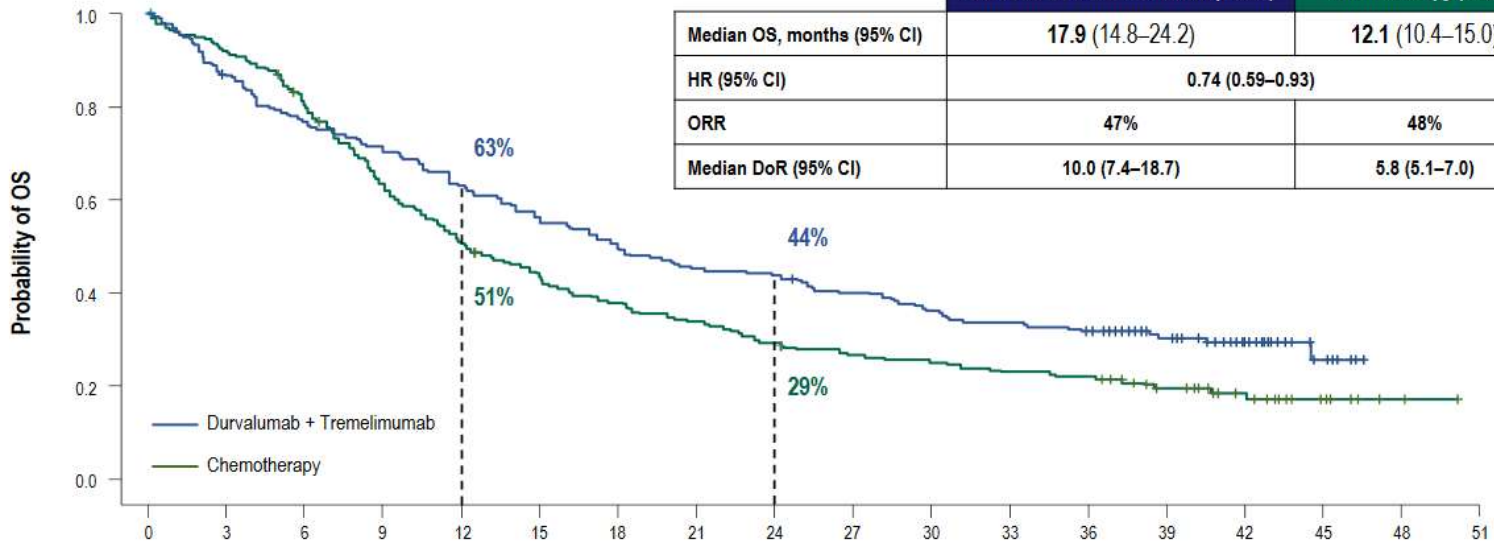
	Durvalumab + Tremelimumab (n=342)	Chemotherapy (n=344)
Median OS, months (95% CI)	**15.1** (13.1–18.0)	**12.1** (10.9–14.0)
HR (95% CI)	0.85 (0.72–1.02)	
Log-rank P value*	0.0751	

	ITT Population		
Co-primary #1 population / Co-primary #2 population	Durvalumab n=346	Durvalumab + Tremelimumab n=342	Chemotherapy n=344
Objective response rate*	26%	36%	49%
Cisplatin eligible	27% (53/197)	37% (71/194)	51% (99/193)
Cisplatin ineligible	24% (36/149)	36% (53/148)	46% (70/151)
Best objective response*			
Complete response	8%	8%	6%
Partial response	18%	28%	43%
Stable disease ≥8 weeks	20%	19%	23%
Progressive disease	53%	42%	18%
Median duration of response*, months (95% CI)	9.3 (5.8–20.5)	11.1 (7.9–18.5)	5.7 (5.6–6.2)

Powles, ESMO 2020.

Combination treatment in PD-L1-high population

	Durvalumab + Tremelimumab (n=205)	Chemotherapy (n=207)
Median OS, months (95% CI)	**17.9** (14.8–24.2)	**12.1** (10.4–15.0)
HR (95% CI)	0.74 (0.59–0.93)	
ORR	47%	48%
Median DoR (95% CI)	10.0 (7.4–18.7)	5.8 (5.1–7.0)



Number at risk

Durva + Treme	205	177	156	144	129	114	101	92	89	81	73	68	63	41	21	6	0	0
Chemotherapy	207	186	161	126	101	86	74	66	57	51	48	44	42	27	16	8	2	0

Powles, ESMO 2020.

Safety summary

	Durvalumab n=345	Durvalumab + Tremelimumab n=340	Chemotherapy n=313
Treatment-related AEs			
Any grade	56%	75%	90%
Grade 3 or 4	14%	28%	60%
Grade 5	1%	1%	<1%
Treatment-related serious AEs	9%	23%	16%
Treatment-related AEs leading to discontinuation	6%	16%	12%
Treatment-related AEs of special interest*			
Any grade	26%	49%	15%
Grade 3 or 4	6%	12%	2%
Systemic corticosteroid use	11%	26%	1%

*Excluding infusion/hypersensitivity reactions.

Powles, ESMO 2020.

Nivolumab plus cabozantinib versus sunitinib in first-line treatment for advanced renal cell carcinoma: first results from the randomized phase 3 CheckMate 9ER trial

Toni K. Choueiri, Thomas Powles, Mauricio Burotto, Maria T. Bourlon, Bogdan Zurawski, Víctor Manuel Oyervides Juárez, James J. Hsieh, Umberto Basso, Amishi Y. Shah, Cristina Suarez, Alketa Hamzaj, Carlos Barrios, Martin Richardet, David Pook, Yoshihiko Tomita, Bernard Escudier, Joshua Zhang, Burcin Simsek, Andrea B. Apolo, Robert J. Motzer

Study design

Stratification factors:
- IMDC risk score
- Tumor PD-L1 expression[a]
- Geographic region

N = 651

Key inclusion criteria[1,2]
- Previously untreated advanced or metastatic RCC
- Clear cell component
- Any IMDC risk group

R 1:1

- NIVO 240 mg IV Q2W + CABO 40 mg PO QD
- SUN 50 mg PO QD, cycle of 4 weeks on/ 2 weeks off

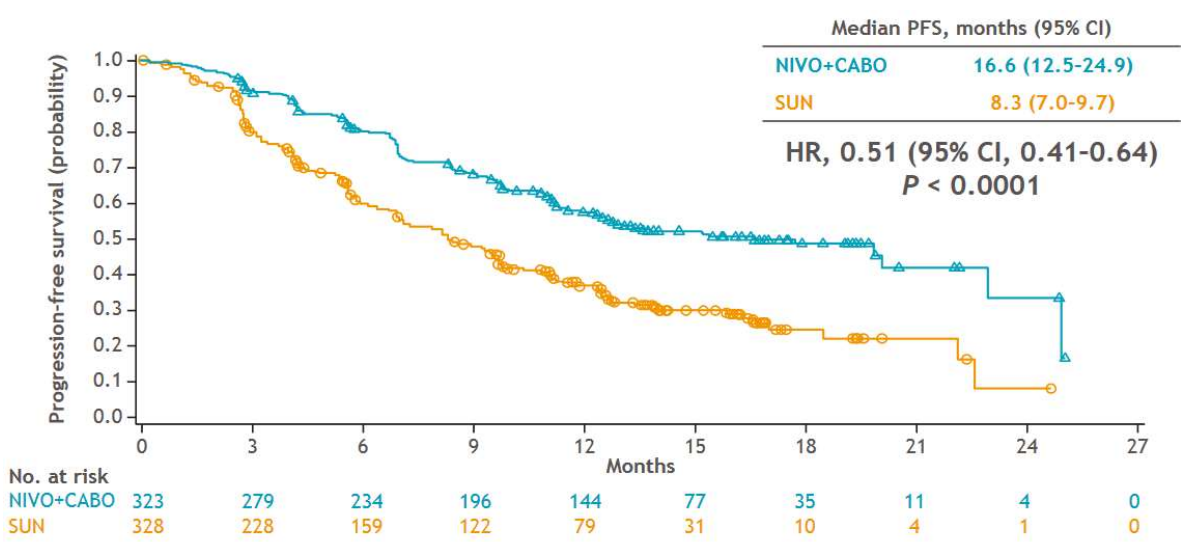
Treat until RECIST v1.1-defined progression or unacceptable toxicity[b]

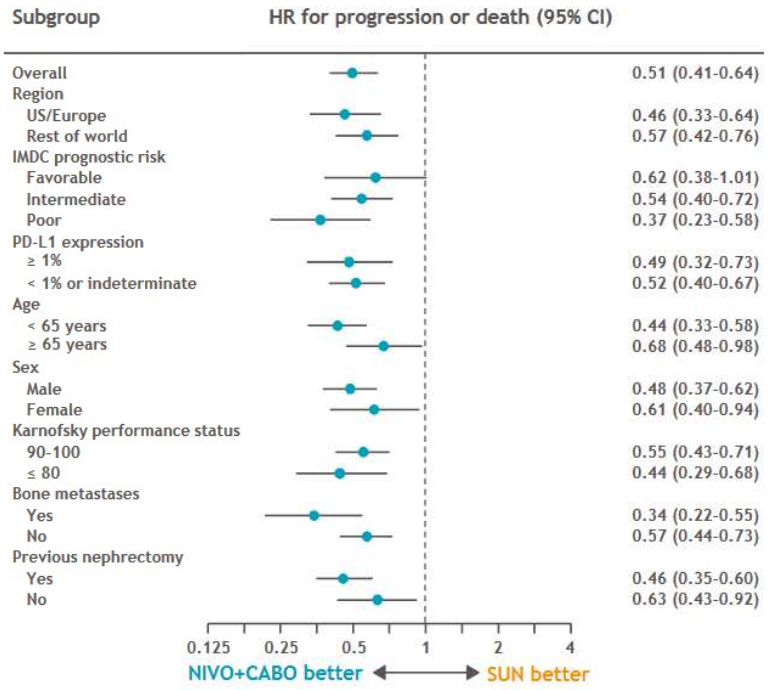
Median study follow-up, 18.1 months (range, 10.6-30.6 months)

Primary endpoint: PFS
Secondary endpoints: OS, ORR, and safety

Choueiri, ESMO 2020.

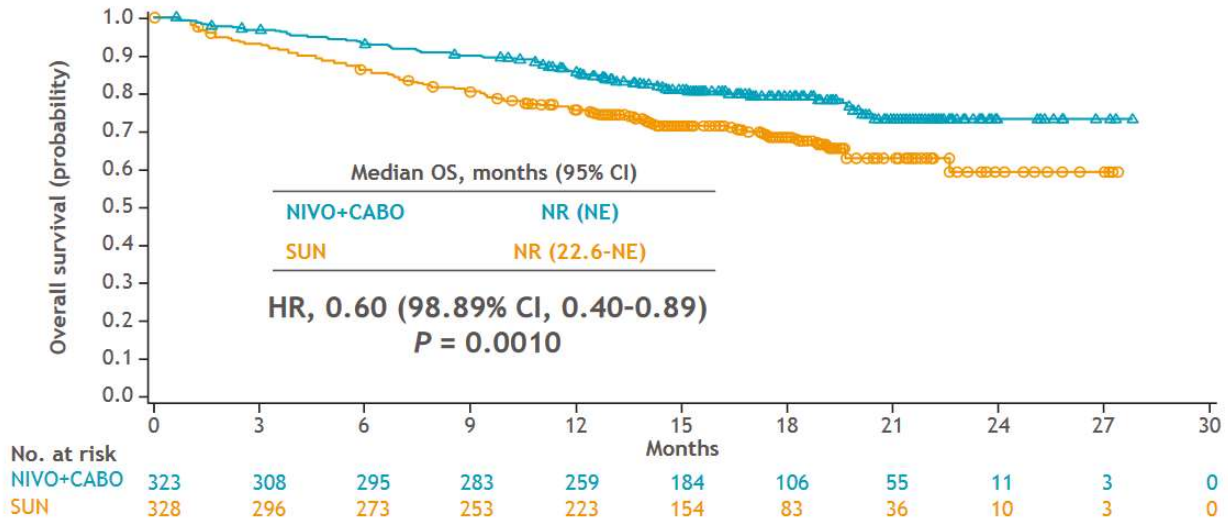
Primary endpoint: PFS

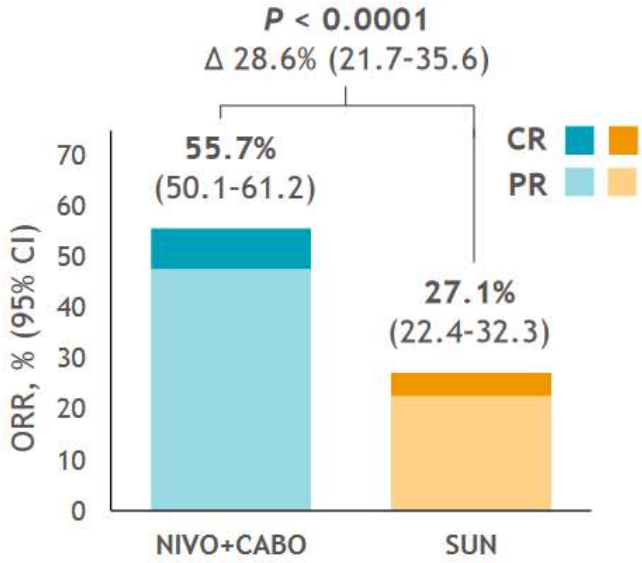




Choueiri, ESMO 2020.

Secondary endpoints: OS and ORR

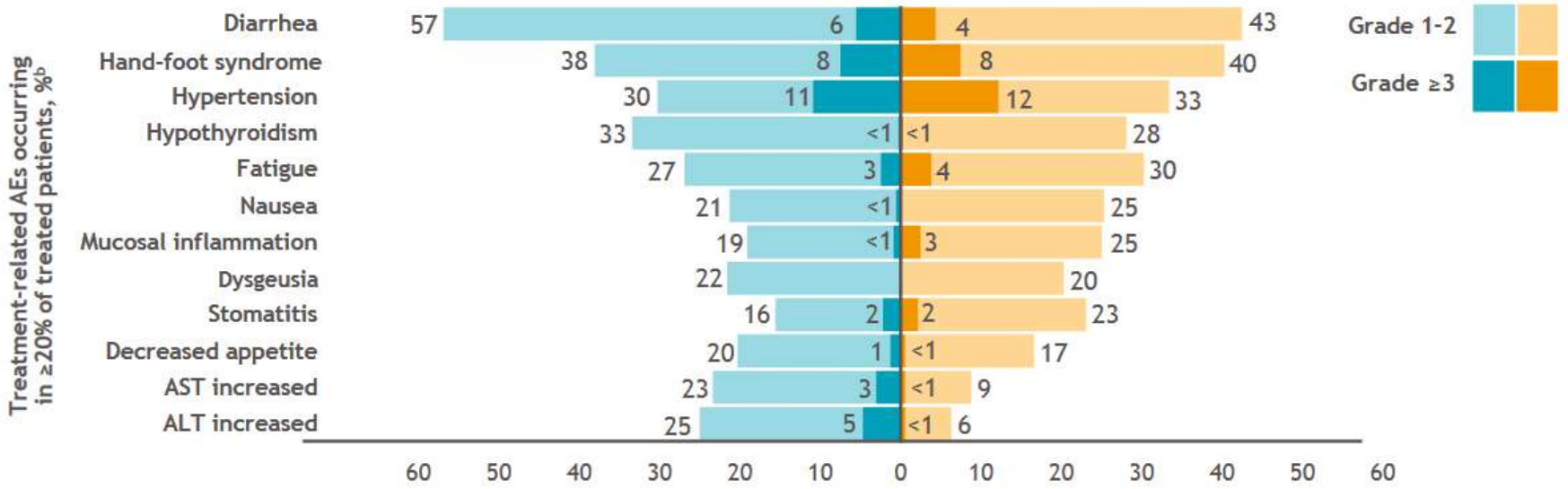




Choueiri, ESMO 2020.

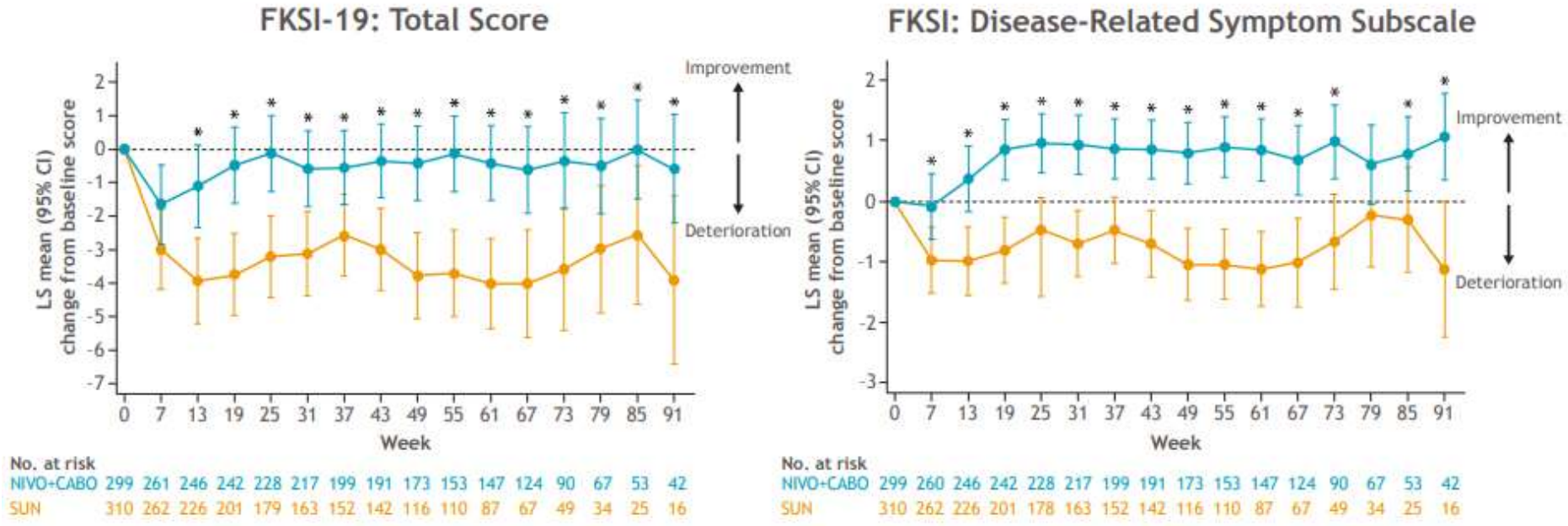
Safety summary

Events, %[a]	NIVO+CABO, n = 320		SUN, n = 320	
	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
All-cause AEs	100	75	99	71
Treatment-related AEs	97	61	93	51



Choueiri, ESMO 2020.

Health-related quality of life



Choueiri, ESMO 2020.

Cabozantinib in combination with atezolizumab as first-line therapy for advanced clear-cell renal cell carcinoma: results from the COSMIC-021 study

Sumanta Pal, Che-Kai Tsao, Cristina Suarez, William Kelly, Lance Pagliaro, Ulka Vaishampayan, Yohann Loriot, Sandy Srinivas, Bradley McGregor, Ashok Panneerselvam, Dominic Curran, Toni K. Choueiri, Neeraj Agarwal

Study design

Advanced or metastatic ccRCC
- No prior systemic therapy for RCC
- Measurable disease per RECIST v1.1
- ECOG PS 0 or 1

Expansion Cohorts

April 2018*	January 2019*
Cabozantinib 40 mg QD PO + Atezolizumab 1200 mg Q3W IV (N=30)	Cabozantinib 60 mg QD PO + Atezolizumab 1200 mg Q3W IV (N=30)

Tumor assessments per RECIST v1.1 by the investigator every 6 weeks for the first year and every 12 weeks thereafter; treatment until loss of clinical benefit or intolerable toxicity.

- 10 patients with previously untreated ccRCC were enrolled in the dose-escalation phase (4 at a dose level of 40 mg and 6 at a dose level of 60 mg)
- Data are presented for all 70 ccRCC patients with a data cutoff of July 21, 2020 and a median follow-up of 25.8 months (range, 20-33) for the 40 mg dose group and 15.3 months (range, 10-32) for the 60 mg dose group

Primary Endpoint: ORR by the investigator per RECIST v1.1
Secondary Endpoint: Safety
Exploratory endpoints include PFS and correlations of biomarkers with outcomes

Pal, ESMO 2020.

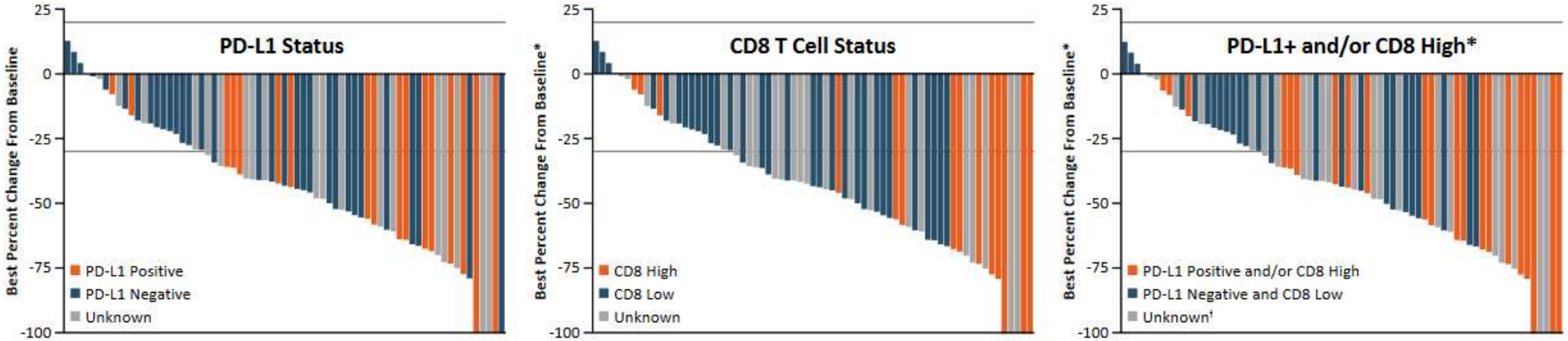
Primary endpoint: response rate

	Cabozantinib 40 mg + Atezolizumab 1200 mg (N=34)	Cabozantinib 60 mg + Atezolizumab 1200 mg (N=36)
Objective response rate (80% CI), %	53 (41–65)	58 (46–70)
Best overall response, n (%)		
Complete response	1 (3)	4 (11)
Partial response	17 (50)	17 (47)
Stable disease	14 (41)	12 (33)
Progressive disease	2 (6)	2 (6)
Missing	0	1 (3)
Disease control rate,* %	94	92
Duration of response, median (range), mo	NE (12.4–NE)	15.4 (8.1–NE)
Time to objective response, median (range), mo	1.4 (1–19)	1.5 (1–7)

Pal, ESMO 2020.

Correlative studies

Best Percent Change in Tumor Target Lesions



Best Overall Response

PD-L1 Status (SP142 CPS)	CR or PR N (%)	SD or PD N (%)	p value‡
Positive	15 (88%)	2 (12%)	0.001
Negative	13 (39%)	20 (61%)	

CD8 T Cell Status	CR or PR N (%)	SD or PD N (%)	p value‡
High	11 (79%)	3 (21%)	0.05
Low	14 (44%)	18 (56%)	

PD-L1+ and/or CD8 High	CR or PR N (%)	SD or PD N (%)	p value‡
Positive or High	18 (86%)	3 (14%)	0.0003
Negative and Low	8 (31%)	18 (69%)	

Pal, ESMO 2020.

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Adverse events

	Cabozantinib 40 mg + Atezolizumab 1200 mg (N=34)		Cabozantinib 60 mg + Atezolizumab 1200 mg (N=36)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Any AE, n (%)	33 (97)	24 (71)	36 (100)	24 (67)
Diarrhea	23 (68)	3 (9)	24 (67)	7 (19)
Fatigue	22 (65)	2 (6)	20 (56)	2 (6)
Nausea	14 (41)	0	16 (44)	1 (3)
Dysgeusia	12 (35)	0	21 (58)	0
Hypertension	12 (35)	8 (24)	12 (33)	5 (14)
ALT increased	11 (32)	1 (3)	12 (33)	5 (14)
PPE	10 (29)	0	20 (56)	0
Stomatitis	10 (29)	0	10 (28)	0
AST increased	9 (26)	0	14 (39)	2 (6)
Hypophosphatemia	9 (26)	5 (15)	3 (8)	1 (3)
Decreased appetite	8 (24)	0	19 (53)	0
Pruritus	8 (24)	1 (3)	5 (14)	0
Hypothyroidism	6 (18)	0	10 (28)	0
Weight Decreased	6 (18)	0	9 (25)	1 (3)
Lipase Increased	5 (15)	1 (3)	8 (22)	3 (8)
Mucosal inflammation	4 (12)	0	8 (22)	2 (6)
Proteinuria	2 (6)	0	8 (22)	1 (3)

Pal, ESMO 2020.

GU summary and trends

- Urothelial Cancer (DANUBE Trial):
  - No statistical benefit for co-primary endpoints of OS in 1L mUC:
    - Durvalumab vs. chemo in PD-L1 +
    - Durvalumab + Tremelimumab in all comers
    - Results from phase III Nivolumab+ Ipilimumab (Nivo+Ipi) vs. Chemotherapy (CheckMate901) are pending.

- Renal Cell Carcinoma (CHECKMATE 9ER, COSMIC 021):
  - Cabozantinib + Nivolumab improved PFS, OS, ORR and QOL over sunitinib in 1L metastatic ccRCC of all IMDC risk groups -> potential new standard 1st line.
    - Cabozantinib + Nivo/Ipi vs. Nivo/Ipi phase III trial in intermediate/poor risk is ongoing (COSMIC-313)
  - Cabozantinib + Atezolizumab is clinically active and safe in metastatic ccRCC
    - Phase III of cabozantinib +/- atezolizumab in RCC previously treated with immune checkpoint inhibitors is ongoing (CONTACT-03)

EE [2]2

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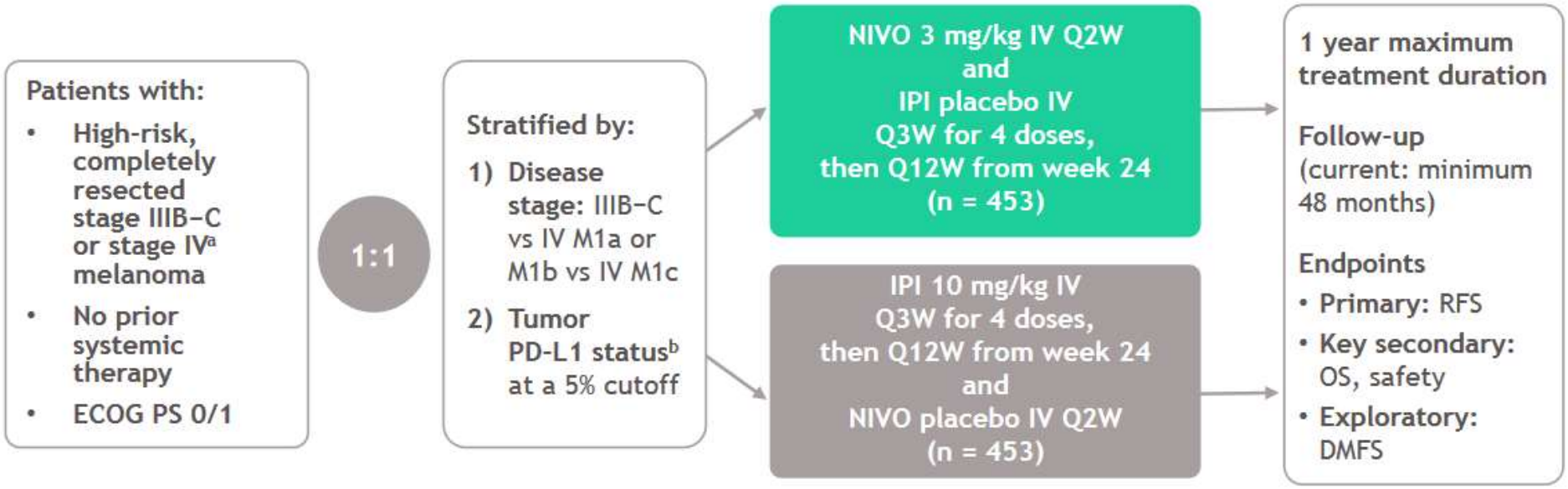
Webinar outline

- Genitourinary cancers
- Melanoma
- Head and neck cancer
- Gastrointestinal cancer
- Novel agents

Adjuvant nivolumab vs ipilimumab in resected stage III/IV melanoma: 4-year recurrence-free and overall survival results from CheckMate 238

Jeffrey Weber, Michele Del Vecchio, Mario Mandalá, Helen Gogas, Ana M. Arance, Stephane Dalle, C. Lance Cowey, Michael Schenker, Jean-Jacques Grob, Vanna Chiarion-Sileni, Iván Márquez-Rodas, Marcus O. Butler, Michele Maio, Mark R. Middleton, Luis de la Cruz-Merino, Maurice Lobo, Veerle de Pril, James Larkin, Paolo A. Ascierto

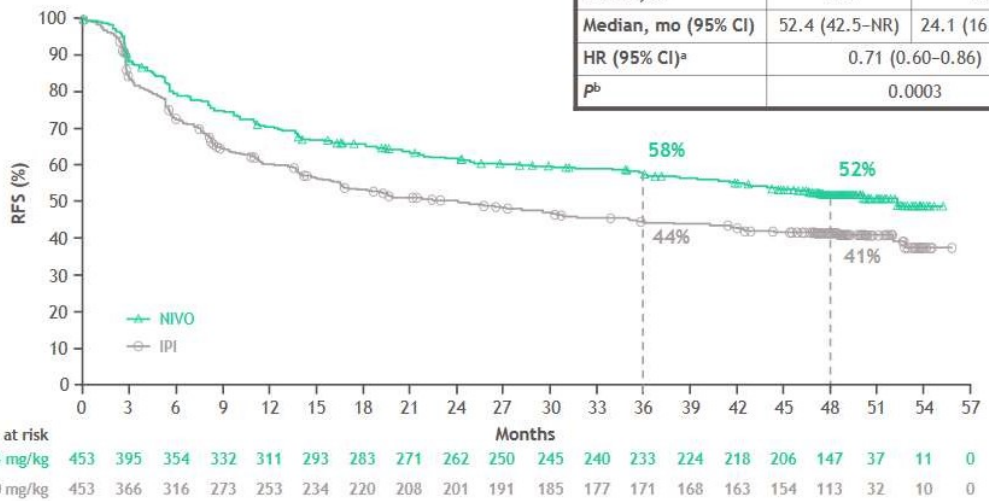
Study design



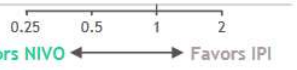
Weber, ESMO 2020.

Primary endpoint: 48-month RFS

	NIVO (n = 453)	IPI (n = 453)
Events, n	212	253
Median, mo (95% CI)	52.4 (42.5–NR)	24.1 (16.6–35.1)
HR (95% CI)[a]	0.71 (0.60–0.86)	
P[b]	0.0003	



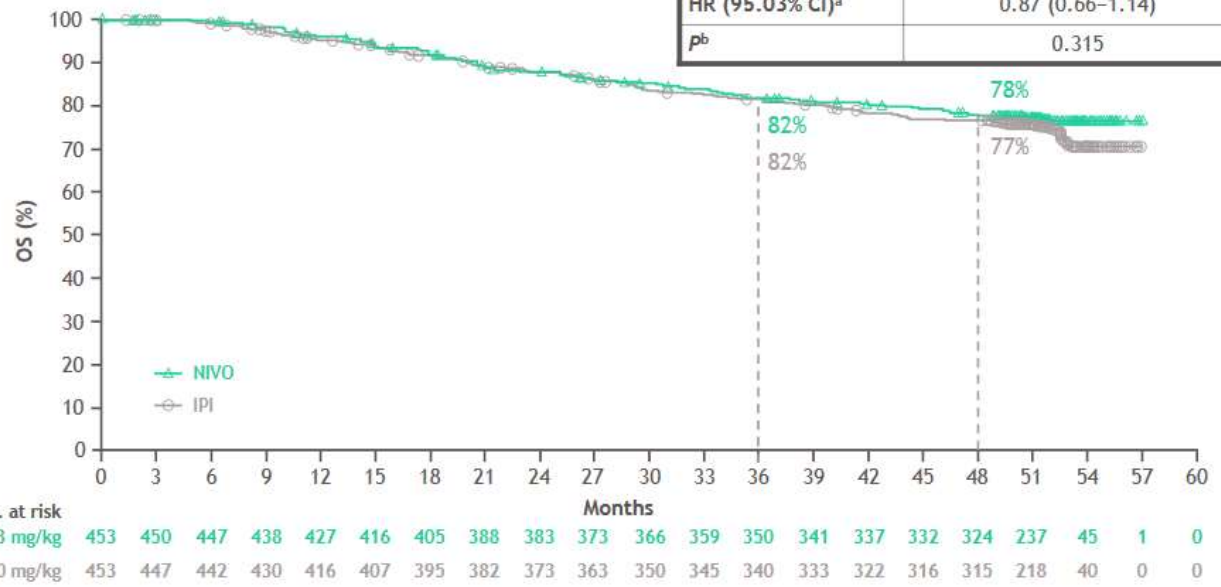
Subgroup		Unstratified HR (95% CI)
Overall	Overall	0.72 (0.60–0.86)
Age	< 65 years	0.72 (0.58–0.89)
	≥ 65 years	0.72 (0.51–1.00)
Sex	Male	0.74 (0.59–0.93)
	Female	0.69 (0.52–0.93)
Stage	IIIB	0.70 (0.50–0.98)
	IIIC	0.74 (0.57–0.96)
	IV M1a–M1b	0.65 (0.41–1.03)
	IV M1c	1.13 (0.44–2.93)
	Not reported	–
Stage III: ulceration	Absent	0.65 (0.49–0.86)
	Present	0.79 (0.58–1.07)
	Not reported	0.55 (0.17–1.74)
Stage III: lymph node involvement	Microscopic	0.71 (0.50–1.00)
	Macroscopic	0.75 (0.58–0.97)
	Not reported	0.47 (0.19–1.13)
Tumor PD-L1 status[a]	< 5% or indeterminate	0.74 (0.59–0.91)
	≥ 5%	0.67 (0.47–0.96)
BRAF mutation status	Positive	0.79 (0.60–1.05)
	Negative	0.69 (0.53–0.91)
	Not reported	0.66 (0.38–1.12)



Weber, ESMO 2020.

Secondary endpoint: 48-month OS

	NIVO (n = 453)	IPI (n = 453)
Events, n	100	111
Median, mo (95% CI)	NR	NR
HR (95.03% CI)[a]	0.87 (0.66–1.14)	
P[b]	0.315	



Weber, ESMO 2020.

Late-emergent TRAEs

TRAE[a]	Nivolumab (n = 452), n (%)		Ipilimumab (n = 453), n (%)	
	Any grade	Grade 3–4	Any grade	Grade 3–4
Any	18 (4.0)	3 (0.7)	25 (5.5)	7 (1.5)
Arthralgia	2 (0.4)	0	1 (0.2)	0
Colitis	2 (0.4)	0	2 (0.4)	2 (0.4)
Diabetic ketoacidosis	1 (0.2)	1 (0.2)	0	0
Diarrhea	1 (0.2)	1 (0.2)	4 (0.9)	1 (0.2)
Maculopapular rash	1 (0.2)	0	2 (0.4)	1 (0.2)
Pneumonitis	1 (0.2)	1 (0.2)	0	0
Pruritus	1 (0.2)	0	3 (0.7)	0
Vitiligo	1 (0.2)	0	2 (0.4)	0
Fatigue	0	0	2 (0.4)	0
Increased lipase	0	0	2 (0.4)	1 (0.2)
Pyrexia	0	0	2 (0.4)	0
Bone marrow failure	0	0	1 (0.2)	1 (0.2)
Immune thrombocytopenic purpura	0	0	1 (0.2)	1 (0.2)
Rash	0	0	1 (0.2)	1 (0.2)
Secondary adrenocortical insufficiency	0	0	1 (0.2)	1 (0.2)

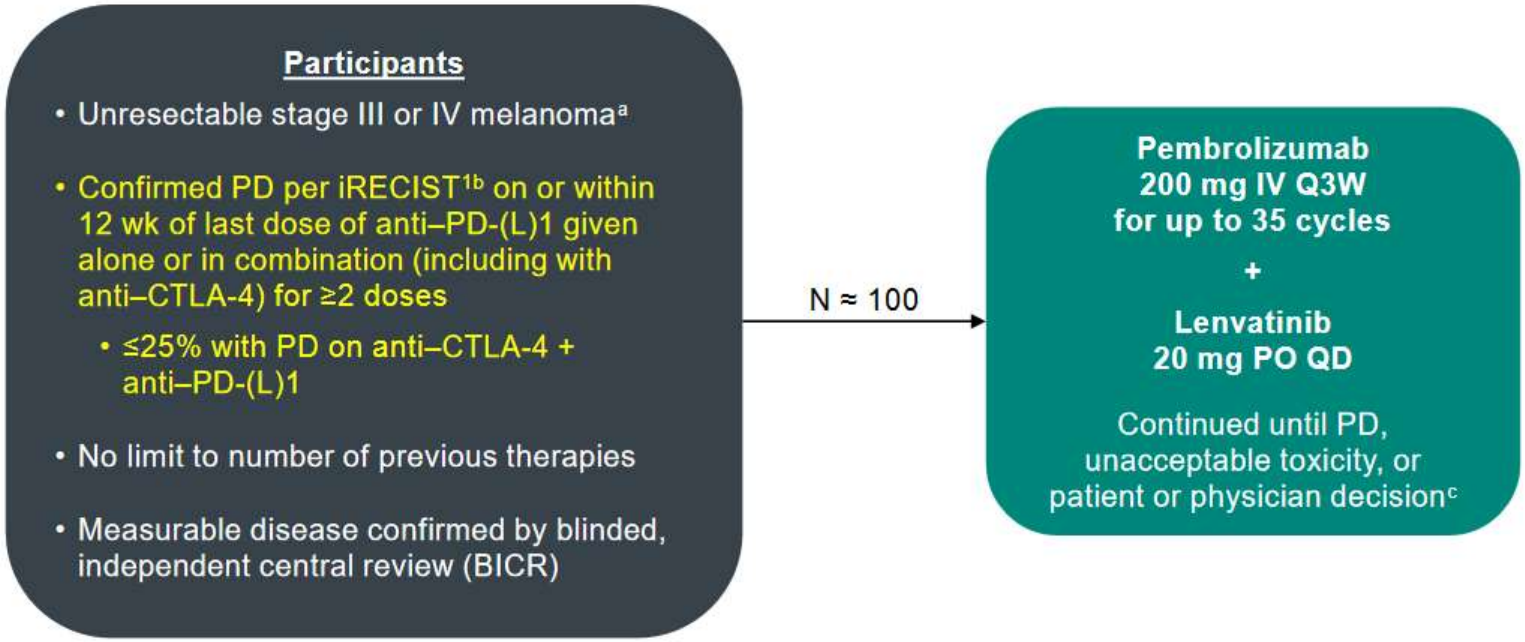
As reported previously, at 18 months of follow-up, all patients had been off study treatment for > 100 days; grade 3–4 TRAEs were reported in 14.4% patients treated with NIVO and 45.9% patients treated with IPI[1]

Weber, ESMO 2020.

Lenvatinib Plus Pembrolizumab For Advanced Melanoma That Progressed on a PD-1 or PD-L1 Inhibitor: Initial Results of LEAP-004

Ana Arance, Steven J. O'Day, Luis de la Cruz Merino, Teresa M. Petrella, Rahima Jamal, Lars Ny, Ana Carneiro, Alfonso Berrocal, Ivan Márquez-Rodas, Anna Spreafico, Victoria Atkinson, Fernanda Costa Svedman, Alan D. Smith, Ke Chen, Scott J. Diede, Clemens Krepler, Georgina V. Long

Study design



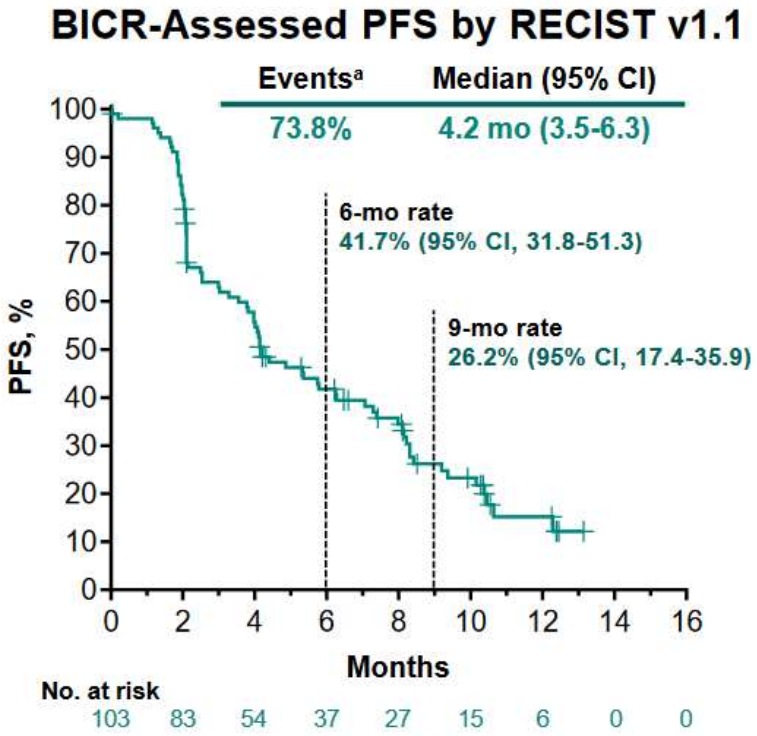
Arance, ESMO 2020.

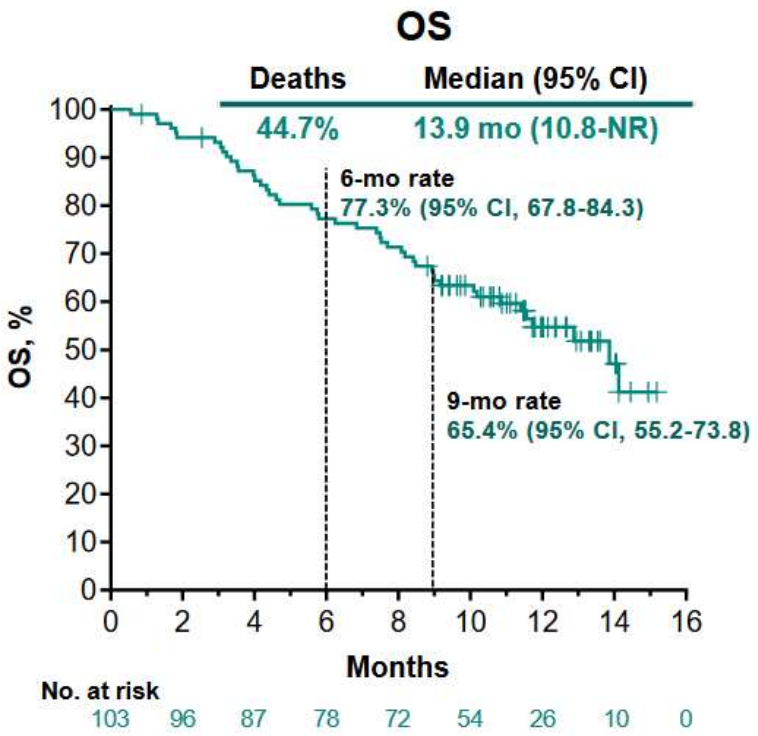
Primary endpoint: ORR

	Total Population N = 103	PD on Prior Anti–CTLA-4 + Anti–PD-(L)1 Yes n = 29	PD on Prior Anti–CTLA-4 + Anti–PD-(L)1 No n = 74
ORR, % (95% CI)	**21.4% (13.9-30.5)**	**31.0% (15.3-50.8)**	**17.6% (9.7-28.2)**
DCR, % (95% CI)	65.0% (55.0-74.2)	62.1% (42.3-79.3)	66.2% (54.3-76.8)
Best overall response, n (%)			
CR	2 (1.9%)	1 (3.4%)	1 (1.4%)
PR	20 (19.4%)	8 (27.6%)	12 (16.2%)
SD	45 (43.7%)	9 (31.0%)	36 (48.6%)
PD	31 (30.1%)	10 (34.5%)	21 (28.4%)
Not assessed[a]	5 (4.9%)	1 (3.4%)	4 (5.4%)

Arance, ESMO 2020.

Secondary endpoints: PFS and OS





Arance, ESMO 2020.

Adverse events

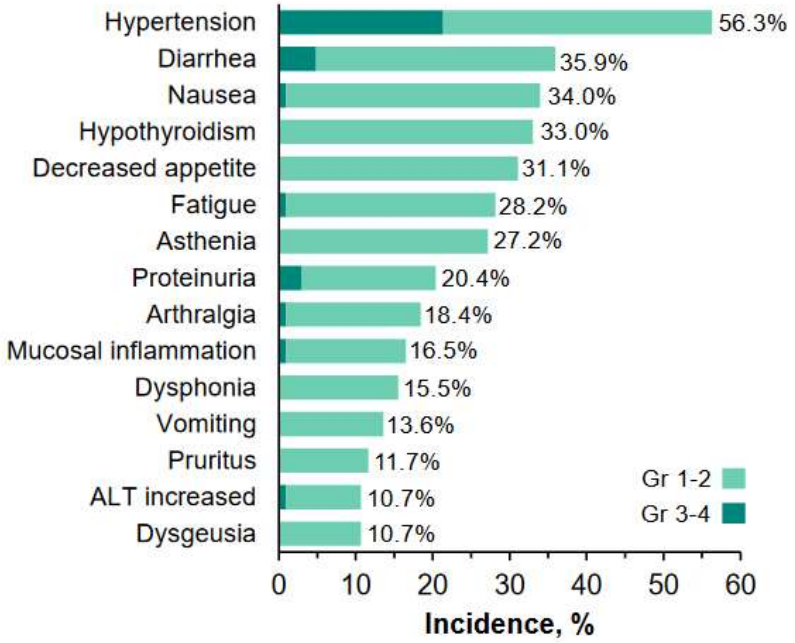
Summary

n (%)	N = 103
Any grade	99 (96.1%)
Grade 3-5	46 (44.7%)
Grade 3	41 (39.8%)
Grade 4	4 (3.9%)
Grade 5	1 (1.0%)[a]
Serious	19 (18.4%)
Led to discontinuation[b]	8 (7.8%)
Led to interruption[b]	61 (59.2%)
Led to len dose reduction	55 (53.4%)

Median (range) duration of treatment

- 6.0 mo (4 d-14.9 mo) for len
- 5.5 mo (1 d-14.5 mo) for pembro

Incidence ≥10%

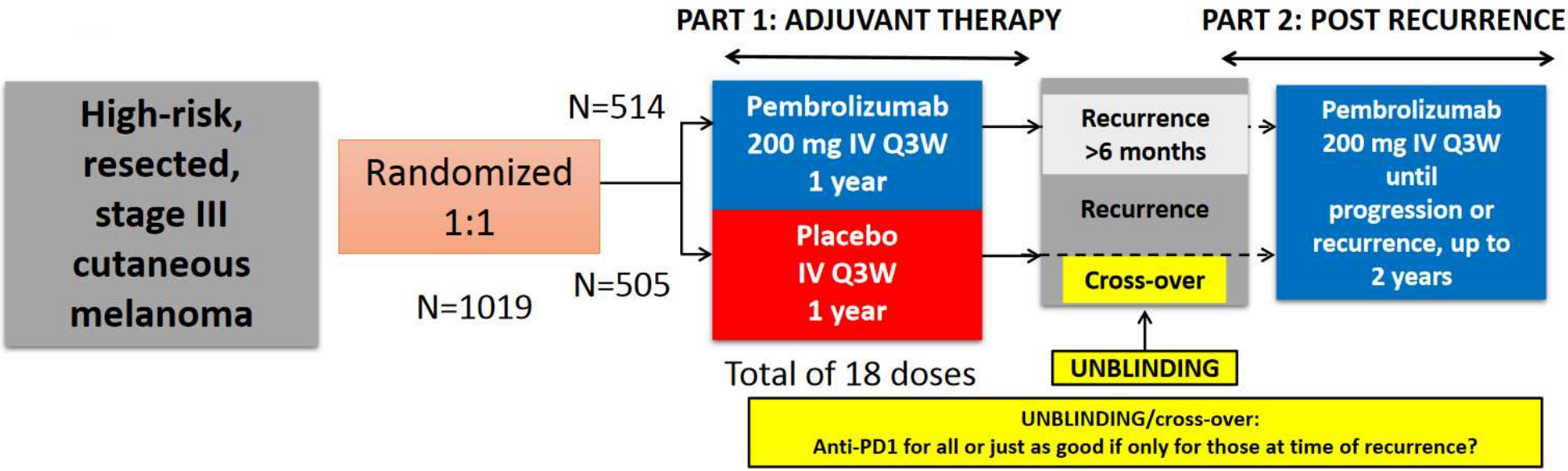


Arance, ESMO 2020.

Pembrolizumab versus placebo after complete resection of high-risk stage III melanoma: final results regarding distant metastasis-free survival results from the EORTC 1325-MG/Keynote 054 double-blinded phase 3 trial

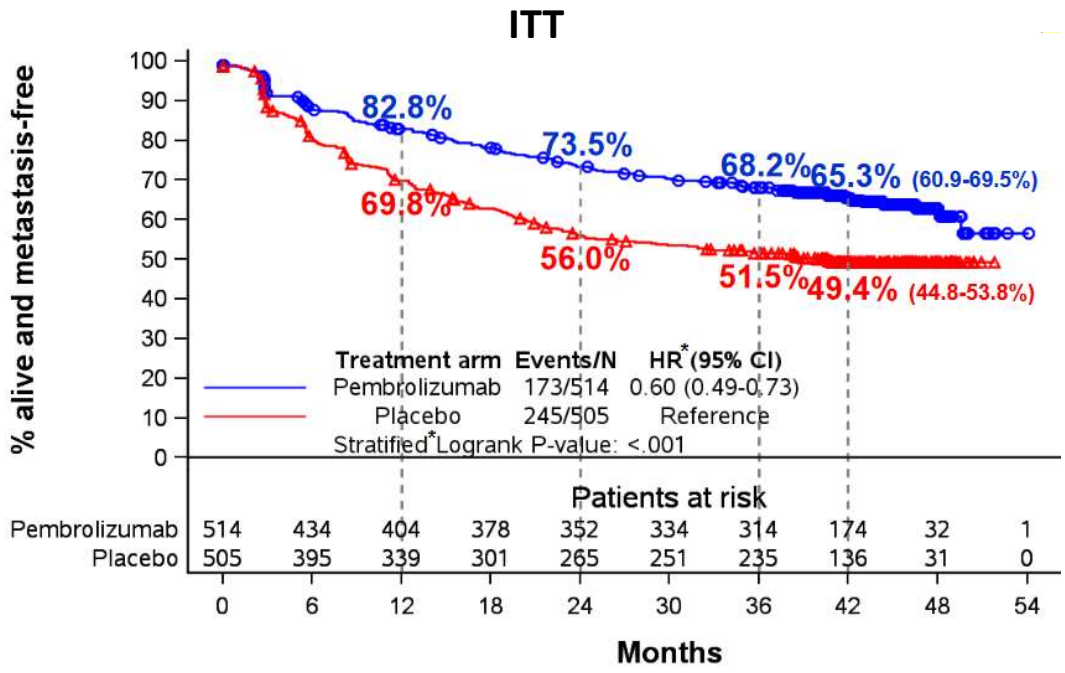
Alexander MM Eggermont, MD, PhD, Christian U Blank, MD, PhD, Mario Mandala, MD, Georgina V Long, MD, PhD, Victoria Atkinson, MD, Stéphane Dalle, MD, Andrew Haydon, MD, Andrey Meshcheryakov, MD, Adnan Khattak, MD, Matteo S Carlino, MD, PhD, Shahneen Sandhu, MD, Susana Puig, MD, PhD, Paolo A Ascierto, MD, Alexander van Akkooi, MD, PhD, Clemens Krepler, MD, Nageatte Ibrahim, MD, Sandrine Marreaud, MD, Michal Kicinski, PhD, Stefan Suciu, PhD, Caroline Robert, MD, PhD

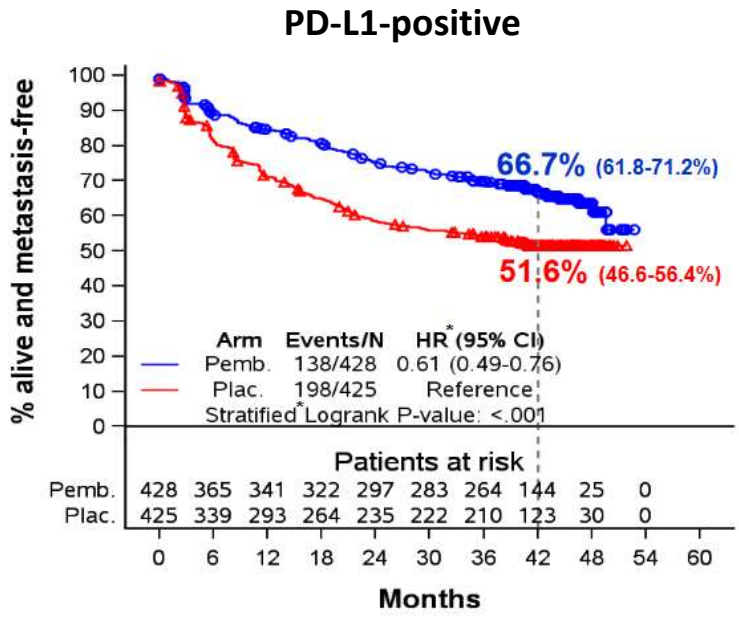
Study design



Eggermont, ESMO 2020.

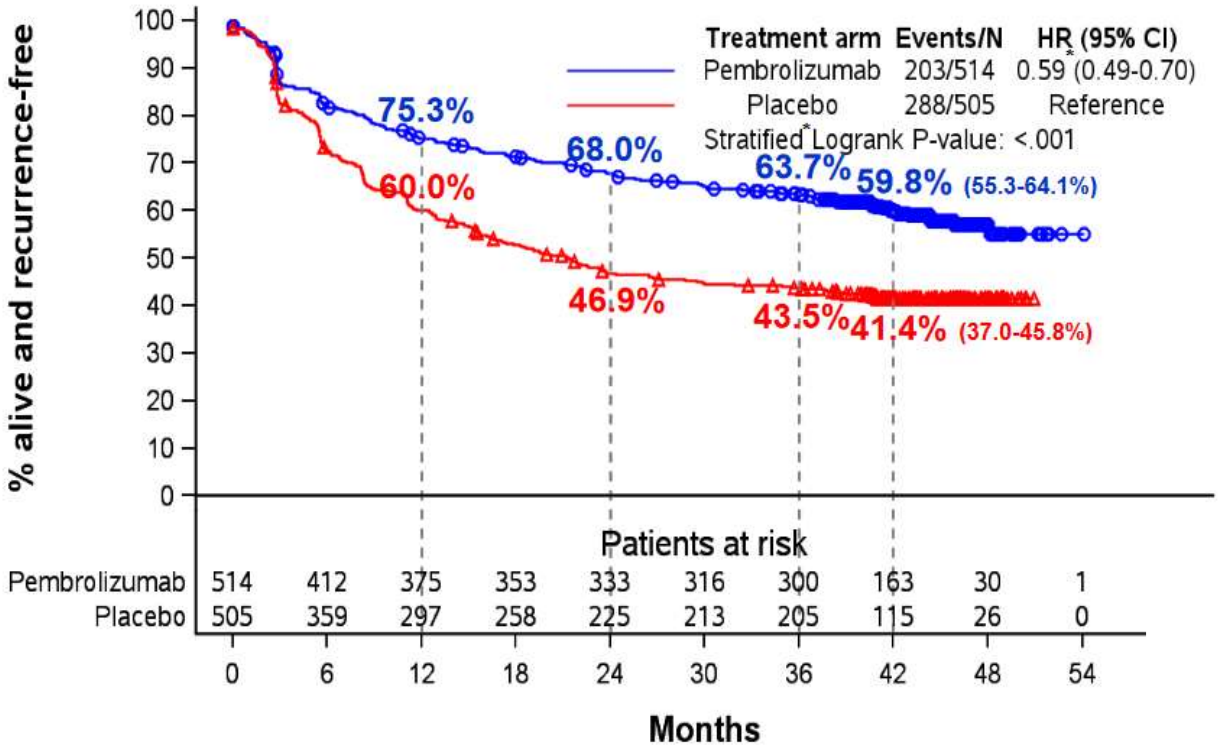
Secondary endpoint: final DMFS analysis





Eggermont, ESMO 2020.

Updated primary endpoint analysis: RFS



Eggermont, ESMO 2020.

Immune-related adverse events

	Pembrolizumab (n=509)		Placebo (n=502)	
	Grade ≥1	Grade ≥3	Grade ≥1	Grade ≥3
Any irAE	37.7%	7.7%	9.0%	0.6%
Endocrine disorders	23.4%	1.6%	5.0%	0%
Respiratory/thoracic disorders	4.9%	0.8%	0.6%	0%
Vitiligo or severe skin reactions	5.9%	1.0%	1.6%	0%
Gastrointestinal disorders	4.1%	2.2%	0.8%	0.4%
Hepatobilliary disorders	1.8%	1.4%	0.2%	0.2%
Other irAEs	3.3%	1.2%	1.0%	0%

Eggermont, ESMO 2020.

Melanoma summary and trends

- Adjuvant therapy stage IIIB/C/IV (Checkmate-238 Trial):
  - 48 month relapse-free survival shows NIVO still superior to IPI; HR=0.71, P=0.0003
  - Patients with in transit metastases also benefit
  - No difference in overall survival noted between the arms
- Adjuvant therapy stage IIA/B/C (Keynote-054 Trial):
  - 42 month relapse-free survival shows PEMBRO still superior to placebo; HR=0.59, P=0.001
  - 42 month distant metastases-free survival also superior for PEMBRO
  - Grade 3-5 immune-related adverse events low at 7.7%
- Metastatic therapy stage IV (LEAP-004 Trial):
  - 31% response rate in PD-1 refractory patients
  - Median PFS was 4.2 months and median OS was 13.2 months
  - 7.8% of patients stopped therapy due to treatment-related adverse events

Society for Immunotherapy of Cancer

Webinar outline

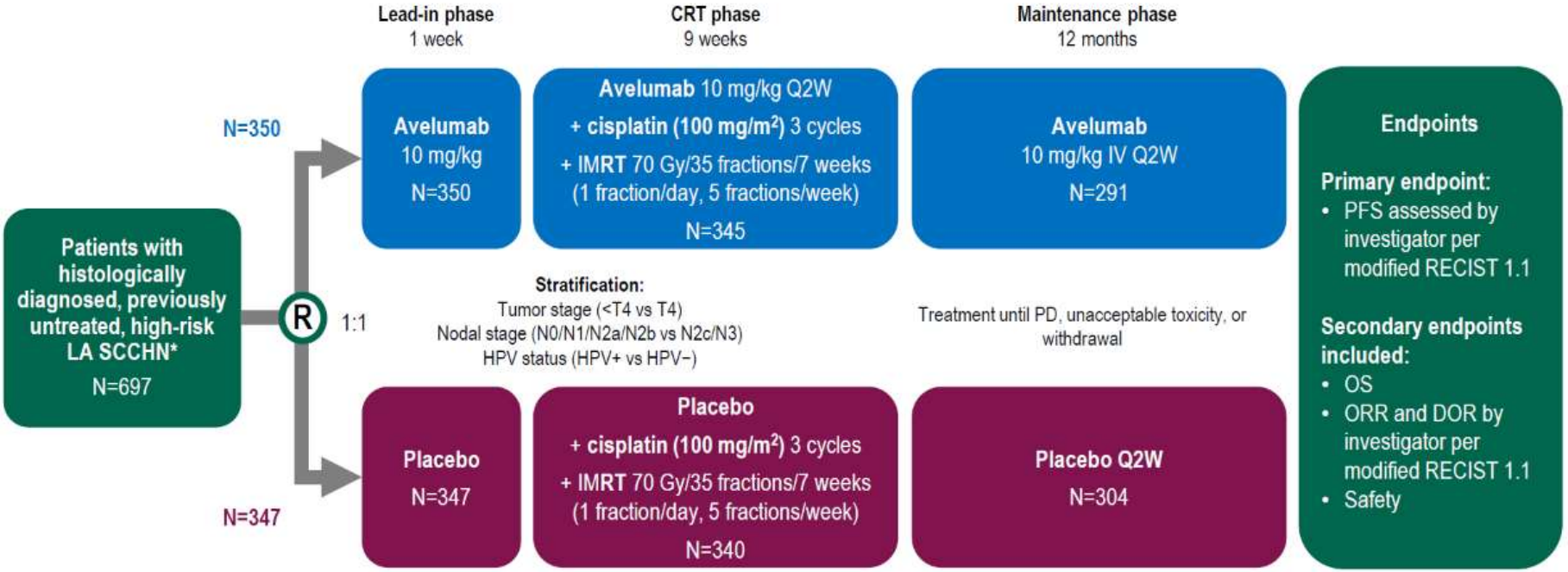
- Genitourinary cancers
- Melanoma
- Head and neck cancer
- Gastrointestinal cancer
- Novel agents

Society for Immunotherapy of Cancer

Primary results of the phase 3 JAVELIN Head & Neck 100 trial: avelumab plus chemoradiotherapy (CRT) followed by avelumab maintenance vs CRT in patients with locally advanced squamous cell carcinoma of the head and neck (LA SCCHN)

E.W. Cohen, R.L. Ferris, A. Psyrri, R.I. Haddad, M. Tahara, J. Bourhis, K. Harrington, P. M-H. Chang, J-C. Lin, A. Razaq, M.M. Teixeira, J. Lovey, J. Chamois, A. Rueda, C. Hu, M.V. Dvorkin, S. De Beukelaer, D. Pavlov, H. Thurm, N. Lee

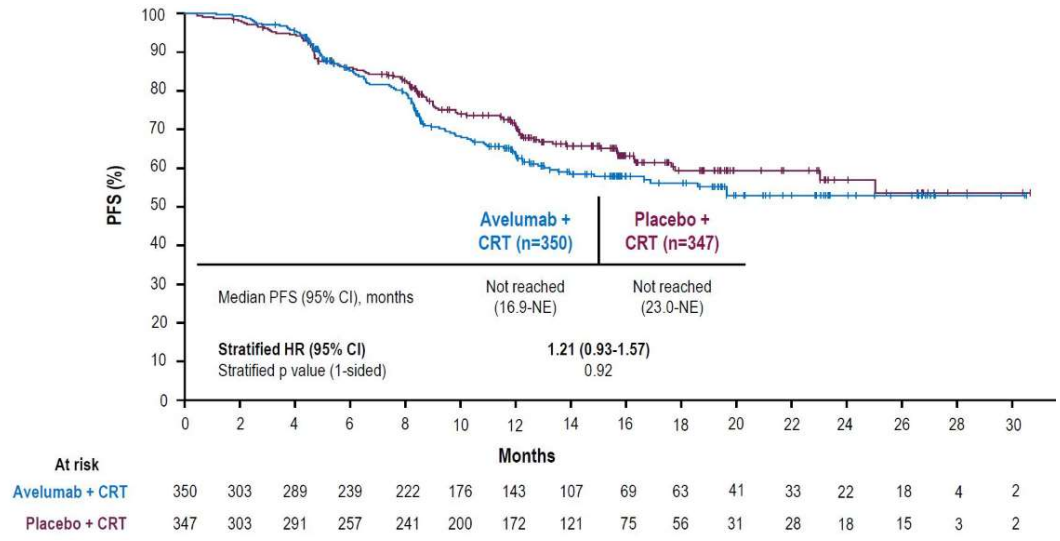
Study design

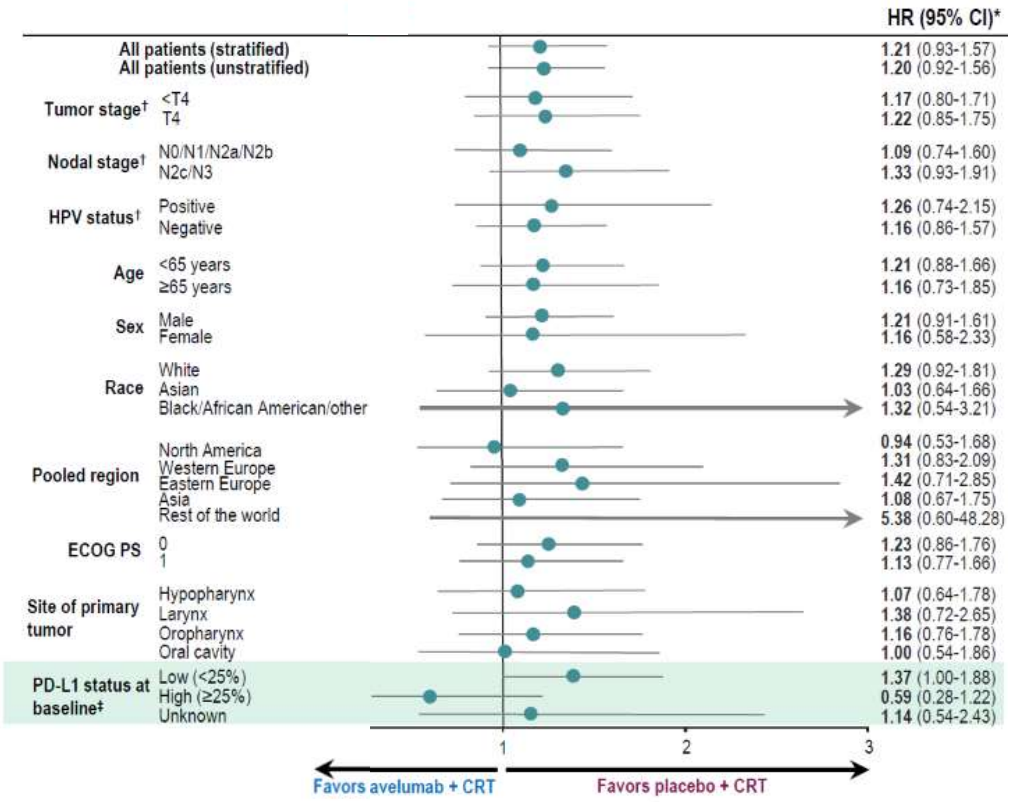


Cohen, ESMO 2020.

Society for Immunotherapy of Cancer

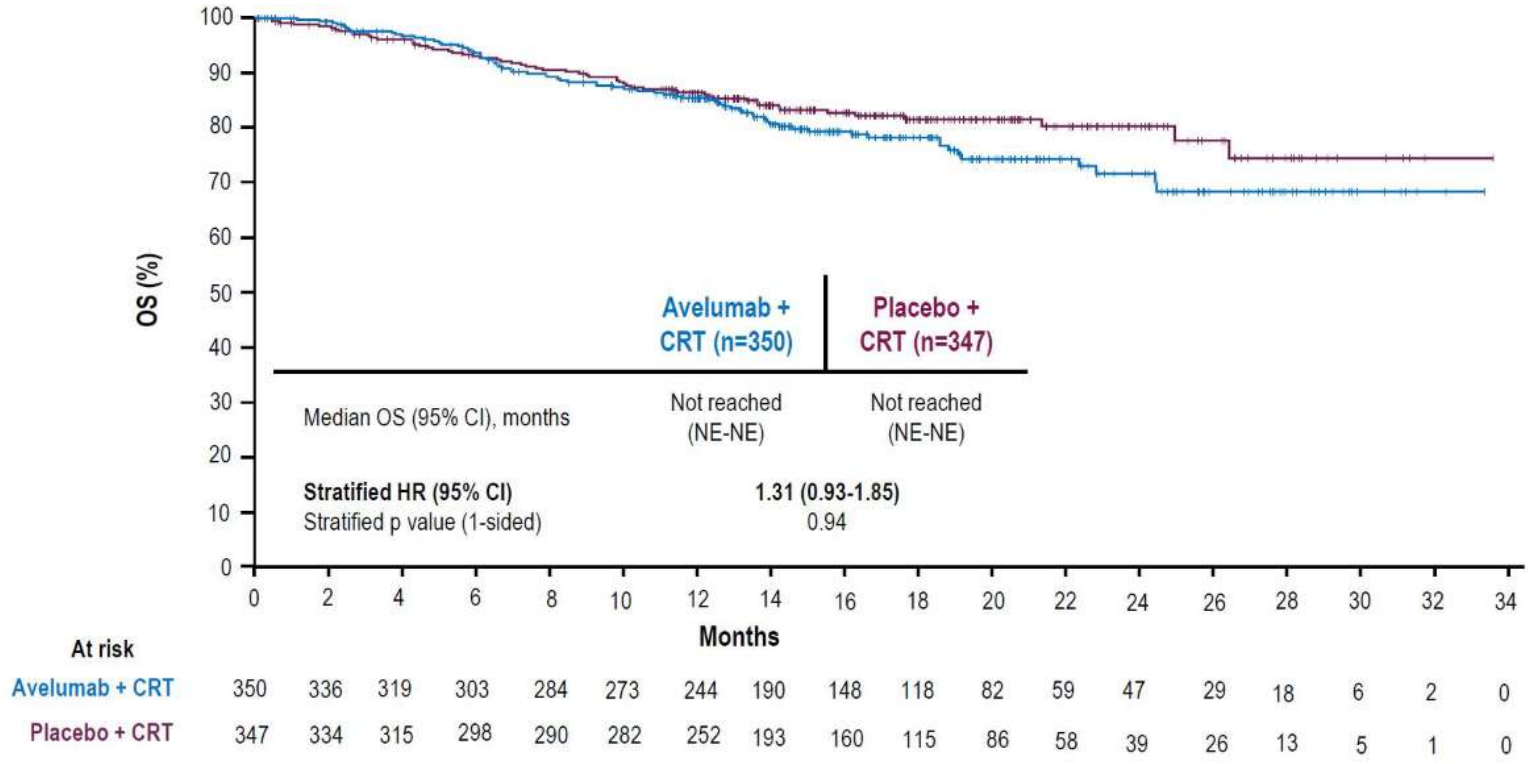
Primary endpoint: PFS





Cohen, ESMO 2020.

Secondary endpoint: OS



Cohen, ESMO 2020.

Adverse events

	Avelumab + CRT (n=348)		Placebo + CRT (n=344)	
	All grades	Grade 3/4	All grades	Grade 3/4
Any TRAE, %*	**98**	**66/14**	**99**	**63/11**
Nausea	55	6	55	5
Anemia	53	12	50	13
Dry mouth	42	1	43	1
Mucosal inflammation	41	14	37	13
Radiation skin injury	39	5	40	5
Dysphagia	38	14	40	14
Weight decreased	35	4	43	6
Decreased appetite	33	7	33	5
Dysgeusia	30	0	34	1
Neutropenia	30	16	28	15
Fatigue	29	4	34	3
Vomiting	28	5	31	6
Stomatitis	27	7	28	8
Blood creatine increased	22	2	20	1
Hypomagnesemia	22	1	18	1
Neutrophil count decreased	18	11	17	9
Oropharyngeal pain	18	3	23	2
Infusion-related reaction, %	22	2	3	<1

Cohen, ESMO 2020.

Webinar outline

- Genitourinary cancers
- Melanoma
- Head and neck cancer
- Gastrointestinal cancer
- Novel agents

Nivolumab plus chemotherapy versus chemotherapy as first-line treatment for advanced gastric cancer/gastroesophageal junction cancer/esophageal adenocarcinoma: first results of the CheckMate 649 study

Markus Moehler, Kohei Shitara, Marcelo Garrido, Pamela Salman, Lin Shen, Lucjan Wyrwicz, Kensei Yamaguchi, Tomasz Skoczylas, Arinilda Campos Bragagnoli, Tianshu Liu, Michael Schenker, Patricio Yanez, Mustapha Tehfe, Valerie Poulart, Dana Cullen, Ming Lei, Kaoru Kondo, Mingshun Li, Jaffer A. Ajani, Yelena Y. Janjigian

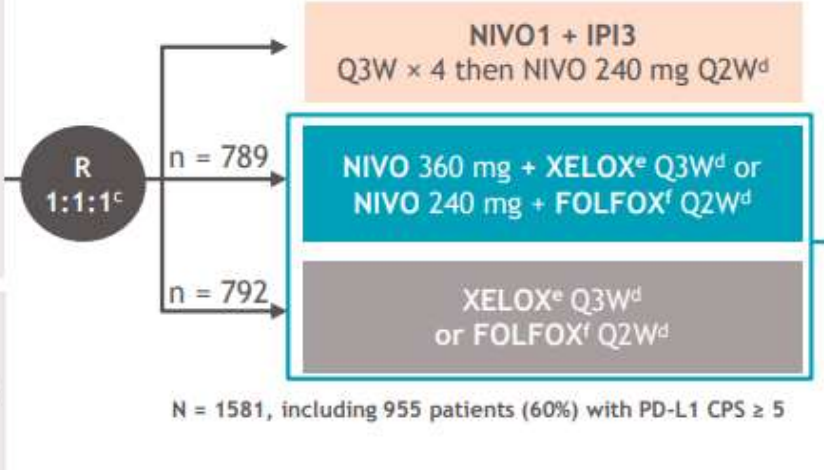
Study design

Key eligibility criteria

- Previously untreated, unresectable, advanced or metastatic gastric/GEJ/ esophageal adenocarcinoma
- No known HER2-positive status
- ECOG PS 0-1

Stratification factors

- Tumor cell PD-L1 expression (≥ 1% vs < 1%[b])
- Region (Asia vs United States/Canada vs ROW)
- ECOG PS (0 vs 1)
- Chemo (XELOX vs FOLFOX)



Dual primary endpoints:

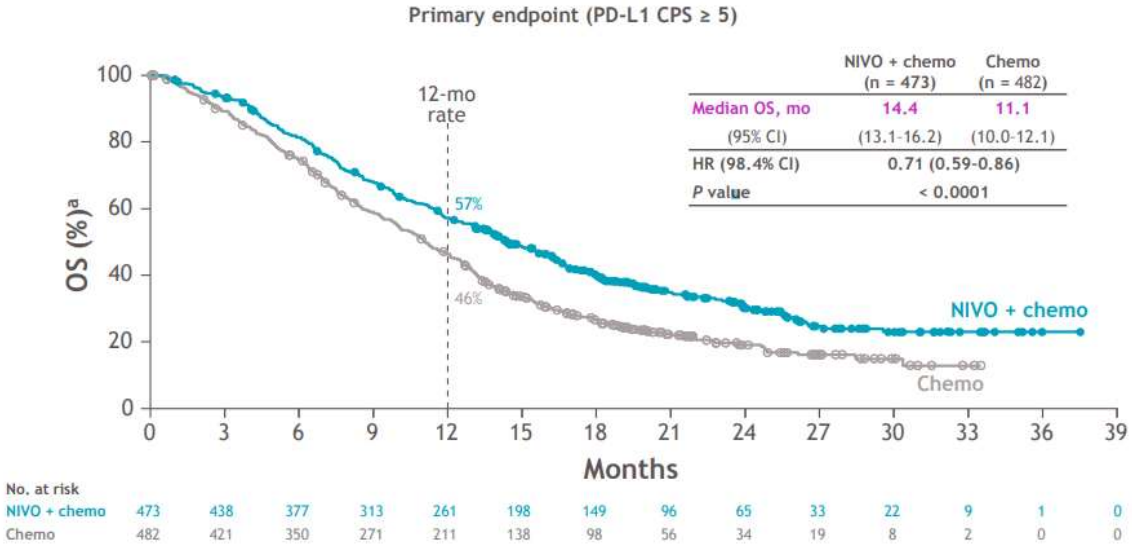
- OS and PFS[g] (PD-L1 CPS ≥ 5)

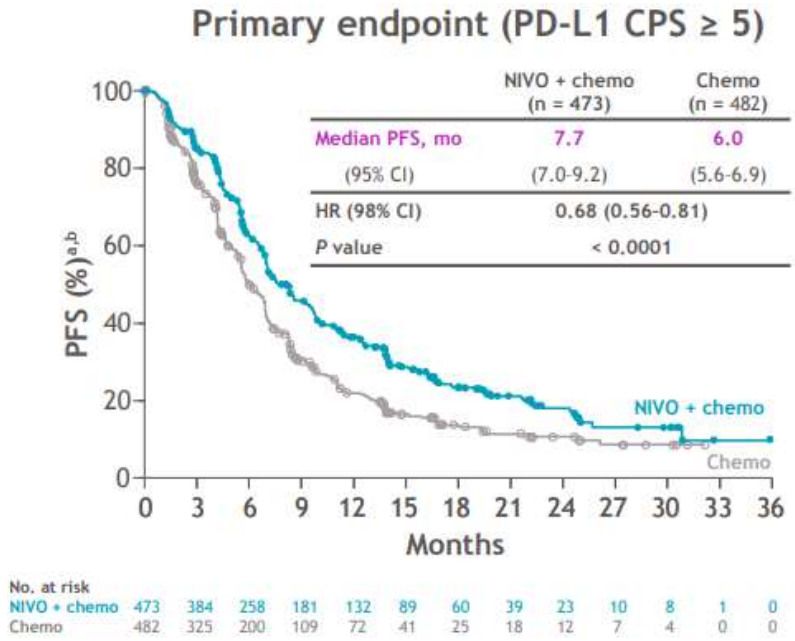
Secondary endpoints:

- OS (PD-L1 CPS ≥ 1 or all randomized)
- OS (PD-L1 CPS ≥ 10)
- PFS[g] (PD-L1 CPS ≥ 10, 1, or all randomized)
- ORR[g]

Moehler, ESMO 2020.

Primary endpoints – OS and PFS in PD-L1 CPS ≥ 5

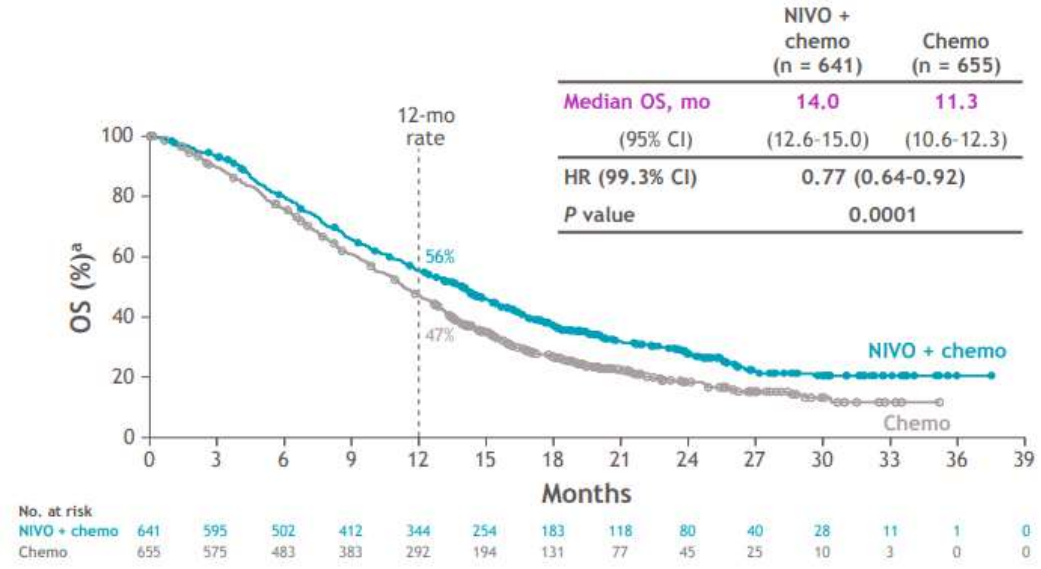




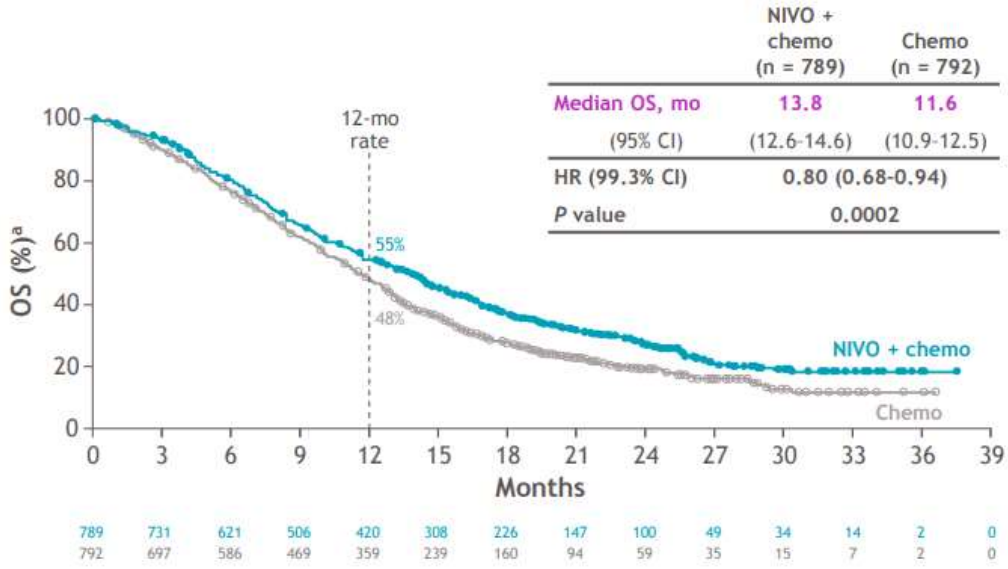
Moehler, ESMO 2020.

Secondary endpoint – OS in all patients

PD-L1 CPS ≥ 1



All randomized



Moehler, ESMO 2020.

Safety summary

Treatment-related adverse events				
%	Nivo + chemo (n=782)		Chemo (n=767)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Any TRAEs	94	59	89	44
Serious TRAEs	22	17	12	10
TRAEs leading to discontinuation	36	17	24	9
Treatment-related deaths	N = 12		N = 4	

TRAEs with potential immunologic etiology				
%	Nivo + chemo (n=782)		Chemo (n=767)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Endocrine	14	<1	<1	0
Gastrointestinal	34	5	27	3
Hepatic	26	4	17	2
Pulmonary	5	2	<1	<1
Renal	3	<1	1	<1
Skin	27	3	14	<1

Moehler, ESMO 2020.

Webinar outline

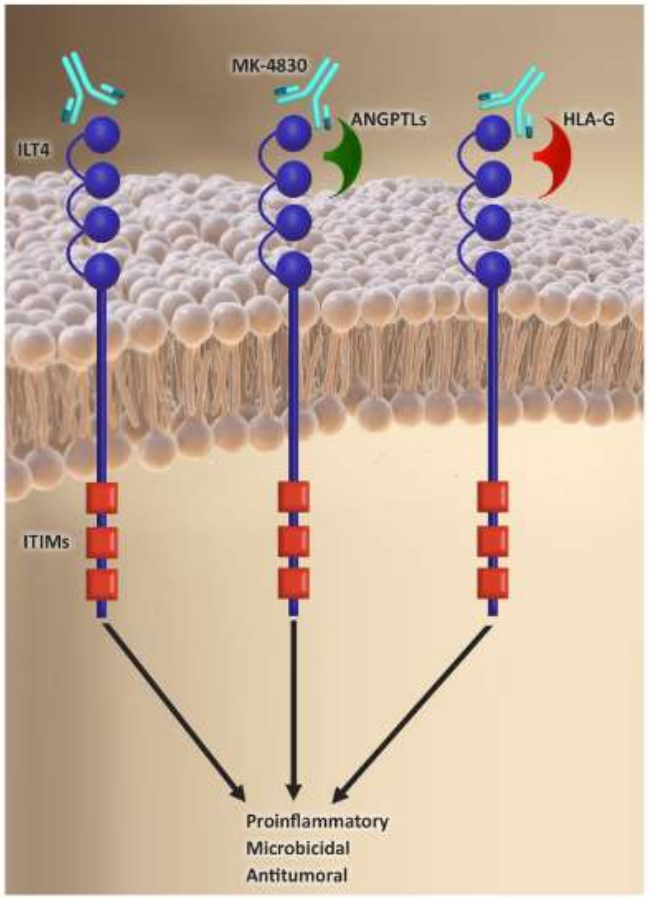
- Genitourinary cancers
- Melanoma
- Head and neck cancer
- Gastrointestinal cancer
- Novel agents

Initial Results of a Phase 1 Study of MK-4830, a First-in-Class Anti-Immunoglobulin-Like Transcript 4 Myeloid-Specific Antibody in Patients With Advanced Solid Tumors

Lillian L. Siu, Ding Wang, John Hilton, Ravit Geva, Drew Rasco, Anson K. Abraham, Julia F. Markensohn, Leah Suttner, Shabana Siddiqi, Rachel A. Altura, Corinne Maurice-Dror

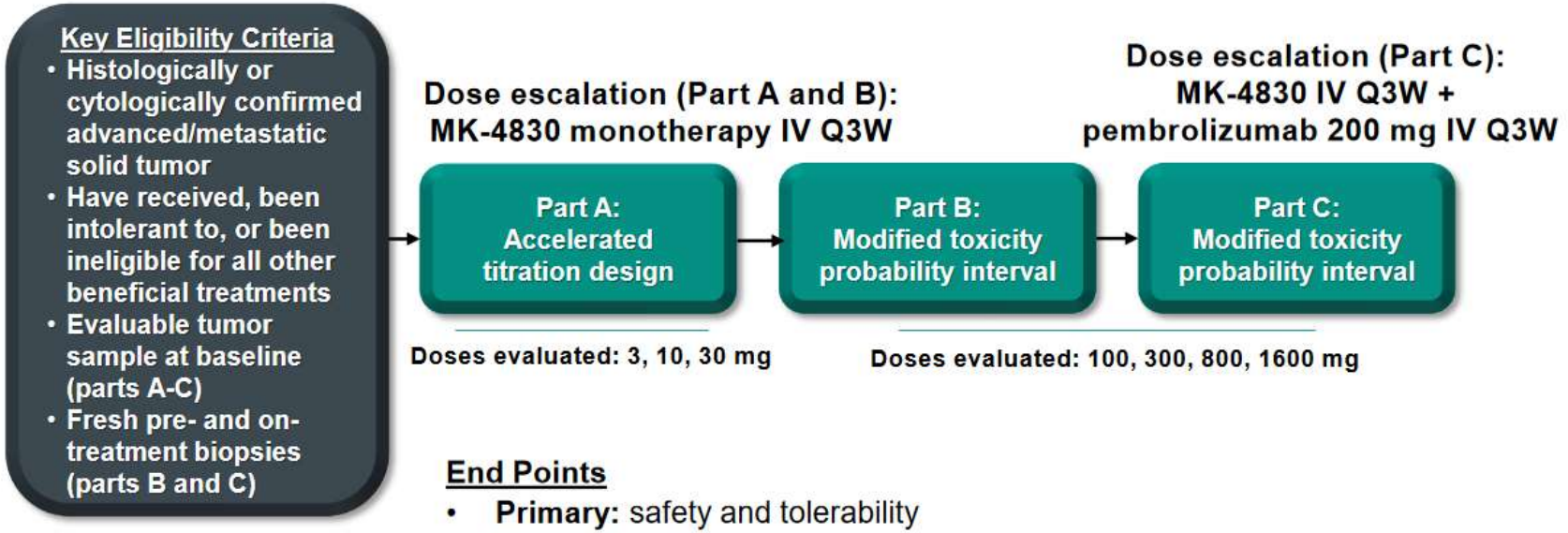
MK-4830

- Myeloid infiltration in tumors is associated with poor prognosis
- Immunoglobulin-like transcript 4 (ILT4) is an inhibitory receptor highly expressed by myeloid cells (APCs, MDSCs, macrophages, granulocytes)
- Expression of ILT4 and its major ligand, HLA-G, are associated with poor prognosis in multiple tumor types
- Targeting ILT4 may relieve myeloid suppressive activity in the tumor microenvironment and result in an antitumor response
- MK-4830 catalyzes reprogramming of tumor-associated macrophages, relieving myelosuppression and enhancing T-cell function



Siu, ESMO 2020.

Study design



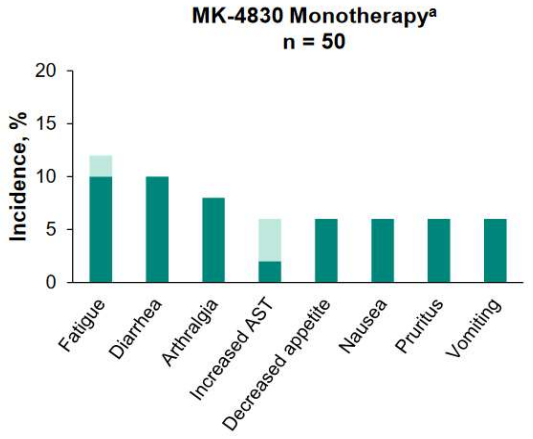
End Points

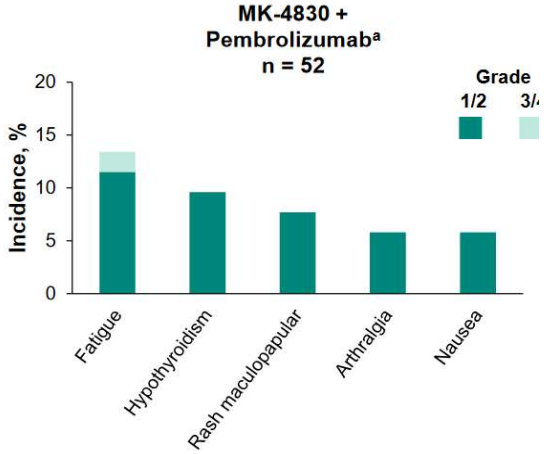
- **Primary:** safety and tolerability
- **Secondary:** PK
- **Tertiary/Exploratory:** ORR per RECIST v1.1; PD (receptor occupancy)

Siu, ESMO 2020.

Safety

AE, n (%)	MK-4830 Monotherapy[a] n = 50	MK-4830 + Pembrolizumab[a] n = 52
Any-grade	50 (100)	48 (92)
Grade 3-5	23 (46)	23 (44)
Led to discontinuation	2 (4)	1 (2)
Serious	14 (28)	18 (35)
Serious and led to discontinuation	0	0
Led to death[b]	2 (4)	0
Any-grade TRAE	24 (48)	28 (54)
Grade 3-4 TRAE	3 (6)	4 (8)
TRAE led to discontinuation	1 (2)	1 (2)
Serious TRAE	0	4 (8)
Serious TRAE and led to discontinuation	0	0
Led to death	0	0

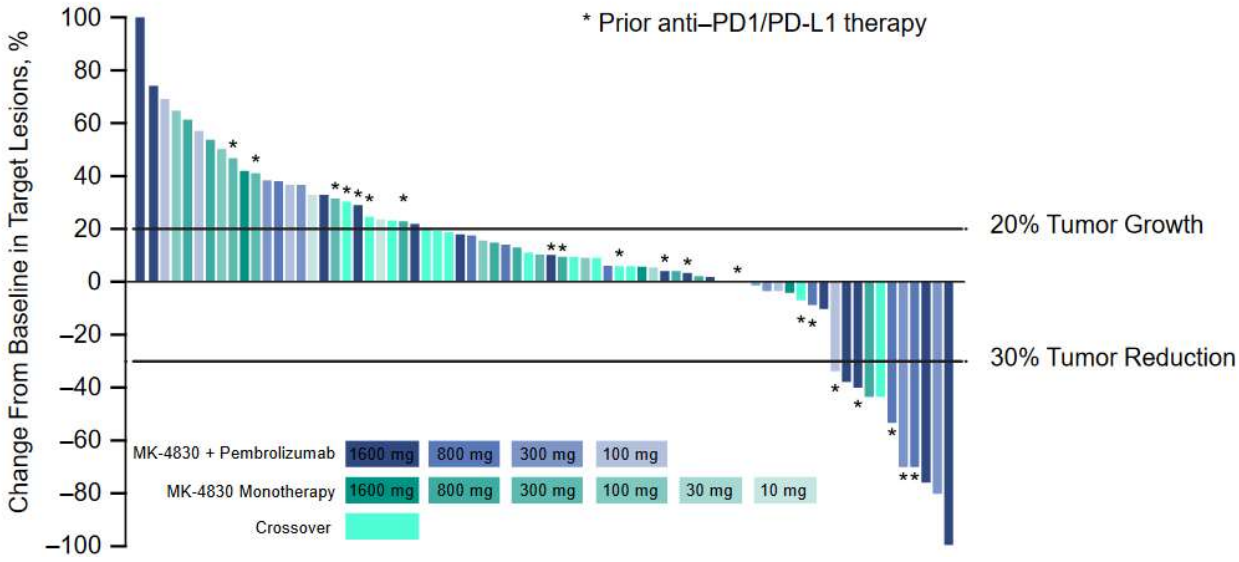




Siu, ESMO 2020.

Efficacy

%	MK-4830	MK-4830 + pembro	Crossover to combo
ORR	2	24	6
CR	0	3	0
PR	2	21	6
SD	22	26	6
PD	68	47	17
No RECIST assessment	8	3	72



Siu, ESMO 2020.

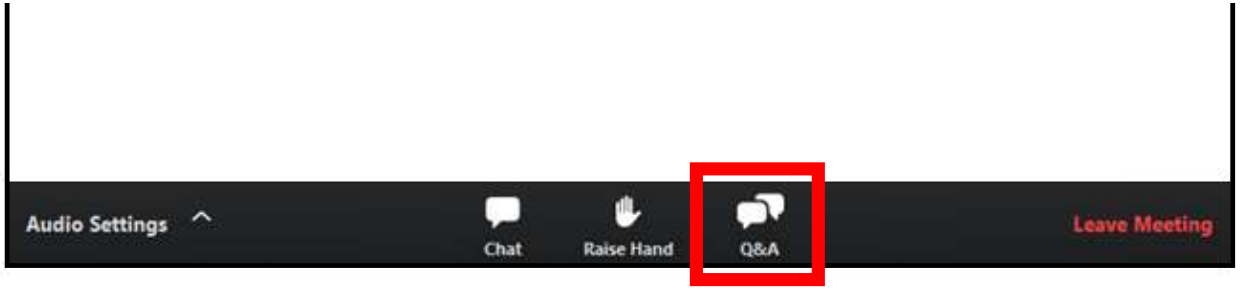
HN, GI and Novel Agents

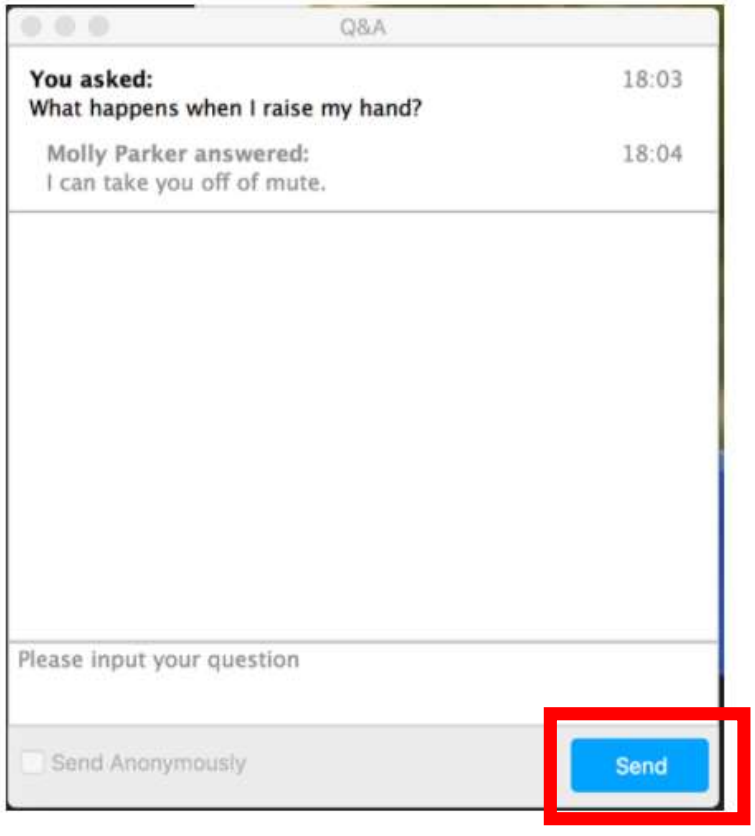
- Head and Neck (JAVELIN HN 100):
  - No benefit in PFS or OS with avelumab added to chemoradiation in locally advanced high-risk SCCHN
  - KEYNOTE-412 results with pembrolizumab are pending
- Esophageal/GEJ/Gastric (CHECKMATE 649):
  - Nivolumab + chemotherapy in PD-L1 positive (CPS$\geq$5) patients produced statistically significant benefit in mPFS (Δ1.7 m) and mOS (Δ3.3 m) compared to chemotherapy alone -> potential new standard 1st line treatment
- Novel agents (MK4830-001):
  - MK4830 has a novel MOA by targeting myeloid populations, antitumor activity seen in both ICI-naïve and ICI-pretreated patients across different tumor types

Society for Immunotherapy of Cancer

How to Submit Questions

- Click the “Q&A” icon located on at the bottom of your Zoom control panel
- Type your question in the Q&A box, then click “Send”
- Questions will be answered in the Question & Answer session at the end of the webinar (as time permits)





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- Questions and comments: connectED@sitcancer.org

Thank you for attending the webinar!

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