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Avelumab 1L maintenance + best supportive care (BSC) vs BSC alone with 1L chemotherapy for advanced urothelial carcinoma: subgroup analyses from JAVELIN Bladder 100

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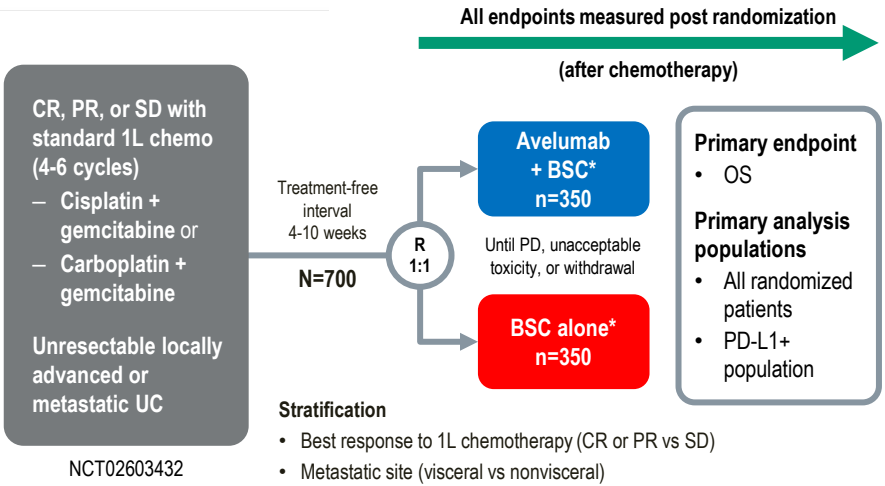
Disclosures for Dr Grivas

- Consulting role: AstraZeneca, Bayer, Bristol Myers Squibb, Clovis Oncology, Driver, EMD Serono, Exelixis, Foundation Medicine, GlaxoSmithKline, Genentech, Genzyme, Heron Therapeutics, Janssen, Merck, Mirati Therapeutics, Pfizer, Roche, Seattle Genetics, QED Therapeutics
- Educational program participation: Bristol Myers Squibb
- Institutional research funding: AstraZeneca, Bavarian Nordic, Bayer, Bristol Myers Squibb, Clovis Oncology, Debiopharm, Genentech, GlaxoSmithKline, Immunomedics, Kure It Cancer Research, Merck, Mirati Therapeutics, Oncogenex, Pfizer, QED Therapeutics
- This trial was sponsored by Pfizer and is part of an alliance between Pfizer and Merck KGaA, Darmstadt, Germany

Disclosures over past 3 years

Avelumab 1L maintenance + BSC significantly prolonged OS vs BSC alone in the JAVELIN Bladder 100 phase 3 trial



NCT02603432

- Median OS in all randomized patients[1]
  - **Avelumab 1L maintenance + BSC**: **21.4 months** (95% CI, 18.9, 26.1)
  - **BSC alone: 14.3 months** (95% CI, 12.9, 17.9)
  - **HR 0.69** (95% CI, 0.56, 0.86); P<0.001
- The safety profile of avelumab 1L maintenance was manageable and consistent with previous studies of avelumab monotherapy[1,2]

OS benefit with avelumab + BSC vs BSC alone was analyzed in patient subgroups

1L, first line; **BSC**, best supportive care; **CR**, complete response; **HR**, hazard ratio; **OS**, overall survival; **PR**, partial response; **R**, randomization; **SD**, stable disease; **UC**, urothelial carcinoma
* 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

1. Powles T, et al. J Clin Oncol. 2020;38:abstract LBA1. 2. Kelly K, et al. Cancer. 2018;124:2010-17.

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Subgroup baseline characteristics reflected physician's choice of 1L chemotherapy regimen

	Gemcitabine + cisplatin (N=389)*		Gemcitabine + carboplatin (N=269)*	
	Avelumab + BSC (N=183)	BSC alone (N=206)	Avelumab + BSC (N=147)	BSC alone (N=122)
Median age, years	66	67	71	74
ECOG performance status, %				
0	68	66	51	53
1	32	34	49	44
Creatinine clearance, %				
≥60 mL/min	64	64	36	44
<60 mL/min	36	33	63	55
Site of baseline metastasis, %				
Visceral	56	59	54	48
Nonvisceral†	44	41	46	52
PD-L1 status, %‡				
Positive	55	48	50	44
Negative	38	36	44	43
Unknown	7	17	5	12
Best response to 1L chemotherapy, %				
CR or PR	72	72	73	67
SD	28	28	27	33

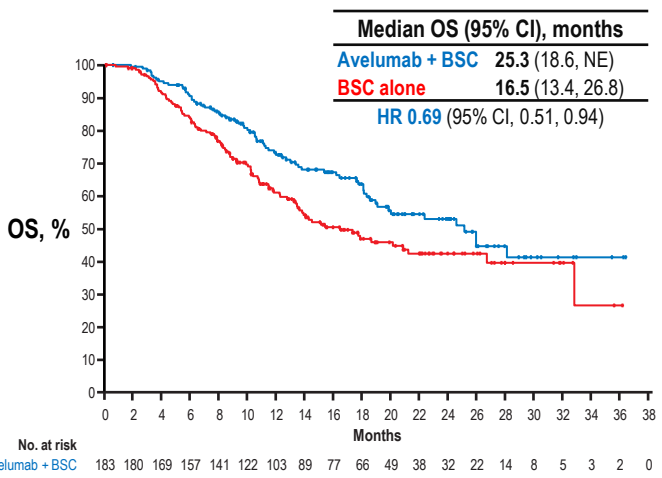
* 40 additional patients switched platinum regimens while receiving 1L chemotherapy (20 per arm)

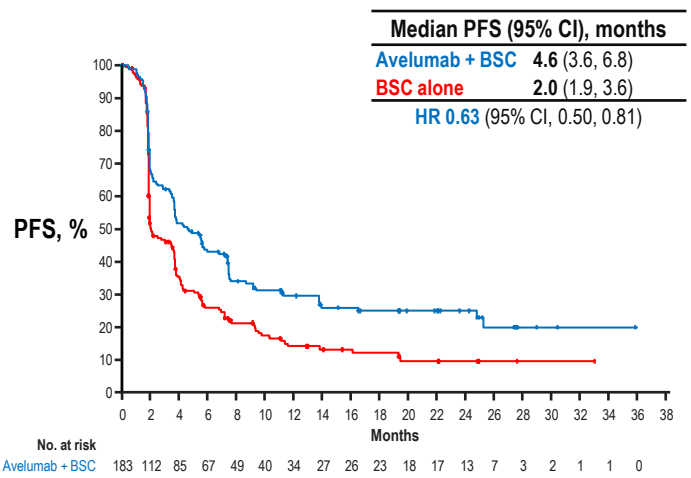
† Nonvisceral includes patients with locally advanced disease or only nonvisceral disease, including bone metastasis

‡ 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)

OS and PFS benefit with avelumab 1L maintenance occurred irrespective of 1L chemotherapy regimen

Gemcitabine + cisplatin (N=389)

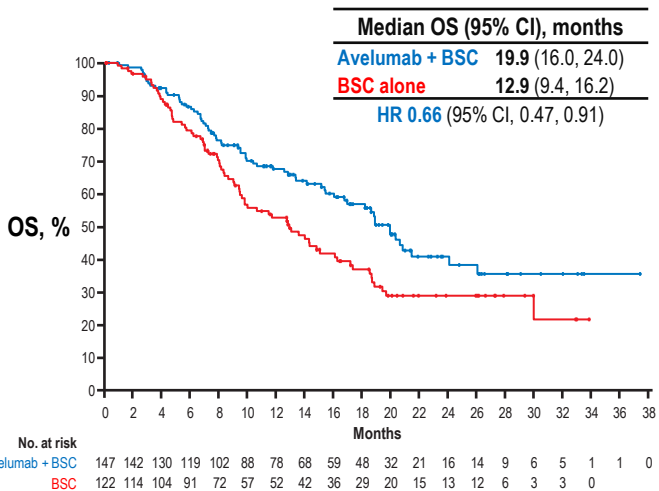


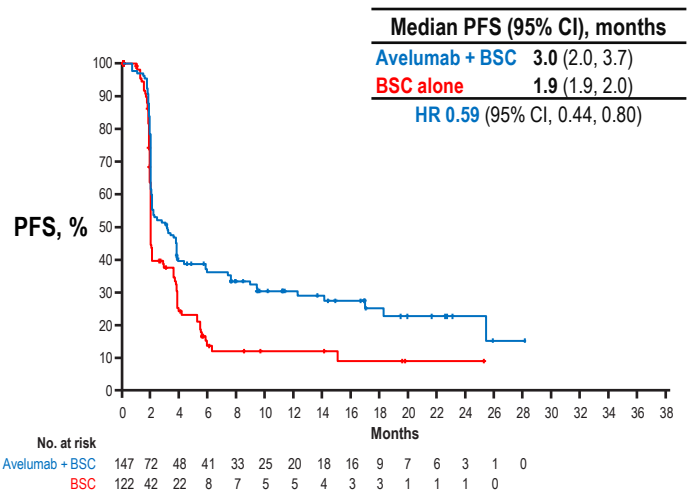


NE, not estimable; **PFS**, progression-free survival
OS and PFS were measured post randomization (after chemotherapy)

OS and PFS benefit with avelumab 1L maintenance occurred irrespective of 1L chemotherapy regimen

Gemcitabine + carboplatin (N=269)





OS and PFS were measured post randomization (after chemotherapy)

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Selected baseline characteristics by best response to 1L chemotherapy

	Complete response (N=179)		Partial response (N=326)		Stable disease (N=195)	
	Avelumab + BSC (N=90)	BSC alone (N=89)	Avelumab + BSC (N=163)	BSC alone (N=163)	Avelumab + BSC (N=97)	BSC alone (N=98)
Median age, years	71	69	67	69	69	69
ECOG performance status, %						
0	63	63	64	62	54	55
1	37	37	36	37	46	43
Creatinine clearance, %						
≥60 mL/min	50	66	57	54	44	50
<60 mL/min	50	30	42	45	56	49
Site of baseline metastasis, %						
Visceral	46	39	61	64	53	52
Nonvisceral*	54	61	39	36	47	48
PD-L1 status, %†						
Positive	67	60	48	46	52	42
Negative	28	28	47	40	39	41
Unknown	6	12	5	13	9	17

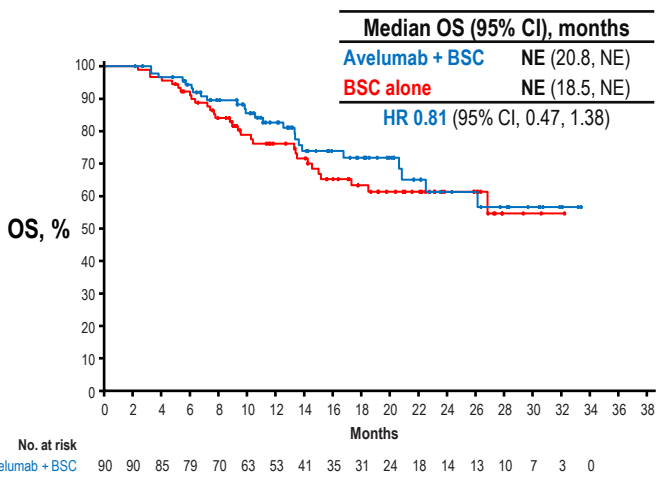
CR (ie, no evidence of disease at baseline), PR, and SD at baseline was based on either blinded independent central review (BICR) or investigator assessment up to protocol amendment 3, or investigator assessment only from protocol amendment 3 (19 Dec 2016) onward

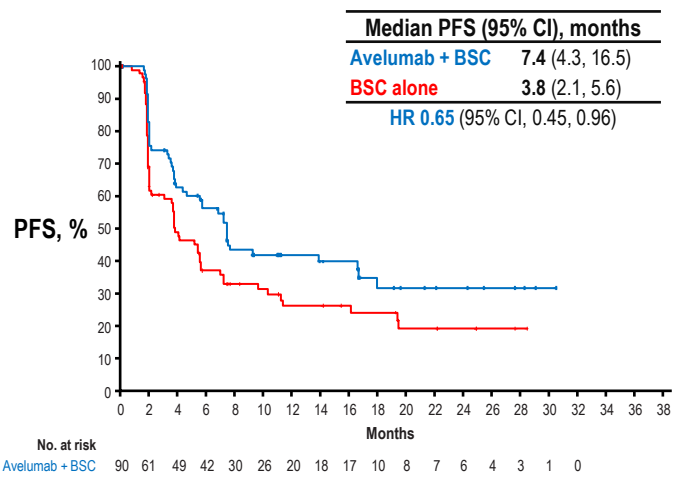
* Nonvisceral includes patients with locally advanced disease or only nonvisceral disease, including bone metastasis

† 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)

OS and PFS benefit with avelumab 1L maintenance was observed irrespective of best response to 1L chemotherapy

Complete response (N=179)

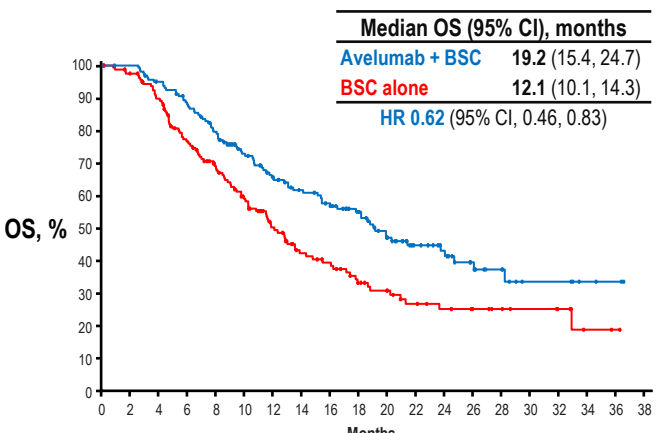


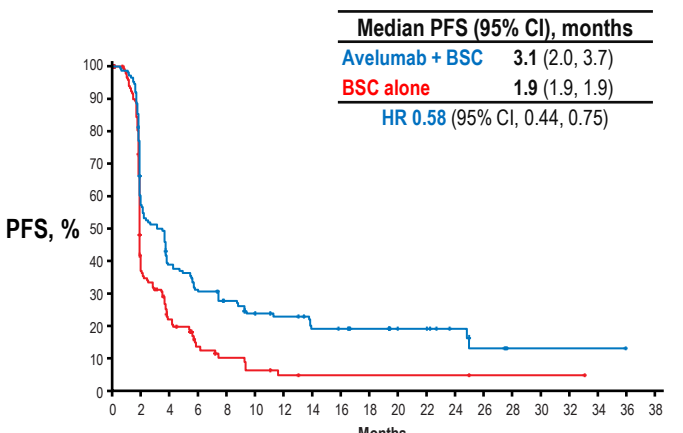


OS and PFS were measured post randomization (after chemotherapy); CR (ie, no evidence of disease at baseline), PR, and SD at baseline was based on either BICR or investigator assessment up to protocol amendment 3, or investigator assessment only from protocol amendment 3 (19 Dec 2016) onward

OS and PFS benefit with avelumab 1L maintenance was observed irrespective of best response to 1L chemotherapy

Partial response (N=326)

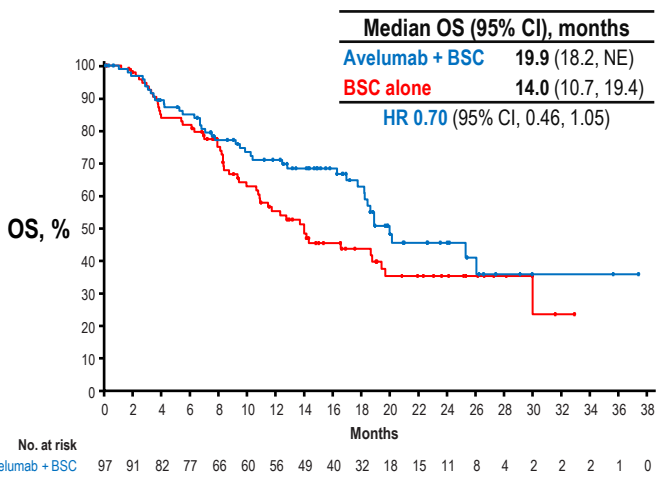


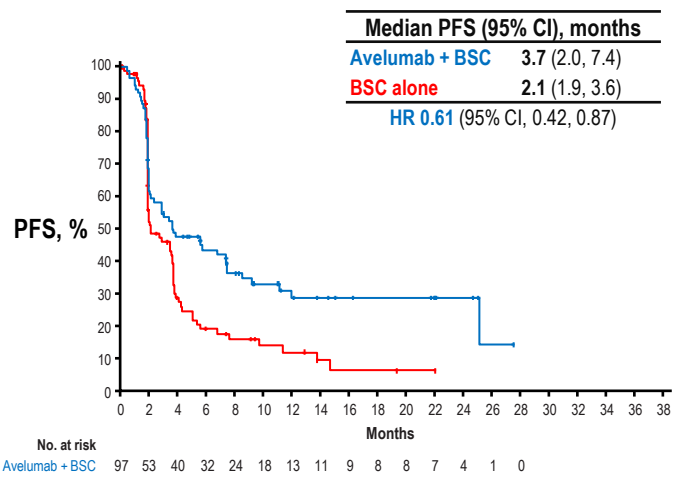


OS and PFS were measured post randomization (after chemotherapy); CR (ie, no evidence of disease at baseline), PR, and SD at baseline was based on either BICR or investigator assessment up to protocol amendment 3, or investigator assessment only from protocol amendment 3 (19 Dec 2016) onward

OS and PFS benefit with avelumab 1L maintenance was observed irrespective of best response to 1L chemotherapy

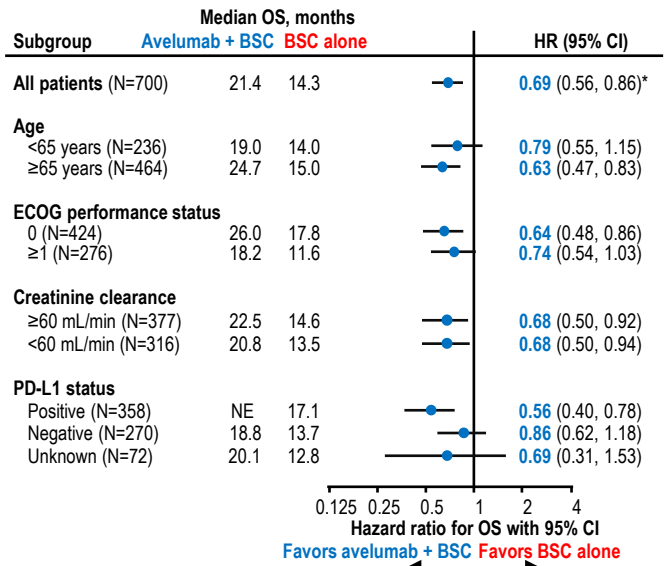
Stable disease (N=195)

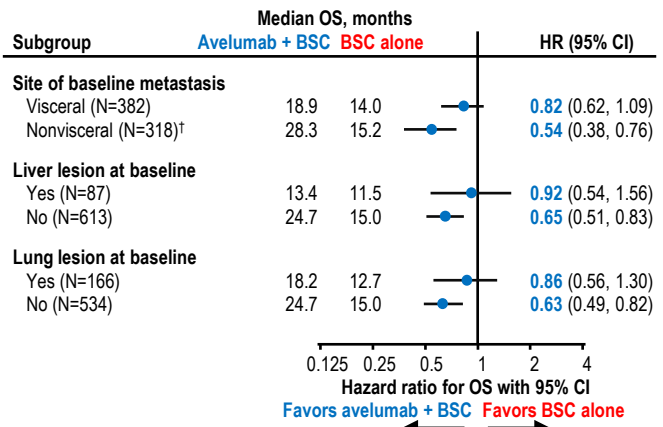




OS and PFS were measured post randomization (after chemotherapy); CR (ie, no evidence of disease at baseline), PR, and SD at baseline was based on either BICR or investigator assessment up to protocol amendment 3, or investigator assessment only from protocol amendment 3 (19 Dec 2016) onward

OS benefit with avelumab 1L maintenance was observed across additional prespecified subgroups





No significant treatment-by-subgroup interaction (at 0.05 level) was observed for any subgroup variable

OS was measured post randomization (after chemotherapy)
* Stratified (all other analyses are unstratified)
† Nonvisceral includes patients with locally advanced disease or only nonvisceral disease, including bone metastasis

Conclusions

- In the JAVELIN Bladder 100 trial, avelumab 1L maintenance + BSC provided an OS and PFS benefit vs BSC alone across prespecified subgroups
- OS and PFS were longer with avelumab 1L maintenance + BSC vs BSC alone in patients who had received 1L cisplatin- or carboplatin-containing chemotherapy, and irrespective of CR, PR, or SD with 1L chemotherapy
- These results support the approval of avelumab 1L maintenance in the US[1] and its inclusion in NCCN and ESMO guidelines as a new standard of care for 1L treatment of advanced UC[2,3]
- Additional data are available via QR code on the final slide

QR, quick response

1. US Food and Drug Administration. 1 Jul 2020. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-avelumab-urothelial-carcinoma-maintenance-treatment
2. NCCN Guidelines: bladder cancer, v6.2020. 16 Jul 2020. https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf
3. ESMO eUpdate – Bladder Cancer Treatment Recommendations. 16 Jul 2020. https://www.esmo.org/guidelines/genitourinary-cancers/bladder-cancer/eupdate-bladder-cancer-treatment-recommendations4

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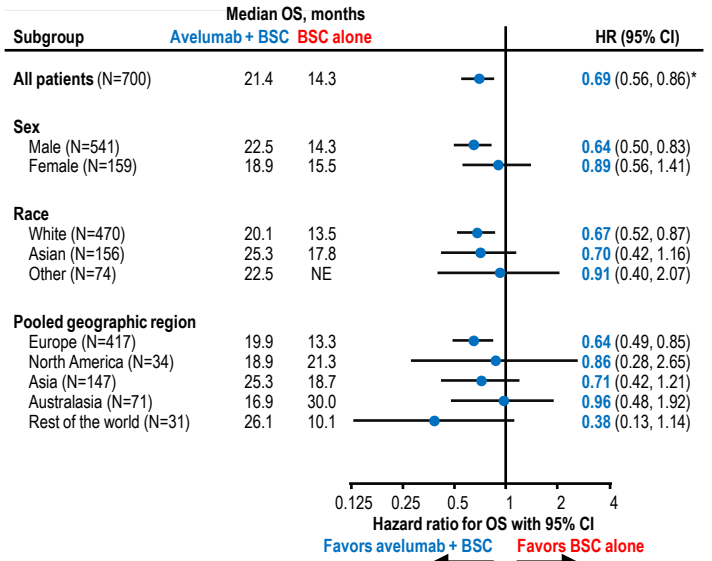
Additional data

Available via QR code

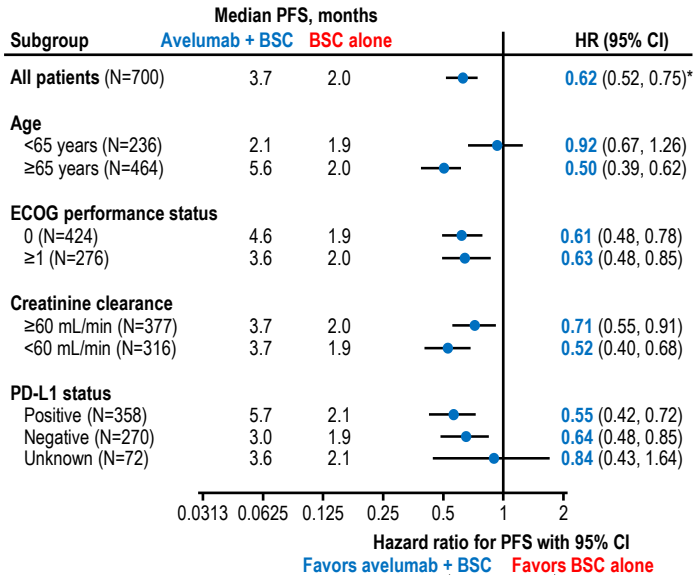
OS in additional subgroups

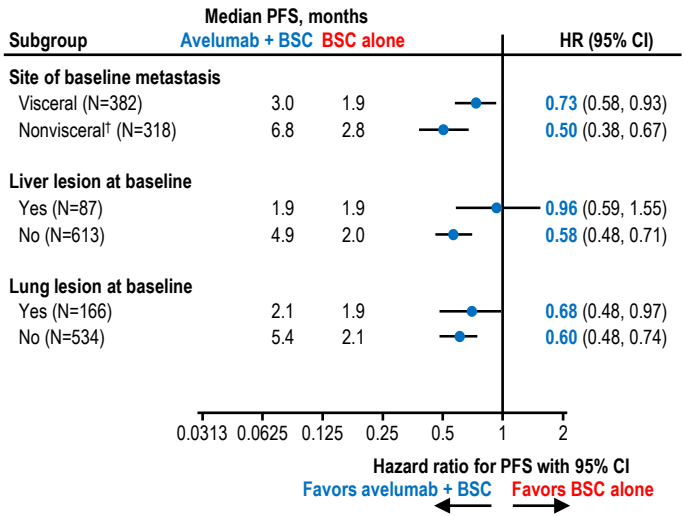


No significant treatment-by-subgroup interaction (at 0.05 level) was observed for any subgroup variable

OS was measured post randomization (after chemotherapy)
*Stratified (all other analyses are unstratified)

PFS in additional subgroups





PFS was measured post randomization (after chemotherapy)
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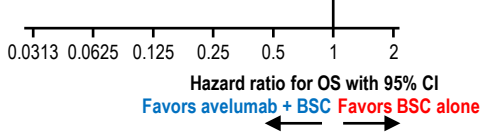
PFS in additional subgroups

Subgroup	Median PFS, months: Avelumab + BSC	Median PFS, months: BSC alone	HR (95% CI)
All patients (N=700)	3.7	2.0	**0.62** (0.52, 0.75)*
Sex			
Male (N=541)	3.8	2.0	**0.60** (0.49, 0.74)
Female (N=159)	3.0	1.9	**0.69** (0.47, 1.01)
Race			
White (N=470)	20.1	13.5	**0.65** (0.52, 0.81)
Asian (N=156)	25.3	17.8	**0.55** (0.37, 0.80)
Other (N=74)	22.5	NE	**0.64** (0.36, 1.11)
Pooled geographic region			
Europe (N=417)	19.9	13.3	**0.66** (0.52, 0.84)
North America (N=34)	18.9	21.3	**0.20** (0.06, 0.61)
Asia (N=147)	25.3	18.7	**0.57** (0.39, 0.85)
Australasia (N=71)	16.9	13.5	**0.83** (0.46, 1.49)
Rest of the world (N=31)	26.1	17.8	**0.32** (0.13, 0.81)



PFS was measured post randomization (after chemotherapy)
*Stratified (all other analyses are unstratified)

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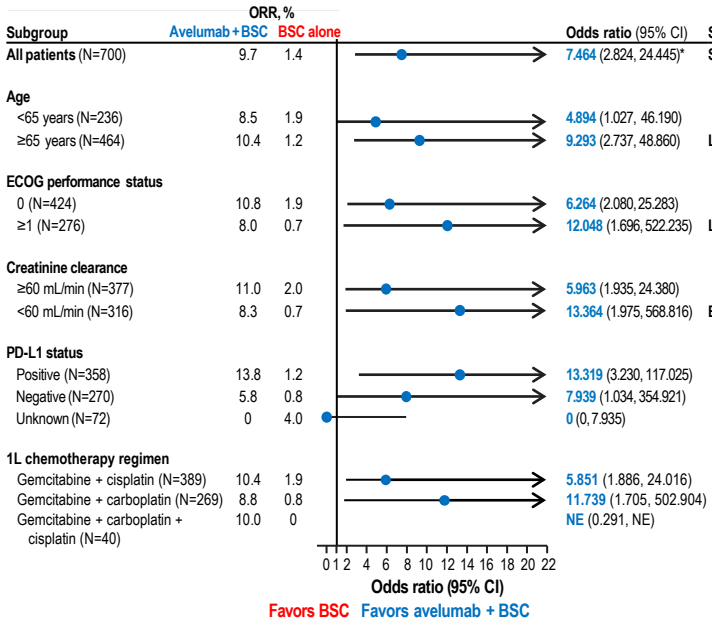
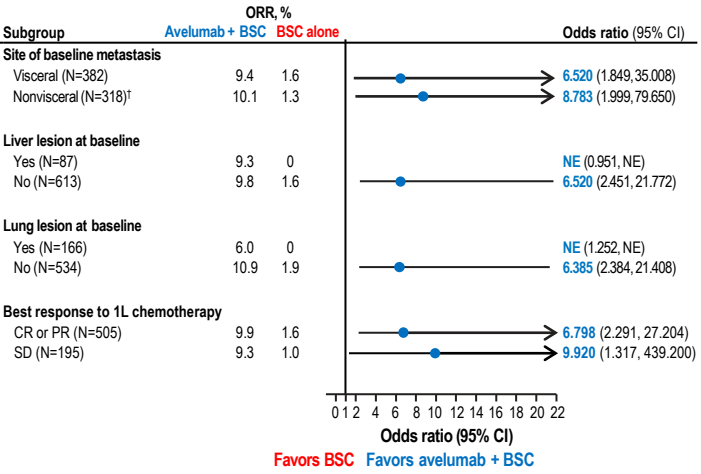
Confirmed ORR in prespecified subgroups





ORR was measured post randomization (after chemotherapy)
*Stratified (all other analyses are unstratified)
†Nonvisceral includes patients with locally advanced disease or only nonvisceral disease, including bone metastasis

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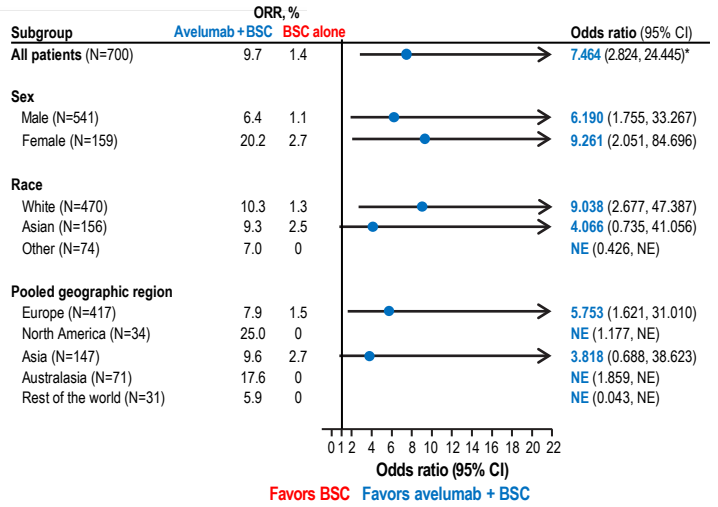
Confirmed ORR by prespecified subgroups



ORR was measured post randomization (after chemotherapy)
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