IMpower110: Interim overall survival analysis of a Phase III study of atezolizumab monotherapy vs platinum-based chemotherapy as first-line treatment in PD-L1–selected NSCLC

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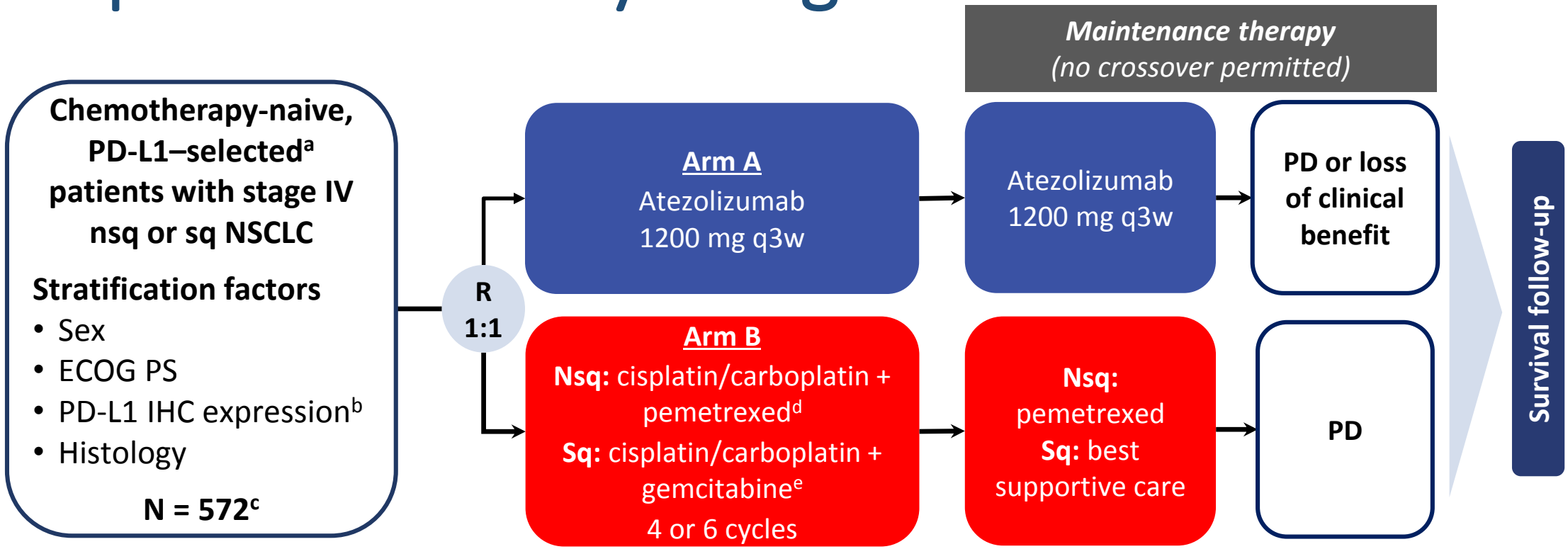
Background

- Anti–PD-1 monotherapy or PD-L1/PD-1 inhibitors in combination with platinum-based doublet chemotherapy, with or without bevacizumab, are 1L standards of care in metastatic NSCLC[1,2]
  - Tumor PD-L1 expression level and histology are used to determine treatment regimens
- In the Phase II BIRCH study, atezolizumab monotherapy demonstrated tolerability and efficacy in PD-L1–selected patients with advanced NSCLC across lines of therapy[3]
- The Phase III IMpower110 study (NCT02409342) evaluates atezolizumab monotherapy as 1L treatment in PD-L1–selected patients, independent of tumor histology
  - We report results of the interim OS analysis in IMpower110

1L, first-line. 1. NCCN Clinical Practice Guidelines. NSCLC. V7.2019; 2. Planchard D, et al. *Ann Oncol*. 2018;29(Suppl 4):iv192-iv237; 3. Peters S, et al. *J Clin Oncol*. 2017;35(24):2781-2789.

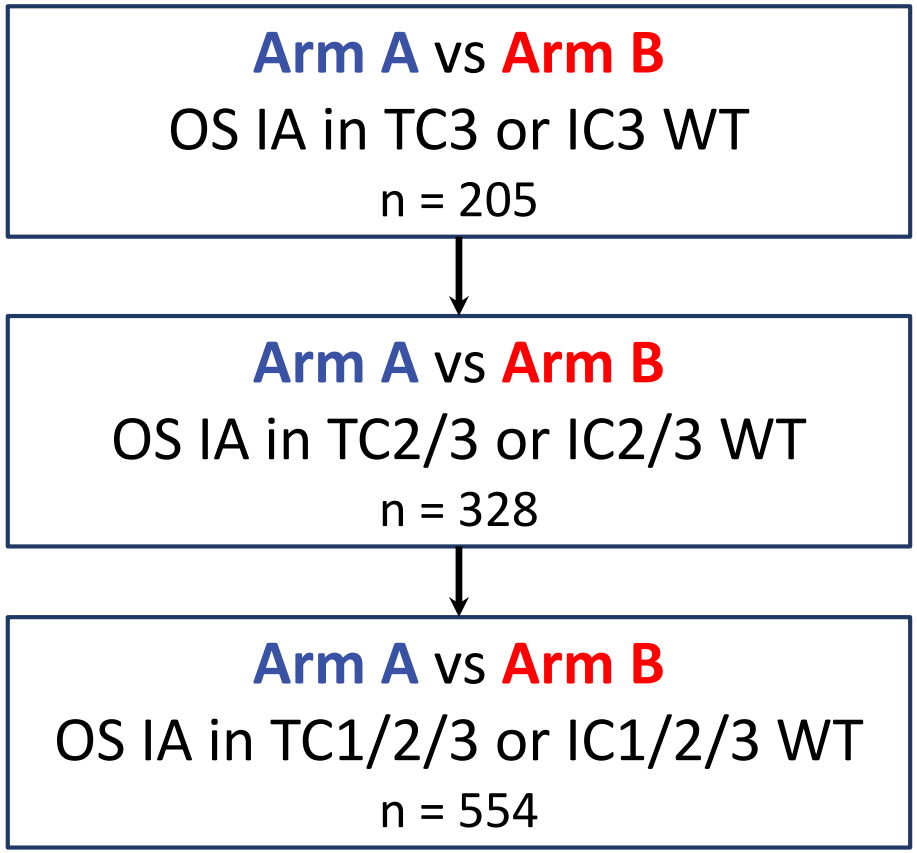
IMpower110 Study Design



- Primary endpoint: OS in WT population[f]
- Key secondary endpoints: investigator-assessed PFS, ORR and DOR (per RECIST 1.1)

IC, tumor-infiltrating immune cells; IHC, immunohistochemistry; nsq, non-squamous; sq, squamous; TC, tumor cells; WT, wild-type.
[a] PD-L1 expression (VENTANA SP142 IHC assay) ≥ 1% on TC or IC. [b] TC1/2/3 and any IC vs TC0 and IC1/2/3. [c] 554 patients in the WT population. [d] Cisplatin 75 mg/m^2 or carboplatin area under the curve (AUC) 6 + pemetrexed 500 mg/m^2 IV q3w. [e] Cisplatin 75 mg/m^2 + gemcitabine 1250 mg/m^2 or carboplatin AUC 5 + gemcitabine 1000 mg/m^2 IV q3w. [f] WT population excludes patients with *EGFR*+ and/or *ALK*+ NSCLC.

Statistical Testing Plan



- The primary OS endpoint was tested hierarchically in the following order: TC3 or IC3 WT → TC2/3 or IC2/3 WT → TC1/2/3 or IC1/2/3 WT
- The secondary endpoint of PFS can be formally tested only when the primary endpoint is positive among all 3 populations

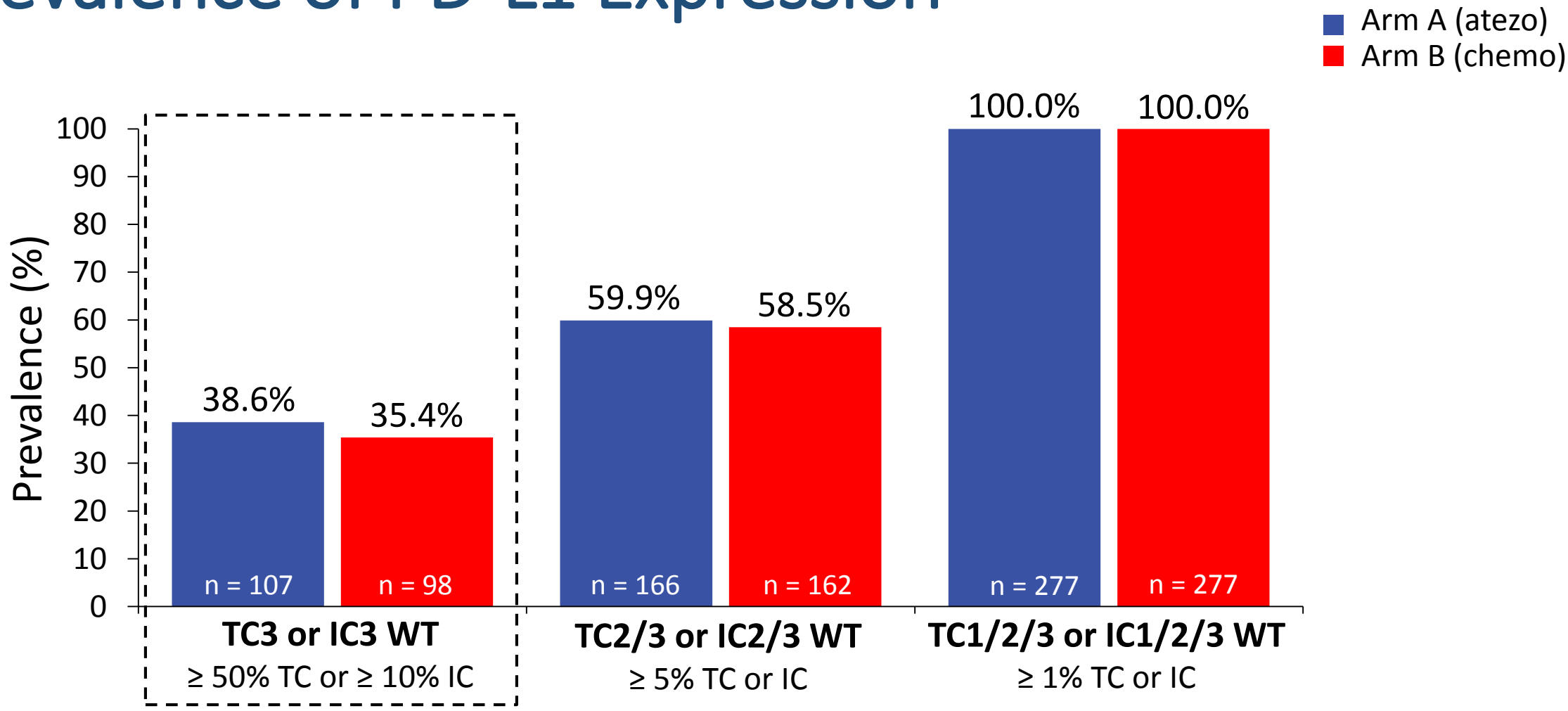
IA, interim analysis. WT, wild-type (excluding patients with *EGFR+* and/or *ALK+* NSCLC).
Data cutoff: September 10, 2018.

Baseline Characteristics

Characteristic	TC1/2/3 or IC1/2/3 WT		TC3 or IC3 WT	
n (%)	Arm A (atezo) n = 277	Arm B (chemo) n = 277	Arm A (atezo) n = 107	Arm B (chemo) n = 98
Age < 65 y	143 (51.6)	134 (48.4)	59 (55.1)	43 (43.9)
Male	196 (70.8)	193 (69.7)	79 (73.8)	64 (65.3)
White	227 (81.9)	240 (86.6)	87 (81.3)	82 (83.7)
Asian	45 (16.2)	30 (10.8)	20 (18.7)	15 (15.3)
Never used tobacco	37 (13.4)	35 (12.6)	9 (8.4)	15 (15.3)
Non-squamous histology	192 (69.3)	193 (69.7)	80 (74.8)	75 (76.5)
ECOG PS 0	97 (35.0)	102 (36.8)	35 (32.7)	38 (38.8)

Data cutoff: September 10, 2018.

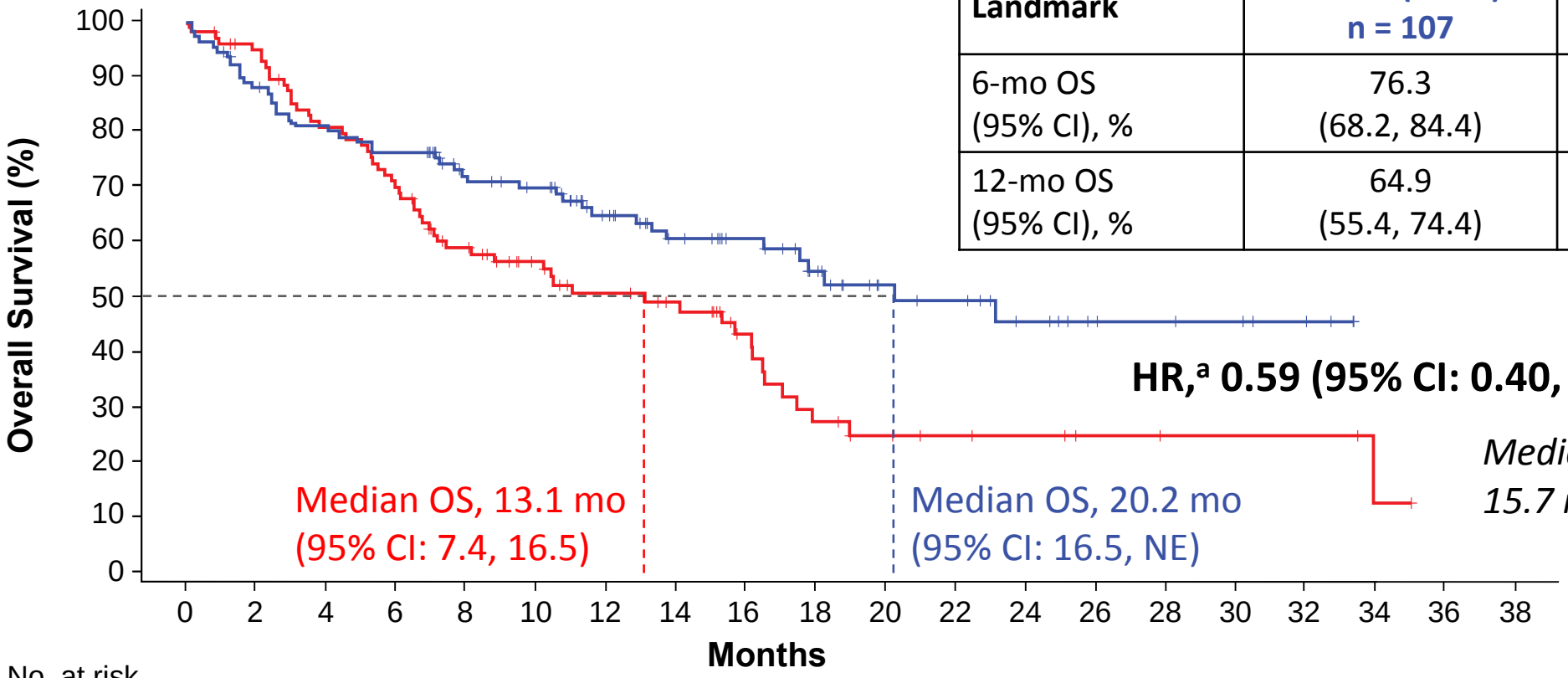
Prevalence of PD-L1 Expression[a]



[a] PD-L1 status determined using the SP142 PD-L1 IHC assay.
Data cutoff: September 10, 2018.

OS: TC3 or IC3 WT

Landmark	Arm A (atezo) n = 107	Arm B (chemo) n = 98
6-mo OS (95% CI), %	76.3 (68.2, 84.4)	70.1 (60.8, 79.4)
12-mo OS (95% CI), %	64.9 (55.4, 74.4)	50.6 (40.0, 61.3)



HR,[a] 0.59 (95% CI: 0.40, 0.89); *P* = 0.0106[b]

Median follow-up, 15.7 mo (range, 0-35)

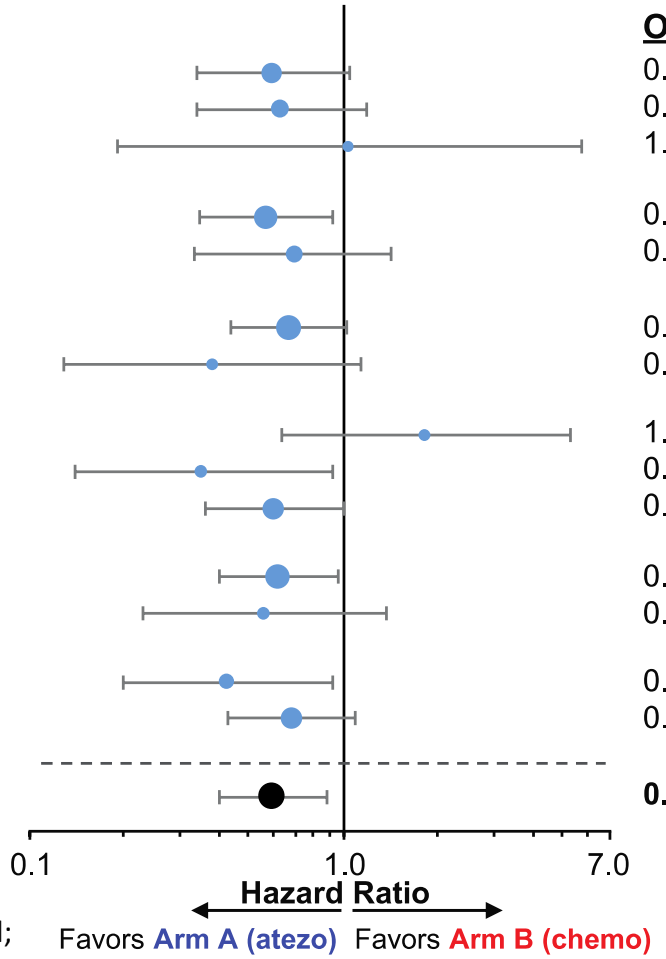
No. at risk

Atezolizumab	107	94	85	80	66	61	48	40	34	25	18	16	11	7	6	5	2	
Chemotherapy	98	89	75	65	50	40	33	28	19	12	9	7	6	4	3	3	3	1

NE, not estimable. [a] Stratified. [b] Stratified log-rank.
Data cutoff: September 10, 2018.

TC3 or IC3 WT: OS in Key Subgroups

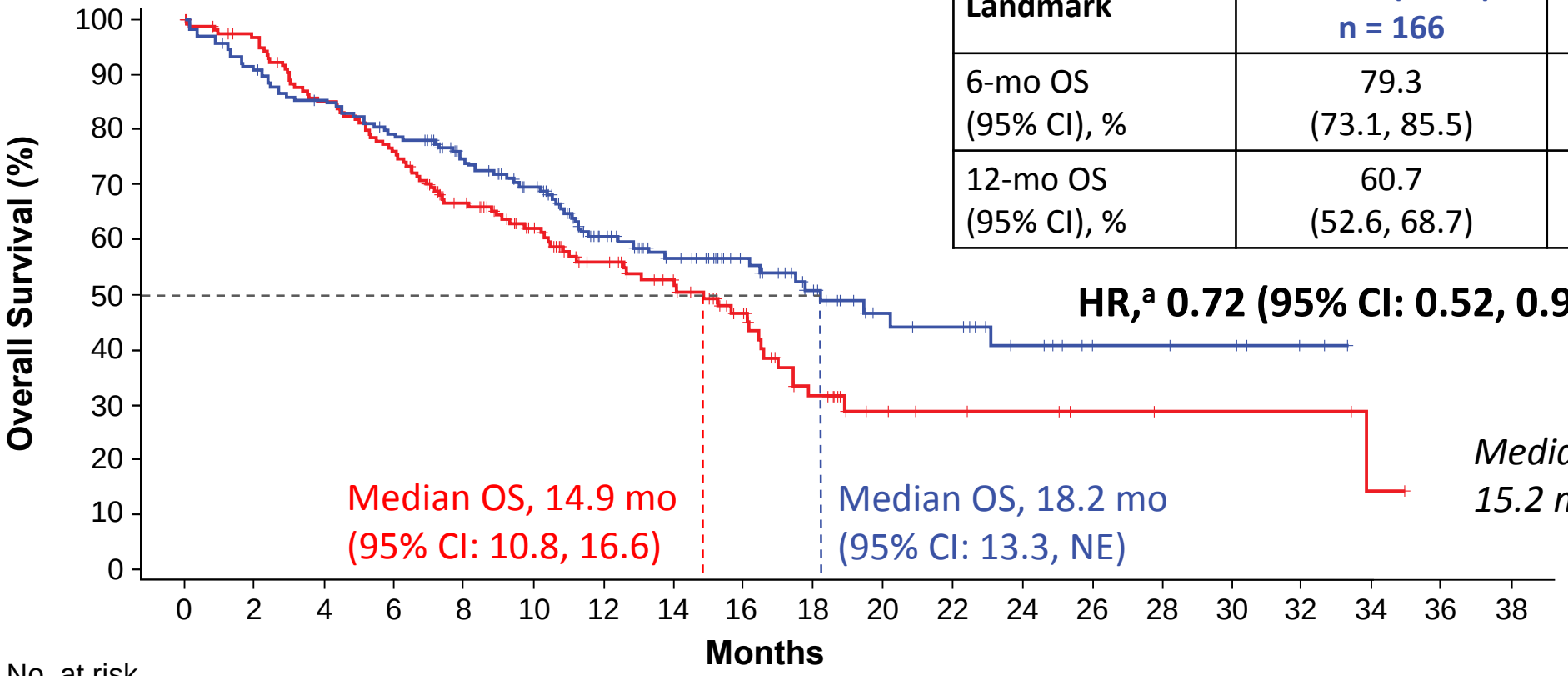
Subgroup[a]	n (%)	OS HR (95% CI)[b]	Median OS, mo	
			Arm A	Arm B
< 65 years	102 (49.8)	0.59 (0.34, 1.04)	NE	13.1
65-74 years	80 (39.0)	0.63 (0.34, 1.19)	17.8	10.4
75-84 years	22 (10.7)	1.04 (0.19, 5.70)	NE	16.2
Male	143 (69.8)	0.57 (0.35, 0.93)	23.1	13.1
Female	62 (30.2)	0.69 (0.34, 1.39)	17.8	14.1
White	169 (82.4)	0.67 (0.44, 1.03)	17.8	13.1
Asian	35 (17.1)	0.38 (0.13, 1.13)	NE	14.1
Never used tobacco	24 (11.7)	1.83 (0.63, 5.31)	8.0	15.9
Current tobacco user	49 (23.9)	0.35 (0.14, 0.88)	NE	10.2
Previous tobacco user	132 (64.4)	0.60 (0.36, 1.00)	23.1	13.1
Non-squamous histology	155 (75.6)	0.62 (0.40, 0.96)	20.2	10.5
Squamous histology	50 (24.4)	0.56 (0.23, 1.37)	NE	15.3
ECOG PS 0	73 (35.6)	0.42 (0.20, 0.92)	NE	15.7
ECOG PS 1	132 (64.4)	0.69 (0.43, 1.10)	16.5	13.1
All TC3 or IC3 WT patients	**205 (100)**	**0.59 (0.40, 0.89)[c]**	**20.2**	**13.1**



[a] The 1 patient in the ≥ 85 years subgroup is not included; 1 patient's race was unknown. [b] Unstratified. [c] Stratified.
Data cutoff: September 10, 2018.

OS: TC2/3 or IC2/3 WT

Landmark	Arm A (atezo) n = 166	Arm B (chemo) n = 162
6-mo OS (95% CI), %	79.3 (73.1, 85.5)	76.1 (69.3, 82.8)
12-mo OS (95% CI), %	60.7 (52.6, 68.7)	56.0 (47.7, 64.3)



HR,[a] 0.72 (95% CI: 0.52, 0.99); *P* = 0.0416[b,c]

Median follow-up, 15.2 mo (range, 0-35)

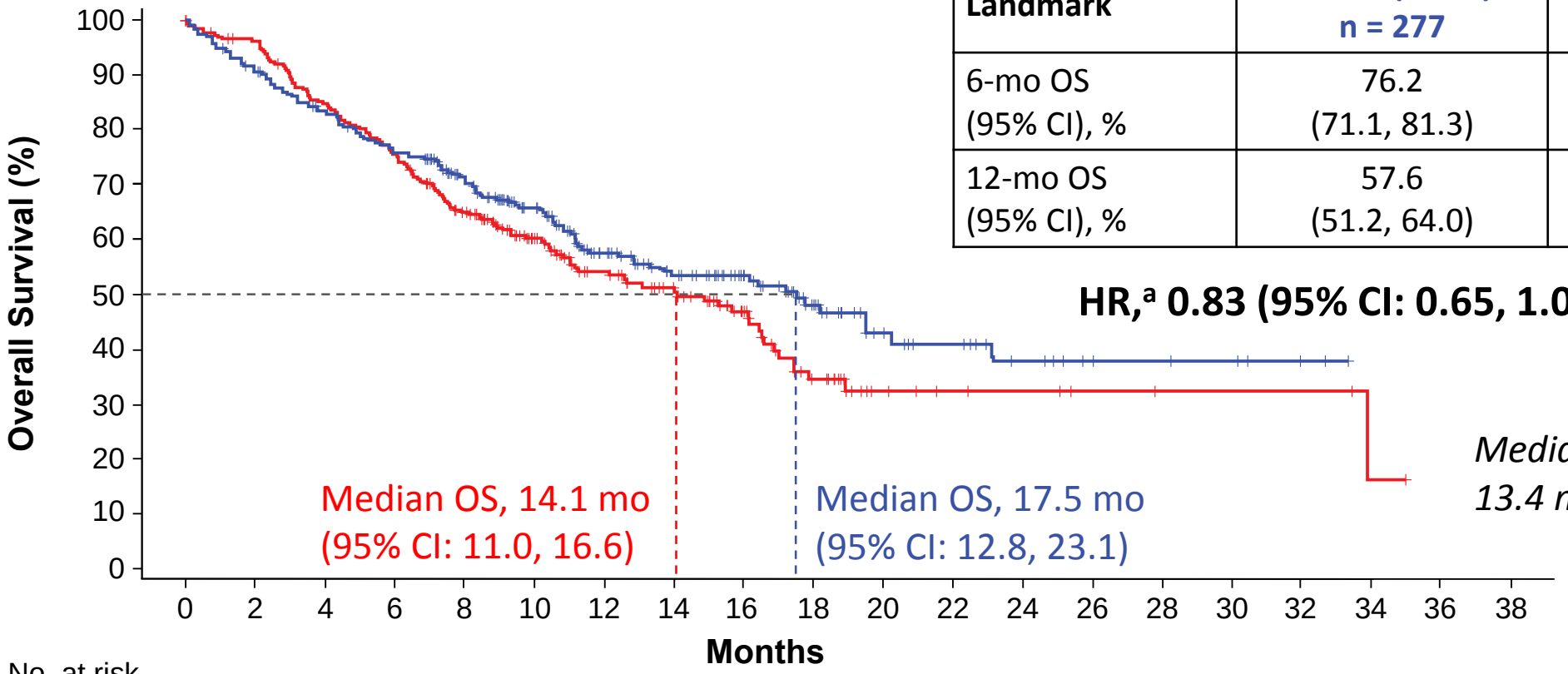
No. at risk

Atezolizumab	166	151	139	128	108	92	66	54	42	30	19	17	11	7	6	5	2
Chemotherapy	162	150	131	117	95	75	57	46	32	17	9	7	6	4	3	3	3	1

[a] Stratified. [b] Stratified log-rank. [c] Not crossing the pre-specified alpha boundary.
Data cutoff: September 10, 2018.

OS: TC1/2/3 or IC1/2/3 WT

Landmark	Arm A (atezo) n = 277	Arm B (chemo) n = 277
6-mo OS (95% CI), %	76.2 (71.1, 81.3)	75.7 (70.5, 80.9)
12-mo OS (95% CI), %	57.6 (51.2, 64.0)	54.3 (47.7, 60.8)



HR,[a] 0.83 (95% CI: 0.65, 1.07); *P* = 0.1481[b,c]

Median follow-up, 13.4 mo (range, 0-35)

No. at risk

Atezolizumab	277	252	226	204	170	134	93	74	58	37	22	17	11	7	6	5	2
Chemotherapy	277	254	223	199	153	108	79	63	43	24	10	7	6	4	3	3	3	1

[a] Stratified. [b] Stratified log-rank. [c] For descriptive purposes only.
Data cutoff: September 10, 2018.

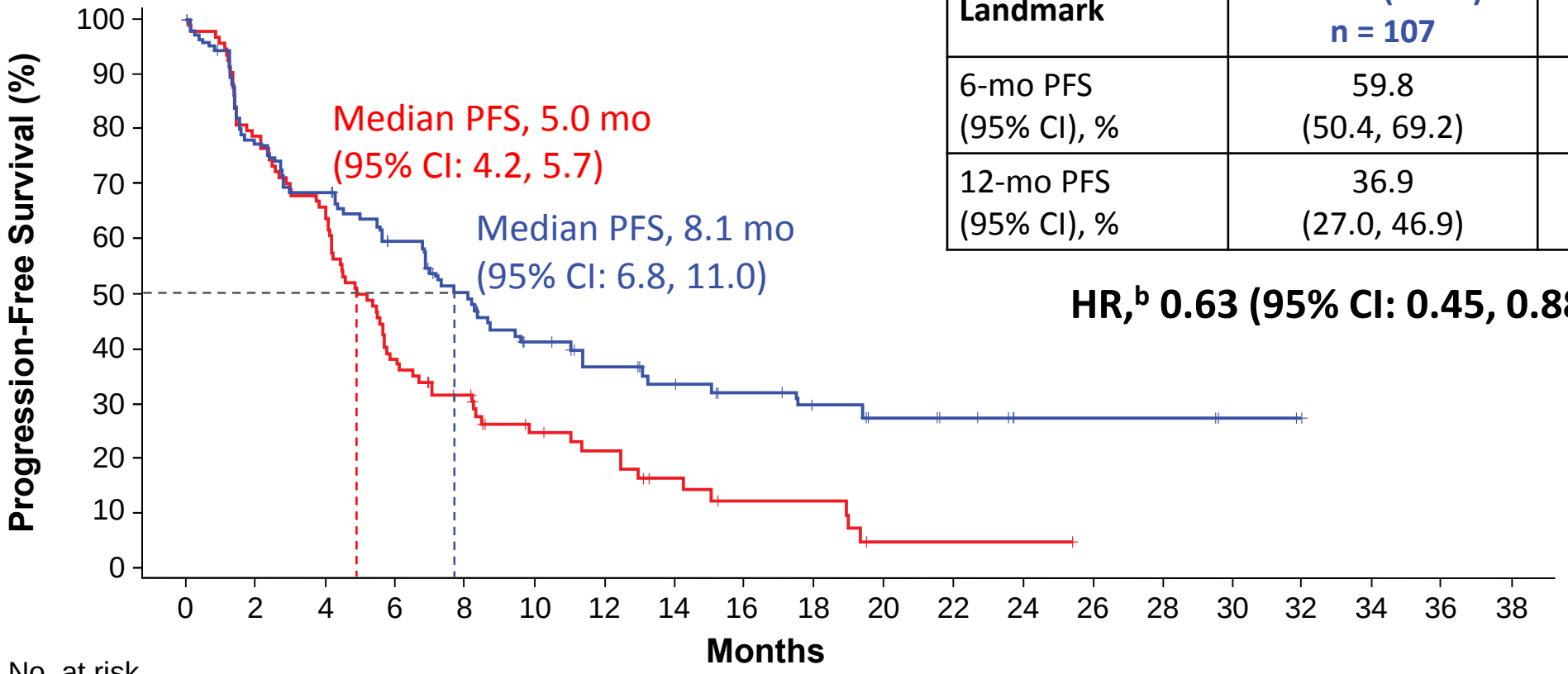
Subsequent Cancer Therapies

	TC1/2/3 or IC1/2/3 WT	
	Arm A (atezo) n = 277	Arm B (chemo) n = 277
Patients with ≥ 1 therapy, n (%)	82 (29.6)	137 (49.5)
Chemotherapy	77 (27.8)	68 (24.5)
Immunotherapy	7 (2.5)	80 (28.9)
Targeted therapy	14 (5.1)	12 (4.3)

- The proportion of patients who received different classes of subsequent cancer therapies was similar across the PD-L1 subgroups

Data cutoff: September 10, 2018.

PFS[a]: TC3 or IC3 WT



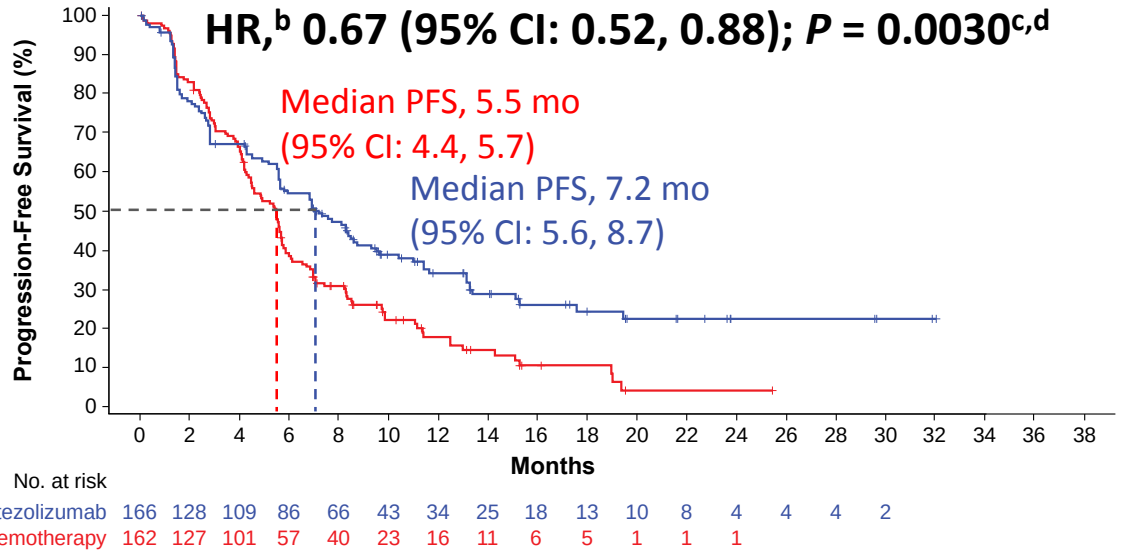
Landmark	Arm A (atezo) n = 107	Arm B (chemo) n = 98
6-mo PFS (95% CI), %	59.8 (50.4, 69.2)	38.3 (28.5, 48.1)
12-mo PFS (95% CI), %	36.9 (27.0, 46.9)	21.6 (12.6, 30.6)

HR,[b] 0.63 (95% CI: 0.45, 0.88); *P* = 0.0070[c,d]

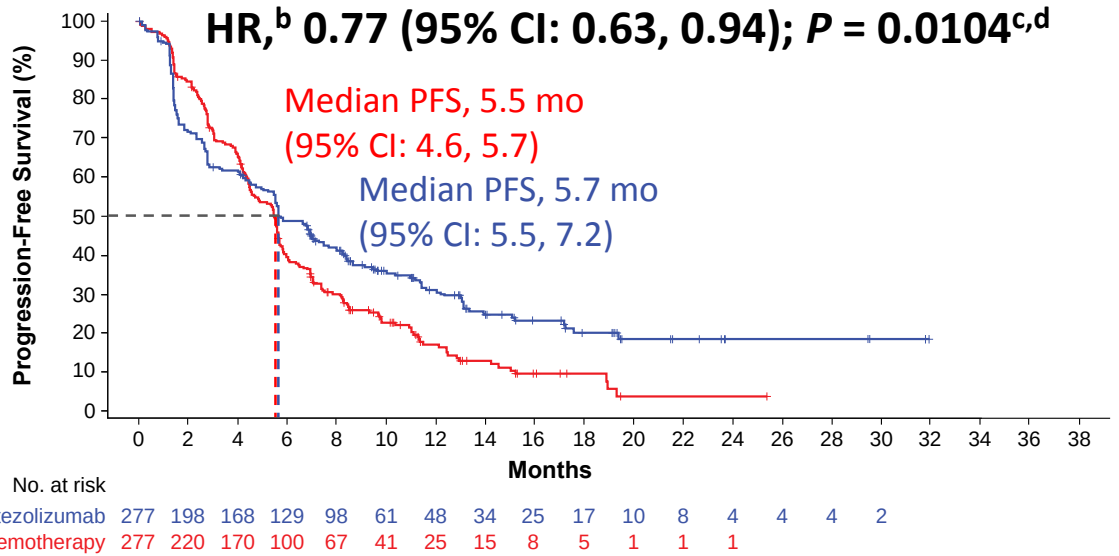
[a] Investigator assessed per RECIST 1.1. [b] Stratified. [c] Stratified log-rank. [d] For descriptive purposes only.
Data cutoff: September 10, 2018.

PFS[a]: TC2/3 or IC2/3 and TC1/2/3 or IC1/2/3 WT

TC2/3 or IC2/3 WT

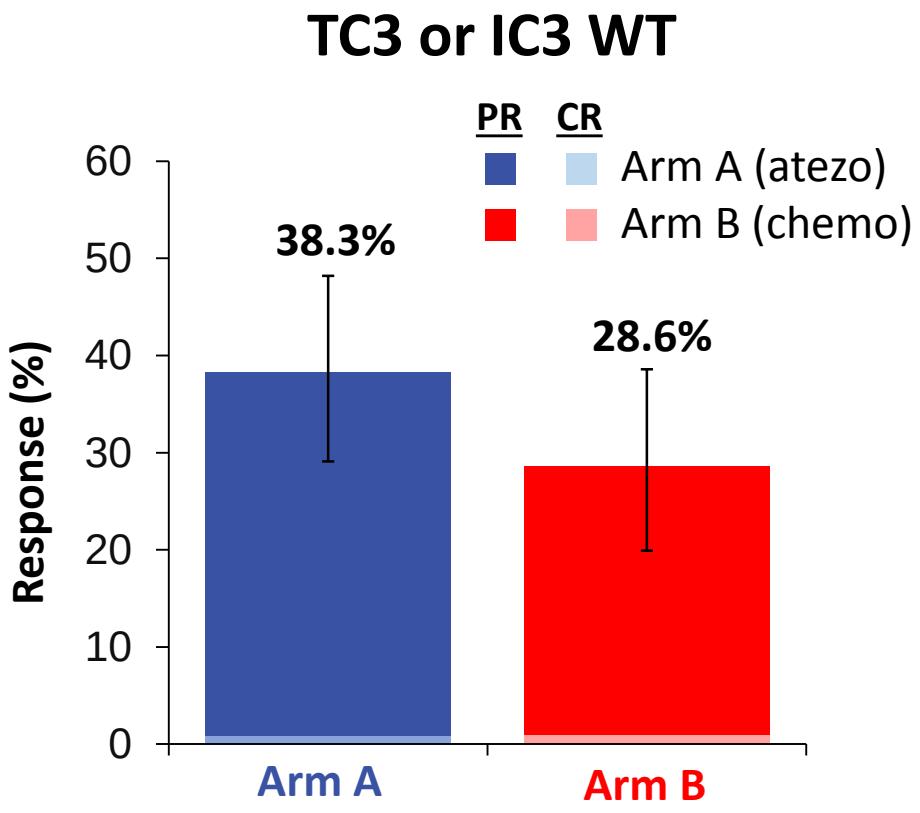


TC1/2/3 or IC1/2/3 WT



[a] Investigator assessed per RECIST 1.1. [b] Stratified. [c] Stratified log-rank. [d] For descriptive purposes only.
Data cutoff: September 10, 2018.

Confirmed ORR and DOR



	Arm A	Arm B
Median DOR (range), mo	**NE (1.8+ to 29.3+)**	**6.7 (2.6 to 23.9+)**

	Arm A (atezo)	Arm B (chemo)
TC2/3 or IC2/3 WT	**n = 166**	**n = 162**
ORR (95% CI), %	30.7 (23.8, 38.3)	32.1 (25.0, 39.9)
Median DOR (range), mo	NE (1.8+ to 29.3+)	5.8 (2.6 to 23.9+)
TC1/2/3 or IC1/2/3 WT	**n = 277**	**n = 277**
ORR (95% CI), %	29.2 (24.0, 35.0)	31.8 (26.3, 37.6)
Median DOR (range), mo	NE (1.8+ to 29.3+)	5.7 (2.4 to 23.9+)

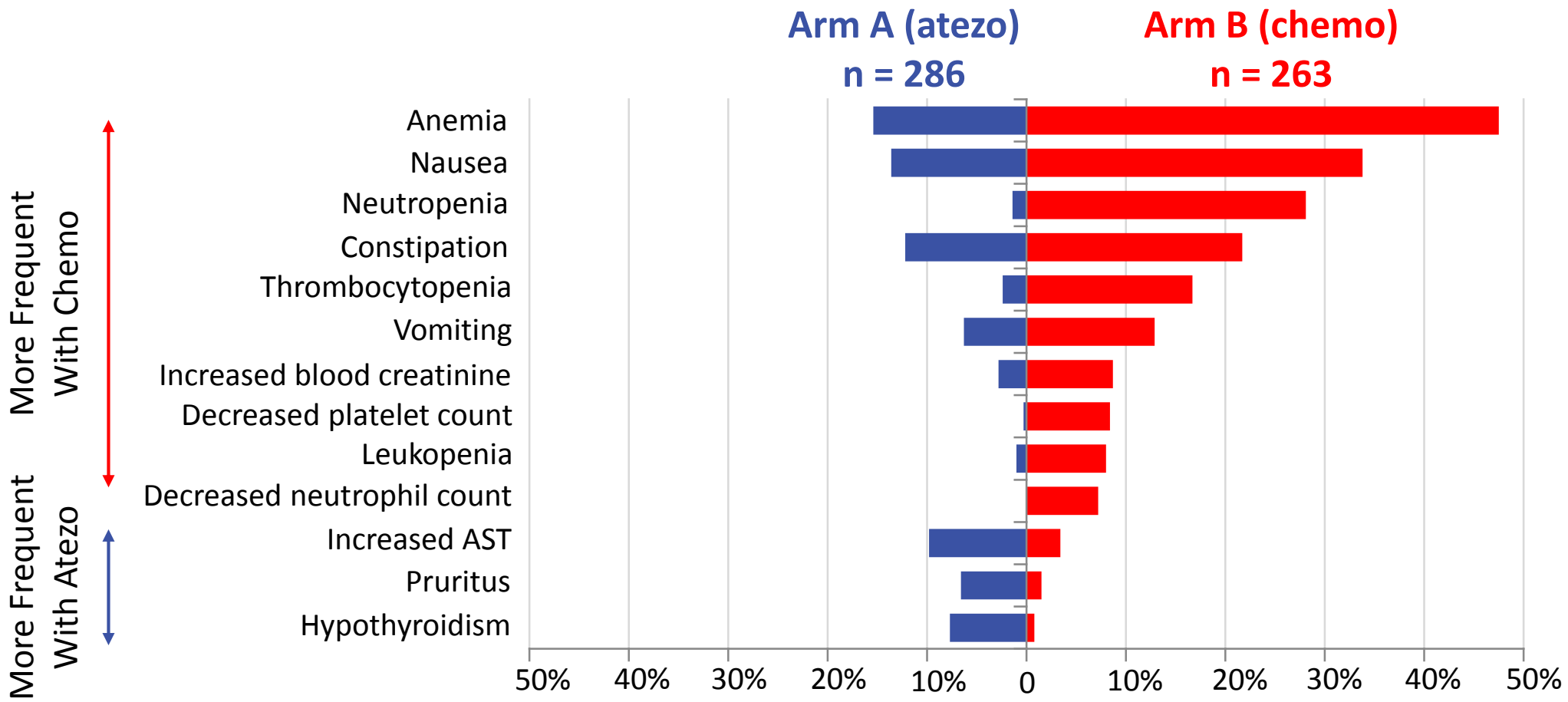
CR, complete response; PR, partial response.
+, censored. Data cutoff: September 10, 2018.

Safety Summary

	Arm A (atezo) n = 286	Arm B (chemo) n = 263			
Median treatment duration (min-max), mo	5.3 (0-33)	Pem 3.5 (0-20)	Gem 2.6 (0-5)	Carb 2.3 (0-5)	Cis 2.1 (0-5)
Any-cause AE, n (%)	258 (90.2)	249 (94.7)			
Related AE	173 (60.5)	224 (85.2)			
Grade 3-4 AE, n (%)	91 (31.8)	141 (53.6)			
Related Grade 3-4 AE	37 (12.9)	116 (44.1)			
Serious AE, n (%)	81 (28.3)	75 (28.5)			
Related serious AE	24 (8.4)	41 (15.6)			
Grade 5 AE, n (%)	11 (3.8)	11 (4.2)			
Related Grade 5 AE	0	1 (0.4)			
AE leading to any treatment withdrawal, n (%)	18 (6.3)	43 (16.3)			
Atezo AESI, n (%)	115 (40.2)	44 (16.7)			
Grade 3-4 atezo AESI	19 (6.6)	4 (1.5)			
Atezo AESI requiring use of corticosteroids, n (%)	22 (7.7)	1 (0.4)			

AE, adverse event; AESI, adverse event of special interest; carb, carboplatin; cis, cisplatin; gem, gemcitabine; pem, pemetrexed. Data cutoff: September 10, 2018.

All-Cause AEs (≥ 5% difference between arms)



AST, aspartate aminotransferase.
Data cutoff: September 10, 2018.

Conclusions

- Atezolizumab monotherapy showed statistically significant and clinically meaningful OS improvement in the TC3 or IC3 WT population vs platinum-based chemotherapy (HR, 0.59 [95% CI: 0.40, 0.89]; *P* = 0.0106)
- The OS testing boundary was not crossed in the TC2/3 or IC2/3 WT population. Therefore, the TC1/2/3 or IC1/2/3 WT population was not formally tested
  - IMpower110 will continue to the OS final analysis
- In the TC3 or IC3 WT population, atezolizumab showed meaningful improvement in PFS, ORR and DOR vs chemotherapy
- The safety profile of atezolizumab was consistent with prior observations; no new or unexpected safety signals were identified
- Additional biomarker analyses will be presented at a future congress
  - PD-L1 IHC by SP263 and 22C3, and bTMB
- Atezolizumab represents a promising 1L treatment option in patients with PD-L1–high NSCLC

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