Pembrolizumab versus placebo as adjuvant therapy for completely resected stage IB–IIIA non-small-cell lung cancer (PEARLS/KEYNOTE-091): an interim analysis of a randomised, triple-blind, phase 3 trial

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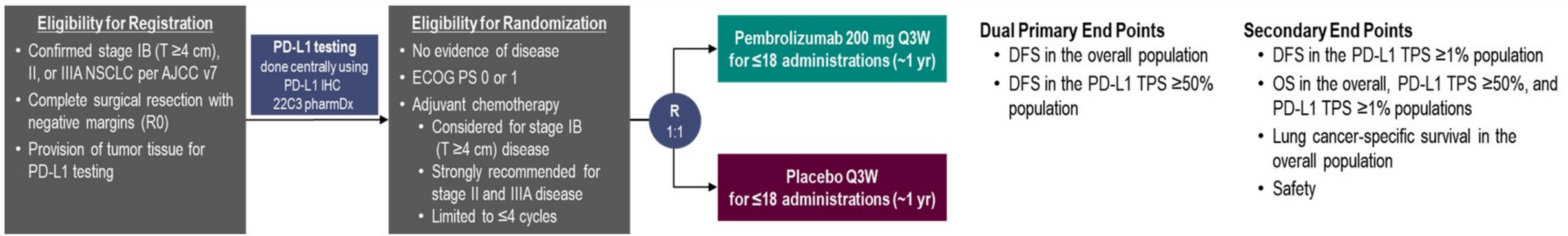


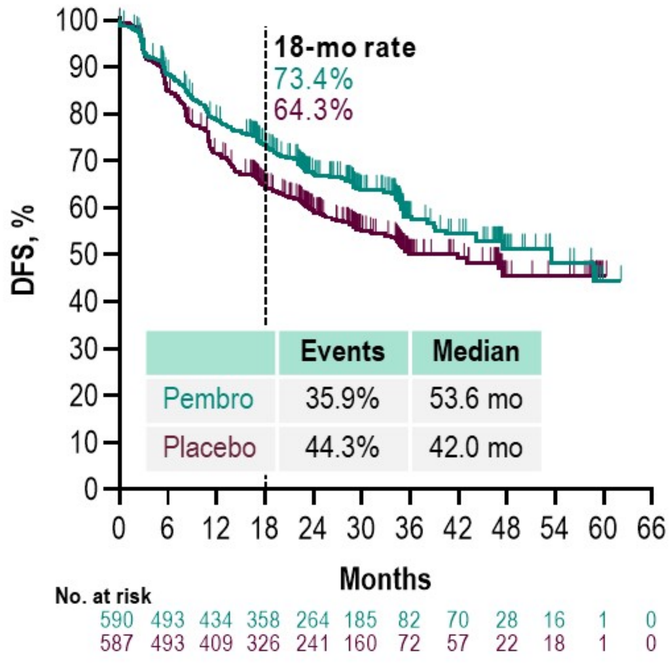
Stratification Factors: disease stage (IB vs II vs IIIA), PD-L1 TPS (<1% vs 1-49% vs ≥50%), adjuvant chemotherapy (yes vs no), geographic region (Asia vs E. Europe vs W. Europe vs ROW)

Characteristic	Overall		PD-L1 TPS ≥50%	
	Pembro (N = 590)	Placebo (N = 587)	Pembro (N = 168)	Placebo (N = 165)
Age, median (range), y	65.0 (31-87)	65.0 (37-85)	64.5 (38-82)	65.0 (37-85)
Male sex	68.0%	68.7%	72.0%	70.3%
Geographic region				
Asia	18.0%	17.9%	17.3%	17.6%
Eastern Europe	19.7%	19.3%	18.5%	18.2%
Western Europe	51.4%	51.3%	53.6%	53.9%
Rest of world	11.0%	11.6%	10.7%	10.3%
ECOG PS 1	35.6%	41.6%	31.0%	38.8%
Current/former smoker	85.3%	88.8%	91.7%	92.1%
Nonsquamous histology	67.5%	61.8%	61.3%	63.6%
Received adjuvant chemotherapy	85.8%	85.9%	85.1%	85.5%
Pathologic stage[a]				
IB	14.2%	14.5%	12.5%	13.3%
II	55.8%	57.6%	56.5%	56.4%
IIIA	30.0%	27.6%	31.0%	30.3%
EGFR mutation[b]	6.6%	5.8%	3.6%	3.0%
ALK translocation[c]	1.2%	1.2%	1.8%	0.0%

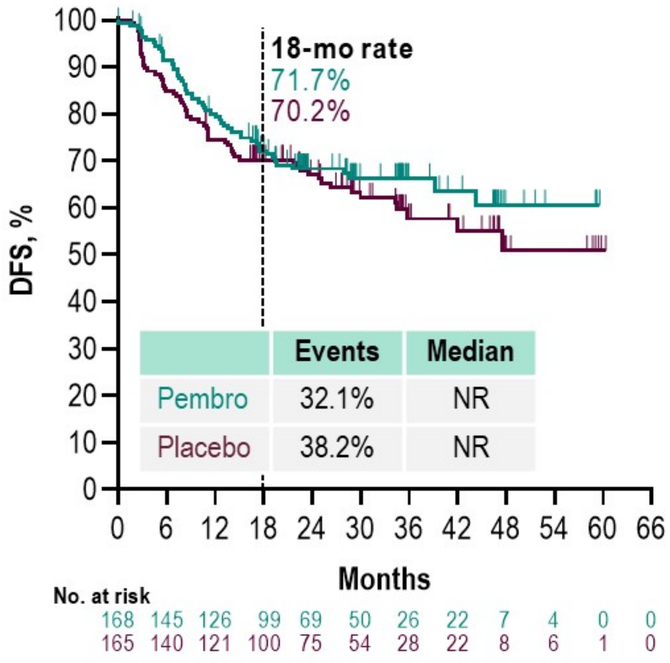
[a]2 (0.3%) participants in the placebo arm had stage IV disease; neither had TPS ≥50%.
[b]*EGFR* mutation status was unknown for 56.9% of participants (59.5% with TPS ≥50%).
[c]ALK translocation status was unknown for 63.5% of participants (65.2% with TPS ≥50%).

PEARLS/KEYNOTE-091:
Primary Results From the Protocol-Specified Second Interim Analysis (IA2)

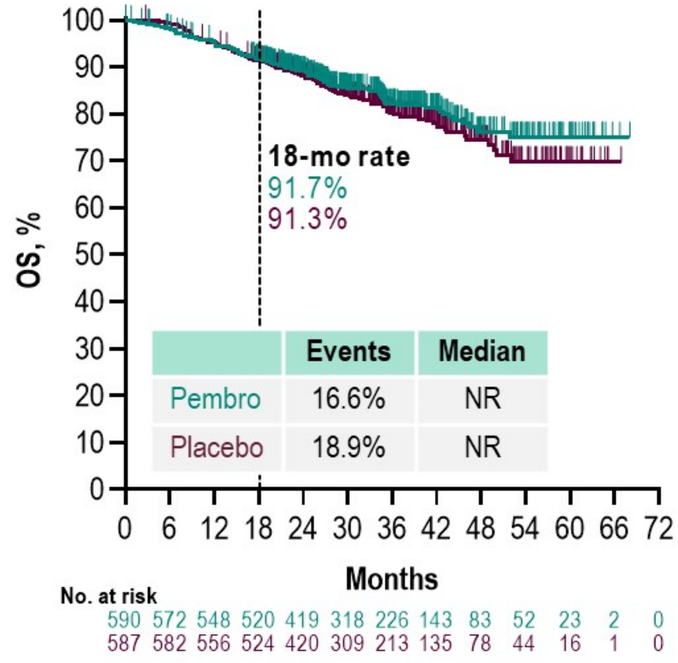
DFS, Overall Population
HR 0.76 (95% CI 0.63-0.91)
***P* = 0.0014**



DFS, PD-L1 TPS ≥50% Population
HR 0.82 (95% CI 0.57-1.18)
***P* = 0.14**



OS, Overall Population
HR 0.87 (95% CI 0.67-1.15)
***P* = 0.17**



- DFS benefit generally consistent across most protocol-specified subgroups, including PD-L1 TPS <1% (HR 0.78, 95% CI 0.58-1.03) and 1-49% (HR 0.67, 95% CI 0.48-0.92)
- Overall safety profile generally as expected for pembrolizumab monotherapy

Median follow-up, defined as time from randomization to the IA2 data cutoff date of September 20, 2021, was 35.6 mo (range, 16.5-68.0).

Paz-Ares L et al. *Ann Oncol* 2022; 2022-4;33:451-453 (Abstr VP3-2022).

Objective: Explore the Potential Impact of the Type of Surgical Resection, Baseline Disease Burden, and Use of Adjuvant Chemotherapy on DFS at IA2

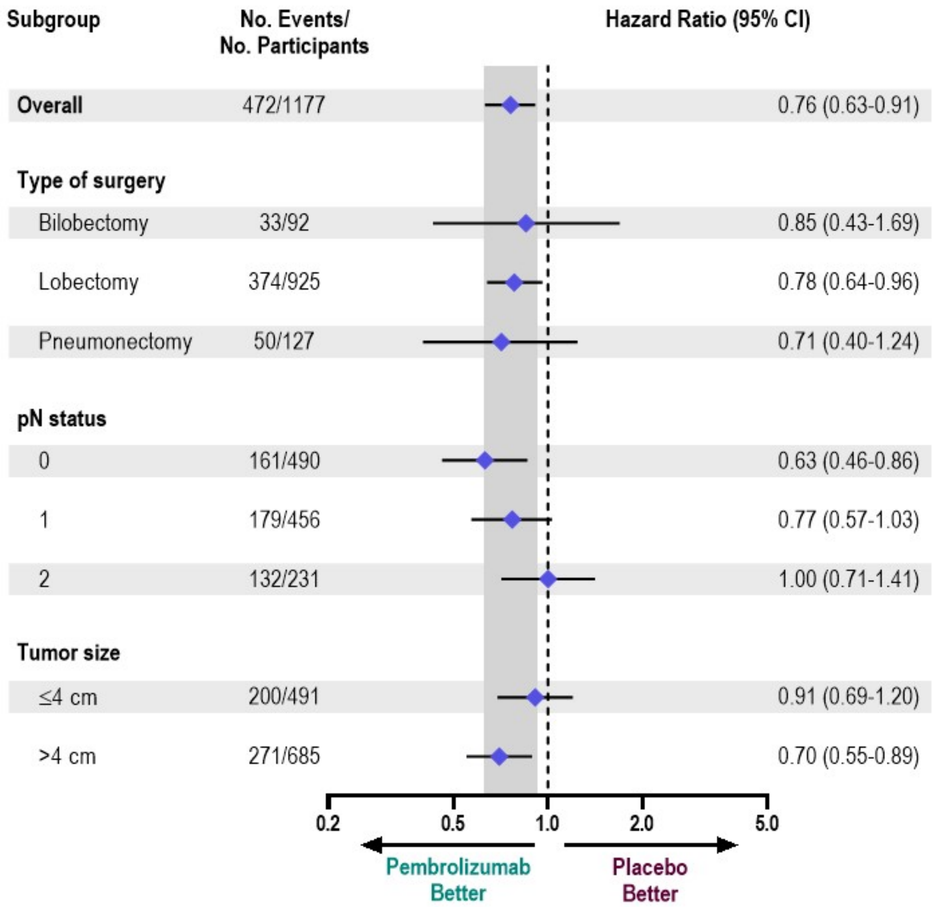
	Pembro (N = 590)	Placebo (N = 587)
Type of surgery, n (%)		
Bilobectomy	47 (8.0)	45 (7.7)
Lobectomy	461 (78.1)	464 (79.0)
Pneumonectomy	65 (11.0)	62 (10.6)
Other	17 (2.9)	16 (2.7)
pN status, n (%)		
0	233 (39.5)	257 (43.8)
1	233 (39.5)	223 (38.0)
2	124 (21.0)	107 (18.2)
Tumor size, n (%)		
≤4 cm	252 (42.7)	239 (40.7)
>4 cm	337 (57.1)	348 (59.3)
Missing	1 (0.2)	0

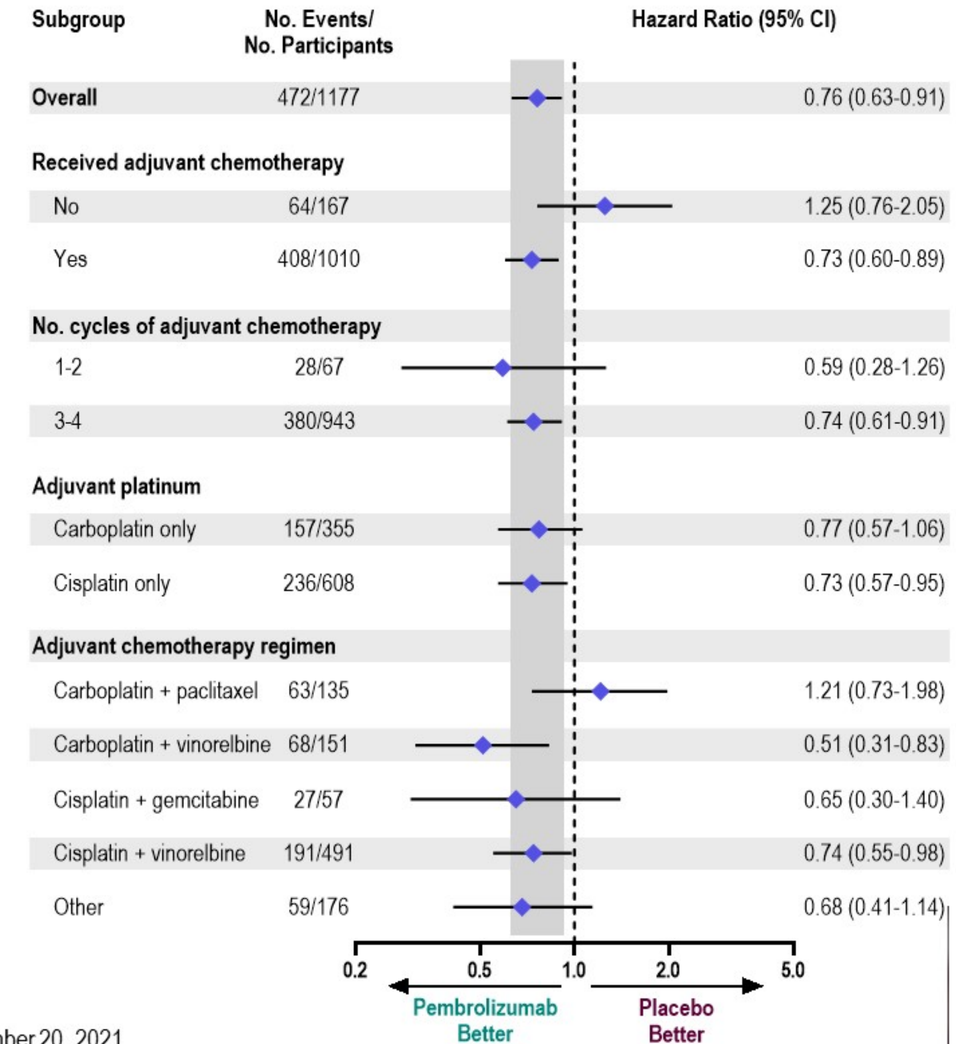
	Pembro (N = 590)	Placebo (N = 587)
Received adjuvant chemotherapy		
No, n (%)	84 (14.2)	83 (14.1)
Reason for not receiving, n		
Participant refused	36	30
Physician decision[a]	46	47
Unknown	2	6
Disease stage in those who did not receive, n		
IB	24	30
II	48	43
IIIA	12	10
Yes, n (%)	506 (85.8)	504 (85.9)
1-2 cycles	35 (5.9)	32 (5.5)
3-4 cycles	471 (79.8)	472 (80.4)

	Pembro (N = 590)	Placebo (N = 587)
Type of adjuvant platinum, n (%)		
Carboplatin-based only	184 (31.2)	171 (29.1)
Cisplatin-based only	301 (51.0)	307 (52.3)
Carboplatin- and cisplatin-based	21 (3.6)	26 (4.4)
Adjuvant regimen, n (%)		
Carboplatin + paclitaxel	60 (10.2)	75 (12.8)
Carboplatin + vinorelbine	81 (13.7)	70 (11.9)
Cisplatin + gemcitabine	27 (4.6)	30 (5.1)
Cisplatin + vinorelbine	241 (40.8)	250 (42.6)
Other	97 (16.4)	79 (13.5)

[a]Based on unfavorable benefit/risk profile for the individual participant.
Data cutoff date: September 20, 2021.

Results: DFS in Subgroups Related to Surgical Resection, Disease Burden, and Use of Adjuvant Chemotherapy





95% CIs of all subgroups overlapped the 95% CI of the overall population and included the overall HR of 0.76. Data cutoff date: September 20, 2021.

DFS was defined as time from randomization to locoregional or metastatic recurrence assessed per RECIST v1.1 by investigator review, appearance of second NSCLC primary or other malignancy, or death from any cause, whichever occurred first. DFS was not analyzed in subgroups of <50 participants in the overall population. Receipt of adjuvant chemotherapy was a protocol-specified subgroup; all other subgroups are exploratory.

Conclusions

- In this exploratory analysis, pembrolizumab generally improved DFS regardless of the type of surgical resection, degree of lymph node involvement, tumor size, and type and extent of adjuvant chemotherapy
  - Exploratory subgroup analysis results should be interpreted with caution due to the lack of power and lack of multiplicity adjustment
- Together with the overall efficacy and safety findings, these data support the benefit of adjuvant pembrolizumab for stage IB (T ≥4 cm) to IIIA NSCLC following complete resection and, if recommended, adjuvant chemotherapy

Thankyou