MADRID 2026 ESMO congress

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Final analysis of adjuvant pembrolizumab (pembro) in resected early-stage non–small-cell lung cancer (NSCLC): Phase 3 PEARLS/KEYNOTE-091 study

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Background

At the second interim analysis (IA2) of PEARLS/KEYNOTE-091 of participants (pts) with resected, stage IB–IIIA NSCLC, adjuvant pembro improved DFS vs placebo in the ITT population (HR, 0.76; 95% CI, 0.63–0.91; *P* = 0.0014) and in the subgroup that received chemotherapy (chemo; HR, 0.73; 95% CI, 0.60–0.89). We report results, including OS, from the final analysis (FA) of PEARLS/KEYNOTE-091 (NCT02504372).

Methods

Eligible pts aged ≥18 y with completely resected, pathologically confirmed stage IB (T ≥4 cm), II, or IIIA NSCLC per AJCC v7 received ≤4 cycles of adjuvant chemo per local guidelines and were randomized 1:1 to 18 cycles (~1 y) of adjuvant pembro 200 mg or placebo Q3W. Primary endpoints were DFS per RECIST v1.1 by investigator assessment in the ITT and PD-L1 TPS ≥50% populations. Secondary endpoints included OS, lung cancer–specific survival (LCSS), and safety.

Results

1177 pts were included in the ITT population (pembro, n = 590; placebo, n = 587). Median follow-up from randomization to data cutoff (Jan 21, 2026) was 87.7 (range, 68.6–120.1) mo. 6-y OS (95% CI) was 68.5% (64.5%–72.1%) for pembro and 66.4% (62.4%–70.1%) for placebo (HR, 0.98; 95% CI, 0.81–1.18; P = 0.41826) in the ITT population and 68.9% (64.6%–72.8%) and 65.4% (61.0%–69.4%), respectively, in pts who received chemo (HR, 0.91; 95% CI, 0.74–1.12). DFS and LCSS results are in the table. Grade ≥3 AEs occurred in 197/580 pts (34.0%) with pembro and 149/581 (25.6%) with placebo. Grade ≥3 immune-mediated AEs and infusion reactions occurred in 46 (7.9%) and 11 pts (1.9%), respectively.

Conclusions

At the final analysis of PEARLS/KEYNOTE-091, adjuvant pembrolizumab continued to demonstrate a consistent DFS benefit versus placebo in resected early-stage NSCLC, with a favorable trend in LCSS. Safety remained manageable. While OS did not show a statistically significant improvement, it was a secondary endpoint and the study was not powered to detect an OS benefit.Table: 2511O

	ITT Population		Pts Who Received Chemo	
	Pembro (n = 590)	Placebo (n = 587)	Pembro (n = 506)	Placebo (n = 504)
DFS				
Median (95% CI), mo	58.7 (47.0–70.4)	43.3 (35.0–55.6)	58.7 (47.0–70.5)	39.1 (31.3–51.7)
6-y DFS (95% CI), %	44.0 (39.7–48.2)	39.2 (35.0–43.2)	43.6 (38.9–48.1)	38.1 (33.7–42.5)
HR (95% CI)	0.85 (0.73–0.98)	0.80 (0.68–0.94)		

	ITT Population		Pts Who Received Chemo	
	Pembro (n = 590)	Placebo (n = 587)	Pembro (n = 506)	Placebo (n = 504)
LCSS				
Median (95% CI), mo	NR (NR–NR)	NR (NR–NR)	NR (NR–NR)	NR (NR–NR)
6-y LCSS (95% CI), %	81.3 (77.7–84.4)	76.9 (73.1–80.2)	81.6 (77.7–84.9)	75.0 (70.8–78.7)
HR (95% CI)	0.81 (0.63–1.03)	0.69 (0.53–0.91)		

NR, not reached.

Clinical trial identification

NCT02504372; EU CT, 2015-000575-27.

Editorial acknowledgement

Medical writing assistance was provided by Aisling Towell, PhD, of ICON plc (Blue Bell, PA, USA). This assistance was funded by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Legal entity responsible for the study

EORTC Lung Cancer Group and ETOP.

Funding

Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Disclosure

M.E.R. O'Brien: Financial Interests, Personal, Other, honoraria: Abbvie, Bristol-Myers Squibb, MSD, and Merck Serono; Financial Interests, Personal, Advisory Role: Amgen, AstraZeneca, Eisai Europe, ITeos Therapeutics, MSD, PharmaMar, Pierre Fabre, and Puma Biotechnology; Financial Interests, Personal, Funding, travel, accommodations, and expenses: Bristol-Myers Squibb; Financial Interests, Personal, Research Funding: MSD. L. Paz-Ares: Financial Interests, Personal, Leadership Role: ALTUM Sequencing and Genomica; Financial Interests, Personal, Speaker's Bureau: AstraZeneca, BMS, Lilly, MSD Oncology, Merck Serono, Pfizer, Roche/Genentech; Financial Interests, Personal, Other, travel, accommodation, and expenses: AstraZeneca, BMS, MSD, Pfizer, Roche, and Takeda; Financial Interests, Personal, Other, honoraria: Amgen, AstraZeneca, Bayer, Blueprint Medicines Corporation, BMS, Celgene, Ipsen, Lilly, Merck Serono, Mirati Therapeutics, MSD, Novartis, Pfizer, PharmaMar, Roche/Genentech, Sanofi, Servier, and Takeda; Financial Interests, Institutional, Research Funding: AstraZeneca, BMS, Kura Oncology, MSD, Pfizer and PharmaMar; Financial Interests, Personal, Other, other relationships: Roche; Financial Interests, Personal, Other, and an immediate family member has other relationships: Amgen, Ipsen, Merck Novartis, Pfizer, Sanofi, Servier, and Roche.. U. Dafni: Financial Interests, Personal, Other, Statistical Consultancy: ETOP; Financial Interests, Institutional, Other, Pro-bono consultancy from myself on research work performed by FSF-H for W4O, MCBS: ESMO; Non-Financial Interests, , Leadership Role, Member of the BoD & Manager of this not for profit organization providing statistical expertise and support in Clinical trials, primarily in cancer: FRONTIER SCIENCE FOUNDATION - HELLAS. K. Oselin: Financial Interests, Institutional, Research Grant: Pfizer and Takeda; Financial Interests, Personal, Other, Consulting: Amgen, Takeda, MSD, Janssen, Roche, and AstraZeneca; Financial Interests, Personal, Other, Travel support: MSD and AstraZeneca. E. Esteban Gonzalez: Financial Interests, Personal, Research Funding: MSD. M.D. Isla Casado: Financial Interests, Personal, Advisory Role: Amgen, AstraZeneca, Bayer; Boehringer Ingelheim, Bristol-Myers Squibb, GSK, Janssen, MSD, Pfizer, Roche, Sanofi, and Takeda; Financial Interests, Personal, Speaker's Bureau: Amgen, AstraZeneca, Bayer, Bristol-Myers Squibb, MSD, Pfizer, Roche, Takeda; Financial Interests, Institutional, Research Funding: GSK and MSD. A. Martinez-Marti: Financial Interests, Personal, Advisory Board: AstraZeneca/MedImmune, Bristol-Meyers Squibb, F. Hoffmann La Roche AG, MSD, MSD Oncology, Pfizer, Janssen, Amgen, and Fuchigec; Financial Interests, Personal, Speaker, Consultant, Advisor, Speaker fees: AstraZeneca/MedImmune, Bristol-Meyers Squibb, F. Hoffmann La Roche AG, MSD, MSD Oncology, Pfizer, Janssen, and Amgen; Financial Interests, Personal, Expert Testimony: AstraZeneca/MedImmune, Bristol-Meyers Squibb, F. Hoffmann La Roche AG, and MSD Oncology; Financial Interests, Personal, Other, support for attending meetings/travel: AstraZeneca/MedImmune, Bristol-Meyers Squibb, F. Hoffmann La Roche AG, MSD, MSD Oncology, Pfizer, Janssen, and Lilly.. M. Faehling: Financial Interests, Personal, Advisory Role: AstraZeneca, Bristol-Myers Squibb, MSD, and Roche; Financial Interests, Personal, Speaker's Bureau: AstraZeneca, Bristol-Myers Squibb, Roche, and Sanofi; Financial Interests, Personal, Research Funding: AstraZeneca, MSD, and Roche.. J. Lee: Financial Interests, Personal, Research Funding: MSD. K. Nakagawa: Financial Interests, Personal, Research Funding: MSD. R. Ghori: Financial Interests, Personal, Full or part-time Employment: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. N.M. Shariati: Financial Interests, Personal, Full or part-time Employment: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. S.M. Keller: Financial Interests, Personal, Full or part-time Employment: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA; Financial Interests, Personal, Stocks/Shares: Merck & Co., Inc., Rahway, NJ, USA. M.E. Mauer: Financial Interests, Personal, Full or part-time Employment: EORTC - European Organisation for Research and Treatment of Cancer Headquarters, Brussels, Belgium. N. Jha: Financial Interests, Personal, Full or part-time Employment: EORTC - European Organisation

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