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Pembrolizumab with or without platinum-based chemotherapy as first-line treatment in advanced NSCLC with PD-L1 $\geq 50\%$. PERSEE phase 3 trial (GFPC 01-2020)

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Background

Pembrolizumab (pembro) monotherapy or in combination with chemotherapy are standard first-line options in advanced PD-L1 $\geq 50\%$ NSCLC. We evaluated whether adding platinum-based chemotherapy improves outcomes versus pembro monotherapy.

Methods

This multicentre open-label phase 3 trial enrolled patients (pts) with untreated stage IV or not amenable to radiotherapy stage III PD-L1 $\geq 50\%$ NSCLC, PS 0-1 and no EGFR/ALK alterations. Pts, stratified by histology and presence of brain metastases, were randomised (1:1) to pembro plus platinum-based chemotherapy (pembro-CT) (paclitaxel for squamous, pemetrexed for non-squamous histology) for four cycles followed by maintenance pembro + pemetrexed, or pembro alone. Primary endpoint was progression free survival (PFS) by blinded central review (BCR) per RECIST v1.1. Key secondary endpoints included investigators assessed PFS, overall survival (OS), objective response rate (ORR), duration of response (DoR) and safety. The study was powered to test the superiority for PFS of pembro-CT over pembro (HR 0.70), with 80% power and a two-sided alpha of 5%.

Results

Between December 2020 and December 2023, 321 pts were randomised across 28 French centres. Median age was 64 years (59-69), 32.4% of pts were female, 2.2% were non-smokers, 23.4% had brain metastases, and 19.6% had squamous histology. At the cut-off date of 7 April 2026, the median follow-up was 38.7 (35.3-41.6) months. By BCR, pembro-CT significantly improved PFS compared with pembro: HR 0.56; 95% CI 0.43-0.74; $p < 0.001$; median 16.1 (11.0-34.1) vs 6.9 (5.5-9.3) months. Median PFS by investigators was 13.7 (9.3-25.4) vs 6.9 (4.7-9.2) months (HR 0.60; 95% CI 0.46-0.78). Median OS was 50.2 (32.6-NR) vs 29.9 (23.4-47.9) months (HR 0.77; 95% CI 0.57-1.05), ORR 77.5% vs 50.3%, DoR 30 (13.1-NR) vs 15.6 (9.8-32.8) months (HR 0.86; 95% CI 0.59-1.24) for pembro-CT and pembro, respectively. Grade ≥ 3 TRAEs occurred in 53.8% and 19.3% of pts in the pembro-CT and pembro arms, respectively.

Conclusions

In first line treatment of advanced PD-L1 $\geq 50\%$ NSCLC, PERSEE demonstrates a significant improvement of PFS with pembro-CT compared to pembro monotherapy and may help refine treatment selection.

Clinical trial identification

EudraCT 2020-002626-86.

Legal entity responsible for the study

CHU Brest and Groupe Français de Pneumo-Cancérologie (GFPC).

Funding

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Disclosure

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