

Phase II Trial of pembrolizumab plus lenvatinib in PD-L1 positive patients with TKI-resistant EGFR-mutated advanced non-small cell lung cancer

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Background

- Lenvatinib plus pembrolizumab exhibits synergistic activity with manageable toxicity across various solid tumors^{1,2}.
- Preclinical and early clinical data indicate this combination modulates the tumor microenvironment and may overcome resistance to prior TKI therapy, supporting its evaluation as a chemotherapy-sparing approach in advanced NSCLC³.
- This trial investigated the efficacy and safety of pembrolizumab combined with lenvatinib in patients with advanced, TKI-resistant, EGFR-mutated NSCLC expressing PD-L1(TPS ≥1%).

Methods

- This phase II, single-arm trial evaluated lenvatinib combined with pembrolizumab in patients with advanced EGFR-mutated NSCLC and PD-L1-positive tumors (TPS ≥1%) who had progressed after one or two prior lines of EGFR TKI therapy. Participants with a T790M mutation were required to have received a third-generation TKI.
- Treatment consisted of oral lenvatinib (20 mg once daily) plus intravenous pembrolizumab (200 mg every 3 weeks) for up to 35 cycles or until disease progression or unacceptable toxicity.
- The primary endpoint was investigator-assessed PFS per RECIST v1.1. Secondary endpoints included OS, ORR, DOR, and safety.

Results

- After a median follow-up of 4.0 months, the median PFS for the overall population was 4.0 months (Figure 1).
- The confirmed ORR was 24.2% (Figure 2), and the disease control rate (DCR) was 90.9% (Figure 2).
- Treatment-related adverse events (TRAEs) occurred in 14 participants (42.4%). Grade ≥3 TRAEs were reported in 6(18.2%) participants.

Conclusions

- In conclusion, the combination of lenvatinib and pembrolizumab demonstrated modest antitumor activity and a manageable safety profile in patients with PD-L1-positive, TKI-resistant, EGFR-mutated advanced NSCLC.
- These findings support its potential as a chemotherapy-free treatment option for this population with an unmet medical need. ClinicalTrials.govNCT05078931.

Figure 1. Progression-free survival (PFS) for lenvatinib plus pembrolizumab in the overall population (data cutoff: December 31, 2025)

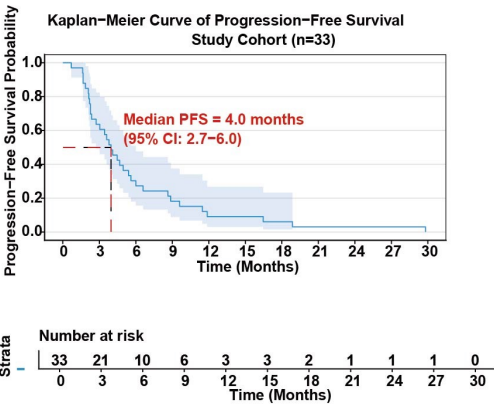
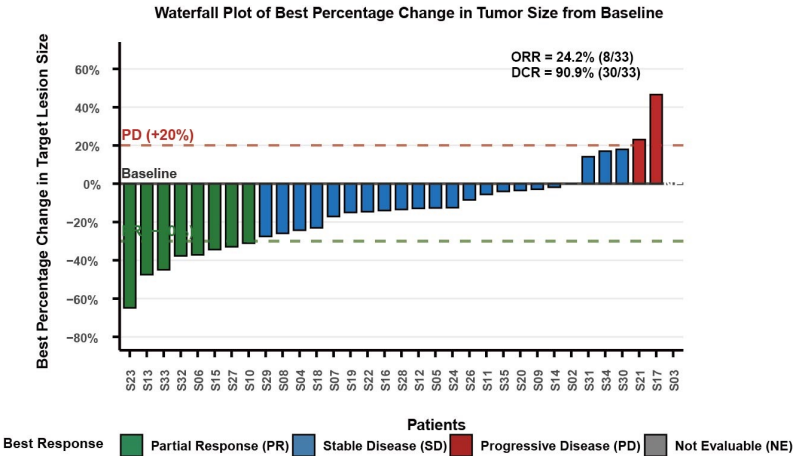


Figure 2. Objective response rate (ORR) for lenvatinib plus pembrolizumab in the overall population (data cutoff: December 31, 2025)



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Disclosure

The presenter declares no competing interests.

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