RESEARCH SUMMARY

First-Line Selpercatinib or Chemotherapy and Pembrolizumab in *RET* Fusion–Positive NSCLC

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CLINICAL PROBLEM

In patients with advanced, *RET* fusion–positive non–small-cell lung cancer (NSCLC), the RET kinase inhibitor selpercatinib has shown promise in nonrandomized studies, but data comparing this drug with existing therapies are lacking.

CLINICAL TRIAL

Design: A phase 3, multinational, open-label, randomized trial assessed the efficacy and safety of selpercatinib as compared with control therapy in patients with unresectable, stage IIIB, IIIC, or IV, nonsquamous, *RET* fusion–positive NSCLC who had not previously received systemic treatment for metastatic disease.

Intervention: 261 patients were randomly assigned in a 1.6:1 ratio to receive either selpercatinib (160 mg twice daily in continuous 21-day cycles) or control therapy (platinum-based chemotherapy with or without pembrolizumab every 21 days). The primary end point was progression-free survival.

RESULTS

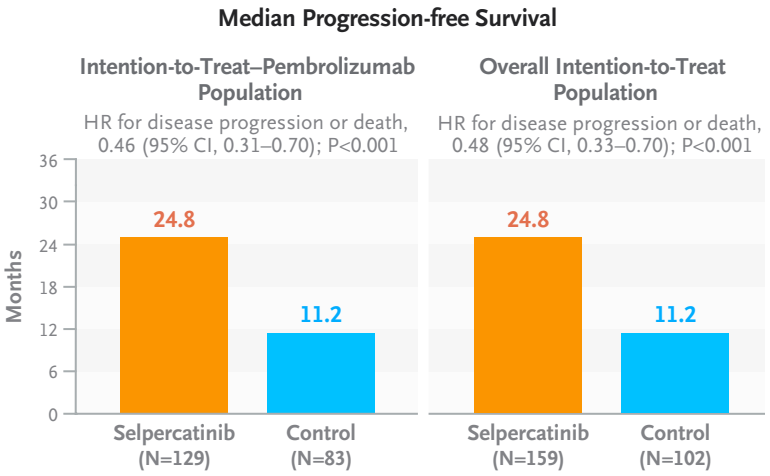
Efficacy: Progression-free survival was significantly longer with selpercatinib than with control therapy both in the population of patients whose physician had intended to treat them with pembrolizumab in the event that they were assigned to the control group (intention-to-treat–pembrolizumab population) and in the overall intention-to-treat population.

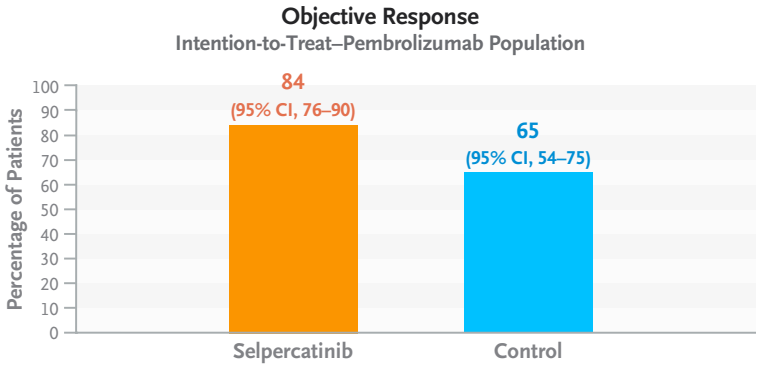
Safety: Adverse events that occurred at a higher incidence with selpercatinib included elevated liver-function values, hypertension, diarrhea, edema, and prolonged QTc interval.

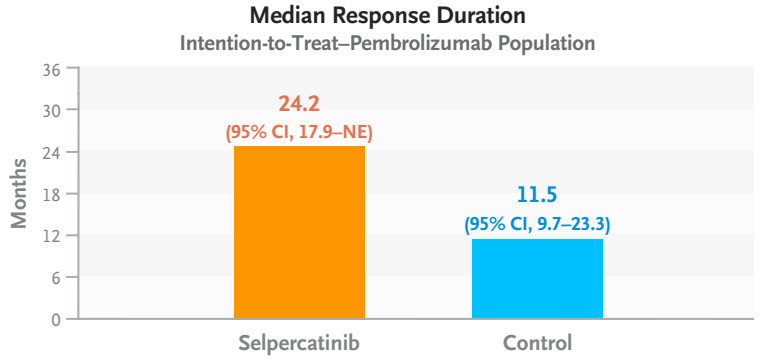
LIMITATIONS AND REMAINING QUESTIONS

- Overall survival data remain immature.
- The trial was open-label, and there was a high rate of crossover both within the trial itself and to commercially available selective RET inhibitors.

Links: Full Article | NEJM Quick Take | Science behind the Study







CONCLUSIONS

In patients with *RET* fusion–positive advanced NSCLC, first-line selpercatinib was associated with longer progression-free survival than chemotherapy and pembrolizumab.