

Selpercatinib in RET fusion-positive non-small-cell lung cancer (SIREN): An international, real-world analysis

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Introduction: RET gene fusions are rare genetic drivers in non-small cell lung cancer (NSCLC).

Selective RET-inhibitors like selpercatinib have shown therapeutic activity in early clinical trials but their efficacy in the real-world setting is unknown.

Methods: A retrospective efficacy and safety analysis was performed on data from RET fusion-positive NSCLC patients who participated in a selpercatinib access program between August 2019 and January 2021. Twenty-seven centers in twelve different countries contributed to this dataset: Australia (1 center), Austria (8), Canada (2), Finland (1), France (2), Germany (4), Italy (2), Netherlands (2), Spain (1), Slovenia, (1), Sweden (2), and Switzerland (1).

Results: Data from 50 patients with RET fusion-positive advanced NSCLC treated with selpercatinib

were analyzed. Most patients were Non-Asian (90%), female (60%), never smoker (74%), with a median age of 65 years (range, 38-89) and 32% had known brain metastasis at time of selpercatinib treatment. Overall, 13 patients were treatment-naïve, while 37 were pretreated with a median of 3 lines of therapy (range, 1-8). The objective response rate (ORR) was 68% (95% CI, 53-81) in the overall population. The disease control rate was 92%. Median progression-free survival was 15.6 months (95% CI, 8.8-22.4) after a median follow-up of 9 months. In patients with measurable brain metastases (n=8) intracranial ORR reached 100%. In total, 88% of patients experienced treatment-related adverse events (TRAEs), a large majority of them being grade 1/2; most common grade ≥3 TRAEs were increased liver enzyme levels (in 10% of patients), prolonged QTc time (4%), abdominal pain (4%), hypertension (4%) and fatigue/asthenia (4%). None of patients discontinued selpercatinib treatment for safety reasons. No new safety concerns were observed, nor any treatment-related death.

Conclusions: In this real-world setting, the selective RET-inhibitor selpercatinib demonstrated durable systemic and intracranial antitumor activity in RET fusion-positive NSCLC and was well tolerated.

Conflict of Interests:

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