Patient-Reported Outcomes Reinforce Clinical Benefits of Tarlatamab in Small Cell Lung Cancer

Tarlatamab was approved by the FDA in May 2024 for patients who progressed after platinum-based chemotherapy.

Tarlatamab (Imdelltra; Amgen) demonstrated moderate and long-lasting tolerability with a strong benefit-risk profile in previously treated small cell lung cancer (SCLC), with favorable patient-reported outcomes (PROs) across a spectrum of functional outcomes and symptoms.

SCLC is the most aggressive type of lung cancer, accounting for approximately 15% of all diagnoses. It is commonly seen in patients with a long history of tobacco use, specifically smoking cigarettes, although it can also be caused by exposure to chemicals, such as radon. The majority of patients with SCLC have advanced disease by the time of diagnosis, and the 5-year survival rate remains poor at less than 10%. Emerging research indicates that, like other cancers, SCLC is responsive to immunotherapies, potentially offering patients additional or alternative options to standard chemotherapy or radiotherapy.[1]

Bispecific antibody interacting with cancer cells | Image Credit: © ProArt Studios - stock.adobe.com

DLL3 has emerged as a promising target for therapy due to its high expression in 85% to 94% of SCLC cases. Tarlatamab, a bispecific T-cell engager, is designed to recognize DLL3 on cancer cells and CD3 on T-cells, facilitating T-cell-driven destruction of DLL3-positive tumor cells. In May of 2024, tarlatamab received accelerated approval for treatment of extensive stage SCLC with disease progression on or after platinum-based chemotherapy, based on data from the DeLLphi-301 trial (NCT05060016).[1-3]

The phase 2 trial results demonstrated promising efficacy, with an overall response rate (ORR) of 40% (95% CI: 31–51) and a median duration of response (DOR) of 9.7 months (range: 2.7–20.7+). Notably, among the 69 patients with available platinum sensitivity data, response rates varied based on prior treatment resistance. In patients with platinum-resistant SCLC—defined as disease progression within 90 days of their last platinum-based therapy—the ORR reached 52% (95% CI: 32–71). In contrast, those with platinum-sensitive disease, progressing at least 90 days after their last platinum treatment, had an ORR of 31% (95% CI: 18–47). These findings highlight the drug's activity, particularly in the platinum-resistant population, where treatment options are limited.[4]

Emerging data from a study of PROs of SCLC patients treated with tarlatamab has demonstrated encouraging results, with high PRO completion rates and trends toward symptom improvement, further supporting the clinical benefits underlying the drug's approval. Patients received intravenous tarlatamab every 2 weeks at either 10 mg or 100 mg until disease progression or loss of clinical benefit. PROs were assessed using multiple validated tools, including the European Organization for Research and Treatment of Cancer 30-item Quality of Life Questionnaire (EORTC-QLQ-C30), the 13-item lung cancer module (LC13), the Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE), and the GP5 question from the Functional Assessment of Cancer Therapy—General Form (FACT-GP5).[4]

Patients completed PRO assessments at cycle 1 (days 1, 8, and 22), cycle 2 (days 1 and 15), and then every 6 weeks starting from cycle 3. Additionally, median time to deterioration (TTD) was assessed for symptom and functional scales. Among the 100 patients who were PRO-evaluable at the target 10 mg dose, completion rates for the EORTC-QLQ-C30 and LC13 remained consistently high (greater than 80%) throughout the trial.[4]

Analysis of PROs suggested improvements in key quality-of-life metrics. Patients reported a reduced symptom burden, particularly for dyspnea, with improvements becoming more pronounced in later treatment cycles (greater than or equal to a 10-point reduction). Chest pain and cough remained stable over time. Median TTD exceeded 6 months for cough and dyspnea, although deterioration in chest pain was not estimable, suggesting durable symptom control.[4]

Additionally, tarlatamab was well tolerated, with most patients experiencing no or only minimal bother from side effects after baseline. Patient-reported adverse events were generally mild to moderate in severity and occurred infrequently.[4]

The PROs provide valuable insight into the patient experience with tarlatamab, reinforcing its potential to not only extend survival but also maintain or improve quality of life for individuals with previously treated SCLC. Future studies will help refine its role in treatment sequencing and explore potential combinations to enhance patient outcomes.

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