Pfizer's lung cancer drug trial fails to show significant improvement in overall survival

Pfizer Inc., announced topline results from the Phase 3 SigVie-002 study (previously known as Be6A Lung-01) evaluating sigvotatug vedotin, an investigational, potential first-in-class integrin beta-6 (IB6) directed antibody-drug conjugate (ADC). The study enrolled adults with locally advanced, unresectable or metastatic non-squamous non-small cell lung cancer (NSCLC) who had received one or more lines of prior therapy.

In the overall population, sigvotatug vedotin did not show a statistically significant improvement in the primary endpoint of overall survival (OS) compared to docetaxel. The safety profile of sigvotatug vedotin was manageable and consistent with prior studies.

Encouragingly, in patients who received only one prior line of systemic therapy, which represents two-thirds of the study population, a stronger trend was observed for OS and progression-free survival (PFS) for sigvotatug vedotin over docetaxel, said the company. In the exploratory analysis, no clear IB6 expression-response relationship was observed. Detailed results from SigVie-002 will be submitted for presentation at a future medical congress.

“Patients with previously treated advanced NSCLC are a historically difficult-to-treat population, and there is clearly more work to be done to improve the outcomes for this population,” said Jeff Legos, Chief Oncology Officer, Pfizer. “Although the overall study results did not demonstrate superiority over docetaxel, it is encouraging that second-line patients treated with sigvotatug vedotin achieved strong efficacy outcomes compared to an established standard of care, alongside a manageable safety profile. This observed clinical benefit, along with our Phase 1 combination data in the first-line setting, reinforces our confidence in the potential of the sigvotatug vedotin program, including an ongoing Phase 3 trial in combination with pembrolizumab in first-line advanced NSCLC.”

“It is important not to underestimate the activity of docetaxel as a comparator in this setting. Patients enrolled in this trial were heavily pre-treated, with most having previously received both platinum-based chemotherapy and immunotherapy, yet docetaxel continues to provide meaningful clinical benefit. Although the study did not meet its overall survival endpoint, in second-line patients the data suggest a clinically meaningful survival benefit for sigvotatug vedotin over docetaxel, supporting continued scientific evaluation of sigvotatug vedotin in earlier lines in combination with immunotherapy,” said Solange Peters, M.D., PhD, Chair of Medical Oncology & Thoracic Cancers Clinic, Lausanne University Hospital, Switzerland.

“The ability of sigvotatug vedotin to induce immunogenic cell death provides a strong rationale for combination approaches with immunotherapy, particularly in earlier treatment settings where immune competence is better preserved. In this context, the promising phase 1 efficacy signals observed in treatment-naïve patients with high PD-L1 expression warrant further evaluation and may represent a more effective clinical application of this strategy.”

In NSCLC, IB6 is expressed on approximately 90% of tumors. IB6 is associated with poor prognosis. Sigvotatug vedotin is a novel ADC designed for high target selectivity of IB6 and rapid internalization, which may help limit binding to other integrins more likely to be expressed in normal tissues and potentially reduce off-target toxicity.

Pfizer is evaluating sigvotatug vedotin in several ongoing studies across multiple stages and patient populations in NSCLC and other solid tumors, including an ongoing Phase 3 study evaluating sigvotatug vedotin + pembrolizumab in 1L NSCLC with PD-L1 tumor proportion score (TPS) =50%; and exploration of sigvotatug vedotin in novel combinations, including with PF'4404, the novel bispecific antibody targeting PD-1 and VEGF, in early-stage lung cancers and other IB6-expressing tumors.

Since the acquisition of Seagen, Pfizer has continued to advance a broad ADC portfolio spanning marketed medicines and pipeline programs. Pfizer is progressing multiple differentiated ADC candidates, including fetrastobart vedotin, a PD-L1–directed ADC currently in Phase 3 in NSCLC, additional IB6-targeted ADCs with alternate payloads, and early-stage candidates exploring novel targets and payloads, including topoisomerase I (Topo1) inhibitors and novel auristatin-based payloads. This breadth reinforces the strength of Pfizer's Oncology pipeline, including the potential for novel combinations with its investigational PD-1xVEGF bispecific antibody, supporting the company's goal of delivering eight potential Oncology breakthroughs by 2030.

SigVie-002 is an ongoing, open-label randomized, Phase 3, global study evaluating sigvotatug vedotin compared with docetaxel in adult participants with previously treated locally advanced, unresectable or metastatic NSCLC. Patients were randomized to receive sigvotatug vedotin administered intravenously on Days 1 and 15 of each 28-day cycle or docetaxel administered intravenously on Day 1 of each 21-day cycle. The primary endpoint of this trial is overall survival (OS). The study enrolled 703 participants. Descriptive, secondary endpoints include progression-free survival (PFS), confirmed objective response rate (ORR) and duration of response (DOR) per RECIST v1.1 as assessed by blinded independent central review (BICR), said the company.

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