BIOPHARMA DIVE

# Merck suffers bad week as 3 Keytruda combination trials fail

The studies are part of Merck's strategy to sustain market exclusivity for its $21 billion immunotherapy as key patent expirations approaches.

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*A molecular model of Merck & Co.'s cancer immunotherapy Keytruda.*
*Dr_Microbe via Getty Images*

Merck & Co.'s reputation for picking winners in cancer treatment took a hit this week as the New Jersey-based drugmaker reported three separate failures of trials that combined its immunotherapy Keytruda with other agents.

The data demonstrate the challenges drug developers will have improving on Keytruda, on track to be the world's biggest-selling drug this year. Merck reported Keytruda sales of $18 billion through the first nine months of 2023.

The biggest setback is from a lung cancer trial of a coformulation of Keytruda with a different type of immunotherapy called vibostolimab, an approach that could help Merck fight off biosimilar competition after its main Keytruda patent expires in 2028.

The trial, called KeyVibe-002, was designed to see if the combination could improve on chemotherapy treatment in people with non-small cell lung cancer that has spread beyond the lungs,



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who have progressed after treatment with an immunotherapy and chemotherapy. Combined with the chemotherapy docetaxel, the Keytruda-vibostolimab combination didn't significantly delay disease progression when compared with docetaxel alone.

Earlier this year, Merck released results from another part of the trial, which tested the Keytruda-vibostolimab combination alone against docetaxel. Those results were also negative for the combination.

The KeyVibe-002 trial results, released at a European medical meeting, could cast continued doubt on drugs from vibostolimab's class, called TIGIT inhibitors. TIGIT inhibition is a novel approach that developers hope can work hand-in-hand with Keytruda, Opdivo and other drugs from that class, called PD-1 blockers. TIGIT drugs from Bristol Myers Squibb, Gilead and Roche have experienced clinical setbacks, although more recent Roche data have been more positive.

Merck currently is running four Phase 3 trials of the combination in lung cancer along with one in melanoma.

The other two trial failures were with marketed drugs that Merck collaborates on with other drugmakers. The first was another trial in non-small cell lung cancer that combined Keytruda with Lynparza, an AstraZeneca drug, to keep disease at bay following an initial line of therapy that combined Keytruda and chemotherapy.

The trial, called KEYLYNK-008, was stopped at an interim analysis when data monitors saw that the Keytruda-Lynparza combination maintenance therapy didn't help patients live longer or delay progression longer than Keytruda plus chemotherapy maintenance.

The third trial sought to expand use of Keytruda in combination with Eisai's Lenvima in endometrial cancer, where the pairing now

is approved for use in patients with a mutation called mismatch-repair proficient in patients who have progressed on an earlier line of treatment and aren't candidates for surgery or radiation therapy.

The LEAP-001 trial sought to demonstrate that the Keytruda-Lenvima would outperform a chemotherapy combination as a first-line treatment, but missed both on overall survival and progression-free survival measures.

Merck reported Lynparza collaboration revenue of $884 million and Lenvima collaboration revenue of $734 million through the first nine months of 2023.