PHARMA

Merck's Keytruda flunks pivotal studies in early-stage lung and skin cancers

By **Angus Liu**
Aug 29, 2024 10:16am

Merck & Co. | Keytruda | non-small cell lung cancer | PD-1/L1

Merck announced that two phase 3 studies of its PD-1 inhibitor Keytruda have failed. (iStock / Getty Images Plus)

A Merck & Co. effort to move its PD-1 behemoth Keytruda into early treatment of lung cancer has reached a dead end, along with another bid to expand into a type of early-stage skin cancer.

Merck has decided to stop (https://www.businesswire.com/news/home/20240829788910/en/Merck-Provides-Update-on-Phase-3-KEYNOTE-867-and-KEYNOTE-630-Trials) the phase 3 KEYNOTE-867 trial for Keytruda in inoperable stage 1 or 2 non-small cell lung cancer, the company said Thursday.

During a planned interim analysis, Keytruda's addition to radiation not only failed to improve patients' risk of disease worsening or death, but it led to higher rates of adverse events, including ones that resulted in death, Merck said. The study tested the pairing against stereotactic body radiotherapy alone.

After reviewing the data, an independent data monitoring committee ruled that the benefit-risk profile of the Keytruda-radiotherapy regimen didn't support continuing the trial, according to Merck.

The flop in early-stage disease doesn't affect Keytruda's position in metastatic NSCLC, where it's the first-line standard of care. In October, the PD-1 inhibitor also snagged a key FDA approval as a continuous treatment both before and after surgery in resectable NSCLC.

Still, the early-stage NSCLC setback comes as Merck's efforts to further enhance Keytruda in metastatic NSCLC have encountered some difficulties, and ahead of a potential challenge (https://www.fiercepharma.com/pharma/merck-cmo-akeso-summits-keytruda-head-head-win-maybe-another-option-issue) from a PD-1/VEGF bispecific antibody by Akeso and Summit Therapeutics.

In two recent back-to-back failures, Merck found (https://www.fiercepharma.com/pharma/mercks-lynparza-keytruda-plan-sputters-2nd-lung-cancer-trial-will-adc-work) that using its AstraZeneca-partnered Lynparza during the maintenance treatment phase of newly diagnosed metastatic NSCLC didn't work out across nonsquamous (https://www.fiercepharma.com/pharma/mercks-lynparza-keytruda-plan-sputters-2nd-lung-cancer-trial-will-adc-work) and squamous (https://www.fiercepharma.com/pharma/merck-lynparza-fails-improve-keytruda-first-line-lung-cancer) histologies, separately, in two phase 3 studies.

In addition, a combination of Keytruda and Merck's investigational anti-TIGIT antibody vibostolimab was found (https://www.fiercebiotech.com/biotech/merck-co-digs-tigit-fail-sharing-survival-data-phase-2-lung-cancer-trial) to be less effective than the chemotherapy docetaxel in a phase 2 trial in previously treated metastatic NSCLC. Merck still has three ongoing phase 3 trials for MK-7684A, a fixed-dose combo of Keytruda and vibostolimab, in different NSCLC settings.

In the wake of Merck's latest setback, the search for a viable PD-1/L1 inhibitor in stage 1 or 2 unresected NSCLC is still ongoing for at least one other company. AstraZeneca is conducting the phase 3 PACIFIC-4 trial, testing the addition of its PD-L1 inhibitor Imfinzi to radiotherapy in a similar design to Merck's KEYNOTE-867 trial. The AZ study started about three months earlier than its Merck counterpart, and it has a separate cohort examining the British pharma's Tagrisso following radiotherapy in EGFR-mutant tumors.

In a second setback for Keytruda that Merck unveiled Thursday, the New Jersey pharma is discontinuing the phase 3 KEYNOTE-630 trial for Keytruda as an adjuvant treatment in patients with high-risk locally advanced cutaneous squamous cell carcinoma (cSCC) following surgery and radiation.

An independent data monitoring committee recommended that the study be stopped for futility. On the study's primary endpoint of recurrence-free survival, Keytruda missed the mark in preventing disease recurrence or death compared with placebo. What's more, patients' life expectancy also didn't favor Keytruda, although the overall survival endpoint was not formally tested because of the primary endpoint flop.

JHU 2077
Merck Sharp v. Johns Hopkins
IPR2024-00624

Before the latest trial miss, Keytruda gained approvals in recurrent or metastatic cSCC or locally advanced cSCC that's not curable by surgery or radiation.

Merck & Co. | Keytruda | non-small cell lung cancer | PD-1/L1 | cutaneous squamous cell carcinoma | Clinical Data | Pharma

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ATTEND EVENTS

25-26 SEP
Medical Affairs Strategic Summit West
San Diego, CA

25-27 SEP
Fierce Clinical Summit
Philadelphia, PA

30-01 SEP-OCT
New Product Planning Summit
Boston, MA

SPONSORED PHARMA

Understanding SPMS: Insights from Dr. Jiwon Oh

Sponsored by **SANOFI**
Sep 27, 2024 08:00am

Diagnosing multiple sclerosis (MS) can be an incredibly complex process for both patients and doctors. With symptoms that often overlap with, or mimic other conditions, making a definitive diagnosis is challenging and could potentially take months or even years.

Advancements in research are essential for improving diagnostic accuracy and enabling earlier intervention, which can significantly enhance the quality of life for individuals living with MS.

In this episode, sponsored by Sanofi, we have the privilege of speaking with Dr. Jiwon Oh, a distinguished neurologist, scientist, and Medical Director of the BARLO Multiple Sclerosis (MS) Centre at St. Michael's Hospital, University of Toronto.

Dr. Oh is also the principal investigator for several key studies, including the Canadian Prospective Cohort Study to Understand Progression in MS (CanProCo) that aims to deepen our understanding of MS progression.

Today, she delves into the complexities of secondary progressive MS (SPMS), discussing everything from the need to reassess its various subtypes to the importance of clinical trials focusing on non-relapsing SPMS patients.

"The significance of a trial that focuses exclusively on non-relapsing SPMS is that there have been very few trials looking at progressive MS in general," Dr. Oh explains, outlining how progress is now starting to be made in this field.

"It's a challenging population to study. It's a tricky and risky population to study. But in clinical practice, these are the types of patients where we truly have the greatest unmet need."

To learn more about the challenges that this unmet need is currently presenting, and some of the ways in which researchers such as Dr. Oh are working to bridge this gap, tune into the full episode.

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Warren, others urge government to allow generics to Novo's blockbuster GLP-1s ahead of CEO hearing

By **Zoey Becker**
Sep 23, 2024 05:28pm

Novo Nordisk | Elizabeth Warren | Ozempic (semaglutide) | Wegovy

Novo Nordisk's CEO Lars Fruergaard Jorgensen is set to appear before the Senate HELP committee at a Tuesday hearing. (Becky Wright/Getty Images)

Ahead of a Senate hearing centered on high prices for Novo Nordisk's in-demand semaglutide medications, lawmakers are pressing the government to use its "march-in" rights and allow generic versions of the drugs to enter the market.

Sen. Elizabeth Warren, D-Massachusetts, Rep. Lloyd Doggett, D-Texas, and other legislators penned a letter (https://doggett.house.gov/sites/evo-subsites/doggett.house.gov/files/evo-media-document/1498%20Weight%20Loss%20Drug%20Letter%209.23.24.pdf) (PDF) to secretary of the Department of Health and Human Services (HHS), Xavier Becerra, urging the agency to use its authority to dole out licenses to generic semaglutide makers in order to promote competition and bring down prices.

"By utilizing your competitive licensing authority to permit generic competitors to Wegovy and Ozempic, you can stabilize supplies at a time of enormous demand and lower outrageous prices that have severely limited access to these life-changing drug," the lawmakers wrote.

"March-in" rights were introduced as part of the Bayh-Dole Act of 1980, enabling the government to grant licenses for any patented invention that is "used or manufactured by or for the United States" under certain circumstances. The move has never been used (https://crsreports.congress.gov/product/pdf/IF/IF12582) despite numerous attempts (https://www.warren.senate.gov/newsroom/press-releases/warren-king-doggett-urge-hhs-to-exercise-march-in-rights-for-life-saving-cancer-drug-xtandi-to-dramatically-lower-its-price-for-millions-of-americans) to pressure the government into using the legal authority.

A market exclusivity period is allotted to patented products as a reward for the investments drugmakers pour into the development process. Companies often use this reasoning to justify high prices, an argument that the lawmakers say has been "debunked time and time again." The lawmakers say Ozempic and Wegovy have generated more than $38 billion in combined revenue, while Novo spent $4.71 billion on R&D last year.

A clutch of advocacy groups including Public Citizen and Doctors for America made similar arguments in their own separate letter (https://www.citizen.org/article/groups-urge-secretary-becerra-to-license-competition-on-diabetes-and-weight-management-drugs/#_ftn21) to Becerra, noting that the savings generated from generic versions of Ozempic and Wegovy could add up (https://www.citizen.org/article/estimate-of-savings-from-generic-competitors-to-ozempic-and-wegovy/) to more than $10 billion yearly.

The efforts come just before Novo's CEO, Lars Fruergaard Jørgensen, is set to testify at a Senate hearing on his company's pricing.

Earlier this year, the Senate Committee on Health, Education, Labor and Pensions (HELP) launched an investigation into the company's pricing, finding that it charges $969 per month in the U.S. for Ozempic versus $155 in Canada, $122 in the company's home country of Denmark and $59 in Germany, with similar discrepancies in Wegovy pricing.

HELP committee chair Sen. Bernie Sanders, I-Vermont, later threatened to subpoena the company into appearing at a September 24 hearing on the matter, and Novo's CEO eventually agreed to participate.

Along with the lawmakers speaking out ahead of the hearing, Médecins Sans Frontières/Doctors Without Borders (MSF) took the opportunity to publicly call on (https://msfaccess.org/ahead-us-senate-hearing-msf-calls-pharmaceutical-corporations-eli-lilly-novo-nordisk-and-sanofi) diabetes drugmakers Novo, Sanofi and Eli Lilly to lower prices and allow generics to enter the market.

Fruergaard's appearance at the hearing follows a separate high-profile pricing probe that saw the CEOs of Bristol Myers Squibb, Johnson & Johnson and Merck testify before a Senate committee. The U.S. Chamber of Commerce previously wrote in a statement (https://www.fiercepharma.com/pharma/sanders-wants-subpoena-novo-nordisk-exec-langa-answer-questions-us-semaglutide-pricing) in response to the Novo subpoena threat that Sanders was "abusing the power of his committee to intimidate companies."

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