Ovarian cancer drug to enter phase II clinical trial

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Our Center for Cancer Drug Discovery building—now the home of our drug discovery scientists. Credit: Institute of Cancer Research

An innovative cancer drug discovered by scientists at The Institute of Cancer Research, London, is set to enter a new clinical trial.

The drug, called idetrexed and formerly known by experimental drug names including BTG945, ONX-0901 and CT900, was created by scientific teams in what is now the ICR's Center for Cancer Drug Discovery.

It has already shown particular promise in ovarian cancer in a first-in-human, phase I trial led by researchers at the ICR and our partner hospital, The Royal Marsden NHS Foundation Trust.

The phase II trial will further test idetrexed's effectiveness and safety in a larger group of patients, specifically with ovarian cancer.

Idetrexed is set to undergo the larger trial thanks to a new agreement between US-based pharmaceutical company Algok Bio and BTG International, which partnered with the ICR earlier in the drug's development. Cancer Research UK also helped to fund earlier research.

Algok Bio's exclusive license agreement with BTG grants the former the rights to develop and commercialize idetrexed worldwide. Under the agreement, Algok Bio will make an upfront payment to BTG and additional payments contingent on achieving specific regulatory and sales milestones, as well as tiered royalty payments.

Algok Bio will soon initiate pivotal studies for registering idetrexed for ovarian cancer treatment. Additional clinical programs exploring other indications and combination regimens with standard care will also be pursued.

About idetrexed

Idetrexed is a potent thymidylate synthase inhibitor that triggers cell death while selectively targeting the alpha folate receptor (FRα), which is highly expressed in cancer cells compared to normal tissues across a variety of solid tumors.

A phase I study conducted by the ICR and The Royal Marsden, the results of which were published in *Clinical Cancer Research* last year, treated 109 cancer patients, including ovarian cancer patients resistant to platinum-based chemotherapy, with idetrexed.

Among 25 platinum-resistant ovarian cancer patients with high or medium expression of FRα who received the recommended phase II dose, tumor shrinkage was observed in nine patients (overall response rate 36%; 95% CI, 18–57.5).

According to the World Health Organization, ovarian cancer is the seventh most commonly diagnosed cancer in women worldwide, with over 300,000 new cases diagnosed each year. More than 90% of ovarian cancer cases express FRα, with high levels of overexpression also observed in endometrial, triple-negative breast cancer, and mesothelioma.

Kidney, lung, colorectal, and gastric cancers also exhibit varying degrees of expression.

The development of idetrexed by Algok Bio holds significant promise for the treatment of these cancers, and the exclusive license agreement with BTG represents a major milestone in the development of this innovative therapy.

Professor Udai Banerji, principal investigator of the idetrexed phase I study and co-director of Drug Development at the ICR and The Royal Marsden, said, "Idetrexed is a small molecule targeting FRα-

overexpressing cancers that has shown significant single agent activity in phase I clinical trials. In a similar stage of development, idetrexed has shown comparable efficacy to drugs such as antibody drug conjugates that have gone on to successful late phase development.

"This drug has significant potential as a possible future treatment for ovarian cancer and I am thrilled that it is now advancing to the next stage of clinical development. I wish Algok Bio the very best to develop this drug for patients with ovarian cancer and other FRα-overexpressing cancers."

Dr. Sung Chul Kim, President and Founder of Algok Bio, said, "As the only small molecule drug with a unique mechanism of action currently targeting FRα, the efficacy and safety profiles in early clinical studies were highly promising and competitive with other antibody-drug conjugate drugs. We are thrilled to be a part of this development program and believe it holds significant potential as an effective treatment for ovarian cancer patients."

More information: Susana Banerjee et al, A Phase I Trial of CT900, a Novel α-Folate Receptor–Mediated Thymidylate Synthase Inhibitor, in Patients with Solid Tumors with Expansion Cohorts in Patients with High-Grade Serous Ovarian Cancer, *Clinical Cancer Research* (2022). DOI: 10.1158/1078-0432.CCR-22-1268

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