

Novel targeted cancer therapies demonstrate activity and safety in metastatic solid tumors

June 3 2024



Credit: Pixabay/CC0 Public Domain

Two early-phase clinical trials presented at the 2024 American Society of Clinical Oncology ([ASCO](#)) Annual Meeting by researchers from The University of Texas MD Anderson Cancer Center demonstrate promising responses and safety profiles in heavily pretreated patients

with advanced solid tumors.

The studies were featured in an oral abstract session highlighting the development of new molecularly targeted agents.

Novel antibody-drug conjugate targeting CEACAM5 shows activity in advanced colorectal cancer

Preliminary data from a [Phase I study](#) evaluating the novel antibody-drug conjugate (ADC) M9140 demonstrated encouraging activity in heavily pretreated patients with advanced colorectal cancer. The study was presented by principal investigator Scott Kopetz, M.D., Ph.D., professor of Gastrointestinal Medical Oncology and associate vice president for Translational Integration.

The trial treated 40 patients from the U.S., Europe and Japan across seven different dose levels. Among them, 10% experienced a partial response and 42.5% achieved stable disease. With a preliminary median progression-free survival of 6.7 months, the results suggest M9140 may offer a potential new approach for treating this disease.

"Patients with advanced colorectal cancer typically face a challenging prognosis, so there's a critical need for new treatment options," Kopetz said. "I'm encouraged by the positive response in many of these patients and eagerly anticipate the results from the ongoing trial."

M9140 is the first ADC with a topoisomerase 1 inhibitor payload designed to target the cell surface protein CEACAM5, which is found in over 90% of colorectal cancers.

The most common adverse events were hematological, including neutropenia, thrombocytopenia and anemia. Notably, there were no reports of interstitial lung disease or ocular toxicity, which are commonly associated with similar ADCs. The data suggest that M9140 has a manageable safety profile, leading researchers to determine the maximum tolerated dose at 2.8 mg/kg, with recommended doses for further study set at 2.4 and 2.8 mg/kg.

Further evaluation is ongoing in a randomized expansion study to determine the long-term potential and effectiveness of this treatment.

USP1 inhibitor shows manageable safety profile and signs of early anti-tumor activity in patients with metastatic solid tumors

Preliminary data from the [first-in-human Phase I trial](#) of RO7623066—a first-in-class inhibitor of ubiquitin-specific peptidase 1 (USP1)—show a promising safety profile as a single agent and signs of early anti-tumor activity for patients with advanced solid tumors. The data were presented by Timothy Yap, M.B.B.S., Ph.D., professor of Investigational Cancer Therapeutics and vice president and head of clinical development in MD Anderson's Therapeutics Discovery division.

On the trial, researchers observed a partial response in one patient with advanced fallopian tube cancer, while 5 of 29 (17%) patients had stable disease for greater than 16 weeks. Consistent with preclinical data, preliminary clinical anti-tumor activity of the RO7623066 combination with the PARP inhibitor olaparib appeared to be associated with BRCA1 mutation status.

"RO7623066 has demonstrated a manageable safety profile in combination with olaparib with early signals of anti-tumor activity in

patients with metastatic solid tumors," Yap said. "Further evaluation of the combination of RO7623066 and olaparib currently is ongoing to determine the recommended dose for expansion and recommended Phase II dose."

RO7623066, or KSQ-4279, is an oral, selective, small molecule, targeting USP1, a deubiquitinating enzyme that regulates the translesion synthesis and Fanconi Anemia DNA repair pathways.

The trial enrolled 70 heavily pretreated patients with [advanced solid tumors](#) in three arms comprising dose escalation studies investigating RO7623066 as a single agent, in combination with olaparib, and in combination with the chemotherapy carboplatin, respectively.

The most common side effect as a single agent and in combination with olaparib was anemia. The most common grade three or higher adverse events were hyponatremia with single agent and anemia in combination with olaparib. Both dose interruption and drug discontinuation rates were low. Further evaluation of RO7623066 in combination with olaparib is ongoing with additional measures introduced to address the occurrence of anemia.

Pharmacokinetic and pharmacodynamic data suggested the drug effectively targeted USP1, as expected, in a near dose-proportional exposure.

More information: Scott Kopetz et al, [First-in-human trial of M9140, an anti-CEACAM5 antibody drug conjugate \(ADC\) with exatecan payload, in patients \(pts\) with metastatic colorectal cancer \(mCRC\)](#)

Timothy A. Yap et al, [First-in-human phase I trial of the oral first-in-](#)

[class ubiquitin specific peptidase 1 \(USP1\) inhibitor KSQ-4279 \(KSQi\)](#)

Provided by University of Texas M. D. Anderson Cancer Center

Citation: Novel targeted cancer therapies demonstrate activity and safety in metastatic solid tumors (2024, June 3) retrieved 26 June 2024 from

<https://medicalxpress.com/news/2024-06-cancer-therapies-safety-metastatic-solid.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.