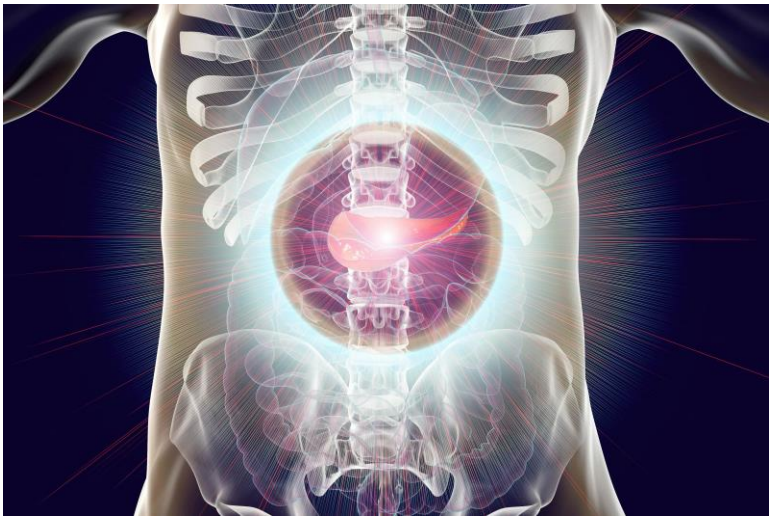
Avutometinib With Defactinib Granted FDA Orphan Drug Designation to Treat Pancreatic Cancer

The designation is based off positive results from the RAMP 205 trial presented at the ASCO Annual Meeting.

The FDA has granted orphan drug designation (ODD) to avutometinib, a RAF/MEK clamp, in combination with defactinib, a selective FAK inhibitor, for the treatment of pancreatic cancer, according to a news release from Verastem Oncology.[1]



Verastem presented initial safety and efficacy results from the ongoing RAMP 205 trial at the American Society of Clinical Oncology (ASCO) Annual Meeting in June 2024. The trial assessed avutometinib and defactinib in combination with current standard of care gemcitabine and nab-paclitaxel in first-line metastatic pancreatic cancer.[1]

“We believe avutometinib and defactinib in combination with standard of care has an opportunity to provide a different approach in treating this challenging cancer,” Dan Paterson, president and chief executive officer of Verastem Oncology, said in the news release.[1]

In the RAMP 205 trial, patients in the dose level 1 cohort had an overall response rate of 83% (5/6), with 1 dose-limiting toxicity observed in that cohort as of May 14, 2024. Additionally, of the 26 patients in all the cohorts who had an opportunity for their first scan while on treatment, 21 experienced a reduction of the change in target lesion sum of diameters.[2]

John Hayslip, MD, chief medical officer of Verastem Oncology, said that “the initial interim results from the RAMP 205 trial…are encouraging, and demonstrate the importance of targeting the RAS/MAPK pathway, as more than 90% of pancreatic tumors have a KRAS mutation.”[2]

The combination of avutometinib and defactinib could potentially create a more complete and durable anti-tumor response by developing maximal RAS/MAPK pathway inhibition. In March 2024, the FDA granted ODD for avutometinib alone or with defactinib in recurrent low-grade serious ovarian cancer (LGSOC).[1,3]

RAMP 301, a phase 3 confirmatory trial to compare avutometinib alone or with defactinib to standard chemotherapy, is ongoing. Patients will be randomly assigned to receive either 3.2 mg of avutometinib twice weekly plus 200 mg of defactinib twice daily, or 1 of 5 possible chemotherapies.[1,3]

Avutometinib and defactinib was also granted Breakthrough Therapy Designation for the treatment of all patients with LGSOC, regardless of KRAS status, after they received 1 or more prior lines of therapy.1

An ODD provides certain benefits to drug developers for certain investigational treatments for diseases or conditions that affect fewer than 200,000 people in the United States. These benefits include tax credits for clinical trials, and the potential for several years of market exclusivity once the drug is approved.[1]

"We look forward to reporting updated data from across dose cohorts in the ongoing RAMP 205 trial in the first quarter of 2025," Paterson continued.[1]

About the Trial

Trial Name: Study of Avutometinib (VS-6766) +Defactinib With Gemcitabine and Nab-paclitaxel in Patients With Pancreatic Cancer (RAMP205)

ClinicalTrials.gov ID: NCT05669482

Sponsor: Verastem, Inc.

Completion Date (estaimted): December 31, 2025.

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