RAMP 201 (RAF AND MEK PROGRAM) ABOUT VERASTEM ONCOLOGY'S PHASE 2 REGISTRATION-DIRECTED TRIAL OF VS-6766 AND DEFACTINIB IN RECURRENT LOW-GRADE SEROUS OVARIAN CANCER (LGSOC)

RAMP201study.com

About the Study[1]

- The study sponsor is Verastem Oncology, in collaboration with the European Network of Gynaecological Oncological Trial Groups (ENGOT) and the Gynecologic Oncology Group (GOG) Foundation
- The Phase 2 study will evaluate the efficacy and safety of VS-6766 alone and in combination with defactinib in patients with recurrent low-grade serous ovarian cancer (LGSOC)
- An estimated 100 participants in the U.S. and EU are expected to be enrolled in the study
- Additional information about the study can be found here on ClinicalTrials.gov (NCT04625270), or by visiting RAMP201study.com

Trial Design[1]

- The study is an open-label trial, meaning that the investigator conducting the trial and the patient will know which medication they are being treated with
- The study will determine the optimal regimen of either VS-6766 alone (monotherapy), or VS-6766 in combination with defactinib, in patients with recurrent LGSOC
- The primary outcome measure being evaluated is confirmed overall response rate
- Study investigators will also measure key secondary outcomes including:
  - Duration of response
  - Disease control rate
  - Progression-free survival
  - Overall survival
  - Safety

Inclusion Criteria[1]

To participate, patients must meet certain eligibility requirements.

- Histologically proven LGSOC (ovarian, peritoneal)
- Progression or recurrence of LGSOC after at least one prior systemic therapy for metastatic disease
- Measurable disease according to RECIST 1.1
- An Eastern Cooperative Group (ECOG) performance status ≤ 1
- Adequate organ function
- Adequate recovery from toxicities related to prior treatments
- Agree to use highly effective method of contraceptive, if of childbearing age

Exclusion Criteria[1]

- Systemic anti-cancer therapy within 4 weeks of the first dose of study therapy
- Co-existing high-grade ovarian cancer or another histology
- History of prior malignancy with recurrence within 3 years from the time of enrollment
- Major surgery within 4 weeks
- Symptomatic brain metastases requiring steroids or other interventions
- Known SARS-Cov2 infection (COVID-19) within 28 days prior to first dose of study therapy
- For subjects with prior MEK exposure, Grade 4 toxicity deemed related to the MEK inhibitor
- Active skin disorder that has required systemic therapy within the past year
- History of rhabdomyolysis
- Concurrent ocular disorders
- Concurrent heart disease or severe obstructive pulmonary disease
- Subjects with the inability to swallow oral medications

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Study Principal Investigators

- Susana Banerjee, M.D., Ph.D., Medical Oncologist and Research Lead for the Gynaecology Unit at The Royal Marsden and Team Leader at The Institute of Cancer Research, London, Global and Principal European Investigator
- Rachel Grisham, M.D., Section Head, Ovarian Cancer and Director, Gynecologic Medical Oncology at Memorial Sloan Kettering Cancer Center in Westchester, NY, Principal U.S. Investigator

For additional information on this trial, including the site locations, please visit: RAMP201study.com or contact ClinicalTrials@verastem.com.

About VS-6766 and Defactinib

VS-6766 and defactinib are investigational treatments that target critical signaling pathways in tumors. These signaling pathways are abnormal in cancer and promote cancer cell survival and tumor growth. VS-6766 is an investigational oral small-molecule compound with a unique mechanism to block a signaling pathway called RAF/MEK. Defactinib is an investigational oral small molecule inhibitor of the focal adhesion kinase (FAK) and the related protein kinase (PYK2) signaling pathways.

KRAS Targeting

RAS gene mutations, including KRAS, are present in approximately 30 percent of all human cancers, have historically presented treatment challenges and are often associated with significantly worse prognosis.[2] The combination of VS-6766 and defactinib is being evaluated in patients with LGSOC, as well as KRAS positive non-small cell lung cancer (NSCLC), colorectal cancer, pancreatic cancer, KRAS positive endometrial cancer and KRAS-G12V positive NSCLC.

References: 1. ClinicalTrials.gov. A Study of VS-6766 v. VS-6766 + Defactinib in Recurrent Low-Grade Serous Ovarian Cancer With and Without a KRAS Mutation. Available at: https://clinicaltrials.gov/ct2/show/NCT04625270?tem=vs-6766&draw=2&rank=1. Accessed December 4, 2020.
2. Baines, A. T., Xu, D., & Der, C. J. (2011). Inhibition of Ras for cancer treatment: the search continues. Future medicinal chemistry, 3(14), 1787–1808. https://doi.org/10.4155/fmc.11.121

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