RAMP 202 (RAF AND MEK PROGRAM) ABOUT VERASTEM ONCOLOGY'S PHASE 2 REGISTRATION-DIRECTED VS-6766 AND DEFACTINIB TRIAL IN PREVIOUSLY TREATED KRAS-POSITIVE NON-SMALL CELL LUNG CANCER (NSCLC)

RAMP202study.com

About the Study[1]

The study called RAMP 202, is sponsored by Verastem Oncology

- RAMP 202 is a Phase 2 study that will evaluate the efficacy and safety of VS-6766 alone and in combination with defactinib in patients with KRAS-positive (KRAS+) non-small cell lung cancer (NSCLC), following treatment with a platinum-based regimen and immune checkpoint inhibitor
- 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 (NCT04620330), or by visiting RAMP202study.com

Trial Design[1]

- RAMP 202 is an open-label trial, meaning that the investigator conducting the trial and the patient will know which experimental medication they are being treated with
- RAMP 202 will determine the optimal regimen of either VS-6766 alone, also called monotherapy, or VS-6766 in combination with defactinib, in patients with KRAS-G12V positive NSCLC
- 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.

- Male or female subjects at least 18 years of age
- Histologic or cytologic evidence of NSCLC
- Known KRAS mutation (KRAS positive)
- The subject must have received appropriate prior therapy
- 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 a 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
- History of prior malignancy, with the exception of curatively treated malignancies
- Major surgery within 4 weeks (excluding placement of vascular access)
- History of treatment with a direct and specific inhibitor of MEK or KRAS
- Exposure to strong CYP2C9 and CYP3A4 inhibitors or inducers within 7 days prior to the first dose and during the course of therapy
- Symptomatic brain metastases requiring steroids or other local interventions
- Known SARS-Cov2 infection (COVID-19) within 28 days prior to first dose of study therapy
- Active skin disorder that has required systemic therapy within the past 1 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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RAMP 202

Study Principal Investigators

- D. Ross Camidge, M.D., Ph.D., Director of Thoracic Oncology at the University of Colorado School of Medicine and University of Colorado Cancer Center member, Principal U.S. Investigator
- Silvia Novello, M.D., Ph.D., Professor of Respiratory Medicine at the Department of Clinical and Biological Sciences of the University of Turin, Italy, Principal European Investigator

For additional information on this trial, including the site locations, please visit: RAMP202study.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. The combination of VS-6766 and defactinib is being evaluated in patients with KRAS+ NSCLC, low-grade serous ovarian cancer, colorectal cancer, pancreatic cancer, KRAS+ endometrial cancer and KRAS-G12V+ 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/ct2show/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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