Amethyst NSCLC Trial: Phase 2 Trial of MGCD265 in Patients (pts) with Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) with Activating Genetic Alterations in Mesenchymal-Epithelial Transition Factor (MET)


1. University of California San Diego, La Jolla, CA, USA
2. Clearview Cancer Institute, Huntsville, AL, USA
3. Henry Ford Health System, Detroit, MI, USA
4. Rigshospitalet, Copenhagen, Denmark, Denmark
5. UC San Diego Health System, San Diego, CA, USA
6. Dana-Farber Cancer Institute, Boston, MA, USA
7. University of Tennessee Health Science Center, Memphis, TN, USA
8. Dana-Farber Cancer Institute, Boston, MA, USA
9. Princess Margaret Hospital, Toronto, ON, Canada
10. Princess Margaret Hospital, Toronto, ON, Canada
11. National Cancer Institute, Bethesda, MD, USA
12. Memorial Sloan Kettering Cancer Center, New York, NY, USA
13. University of California San Diego, La Jolla, CA, USA
14. University of California San Diego, La Jolla, CA, USA
15. University of California San Diego, La Jolla, CA, USA
16. University of California San Diego, La Jolla, CA, USA

BACKGROUND

- MET is a receptor tyrosine kinase for hepatocyte growth factor (HGF) and activates cellular signaling pathways that are important for tissue homeostasis.
- Genetic alterations in MET, including mutations and/or gene amplification, occur in approximately 7% of NSCLC and function as oncogenic drivers that promote cancer development and progression.
- Various mutations located at or near the exon 14 splice site of the MET gene (METex14del) result in loss of expression of the MET protein.
- MET is a receptor tyrosine kinase for hepatocyte growth factor (HGF). The primary ligand of MET is HGF, a cytokine that plays a critical role in the proliferation and survival of several cell types, including fibroblasts, epithelial cells, and hematopoietic cells.
- Absence of this receptor leads to the loss of expression of the MET protein and the inhibition of cell proliferation and survival.

STUDY OBJECTIVES

PRIMARY OBJECTIVE:
- To determine the tumor response to MGCD265 in selected patient population.

SECONDARY OBJECTIVES:
- To evaluate the safety and tolerability of METex14del.
- To assess efficacy endpoints with MGCD265 treatment in selected population.
- To assess correlation between selected tumor gene alterations using different analytical techniques in tumor tissue and ctDNA.
- To assess change in genetic alteration status in ctDNA with MGCD265 treatment over time in the selected population.

METHODS

- Study Design:
  - Initial n=10 per arm: Early Evaluation
  - Expansion n~55: Genetic Pre-Screening

- Dosages and Assessments:
  - MGCD265 is a potent and selective inhibitor of MET. It is an orally available small molecule RTK inhibitor.
  - The primary endpoint is Objective Response Rate (ORR) in accordance with RECIST 1.1.

- Summary:
  - MGCD265 is a global, open-label, parallel phase 2 trial evaluating the tumor response to MGCD265 in patients with locally advanced, or metastatic NSCLC exhibiting an activating genetic alteration of MET.

KEY EXCLUSION CRITERIA:
- Prior treatment with a small molecule or antibody inhibitor of MET or HGF
- Prior positive test for EGFR mutation or ALK rearrangement
- Symptomatic or unstable bone metastases
- Unstable angina pectoris, congestive heart failure of NYHA Class ≥ 3, or QTc > 480 msec

REFERENCES

3. Amethyst NSCLC Trial (265-109) NCT02544633

Study Trial Information: www.mirati.com