**BACKGROUND**

Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) are the standard of care for patients with EGFR-mutated non-small cell lung cancer (NSCLC).

**STUDY OBJECTIVES**

- Evaluate the safety, tolerability, and clinical activity of lerociclib in combination with osimertinib.
- Assess correlation between changes in cell-free DNA (cfDNA) with clinical outcomes.

**METHODS**

- Dose escalation study (Part 1).
- Patients received 24-hour continuous dosing with lerociclib.
- PK of lerociclib (maximal concentration, Cmax) was assessed.

**RESULTS**

- Coadministration of osimertinib had minimal impact on the PK of lerociclib.
- Minimal dose reduction occurred in patients receiving the 300 mg and 400 mg QD dose levels.
- There were no AEs leading to lerociclib/osimertinib discontinuation or death.

**CONCLUSIONS**

- Continuous lerociclib dosing with osimertinib resulted in a dose-dependent decline and subsequent plateau of blood concentrations of lerociclib.
- This study provides preliminary evidence of the potential for combination therapy with lerociclib and osimertinib.

**Table 1. Patient Demographics and Disease Characteristics**

- **Patient characteristics**:
  - Median age: 64.5 years (range: 20-86).
  - ECOG PS: 0 (57.1%), 1 (42.9%).
  - Gender: Female (83.3%), Male (16.7%).
  - Prior treatments: cp (80.8%), paclitaxel (79.2%), erlotinib (21.9%), osimertinib (57.1%).
  - EGFR mutations: Exon 19 deletion (66.7%), T790M (57.1%).

**Table 2. Best Overall Response (Confirmed)**

- **Best overall response**:
  - Partial response (57.1%), stable disease (26.9%), progressive disease (16.7%).
  - No confirmed complete responses were observed.

**Table 3. Tumor Biomarkers at Baseline (n=23)**

- **Baseline tumor biomarkers**:
  - PIK3CA E545K: 7 (30.4%), EGFRC797S: 5 (21.7%), PTEN109H: 4 (17.4%), EGFRT790M: 2 (8.7%).
  - L858R mutations were not observed.

**Figure 1. Tumor Biomarkers at Baseline**

- Visual representation of tumor biomarkers at baseline.

**Figure 2. Median Neutrophils (Absolute) by Visits**

- Graph showing median neutrophil count over time.

**Figure 3. Tumor Burden at Baseline**

- Baseline tumor burden visualization.

**Figure 4. Baseline Tumor Burden Compared to Baseline Tumor Burden (AUC)**

- Comparison of baseline tumor burden.

**Figure 5. EGFR Mutation Frequency at Baseline**

- Distribution of EGFR mutation frequency at baseline.

**Figure 6. Change in cfDNA Allele Fraction**

- Graph depicting change in cfDNA allele fraction.

**Figure 7. Plasma and Tumor Biomarkers at Baseline**

- Visual comparison of plasma and tumor biomarkers at baseline.

**Table 4. Any Progression/Death in Patients with Baseline Tumor Burden**

- **Any progression/death**:
  - Median time to progression: 8 (range: 0.1-10) months.
  - Overall survival: 15 (range: 0.1-22) months.