**INTRODUCTION**

- Poziotinib (NOV120101) is an oral, irreversible inhibitor of EGFR, HER2 and HER4.
- Preclinical studies conducted in cell lines and xenograft models of NSCLC revealed that Poziotinib has more potent activity than gefitinib, erlotinib and even afatinib in lung cancer models with activating EGFR mutations or T790M mutation.
- A phase I study to investigate the safety and maximum tolerated dose (MTD) of Poziotinib in genetically-unselected patients with advanced solid cancers including NSCLC showed 14/75 (19%) of patients experienced partial response (PR), with the MTD of 24 mg once daily and acceptable toxicity profile (unpublished data), supporting further clinical development of Poziotinib.
- This phase II open-label, single-arm study was conducted to explore the anti-cancer activity and safety of Poziotinib in patients with advanced or metastatic lung adenocarcinoma with activating EGFR mutations, who developed acquired resistance (AR) to EGFR TKIs based on the JAK3 criteria.
- Clinical Trial.gov identifier: NCT01718847

**METHODS AND MATERIALS**

- Patients received Poziotinib at a dose of 16 mg once daily in 28-day cycles.
- The primary endpoint was progression-free survival (PFS).
- All tumor responses were evaluated by independent review and, in a supportive manner, by investigator.
- Safety assessments included treatment-emergent adverse events (TEAEs), laboratory tests, vital signs, X-ray, ECGs and LEVF by a multi-institutional review.
- EGFR mutation analysis in tumor tissue and blood samples were conducted using Ion Torrent deep-sequencing and PANAMutyper™ EGFR kit, respectively.
- MET amplification or overexpression in tumor tissue were assessed by FISH and immunohistochemistry.

**RESULTS**

**Efficacy**

- Between December 2012 and September 2014, 39 patients received at least one dose of Poziotinib with at least one tumor assessment after baseline.

**Safety and tolerability**

- Most patients required at least one dose reduction; 15 with one dose reduction; 15 with two dose reductions. Two events (one myositis and one rash) led to permanent discontinuation.
- There was no treatment-related death.

**Performance of T790M mutation in plasma assay**

- 39 patients received at least one dose of poziotinib.
- Five out of six patients with tissue/plasma showed PD to poziotinib.

**EGFR Mutational status in tumor tissue at baseline**

- 1. The possible mechanism of AR to prior EGFR-TKIs

**CONCLUSION**

- Poziotinib showed modest efficacy in patients with EGFR-mutant lung adenocarcinoma who had progressed on erlotinib or gefitinib.
- As might be expected, most patients developed AR to prior EGFR-TKIs due to secondary acquisition of EGFR T790M mutations.
- These results suggesting that poziotinib may not overcome AR secondary to EGFR T790M mutation in EGFR mutant lung adenocarcinoma.
- The exploratory biomarker analysis suggested that plasma T790M assay may be more correlated with clinical benefit with Poziotinib.

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**REFERENCES**


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