Phase I/II study exploring safety and efficacy of APL-101 plus frontline osimertinib in EGFR-mutated metastatic non-small cell lung cancer

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Introduction

- Activation of MET signaling has been described as a driver of primary resistance to EGFR tyrosine kinase inhibitors (TKI)1
- Copy number gains in MET have been described in EGFR mutated non-small cell lung cancers (NSCLC) that are resistant to osimertinib and also treatment-naive samples2
- Combination of osimertinib with MET-TKIs has shown to be safe with encouraging antitumor activity following disease progression on osimertinib3,4
- APL-101 is a specific ATP-competitive small-molecule MET inhibitor that has shown favorable safety profile in advanced solid tumors with MET dysregulation (NCT03175224)

Hypothesis

- We hypothesize that combination therapy with MET inhibitor, APL-101, and EGFR-TKI osimertinib has the potential to induce deep and durable responses in patients with EGFR mutated lung cancer

Key Eligibility Criteria

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<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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<tr>
<td>Metastatic NSCLC with TKI-sensitive EGFR mutations</td>
<td>Prior treatment with osimertinib in metastatic setting</td>
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<td>Measurable disease by RECIST 1.1 with at least one lesion accessible for core biopsy</td>
<td>Prior immunotherapy treatment in metastatic setting</td>
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<td>Planning to initiate treatment with osimertinib 80 mg daily</td>
<td>Presence of symptomatic and unstable brain metastasis</td>
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Study Objectives

- Phase I = dose escalation phase, determine maximum tolerated dose (MTD) and dose-limiting toxicities
- Toxicity assessed by CTCAE v 5.0
- Standard 3+3 design
- Phase II = MTD cohort expansion phase
- Progression free survival at 1 year
- Overall response rate, duration of response, overall survival
- Exploratory analyses will investigate genomic alterations underlying drug tolerance and identify biomarkers that are prognostic and predictive of treatment response

Study Information

- Status: Recruiting to dose level 2
- Protocol Number: 202104039
- ClinicalTrials.gov Identifier: NCT04743505

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References
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