Phase 1b Study of Ficlatuzumab (AV-299), an Anti-Hepatocyte Growth Factor Monoclonal Antibody, in Combination With Gefitinib in Asian Patients With NSCLC

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Objectives

- To determine the safety, tolerability, dose-limiting toxicity (DLT), and recommended phase 2 dose (RP2D) of ficlatuzumab in combination with gefitinib in the subsequent Phase 2 study
- To determine the PK profile of ficlatuzumab in combination with gefitinib
- To determine the potential of ficlatuzumab in combination with gefitinib to induce the expected increase in total HGF levels upon ficlatuzumab administration, suggesting efficacy in NSCLC

Methods

- **Study Design**: This study used a standard 3 + 3 dose escalation design
- **Eligibility Criteria**: Enrollment criteria included patients with advanced NSCLC who had failed standard chemotherapy or who had progressed after previous EGFR TKI therapy
- **Treatment Protocol**: Patients received ficlatuzumab 20 mg/kg intravenously every 2 weeks plus gefitinib 250 mg orally once daily in Cycle 1
- **Safety Monitoring**: Patients were monitored for DLT during Cycle 1 after the first dose of ficlatuzumab
- **PK Profile**: Patients who had DLTs during Cycle 1 were replaced with 6 additional patients to establish the RP2D
- **Efficacy Evaluation**: Primary efficacy endpoint was the ORR evaluated by central review

Key Eligibility Criteria

- **Primary Objective**: To determine the recommended phase 2 dose of ficlatuzumab in combination with gefitinib
- **Secondary Objectives**: To determine the PK profile of ficlatuzumab in combination with gefitinib
- **Safety and Tolerability**: To determine the safety, tolerability, and drug-drug interactions
- **Efficacy**: To determine the ORR and duration of response

Results

- **Patient Demographics**: The majority of patients were male (78%) and Asian (91%)
- **ORR**: Three of 30 patients (10%) achieved a complete response, and 10 patients (33%) achieved a partial response
- **PK Profile**: The mean (SD) AUC of ficlatuzumab was 1,741 (96) µg•d/mL in Cycle 1, increasing to 2,134 (71) µg•d/mL in Cycle 2
- **Safety and Tolerability**: The most common adverse events were dermatitis acneiform (67%) and diarrhea (40%)

Conclusions

- The combination of ficlatuzumab and gefitinib was well tolerated.
- The RP2D of ficlatuzumab 30 mg/kg intravenously every 2 weeks plus gefitinib 250 mg orally was likely safe and active.
- All patients experienced the expected increase in total HGF levels upon ficlatuzumab administration, suggesting target engagement.
- A phase 2 trial has been completed, with time to Cmax and AUC obtained at 7.5 hours after Cycle 1.

References