Elevated levels of KL-6 are observed in lung cancer patients with and without EGFR mutations (16). KL-6, a plasma glycoprotein, is a non-specific pulmonary inflammatory biomarker. Its levels have been associated with disease progression in patients with inflammatory lung disease, including bronchial dysplasia, chronic bronchitis, and bronchiectasis (17). The exact mechanism of action for KL-6 is not fully understood, but it is believed to play a role in the repair of lung tissue (18).

Methods

Plasma and serum samples were collected at baseline, after 2 cycles (Cycle 3 Day 1 [C3D1]), and after 4 cycles (Cycle 5 Day 1 [C5D1]), and at disease progression from promising treated patients with EGFR ex20ins-positive mNSCLC who received once-daily mobocertinib 160 mg orally (28-day cycles) in a phase 1/2 study (NCT02716116). KL-6 concentrations were measured in 12 EGFR mNSCLC plasma using the Nexropol KL-6 assay (Tekedia Medical Co., Ltd.) and in 5 of the 12 patients assessed for SP-D (Figure 1). Circulating serum SP-D (ng/mL) concentrations were measured using the Quanturate human SP-D ELISA kit (R&D Systems, Inc.) and in 1 of the 5 patients assessed for SP-D (Figure 2).

Results

The number of patients assessed for KL-6 and SP-D at each time point are shown in Figure 1. The number of patients assessed for KL-6 at baseline was 97, and for SP-D was 72. The number of patients assessed at C3D1 was 28 for KL-6 and 5 for SP-D, and at C5D1 was 72 for KL-6 and 41 for SP-D. Baseline KL-6 and SP-D concentrations are shown in Table 1. The geometric mean of KL-6 was 617.50 U/mL and 40.23 ng/mL for SP-D, respectively. The geometric mean of KL-6 concentration at baseline relative to the incidence of pulmonary AE was 0.53 (95% CI: 0.37–0.75) (P = 0.008) (Figure 3). The geometric mean KL-6 concentration declined to a greater extent in patients who achieved PR compared to SD or PD (Figure 4).

Conclusions

Baseline KL-6 and SP-D concentrations are not predictive of response outcomes or occurrence of pulmonary AEs in patients with mNSCLC treated with mobocertinib. Decrease in plasma KL-6 concentration is significantly associated with achievement of PR or SD in patients receiving mobocertinib. No correlation was observed between change in SP-D concentration and response to mobocertinib. Circulating levels of KL-6 are a potential indicator of response in patients with mNSCLC receiving mobocertinib therapy.