**INTRODUCTION**

- Insulin-like growth factor (IGF) signaling mediates proliferation and survival in NSCLC cells in SCLC.
- It is known that IGF signaling is activated in NSCLC, and IGF receptor (IGF-1R) and IGF-1 are known to affect glucose metabolism via the IGF-IR (Figure 1).

**METHODS**

**Study design**

- The study consists of a 3+3 design; dose-escalation part (reported here) followed by the expansion part at the recommended Phase II dose (RPTD/MTD) maximum tolerated dose (MTD, Figure 2).
- Phase Ib trial (NCT02191891) evaluated xentuzumab in combination with afatinib based on the occurrence of DLTs (range) in the first 12 patients (n=3).

**RESULTS**

- No DLTs were observed in Cycle 1 or any other treatment cycles.
- Two treatment-related grade 3 AEs were observed: xentuzumab 1,000 mg/week + afatinib 30 mg/day stenomatis (n=1); xentuzumab 1,000 mg/week + afatinib 40 mg, interstitial lung disease (ILD; n=1).
- The combination demonstrated a clinically manageable safety profile.
- It is feasible to combine an IGF antibody and EGFR TKI; the MTD and RP2D were confirmed as xentuzumab 1,000 mg/week + afatinib 30 mg/day.

**CONCLUSIONS**

- The combination of xentuzumab and afatinib is feasible and well-tolerated in patients with NSCLC harboring an I716V activating mutation.
- It is ongoing in Japan, Korea, Singapore, and Taiwan.

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