Safety and Preliminary Clinical Activity of Repotrectinib in Patients with Advanced ROS1/TRK Fusion-Positive Solid Tumors (TRIDENT-1 Study)

INTRODUCTION

The present study was a single-arm, open-label, global registrational Phase 2 trial designed to investigate the efficacy and safety of repotrectinib, an oral multi-targeted RET (ROS1, TRK), ALK, and NTRK inhibitor in patients with advanced ROS1 or TRK (ROS1 and TRK TKI) fusion-positive solid tumors.

METHODS: STUDY DESIGN AND PATIENTS

Patients received oral repotrectinib 180 mg, 240 mg, 360 mg, 480 mg, 600 mg, or 800 mg QD or above. Patients were allowed to receive prior therapy: TKI treatment: crizotinib, entrectinib and entrectinib+trametinib.

RESULTS:

Preliminary efficacy results from 38 patients with ROS1+ tumors at 180 mg QD and above were presented. Repotrectinib was well tolerated, with common TEAEs including fatigue, nausea, and anemia. Dose interruptions and reductions occurred in 32% of patients, with most occurring at the 240 mg dose.

RESULTS: EFFICACY

Confirmd ORR, n/N (%) 7/18 (39%) 
Intracranial ORR (IC-ORR), n/N (%) 3/3 (100%) 
Confirmed ORR, n/N (%) 10/11 (91%) 
Clinical Benefit Rate, n/N (%) 5/7 (71%) 
Median follow-up time, months 20.1 
95% CI (%) (29 – 100) 
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Confirmed ORR, n/N (%) 10/11 (91%) 
Clinical Benefit Rate, n/N (%) 5/7 (71%) 
Median follow-up time, months 20.1 
95% CI (%) (29 – 100)

RESULTS: SAFETY

Fatigue 28 (30.1) 17 (18.3) 9 (9.7) 2 (2.2) --- --- --- ---
Upper respiratory tract infection 11 (11.8) 6 (6.5) 5 (5.4) --- --- --- ---
Abdominal pain 10 (10.8) 8 (8.6) 2 (2.2) --- --- --- ---
ALT elevation 20 (21.9) 17 (18.3) 8 (8.6) 5 (5.4) --- --- --- ---
AST elevation 20 (21.9) 17 (18.3) 8 (8.6) 5 (5.4) --- --- --- ---
Grade 5 TEAEs: respiratory failure (n=2), pneumonia, sepsis, sudden death (n=1 each); only the case of sudden death was determined to be possibly related to treatment.

RESULTS: EFFICACY

Figure 1. Preliminary Efficacy Results in 38 Patients with ROS1+ Tumors at 180 mg QD and Above

Table 1. Common Treatment-Emergent Adverse Events (TEAEs) Occurring at ≥ 3% in 38 Patients with ROS1+ Tumors at 180 mg QD and Above

RESULTS: EFFICACY

Figure 2. Preliminary Efficacy Results in 38 Patients with ROS1+ Tumors at 180 mg QD and Above

REFERENCES