Efficacy and Safety of Taletrectinib in Patients With ROS1+ Non-Small Cell Lung Cancer (NSCLC): Interim Analysis of GlobalTrust-II Study

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Background

- Taletrectinib is a next-generation, CNS-active, ROS1 TKI with selectivity over TRKB.
- Clinical exposures at steady state sufficient to inhibit both ROS1 and TRKB.
- Taletrectinib previously demonstrated high overall response rate (ORR) and activity against G2032R, and had a favorable safety profile in the regional Trust-II study (NCT03620577).
- Based on these findings, Taletrectinib was granted a breakthrough therapy designation by FDA for refractory patients with advanced or metastatic ROS1+ NSCLC who are ROS1 TKI-treatment-naive or previously treated with crizotinib.

Objectives

- Evaluate the efficacy and safety of taletrectinib in patients with advanced or metastatic ROS1+ NSCLC and other solid tumors.

Methods

- **TRUST-II** (NCT04918811), a global phase 2, multicenter, open-label, single-arm study in patients with ROS1+ tumors, has 4 cohorts

**Study Design**

- Taletrectinib was administered in 21-day cycles.
- Tumor assessments were performed every 3 months.
- Treatment ongoing

**Endpoints**

- Efficacy: ORR, cORR, mPFS, DCR, DoR, OS
- Safety: TEAEs, AEs, Dose reduction due to AE

**Population**

- TKI-naive patients: n=52 (21.5%)
- TKI-pretreated patients: n=46 (43.0%)
- No treatment-related deaths
- TEAEs led to dose reduction in 34% of patients, the most common was increased liver enzymes (23%)

**Results**

- Intracranial responses were robust in both TKI-naive (80%) and TKI-pretreated patients (63%)
- Grade 5 TEAEs: 3 (2.8%)
- Grade 4 TEAEs: 3 (2.8%)
- All Grade TEAEs: 67 (62.6%)
- TEAEs led to dose reduction in 33% of patients, the most common was increased liver enzymes (23%)
- Patients with TKI-pretreated: n=46
- TEAEs most common in grade 1-2

**Safety**

- Median duration of exposure: 4.8 months (range: 0.03–18.9)
- Most common TEAEs: ALT (4%); AST (3%); diarrhea (3%); rash (2%)
- Most TEAEs were grade 1–2
- TEAEs were dose-related in 33% of patients, the most common was increased liver enzymes (23%)
- 10 patients had a TEAE leading to treatment discontinuation
- No treatment-related deaths were reported

**Conclusion**

- Taletrectinib demonstrated a favorable safety profile in TRUST-II, and was generally well tolerated.
- Safety and efficacy were consistent with data from other ROS1 TKI trials.
- Taletrectinib is currently ongoing.

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References