Safety and Efficacy of Tenalisib Given in Combination with Romidepsin in Patients with Relapsed/Refractory T-Cell Lymphoma: Final Results from a Phase III/II Open Label Multi-Center Study

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Introduction

Tenalisib (RPE653), a highly selective PI3Kδ and SKI inhibitor, has shown promising activity as a single agent in patients with TCL, with a differentiated and favorable safety profile. In vitro studies in TCL lines showed synergistic potential of the combination of tenalisib and romidepsin. This combination was evaluated in patients with R/R TCL lymphomas. The data presented is the final data set for the study.

Methods

Study Design:
- This was a multi-center, open label, Phase III trial (Protocol ID: RPE530Romipolin-1805) in patients with TCL lymphomas (NCT03770000).
- The Phase I was a 3+3 dose escalation study to determine the MTD/optimal dose of the combination. The Phase II was an expansion cohort at the MTD/optimal dose.
- DLT assessment period was 28-days.
- Primary and secondary endpoints: Safety, tolerability and MTX. Secondary endpoints: PK, ORR and DFS.
- Response assessed as per Lugano classification (Cheun 2016) & Global assessment (Osten 2011) respectively.

Figure 1: Study Design

Results: Safety

- No DLTs were reported in the dose escalation phase and Tenalisib 800 mg BID plus Romidepsin 14 mg/m² was considered as the optimal dose for expansion cohorts.
- No unexpected AEs or increased frequency of exiting AEs for individual agents.

Table 3: Incidence of Related Adverse Events (AEs ≥ 10%)

Table 2: Incidence of Related Adverse Events (AEs ≥ 15% in patients)

Table 4: Demographics of all subjects

Pharmacokinetics

- Co-administration of romidepsin along with tenalisib did not significantly alter the PK of either agents.

Figure 3a: Plasma concentrations of Romidepsin

Figure 3b: Plasma concentrations of Tenalisib and its metabolite (N0385)

Figure 4a: Clinical response in PTCL patients

Figure 4b: Clinical response in CTL patients

Figure 5a: Best response in efficacy evaluable PTCL patients (n=12)

Figure 5b: Best response in efficacy evaluable CTL patients (n=15)

Conclusion

- The combination of tenalisib and romidepsin demonstrated a favorable safety profile and promising-tumor activity in patients with R/R TCL.
- No DLT was reported with the combination at any dose level in the dose escalation.
- Co-administration of romidepsin along with tenalisib did not significantly alter the PK of either agents.
- Overall efficacy response in both PTCL & CTL continues to be encouraging and supports further development of Tenalisib in patients with T-cell lymphomas.