(PS2056) PHASE 1 FIRST-IN-HUMAN STUDY OF AUR112, A HIGHLY SELECTIVE MALT1 INHIBITOR, IN RELAPSED LYMPHOID MALIGNANCIES

Topic: 18. Indolent and mantle-cell non-Hodgkin lymphoma - Clinical

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Background

MALT1 (mucosa-associated lymphoid tissue lymphoma translocation protein 1) is a central regulator of B-cell and T-cell receptor signaling and is implicated in the pathogenesis of multiple lymphoid malignancies. Aberrant activation of the CARD11-BCL10-MALT1 (CBM) complex activates canonical NF-κB pathway crucial for cell proliferation and survival, supporting investigation of MALT1-targeted inhibition. AUR112 is an oral selective small-molecule MALT1 inhibitor with acceptable pre-clinical safety, efficacy, and adequate DMPK profile[1].

Aims

To present early results from a phase 1, first-in-human, dose escalation study (NCT06755450; CTRI/2025/01/078964) of AUR112 in relapsed lymphoid malignancies.

Methods

Eligible patients aged ≥ 18 years with all different subtypes of lymphoid malignancies, including CLL, Eastern Cooperative Oncology Group performance status (ECOG PS) ≤1 were enrolled in three sequential dose cohorts at doses ranging from 100-400 mg once daily. Safety assessments included adverse events and dose-limiting toxicities (DLTs). PK parameters were evaluated after single and multiple dosing. PD effects were assessed using cytokine inhibition and exploratory biomarkers. Tumor responses were assessed by modified Lugano for lymphoma and International Workshop criteria for CLL (iWCLL). Based on the efficacy and PK from 100 mg and 200 mg cohorts and following enrollment of a single patient with T-cell lymphoma at 400 mg, further enrollment is being focused on lower dosages.

Results

At a cutoff of 31 Jan 2026, sixteen patients with relapsed lymphoid malignancies were treated: Hodgkin lymphoma (n=7), CLL (n = 2), diffuse large B-cell Lymphoma (n = 3), one patient each with follicular, mantle cell, marginal zone, and T-cell lymphoma. Median age was 36.5 years (range 20-71), and 44% were male. Most patients (81.5%) had received ≥3 prior lines of therapy. Ninety Treatment-emergent AEs were reported in 15/16 (93.75%) patients enrolled. Most AEs (69/90; 76.7%) were lower grades (Grade 1/2). Only one patient developed a DLT of Grade 3 neutropenia (100 mg). Objective responses were observed in 55.6% (5/9) and 75% (3/4) among evaluable patients in 100 mg QD and 200 mg QD cohorts, respectively, with an ORR of 61.5 % (8/13) across the two cohorts. PK analyses demonstrated dose-proportional exposure from 100 mg to 200 mg. Most patients showed IL-2 levels below the lower limit of quantification post-dosing, consistent with PD activity.

Summary/Conclusion

AUR112 demonstrated encouraging clinical activity with manageable safety profile in relapsed lymphoid malignancies across histological subtypes. Pharmacokinetics / Pharmacodynamics findings support continued dose expansion at dosages ≤200 mg daily dose. Activity in selected lymphoid malignancies, including Chronic Lymphocytic Leukemia (CLL), Follicular Lymphoma (FL), Marginal Zone Lymphoma (MZL), Mantle Cell Lymphoma (MCL), Waldenstrom's Macroglobulinemia, and Activated B-cell like Diffuse Large B-cell Lymphoma (ABC-DLBCL) is being explored as part of Dose Expansion.

[1] Balasubramanian WR et al. Discovery of AUR-112, a novel MALT1 protease inhibitor for the treatment of B-cell lymphomas. Proc. AACR 2023; Abstract C127