TPS7083 **Poster Session**

SOUNDTRACK-E: A phase 1/2, open-label, multicenter study to evaluate the safety and efficacy of AZD0486 monotherapy or combination therapy in patients with mature B-cell malignancies.

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Background: AZD0486 is an IgG4 fully human CD19xCD3 bispecific T-cell engager that binds CD3 with low affinity to potentially reduce cytokine release upon T-cell activation while preserving effective T-cell cytotoxicity against malignant B cells. In a first-in-human phase 1 trial (NCT04594642), AZD0486 was active and well tolerated in patients (pts) with relapsed/refractory (R/R) follicular lymphoma or R/R diffuse large B-cell lymphoma (Gaballa S, et al. *Blood*. 2024;144:868; Hou JZ, et al. *Blood*. 2024;144:341). This study assesses fixed-duration subcutaneous (SC) AZD0486 monotherapy in B-cell malignancies and fixed-duration SC or intravenous AZD0486 in combination with other anticancer agents. This study is the first to evaluate SC AZD0486, and the first to evaluate AZD0486 in chronic lymphocytic leukemia (CLL). **Methods:** SOUNDTRACK-E (NCT06564038) is a phase 1/2 dose-escalation, global, multicenter trial of AZD0486 with 3 substudies. The study is recruiting pts aged ≥18 years with Eastern Cooperative Oncology Group performance status 0–2 and a histologically confirmed diagnosis. Pts with clinically significant central nervous system events (eg, seizure, stroke) or cardiovascular disease are excluded. Substudy 1 evaluates SC AZD0486 in R/R CLL/small lymphocytic lymphoma and includes a monotherapy cohort (1A; ≥2 prior lines of therapy [pLOT] with Bruton tyrosine kinase inhibitor exposure) and a cohort that receives combination with acalabrutinib (1B; ≥1 pLOT). Substudy 2 evaluates SC AZD0486 in R/R mantle cell lymphoma and includes a monotherapy cohort (2A; ≥2 pLOT) and a cohort that receives combination with acalabrutinib (2B; ≥1 pLOT). Substudy 3 evaluates AZD0486 in combination with R-CHOP in pts with untreated large B-cell lymphoma with International Prognostic Index ≥2, or R/R B-cell non-Hodgkin lymphoma with ≥1 pLOT. In each cohort, AZD0486 is administered via a double step-up dosing schedule in cycle 1; the target dose is given every 2 weeks. Treatment is administered for 24 (28-day) cycles in substudy 1, 12 (28-day) cycles in substudy 2, and 17 (21-day) cycles in substudy 3. Pts in cohorts 1B and 2B receive acalabrutinib 100 mg orally BID beginning at cycle 2. In substudy 3, R-CHOP is administered once every 3 weeks for 6 cycles. Dose escalation decisions will be based on a modified probability interval (mTPI-2) design. Approximately 46 pts for each cohort in substudies 1 and 2 and 36 pts in substudy 3 (~200 total pts) will be recruited. Primary objectives are to assess safety and tolerability, and to determine the recommended phase 2 dose for AZD0486 as monotherapy and combination therapy in mature B-cell malignancies. Secondary objectives include efficacy endpoints, pharmacokinetics, and immunogenicity. Enrollment opened in October 2024. Clinical trial information: NCT06564038. Research Sponsor: AstraZeneca.