P1152 RESULTS FROM A PHASE I PHARMACOKINETIC (PK) AND SAFETY STUDY OF TRPH-222, A NOVEL CD22-TARGETING ANTIBODY-DRUG CONJUGATE, IN PATIENTS WITH RELAPSED/REFRACTORY B-CELL NON-HODGKIN LYMPHOMA (R/R NHL)

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

Francisco J. Hernandez-Ilizaliturri1, John Kuruvilla2, Beth A. Christian3, Ian W. Flinn4, Sarit E. Assouline5, Matthew L. Ulrickson6, Daniel J. Landsburg7, Monic Stuart8, Henry Lowman8, Nancy Levin8, Dorothea Maetzel9, Natasja N. Viller9, Ann MacLaren8

1 Department of Medicine, Roswell Park Cancer Institute, Buffalo, NY, United States; 2 The Princess Margaret Hospital, Toronto, ON, Canada; 3 The Ohio State University, Columbus, OH, United States; 4 Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, United States; 5 Division of Hematology, Sir Mortimer B. Davis-Jewish General Hospital, Department of Oncology, McGill University, Montreal, QC, Canada; 6 Banner MD Anderson Cancer Center, Gilbert, AZ, United States; 7 Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, United States; 8 Triphase Accelerator, La Jolla, CA, United States; 9 Triphase Accelerator, Toronto, ON, Canada

**Background:** TRPH-222 is a novel antibody-drug conjugate (ADC) comprised of a humanized anti-CD22 monoclonal antibody and maytansine, a potent microtubule inhibitor, joined by a novel third-generation linker conjugation technology (SMARTag®). This approach enables site-specific conjugation of the maytansine payload while tightly controlling drug:antibody ratio (DAR), resulting in a highly stable anti-CD22 ADC with a non-cleavable linker designed to widen the therapeutic window.

**Aims:** The primary objectives of this first in human study are to determine the safety, tolerability and pharmacokinetics (PK) of TRPH-222 monotherapy in patients with R/R NHL.

**Methods:** TRPH-222-100 is an open-label, multicenter study comprised of dose-escalation and dose-expansion stages. TRPH-222 was administered IV once every 3 weeks. 22 patients were enrolled in dose-escalating cohorts of TRPH-222 (0.6 mg/kg to 10 mg/kg) from DLBCL, FL, TFL, MCL and MZL histologies, and 10 patients in a dose-expansion cohort (7.5 mg/kg) focusing on DLBCL and FL histologies.

**Results:** As of January 7, 2022, 32 NHL patients have been enrolled: 15 indolent (14 FL and 1 MZL) and 17 aggressive histologies (15 DLBCL, 1 TFL and 1 MCL). Patients had a median age of 64.5 years, a median of 4 prior lines of therapy including 7 patients receiving prior CAR-T treatment.

Three DLTs occurred in 2 patients during the study and comprised Grade 3 and 4 transaminase elevations; one each at 4.2 and 10 mg/kg and one Grade 3 thrombocytopenia at 4.2 mg/kg. Treatment-related serious adverse events (AEs) occurred in 2 patients (6.3%), caused by thrombocytopenia and pyrexia (both at 7.5 mg/kg TRPH-222). AEs were more prevalent at doses ≥7.5 mg/kg and less prevalent at lower doses. There was a trend to higher grade AEs in patients with aggressive histologies, compared to indolent ones. The most frequent (≥ 5%) treatment-emergent related AEs (Grade ≥3) included thrombocytopenia (34%), neutropenia (22%), ALT/AST elevation (6%), dry eye (6%) and blurred vision (6%). Cytopenias were non-febrile, infrequent, asymptomatic and resolved without significant intervention. Ocular findings were consistent with known epithelial keratopathy of ADCs and were generally low grade and resolved to ≤ Grade 1 with dose interruptions and/or reductions. Overall, TRPH-222 demonstrated a favourable safety profile with most AEs being predominantly low grade, tolerable, easily managed and reversible.

Preliminary efficacy results suggest evidence of anti-tumor activity, most notably in patients with R/R FL. Of the 13 response-evaluable FL patients, 4 complete responses (CR) and 2 partial responses (PR) were observed, with an overall response rate (ORR) of 46% and a complete response rate (CRR) of 31%. Four patients with metabolic CRs maintained these CRs for long periods off treatment; 3 patients remain in CR with responses maintained for up to 25
months. Responses were generally early, durable and CRs were maintained off-therapy. Beyond FL, CRs were also observed in 1 DLBCL patient and in 1 MCL patient.

Summary/Conclusion: TRPH-222 was found to be well tolerated at higher dose levels than evaluated for other ADCs. TRPH-222 monotherapy resulted in robust and durable CRs in FL across dose levels where patients were able to discontinue TRPH-222 while remaining in remissions. Collectively, these characteristics of TRPH-222 are favorable for further development in the indolent lymphoma setting either as monotherapy or in combination with other anti-tumor agents in B-cell lymphoma patients.