TPS2681 Poster Session

A phase I, multicenter, open-label study of UB-VV111 in combination with rapamycin in relapsed/refractory CD19+ B-cell malignancies.

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Background: Autologous, ex vivo-manufactured chimeric antigen receptor (CAR) T cells directed against CD19 have demonstrated clinical activity. These products have gained approvals in the relapsed/ refractory (R/R) setting in multiple B-cell malignancies (BCMs), including large B-cell lymphoma (LBCL) and chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). However, challenges in product availability due to limited manufacturing capacity, the need for apheresis and lymphodepletion, failure to prior ex vivo CAR T therapy, and the level of patient fitness needed to wait for and receive ex vivo autologous CAR T therapy all pose significant challenges to the field, presenting significant unmet clinical need. UB-VV111 is a third-generation, self-inactivating, replication-incompetent lentiviral vector (LVV) investigational drug product comprising an envelope with cocal virus fusion glycoprotein (cocal) and surface engineered with a membrane-bound multidomain fusion (MDF) protein. The MDF protein contains CD58, CD80, and anti-CD3 single-chain variable fragment (scFv) components that provide both T-cell tropism and activation signals thought to be critical for effective CAR T-cell generation. UB-VV111 addresses the limitations of currently available autologous CD19-directed CAR T therapies to deliver a product that would generate CD19-directed cells in the patient. UB-VV111 is to be administered by either intranodal (IN) or intravenous (IV) route of administration (ROA). Administration of UB-VV111 by either the IN or IV ROA is expected to transduce T cells to generate CAR T cells designed to bind to CD19 antigen to mediate cell killing and express the rapamycin-activated cytokine receptor (RACR) system which, in the presence of rapamycin, is designed to enhance specific enrichment and expansion of transduced cells. **Methods:** Study UB-VV111-01 (INVICTA, [NCT06528031CO]) is a first-in-human, global, multicenter, dose-finding study of UB-VV111 administered IN or IV +/- rapamycin in CAR-naïve and CAR-exposed subjects with R/R LBCL and CLL/SLL. Dose escalation will proceed independently for each ROA using a Bayesian optimal interval (BOIN) design. Confirmation of CD19 expression will be required for all subjects with prior CD19-directed therapy. Major eligibility criteria include adults with R/R LBCL/CLL/SLL following at least 2 lines of prior therapy who have standard organ function, measurable disease according to Lugano 2014 (LBCL) or iwCLL 2018 (CLL/SLL), ECOG 0 or 1, and no prior allogeneic transplant. Primary objectives include determining the safety profile, maximum tolerated/administered dose, and recommended Phase 2 dose of UB-VV111 +/- rapamycin. Secondary/exploratory objectives include measuring preliminary antitumor activity (magnitude and durability), as well as translational correlates of safety/efficacy. Clinical trial information: NCT06528301. Research Sponsor: Umoja Biopharma.