(PB3777) A PHASE 1/2, OPEN-LABEL, MULTICENTER STUDY OF UB-VV400 IN COMBINATION WITH RAPAMYCIN IN RELAPSED OR REFRACTORY B-CELL MALIGNANCIES

Topic: 19. Large B cell lymphomas - Clinical

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Background

Autologous, ex vivo-manufactured chimeric antigen receptor (CAR) T cells have demonstrated clinical activity in hematologic malignancies. 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 mantle cell lymphoma (MCL). 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-VV400 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 T-cell adhesion, activation, and costimulation components that promote both T-cell tropism and activation signals thought to be critical for effective CAR T-cell generation. UB-VV400 is designed to generate CD22-directed CAR T cells in a patient, thus addressing the delivery limitations that exist for currently available autologous ex vivo CD19-directed CAR T therapies. CD22 is an attractive therapeutic target because, like CD19, its expression is restricted to B cells, including both normal and malignant B cells. Moreover, CD22 offers an alternative target for patients who progress or relapse after exposure to CD19-directed therapies. UB-VV400 is designed to transduce T cells in vivo to generate CAR T cells that bind to CD22 antigen to mediate cell killing and express the rapamycin-activated cytokine receptor (RACR) system which, in the presence of rapamycin, provides specific pro-survival and expansion signals to transduced cells.

Methods

Study UB-VV400-03 is a Phase 1/2, open-label, multicenter study of UB-VV400 administered intravenously (IV) in combination with rapamycin in adult participants with R/R CD22-positive BCMs, including LBCL and MCL. In Phase 1, dose escalation will proceed independently for each disease cohort using a Bayesian optimal interval (BOIN) design. Confirmation of CD22 expression will be required for all participants. Major eligibility criteria include adults with R/R LBCL or MCL who provide informed consent and who have standard organ function, measurable disease according to Lugano 2014, ECOG 0 or 1, and no prior allogeneic transplant. Primary objectives for Phase 1 include determining the safety profile, maximum tolerated/administered dose, and recommended Phase 2 dose of UB-VV400 + rapamycin. The primary objective in Phase 2 is to assess the antitumor activity (overall response rate); durability of response and pharmacokinetics (PK) will be assessed as a secondary objective. In both parts of the study, pharmacodynamics will be evaluated as exploratory objectives.

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