TPS2668 Poster Session

A phase 1, first-in-human study of DS-2243, an HLA-A*02/NY-ESO–directed bispecific T-cell engager, in patients with advanced solid tumors.

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Background: NY-ESO-1 and LAGE-1 are homologous proteins commonly expressed in various malignancies but not in normal tissues other than the testis and placenta. Tumor types showing prevalent NY-ESO-1 and/or LAGE-1 expression include synovial sarcoma (SS), myxoid/round cell liposarcoma (MRCLS), non-small cell lung cancer (NSCLC), and urothelial carcinoma (UC). Both NY-ESO-1 and LAGE-1 undergo intracellular proteolytic processing to generate the same highly immunogenic 9-mer NY-ESO peptide (SLLMWITQC), which is presented on the cell surface in association with HLA-A*02 major histocompatibility complex molecules. DS-2243 is a bispecific antibody and T-cell engager with an effectorless Fc region. It is designed to target HLA-A*02/NY-ESO peptide complexes on tumor cells and specific molecules on T-cells, redirecting T-cell–mediated cytotoxicity toward the tumor. **Methods:** DS2243-054(NCT06644755) is a Phase 1, first-in-human, open-label, multicenter, 2-part, dose-escalation and -expansion trial of DS-2243. Patients must be ≥18 years of age and have HLA-A*02-positive advanced or metastatic SS, MRCLS, squamous or adenocarcinoma NSCLC, or UC, and be unable to tolerate standard treatments, or have relapsed disease after or be refractory to such treatment. Patients with NSCLC or UC in dose escalation and all patients in dose expansion must have NY-ESO protein expression confirmed in tumor tissue by immunohistochemistry in a central laboratory. Further inclusion criteria include the presence of ≥1 measurable lesion per Response Evaluation Criteria in Solid Tumours, version 1.1 (RECIST 1.1) and Eastern Cooperative Oncology Group performance status of 0 or 1. The primary objective of dose escalation is to evaluate the safety and tolerability of DS-2243 and determine the maximum tolerated dose and/or recommended dose for expansion (RDE). The dose-expansion part includes 4 cohorts defined by tumor type—SS/MRCLS, squamous NSCLC, adenocarcinoma NSCLC, and UC—in which patients receive DS-2243 at the RDE. The primary objectives of dose expansion are to evaluate safety and determine the objective response rate (ORR) assessed by the investigator per RECIST 1.1. Safety endpoints include dose-limiting toxicities (dose escalation only) and treatment-emergent adverse events. Secondary outcome measures include ORR (dose escalation only), time to response, duration of response, progression-free survival (all assessed by the investigator per RECIST 1.1), and overall survival. The planned sample size is ~150 patients; enrollment is ongoing. Clinical trial information: NCT06644755. Research Sponsor: Daiichi Sankyo, Inc.