

PHASE 2 STUDY OF SEA-CD40 COMBINATION THERAPIES IN ADVANCED MALIGNANCIES (SGNS40-002, TRIAL IN PROGRESS)

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Background While immunotherapy has improved outcomes for patients with metastatic non-small cell lung cancer (NSCLC) and melanoma, most progress despite standard treatment. Therefore, treatments with the potential to enhance the efficacy of existing immunotherapy-based regimens are being actively examined to further improve outcomes in these diseases.

CD40 is a tumor necrosis factor receptor expressed on multiple immune cell populations as well as on tumor cells. CD40 activation drives B- and T-cell activation to evoke tumor-specific cytotoxic T-cell responses. SEA-CD40 is an investigational, receptor-agonistic, nonfucosylated, humanized IgG1 monoclonal antibody (mAb) directed to CD40. SEA-CD40 binds with high affinity to FcγRIIIa and CD40, resulting in enhanced effector function and CD40 agonism, allowing amplification of immune stimulation and antitumor activity.

Preclinical studies have shown that SEA-CD40 combined with chemotherapy and pembrolizumab resulted in significant antitumor activity. This combination regimen has also demonstrated a tolerable safety profile, encouraging antitumor activity, and evidence of persistent immune activation in an ongoing phase 1 study (SGNS40-001, NCT02376699). Given the preclinical and clinical data supporting SEA-CD40 combined with pembrolizumab and/or chemotherapy, further investigation into additional diseases is warranted.

Methods SGNS40-002 (NCT04993677) is a phase 2, open-label, multicenter trial designed to assess the antitumor activity, safety, and tolerability of SEA-CD40 in combination with pembrolizumab and/or chemotherapy in adults (≥18 years) with NSCLC or melanoma. Five indication-specific cohorts will explore 2 different regimens: cohorts 1–3 will receive SEA-CD40 with pembrolizumab while cohorts 4 and 5 will receive SEA-CD40, pembrolizumab, carboplatin, and pemetrexed.

Cohort 1 will enroll patients with relapsed or refractory metastatic melanoma (≤3 prior lines of therapy, including an anti-programmed death/ligand 1 (PD-1/PD-L1) mAb within 90 days), cohort 2 will enroll patients with metastatic uveal melanoma, and cohort 3 will enroll patients with metastatic PD-1/PD-L1-naïve melanoma. Patients in cohorts 2 and 3 must have no prior therapy for advanced disease except adjuvant/neoadjuvant therapy. Cohorts 4 and 5 will include patients with NSCLC with a PD-L1 tumor proportion score of 1–49% or <1%, respectively.

The primary endpoint is investigator-assessed confirmed objective response rate per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1). Secondary endpoints include incidence of adverse events; laboratory abnormalities; treatment interruptions, reductions or discontinuations; disease

control rate; duration of response; progression-free survival; and overall survival. Exploratory endpoints include pharmacokinetic parameters, antidrug antibodies, biomarkers of response, and patient-reported quality of life. Enrollment is ongoing in North America and Europe.

Trial Registration NCT04993677

Ethics Approval Institutional review boards or independent ethics committees of participating sites approved the trial, which will be conducted in compliance with the Declaration of Helsinki and International Conference on Harmonization Guidelines for Good Clinical Practice. All patients will provide written informed consent.

Consent All patients will provide written informed consent.

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