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

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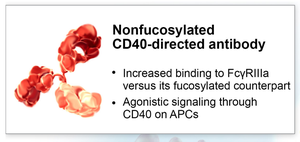
Background and Rationale

- While immunotherapy has improved outcomes for patients with NSCLC and melanoma, most progress despite standard treatment.[1] Novel treatments to improve outcomes are currently needed
- CD40 is a tumor necrosis factor receptor expressed on multiple immune cell populations and on tumor cells[2]
- SEA-CD40 is a receptor-agonistic, nonfucosylated IgG1 antibody directed to CD40. SEA-CD40 has enhanced binding to FcγRIIIa, resulting in increased effector function and CD40 agonism, thereby allowing amplification of immune stimulation and antitumor activity[3]
- SEA-CD40 combined with pembrolizumab and/or chemotherapy has demonstrated a tolerable safety profile, encouraging antitumor activity, and evidence of persistent immune activation in an ongoing phase 1 study[4]
- Given existing data supporting SEA-CD40 combined with pembrolizumab and/or chemotherapy, investigation into additional diseases is warranted. This study will evaluate whether the addition of SEA-CD40 to standard of care treatments in NSCLC and melanoma, can improve response rates and/or survival

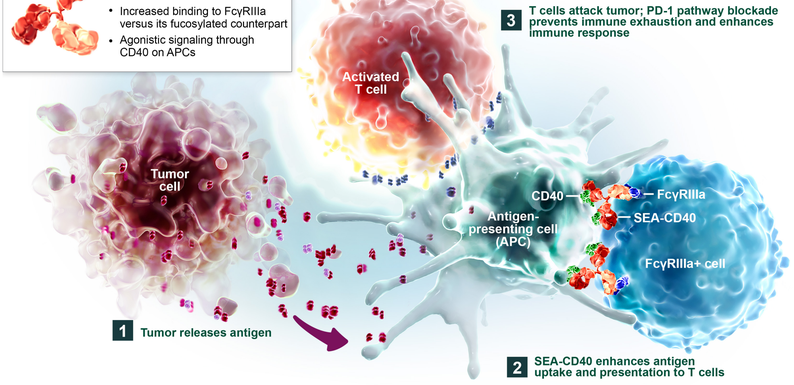
Proposed Mechanism of Action of SEA-CD40



Nonfucosylated CD40-directed antibody

- Increased binding to FcγRIIIa versus its fucosylated counterpart
- Agonistic signaling through CD40 on APCs

Proposed Mechanism of Action of SEA-CD40 in Combination with an Anti-PD-1 Agent*



***SEA-CD40 is an investigational agent, and its safety and efficacy have not been established.**

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Abbreviations

ADA, antidrug antibody; AE, adverse event; CR, complete response; AJCC, American Joint Committee on Cancer; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire; HRQoL, health-related quality of life; IgG1, immunoglobulin G1; mAB, monoclonal antibody; NSCLC, non-small cell lung cancer; NSCLC-SAQ, Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; ORR, objective response rate; OS, overall survival; PD-(L)1, programmed death/ligand 1; PFS, progression-free survival; PK, pharmacokinetics; PR, partial response; PRO, patient-reported outcome; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease; SOC, standard of care.

Disclosures: This study is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. Dr. Salama reports consultant agreements with Regeneron, Novartis, and Pfizer. Dr. Salama reports contracted research with Ideaya, BMS, Merck, Nektar, Replimune, and Seagen.

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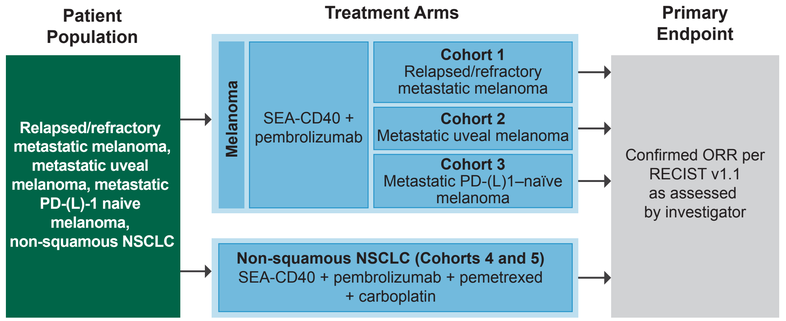
Study Design

- 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



Estimated enrollment: 200 participants

Endpoints

Primary

- Confirmed ORR; confirmed CR or PR according to RECIST v1.1[a]

Secondary

- Incidence of AEs, laboratory abnormalities, and dose alterations
- DCR; confirmed CR, PR, and SD[a]
- DOR; duration of confirmed CR or PR[a]
- PFS[a]
- OS

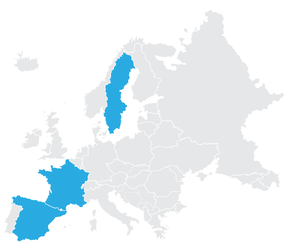
[a]Per investigator assessment.

Summary

- Patients with metastatic NSCLC or melanoma continue to have an unmet need for new therapies that improve outcomes
- This study will evaluate SEA-CD40 in combination with SOC therapies in patients with metastatic NSCLC or melanoma
- Enrollment in Cohorts 2, 4, and 5 is ongoing in North America and Europe

North America

Europe



Eligibility Criteria

Key Inclusion Criteria

Adults aged ≥18 years with histologically or cytologically confirmed diagnosis of unresectable malignancy of 1 of the following types:

Cohort 2: Metastatic Uveal Melanoma

- Must not have received prior treatment for advanced or metastatic disease except for prior adjuvant/neoadjuvant immunotherapy
- No prior liver-directed therapy

Cohorts 4 and 5: Non-Squamous NSCLC

- Participants must have stage IV disease per AJCC Cancer Staging Manual, 8th edition
- No known driver mutations/alterations mutation for which targeted therapy is available
- Must have non-squamous histology
- No prior therapy for metastatic disease
- No prior treatment with anti–PD-(L)1 or PD-L2 agent, or an antibody targeting other immune-regulatory receptors or mechanisms

- Able to provide archival tumor tissue from locations not radiated prior to biopsy. If archival tumor sample is not available a fresh baseline biopsy is required
- ECOG Performance Status score of 0 or 1
- Measurable disease per RECIST v1.1 at baseline

Key Exclusion Criteria

- History of another malignancy within 3 years of first dose of study drug
- Active central nervous system metastases and/or carcinomatous meningitis
- Previous exposure to CD40-targeted therapy
- Currently on chronic systemic steroids in excess of physiologic replacement
- Has had an allogeneic tissue/solid organ transplant
- History of autoimmune disease that has required systemic treatment in the past 2 years

References

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