A PHASE 1 STUDY OF SEA-CD70 IN MYELOID MALIGNANCIES

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Disease Background

Acute Myeloid Leukemia

- In 2020, it is estimated that nearly 20,000 new cases of AML will be diagnosed in the United States and over 11,000 deaths due to AML will occur[1].
- Despite recent therapeutic advances improving remission rates for newly diagnosed AML, the majority of patients will go on to relapse, and the prognosis remains poor for most patients with relapsed or refractory disease.
  - A recent phase 3 trial in the higher risk relapsed or refractory AML population reported a CR rate of 12% and median OS of 3.3 months in the control arm with no statistically significant difference in response rates or survival between the experimental arm and investigator's choice of available therapies[2].
  - Treatment in a clinical trial is generally recommended for these patients.

1. ACS. Key statistics for acute myeloid leukemia (AML). 2020; www.cancer.org Accessed: Oct 26, 2020.
2. Roboz et al. J Clin Oncol. 2014; 32(18):1919-26.

Disease Background

- Myelodysplastic Syndromes
  - The annual age-adjusted incidence of MDS is approximately 2 to 4 per 100,000 in the US, but the incidence rises substantially to 7 per 100,000 in 60 to 69 year-olds and 36 per 100,000 in people over 80 years of age[1].
  - Prognosis in MDS depends on a number of risk factors. For patients with intermediate or high risk MDS, allogeneic hematopoietic cell transplant (allo-HCT) is the preferred treatment.
  - However, the majority of higher-risk MDS patients are not eligible for allo-HCT due to age, comorbidities, and/or donor availability. For these patients, hypomethylating agent (HMA) therapy is the standard of care treatment[2].
  - HMA therapy is not curative; there is no standard treatment for patients who do not respond to or relapse following HMA treatment[3]

1. Zeidan et al. Blood Rev. 2019; 34:1-15.
2. Fenaux et al. Lancet Oncol. 2009; 10(3):223-32.
3. Greenberg et al. J Natl Compr Canc Netw. 2017; 15(1):60-87.

SEA-CD70 Target

- CD70 (CD27L) is a member of the tumor necrosis factor superfamily that is transiently expressed on T and B lymphocytes and myeloid cells following activation.
- CD70 and its ligand, CD27, may play a role in malignant blast cell survival and/or tumor immune evasion.
- CD70 is aberrantly expressed in a variety of hematologic cancers and carcinomas and may play a role in tumor cell survival or tumor immune evasion.
- Both CD70 and CD27 have been reported to be expressed on AML and MDS blasts[1].
- CD70-CD27 interactions may also play a role in regulating antitumor immune responses, and thus disrupting CD70-CD27 signaling may counteract tumor cell immune evasion in myeloid malignancies.

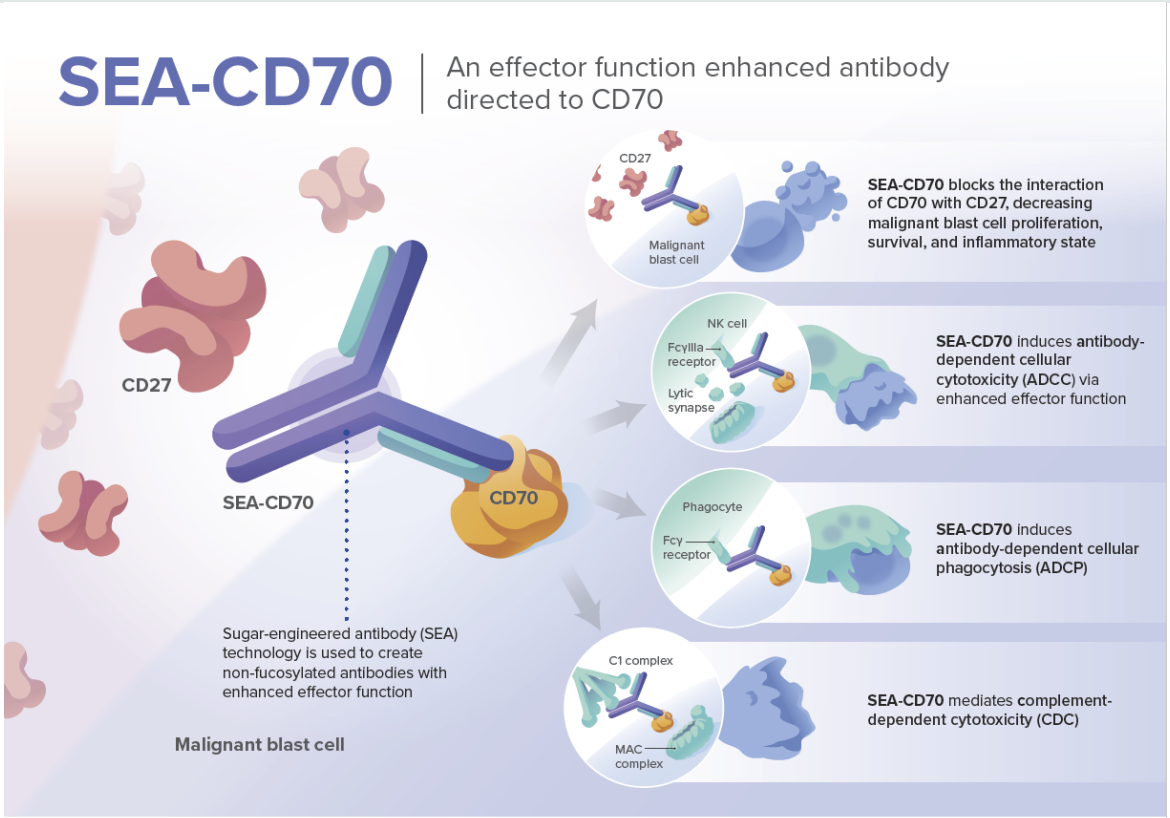
1. Schurch et al. Front Oncol. 2018 8:152.

Background Studies

- SEA-CD70 mediates potent target killing through Fc-dependent antibody effector functions, including antibody-dependent cellular cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), and complement-dependent cytotoxicity (CDC) in vitro[1].
- SEA-CD70 can also disrupt CD70-CD27 signaling in vitro, therefore interfering with CD70-CD27 pro-survival activity[1].
- In vivo, SEA-CD70 delayed tumor growth and increased survival in subcutaneous AML xenograft mouse tumor models both as a single agent and when combined with azacitidine[1].

1. Diolaiti et al. Blood 2020 136(Supplement 1): 23.

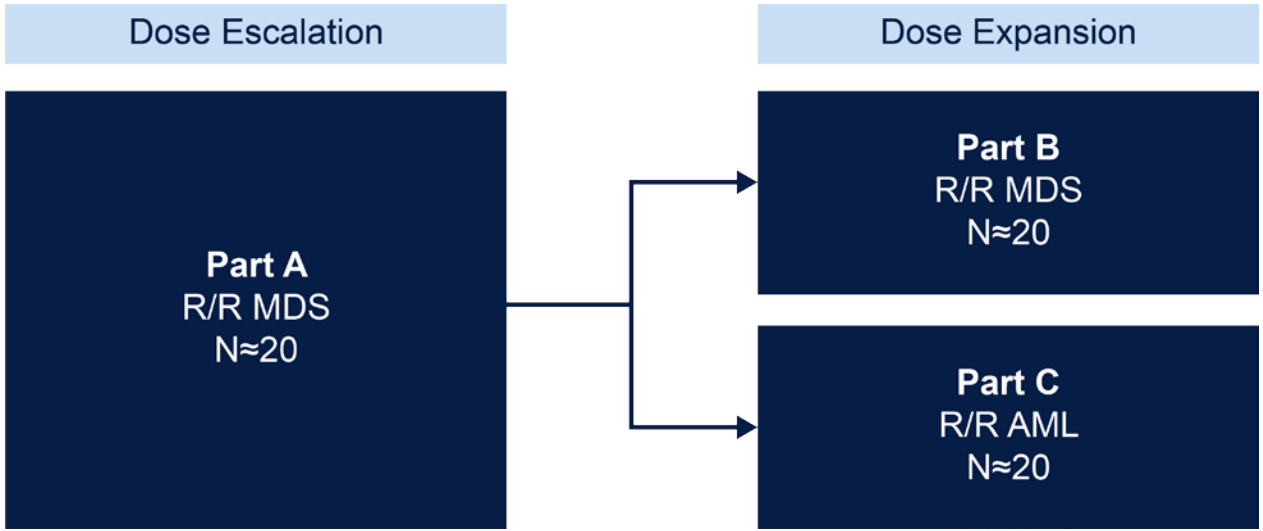
SEA-CD70 Proposed Mechanism of Action



SEA-CD70 is an investigational agent, and its safety and efficacy have not been established.

SGNS70-101 Study Design

SGNS70-101 is a phase 1, open-label, dose-escalation, and cohort expansion study designed to evaluate the safety, tolerability, pharmacokinetic, and antitumor activity of SEA-CD70 in adults with myeloid malignancies.



Objectives

Primary Objectives

- Evaluate the safety and tolerability of SEA-CD70
- Identify the maximum tolerated dose or recommended expansion dose of SEA-CD70

Secondary Objectives

- Assess the antitumor activity of SEA-CD70, including complete remission (CR) rate, overall response rate (ORR), hematologic improvement (HI) rate for subjects with MDS, and event-free survival (EFS)
- Assess the pharmacokinetics of SEA-CD70
- Assess the immunogenicity of SEA-CD70

Eligibility

Key Inclusion Criteria

- Parts A and B: Subjects with relapsed or refractory (HMA-failure) MDS with no other therapeutic options available that are known to provide clinical benefit in MDS
- Part C: Subjects with relapsed or refractory AML, and who have received 2 or 3 prior regimens, or 1 prior regimen with additional high-risk features

Key Exclusion Criteria

- History of another malignancy within 3 years prior
- Prior allogeneic hematopoietic stem cell transplant
- Central nervous system leukemia

Study Sites

- 8 sites active
- Study start: August 2020
- Additional sites opening across the US and EU

Acknowledgements

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Disclosures

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