



Magrolimab + Azacitidine versus Azacitidine + Placebo in Untreated Higher Risk Myelodysplastic Syndrome: The Phase 3, Randomized, Double-Blind ENHANCE Study

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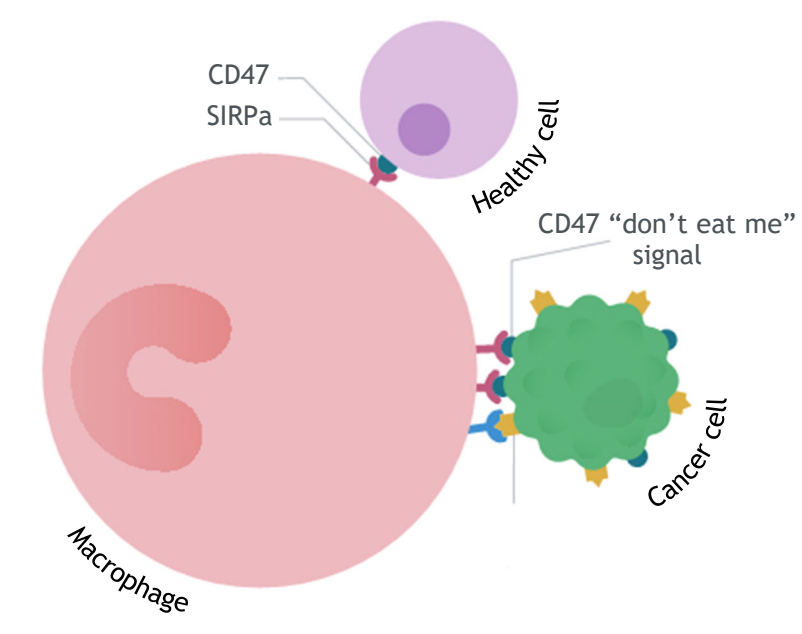
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Background

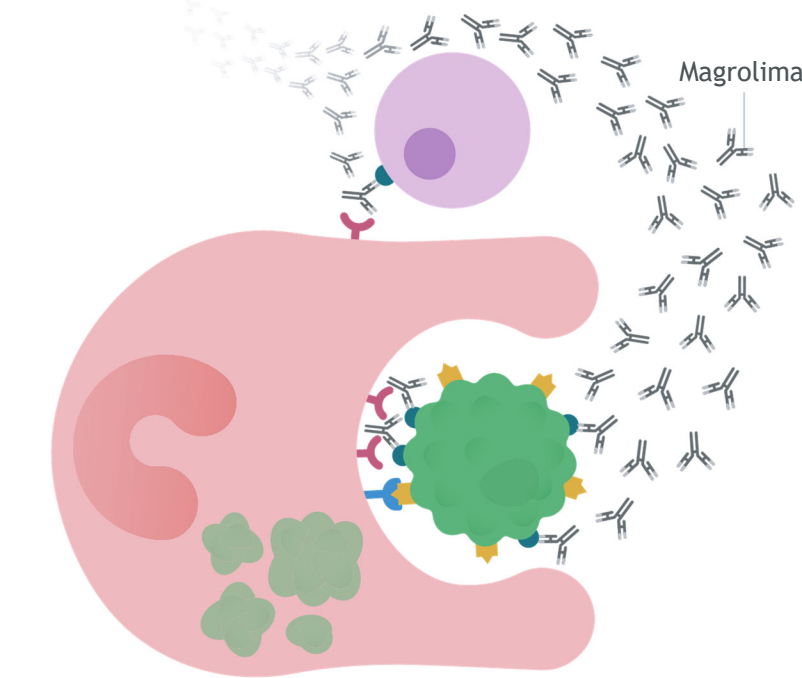
- Myelodysplastic syndrome (MDS) is a clonal myeloid disorder characterized by cytopenia and ineffective hematopoiesis¹.
- MDS is a disease of the elderly, with a median age of 71-76 years at diagnosis^{2,3}; prognosis and treatment are guided by the Revised International Prognostic Scoring System (IPSS-R) criteria⁴.
- Patients with intermediate, high and very high risk MDS (HR-MDS) have a median overall survival (OS) of 0.8 to 3 years⁴.
- Despite the high unmet need in this patient population, azacitidine and decitabine are the only approved therapies for HR-MDS to date⁵.
- Magrolimab is a first-in-class monoclonal antibody that blocks the macrophage inhibitory immune checkpoint cluster of differentiation (CD)47, a “do not eat me” signal overexpressed on tumor cells⁶.
- Binding of magrolimab to CD47 leads to phagocytosis of tumor cells⁶.
- Azacitidine increases expression of prophagocytic “eat me” signals, facilitating synergy with magrolimab⁷.
- In an ongoing Phase 1b study, the combination of magrolimab + azacitidine induces an overall response rate (ORR) of 91%, a complete response rate of 42% (with no duration of response [DOR] reached), and an acceptable safety profile without significant immune-related adverse events⁸.
- ENHANCE (NCT04313881) is a Phase 3 trial comparing the efficacy and safety of magrolimab + azacitidine with that of azacitidine + placebo in previously untreated patients with HR-MDS⁹.

Magrolimab Mechanism of Action⁸

No phagocytosis



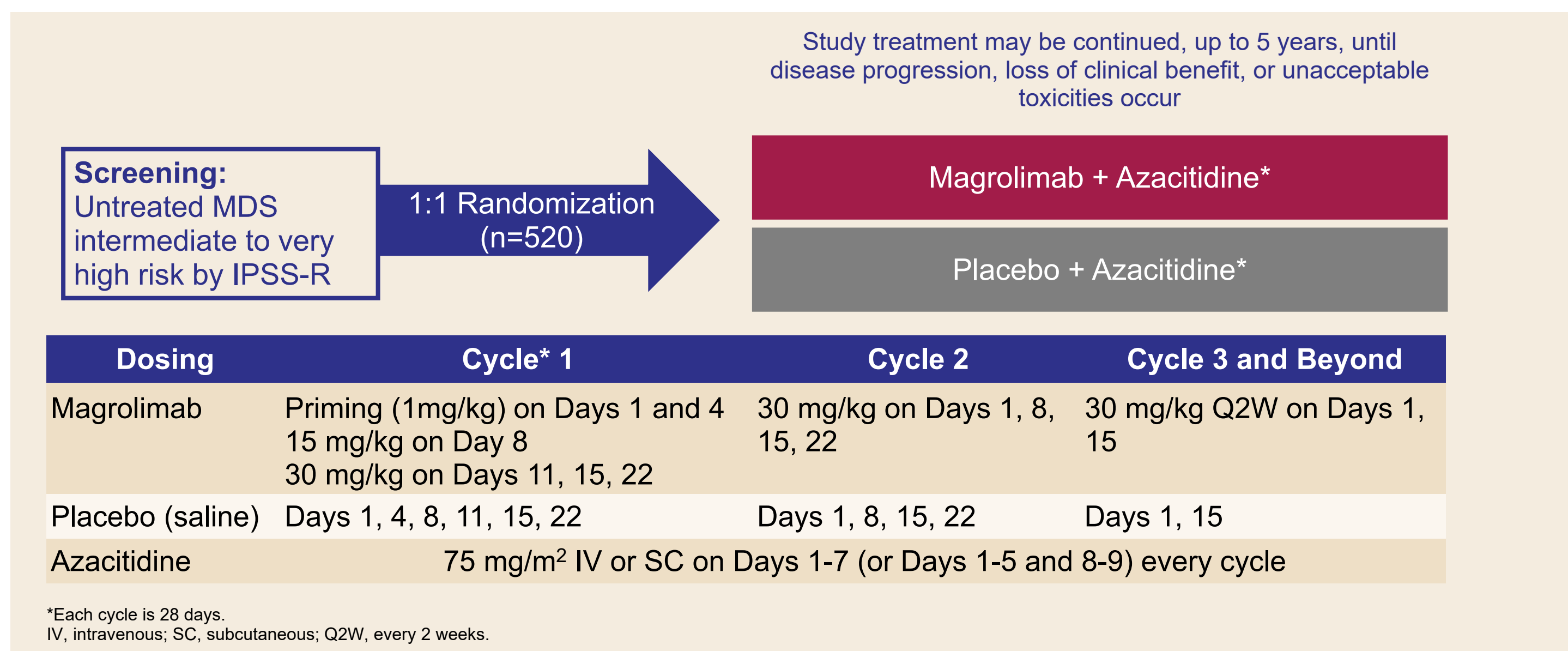
Phagocytosis



Objectives

- To evaluate the efficacy of magrolimab + azacitidine compared to that of azacitidine + placebo in previously untreated patients with HR-MDS by IPSS-R.
- To evaluate safety, pharmacokinetics, pharmacodynamics, and immunogenicity of magrolimab + azacitidine.

Study Design

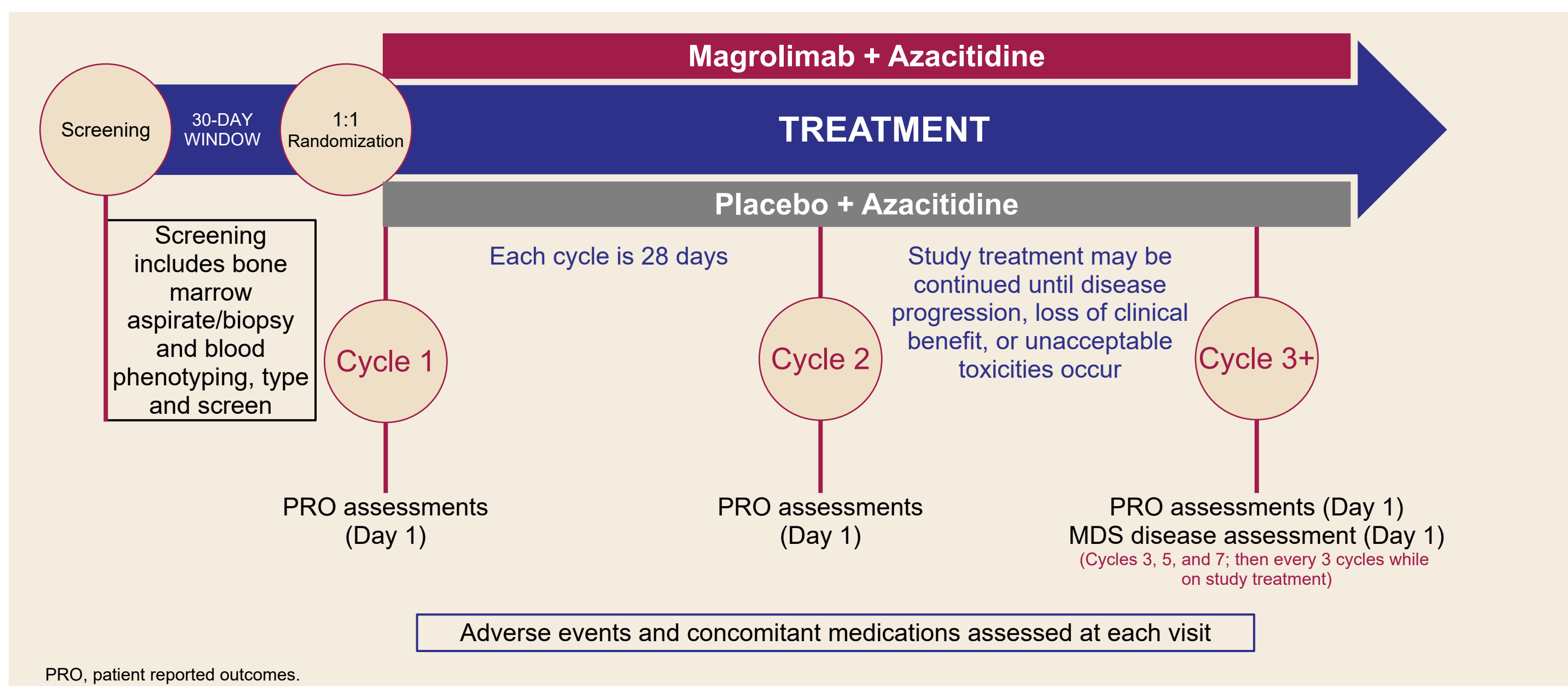


Endpoints

Primary Endpoints:	Secondary Endpoints:		
♦ CR rate*	♦ Duration of CR	♦ MRD-negative response rate	♦ Safety
♦ OS	♦ ORR and DOR	♦ Time to transformation to AML	♦ Anti-magrolimab antibody rate
Exploratory:	♦ RBC transfusion independence rate	♦ Serum concentration of magrolimab	♦ FACT-Anemia response rate
♦ Biomarkers	♦ PFS	♦ EFS	

*Based on Investigator-assessed International Working Group 2006 MDS criteria¹⁰. AML, acute myeloid leukemia; CR, complete response; EFS, event free survival; FACT, Functional Assessment of Cancer Therapy; MRD, minimal residual disease; PFS, progression-free survival; RBC, red blood cell.

ENHANCE Key Assessments and Timing



Patient Eligibility

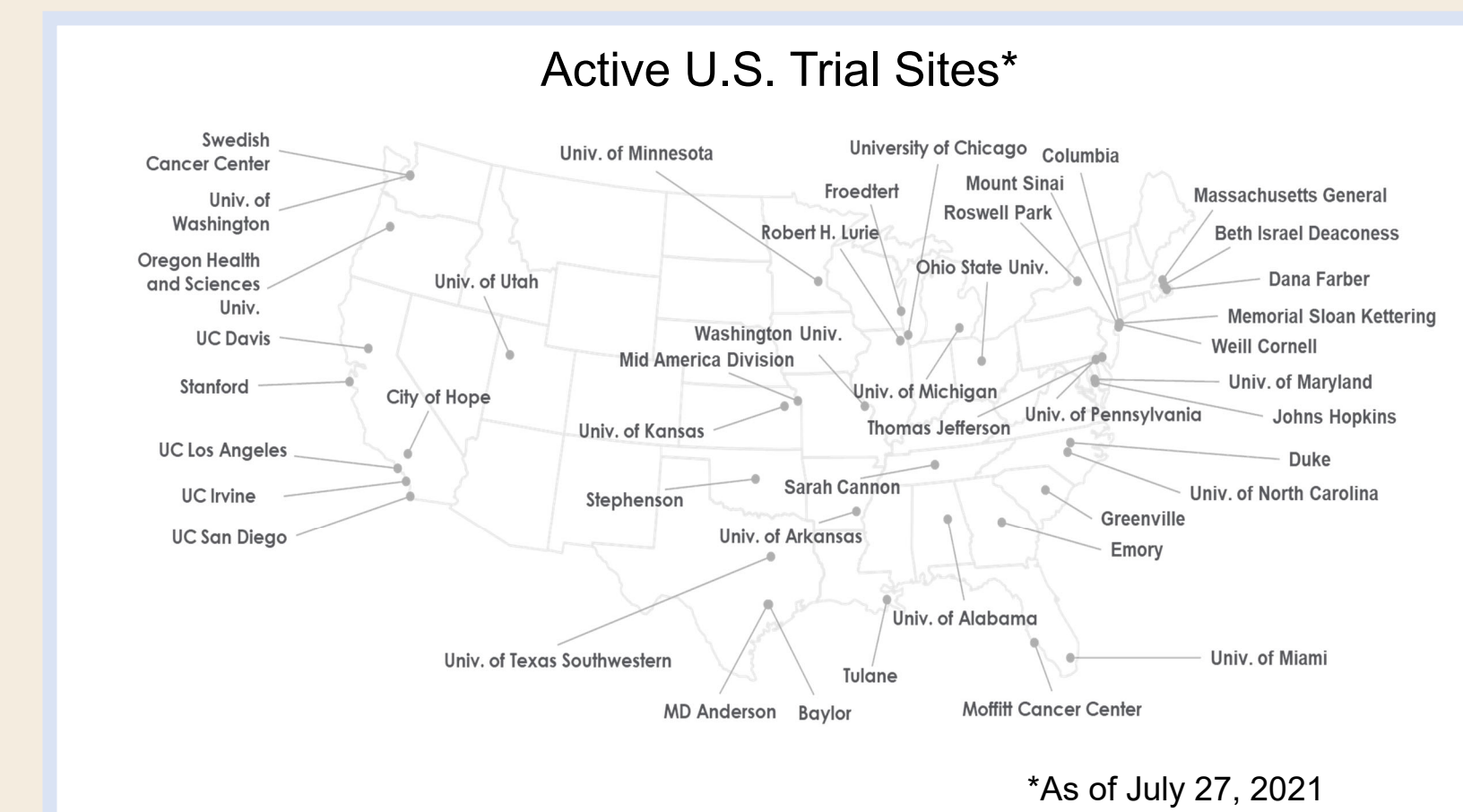
ENHANCE Key Inclusion and Exclusion Criteria

Key Inclusion Criteria	Key Exclusion Criteria
♦ Previously untreated individuals with intermediate to very high risk MDS by IPSS-R	♦ Prior treatment with CD47 or Signal-regulatory protein alpha (SIRPα)-targeting agents
♦ Adequate performance status and hematologic, liver, and kidney function	♦ Any prior antileukemic therapy for treatment of intermediate, high, very high risk MDS per IPSS-R
	♦ Contraindications to azacitidine
	♦ Clinical suspicion of active central nervous system involvement by MDS
	♦ Known active or chronic hepatitis B or C infection or human immunodeficiency virus
	♦ Pregnancy or active breastfeeding

Note: Other protocol-defined inclusion/exclusion criteria may apply.

Enrollment

- The study opened to accrual in September 2020 and, as of August 2021, is currently recruiting participants at 46 study sites in the United States and 41 sites internationally.



Country	Number of Sites
United States of America	46
Australia	16
France	5
Hungary	5
Spain	4
New Zealand	3
Finland	2
United Kingdom	2
Hong Kong	1
Italy	1
Poland	1
Switzerland	1

- ♦ Additional information available at ClinicalTrials.gov <https://clinicaltrials.gov/ct2/show/NCT04313881>

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Acknowledgments

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