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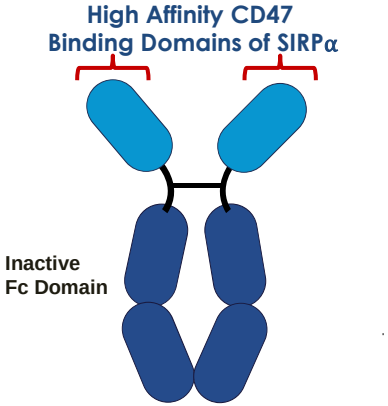
ASH Conference Call

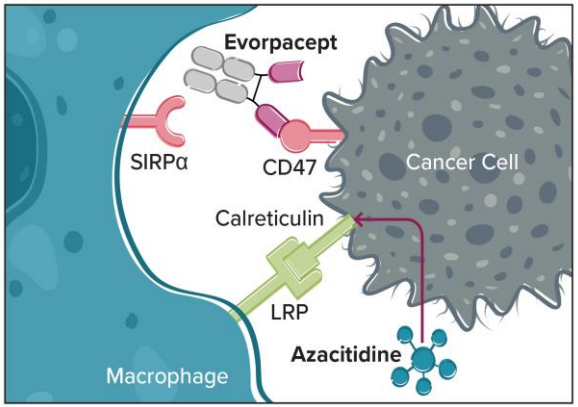
December 13, 2021

Evorpacept: Targeting CD7 as a Myeloid Checkpoint in MDS

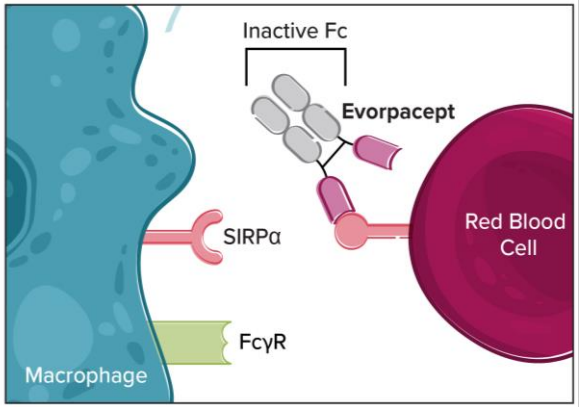
- **CD47, a marker of self, is upregulated by tumors to evade the immune system**
- **CD47-SIRPα signaling represents a myeloid checkpoint mechanism in cancer**
- **CD47 engages SIRPα and signals the macrophage to ignore the cell on which it is expressed**



Molecular weight half the size of a typical antibody



Evorpacept increases pro-phagocytic signal provided by azacitidine



While sparing normal hematopoietic cells from destruction

Kauder, SE. et al. PLoS ONE. 2018 August;13(8): e0201832

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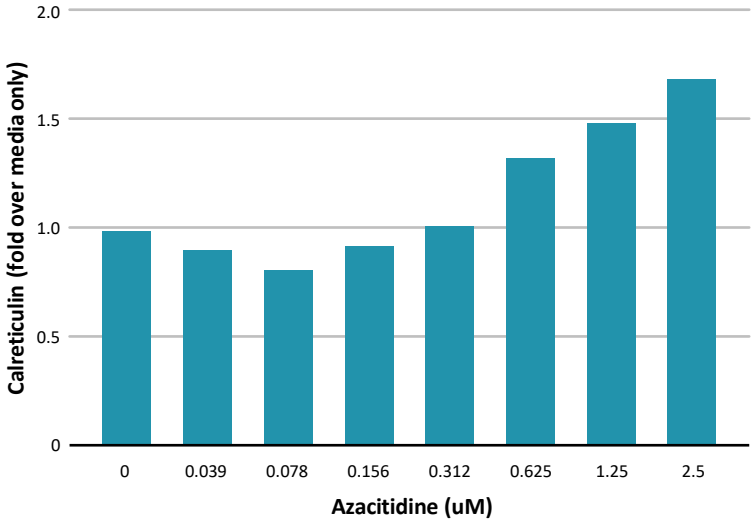
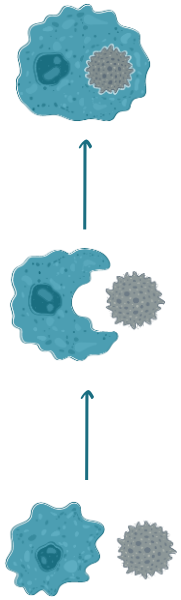
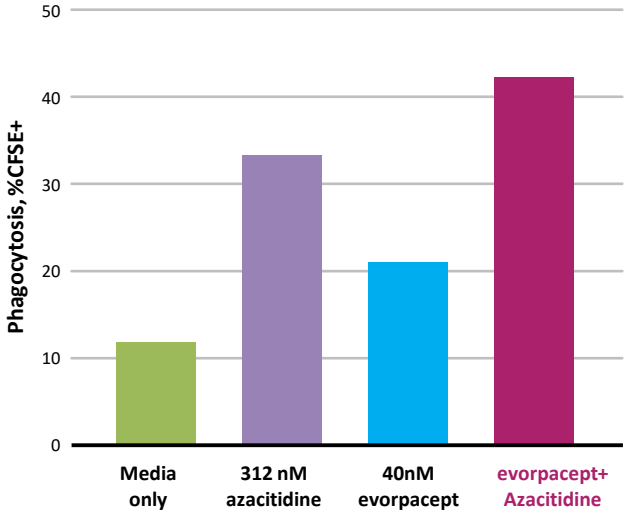
Preclinical: Evorpacept increases phagocytosis of leukemia cells in combination with backbone MDS drug azacitidine







Azacitidine induces calreticulin display
Evorpacept increases phagocytosis in combination with azacitidine

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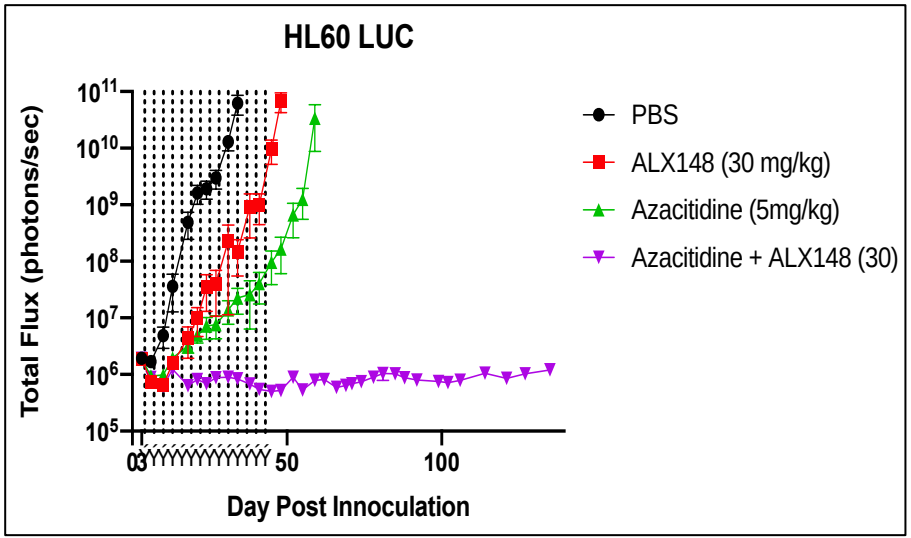
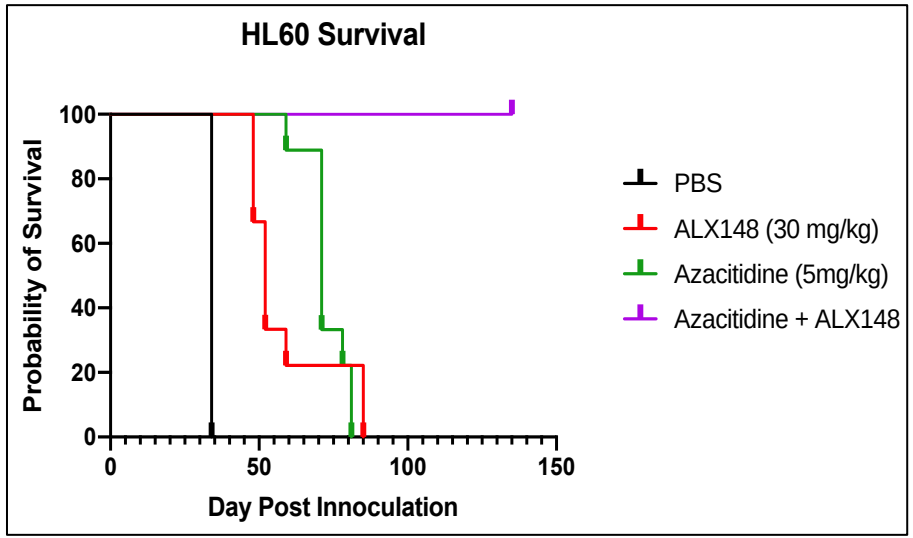
Evorpacept (ALX148) + AZA Combination Significantly Increases Efficacy in Disseminated AML Xenograft Model





Chen et al., ASH 2020 Abstract #1965

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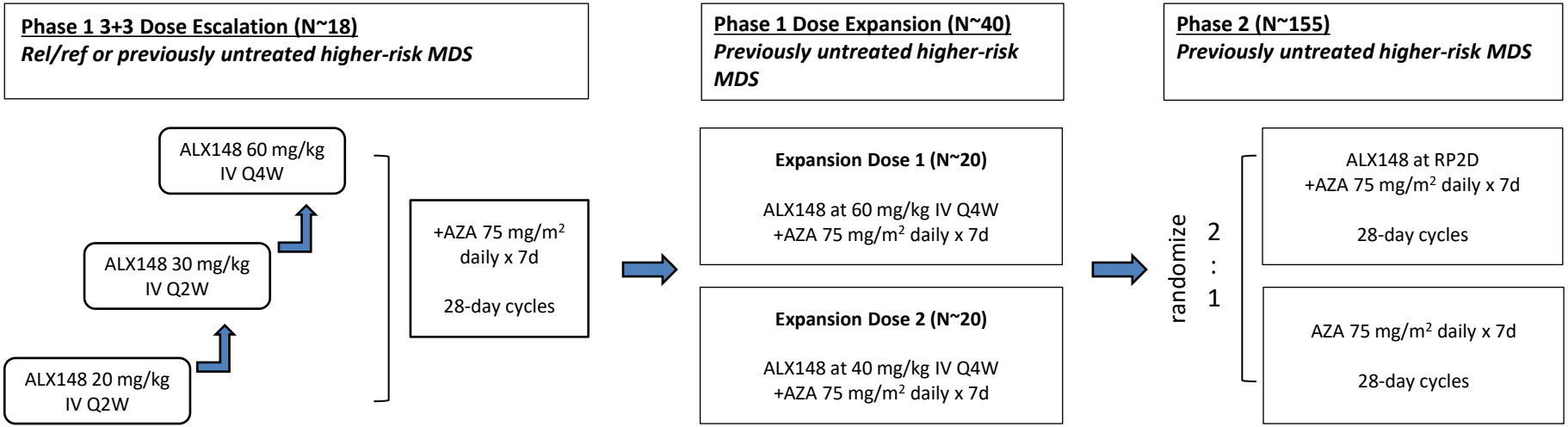
ASPEN-02 Study Design

Incorporation of dose optimization in Phase 1 prior to initiation of randomized phase 2 study



Professor Guillermo Garcia-Manero, M.D.

For the last 15 years, Dr. Garcia-Manero's efforts have focused on improving the outcomes and quality of life of patients with leukemia and in particular myelodysplastic syndromes. His work centers around the understanding of the pathophysiology of these disorders in an attempt to develop new therapeutic interventions. He currently leads the largest MDS program in the world and directs the MDS/AML Moon Shot ® program at MD Anderson. This work has resulted in over 500 publications in the areas of biology, therapy and prognostication of these disorders, and development of multiple therapeutic clinical trials.

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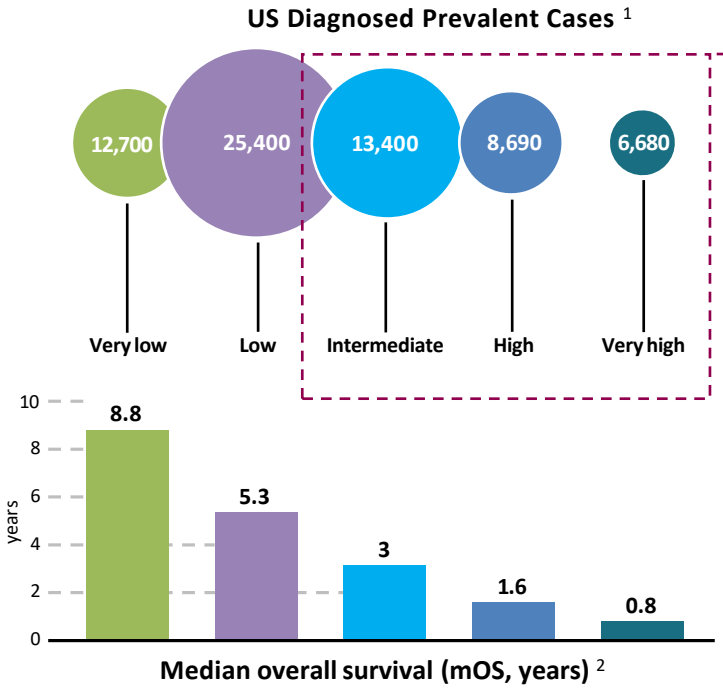
Patients with higher risk MDS represent an area of high unmet need



Higher Risk (HR) MDS

Bone marrow transplant

<10%
Receive allogeneic transplant [3]

Azacitidine, Decitabine

17%
Treated with azacitidine achieve a CR [4]

Overall MDS

Nearly all pts transfused due to cytopenias

41 of 100
Will die from cytopenia-related causes [5]

Revised international prognostic scoring system (IPSS-R).
[1]Estimated: Decision Resource Group 2019 MDS Report
[2]Greenberg, *Blood,* 2012

[3]Zeidan, *Leukemia & Lymphoma*, 2018
[4]Fenaux, *Lancet Oncology,* 2009
[5]Steensma, *Leukemia & Lymphoma,* 2015

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Current Standard of Care Benchmarks for Higher Risk and Relapsed/Refractory MDS

MDS Population/ Treatment/ Study Type	N	ORR (%)	CRR (%)	mOS (mo)
1L HR-MDS Azacitidine AZA-001 (Ph 3)[1]	179	29*	17	24.5
1L HR-MDS with TP53 mutation and complex cytogenetics Azacitidine (retrospective)[2]	261	~63	~22	10.7
≥2L MDS Venetoclax+azacitidine (Phase 1b)[3]	38	40	8	-
2L MDS Guadecitabine (Phase 2)[4]	56	14.3	3.6	7.1

*CR+PR per IWG 2000 criteria

[1]Fenaux et al, Lancet Onc 2009; [2]Montalban-Bravo, Blood 2020; [3]Zeidan et al, ASH 2019; [4]Sebert et al, Haemotologica 2019

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Evorpacept (ALX148), a CD47-Blocking Myeloid Checkpoint Inhibitor, in Combination with Azacitidine: A Phase 1/2 Study in Patients with Myelodysplastic Syndrome (ASPEN-02)

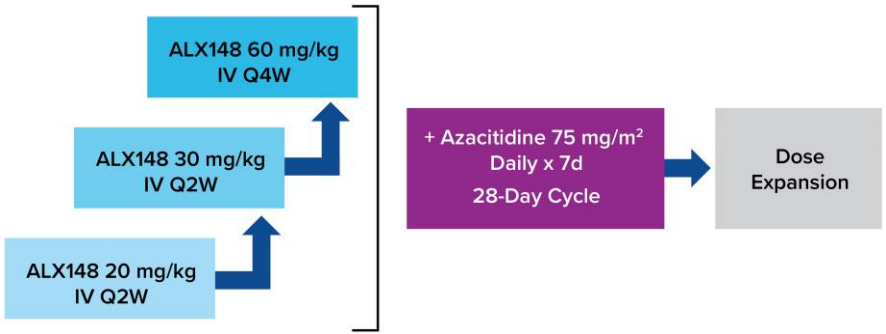
Guillermo Garcia-Manero[1], Harry Erba[2], Srinivasa Sanikommu[3], Jessica Altman[4], Hamid Sayar[5], Bart Scott[6], Abraham Fong[7], Shanhong Guan[7], Feng Jin[7], Alison Forgie[7], Jaume Pons[7], Sophia Randolph[7], Michael Byrne[8]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [2]Duke Cancer Institute, Durham, NC, US; [3]Levine Cancer Institute, Charlotte, NC, US; [4]Robert H Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL, US; [5]Indiana University Simon Comprehensive Cancer Center, Indianapolis, IN, US; [6]Fred Hutchinson Cancer Research Center, Seattle, WA, US; [7]ALX Oncology Inc., South San Francisco, CA, US; [8]Vanderbilt-Ingram Cancer Center, Nashville, TN, US

ASPEN-02 Phase 1 Design

- **Using a 3+3 dose escalation, subjects were administered escalating doses of intravenous evorpacept (20 mg/kg Q2W, 30 mg/kg Q2W, or 60 mg/kg Q4W) combined with azacitidine (75 mg/m^2 IV/SC x 7d) in a 28-day treatment cycle.**
- **The primary Phase 1 objective is to characterize the safety and tolerability of evorpacept administered in combination with azacitidine.**
- **The primary Phase 1 endpoint is the frequency of first cycle dose-limiting toxicities (DLTs).**
- **Eligible patients include adults with a documented diagnosis of relapsed/refractory (R/R) MDS or higher risk (HR) previously untreated MDS (IPSS-R score >3.5) and a baseline ECOG status of 0-2. For patients with R/R MDS, prior exposure to hypomethylating agents (HMA) is allowed. Patients with previously untreated HR-MDS must have had no prior exposure to HMA or cytotoxic chemotherapy for the treatment of MDS (prior use of single agent lenalidomide for low or intermediate-1 risk MDS with deletion 5q abnormality is allowed) and must be appropriate candidates for single-agent azacitidine treatment.**
- **Response assessments were performed by the investigator per IWG criteria.[4]**

Figure 3. Phase 1 Study Schema



Patient Baseline Characteristics

- **22 patients with R/R or previously untreated HR-MDS have been enrolled in the Phase 1 (Table 1) as of the data cutoff date of 25-Oct-2021.**
- **6 of 9 patients with previously untreated HR-MDS had therapy related disease.**
- **All patients with R/R MDS had failed 1 or more prior HMA regimen.**
- **Among the 9 patients enrolled with previously untreated HR-MDS, 7 (78%) had a TP53 mutation together with complex (>3) cytogenetic abnormalities.**

Table 1. Patient Baseline Characteristics

		Phase 1 n=22
Median age, years (range)		70.5 (56 – 81)
Sex, n	F M	8 14
Race, n	White Black Unknown	17 4 1
ECOG PS, n	0 1 2	6 16 0
MDS status, n	Previously untreated HR-MDS • Therapy related	9 6
	Rel/Ref MDS • Prior HMA treatment	13 13
IPSS-R score	Mean Median Min-Max	6.0 5.8 1.0-10.0
Mutation status, n (%)	TP53 ASXL1 TET2 DNMT3A SF3B1 SRSF2 RUNX1	8 (36) 4 (18) 3 (14) 2 (9) 1 (4.5) 1 (4.5) 1 (4.5)
Cytogenetic Risk at Diagnosis, n (%)	Very Good Good Intermediate Poor Very Poor N/A	0 2 (9) 0 2 (9) 8 (36) 10 (45)

N/A: not available

Safety

- **Evorpacept in combination with azacitidine was well tolerated with no dose-limiting toxicities observed, and most adverse events (AE) were of low grade and frequency.**
- **21 (95.5%) patients administered ALX148 + azacitidine experienced any treatment emergent AE (TEAE), with 10 (45.5%) patients experiencing any AE considered possibly related to ALX148 treatment.**
- **The most common treatment related AEs (TRAE) observed with evorpacept + azacitidine were Grade 1-2 infusion related reactions (IRR) (n=4; 18%) (Table 2b). All patients experiencing IRRs were able to complete evorpacept infusions and did not experience recurrence of IRRs with subsequent cycles.**
- **13 (59%) patients experienced any TEAE ≥Grade 3 in severity, with a total of 2 (9%) patients experiencing any ≥Grade 3 TRAE (both with transient neutropenia/neutrophil count decreased); there was 1 (4.5%) G5 TEAE of sepsis unrelated to study treatment.**
- **No patients (0%) experienced any serious adverse event (SAE) considered related to evorpacept treatment.**

Table 2a: Most Common (>2 Subjects) Treatment Emergent AEs (All Causality)

	20 mg/kg Q2W (N=3)		30 mg/kg Q2W (N=3)		60 mg/kg Q4W (N=16)		Total (N=22)
Adverse Event, n	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4	All Grade n (%)
Blood Creatinine Increased	2	–	1	–	2	–	5 (23)
Constipation	1	–	1	–	2	1	5 (23)
Diarrhea	1	–	1	–	3	–	5 (23)
Fatigue	–	–	–	–	4	1	5 (23)
Neutropenia/Neutrophil Count Decreased	–	–	–	1	1	3	5 (23)
Anemia	1	1	1	–	–	1	4 (18)
Dizziness	–	–	1	–	3	–	4 (18)
Dyspnoea	1	–	–	–	2	1	4 (18)
Febrile Neutropenia	–	2	–	–	–	2	4 (18)
Infusion Related Reaction	–	–	–	–	4	–	4 (18)
Nausea	–	–	1	–	3	–	4 (18)
Abdominal Pain	1	–	1	–	1	–	3 (14)
Contusion	1	–	1	–	1	–	3 (14)
Platelet Count Decreased	–	2	–	1	–	–	3 (14)
Pneumonia	–	1	–	–	–	2	3 (14)
Transfusion Reaction	2	–	–	–	1	–	3 (14)
Vomiting	1	–	–	–	2	–	3 (14)

Table 2b: Most Common (>1 Subject) Evorpacept-Related AEs

	20 mg/kg Q2W (N=3)		30 mg/kg Q2W (N=3)		60 mg/kg Q4W (N=16)		Total (N=22)
Adverse Event, n	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4	All Grade n (%)
Infusion Related Reaction	–	–	–	–	4	–	4 (18)
Constipation	1	–	–	–	2	–	3 (14)
Neutropenia/Neutrophil Count Decreased	–	–	–	–	1	2	3 (14)
Nausea	–	–	1	–	1	–	2 (9)
Vomiting	1	–	–	–	1	–	2 (9)

Data Cutoff 25Oct2021; Safety population (n=22); Table includes all ≥G3 evorpacept-related AEs.

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Efficacy in IWG Response-Evaluable Patients

- **Previously untreated HR-MDS: 3 out of 6 subjects achieved a response**
  - 2 CR ([n=1 at 20 mg/kg Q2W, n=1 at 60 mg/kg Q4W] both subjects also achieved cytogenetic response),
  - 1 marrow CR with HI-E and HI-P (20 mg/kg Q2W),
  - 2 SD (n=2 at 60 mg/kg Q4W)
  - 1 PD (30 mg/kg Q2W)
- **R/R MDS: 5 out of 8 subjects achieved a response**
  - 5 marrow CR (n=1 at 20 mg/kg Q2W, n=4 at 60 mg/kg Q4W)
  - 2 SD (n=2 at 30 mg/kg Q2W)
  - 1 PD (60 mg/kg Q4W).
  - One subject had a G5 event unrelated to study treatment and was not evaluable for IWG response.
- **Among the 2 patients with CR, 1 proceeded to stem cell transplant and 1 has ongoing CR with full count recovery and remains on treatment and is transfusion independent.**
- **Overall, 3 patients have been able to proceed to stem cell transplant.**
- **The median follow up time on study is 3.4 months.**
- **Decrease in bone marrow blasts was observed in subjects with both previously untreated HR-MDS and R/R MDS (Figure 4).**

Table 3: Best Overall Response by IWG Criteria[4]

	Previously Untreated HR-MDS (N=6)	Previously Untreated HR-MDS with TP53 mutation (N=5)	Relapsed/Refractory MDS (N=9)[#]
ORR	3 (50%)	3 (60%)	5 (56%)*
CR	2 (33%)	2 (40%)	0
PR	0	0	0
Marrow CR	1 (17%) with HI	1 (20%) with HI	5 (56%)*
HI	0	0	0
SD	2 (33%)	1 (20%)	2 (22%)
PD	1 (17%)	1 (20%)	1 (11%)

Data Cutoff 25Oct2021; Response evaluable population (n=15); *includes 3 unconfirmed responses; [#]1 subject had G5 event unrelated to treatment prior to first disease assessment; ORR – Objective response rate; CR – Complete response; PR – Partial response; HI – Hematologic improvement; E – Erythroid; P – Platelet; SD – Stable disease; PD – Disease progression; IWG – international working group.

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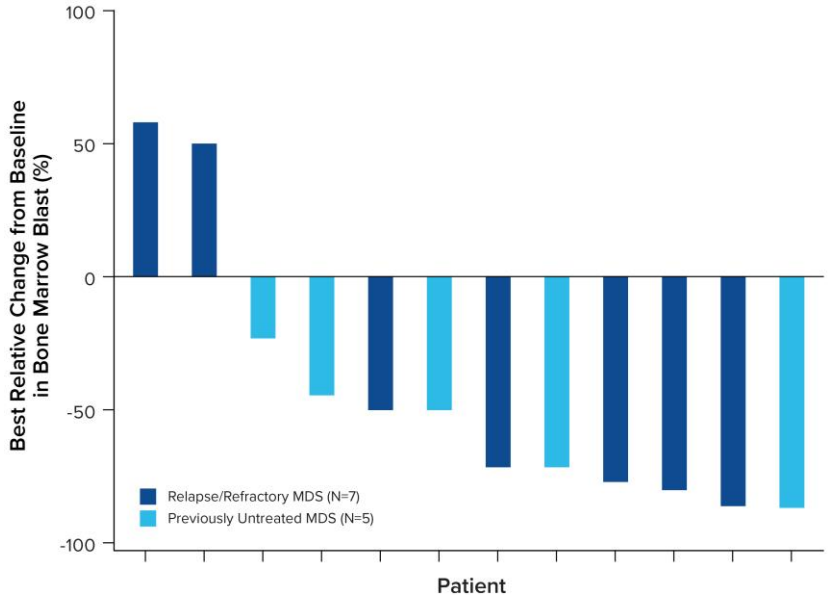
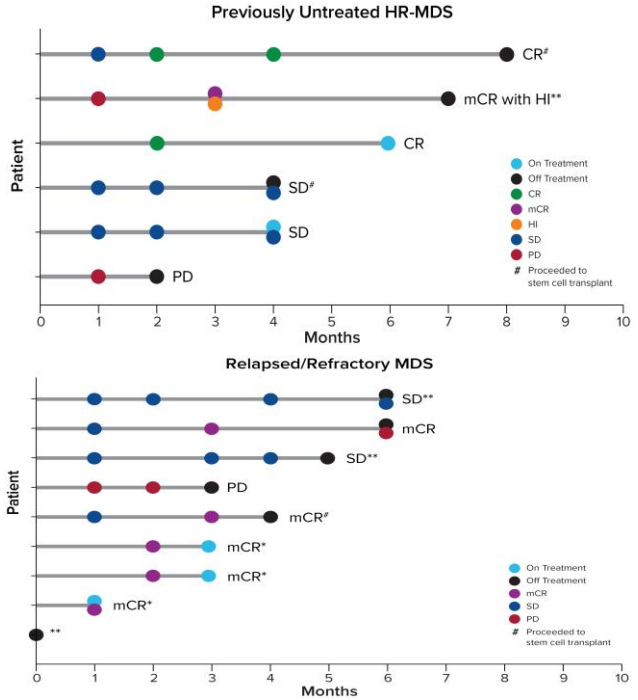
Efficacy

Figure 4. Change in Bone Marrow Blast Percentage from Baseline



Data Cutoff 25Oct2021; Response-evaluable population (n=15); 2 subjects (1 Relapsed/Refractory and 1 Previously Untreated) with missing data and 1 subject with G5 unrelated event not represented on graph.

Figure 5. Duration of Response



Data Cutoff 25Oct2021; Response-evaluable population (n=15); *Unconfirmed responses; **Off treatment due to disease progression (n=1), investigator decision (n=2), and G5 unrelated event (n=1).

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Changes in Hemoglobin Level and RBC Transfusion Frequency

- Preliminary data indicate a trend towards improvement in hemoglobin levels and decrease in RBC transfusion frequency in patients with previously untreated HR-MDS treated with evorpacept + azacitidine, but no clear change from baseline in patients with R/R MDS.
- 2 out of 4 patients with untreated HR-MDS and transfusion dependence at baseline developed transfusion independence on study

Figure 6a. Changes in Hemoglobin Level on Treatment

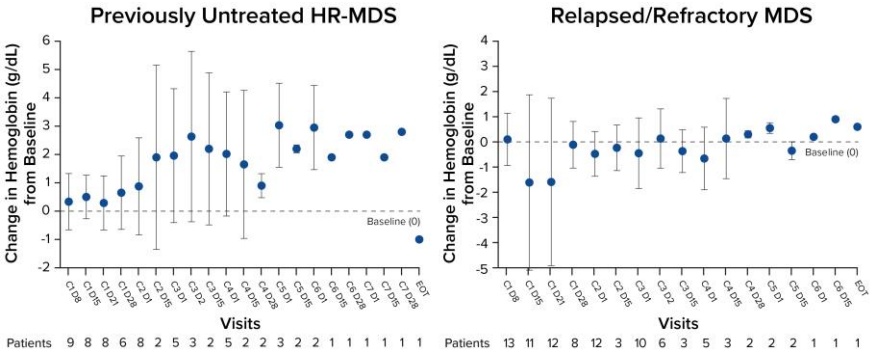
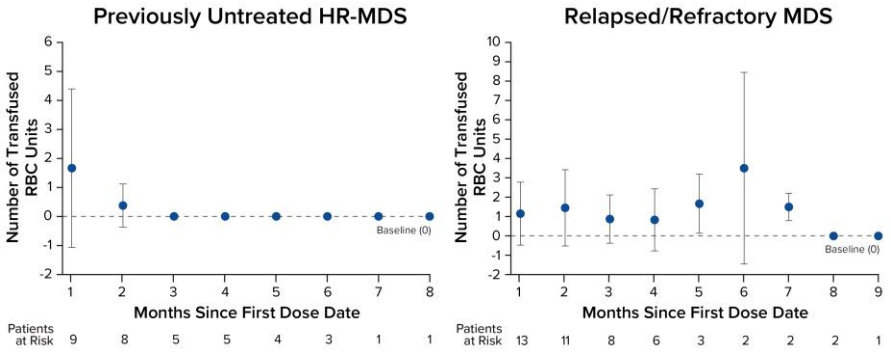


Figure 6b. RBC Transfusion Frequency on Treatment

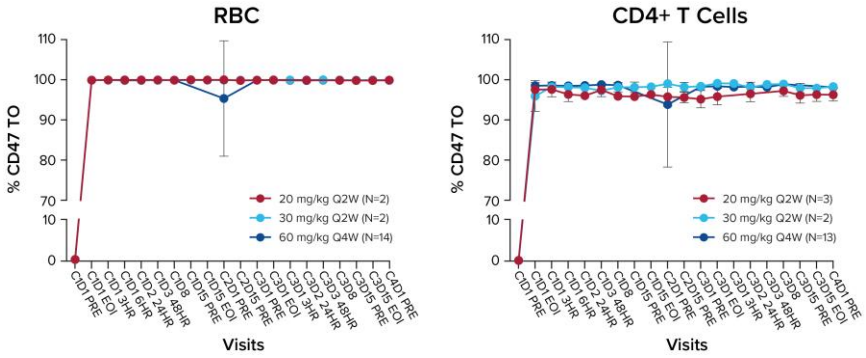


Data Cutoff 25Oct2021; Parameters presented as mean ± SD; Safety population (n=22).

Preliminary Phase 1 PK and PD Results

- Overall, evorpacept exhibited dose-proportional PK, consistent with results from prior studies.
- Full CD47 target occupancy (TO) was observed on peripheral blood RBCs and CD4+ T cells throughout the dosing interval, including at both peak and trough concentrations of evorpacept, across the three dose levels evaluated.

Figure 8. Preliminary CD47 Target Occupancy in Peripheral Blood



Data Cutoff 25Oct2021; One subject in the 60 mg/kg Q4W cohort had reduced CD47 TO due to dose delay prior to C2D1; Parameters presented as mean +/- SD; PRE – pre-infusion; EOI – end of infusion.

Figure 7. Evorpacept Concentration-Time Profiles Following IV Infusion at 20 mg/kg Q2W, 30 mg/kg Q2W, and 60 mg/kg Q4W (Cycle 1, Day 1)

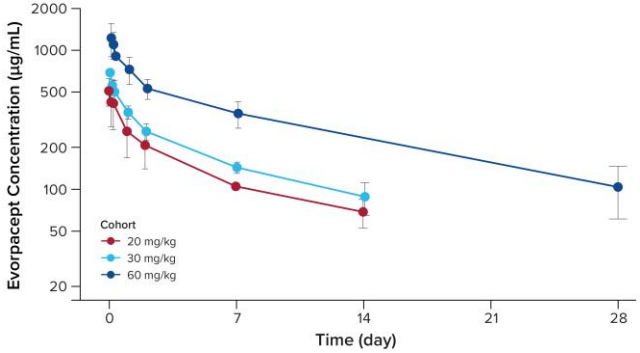


Table 4: Evorpacept PK Parameters Following IV Infusion at 20 mg/kg Q2W, 30 mg/kg Q2W, and 60 mg/kg Q4W (Cycle 1, Day 1)

Parameters	20 mg/kg Q2W (N=3)	30 mg/kg Q2W (N=3)	60 mg/kg Q4W (N=6)
C_{max} (µg/mL)	446 ± 137	628 ± 113	1250 ± 319
AUC_{inf} (µg*h/mL)	66200 ± 16000	81200 ± 16500	222000 ± 70800
CL (mL/h/kg)	0.313 ± 0.068	0.379 ± 0.069	0.296 ± 0.101
Vss (mL/kg)	78.2 ± 21.3	83.9 ± 16.2	94.0 ± 15.9

Data Cutoff 18Jun2021; Parameters presented as mean ± SD.

Conclusion

Initial data suggest that evorpacept is well tolerated in combination with azacitidine and demonstrates promising preliminary activity in patients with MDS

- The combination displays a favorable initial safety profile that is similar to azacitidine monotherapy.
- No dose limiting toxicities were observed and the maximum administered dose was 60 mg/kg Q4W.
- Evorpacept + azacitidine demonstrates complete remissions with cytogenetic responses, hematologic improvement, and transfusion independence in patients with previously untreated higher risk MDS including:
  - TP53 mutation associated with complex cytogenetic abnormalities
  - Therapy-related MDS
  - Prior HMA failure
- Clinical response was observed in patients with R/R MDS that had failed 1 or more prior HMA regimen(s).
- Enrollment in the Phase 1 dose expansion is ongoing to determine the optimal dose of evorpacept in combination with azacitidine for the randomized Phase 2 portion of this study (NCT0441751).

1. Weiskopf, K., *Eur J Cancer*. 2017 May;76:100-109; 2. Kauder, S.E. et al., *PLoS ONE*. 2018 August;13(8): e0201832; 3. Chen et al. ASH 2020. Poster #1965; 4. Cheson et al. *Blood*. 2006.

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