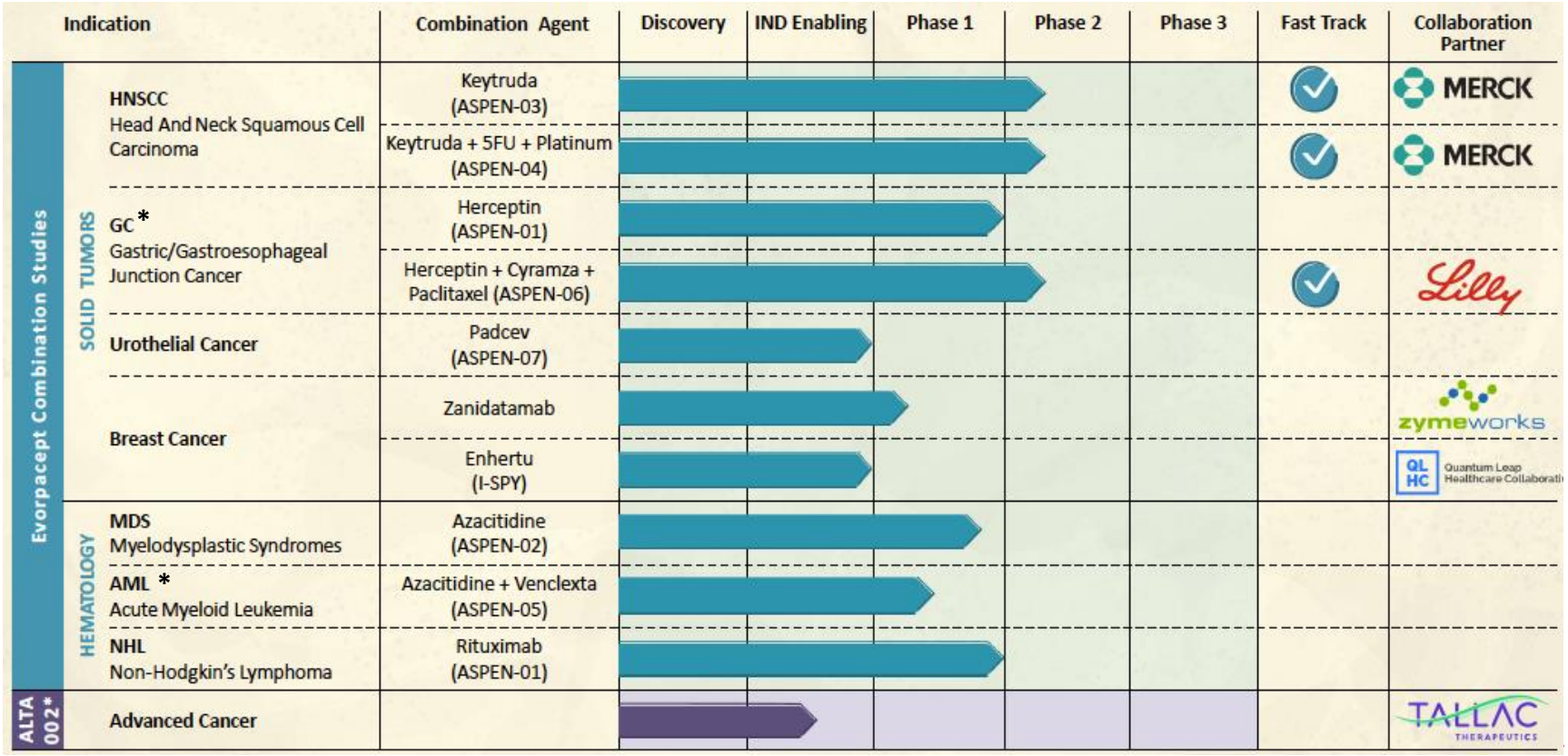
ALX ONCOLOGY

ASH Conference Call

December 13, 2022

ALX Oncology Pipeline: Maximizing the Innate Immune Response Against Cancer



*** Orphan Drug Designation**

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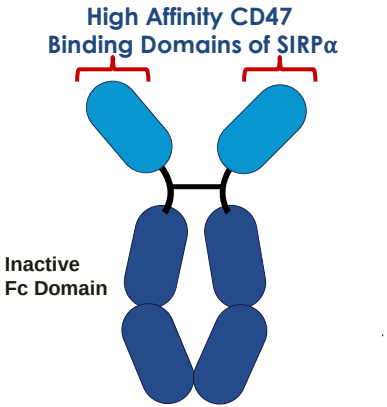
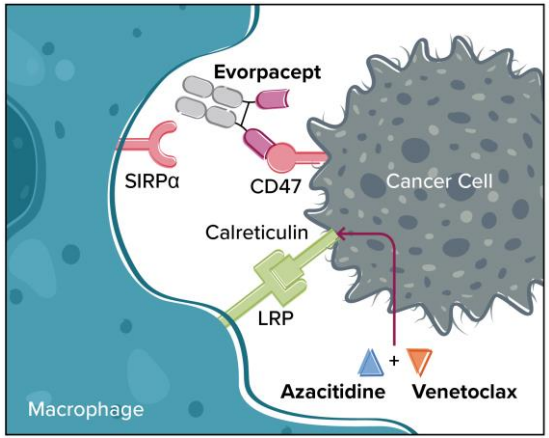
Evorpacept Targets the CD47 Checkpoint Unleashing the Anti-Cancer Immune Response in AML

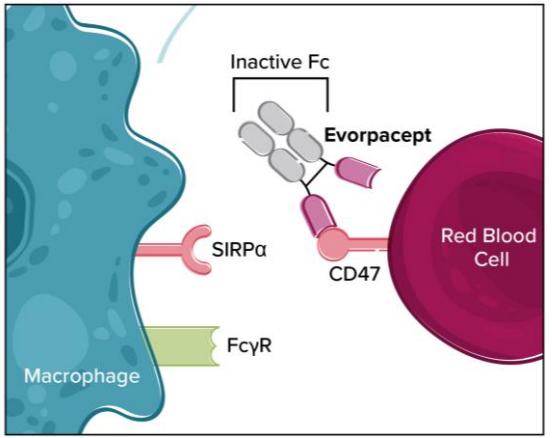
- CD47, a marker of self, is upregulated by tumors to evade the immune system
- Evorpacept blocks CD47, activating the innate immune response against the cancer cell



Molecular weight half the size of a typical antibody



Evorpacept blocks CD47-SIRPα interaction maximizing azacitidine and venetoclax anti-leukemic activity



Evorpacept spares normal cells from destruction, minimizing toxicity

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

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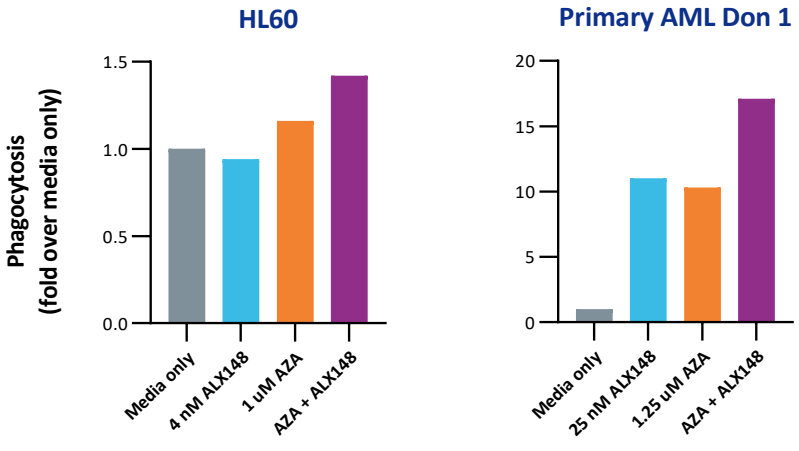
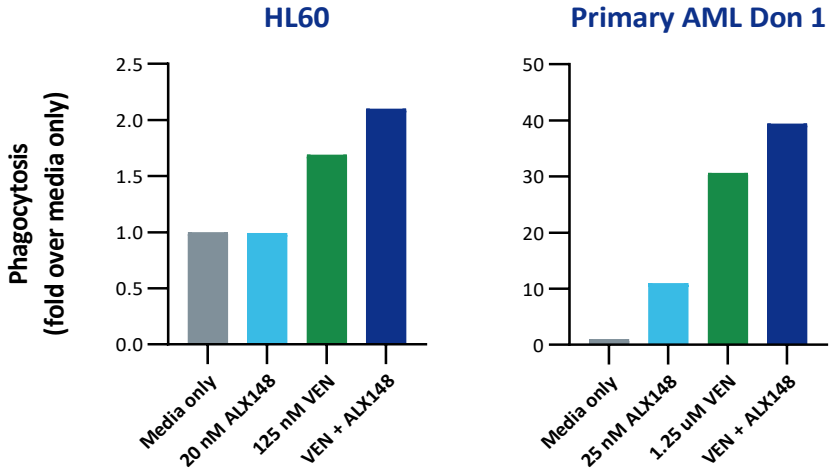
Evorpacept Enhances Phagocytosis of AML Blasts in Combination with AZA and VEN



Evorpacept + azacitidine enhances phagocytosis of AML blasts compared with either agent alone



Evorpacept + venetoclax enhances phagocytosis of AML blasts compared with either agent alone

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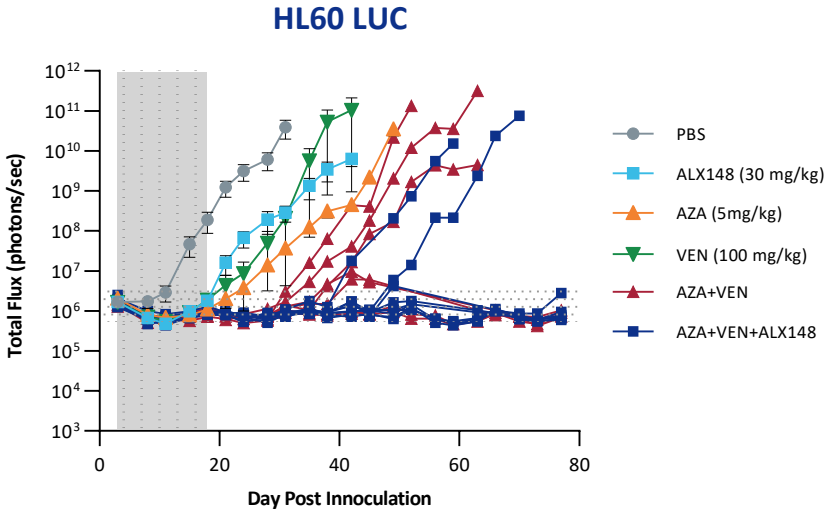
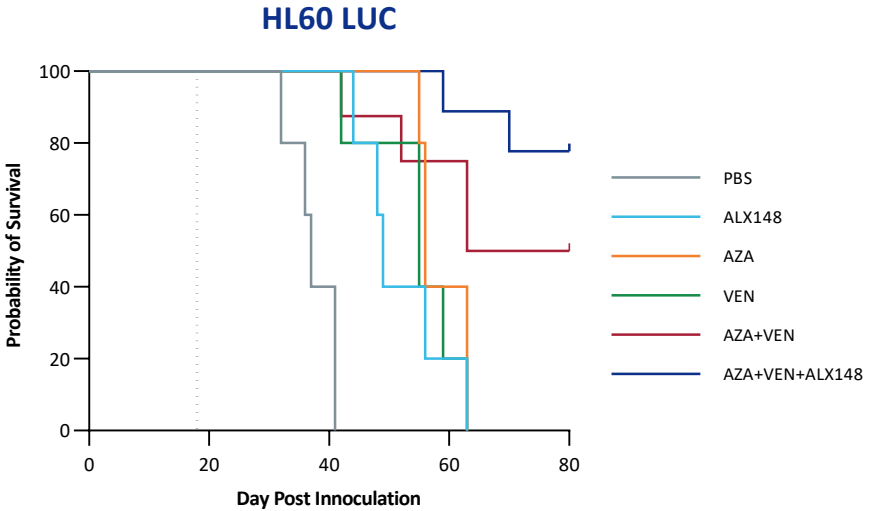
Combining Evorpacept with VEN and AZA Inhibits Tumor Growth and Prolongs Survival in AML Xenograft Model



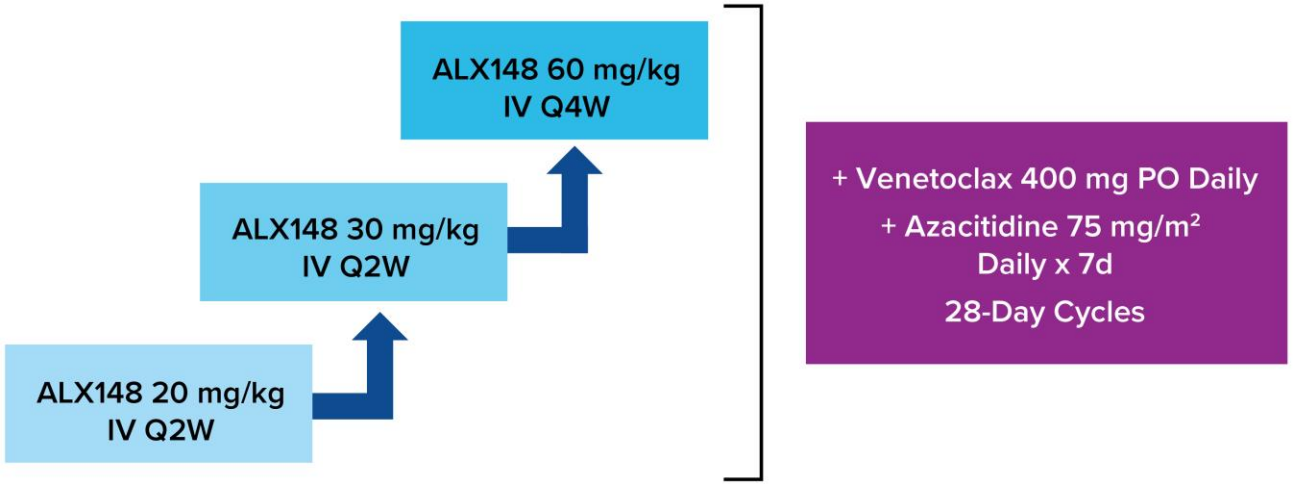
Increased inhibition of AML cell growth with addition of evorpacept to venetoclax + azacitidine backbone



Improved survival with addition of evorpacept to venetoclax + azacitidine backbone

ASPEN-05: Phase 1a Study to Evaluate Safety of Evorpacept in Combination with VEN + AZA in AML

Phase 1a Dose Escalation Study Schema



Q2W – Every 2 weeks; **Q4W** – Every 4 weeks

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Professor Harry Erba, M.D.

Dr. Erba is Director of the Leukemia Program in the Division of Hematologic Malignancies and Cellular Therapy in the Department of Medicine and Medical Directory for the Hematologic Malignancies Inpatient Service at Duke University. He also serves as the Chair of the SWOG Leukemia Committee.

His research interests are focused on the development of novel therapies for acute myeloid leukemia, myelodysplastic syndromes, myeloproliferative neoplasms, and acute lymphoblastic leukemia. He has been the Principal Investigator for numerous studies evaluating small molecular inhibitors, antibody-drug conjugates and cytotoxic chemotherapy for these diseases.

AML Remains an Area of Unmet Need with Rising Incidence and Low 5-year Survival Rate

U.S. AML Statistics

Estimated New Cases in 2022	20,050
% of All New Cancer Cases	1.0%
Estimated Deaths in 2022	11,540
% of All Cancer Deaths	1.9%

5-Year Relative Survival

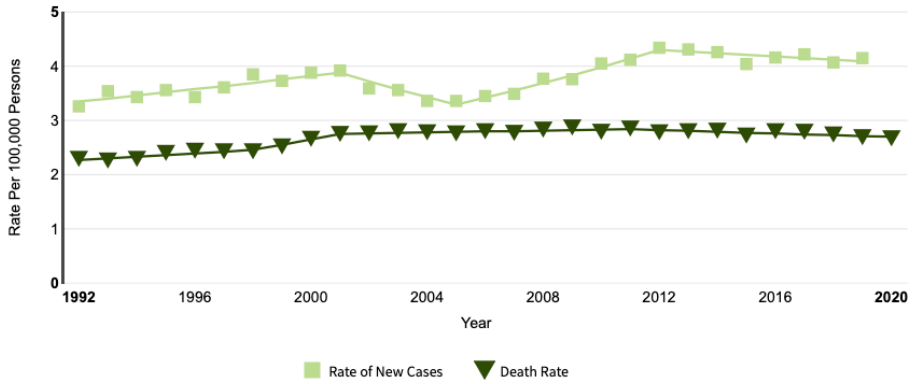
30.5%

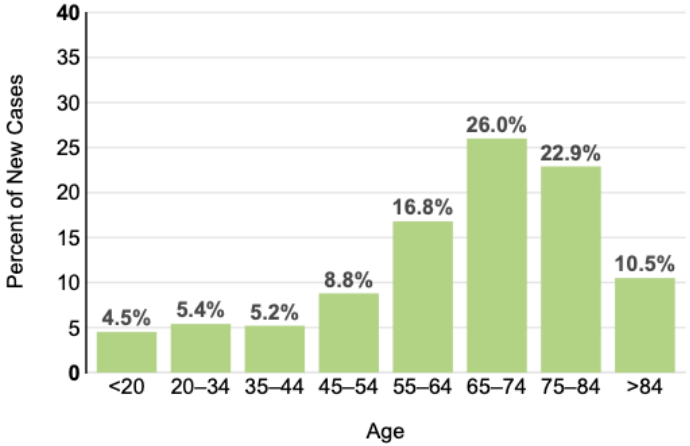
2012–2018

Acute myeloid leukemia is most frequently diagnosed among people aged 65–74.

Median Age At Diagnosis

68





https://seer.cancer.gov/statfacts/html/amyl.html (Nov 2022)

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Poor Outcomes with VEN + AZA in Relapsed/Refractory AML After Prior VEN + AZA Treatment

	1L Unfit AML VEN + AZA VIALE-A (Ph 3)[1]	R/R AML after prior VEN + AZA (Retrospective)[2]
N	286	41
CRR (%)	36.7	Not reported
CR + CRi (%)	66.4	Not reported
mOS (mo)	14.7	2.4

[1]DiNardo, NEJM 2020; [2]Maiti, Haematologica 2020

Evorpacept, a CD47-Blocking Myeloid Checkpoint Inhibitor, in Combination with Azacitidine and Venetoclax in Patients with Acute Myeloid Leukemia (ASPEN-05): Results from Phase 1a Dose Escalation Part

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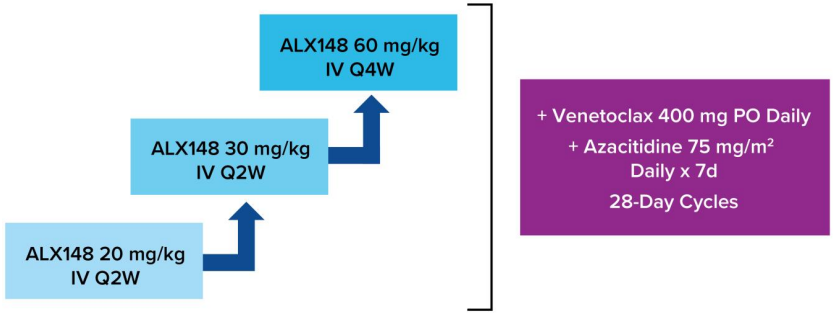
*Co-First Authors

ASPEN-05 Phase 1a Study Design and Key Eligibility

- Phase 1a dose escalation part endpoints to evaluate safety and maximum tolerated dose of evorpacept in combination with VEN + AZA:
  - frequency of first cycle dose-limiting toxicities (DLTs)
  - characterize the pharmacokinetic (PK) profile
  - assess anti-leukemic activity using the ELN 2017 response criteria
- Study enrolled adult subjects with:
  - relapsed/refractory (R/R) AML, or
  - newly diagnosed (ND) AML with adverse risk genetics and considered ineligible for intensive induction therapy

Figure 3. Phase 1a Dose Escalation Study Schema



Q2W – Every 2 weeks; **Q4W** – Every 4 weeks

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ASPEN-05 Phase 1a Patient Population is Heavily Enriched for Poor Risk Disease Features

Table 1. Patient Baseline Characteristics

		Phase 1 (N=14)
Age, Years (median, range)		71 (50-82)
Sex, n	Male	10
	Female	4
Race, n	White	8
	Black or African American	2
	Native Hawaiian or Other Pacific Islander	1
	Asian	3
AML status, n	Relapsed or Refractory	11
	Number of Prior Treatment Regimens (median, range)	1 (1-2)
	Prior Venetoclax, n	9
	Venetoclax-Naïve, n	2
	Prior Hypomethylating Agents, n	5
	Newly Diagnosed	3
WHO AML Classification at Screening, n	AML with Myelodysplasia-Related Changes	5
	Therapy-Related Myeloid Neoplasms	2
	AML, NOS	4
	Unknown/Missing	3
Cytogenetic Risk at Screening, n	Intermediate	1
	Adverse	13
Bone Marrow Myeloblast Percentage at Baseline (median, range)		27 (5-84)
Mutation Status, n (%)	DNMT3A	3 (21)
	RUNX1	2 (14)
	ASXL1	2 (14)
	TP53 Mutation	11 (79)
	Other	8 (57)

- As of October 3, 2022, 14 subjects were treated at evorpacept doses of:
  - 20 mg/kg Q2W (N=4)
  - 30 mg/kg Q2W (N=4)
  - 60 mg/kg Q4W (N=6)
- 11 subjects had relapsed/refractory AML with a median of 1 prior line of therapy:
  - 9 with prior VEN
  - 5 with a prior hypomethylating agent
- 3 subjects had newly diagnosed AML:
  - 2 with therapy-related AML
  - 3 with TP53 mutation
- Bone marrow studies at screening:
  - Median blast percentage of 27%
  - 13 subjects with adverse risk and 1 with intermediate risk cytogenetics
  - Mutations in TP53 (N=11), DNMT3A (N=3), ASXL1, and RUNX1 (N=2 each)

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Evorpacept Was Generally Well Tolerated in Combination with VEN+AZA

Table 2a. Evorpacept-Related AEs (All Patients)

Adverse Event, n	20 mg/kg Q2W (N=4)		30 mg/kg Q2W (N=4)		60 mg/kg Q4W (N=6)		Total (N=14)
	Grade 1/2	Grade ≥3	Grade 1/2	Grade ≥3	Grade 1/2	Grade ≥3	All Grades (%)
Vomiting	1	–	1	–	–	–	2 (14)
Nausea	1	–	–	–	–	–	1 (7)
CRS	–	–	–	–	–	1	1 (7)
Metabolic Acidosis	–	–	–	–	1	–	1 (7)

*Full table of treatment emergent AEs (Table 2b) included in poster

- An MTD of evorpacept was not reached. The maximum administered dose was 60 mg/kg Q4W.
- The most common evorpacept-related AE was low grade vomiting (n=2; 14%). There were no evorpacept-related cytopenias reported.
- One DLT of Grade 3 cytokine release syndrome in the 60 mg/kg Q4W cohort.
- The most frequent Grade ≥3 AEs of any causality:
  - febrile neutropenia (n=6; 43%)
  - anemia (n=5; 36%)
  - AST increased (n=5; 36%)
  - pneumonia (n=4; 29%)
- There were no evorpacept-related deaths on study.

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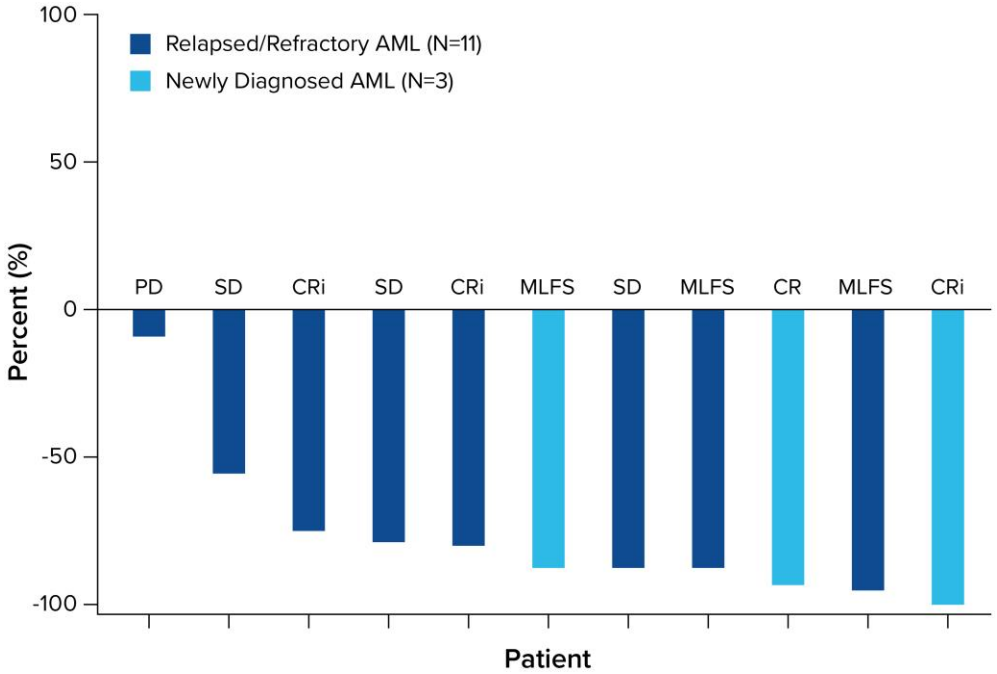
A Reduction in Bone Marrow Blasts Was Observed in All Patients

A reduction in bone marrow blasts was observed across all dose cohorts, including in all R/R VEN-exposed subjects and those refractory to their last cycle of VEN-containing therapy.

Figure 4. Best Percent Change in Bone Marrow Blast % from Baseline



Note: One subject with missing data, two subjects with no post-baseline disease assessment (1 DLT, 1 death).

CR – complete remission
CRi – complete remission with incomplete hematologic recovery
MLFS – morphologic leukemia free state

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Preliminary Evidence of Anti-Leukemic Activity Observed with Evorpacept + VEN + AZA

- Among 13 response evaluable subjects:
  - 3/3 subjects with newly diagnosed AML achieved a response (1 CR, 1 CRi, 1 MLFS).
  - 2/2 subjects with relapsed/refractory VEN-naïve AML achieved a response (2 CRi).
  - 2/8 with relapsed/refractory VEN-exposed AML achieved a response (2 MLFS).

Table 3. Objective Responses per Modified ELN Criteria[#]

	Newly Diagnosed (N=3)	Rel/Ref (N=10)		Overall (N=13) n (%)
		VEN-Naïve (N=2)	Prior VEN (N=8)	
ORR	3	2	2	7 (54)
CR	1	0	0	1 (8)
CRi	1	2	0	3 (23)
PR	0	0	0	0
MLFS	1	0	2	3 (23)
SD	0	0	4	4 (31)
PD	0	0	1	1 (8)
Death	0	0	1	1 (8)*

One patient not included due to DLT and no post-baseline disease assessment; [#]Per Döhner H et al. *Blood*. 2017 with addition of CRh; *Grade 5 pneumonia prior to first post-baseline disease assessment, considered related to disease.

CR – complete remission
CRi – complete remission with incomplete hematologic recovery
MLFS – morphologic leukemia free state

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Initial Responses Observed as Early as the First 1-2 Cycles of Treatment

Figure 5a. Responses Over Time – Relapsed/Refractory AML Patients

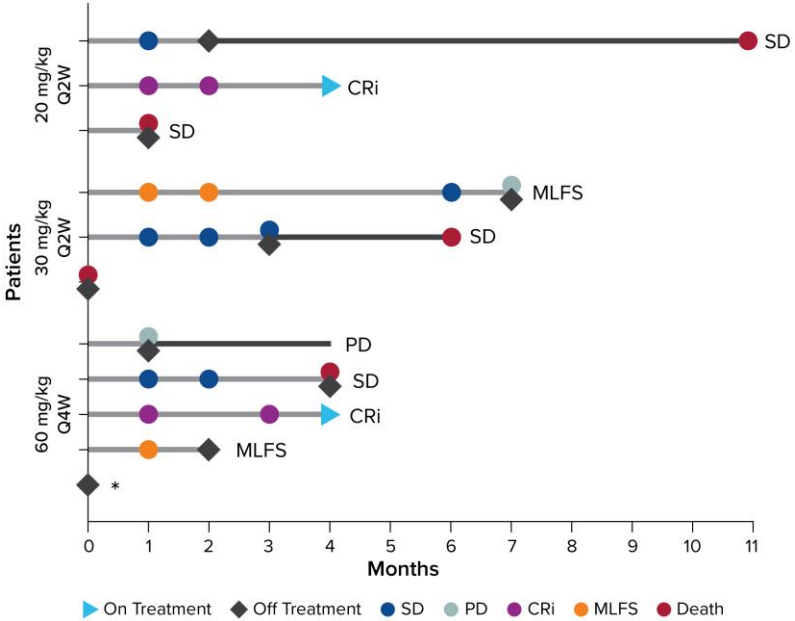
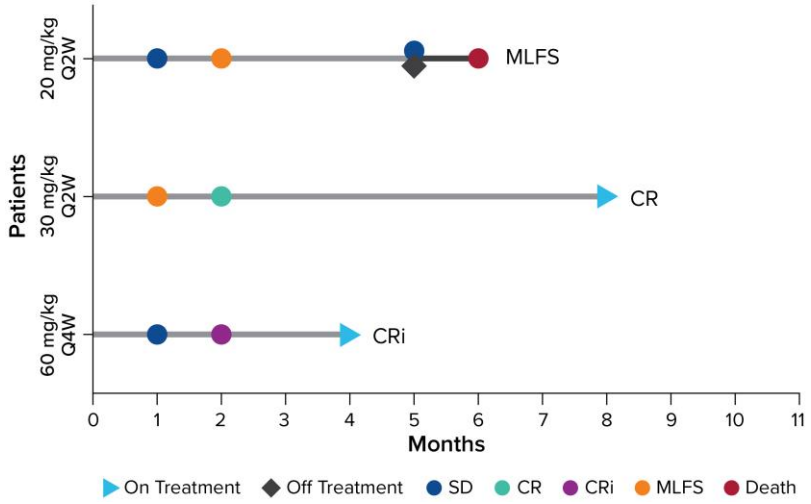


Figure 5b. Responses Over Time – Newly Diagnosed AML Patients



SD – Stable Disease; **CR** – Complete Remission; **CRi** – Complete Remission with Incomplete Hematologic Recovery; **MLFS** – Morphologic Leukemia-Free State; **PD** – Progressive Disease; *Patient not response evaluable.

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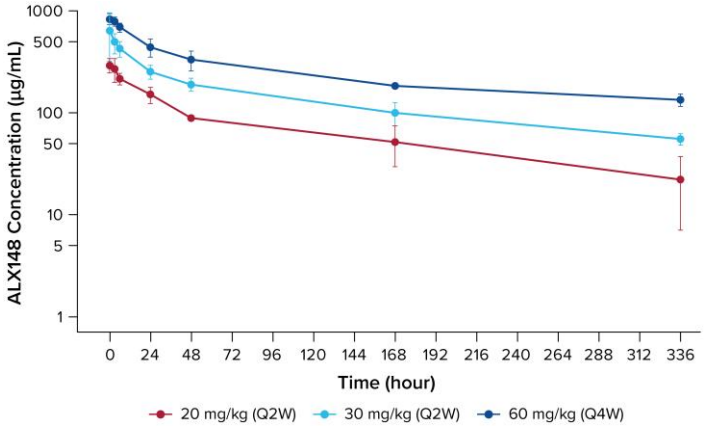
Preliminary ASPEN-05 Phase 1a PK and PD Results: Linear PK and Robust CD47 Occupancy

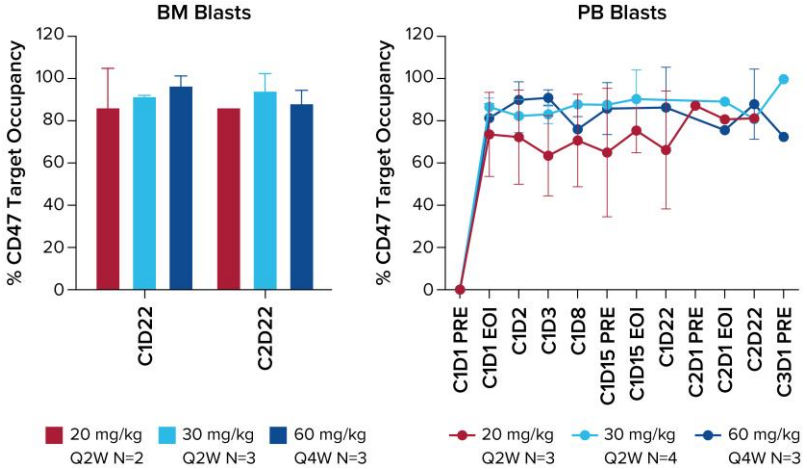
Figure 7. ALX148 Concentration-Time Profiles Following First ALX148 IV Infusion at 20 mg/kg Q2W, 30 mg/kg Q2W, and 60 mg/kg Q4W



Pre – Predose; **EOI** – End of Infusion.

Preliminary PK data indicate dose-proportional pharmacokinetics that are consistent with results from prior studies.

Figure 6. CD47 Occupancy in Bone Marrow (left) and Peripheral Blood (right) Blasts



Preliminary data indicate robust CD47 occupancy in both peripheral blood and bone marrow blasts across all dose levels throughout the dosing interval.

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Conclusions

- Evorpacept is a next generation CD47-blocker designed to maximize the innate and adaptive immune response against cancer cells.
- Evorpacept in combination with standard VEN and AZA was well tolerated with no MTD reached in patients with AML and no evorpacept-related cytopenias. The maximum administered evorpacept dose was 60 mg/kg Q4W.
- Preliminary dose-proportional pharmacokinetics were seen along with robust CD47 occupancy in both peripheral blood and bone marrow blasts across all dose levels evaluated.
- Encouraging initial anti-leukemic activity was observed in patients with poor risk AML, including newly diagnosed TP53 mutated AML and R/R AML (both VEN-naïve and after prior VEN treatment).
- These results support further evaluation of evorpacept in hematologic malignancies, including in combination with VEN and AZA for AML (NCT04755244) and in combination with AZA for MDS (NCT04417517).

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