Aspacytarabine (BST-236) as Monotherapy is Safe, Well-tolerated and Effective for the Treatment of Adults with Newly Diagnosed Acute Myeloid Leukemia Unfit for Intensive Therapy. Results of a Phase 2 Study (NCT03435848)

Jessica K. Altman[1], Jamie Koprivnikar[2] , James McCloskey[2], Vamsi Kota[3], Keng, Michael[4], Dale L. Bixby[5], Olga Frankfurt[1], Ashkan Emadi[6], Tsila Zuckerman[7], Micah Burch[8], Moshe Levy[8], Selina M. Luger[9], Bhavana Bhatnagar[10], Ofir Wolach[11], Chezi Ganzel[12], Mary-Beth M. Percival[13], Gail Roboz[14], Michael Craig[15], Itai Levi [16], Anna Gourevitch[16], Liat Flaishon[17], Darrel Cohen[17], Shoshi Tessler[17], Chen Blumberg[17], Stela Gengrinovitch[17], Ruth Ben Yakar[17], Jacob M. Rowe[7,12]

[1]Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago, IL, USA; [2]John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ, USA; [3]Georgia Cancer Center, Augusta University, Augusta, GA, USA; [4]University of Virginia Cancer Center, Charlottesville, VA, USA; [5]University of Michigan Comprehensive Cancer Center, Ann Arbor, MI, USA; [6]University of Maryland School of Medicine, Baltimore, MD, USA; [7]Rambam Health Care Campus, Haifa, Israel; [8]Baylor Scott & White Research Institute, Dallas, TX, USA; [9]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; [10]Arthur G James Cancer Hospital Comprehensive Cancer Center, The Ohio State University, Columbus, OH, USA; [11]Rabin Medical Center, Petach Tikva, Israel; [12]Shaare Zedek Medical Center, Jerusalem, Israel; [13]Seattle Cancer Care Alliance, Seattle, WA, USA; [14]Weill Cornell Medical College - Sandra and Edward, New York City, NY, USA; [15]West Virginia University, Morgantown, WV, USA; [16]Soroka University Medical Center, Beer Sheva, Israel; [17]Biosight Ltd., Lod, Israel;

PHASE 2, OPEN LABEL, SINGLE ARM, MULTI-CENTER STUDY TO ASSESS THE EFFICACY AND SAFETY OF ASPACYTARABINE AS SINGLE-AGENT IN ADULTS WITH NEWLY-DIAGNOSED AML, NOT ELIGIBLE FOR STANDARD INDUCTION THERAPY

AIM

To evaluate the efficacy and safety of aspacytarabine as a single agent for induction and consolidation therapy of newly diagnosed AML patients unfit for standard induction chemotherapy

METHODS

Aspacytarabine (4.5 g/m^2/d, equimolar to 3 g/m^2/d cytarabine) was administered as daily 1-hour IV infusion 6-day courses, for 1-2 induction and 1-3 consolidation courses, to AML patients age ≥75 years or otherwise unfit for intensive chemotherapy. Patients with secondary or therapy related AML, and patients who received prior hypomethylating agents (HMA) ± venetoclax therapy for a preceding condition were eligible.

Primary endpoint: complete remission (CR); Secondary endpoints: safety, overall survival (OS), duration of response (DOR), minimal residual disease (MRD)

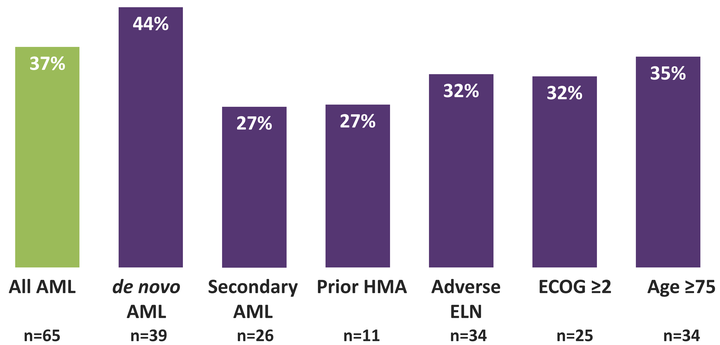
RESULTS

Baseline Characteristics

N		**65**
Age, median, y (range)		75 (54-88)
≥75 years, n (%)		34 (52)
ECOG, n (%)	0-1	40 (62)
	2-3	25 (38)
Secondary AML, n (%)		26 (40)
Secondary to MDS/CMML, n (%)		19 (29)
Secondary to therapy, n (%)		7 (11)
Prior HMA, n (%)		11 (17)
Bone marrow blast percentage, n (%)	<30	22 (34)
	30-50	16 (25)
	>50	27 (41)
ELN risk score, n (%)	Favorable	9 (14)
	Intermediate	16 (25)
	Adverse	34 (52)
	Unavailable	6 (9)

*** Follow up is ongoing; all results, except for CR, are not final**

Complete Remission

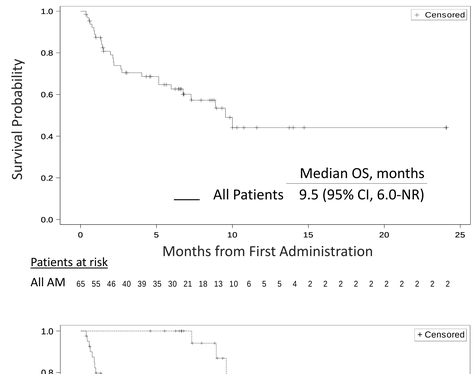


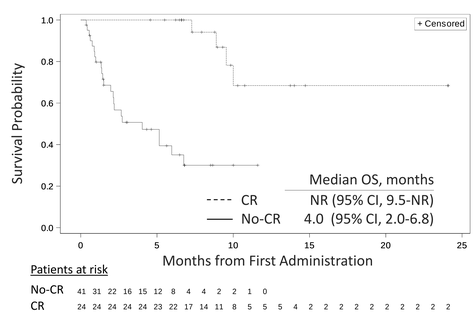
- CRs reached following 1-2 induction courses
- 50% of CRs are MRD$_{neg}$
- Median DOR 6 months (95% CI, 3.9-NR)

Time to Hematological Recovery

	# of Cycles	Days from Cycle D1 Median (Range)
Neu ≥500/ml	65	24.0 (11-39)
Neu ≥1,000/ml	64	25.0 (11-39)
PLT ≥50,000/ml	65	24.0 (11-40)
PLT ≥100,000/ml	61	26.0 (18-40)

Overall Survival





Adverse Events

TEAEs, Grade ≥3 (≥10% of Patients), (%)	
Febrile neutropenia	33 (50)
Thrombocytopenia	18 (27)
Anemia	14 (21)
Leukopenia	14 (21)
Hypokalemia	12 (18)
Sepsis	10 (15)
Neutropenia	9 (14)
Pneumonia	9 (14)
Hypophosphatemia	7 (11)
Hypoxia	7 (11)

TEAEs = Treatment-emergent adverse events (AEs)

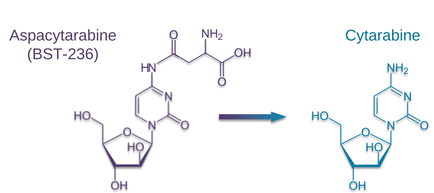
Related SAEs, >1 patient, (%)	
Febrile neutropenia	6 (9)
Sepsis	4 (6)
Pneumonia	3 (5)
Thrombocytopenia	3 (5)
Anemia	2 (3)

SAEs = Serious AEs

MECHANISM OF ACTION

Aspacytarabine (BST-236) is a novel antimetabolite, a prodrug of cytarabine, investigated as a new therapeutic agent for treatment of AML and MDS.

Aspacytarabine is administrated as 1-hour I.V. infusion; it is inactive until it is gradually metabolized to cytarabine, with a shorter duration at C$_{max}$ compared to HiDAC administration, leading to reduced exposure to C$_{max}$, cytarabine levels and therefore lower systemic toxicity.



PK Following Aspacytarabine IV Administration (6 g/m^2, Day 1)