AlloNK® Cell Therapy ± Rituximab in Patients with Relapsed or Refractory Non-Hodgkin Lymphoma

Umar Farooq[1]*, Amitkumar Mehta[2], Erin A. Dean[3], Jennifer N. Saultz[4], Joseph Maly[5], Bassam Matter[6], Adam J. Olszewski[7], Ruthee-Lu Bayer[8], Valerie Chacon[9], Gina Chu[9], Gilad Gordon[9], Heather Kelley[9], Thorsten Graef[9‡], Rashmi Khanal[10]

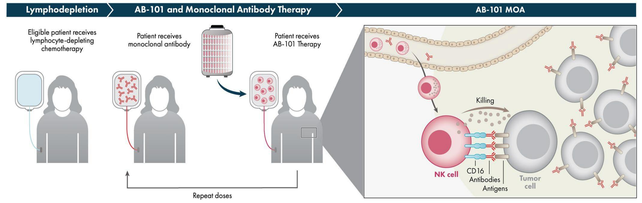
*Presenting author; ‡Corresponding author, [1]University of Iowa, Iowa City, IA; [2]University of Alabama, Birmingham, AL; [3]University of Florida, Gainesville, FL; [4]Oregon Health & Science University, Portland, OR; [5]Norton Cancer Center, Louisville, KY; [6]Cancer Center of Kansas; [7]Brown University Health Cancer Institute, Providence, RI; [8]Northwell Health Cancer Institute, New Hyde Park, NY; [9]Artiva Biotherapeutics, San Diego, CA; [10]Fox Chase Cancer Center, Philadelphia, PA

Introduction

AlloNK® (also referred to as AB-101) is a non-genetically modified, allogeneic, off-the-shelf, cryopreserved natural killer (NK) cell therapy candidate in development for the treatment of cancer and autoimmune diseases. AlloNK has been optimized for combination with monoclonal antibodies (mAbs) to enhance antibody-dependent cellular cytotoxicity (ADCC) and anti-tumor responses through selection of cord blood units (CBUs) with the natural high-affinity variant of CD16 (158V/V polymorphism)[1] to enhance ADCC via combination with mAbs and a killer cell immunoglobulin-like receptor (KIR)-B haplotype[2] for enhanced innate activity in the allogeneic setting.

To date, the therapeutic potential of multi-dose NK-cell/mAb combinations has not been fully assessed due to the limited scale of cell production. AlloNK is a highly scaled product candidate that is being investigated in the outpatient setting, without the requirements for hospitalization or prolonged safety observations compared to genetically modified cell therapies.

For more information on the manufacturing process, see Poster #1765



AlloNK Mechanism of Action– AlloNK enhances a patient's ADCC when undergoing mAb therapy for either hematological or autoimmune indications.[3]

Study Design

AB-101-01 (*NCT04673617*) is a US multi-center, first in human study to investigate the safety, tolerability, and anti-tumor activity with AlloNK ± Rituximab in advanced B-cell malignancies.

Key Inclusion Criteria
- r/r CD20+ B-cell malignancies
- Received ≥2 prior lines of therapy
- ECOG PS 0 or 1
- Prior CAR-T permitted
- No prior allo TX or CNS involvement

Endpoints:
- Safety and tolerability
- PK/PD
- Anti-tumor activity

Lymphodepletion
- Fludarabine 30mg/m²
- Cyclophosphamide 250 or 500 mg/m²
- Cycles 1 and 2 only

AlloNK
- 4 doses per 28-day cycle
- 1 billion (B) or 4B cells per dose (dose finding)

Rituximab *(combo)*
- 375mg/m² per dose
- Cycle 1 and Cycle 2: 3 doses
- Cycle 3 and Cycle 4 : 2 doses

Monotherapy: Limited to one treatment cycle to assess safety, tolerability and PK without the co-administration of a mAb.
Combination: Up to 4 treatment cycles in the absence of toxicity or progressive disease. IL-2 was not used in the Diffuse Large B-Cell Lymphoma (DLBCL) cohort.

All AlloNK administrations (up to 16) were conducted in the outpatient setting.

Demographics & Baseline Characteristics

	Monotherapy N=16	Combo All N=29	Combo CAR T naïve N=14
Age			
Median (range)	*64.5 (29, 80)*	*71 (46, 86)*	*71 (53, 86)*
≥75y, n (%)	*3 (19)*	*6 (21)*	*4 (29)*
Gender			
Male, n (%)	12 (75)	16 (55)	7 (50)
Race, n (%)			
White	*12 (75)*	*25 (86)*	*13 (93)*
ECOG PS 1, n (%)	*9 (56)*	*17 (59)*	*5 (36)*
Cancer Types			
DLBCL	*6 (38)*	*21 (72)*	*11 (79)*
Other aggressive NHL subtypes	*6 (38)*	*6 (21)*	*2 (14)*
Indolent NHL subtypes	*4 (25)*	*2 (6)*	*1 (7)*

	Monotherapy N=16	Combo All N=29	Combo CAR T Naïve N=14
Baseline LDH, n (%)	*n=14*	*n=24*	*n=12*
> 200 U/L (ULN)	*6 (43)*	*14 (58)*	*7 (58)*
Prior lines of systemic therapy Median (min, max)	4 (2, 9)	3 (1, 7)	3 (1, 5)
Refractory to last therapy <6mo, n (%)	13 (81)	17 (59)	8 (57)
Prior Therapies, n (%)			
Prior Alkylating agents	*16 (100)*	*27 (93)*	*13 (93)*
Prior Anthracyclines	*11 (69)*	*19 (66)*	*9 (64)*
Prior Platinum agents	*8 (50)*	*16 (55)*	*7 (50)*
Prior anti-CD20 agents	*16 (100)*	*29 (100)*	*14 (100)*
Prior polatuzumab vedotin	*3 (19)*	*8 (28)*	*3 (21)*
Prior Cell Therapies, n (%)	8 (50)	15 (52)	0
Prior ASCT, n (%)	2 (13)	7 (24)	4 (29)

Safety & Tolerability

Treatment-Emergent Adverse Events (TEAEs)	Rituximab Combo (N=29)			Overall (N=45)		
	All TEAEs	Grade 3 + TEAEs	Grade 3+ Related	All TEAEs	Grade 3 + TEAEs	Grade 3+ Related
Lymphopenia	29 (100)	24 (83)	5 (17)	32 (71)	32 (71)	6 (13)
Neutropenia	26 (90)	24 (83)	5 (17)	38 (84)	36 (80)	7 (16)
Leukopenia	26 (90)	25 (86)	5 (17)	37 (82)	36 (80)	7 (16)
Anemia	16 (55)	16 (55)	4 (14)	17 (38)	17 (38)	4 (9)
Fatigue	15 (52)	1 (3)	0	20 (44)	2 (4)	0
Thrombocytopenia	11 (38)	9 (31)	5(17)	12 (27)	10 (22)	5 (11)
Hypotension	10 (35)	1 (3)	0	12 (27)	2 (4)	0
Cough	7 (24)	1 (3)	0	9 (20)	1 (2)	0
Dyspnea	7 (24)	2 (7)	0	8 (18)	2 (4)	0
Hypokalemia	6 (21)	1 (3)	0	9 (20)	2 (4)	0
Febrile neutropenia	5 (17)	4 (14)	2 (7)	8 (18)	7 (16)	2(4)
Fall	5 (17)	1 (3)	0	5 (11)	1 (2)	0
Injection site reaction	5 (17)	1 (3)	0	5 (11)	1 (2)	0
Infusion related reaction	5 (17)	3 (10)	3 (10)	7 (16)	3 (7)	3 (7)

TEAEs ≥15% and at least 1 Grade 3+

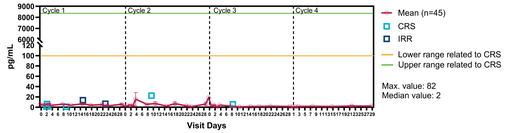
- **AlloNK alone or in combination with rituximab was well, tolerated.**
- **Safety profile was obtained in an outpatient treatment setting without prolonged observation periods in the hospital or need for hospitalization.**
- At this time, no AlloNK associated toxicities patterns identified.
- Main toxicities are hematological in nature and expected with Cy/Flu.
- Infusion related reactions observed with AlloNK.

Cell Therapy Associated TEAEs

Cell Therapy associated AEs, n (%)	Overall (N=45)		Combo (N=29)	
	All	Grade ≥3	All	Grade ≥3
Cytokine release syndrome (CRS)	*4 (9)**	*0*	*2 (7)*	*0*
Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)	0	0	0	0
Graft vs Host Disease (GvHD)	0	0	0	0

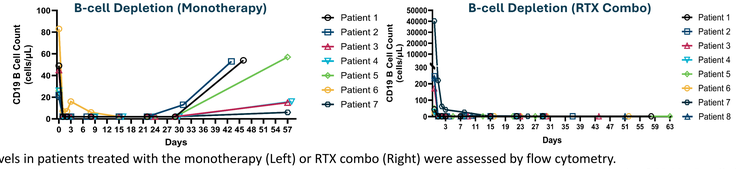
(*) Low grade CRS events were reported in 4 patients, 3 pts experienced Grade 1, and 1 pt experienced Grade 2.

IL-6 Levels Across All Treatment Cycles



- IL-1β, IL-6, IL-8 and TNF-α did not show increased levels in patients, including patients with reported CRS or IRR events.
- **All cases were re-classified by the sponsor as IRRs due to onset (<24h), clinical symptoms, event resolution, and absence of cytokine increases.**

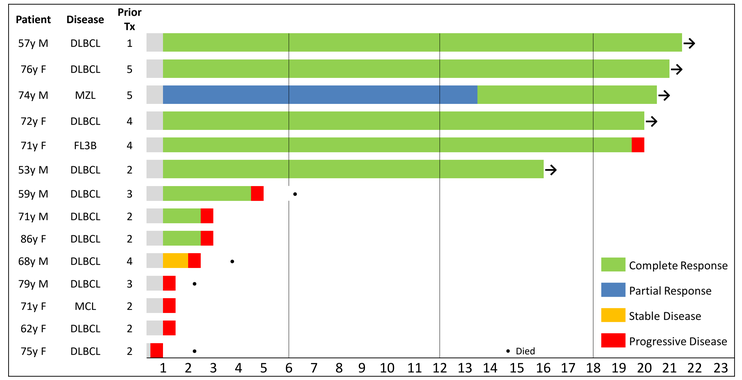
Pharmacodynamics



- Peripheral B-cell levels in patients treated with the monotherapy (Left) or RTX combo (Right) were assessed by flow cytometry.
- All patients in the monotherapy cohort with detectable B cells (n=7) at baseline demonstrated a decline to non-quantifiable levels of CD19+ B-cells by Day 15 and an increase in B-cells approximately 4-8 weeks after the initiation of treatment (Data as of May 15, 2024).
- All patients from the RTX combo cohorts with detectable B cells (n=8) at baseline demonstrated a decline to non-quantifiable levels of CD19+ B-cells by Day 15 and remained depleted over the first cycle of treatment (Data as of March 26, 2024).

Preliminary Efficacy

CAR T Naïve Patients who Received AlloNK® Cells in Combination with Rituximab



Lugano classification	Combo CAR-T naïve N=14
ORR	64%
Complete Response (CR)	9 (64%)
CR at 6mo	*6 (43%)*
CR at 12mo	*6 (43%)*
Partial Response (PR)	0
Median duration of response (DoR, months)	19.4+ (1.0, NR)
Overall Survival (months)	Nor reached (1.01, NR) *(~71% alive)*

- Response to AlloNK (Monotherapy) resulted in a limited CR rate of 25%.
- AlloNK in combination with RTX was effective at all dose levels and led to durable responses.
  - Adding a RTX regimen in combination with AlloNK increased the CR rate to 45%.
  - Particularly, CAR T naïve patients, who were older (median 71y), and received 3 prior therapies including a prior RTX containing regimen, achieved a CR rate of 64%.

Conclusions

- AlloNK alone and in combination with rituximab was safe, well tolerated, and manageable in older and frailer patients in an outpatient setting without the need for hospitalization in relation to AlloNK administration.
- No GvHD, ICANs, study discontinuations, or deaths were related to AlloNK.
- Reported low grade CRS events (n=3 Grade 1 and n=1 Grade 2) were reclassified to IRR based on clinical presentation and absence of cytokine increases during the event.
- AlloNK, in combination with rituximab, was effective at all dose levels and led to durable responses, particularly in patients who did not receive prior CAR-T cell therapy.

References
1. Musolino, A., et al. J Clin Oncol, 2008.
2. Cooley, S., et al. Blood, 2009.
3. Rogers P, et al. Journal for Immuno Therapy of Cancer 2022.

Disclaimer
1. Poster includes data entered as of March 07, 2025. The trial is ongoing, and data is subject to change.
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Contact Email Address: info@artivabio.com