AB-101, an Allogeneic NK Cell Therapy, in Combination with Anti-CD20 Monoclonal Antibodies, Consistently Achieves Deep B-cell Depletion Comparable with CAR T Cell Therapies in Patients with Rheumatologic Diseases

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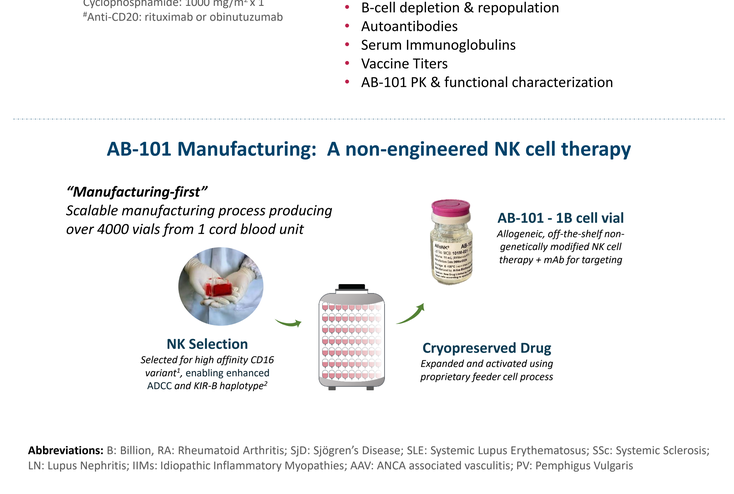
Background

- Deep B-cell depletion is a validated therapeutic strategy in autoimmune disease, but current approaches (CAR T, T-cell engagers) are limited by safety concerns, hospitalization requirements, and restricted access
- AB-101 is an allogeneic, non-genetically modified, off-the-shelf, cryopreserved NK cell therapy designed to enhance antibody-dependent cellular cytotoxicity (ADCC) of B-cell targeting monoclonal antibodies (mAbs), enabling deep B-cell depletion without genetic modification
- In combination with anti-CD20 mAbs, AB-101 has been administered in the outpatient setting, with a favorable safety profile and no CRS or neurotoxicity observed.



Objective

The aim of these analyses was to assess the pharmacokinetic (PK) and pharmacodynamic (PD) activities associated with AB-101 in combination with anti-CD20 mAbs in subjects with autoimmune diseases following a standard conditioning regimen.

Methods

See late-breaker abstract # LB003

AB-101 Treatment Regimen

- AB-101 Dose: 1B or 4B
- Conditioning: Cy/Flu*
- Anti-CD20 mAb# per label

*Fludarabine: 25 mg/m^2 x 3
Cyclophosphamide: 1000 mg/m^2 x 1
#Anti-CD20: rituximab or obinutuzumab

- Phase 2 Basket Trial: RA, SjD, SSc, IIMs
- IIT: RA, SLE, PV, AAV in Community Setting
- Phase 1 / 1b: LN + SLE

Translational Analyses

- B-cell depletion & repopulation
- Autoantibodies
- Serum Immunoglobulins
- Vaccine Titers
- AB-101 PK & functional characterization

AB-101 Manufacturing: A non-engineered NK cell therapy

"Manufacturing-first"
Scalable manufacturing process producing over 4000 vials from 1 cord blood unit

NK Selection
Selected for high affinity CD16 variant[1], enabling enhanced ADCC and KIR-B haplotype[2]

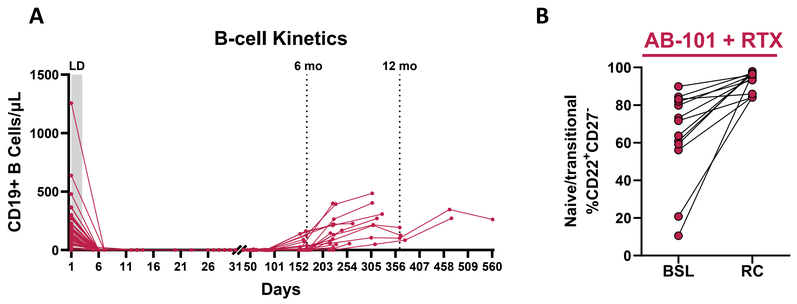
Cryopreserved Drug
Expanded and activated using proprietary feeder cell process

AB-101 - 1B cell vial
Allogeneic, off-the-shelf non-genetically modified NK cell therapy + mAb for targeting

Abbreviations: B: Billion, RA: Rheumatoid Arthritis; SjD: Sjögren's Disease; SLE: Systemic Lupus Erythematosus; SSc: Systemic Sclerosis; LN: Lupus Nephritis; IIMs: Idiopathic Inflammatory Myopathies; AAV: ANCA associated vasculitis; PV: Pemphigus Vulgaris

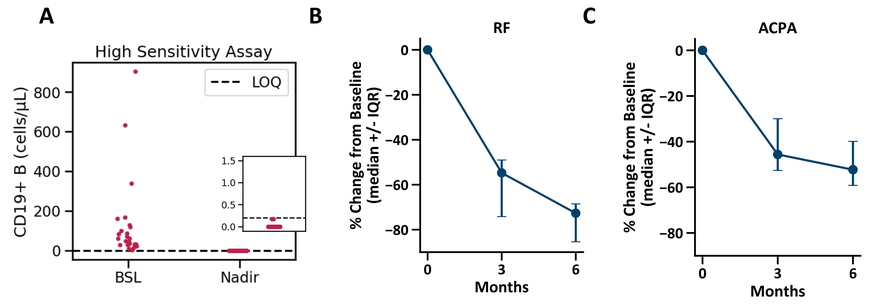
Results

Deep B-cell Depletion is Associated with Immune Reset across Autoimmune Diseases



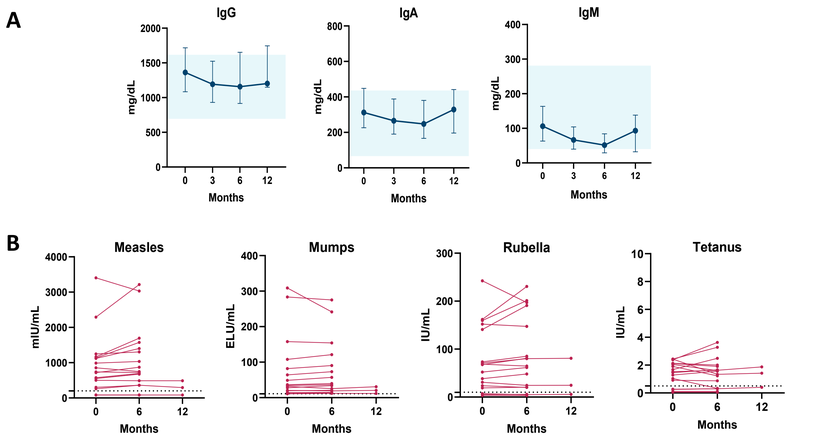
B-cell depletion and reconstitution in autoimmune subjects (A) B-cell depletion observed with reconstitution between 6–12 months post-AB-101 + RTX (n=51). **(B)** B-cell reconstitution post-AB-101 + RTX demonstrated an increase in naïve/transitional B cells (n=13). RTX: rituximab, BSL: Baseline, RC: Reconstitution.

Deep B-cell Depletion with High Sensitivity Assay and Reduced Autoantibodies in RA



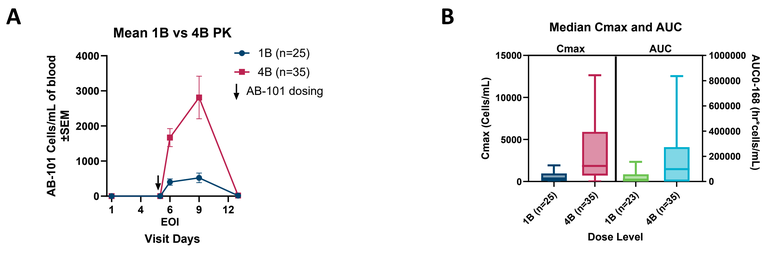
B-cell depletion and autoantibody reduction in RA patients (A) Median CD19+ B cells (cells/µL) at baseline (BSL) and nadir at any time point following AB-101 and RTX (n=28) using a high sensitivity assay. LOQ (limit of quantitation)= 0.2 cells/µL **(B)** Rheumatoid Factor (RF) and **(C)** Anti-CCP (ACPA) levels in RA patients plotted as %change from baseline (median ± IQR) at 0, 3 and 6 months post treatment.

Serum Immunoglobulins and Vaccine Titers Remain Relatively Unchanged



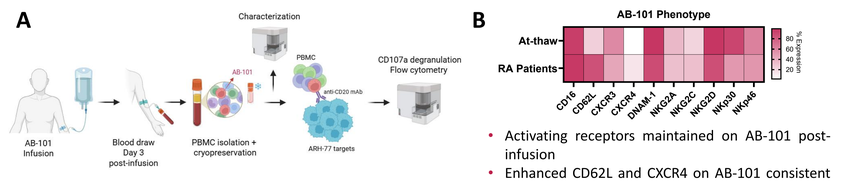
Serum immunoglobulins and vaccine titers in autoimmune subjects (A) Serum levels of immunoglobulins IgG, IgA and IgM. Shaded region indicates normal range, dark blue line indicates median ± interquartile range (IQR). **(B)** Serum levels of vaccination-related antibodies against measles, mumps, rubella and tetanus. Dotted lines indicate seroprotective levels for respective vaccines.

Dose-dependent AB-101 Exposure in Autoimmune Patients

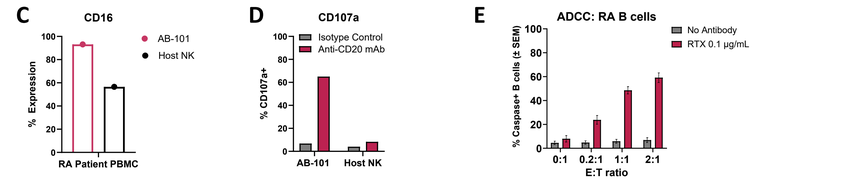


AB-101 PK in autoimmune subjects. (A) AB-101 levels (cells/mL of blood) at 1 billion (1B; n=25) and 4 billion (4B; n=35) dose levels during the first week following the initial dose (up to Day 13) presented as mean ± SEM. **(B)** Median Cmax (cells/mL) and $AUC_{0\text{-}168}$ (area under the plasma concentration-time curve from 0-168h; hr*cells/mL) values for 1B and 4B dose levels. Box plots show median (line), interquartile range (box), and min–max (whiskers).

AB-101 Maintains CD16 Expression in RA Patients and Functional Activity Post-Infusion



- Activating receptors maintained on AB-101 post-infusion
- Enhanced CD62L and CXCR4 on AB-101 consistent with trafficking and tissue homing potential



- High CD16 expression was identified on AB-101 compared to host NK from RA patient PBMC.
- Post-infusion AB-101 from an RA patient showed robust CD107a degranulation against CD20$^+$ targets ± anti-CD20 mAb vs host NK cells.
- AB-101 combined with RTX showed E:T ratio-dependent ADCC against B cells from fresh RA donor PBMCs in vitro.

AB-101 characterization and function in RA (A) Schematic of AB-101 analysis from cryopreserved RA patient PBMCs. **(B)** NK cell marker expression on AB-101 at thaw (n = 9) and in RA PBMCs 3 days post-dose (n = 4). **(C)** CD16 expression on AB-101 and host NK cells in representative RA patient PBMC. **(D)** CD107a expression on AB-101 and host NK cells following 4h co-culture with targets ± anti-CD20 mAb. **(E)** AB-101 mediated ADCC against fresh RA donor B cells (n=3) ± RTX.

Conclusions

Deep B-cell depletion in rheumatologic diseases can be achieved with the AB-101 treatment regimen administered in an outpatient setting, with reduction in autoantibodies but with minimal impact on serum immunoglobulins and vaccine titers. This regimen has the potential to provide clinical benefit in patients with immune-mediated diseases comparable with CAR T cell therapies.

References
1. Musolino, A., et al. J Clin Oncol, 2008.
2. Cooley, S., et al. Blood, 2009.

Disclaimer: Data presented reflect a data cutoff of 03APR2026 and are subject to change.

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