Unmet Need in Atopic Dermatitis (AD)

- AD is a systemic and heterogeneous disease, and its pathophysiology is not well understood.
- Although there has been an increase in effective treatment options, patient satisfaction with treatment is only partially or not met in more than 75% of patients surveyed with moderate to severe AD.
- Current treatment options do not target all the diverse immune cells and cytokines that contribute to the pathogenesis of this disease.

B and T Lymphocyte Attenuator (BTLA)

- BTLA is a co-inhibitory checkpoint receptor that is expressed across a range of immune cells, including T cells (Th1, Th2, Th17, Th22), B cells, and dendritic cells (DCs), which are key cell types contributing to inflammatory diseases such as AD.
- T cell activation requires antigen presentation in the context of MHC to the TCR, and co-stimulation via CD80/86 to CD28.
- BTLA engagement inhibits T cell proliferation and reduces secretion of inflammatory cytokines.
- BTLA engagement on DCs modulates maturation and function, by reducing both antigen presentation by MHC and expression of costimulatory molecules (Figure 1).

ANB032, a BTLA Agonist Antibody

- ANB032 is a humanized IgG4/κ monoclonal antibody to human BTLA that modulates BTLA activity in a non-competitive fashion with its ligand, HVEM.
- ANB032 binds to BTLA on Th1, Th2, Th17, and Th22 T cells and DCs and augments BTLA agonism (Figure 2).
- ANB032’s agonist signal modulates DC maturation and function, reducing antigen presentation and expression of co-stimulatory molecules, including inducing Tregs.
- Cytoxic secretion (Th1, Th2, Th17, & Th22) was inhibited in AD patient-derived PBMCs exposed to ANB032.
- In a Phase 1 first-in-human healthy volunteer study, ANB032 was well-tolerated, had a favorable PK profile, demonstrated robust target engagement and a partial reduction in BTLA expression, consistent with observations in animal models of dermatitis and inflammation (Luu, et al. EADV 2023 Abstract 5603, being presented on Oct. 13 at 8:30 am CET).
- The robust preclinical data and Phase 1 trial results support advancing the clinical development of ANB032 in a Phase 2b study in AD (ARISE AD; NCT05935085).

ANB032 is an inhibitory checkpoint receptor that modulates activation of T cells, B cells, and DCs.

METHODS

Study Design and Subjects

- This global Phase 2b study is a randomized, double-blind, placebo-controlled, parallel-group, multicenter trial (Figure 3).
  - Primary endpoint: Mean change from Baseline in EASI at Week 14.
  - Secondary endpoints: EASI-75, vGQA-AD ≥ 3, AD-involved BSA ≥ 10%.
  - Subjects who are either dupilumab/IL-13 blocker-naïve or -experienced are eligible for enrolment.

Treatment

- Approximately 160 subjects are being randomized in a 1:1:1:1 ratio in 4 equal treatment groups, evaluating 3 subcutaneous (SC) doses of ANB032 and placebo.
- The treatment period is 14 weeks with an additional 12-weeks of follow up.

ANB032 in AD:

- ANB032 is an agonist that augments BTLA activity in a non-competitive fashion with its ligand, HVEM.
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- Bart Burington is no longer employed by AnaptysBio, Inc.

REFERENCES