Efficacy and Safety of ABVV-3373: A Novel Anti-TNF Glucocorticoid Receptor Modulator Antibody Drug Conjugate, in Patients with Moderate to Severe Rheumatoid Arthritis Despite Methotrexate Failure: A Phase 2a Proof of Concept Study

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Background: ABVV-3373 is a novel antibody drug conjugate composed of adalimumab (ADA) linked to a proprietary and highly potent glucocorticoid receptor modulator (the anti-inflammatory payload) currently evaluated for the treatment of rheumatoid arthritis (RA).

Objectives: To assess the efficacy and safety of ABVV-3373 vs ADA in RA patients (pts).

Methods: This was a 24-week (wk) randomized, double-blind, double-dummy, active-controlled Phase 2a study of intravenously (IV)-administered ABVV-3373 100 mg (for 12 wks followed by placebo [PBO] for 12 wks) vs subcutaneous injections of ADA 80 mg every other wk (for 24 wks) in pts on background methotrexate. The primary endpoint was the change from baseline (BL) in DAS28(CRP) at Wk 12. Pre-planned statistical methods incorporating pre-specified historical ADA data both alone (pre-specified success criterion, 2-sided P < 0.1) and supplemented with in-t trial ADA data (pre-specified success criterion, probability >95%) were used to achieve adequate statistical power with a reduced trial size. Assay sensitivity was evaluated through construction of a synthetic PBO arm by propensity score matching, using individual pt-level PBO data from 3 recent sponsor-run trials of similar populations and trial settings. Secondary endpoints included 1) mean change from BL in CDAI, SDAI, DAS28(ESR), HAQ-DI; 2) proportion of pts achieving DAS28(CRP)≤3.2, ACR20/50/70 points at Wk 12 included 1) mean change from BL in CDAI, SDAI, DAS28(ESR), HAQ-DI; 2) proportion of pts achieving DAS28(CRP)≤3.2, ACR20/50/70 responses, HAQ-DI≤0.22. Continuous and categorical efficacy variables were analyzed using mixed effect model repeated measurements and Cochran-Man-Whitney test, respectively; non-responder imputation was applied to missing data. Safety was assessed through the ARTIS national safety monitoring system.

Results: A total of 48 pts were randomized and treated (ABVV-3373: 31; ADA: 17); 46 pts (96%) completed 12 wks of study treatment. BL demographics and disease characteristics were indicative of established RA and similar among the 2 treatment arms and the synthetic PBO arm. ABVV-3373 demonstrated significant improvement in mean DAS28(CRP) at Wk 12 vs the pre-specified historical ADA (2.65 vs -2.13; P=0.002) and numerically greater improvement vs the combined in-t trial and historical ADA arm (2.65 vs -2.29; probability 99%; Figure). Comparable improvements in disease activity and targets were observed for ABVV-3373 and in-t trial ADA. Assay sensitivity was supported by the fact that both ABVV-3373 and ADA arms were superior to synthetic PBO (P<0.001). For secondary endpoints, greater efficacy was observed with ABVV-3373 vs historical ADA; ABVV-3373 was predicted with 79-99% probability to be better than ADA on the combined in-t trial and historical ADA data. 2 serious infections were reported with ABVV-3373 (pneumonia, upper respiratory tract infection) and none with ADA through Wk 12 (Table). 1 event of anaphylactic shock reaction was reported with ABVV-3373. After increasing the duration of IV administration from 3 min to 15-30 min, no similar events were observed.

Conclusion: These data demonstrate the clinical efficacy of ABVV-3373 and its potential to provide improved outcomes for RA pts compared to ADA. The safety profile of ABVV-3373 was generally similar to ADA.

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