agreements with Karolinska Institutet with JA as principal investigator, mainly in the context of safety monitoring of biologics via the ARTIS national safety monitoring system.

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OP0115

EFFICACY AND SAFETY OF ABBV-3373, A NOVEL ANTI-TNF GLUCOCORTICOID RECEPTOR MODULATOR ANTIBODY DRUG CONJUGATE, IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS DESPITE METHOTREXATE THERAPY: A PHASE 2A PROOF OF CONCEPT STUDY

F. Buttgerit¹, J. Aelion², B. Rojkovich³, A. Zubrzycka-Sienkiewicz⁴, T. Radstake⁵, S. Chen⁵, D. Arian⁵, H. Kupper⁶, H. Amital^{7,8}. ¹Charité University Medicine, Department of Rheumatology and Clinical Immunology, Berlin, Germany; ²West Tennessee Research Institute, Jackson, United States of America; ³Buda Hospital of the Hospitaller Order of St. John of God, Rheumatology, Budapest, Hungary; ⁴Reumatika – Centrum Reumatologii, ARS Rheumatica sp.z.o.o, Warsaw, Poland; ⁵AbbVie, Immunology, North Chicago, United States of America; ⁶AbbVie Deutschland GmbH & Co. KG, Immunology, Ludwigshafen, Germany; ⁷Sheba Medical Center, Department of Medicine 'B' and Zabudowicz Center for Autoimmune Diseases, Ramat Gan, Israel; ⁸Affiliated to Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Background: ABBV-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 ABBV-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 ABBV-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 $P \leq 0.1$) and supplemented with in-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 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-Mantel-Haenszel test, respectively; non-responder imputation was applied to missing categorical data. Treatment-emergent adverse events were summarized through Wk 12.

Results: A total of 48 pts were randomized and treated (ABBV-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. ABBV-3373 demonstrated significant improvement in mean DAS28(CRP) at Wk 12 vs the pre-specified historical ADA (-2.65 vs -2.13; $P=0.022$) and numerically greater improvement vs the combined in-trial and historical ADA arm (-2.65 vs -2.29; probability 90%; Figure). Comparable improvements in disease activity and targets were observed for ABBV-3373 and in-trial ADA. Assay sensitivity was supported by the fact that both ABBV-3373 and ADA arms were superior to synthetic PBO ($P<0.001$). For secondary endpoints, greater efficacy was observed with ABBV-3373 vs historical

ADA; ABBV-3373 was predicted with 79-99% probability to be better than ADA based on the combined in-trial and historical ADA data. 2 serious infections were reported with ABBV-3373 (pneumonia, upper respiratory tract infection) and none with ADA through Wk 12 (Table). 1 event of anaphylactic shock reaction was reported with ABBV-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 ABBV-3373 and its potential to provide improved outcomes for RA pts compared to ADA. The safety profile of ABBV-3373 was generally similar to ADA.

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Figure. Analysis of Primary, Secondary, and Additional Efficacy Endpoints at Week 12

* $P < 0.05$ for ABBV-3373 vs historical ADA, in-trial ADA, and synthetic placebo, respectively. [†] ABBV-3373 better than ADA based on the historical/in-trial ADA; the success criterion was probability >95%. ADA, adalimumab; ACR20/50/70, ≥20%/50%/70% improvement in American College of Rheumatology response criteria; BL, baseline; CDAI, clinical disease activity index; DAS28(CRP), 28-point disease activity score based on C-reactive protein; DAS28(ESR), 28-point disease activity score based on erythrocyte sedimentation rate; HAQ-DI, health assessment questionnaire disability index; LRA, low disease activity; MCID, minimal clinically important difference (change from baseline in HAQ-DI < 0.22); SDAI, simplified disease activity index. [‡] Efficacy endpoints based on non-responder imputation. ABBV-3373 vs in-trial ADA comparison was not adequately powered due to small sample sizes. For ABBV-3373 vs combined ADA the probability of ABBV-3373 being better than ADA is presented. [§] Historical ADA cohort (patients receiving ADA 80 mg every other week) was not included. ^{||} Analysis only included patients with baseline HAQ-DI < 0.22. Forty-seven patients met the criterion.

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OP0116

ELDERLY PATIENTS ARE NOT AT INCREASED RISK OF SERIOUS INFECTIONS WHEN RECEIVING bDMARDs OR JAK INHIBITORS COMPARED TO csDMARD TREATMENT

A. Strangfeld¹, B. Manger², M. Worsch³, T. Schmeiser⁴, A. Zink¹, M. Schaefer¹.

¹German Rheumatism Research Centre, Epidemiology and Health Care Research, Berlin, Germany; ²University Hospital Erlangen, Faculty of Medicine, Erlangen, Germany; ³Private Practice, Mühlhausen, Germany; ⁴Private Practice, Cologne, Germany

Background: Elderly rheumatoid arthritis (RA) patients are generally at increased risk of serious infections (SI). At the same time, treatment with bDMARDs has been associated with a higher SI risk than treatment with csDMARDs (1). However, long-term use of bDMARDs did not increase the risk of SI in a small group of elderly patients over 65 (2). The extent to which elderly patients are exposed to a higher SI risk when treated with JAK inhibitors (JAKi) is an open question.

Objectives: To assess the effects of bDMARDs and specifically JAKi on the risk of SI in elderly patients with RA.

Methods: The German register RABBIT is a prospective, longitudinally followed cohort of RA patients enrolled with a new start of a DMARD after at least one csDMARD failure. This analysis comprises patients over 70 years of age who were enrolled between 01/2007 and 04/2020 and had at least one follow-up.

Table 1. Treatment Emergent Adverse Events up to Week 12

Event, n (%)	ADA (N = 17)	ABBV-3373 (N = 31)
Adverse event (AE)	12 (70.6)	11 (35.5)
AE with reasonable possibility of being drug related ^a	3 (17.6)	2 (6.5)
Severe AE	0	1 (3.2)
Serious AE	0	4 (12.9) [#]
AE leading to Discontinuation of Study Drug	1 (5.9)	1 (3.2)
Serious infections	0	2 (6.5)
Opportunistic infection excluding Tuberculosis	0	0
Allergic Reactions Including Hypersensitivity, Angioedema, and Anaphylaxis	2 (11.8) ^{&}	1 (3.2) [^]
Systemic glucocorticoid events	0	0
All deaths	0	0

^aAs assessed by investigator. [#]Serious AEs: 1 non-cardiac chest pain, 1 pneumonia, 1 upper respiratory tract disease and 1 anaphylactic shock. [&]1 Type I hypersensitivity, 1 Pruritus [^]1 Anaphylactic shock