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FRI0108

SHORT-TERM EFFICACY OF BCD-089, NOVEL MONOCLONAL ANTI-IL-6 RECEPTOR ANTIBODY, IN COMBINATION WITH METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS: 12-WEEK RESULTS OF PHASE 2 AURORA STUDY

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Background: In the previous phase 1 study BCD-089 (INN: levilimab) was well-tolerated, had favorable safety profile and low immunogenicity¹. Here we report 12-week efficacy and safety results of ongoing phase 2 clinical study of BCD-089 in patients with active RA.

Objectives: This study is aimed to assess efficacy and safety of 2 dosing regimens of BCD-089 in patients with MTX-IR active RA.

Methods: During this multicenter double-blind placebo-controlled randomized clinical study (NCT03455842) 105 MTX-IR patients with active RA (ACR2010) were assigned (1:1:1) to receive 162 mg of BCD-089 s.c. (QW arm and Q2W arm) or PBO. MTX (10-25 mg/week) was used in all groups. After completion of 12-week blinded period patients from QW/Q2W arms continued the treatment, patients from PBO arm were switched to BCD-089 Q2W until Wk56. The primary efficacy endpoint was the rate of ACR20 at Wk12. Secondary endpoints included ACR50/70 and DAS28-CRP(4). The safety was routinely evaluated.

Results: The efficacy analysis showed that 95% confidence interval for BCD-089 treatment effect relative to PBO was [38.45 – 81.55] for QW arm and [16.53 – 63.4] for Q2W arm, which confirms the superiority to PBO of either dosing regimens. Summary of efficacy results is presented in table 1.

The majority of adverse events (AE) were laboratory abnormalities. The spectrum of AEs is similar to other IL6R inhibitors (Table 2). Three serious AE (SAEs) were reported: community-acquired pneumonia (QW arm, treatment-related), acute cholecystitis (PBO arm, not related, did not lead to treatment discontinuation), and acute heart failure leading to death (Q2W arm, not related). One case of moderate local reaction (erythema) was reported in QW arm.

Conclusion: BCD-089 in combination with MTX had superior efficacy compared with MTX plus PBO in MTX-IR patients with active RA. BCD-089 showed safety profile consistent with other IL6R inhibitors. Further clinical studies are needed.

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Table 1. Safety results (full analysis set), n (%)

Efficacy parameter	BCD-089 QW+MTX (n=35)	BCD-089 Q2W+MTX (n=35)	PBO +MTX (n=35)	p-value (Fisher's exact test)
ACR20	27 (77.1%)	20 (57.1%)	6 (17.1%)	<0.0001
ACR50	18 (51.4%)	11 (31.4%)	2 (5.7%)	0.0001
ACR70	10 (28.6%)	7 (20.0%)	1 (2.9%)	0.0106
DAS28-CRP(4) < 3.2	20 (57.1%)	10 (28.6%)	1 (2.9%)	<0.0001

Table 2. Safety results (full analysis set), n (%)

Safety parameter	BCD-089 QW+MTX (n=35)	BCD-089 Q2W+MTX (n=35)	PBO+MTX (n=35)
Any AE	26 (74.29%)	23 (65.71%)	14 (40.0%)
Any SAE	1 (2.86%)	1 (2.86%)	1 (2.86%)
Any grade 3-4 AE	10 (28.57%)	6 (17.14%)	2 (5.71%)

Grade 3-4 Neutropenia	3 (8.57%)	3 (8.57%)	0 (0.00%)
AE of special interest			
ALT/AST increased	4 (11.43%)	5 (14.29%)	1 (2.86%)
Leucopenia/Neutropenia	5 (14.29%)	6 (17.14%)	1 (2.86%)
Infections and infestations	2 (5.71%)	1 (2.86%)	2 (5.71%)
Total cholesterol increased	8 (22.86%)	8 (22.86%)	2 (5.71%)
AEs leading to treatment discontinuation	0 (0.00%)	1 (2.86%)	0 (0.00%)
Deaths	0(0.00%)	1(2.86%)	0(0.00%)

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EFFECTIVENESS AND SAFETY OF INFliximab, GOLIMUMAB AND GOLIMUMAB-IV IN RHEUMATOID ARTHRITIS PATIENTS FROM A PROSPECTIVE OBSERVATIONAL REGISTRY

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Background: Long-term registries are essential to evaluate new therapies in a patient population that differs from clinical trials and usually varies over time.

Objectives: To describe the profile of rheumatoid arthritis (RA) patients treated with infliximab (IFX), golimumab subcutaneous (GLM) or intravenous (GLM-IV) in Canadian routine care, along with its effectiveness and safety.

Methods: 1577 RA patients treated with IFX, GLM or GLM-IV were enrolled into the Biologic Treatment Registry Across Canada (BioTRAC) between 2006-2015, 2010-2017 and 2014-2017, respectively. Study visits occurred at baseline and every 6 months thereafter. Effectiveness was assessed with changes in TJC28, SJC28, MDGA, PtGA, pain, HAQ, and acute phase reactants. Safety was evaluated with the incidence of adverse events (AEs) and drug survival.

Results: Of the 890 IFX-, 530 GLM- and 157 GLM-IV-treated patients, the proportion of females were 75.7%- 77.1%, the mean age were 55.8-57.7 and the mean disease duration were 6.5-8.6 years. Most patients were bio-naïve (> 80%).

A significant decrease in disease duration and disease activity scores (DAS, TJC, SJC, HAQ, AM stiffness, MDGA, PtGA, CRP, ESR) were observed in the IFX cohort over time (p<0.001). Interestingly, baseline disease duration and disease activity scores for the GLM cohort (DAS, TJC, SJC, PtGA, Pain, CRP, ESR) were higher than in the IFX cohort from 2010-2012 when GLM was first introduced while the mean MDGA remained the same between the two groups.

Treatment with IFX, GLM and GLM-IV significantly improved all disease parameters over time (P<0.001) from baseline to 6 months and up to 120, 78 and 42 months, respectively. The proportion of patients in SDAI remission at 12, 24 and 36 months reached 16.2%, 20.8% and 22.8% in IFX-patients; 34.7%, 47.5% and 52.7% in GLM-patients and 33.8%, 47.5% and 61.9% in GLM-IV-patients (p=0.1978 and p=0.0081 vs IFX).

AEs were reported for 61.5%, 67.4% and 59.2% (105, 113 and 82.6 events/100 PYs) and SAEs for 21.2%, 15.5% and 3.8% (11.7, 34.4 and 9.0 events/100 PYs) covering 2714, 1077 and 257 years of exposure for IFX, GLM and GLM-IV-treated patients, respectively. The most frequently occurring AEs were arthralgia and upper respiratory tract infection (>5%). Eighteen, 7 and 1 deaths occurred among IFX-, GLM- and GLM-IV-treated patients, respectively. The proportion of patients who discontinued treatment were 74.0% over a mean 3.0 years of exposure to IFX-,