OP0028 EFFICACY AND SAFETY OF BCD-085, A NOVEL IL-17 INHIBITOR, IN ANKYLOSING SPONDYLITIS. RESULTS OF PHASE 2 CLINICAL STUDY

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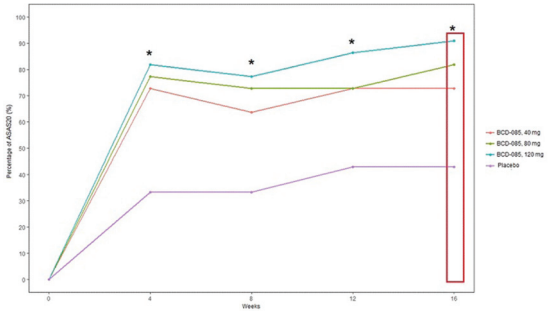
Background: BCD-085 is an innovative humanised monoclonal antibody against interleukin-17 with genetically modified Fc- and CDR-regions, aimed to improve treatment outcomes in patients with several autoimmune disorders.
Objectives: This abstract presents the results of double-blind placebo controlled dose-finding phase II clinical study of efficacy and safety of subcutaneous BCD-085 in patients with ankylosing spondylitis.
Methods: The study was conducted as international multicenter randomised double-blind placebo controlled study. The study enrolled 88 adults with active AS. Patients were randomised in 4 study arms in 1:1:1:1 ratio to receive 40, 80 or 120 mg of BCD-085 or placebo. In the active period of the study, patients received the test drug/placebo SC injections once weekly for the first three weeks of treatment and then every other week till Wk 12. After Wk 12 all patients underwent follow-up for 4 weeks.
Results: Efficacy: BCD-085 is superior to placebo in doses 80 and 120 mg. ASAS20 at wk 16 was reached by 81.82%, 90.91% and 42.86% of patients in BCD-085 80 mg, 120 mg and placebo arm respectively (p=0.008, 95% CI for difference in proportion [12.36%; 65.56%]; p=0.001, 95% CI: 23.71% to 72.39%], superiority margin 10%). Significant reduction of AS activity was revealed for all BCD-085 arms: by Wk 4 BASDAI and ASDAS-CRP scores decreased and maintained achieved levels till the end of the study. Other secondary endpoints (ASAS40, ASAS5/6, BASMI, BASFI, BASDAI, MASES, chest expansion, QoL, spinal pain) had the corresponding dynamics: by the time of second evaluation (Wk 1 for spinal pain, Wk 4 for other endpoints) significant improvement with no further negative changes was revealed. For all evaluated endpoints the most pronounced response was established for BCD-085 120 mg arm. In placebo arm no significant dynamics was shown.
Safety: All arms had highly similar safety profiles. Most of AEs were presented as mild or moderate laboratory abnormalities (ANC decreased, WBC increased) and moderate arterial hypertension. The rates of AEs were equivalent for all BCD-085 doses and placebo. There were no cases of SAEs, treatment discontinuation due to safety reasons or local reactions. Immunogenicity assessment did not detect formation of binding antibodies.

Abstract OP0028 – Table 1. Summarised safety data

Parameter	Arm				P-value
	BCD-085 40 mg (n=22)	**BCD-085 80 mg (n=22)**	**BCD-085 120 mg (n=22)**	**Placebo (n=22)**	
Any AE	11 (50.00%)	6 (27.27%)	4 (18.18%)	7 (31.82%)	0.183
Therapy-related AEs	5 (22.73%)	4 (18.18%)	1 (4.55%)	5 (22.73%)	0.354
Grade 3–4 AEs	1 (4.55%)	2 (9.09%)	0	1 (4.55%)	0.900



Abstract OP0028 – Figure 1. ASAS20 response throughout the study (* – statistically significant difference between BCD-085 and placebo arms).

Conclusions: Treatment with BCD-085 leads to significant improvement in all AS symptoms in comparison with placebo. The dose of 120 mg of BCD-085 had the most pronounced effect. The drug was well tolerated in all doses with no differences with placebo in safety profiles.
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OP0029 CLINICAL EFFECT OF VEDOLIZUMAB ON ARTICULAR MANIFESTATIONS IN PATIENTS WITH SPONDYLOARTHRITIS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE

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Background: Data on the effects of vedolizumab on joint manifestations remain controversial.[1,2]
Objectives: The purpose of this study was to[1] evaluate baseline characteristics of crohn's disease (CD) and ulcerative colitis (UC) patients treated with vedolizumab,[2] assess the effect of vedolizumab on joint manifestations in patients with inflammatory bowel disease (IBD)-associated Spondyloarthritis (SpA), and[3] evaluate new onset of SpA under VDZ.
Methods: This single-centre, retrospective and observational study was conducted from July 2014 to July 2017. The charts of all patients with IBD who had undergone treatment with vedolizumab for more than 3 months were reviewed. The patients' demographic and clinical characteristics were collected. Data on IBD-associated SpA were collected as well as new onset of SpA under VDZ. The ASAS criteria were used to establish the diagnosis of SpA.
Results: Patient characteristics and main results are shown in table 1. A total of 171 patients diagnosed with IBD were treated with vedolizumab from July 2014 to July 2017. Notably, 97.1% of patients had been previously treated with at least one TNF-α inhibitor. All patients included in this study completed the induction phase at last observation, and the mean follow-up of the entire cohort was 14.3 ±12.0 months. Ten (5.8%) patients had a history of IBD-associated SpA but were in clinical remission at the time of initiation of VDZ, whereas 4 (2.4%) had active SpA when VDZ was started. First, no clinical benefit on SpA following initiation of VDZ was found in those 4 patients with active SpA. Second, exacerbation of SpA in patients with clinical remission at initiation of VDZ was found in 6/10 patients whereas no effect was reported in the remaining 4/10 patients. All those 14 patients with IBD-associated SpA were under TNF inhibitors just before starting VDZ. Finally, new onset of SpA induced by VDZ was reported in 1 patient.

Abstract OP0029 – Table 1. Characteristics of patients and main results

Variable	n=171
Age (years), mean±SD	37.8±12.9
Female gender, n (%)	110 (64.3)
Body mass index (kg/m²), mean±SD	23.7 (4.8)
Type of disease, n (%)	104 (60.8)
- Crohn's disease	67 (39.2)
- Ulcerative colitis	
Duration of disease (years), mean±SD	10.5 (7.6)
Duration of follow-up under vedolizumab (months), mean±SD	14.3 (12.0)
IBD-associated SpA, n (%)	157 (91.8)
- No history	10 (5.8)
- History (inactive at initiation of VDZ)	4 (2.4)
- Active at initiation of VDZ	
Clinical benefit on SpA following initiation of VDZ (n=4)	4/4 (100)
- No clinical benefit	0/4 (0)
- Improvement	
Exacerbation of SpA in patients with clinical remission at initiation of VDZ (n=10)	6 (60) 4 (40)
- Yes	
- No	
New onset of SpA induced by VDZ	1 (<1)

Conclusions: Vedolizumab does not seem to show any efficacy in IBD-associated SpA and might even induce exacerbation or new onset of SpA. Inception cohort studies are needed to better evaluate the effect of vedolizumab on joint manifestations.

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WEDNESDAY, 13 JUNE 2018: RA therapy – new molecules and new strategies

OP0030 CORTICOSTEROID BRIDGING STRATEGIES WITH METHOTREXATE MONOTHERAPY IN EARLY RHEUMATOID AND UNDIFFERENTIATED ARTHRITIS; A COMPARISON OF EFFICACY AND TOXICITY IN THE TREACH AND IMPROVED STUDIES

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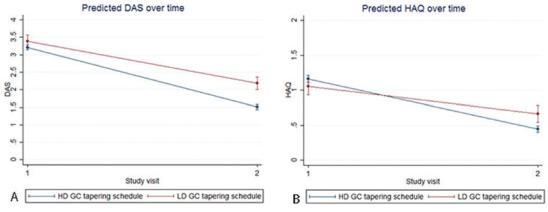
Background: What is the optimal glucocorticoid (GC) bridging therapy with MTX monotherapy in early arthritis?
Objectives: To compare short term clinical efficacy of high and low dose GC tapering schedules with MTX monotherapy in 2 clinical trials in early rheumatoid arthritis (RA) and undifferentiated arthritis (UA) patients.
Methods: In tREACH, early RA and UA (arthritis in ≥1 joint(s),<1 year symptoms) patients were randomised to 3 different treatment arms. For this analysis we only use the data of arm C: oral GCs (prednisone) (15 mg/day, tapered to 0 in 10 weeks) with MTX monotherapy (25 mg/week); low dose GC tapering schedule (LDGC).
In IMPROVED RA and UA (arthritis in ≥1 joint and ≥1 other painful joint,<2 years symptoms) patients were treated with prednisone (60 mg/day, tapered in 7 weeks to 7.5 mg/day, continued to 4 months)+MTX monotherapy (25 mg/week); high dose GC tapering schedule (HDGC). We compared%DAS-remission (<1.6) and low disease activity (≤2.4) at first evaluation (3 months tREACH, 4 months IMPROVED) and DAS and HAQ over time. After multivariate normal imputation we applied generalised estimating equations (GEE) for linear outcomes and logistic regression models for binary outcomes, adjusted for potential baseline confounders (figure 1). Adverse events were compared between treatment arms using χ2-square tests.
Results: Patients with a HDGC (n=610) had shorter symptom duration and higher HAQ, were less often seropositive (ACPA positive 56.0% vs 77.3%, RF positive 58.1% vs 65%) and more often had UA (20.3% vs 2.1%) than patients with a LDGC (n=97). Baseline DAS was comparable.
At the first evaluation time point (median 3.06 (IQR 2.99–3.22) months in LDGC, 4.01. (3.8–4.17) in HDGC) DAS and HAQ had decreased significantly less after 3 months LDGC: DAS β (95% CI) 0.500 (0.276; 0.725), and HAQ 0.330 (0.189; 0.470) than after 4 months HDGC (figure 1).
Compared to the HDGC patients, patients with the LDGC had a significantly lower chance of achieving DAS-remission 63.4% vs 28.9% (OR (95% CI) 0.215 (0.124; 0.373) and low disease activity 80.6% vs 55.7% ((OR (95% CI) 0.249 (0.143; 0.435)). Presence of ACPA was positively associated with achieving DAS-remission in the HDGC group, but not in the LDGC group. Per 100 patient years, 7.98 serious adverse events were reported in the HDGC and 23.4 in the LDGC (p=0.004). Hypertension, hyperglycemia (>7.8 mmol/L), gastrointestinal complaints and liverenzymes above normal were reported in similar frequencies across all groups. In patients with a LDGC more headaches, skin rashes, creatinine above normal range and any decrease in haematology blood counts were reported (data not shown).



Abstract OP0030 – Figure 1 A: Predicted DAS over time, B: PRedicted HAQ over time. All predictions are from multiple imputed models, adjusted for age, gender body mass index, presence of ACPA, presence of rheumatoid factor, symptom duration, effect over time (in GEE) and baseline DAS (for binary out-comes). DAS, Disease Activity Score; HAQ Health Assessment Questionnarie; HD GC, high dose glucocorticoids, LD GC, low dose glucocorticoids

Conclusions: In early arthritis patients, GC bridging therapy with prednisone 60 mg daily tapered in 7 weeks to and continued at 7.5 mg daily in combination with MTX monotherapy was associated with better clinical outcomes and without additional effects than prednisone 15 mg daily tapered to nil in 10 weeks in combination with MTX monotherapy, after correction for baseline age, gender, DAS, body mass index, presence of ACPA, presence of rheumatoid factor, symptom duration, and (in GEE) time from baseline.
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OP0031 THE IMPORTANCE OF ASSESSING MULTIPLICATIVE AND ADDITIVE INTERACTION: EXAMINING THE EFFECT OF GLUCOCORTICOID THERAPY ON MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITISAND CONCOMITANT TYPE II DIABETES

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Background: Glucocorticoids (GC) are widely used to treat rheumatoid arthritis (RA), however they are known to have risks associated with them. It has been shown that GCs increase the risk of diabetes mellitus (DM). A few studies have investigated the long-term effects of GC use on outcomes in DM, but not in RA specifically. As people with RA already have increased risk of cardiovascular (CV) disease, the additional burden of DM and GCs may be important. If the effect of GCs was dependent on DM we would say there is effect modification and this can be on the additive scale, corresponding to variation in the absolute treatment effect, e.g. the risk difference (RD), across DM status, or the multiplicative scale, corresponding to variation in the relative treatment effect e.g. the rate ratio (RR).[1]
Objectives: To examine in patients with RA 1) whether all-cause and CV mortality rates differ by GC and DM status, and 2) whether DM modifies the relationship between GC and all-cause and CV mortality on multiplicative and additive scales.
Methods: Patients with RA and linkage to mortality data were identified from the Clinical Practice Research Datalink (n=9085), a database of primary care electronic medical records in the UK. RR and RD for ever GC use were calculated by DM status. Cox proportional hazards (PH) regression models were fitted with an interaction term for DM and use of GC to assess multiplicative interaction. Additive interaction was measured with the Relative Excess Risk due to Interaction (RERI)[2] where a value different from zero indicates a difference in the absolute effect of treatment.
Results: Those with DM and ever treated with GCs had a 3-fold increased all-cause mortality RR (95% CI: 2.27, 4.09) whilst those without DM had a slightly higher RR (3.46 (95% CI: 2.95, 4.07)). However those with DM had a higher RD: 36.46 deaths per 1000 patient years (pyrs) (95% CI: 27.5, 45.41) compared to those without DM: RD 22.83 deaths per 1000 pyrs (95% CI: 19.83, 25.82) because of higher baseline mortality rates. A similar pattern was seen for CV mortality. The adjusted Cox PH model for all-cause mortality showed no evidence of multiplicative interaction, but there was significant additive interaction (RERI 0.86 (95% CI: 0.18, 1.54)). For CV mortality there was no interaction on either scale.
Conclusions: Methodologically, this study showed assessing interaction on the additive and multiplicative scales can lead to different conclusions and should be considered carefully. In this study significant interaction was seen on additive scale but not on the multiplicative scale due to higher baseline rates in patients with DM. Clinically, this study provides some evidence that long-term GC therapy may be particularly harmful in patients with RA and DM.

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