FRI0117

TOCILIZUMAB USE DIRECTLY AFTER sDMARD FAILURE SHOWS HIGHER RESPONSE RATES AND A LONGER TREATMENT DURATION

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Background: The non-interventional study (NIS) ARATA (NCT02251860) observes the clinical effectiveness and safety of subcutaneous Tocilizumab (TCZ) s.c. treatment under routine conditions over a 2 year period.

Objectives: In this interim analysis, the patients were subgrouped according to their pretreatment: (I) pretreated exclusively with sDMARD or (II) also pretreated with bDMARD.

Methods: TCZ-naïve patients (Pts) (≥18 years) with RA, who receive TCZ s.c. treatment, could be included in the study since 2014. Demographic and disease-specific characteristics, the progression of the disease (rheumatoid activity scores), concomitant medications, adverse events (AE) and patient questionnaires were documented.

Results: In this interim analysis (reporting date 01-FEB-2017), the data of 912 Pts were evaluated. 319 Pts (35%) were pretreated exclusively with sDMARD and 585 Pts (64.8%) were also pretreated with bDMARD. The main reason for a switch to TCZ s.c. was lacking effectiveness of the pretreatment.

In comparison, patients exclusively pretreated with sDMARD demonstrated a shorter median disease duration (6 vs. 9 years), TCZ s.c. was applied at BL more rarely in combination with MTX (23.5% vs. 35.6%) and more rarely with glucocorticoids (59.2% vs. 69.5%). The comorbidity rates were comparable in both groups. However, patients exclusively pretreated with sDMARD suffered half as often from osteoporosis (9.1% vs. 21.2%). Patients Exclusively pretreated with sDMARD had a longer median treatment duration (380.5 vs. 341.0 days) and a higher retention rate to week 52 (78.9% vs. 70.5%). The effectiveness of the TCZ s.c. treatment was examined with 831 patients. More patients with exclusively sDMARD pretreatment achieved a DAS28 remission and remained in remission (figure 1). The change from BL for the CDAI and Dcrt response was higher in the sDMARD subgroup. No new safety signals and no differences between the subgroups for all safety parameters were observed.

Abstract FRI0117 – Figure 1. Clinical remission (DAS28-ESR <2.6) after pretreatment (N=831). DAS28-ESR, Disease activity score 28-erythrocyte sedimentation rate.

Conclusions: The results of the third interim analysis of the NIS ARATA confirm the efficacy of TCZ s.c. observed in the approval trials in clinical practice. A fast and effective reduction of disease activity in the treated RA patients as well as a lasting improvement in all RA progression parameters collected was observed. In case of the earlier application of TCZ s.c., directly after sDMARD failure, higher response rates and a longer retention of the treatment were observed.

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FRI0118

DEKAVIL (F8IL10) – UPDATE ON THE RESULTS OF CLINICAL TRIALS INVESTIGATING THE IMMUNOCYTOKINE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The targeted pharmacodelivery of cytokines by means of antibody-fusion proteins aims at selective accumulation of the active compound at the site of disease while sparing healthy tissues. Dekavil (F8IL10) is a fully human fusion protein composed of the vascular targeting antibody F8 fused to the cytokine interleukin-10. A phase 1 dose escalation study in patients with rheumatoid arthritis (RA) has recently been completed. Dekavil is currently under investigation in a phase 2 clinical study for the treatment of RA.

Objectives: The phase 1 study investigated safety, tolerability and the maximum tolerated dose of Dekavil when administered in combination with methotrexate (MTX). The currently ongoing phase 2 (in patients with active RA despite MTX therapy who had failed anti-TNF treatment) measures the mean change from baseline in DAS28-CRP between F8IL10 and placebo arms as primary endpoint.

Methods: The target population of both RA studies comprises patients with active RA despite MTX therapy who had failed anti-TNF treatment. Dekavil is administered once weekly for 8 consecutive weeks by s.c. injection in combination with a fixed dose of MTX (10–25 mg). The recently completed phase 1 study investigated escalating doses of Dekavil (6–600 µg/kg +MTX). The ongoing randomised multicenter, double-blind, placebo-controlled phase 2 trial assesses therapeutic activity in two treatment groups (Dekavil 30 or 160 µg/kg plus MTX) and one placebo group (placebo plus MTX).

Results: Dekavil was well tolerated up to the highest investigated dose (600 µg/kg) and an MTD was not reached. In 34 out of 35 patients treated in the phase 1 study no SAEs and no SUSARs were reported. One subject (cohort 9, 450 µg/kg) experienced a DLT (G2 purpura), which was accompanied by an SAE (G2 dyspnea, not drug related). The patient fully recovered within one week following corticosteroid administration. The most frequently observed adverse event was mild (G1) injection site reaction and occurred in 60% of the patients. Furthermore, two cases of drug related anaemia (G3 and G2; 160 µg/kg and 450 µg/kg, respectively) were reported in this study. All adverse reactions resolved completely. After 4 cycles of treatment, 36.4% of patients (12/33) exhibited ACR responses. The fraction of responses increased to 45.8% (11/24) after 8 cycles. Two patients achieved an ACR70 for more than 12 months after the last drug administration. As of January 2018, 25 patients have been treated in the phase 2 clinical study and neither SUSARs nor treatment-related deaths were recorded. Immunogenicity assessment is completed for the first 20 study subjects did not reveal an antibody response specific to F8IL10. An interim read-out after 45 patients will provide a more thorough understanding of the therapeutic activity of F8IL10.