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THU0191 NOVEL FORMULATION OF CT-P13 FOR SUBCUTANEOUS ADMINISTRATION IN PATIENTS WITH RHEUMATOID ARTHRITIS: INITIAL RESULTS FROM A PHASE I/III RANDOMISED CONTROLLED TRIAL

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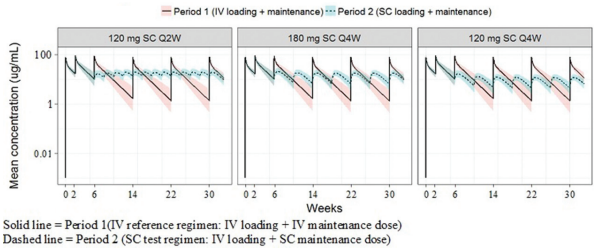
Background: While the treatment with intravenous (IV) CT-P13, an infliximab biosimilar, is effective and well tolerated, a new subcutaneous (SC) CT-P13 formulation (CT-P13 SC) is developed to provide additional, more convenient treatment options and opportunity for self-injection.
Objectives: To find the optimal dose of CT-P13 SC and to evaluate efficacy, PK and safety over the first 30 weeks in patients with rheumatoid arthritis.
Methods: This study consists of 1 cohort with CT-P13 IV, and 3 cohorts with 3 different doses of CT-P13 SC injected biweekly. All enrolled patients initially received CT-P13 IV at Weeks 0 and 2 and patients who received 2 full doses and displayed no safety concerns were randomly assigned to receive either CT-P13 SC or IV at Week 6. Using part 1 result, PK-PD modelling was conducted for the 3 regimens.
Results: A total of 50 patients were enrolled, of whom 48 patients were randomly assigned into 4 cohorts.
Overall, the efficacy results of CT-P13 SC up to Week 30 were comparable to those of CT-P13 IV. Disease improvement by DAS28 and ACR20 were comparable across all 4 cohorts, regardless of the route of administration or dosage of CT-P13 (table 1).
The safety profiles in CT-P13 SC cohorts were generally comparable to CT-P13 IV. One of the 2 patients who experienced a hypersensitivity reaction became anti-drug antibody (ADA) positive at Week 6 and experienced hypersensitivity from Week 2 to 8. All injection site reactions were grade 1 or 2. The proportion of ADA (positive) was lower in the SC cohorts.
In PK-PD modelling, bioavailability was 59% (95% CI, 52%–67%). The dose linearity in SC regimens was confirmed based on Weeks 22 to 30 C_{trough}, AUC_{τ} and $C_{max,\ ss}$ (figure 1). C_{trough} were greater (above 4 μg/mL) than the target exposure (1 μg/mL)[1][2] in all SC regimens. There was a trend towards slightly lower DAS28 score in all SC regimens, which was consistent with the higher C_{trough} comparing with CT-P13 IV. Based on the exposure-response safety analyses, there was no correlation between PK (AUC_{τ} or C_{max}) and safety (IRRs or infections).

Abstract THU0191 – Table 1. Efficacy and safety up to Week 30

		Cohort 1 IV 3 mg/kg (n=13)	Cohort 2 SC 90 mg (n=11)	Cohort 3 SC 120 mg (n=12)	Cohort 4 SC 180 mg (n=12)
DAS28 (CRP), mean ±SD	Week 0	5.4±0.8	6.3±0.8	5.7±0.9	5.5±0.8
	Week 6	3.9±1.5	4.6±1.1	3.9±1.2	3.4±1.2
	Week 22	3.9±1.6	3.7±1.0	3.3±1.4	2.8±1.3
	Week 30	3.3±1.3	3.0±1.1	3.1±1.0	2.7±1.0
ACR20, n (%)	Week 6	8 (61.5)	8 (72.7)	7 (58.3)	7 (58.3)
	Week 22	8 (61.5)	8 (72.7)	9 (75.0)	11 (91.7)
	Week 30	11 (84.6)	10 (90.9)	10 (83.3)	12 (100)
Safety, n (%)	Hypersensitivity/ IRR	0	1 (9.1)	1 (8.3)	0
	Injection site reactions	0	2 (18.2)	0	2 (16.7)
	Infections	4 (30.8)	2 (18.2)	0	4 (33.3)
	ADA	9 (69.2)	3 (27.3)	4 (33.3)	1 (8.3)



Abstract THU0191 – Figure 1. Mean (± SD) Simulated CT-P13 Serum Concentration vs Time Profiles for the Simulated Fixed Dose SC Maintenance Dosing Regimens with Overlaid IV Maintenance Reference Treatment (Semi-Logarithmic Scale). Solid line=Period 1 (IV reference regimen: IV loading+IV maintenance dose). Dashed line=Period 2 (SC test regimen: IV loading+SC maintenance dose)

Abstract THU0191 – Table 2. Summary of Steady State Median (Prediction Interval 5th-95th percentile) CT-P13 Exposure Results

Simulated Dose Regimen	C_{trough} (μg/mL)	$AUC_{22\text{-}30wk}$ (h·μg/mL)	C_{max} (μg/mL)
3 mg/kg IV every 8 weeks	1.53 (0.18 - 5.2)	16725.64 (9328.94 - 26297.08)	76.01 (52.73 - 103.21)
120 mg SC every 2 weeks	13.66 (6.66 - 24.25)	22717.66 (12849.49 - 37845.41)	18.95 (11.38 - 30.81)
180 mg SC every 4 weeks	6.66 (2.55 - 13.7)	17060.69 (9660.52 - 28442.43)	17.47 (11.13 - 26.76)
120 mg SC every 4 weeks	4.44 (1.7 - 9.14)	11375.19 (6440.93 - 18976.74)	11.65 (7.42 - 17.84)

Treatment continuation in patients enrolled with SB4 or oETN who were bionaive until enrollment.
Conclusions: CT-P13 SC showed comparable efficacy and safety with CT-P13 IV. The preliminary results suggest CT-P13 SC as a future alternative treatment of infliximab.

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[1] Takeuchi, et al. 2009.
[2] Mori, et al. 2007.

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THU0192 RETENTION RATES FOR ETANERCEPT: COMPARING THE ORIGINAL WITH A BIOSIMILAR

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Background: Since the first approval of a biosimilar in 2015, the number of biosimilars approved for the treatment of rheumatoid arthritis (RA) in Germany has been increasing. Until now, there are just a few analyses investigating retention rates of biosimilars and the respective originators.
Objectives: To compare treatment survival on SB4 to the originator etanercept (oETN) using real-world data.
Methods: We used data gathered until December 2017 from the prospective, longitudinal RABBIT (***R***heumatoid ***A***rthritis: O***b***servation of ***bi***ologic ***t***herapy) cohort. RA patients are enrolled in RABBIT when they start a biologic, biosimilar or new csDMARD treatment. For comparative analyses, patients starting SB4 either at enrollment or during follow-up were compared to patients enrolled with oETN since 2015. The drug survival rates during the first six months were analysed in biologic naive patients prior to enrollment using Kaplan-Meier curves.