SAT0139

A MULTICENTRE, RANDOMISED, DOUBLE-BLIND, PARALLEL ACTIVE-CONTROLLED CLINICAL TRIAL COMPARING PHARMACOKINETICS, PHARMACODYNAMICS, SAFETY AND EXPLORATORY EFFICACY BETWEEN HLX01 AND EUROPE-SOURCED RITUXIMAB AS A NEW INDICATION IN CHINESE MODERATE TO SEVERE PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Biologic products, such as rituximab and adalimumab, have revolutionized the treatment for chronic inflammatory disorders, providing an option to patients who were non-responsive to conventional systemic therapies. In China, rituximab is only approved for the treatment of certain haematologic malignancies. At present, there are several approved biosimilar drugs in Europe but none in China. HLX01, a China-manufactured proposed rituximab biosimilar, was first developed for patients with non-Hodgkin's lymphoma later as a new drug for the treatment for autoimmune diseases. Currently, HLX01's biosimilar NDA for the treatment of non-Hodgkin's lymphoma is being reviewed by authorities in China.

Objectives: Evaluation of clinical PK, safety and exploratory efficacy in RA patients to support the development of HLX01 for the treatment of autoimmune disease

Methods: We conducted a multi-centre, randomised, double-blind, parallel active-controlled clinical trial to compare the PK, PD safety and exploratory efficacy (ACR20 and DAS28-CRP) between HLX01 and Europe sourced rituximab (EU-RTX) as two-1000 mg intravenous infusions (Days 1 and 15) in moderately to severely active RA patients who have had inadequate response to treatment with disease-modifying antirheumatic drugs (DMARDs). The PK equivalence was achieved if 90% confidence intervals (CIs) for the test-to-reference ratios of area under the curve from time zero to infinity ($AUC_{(0-\infty)}$) and maximum observed concentration (C_{max}) fall within the pre-defined 80-125% equivalence margin.

Results: In the study, a total of 196 patients randomised at 1:1 ratio to HLX01 and EU-RTX and 179 subjects (88 in HLX01 group; 91 subjects in EU-RTX group) were included in the PK pre-protocol set (PPS). The 90% confidence intervals (CI) for the ratio of geometric means for the pairwise comparisons of the primary PK endpoint $AUC_{(0-\infty)}$ (Figure 1), as well as $AUC_{(0-14d)}$, $AUC_{(0-1)}$, $AUC_{(15d-1)}$, $C_{max,1}$, $C_{max,2}$, C_{min} were within the pre-specified limits of 80-125% (Table 1). Based on the ACR20 and DAS28-CRP results at week 24, HLX01 group and EU-RTX group are similar. In addition to the efficacy similarity, there was also no statistical difference in safety and immunogenicity between the two treatment groups.

PK parameters (Unit)	Geometric mean and its ratio				90%CI (%)	Inter- individual variation (%)	Power (%)	
	n	HLX01 (T)	n	MabThera (R)				Ratio (%)
Primary PK variables								
AUC _(0-∞) (μg* ^a h/mL)	88	200753.720	91	192435.090	104.32	96.49, 112.80	32.39	98.45
Secondary PK variables								
C _{max,1} (μg/mL)	88	404.81	91	388.18	104.28	99.54, 109.25	18.99	>99.1
C _{max,2} (μg/mL)	88	480.35	91	464.57	103.40	98.33, 108.72	20.52	>99.1
C _{min} (μg/mL)	88	75.09	91	71.38	105.20	95.09, 116.38	42.62	87.61
AUC _(0-14d) ^a (μg* ^a h/mL)	87	50488.920	91	48072.250	105.03	99.60, 110.75	21.64	>99.1
AUC ₍₀₋₁₎ (μg* ^a h/mL)	88	50722.070	91	48223.080	105.18	99.74, 110.92	21.75	>99.1
AUC _(15d-1) (μg* ^a h/mL)	88	146631.600	91	141854.640	103.37	93.52, 114.25	42.23	92.50

Note: T=1000 mg HLX01 (Shanghai Henlius Biotech, Inc.); R=1000 mg MabThera (Roche Pharma (Schweiz) Ltd.); *Parameter $AUC_{(0-14d)}$ of subjects 017022 in study drug group could not be calculated, thus a total of 87 subjects in HLX01 group were included in the statistical analysis of this parameter.

Conclusion: We report successful demonstration of similarity in PK, safety and initial efficacy between first China-manufactured biosimilar of rituximab, HLX01, and Europe-sourced rituximab in patients with moderately to severely active rheumatoid arthritis. These results support the Phase 3 confirmatory clinical trial for the development of HLX01 for the treatment of rheumatoid arthritis.

Disclosure of Interests: Xiaofeng Zeng: None declared, Yongfu Wang: None declared, Zhenyu Jiang: None declared, Zhuoli Zhang: None declared, Lan He: None declared, Xiao Zhang: None declared, Xin Lu: None declared, Xiumei Liu: None declared, Jian Xu: None declared, Cibo Huang: None declared, Rui Liu: None declared, Xiaoxia Zuo: None declared, Baozeng Zhao Employee of: Employee of Shanghai Henlius Biotech Inc., Wenting Qiu Employee of: Employee of Shanghai Henlius Biotech Inc., Katherine Chai Employee of: I am an employee of Shanghai Henlius, Xinjun Guo Employee of: Employee of Shanghai Henlius Biotech Inc., Xin Zhang Employee of: I am an employee of Shanghai Henlius Biotech, Inc., Eugene Liu Employee of: I am an employee of Shanghai Henlius Biotech, Inc., Alvin Luk Employee of: I am an employee of Shanghai Henlius Biotech, Inc., Weidong Jiang Shareholder of: I am the co-founder of Shanghai Henlius Biotech, Inc., Employee of: I am an employee of Shanghai Henlius Biotech, Inc., Scott Liu Shareholder of: I am the CEO of Shanghai Henlius Biotech, Inc., Employee of: I am an employee of Shanghai Henlius Biotech, Inc., Pei Hu: None declared, Xia Chen: None declared

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SAT0140

COMPARATIVE EFFECTIVENESS OF TOFACITINIB AND NON-TNF AGENTS SINCE 2014. IMPACT OF COMBINATION WITH METHOTREXATE

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Background: Tofacitinib (TOFA), a targeted synthetic DMARD, has been approved for the treatment of rheumatoid arthritis (RA) in Canada since April 2014. This oral agent preferentially inhibits signalling by cytokine receptors associated with JAK1 and JAK3 subunits. It is now indicated for the treatment of psoriatic arthritis (PsA) and ulcerative colitis (UC) since October 2018. Clinical experience with this molecule has been increasing, and questions relating to its efficacy and long-term safety are of interest. Data collection through RHUMADATA[®], a Quebec based clinical database and registry, allows comparison of various advanced treatment options including TOFA and non-TNFi biologic agents (i.e., agents with other modes of action - OMA) such as fusion proteins (abatacept), and IL-6 (sarilumab, tocilizumab) and CD20 inhibitors (rituximab).

Objectives: This analysis compares TOFA and OMAs used with and without methotrexate (MTX).

Methods: Data collected since January 1, 2014 (since TOFA became available in Canada) at the Institut de Recherche en Rhumatologie de Montréal (IRRM) and the Centre de l'Ostéoporose et de Rhumatologie de Québec (CORQ) was extracted from the Rhumadata[®] on January 7,