OP0210

EFFICACY AND SAFETY OF SM03, A RECOMBINANT ANTI-HUMAN CD22 MONOCLONAL ANTIBODY IN CHINESE PATIENTS WITH RHEUMATOID ARTHRITIS: A PHASE II RANDOMIZED, DOUBLE-BLIND, MULTI-DOSE, PLACEBO-CONTROLLED STUDY

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Background: Rheumatoid arthritis (RA) is a common chronic inflammatory rheumatic disease in China. SM03 is a novel chimeric monoclonal antibody (mAb) specific to the B cell restricted antigen CD22 developed for the treatment of rheumatoid arthritis (RA) and other B cell related immunological diseases.

Objectives: We aim to evaluate the efficacy and safety of SM03 in patients with moderately-to-severely active RA in China.

Methods: In this 24-week Phase II randomized, double-blind, multi-dose, placebo-controlled study, 156 patients were randomized with ratio of 1:1:1 to receive 3600mg cumulative dose of SM03 (group A, 600mg * 6 infusions at 0, 2, 4, 12, 14, and 16 week), 2400mg cumulative dose of SM03 (group B, 600mg*4 infusions at 0, 2, 12, and 14 week) and placebo (group C). All patients remained on background treatment of MTX. Efficacy and safety were assessed at weeks 4, 8, 12, 16 and 24. The primary efficacy end point was the American College of Rheumatology 20% improvement criteria (ACR20) response rate at week 24. Safety profile was also assessed.

Results: ACR20 response rates at 24-week were significant for group A (65.3%, $p=0.002$) and B (56.9 %, $p=0.024$) versus group C (34.0%). There is no significant difference in ACR20 between group A and B (Table 1 & Fig 1). We did not observe significant difference in any adverse event (AE) among group A (35.3%), B (51.9%) and C (34.6%) (Table 2). In groups A and B, 13 (12.6%) patients reported treatment-related infection, and 5 (6.8%) patients were positive in anti-drug antibodies analysis. In group A (higher dose), 3.9% patient had AE of treatment-related infections. No patients reported treatment-related severe infection or any malignancies caused by treatment in groups A and B.

Table 1. Summary of ACR/DAS EULAR Responses of Patients with RA to SM03 at Week 24

Response	Group C Placebo+MTX (n=47)	Group A SM03 600mg*6+MTX (n=49)	Group B SM03 600mg*4 +MTX (n=51)
ACR 20	34.0%	65.3% *	56.9% *
ACR 50	17.0%	44.9%**	29.4%
ACR 70	4.3%	18.4%***	9.8%
EULAR response good & moderate	40.4%	75.5%^	70.6%^
EULAR response good	12.8%	30.6%^^^	15.7%
Change of DAS28 from baseline	-0.70	-1.65^^^	-1.38^^^
DAS28≤3.2	14.9%	30.6%	19.6%
DAS28<2.6	8.5%	18.4%	5.9%

Compared with group C(Placebo), results of group A and B were shown respectively

* $P=0.002$, $P=0.024$; ** $P=0.003$; *** $P=0.03$;

^ $P<0.001$, $P=0.003$; ^^ $P=0.034$; ^^ $P=0.008$, $P=0.047$

Table 2. Profile of Adverse Events

Adverse event, N (%)	Group C(N=52)	Group A(N=51)	Group B(N=52)
Any AE	18(34.6)	18(35.3)	27(51.9)
AE-drug related	7(13.5)	5(9.8)	8(15.4)
AE-mild	16 (30.8)	15(29.4)	24(46.2)
AE-moderate	2(3.8)	2(3.9)	3(5.8)
AE-severe	-	1(2.0)	-
AE-leading to discontinuation	-	2(3.9)	-
Serious adverse event, SAE	1(1.9)	1(2.0)	-
AE-1 st cycle(week 0-12)	15	13	22
AE-2 nd cycle(week 12-24)	9	9	14

Conclusion: In Chinese patients with active RA, both 2400mg and 3600mg cumulative dose of SM03, in combination with MTX were efficacious and well tolerated throughout the 24 weeks of treatment. Moreover, SM03 has demonstrated a good safety profile, especially in terms of treatment-related infection, malignancy and immunogenicity.

References: None

Disclosure of Interests: None declared

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Fig 1. Percent of Patients Achieving ACR 20 Response by Visit

OP0211

TIME TO DISCONTINUATION OF TOFACITINIB AND TNF INHIBITORS IN RHEUMATOID ARTHRITIS PATIENTS WITH AND WITHOUT METHOTREXATE: DATA FROM A RHEUMATOID ARTHRITIS COHORT

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Background: Tofacitinib (TOFA) is an oral, small molecule drug used for rheumatoid arthritis (RA) treatment and is prescribed alone or with methotrexate (MTX). ToFA can be used as an alternative to biologic disease modifying anti-rheumatic drugs (bDMARDs) including tumor necrosis factor inhibitors (TNFi).

Objectives: We aimed to evaluate the discontinuation rate of this drug, with and without concurrent MTX in comparison with TNFi, in patients with RA in the Ontario Best Practices Research Initiative (OBRI).

Methods: RA patients enrolled in the OBRI initiating their TOFA or TNFi (adalimumab, certolizumab, etanercept, golimumab, and infliximab) within 30 days prior to or any time after enrolment between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2018 were included. Time to discontinuation (due to any reason) were assessed using Kaplan-Meier survival (adjusted for propensity score using inverse probability of treatment weight) to compare patients with and without MTX use at initiation of TOFA or TNFi.

Results: A total of 565 patients initiated TOFA (n=208) or TNFi (n=357). Of those, 106 (51%) and 222 (62%) were treated with MTX in the TOFA and TNFi group, respectively and mean (SD) disease duration were 13.1 (9.4) and 9.5 (9.4) years. In the TOFA group, 86% were female and mean (SD) age at treatment initiation was 60.4 (10.6) years. In the TNFi group 82% were female and mean age (SD) at treatment initiation was 57.0 (12.6) years. The TOFA group was more likely to have prior biologic use (61.5%) compared with the TNFi group (31%). At treatment initiation, the mean (SD) clinical disease activity index was 24.8 (12.1) in the TOFA group and 21.8 (12.0) in the TNFi group.

Over a mean of 17.3 month follow-up, discontinuation was reported in 75 (36%) and 103 (29%) of all TOFA and TNFi patients, respectively. After adjusting for propensity score, patients treated with TNFi and MTX remained on treatment longer than those treated without MTX (Logrank $p=0.002$) while there was no significant difference in TOFA discontinuation in patients with and without MTX (Logrank $p=0.31$).

Conclusion: In this real world data study, we found that TOFA retention is similar in patients with and without MTX, while patients treated with TNFi and MTX remained on treatment longer than those treated without MTX. Merging data with other RA registries in Canada is proposed to increase study power and to provide more robust results.

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