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.

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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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OP0212

ABATACEPT IN INTERSTITIAL LUNG DISEASE ASSOCIATED WITH RHEUMATOID ARTHRITIS. NATIONAL MULTICENTER STUDY OF 263 PATIENTS

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Background: Interstitial Lung Disease (ILD) is a severe complication of Rheumatoid Arthritis (RA). Several conventional disease-modifying anti-rheumatic drugs (cDMARDs) and biologic (b) DMARDs may induce or impaired ILD-RA. Abatacept (ABA) may be useful in ILD-RA (1).

Objectives: To assess the efficacy and safety of ABA in a large series of ILD-RA for a long-term follow-up.

Methods: Multicenter open-level study of ILD-RA treated with at least 1 dose of ABA. ILD was diagnosed by high-resolution computed tomography (HRCT). We study these outcomes: a) 1-point change Modied Medical Research Council (MMRC); b) forced vital capacity (FVC) and/or DLCO improvement or decline $\geq 10\%$; c) change in HRCT, d) change in DAS28. e) Prednisone dose. Values were collected at 0, 3, 6, 12 and then every 12 months.

Results: We studied 263 patients (150 women/113 men) (mean age; 64.6 ± 10 years), with ILD-RA. At ABA-onset they were smokers or exsmoker (53.8%), positive APCC (88.6%), median [IQR] duration of ILD of 12 [3-41.25] months, mean DLCO (65.7 ± 18.3) and FVC (85.9 ± 21.8).

The ILD-pattern were usual interstitial pneumonia (UIP) (40.3%), non-specific interstitial pneumonia (NSIP) (31.9%) and others (27.8%).

ABA was prescribed at standard subcutaneous (125 mg/w) in 196 (74.5%) or intravenously (10 mg/kg/4 w) in 67 (25.5%); in monotherapy (n=111) or combined with cDMARDs (n=152); especially leflunomide (n=55), MTX (n=46), or antimalars (n=21).

After a mean follow-up of 22.7 ± 19.7 months most outcomes remain stable (Figure). Moreover, DAS28 improved from 4.5 ± 1.5 to 3.1 ± 1.3 ; prednisone dose reduced from a median 7.5 [5-10] to 5 mg [5-7.5] and retention rate was 76.4%. The main adverse effects were serious infections (n=28), neoplasia (n=3), serious infusion reaction (n=1) and myocardial infarction (n=1).

Conclusion: ABA seems effective and relatively safe in ILD-RA.

References:

[1] Fernández-Díaz C et al. Semin Arthritis Rheum. 2018; 48:22-27

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OP0213

THE IMPACT OF TNFA INHIBITORS ON GLUCOCORTICOIDS USE AMONG PATIENTS WITH ARTHRITIS

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Background: Glucocorticoid steroid (GC) use among patients with arthritis is common. The introduction of TNF α inhibitors (TNFi) has been a breakthrough in the treatment of arthritis leading to remission for many patients. However, there is scarce information on the impact of TNFi on the use of GC among patients with inflammatory joint diseases.

Objectives: To explore oral GC use in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA) before and after the initiation of TNFi therapy. Furthermore, to evaluate if patients on long term GC treatment were receiving active preventive osteoporosis treatment and how treatment with TNFi affected the use of topical steroids in patients with PsA.

Methods: Clinical data on patients with RA, PsA and axSpA who initiated TNFi therapy with etanercept, infliximab, adalimumab or golimumab for the first time between 2005-2015 was collected from the ICEBIO registry. ICEBIO is a nationwide registry on all patients treated with biologics for rheumatologic disorders in Iceland. The use of oral GC, topical steroids and bisphosphonates was collected from the Icelandic Prescription Medicines Registry (IPMR) for a period of four years, two years before and after the initiation of TNFi. Medication use was then evaluated by counting the number of individuals receiving a medication in a given year, the total number of prescriptions, and the defined daily dose (DDD). Five controls were randomly selected from IPMR and matched on age, sex and time frame.

Results: 621 patients with RA, PsA or axSpA received 2630 prescriptions (4.2 prescription per patient; 3105 controls received 1337 prescriptions or