Table 2. Changes in RA parameters in patients treated with tofacitinib, n=374 (M±SE).

Disease characteristics	Baseline	Year 1 [#]	Year 2 [#]	Year 3 [#]
C-RP, mg/L	30.1±35.0	8.3±12.8	7.6±10.7	9.4±13.5
ESR, mm/h	35.2±21.2	22.7±17.2	21.9±17.7	22.3±17.3
NTJ from 28	11.2±6.5	4.6±4.9	4.8±5.0	3.9±3.8
NTJ from 28	7.6±5.1	2.4±3.2	1.7±3.1	1.4±2.8

*difference with baseline is significant with $p < 0.000$. [#] - ±28 days

Conclusion: According to the real world data treatment with tofacitinib may provide good response rates in RA patients, refractory to the previous csDMARDs treatment in long-term perspective.

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SAT0142

MATCHING ADJUSTED INDIRECT COMPARISON OF FILGOTINIB VS. TOFACITINIB IN MODERATE-TO-SEVERE ACTIVE RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO METHOTREXATE

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Background: Filgotinib (FILG) is a JAK1 inhibitor that has been investigated in combination with methotrexate (MTX) for the treatment of moderate-to-severe rheumatoid arthritis (RA). To date, no head-to-head trial has compared the efficacy of FILG versus tofacitinib (TOFA).

Objectives: To compare the efficacy of FILG 200 mg + MTX with TOFA 5 mg + MTX using matching adjusted indirect comparison (MAIC).

Methods: MAIC technique uses individual patient data (IPD) from one trial and aggregate data from the other to enable comparison of outcomes after matching on baseline characteristics [1]. An anchored MAIC was conducted using IPD from the FINCH-1 trial of FILG 200 mg + MTX vs adalimumab (ADA) 40 mg + MTX and published data from ORAL STRATEGY [2] trial of TOFA 5 mg + MTX vs ADA 40 mg + MTX. Patients in the FINCH-1 trial were reweighted based on age, sex, race, tender joint count 28, swollen joint count 28, C-reactive protein and patient's global assessment to match baseline characteristics of the comparator. After matching, Wald tests were used to test for significant differences in ACR 20/50/70 and clinical remission outcomes (SDAI≤3.3, CDAI≤2.8, DAS28(CRP)<2.6, Boolean) between FILG + MTX vs TOFA 5 mg + MTX relative to ADA 40 mg + MTX.

Results: After matching, baseline characteristics were balanced across the trial populations [Table 1]. FILG 200 mg + MTX patients experienced significantly greater improvement in 12 week ACR50 and ACR70 outcomes compared to TOFA 5 mg + MTX with a mean difference in difference (DD) of 13.5% ($p < .05$) and 8.3% ($p < .05$) respectively, as well as numerical improvements on other ACR outcomes at 12, 24 and 52 weeks [Figure 1]. At 24 weeks, FILG 200 mg + MTX patients experienced significantly greater improvement in DAS28(CRP) clinical remission compared to TOFA 5 mg + MTX with DD of 10.1% ($p < .05$) [Figure 2] as well as numerical improvements on other efficacy outcomes. At 52 weeks, FILG 200 mg + MTX patients experienced significantly greater improvement in DAS28(CRP) clinical remission compared to TOFA 5 mg + MTX with DD of 13.2% ($p < .05$) [Figure 2] as well as numerical improvements on other efficacy outcomes.

Table 1. Baseline Characteristics of FINCH-1 vs ORAL STRATEGY

CHARACTERISTIC	BEFORE MATCHING		AFTER MATCHING		ORAL STRATEGY	
	FILG 200 + MTX (N=475)	ADA + MTX (N=325)	FILG 200 + MTX (ESS=340)	ADA + MTX (ESS=233)	TOFA 5mg + MTX BID (N=376)	ADA + MTX BID (N=386)
Sex – Female, %	79.8%	81.8%	83.0%	83.0%	83.0%	83.0%
Age (year), mean (SD)	51.8 (12.8)	53.3 (12.9)	50.0 (13.4)	50.7 (13.4)	50.0 (13.4)	50.7 (13.4)
Race – White, %	65.7%	70.5%	76.0%	76.0%	76.0%	76.0%
Tender Joint Count	15.0 (6.4)	14.6 (6.3)	15.6 (6.5)	15.2 (6.7)	15.6 (6.5)	15.2 (6.7)
28, mean (SD)						
Swollen Joint Count	11.2 (5.2)	11.2 (5.0)	11.8 (5.7)	11.0 (5.4)	11.8 (5.7)	11.0 (5.4)
28, mean (SD)						
C-Reactive Protein (mg/L), mean (SD)	16.1 (21.0)	14.6 (18.0)	18.7 (21.9)	16.7 (21.3)	18.7 (21.9)	16.7 (21.3)
Patient global assessment baseline, mean (SD)	67.1 (19.2)	67.0 (19.1)	61.7 (22.0)	60.2 (23.5)	61.7 (22.0)	60.2 (23.5)

ESS = effective sample size; SD = standard deviation

* $p < .05$

Figure 1. ACR20/50/70 relative to ADA 40 mg+ MTX of FILG 200mg + MTX vs TOFA 5 mg + MTX* $p < .05$

* $p < .05$

Figure 2. Clinical Remission outcomes relative to ADA 40 mg+ MTX of FILG 200mg + MTX vs TOFA 5 mg + MTX * $p < .05$

Conclusion: In this MAIC, compared to TOFA 5 mg + MTX, FILG 200 mg + MTX appears to produce improved efficacy outcomes (ACR20/50/70, DAS28(CRP), SDAI, CDAI and Boolean Remission) at weeks 12, 24 and 52.

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SAT0143

A PHASE 1 STUDY IN HEALTHY VOLUNTEERS EXPLORING THE SAFETY, PHARMACOKINETICS AND PHARMACODYNAMICS OF ATI-450: A NOVEL ORAL MK2 INHIBITOR

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Background: ATI-450, is an investigational small molecule inhibitor of the MAPK-activated protein kinase 2 (MK2) signaling pathway. This pathway drives the expression of multiple cytokines including TNF α , IL-1 α and β , and IL-6.

Objectives: We evaluated the safety and tolerability of ATI-450 in healthy volunteers as well as pharmacokinetics (PK) and pharmacodynamics (PD). Here we present data from single and multiple ascending dose cohorts. The aim was to select a dose for evaluation in phase 2 in patients with rheumatoid arthritis.

Methods: Safety, PK and PD were assessed in a randomized, observer-blind, placebo-controlled, phase 1 study in male and female healthy subjects aged 18-55 (n=77).

- Part A: Single Ascending Dose (SAD) (n=32, 8 subjects per dose cohort - 2 placebo, 6 active). A single dose of 10mg, 30mg, 50mg and 100mg was tested.
- Part B: Multiple Ascending Dose (MAD) (n=30, 10 subjects per dose cohort - 2 placebo, 8 active). 10mg BID, 30mg BID and 50mg BID doses were tested over 7 days of administration.

Safety and tolerability of ATI-450 was evaluated based on adverse events, clinical laboratory, vital signs, 12-lead ECG, Holter monitoring, and physical examination. Blood was drawn for PK analysis at 0.5, 1, 2, 4, 6, 8, 12 hours, 24, 36, and 48 hours post dose in the SAD cohort and on day 7 of the MAD cohort. PD of ATI-450 were explored by investigating the inhibition of a target biomarker, phospho-HSP27 (pHSP27) and proinflammatory cytokines, TNF α , IL1 β , IL6 and IL8 in ex-vivo LPS-stimulated blood samples collected 4 and 12 hours post dose on day 7 from subjects in the MAD cohorts.

Results: ATI-450 was generally well tolerated. No serious adverse events or severe adverse events were reported, and no adverse events led to discontinuation of the study medication. The most common adverse events (reported by 2 or more subjects who received ATI-450) observed during the trial were dizziness, headache, upper respiratory tract infection, constipation, nausea, and abdominal pain. All adverse events were mild. A trend of a decrease in absolute neutrophil count (ANC) was observed without correlated clinical sequelae.

ATI-450 had dose proportional PK with a terminal half-life ($t_{1/2}$) of 9-12 hours in the MAD cohort on day 7. A dose and concentration dependent inhibition of ex vivo stimulated cytokines and target biomarker was observed. On day 7, patients in the 50mg BID dose (the dose with the highest degree of inhibition) recorded mean trough drug levels (12 hours post dose) that were 1.4, 2.5, 2.5 and 2.4 times greater than the IC_{50} for TNF α , IL1 β , IL8 and pHSP27 respectively. Mean C_{max} drug levels (4 hours post dose) were 3.6, 6.4, 6.2 and 6.0 times greater than the IC_{50} for TNF α , IL1 β , IL8 and pHSP27 respectively. IL6 levels were inhibited by more than 50% for part of the dosing interval.

Conclusion: Oral ATI-450 was generally well tolerated at all doses with dose proportional PK. The $t_{1/2}$ suggests that once or twice daily oral dosing may be possible. At the 50mg BID dose, marked inhibition of TNF α , IL1 β and IL8, IL6 and pHSP27 was observed. ATI-450 has the potential to be an oral, small molecule drug which can target multiple cytokines. Exploration of its benefit to risk profile in patients with rheumatoid arthritis is warranted.

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SAT0144

DOES POLYPHARMACY IN RHEUMATOID ARTHRITIS PATIENTS AFFECT THE TREAT TO TARGET STRATEGY?

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Background: Polypharmacy (PP) is an important risk factor for drug toxicity, delirium, falls, hospitalizations and death. Patients with rheumatoid arthritis (RA) often have comorbid conditions and have PP. Treat to target strategy (T2T) implies a drug escalation and rheumatologists may not apply it in patients with PP.

Objectives: Our objective was to analyze if PP affects T2T in a real-world scenario.

Methods: Observational, retrospective cohort study. Patients with a new RA diagnosis (ACR/EULAR 2010 criteria) after 2010, over 18 years old, belonging to a Health Management Organization (HMO) from a university tertiary hospital, with a minimum follow-up period of 2 years, were included. PP was defined as consumption greater than or equal to 5 medications at the time of RA diagnosis, regardless of the medication used for RA, administered for a minimum period of 6 months. T2T strategy was defined as accomplished if an escalation in treatment was done when the patient had moderate or high disease activity at medical visit (by DAS28 and/or CDAI), without a significant improvement with respect to the previous visit. Prevalence of PP at RA diagnosis was calculated and RA patients were divided in those with PP at RA diagnosis time and those without. The first 2 years of disease were analyzed and compare between both groups: clinical and demographic characteristics, percentage of visits where T2T was applied, treatments received during that period. A multivariate logistic regression analysis was performed in order to identify factors associated with no T2T compliance.

Results: 147 patients with RA were included, 86% women, with an average age at diagnosis of 60 years (SD: 15.8). The prevalence of PP at RA diagnosis was 12% (17 patients). Table 1 shows the comparison between patients with and without PP. Patients with PP showed a greater frequency of erosions at baseline and after 2 years of disease, a greater use of corticosteroids at 2 years, higher percentage of hospitalizations and a higher mortality. In the multivariate logistic regression analysis, no compliance of the T2T strategy was only associated with the consumption of corticosteroids at 2 years (OR: 0.36, CI95%: 0.15-0.85; p=0.019) and no association was found with PP at the beginning of the disease.

Table 1. Demographic and clinical characteristics in patients with and without polypharmacy.

	Patients without Polypharmacy (n= 127)	Patients with Polypharmacy (n= 17)	P
Male sex, n (%)	18 (13.8)	3 (17.6)	0.6
Mean age at diagnosis (SD)	58.5 (15.6)	70.6 (12.2)	0.9
Positive rheumatoid factor, n (%)	87 (66.9)	12 (70.5)	0.7
Positive anti CCP, n (%)	109 (85.8)	13 (81.2)	0.6
Erosions at baseline, n (%)	25 (19.2)	7 (41.1)	0.03
Active smoker, n (%)	28 (21.5)	3 (17.6)	0.2
Past smoker, n (%)	23 (17.6)	7 (35.2)	
Charlson score, median (IQR)	3 (1-4)	4 (4-5)	<0.0001
Polypharmacy at 2 years, n (%)	17 (13.0)	46.8 (88.2)	<0.0001
Rheumatological consultations in 2 years, mean (DE), (IC 95%)	8.6 (3.3) (8.0-9.2)	8.8 (3.1) (7.2-10.5)	0.6
Corticosteroid therapy at 2 years, n (%)	29 (22.3)	8 (47.0)	0.02
cDMARDs therapy at 2 years, n (%)	114 (87.6)	13 (76.4)	0.2
Biologic therapy at 2 years, n (%)	13 (10)	4 (23.5)	0.1
Erosions at 2 years, n (%)	29 (22.3)	9 (52.9)	0.007
No T2T compliance, n (%)	65 (50)	5 (29.4)	0.1
Hospitalizations, n (%)	12 (9.2)	7 (41.1)	<0.0001
Mortality, n (%)	2 (1.5)	2 (11.7)	0.01

Conclusion: The prevalence of PP in our patients with a new RA diagnosis was 12% and was associated with more baseline erosions, a higher consumption of steroids, and a higher frequency of hospitalizations and mortality during the first 2 years of the disease. No relationship between PP and adherence to the T2T strategy was demonstrated. In the multivariate logistic regression analysis, no compliance with the T2T strategy was only associated to the consumption of corticosteroids at 2 years, may be reflecting a poorer disease control.

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