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SAT0140

SAFETY OF TOFACITINIB THERAPY IN HBsAg CARRIERS WITH RHEUMATOID ARTHRITIS: A PROSPECTIVE STUDY

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Background: Targeted synthetic DMARDs (ts-DMARDs) are becoming more available and affordable in developing countries, where the prevalence of hepatitis B virus (HBV) infection is still an important public health issue. The safety of ts-DMARDs therapy in terms of the reactivation of hepatitis B virus (HBV) infection need more concern. Rare data from a prospective study focus on the use of ts-DMARDs in patients with concurrent rheumatoid arthritis (RA) and HBV infection were available by now.

Objectives: To evaluate the influence of tofacitinib on reactivation of HBV infection in HBsAg carriers with RA.

Methods: In this 52 weeks observation, HBsAg carriers with active RA (DAS28>5.1) despite failed combined treatment with MTX and other non-biological DMARDs were enrolled. Patients must have normal liver function prior to study. All patients received therapy with tofacitinib (5mg twice daily) and concomitant MTX (10-12.5mg/w). Entecavir was prescribed preventively for patients who had a baseline HBV load >2000 copy/ml (group 1), and Lamivudine for patients with HBV load ≤ 2000 copy/ml (group 2). Liver enzymes (AST/ALT) and HBV viral load were monitored every 4 weeks. Increased viral load and abnormal liver function were managed according to expert opinion.

Results: Thirteen patients (10 female) were recruited. Nine patients had a baseline viral load >2000 copy/ml (group 1, with preventive Entecavir), and the other 4 patients had a viral load ≤ 2000 copy/ml (group 2, with preventive Lamivudine). Two patients from group 1 discontinued tofacitinib at week 12 due to ineffectiveness, and both continued taking Entecavir for another 3 months after the discontinuation of tofacitinib.

No reactivation of hepatitis B was observed in patients from group 1. One patient (female, 54 years old) from group 2 underwent a mild increase of both ALT and AST (67 and 56 IU/L, respectively) at week 16. An elevated viral load (4.9e6 copies/ml, baseline 1.4e3) and a HBV YMDD mutant was also found. The tofacitinib treatment continued. After prescription of Adefovir (combined with the pre-existing Lamivudine), both liver enzyme and viral load decreased to normal range in 8 weeks and remained normal throughout the study.

Conclusion: An aggressive Tofacitinib + MTX therapy may be a safe option for HBsAg carriers with cs-DMARDs refractory RA. More active and effective prophylaxis strategy may be recommended to reduce the risk of HBV reactivation during the treatment.

References:

- Chen YM, Huang WN, Wu YD, et al. Reactivation of hepatitis B virus infection in patients with rheumatoid arthritis receiving tofacitinib: a real-world study. *Ann Rheum Dis* 2018; 77:780-2.

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SAT0141

LONG-TERM EFFECTIVENESS OF TOFACITINIB IN CONVENTIONAL DMARDs NON-RESPONDERS WITH RHEUMATOID ARTHRITIS: RESULTS OF RUSSIAN NATIONAL REGISTER

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Background: Tofacitinib is an oral Janus Kinase inhibitor for the treatment of rheumatoid arthritis (RA).

Objectives: To evaluate the three-year effectiveness of tofacitinib in RA conventional synthetic (cs) DMARDs non-responders.

Methods: Data from 374 patients from Russian national register OREL of patients with RA treated with tofacitinib not less than 3 years after failure of conventional DMARDs were included in the statistical analysis. Clinical and laboratory data from 4 consecutive visits with an interval of 12 months between the visits (± 28 days) were analyzed. Treatment with any biologics ever was an exclusion criteria. Demographic (age, sex) and disease-related characteristics of RA (symptoms duration, RF- and ACCP positivity, presence of joint erosions, DAS28, CDAI, number of tender and swollen joints (NTJ, NSJ), erythrocytes sedimentation rate (ESR), C-reactive protein (CRP)) collected. Statistical analysis performed with statistical programs SPSS2017 and GraphPadPrizm. p-value < 0.05 considered as significant.

Results: Baseline characteristics of RA patients, involved in the analysis are presented in table 1.

Table 1. Baseline characteristics of the patients with RA (n=374).

Parameter	Characteristics
Male, n (%)	92 (24.5)
Age, years (mean±SD)	53.4±13.38
Symptoms duration, month (mean±SD)	140±137
Positive rheumatoid factor (RF), n (%)	123(32.8)
Positive antibodies to cyclic citrullinated peptide (ACCP), n (%)	329(87.9)
Erosions of hand joints (X-rays), n (%)	372 (99.4)
BMI, kg/m ² (mean ±SD)	26.8 ± 6.14
Smokers (current and in the past), n (%)	54 (14.4)

Changes in the diseases activity parameters in patients with RA, treated with tofacitinib not less than 3 years after cs DMARD failure are presented in table 2, figure 1, and figure 2.

Figure 1. DAS28 of patients with RA, treated with tofacitinib (n=374) – 3-years follow-up (time-points are presented in years ± 28 days).

Figure 2. DAS28 of patients with RA, treated with tofacitinib (n=374) – 3-years follow-up (time-points are presented in years ± 28 days).

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.

References:

- Signorovitch JE, et al. "Matching-adjusted indirect comparisons: a new tool for timely comparative effectiveness research." *Value in Health* 15.6 (2012): 940-947
- Fleischmann R, et al. "Efficacy and safety of tofacitinib monotherapy, tofacitinib with methotrexate, and adalimumab with methotrexate in patients with rheumatoid arthritis (ORAL Strategy)." *The Lancet* 390.10093 (2017): 457-468

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