**Conclusions:** Older age, hypoalbuminaemia and renal failure might be poor prognosis factors for low dose MTX-induce myelosuppression in RA.
**Disclosure of Interest:** None declared
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## THU0202 UNAFFORDABLE CONVENTIONAL AND ABSENT BIOLOGIC DMARDS: INCREASING THE BURDEN OF RHEUMATOID ARTHRITIS IN FYROM

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**Background:** In the developing world rheumatologists and their patients are struggling to implement treat to target therapy in established Rheumatoid Arthritis (RA)which means they can hardly establish remission and low disease activity which is the mainstay of the RA treatment. The main reason is the lack of conventional synthetic and biological (c and b) DMARDs in the therapeutic armamentarium as well as their high cost which increases already difficult burden of RA.
**Objectives:** The aim of the study is to evaluate the RA treatment and treatment expenses in a group of patients with established RA in FYR of Macedonia including the availability of DMARDs.
**Methods:** We have conducted a cross-sectional study at the University Rheumatology Clinic in Skopje, including 100 patients with established RA, who fulfilled RA classification criteria from 2010. Physical examination, laboratory analyses and DAS28 were performed and all patients filled a questionnaire with 13 questions about treatment expenses and availability.
**Results:** There were 82 females and 18 males, with mean age of 59 and disease duration of 8.3 (SD 7,3) years and moderate disease activity DAS28 3,9+/-1,47 and 75% of seropositive RA (double positive 30%, Ant-CCP positive 30%, RF positive 15%) with mean CRP of 21,5 mg/L They spend from 10 to 100 Euros monthly (on average 27+/-17,6) for the cs DMARDs therapy. Almost 80% think that the cs DMARDs therapy is too expensive for them and 100% of them could not afford to pay or co-pay for b DMARDs. Most of the patients (49%) are using single cs DMARDs. Double and triple c DMARD therapy is used by 32% vs 17%, respectively. Even though it is highly effective, patients consider triple cs DMARD therapy expensive and with very low compliance because of the high costs and low tolerability. Only 2% of the patiens are using b DMARDS using rituximab, the only available biologic DMARD therapy in FYROM. Around 70% are taking low dose prednisolone. Almost 50% of the patients cannot take the cs DMARD therapy with a prescription and have to buy their DMARDS without any coverage from the insurance fund and the same percent have problems to find the c DMARDs with prescription because it is not available. Almost half of the patients have heard about the b DMARDs, most of them from their rheumatologist and 54% of them would like to receive it. The patient's reasons for taking b DMARDs are presented in Graph 1.
**Conclusions:** High expenses and low availability of c DMARDs on prescription and the urgent need for b DMARDs are adding the burden of RA in developing countries including FYROM with the increased need for full coverage for conventional DMARDs and at least partial coverage of biologic DMARDs, especially anti-TNF agents by the insurance companies. The use of biosimilars might be highly appreciated in the future.
**References:**
[1] Aletaha D, Neogi T, Silman AJ et al. 2010 Rheumatoid arthritis classification criteria: An ACR/EULAR collaborative initiative. Arthritis Rheum 2010; 9 (62):2569–2581.
[2] O'Dell JR. Therapies for active rheumatoid arthritis after methotrexate failure N Engl J Med 2013; 369:307–318.
[3] Avci AB, Feist E, Burmester GR. Biologicals in rheumatoid arthritis current and future RMD Open 2015.
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## THU0203 CHANGES IN C-REACTIVE PROTEIN AND LIPID LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH ABT-494, A SELECTIVE JAK-1 INHIBITOR

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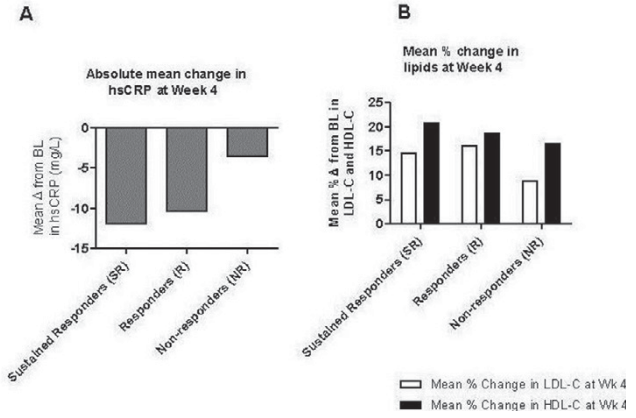
**Background:** In patients (pts) with rheumatoid arthritis (RA) treated with ABT-494, dose-dependent increases in levels of low and high density lipoprotein cholesterol (LDL-C and HDL-C) were observed, along with decreases in levels of C-reactive Protein (CRP). Whether these changes are due to the control of inflammation or a direct effect on CRP production in the liver is not known.
**Objectives:** To explore the relationship between changes in HDL-C or LDL-C and CRP with ABT-494 treatment, and to assess whether the effect on lipids is dependent on improvement of RA signs and symptoms.
**Methods:** Data were from two phase 2b controlled trials of ABT-494 in RA pts with inadequate response or intolerance to TNF inhibitors (TNF-IR, BALANCE-1)[1], or with inadequate response to methotrexate (MTX-IR, BALANCE-2)[2]. Pts treated with placebo or 3,6,12,18 mg ABT-494 twice daily for 12 weeks (wks) are included. Levels of high sensitivity (hs) CRP, total cholesterol (TC), LDL-C and HDL-C were measured at baseline (BL) and Wk 2,4,6, 8 and 12. Atherogenic burden at BL and Wk 12 was assessed by ratio of ApoB:ApoA1 and TC:HDL-C in 6 mg and 12 mg dose groups in both studies. Pearson's coefficients were calculated *post hoc* to assess possible correlations between HDL-C or LDL-C levels (or changes from BL) with other variables including (high sensitivity) hsCRP, at BL and Wk 12. Pts were subgrouped by response: Sustained responders (SR), pts who achieved an ACR20 response at every visit from Wk 2–12; Responders (R), pts who achieved ACR20 at least once, but not at every visit; Non-responders (NR), pts who did not achieve ACR20 at any visit.
**Results:** The ratios of LDL-C:HDL-C[1,2] and TC:HDL-C remained unchanged after 12 wks of treatment with ABT-494. The ratio of ApoB:ApoA1 also remained unchanged from BL to Wk 12: in BALANCE-1, 0.61 to 0.58 for the 6 mg (n=19), and 0.62 to 0.60 for 12 mg (n=11) groups, and in BALANCE-2, 0.62 to 0.64 for the 6 mg (n=18) and 0.69 to 0.66 for 12 mg (n=16) groups. An inverse relationship between LDL-C or HDL-C and hsCRP was observed throughout the treatment period. At Wk 4, among the variables tested, the strongest correlation was observed between changes from BL in hsCRP and LDL-C (-0.29, $p<0.001$) or HDL-C (-0.26, $p<0.001$). Out of 420 pts, 104 pts (25%) were ACR20 SR, 251 pts (60%) were R and 65 pts (15%) were NR. Compared to NR, SR and R had a greater absolute reduction in hsCRP (Fig. 1A). A robust percentage increase in HDL-C was observed in all 3 groups (20.8%, 18.5% and 16.4% in SR, R and NR, respectively). Compared to the SR and R (14.6% and 16%, respectively), a smaller percentage increase in LDL-C was observed in the NR (8.9%) (Fig. 1B).

Figure 1




**Conclusions:** Atherogenic burden did not increase in pts treated with ABT-494 for 12 wks. Compared to non-responders, pts with a clinical response experienced a larger increase in lipids and a larger decrease in hsCRP. Limited data from these phase 2 studies suggest that there might not be an increased risk of cardiovascular events. Results from the larger phase 3 trials can provide more information.
**References:**
[1] Kremer et al. 2016, Arthritis & Rheum;68:2867.
[2] Genovese et al. 2016, Arthritis & Rheum;68:2857.
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## THU0204 RELATIONSHIPS BETWEEN METHOTREXATE DOSAGES AND CLINICAL VARIABLES IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ACHIEVED REMISSION WITH METHOTREXATE MONOTHERAPY: A STUDY USING THE IORRA OBSERVATIONAL COHORT STUDY

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**Background:** Considerable variability exists in the way rheumatologists prescribe methotrexate (MTX) therapy in patients with rheumatoid arthritis (RA), including the dosage [ref.1]. Start higher doses or fast dose escalation are associated with higher efficacy, but also with more toxicity. In addition, factors such as renal function, body size, and age of the patient can affect the optimal dosage of MTX.
**Objectives:** We aimed to study the relationships between MTX dosages and clinical variables in patients with RA who achieved remission with MTX monotherapy.

**Methods:** The "Institute of Rheumatology, Rheumatoid Arthritis (IORRA)" is a single-center prospective observational cohort study established at our institute in 2000. Data (physicians' and patients' disease assessments, laboratory data, and many other patient information) were collected from approximately 5,000 RA patients biannually. More than 99% of RA patients treated at our institute were enrolled in this cohort, and >98% of patients answered and mailed their questionnaires back to us every time. Among the RA patients who were registered in the IORRA cohort study from 2011 through 2015, 603 patients fulfilled the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) Boolean-based definition of remission in RA, at least once and used only MTX as disease-modifying antirheumatic drugs (DMARDs) including biological DMARDs for 5 years. Relationships between MTX dosages and gender, disease duration, height, body weight, body mass index, body surface area, serum creatinine (SCr), estimated glomerular filtration rate (eGFR), creatinine clearance (by Cockcroft-Gault Equation), rheumatoid factor, and anti-cyclic citrullinated peptide antibody when remission was first reached by each patient were analyzed by univariate analyses using Pearson correlation coefficient and Welch's *t* test. Subsequently, a multiple regression analysis was performed.
**Results:** Univariate analyses detected several candidate clinical variables associated with MTX monotherapy dosages in RA patients who achieved remission: height, body weight, body surface area, SCr, eGFR, and CCr ($p$ =0.004, 0.050, 0.241, <0.001, <0.001, and <0.001, respectively). Subsequently, a multiple regression model developed a best-fit model with the following variables; age, height, body weight, and SCr (standardized partial regression coefficient = -0.20, 0.10, 0.07, and -0.22, respectively), while its adjusted coefficient of determination was 0.114.
**Conclusions:** There were significant relationships between MTX monotherapy dosages and age, height, body weight, and renal function in RA patients who achieved remission. However, the low coefficient of determination indicated the model accounted for limited variability with the specified variables.
**References:**
[1] Visser K and van der Heijde D. Optimal dosage and route of administration of methotrexate in rheumatoid arthritis: a systematic review of the literature. Ann Rheum Dis. 2009;68:1094.
**Disclosure of Interest:** M. Tochihara: None declared, Y. Katsumata: None declared, E. Inoue: None declared, Y. Kawaguchi: None declared, E. Tanaka Consultant for: Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Pfizer, Takeda Pharmaceutical, and Ayumi Pharmaceutical, Speakers bureau: Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Pfizer, Takeda Pharmaceutical, and Ayumi Pharmaceutical, A. Nakajima Consultant for: Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company., Speakers bureau: Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company., K. Ikari Grant/research support from: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., Speakers bureau: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., A. Taniguchi Grant/research support from: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer., Speakers bureau: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer., H. Yamanaka Grant/research support from: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Consultant for: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Speakers bureau: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers.
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## THU0205 EFFECTS OF THE JAK1-SELECTIVE INHIBITOR FILGOTINIB ON MULTIBIOMARKER DISEASE ACTIVITY SCORES IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO METHOTREXATE

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**Background:** Filgotinib (GLPG0634, GS-6034) is an oral selective JAK1 inhibitor that has been evaluated in a 24-week phase 2B study (DARWIN 1) on the background of methotrexate (MTX) treatment in active rheumatoid arthritis (RA) patients who were MTX inadequate responders[1].
**Objectives:** To evaluate the effect of filgotinib compared to placebo on a multi-biomarker disease activity (MBDA) score that measures 12 disease-related biomarkers of inflammation and joint injury in RA patients taking background MTX.
**Methods:** Serum samples of RA patients who were on a stable dose of MTX and received either placebo (PBO) or filgotinib 100mg or 200mg once daily (QD), were tested for MBDA components (Crescendo Biosciences, CA, US) at baseline, week 4 and week 12. Median % change from baseline for MBDA score and individual components are reported for week 4 and week 12. Wilcoxon rank-sum test assessed the significance of difference between filgotinib treated groups *vs.* PBO.
**Results:** Baseline MBDA scores and component values (median; interquartile range) were similar in PBO (55; 45–64), 100mg QD (58; 42–66), and 200mg QD (59; 50–67.5) treatment groups. Filgotinib treated patients had reductions in the MBDA score from baseline at both the 100mg and 200mg QD dose levels, but not in the PBO group. At both weeks 4 and 12, these reductions in the filgotinib treated groups were significantly different from the PBO group. Most of the individual components contributed to the decrease in MBDA score, but the largest reductions were observed for serum amyloid A (SAA), C-reactive protein (CRP), and IL-6, and the biomarkers of joint-damage, matrix metalloproteinase 3 (MMP3), MMP1, vascular endothelial growth factor (VEGF), and YKL40 (human cartilage glycoprotein 39). There was an increase in leptin and no change in epidermal growth factor (EGF) concentrations.

Table 1. Median percent change from baseline of MBDA score and component concentrations

| | Week 4 | | | Week 12 | | |
|---|---|---|---|---|---|---|
| | PBO (N=62) | Filgotinib 100mg QD (N=63) | Filgotinib ) 200mg QD (N=68) | PBO (N=65) | Filgotinib 100mg QD (N=62) | Filgotinib par 200mg QD (N=68) |
| MBDA SCORE | -1 | -20*** | -24*** | -5 | -19*** | -24*** |
| CRP | 15 | -57*** | -71*** | -8 | -66*** | -78*** |
| EGF | 14 | -18$^{NS}$ | -8$^{NS}$ | 0 | -10$^{NS}$ | 0$^{NS}$ |
| IL-6 | -15 | -34** | -60*** | -20 | -41** | -63*** |
| LEPTIN | 0 | 8$^{NS}$ | 18$^{NS}$ | 6 | 14$^{NS}$ | 23* |
| MMP-1 | 10 | -16*** | -24*** | -6 | -18** | -26*** |
| MMP-3 | 0 | -24** | -33*** | -9 | -25*** | -43*** |
| RESISTIN | 1 | -12** | -22*** | -1 | -15* | -16*** |
| SAA | 8 | -45*** | -65*** | 7 | -49*** | -67*** |
| TNF-RI | 0 | -11*** | -26*** | 0 | -11*** | -15*** |
| VCAM-1 | 5 | -10*** | -15*** | 0 | -8** | -16*** |
| VEGF | 3 | -16*** | -25*** | -2 | -16*** | -26*** |
| YKL-40 | 2 | -12* | -32*** | -7 | -17$^{NS}$ | -33*** |

p-values comparing % changes between filgotinib and PBO groups NS, p>0.05; *p<0.05; **p<0.01; ***p<0.001.

**Conclusions:** RA patients treated with filgotinib in combination with MTX had significant reductions in the MBDA score that was driven by key RA biomarkers encompassing both inflammation and joint injury. These findings are consistent with the filgotinib efficacy observed in RA patients over 12 weeks.
**References:**
[1] Westhovens R, et al. Ann Rheum Dis 2016;0:1–11. doi:10.1136/annrheumdis-2016–210104.
**Disclosure of Interest:** M. Genovese Grant/research support from: Abbvie, Eli Lilly, Pfizer, Astellas, Vertex, Consultant for: Galapagos, Gilead, Abbvie, Eli Lilly, Pfizer, Astellas, Vertex, W. Li Employee of: Gilead Sciences, L. Goyal Employee of: Gilead Sciences, Y. Pan Employee of: Gilead Sciences, A. Van der Aa Employee of: Galapagos NV, C. Jamoul Employee of: Galapagos NV, P. Harrison Employee of: Galapagos NV, C. Tasset Employee of: Galapagos NV, R. Galien Employee of: Galapagos SASU, J. Tarrant Employee of: Gilead Sciences
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## THU0206 THE JAK1-SELECTIVE INHIBITOR FILGOTINIB REDUCES MULTIPLE MARKERS OF INFLAMMATION LINKED TO VARIOUS PATHOLOGIC CELL TYPES AND PROCESSES IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** JAK1, 2, 3 and TYK2 are cytoplasmic tyrosine kinases that mediate intracellular signaling of many cytokines and growth factors. Filgotinib (GLPG0634, GS-6034) is a JAK inhibitor with high selectivity for JAK1 over other JAK family members. Filgotinib has a favorable safety and efficacy profile in two Phase 2B studies in active rheumatoid arthritis (RA) patients who were methotrexate (MTX) inadequate responders.
**Objectives:** To assess the effect of filgotinib on a background of MTX treatment on markers of inflammation in RA patients.
**Methods:** Serum samples from RA patients who were on a stable dose of MTX and received either placebo (PBO), filgotinib 100mg or 200mg once daily (QD), were collected at baseline, week 4 and week 12 and analyzed for 35 soluble serum biomarkers by validated single-plex or multiplex immunoassays. Median % changes from baseline for biomarkers are reported. Wilcoxon rank-sum test assessed the significance of difference between filgotinib treated groups and PBO.
**Results:** Filgotinib treatment induced a dose-dependent and significant decrease