Health Assessment Questionnaire Disease Index (HAQ-DI) score (Figure 1A). All age groups had similar improvements in PROs such as fatigue, strength of pain, and sleep disturbances (Figure 1B).

Table 1. Mean Disease Activity Score-28 erythrocyte sedimentation rate (DAS28-ESR) and Clinical Disease Activity Index (CDAI) over the course of ICHIBAN. BL, baseline; SD, standard deviation.

		<50 years	50–65 years	>65 years
DAS28-ESR, mean ± SD	n*	777	1237	617
	BL	4.9 ± 1.4	5.3 ± 1.3	5.4 ± 1.3
	Last visit	2.8 ± 1.7	3.1 ± 1.7	3.2 ± 1.7
	Change from BL	-2.0 ± 1.7	-2.2 ± 1.7	-2.2 ± 1.8
CDAI, mean ± SD	n*	768	1217	590
	BL	25.7 ± 12.8	28.4 ± 13.3	28.8 ± 12.8
	Last visit	13.3 ± 12.8	14.6 ± 13.2	14.5 ± 12.8
	Change from BL	-12.5 ± 13.6	-13.8 ± 14.0	-14.3 ± 13.8

*271 patients with missing data at BL**327 patients with missing data at BL

Conclusion: Although elderly patients experienced a higher rate of infections, the proportion of patients withdrawing due to AE was not higher than in the other age groups. Starting with higher baseline disease activity, patients >65 years had similar benefits to disease activity and PROs when compared with younger patients. Overall, these results indicate that long-term TCZ treatment of elderly patients is effective and has an acceptable safety profile.

Figure. Mean (SD) Health Assessment Questionnaire Disease Index (HAQ-DI) score and B) mean (SD) patient-reported outcomes over the course of ICHIBAN. SD, standard deviation.

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POS0616

LONG-TERM EFFECTIVENESS AFTER MULTIPLE CYCLES WITH RITUXIMAB FOLLOWING AN ON-FLARE RETREATMENT STRATEGY IN PATIENTS WITH RHEUMATOID ARTHRITIS

D. Bertrand¹, N. Pype¹, T. Conings¹, D. De Cock¹, S. Pazmino¹, M. Doumen^{1,2}, J. Joly², B. Neerinx^{1,2}, R. Westhovens^{1,2}, P. Verschueren^{1,2}, ¹KU Leuven, Skeletal Biology and Engineering Research Center, Leuven, Belgium; ²UZ Leuven, Rheumatology, Leuven, Belgium

Background: Rituximab is known as an efficacious drug for the treatment of Rheumatoid Arthritis (RA). The recommended administration schedule consist of 2 infusions of 1000 mg with a 2-week interval. In Belgium an on-flare retreatment

strategy is followed, making evaluation of effectiveness over time challenging. Moreover the patient's view on this strategy is unclear.

Objectives: To explore long-term effectiveness and safety of rituximab in daily clinical practice in patients with RA.

Methods: Data of patients diagnosed with RA and treated with rituximab in a tertiary university hospital were retrospectively collected. For every cycle, clinical data were recorded at the time of the first and second infusion, the 16-week visit and the visit on which the treating rheumatologist decided to prescribe a new cycle. Data on demographics, previous RA treatment, disease activity, patient-reported outcomes, adverse events related to rituximab, dose and number of cycles were collected from 01/01/2006 until 01/12/2019 or until discontinuation of rituximab. The visit on which rituximab was prescribed for the first time was considered as the baseline visit. The data were analysed descriptively.

Results: Data of 66 patients with RA were collected. The median (IQR) age was 57.0 (47.0-65.0) years at baseline and 56% (37/66) were female. Most patients were seropositive (RF 91% and ACPA 92%), and had erosive (71%) or nodular disease (53%). The median (IQR) disease duration was 12.5 (4.0-18.3) years. In total, 94% of the patients had failed at least one other biological Disease-modifying Antirheumatic Drug (bDMARD) before starting rituximab. Overall, patients received a median (IQR) of 3 (2-7) cycles of rituximab. Seven of the 66 patients (11%) discontinued rituximab and changed to another bDMARD after a median (IQR) of 1 (1-6) cycles and 11% were treated with a lower dose than 2x1000mg. The median (IQR) interval between the first 2 cycles was 7.0 (6.0-10.0) months, after which this increased to up to one year (interval between cycle 2-3: 10.0 (7.0-13.0) months, cycle 3-4: 12.0 (7.3-15.5) months). The overall median (IQR) follow-up time was 45.5 (14.8-82.3) months. The efficacy of rituximab remained after repeated cycles: after every treatment with rituximab, a reduction in disease activity based on the disease activity score in 28 joints (DAS28) could be noticed (figure 1A). The evolution in patients' (PaGH) and physicians' global health (PhGH) assessment followed the same pattern as the DAS28-score (Figure 1B). High PaGH-scores could be noticed at every start of a new rituximab cycle. The proportion of patients with a PaGH-score above 20 ranged from 84% - 100%, 74% - 100% and 66% - 86% at the first infusion, second infusion and week 16 visits, respectively. Rituximab was considered to be well-tolerated. In total, 23 adverse events in 12 patients were recorded and none of them were serious.

Conclusion: Rituximab can be considered a highly efficacious drug for RA treatment in daily practice. There were no major side effects and there was an increasing treatment interval over time. However, a healthy survivor effect should be kept in mind when interpreting the results. It should be noted that with the on-flare retreatment strategy, every new rituximab cycle was preceded by a rise in PaGH-scores, which reflects a state of impaired wellbeing reported by patients. This should be further studied with qualitative methods and in a randomized trial setting comparing on-flare with fixed-interval retreatment to evaluate optimal effectiveness.

Figure 1. Evolution in median - interquartile range disease activity (DAS28CRP) (A) and patients' (PaGH) and physicians' global health (PhGH) (B) over the different rituximab cycles. The disease activity, PaGH and PhGH were measured at baseline, the time of the first and

second infusion, W16 and the visit on which a new rituximab cycle was prescribed. The dotted lines represent a DAS28CRP-score of 2.6 (remission cut-off) and 3.2 (low disease activity cut-off). C: cycle; W: week; VAS: visual analogue scale.

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POS0617

ANTI INFLIXIMAB ANTIBODIES DETECTED BY A DRUG TOLERANT ASSAY ARE FREQUENT BUT, IN MANY CASES, WITHOUT RELEVANT CLINICAL SIGNIFICANCE

A. Martínez-Feito^{1,2}, B. Hernández-Breijo², M. Novella-Navarro^{2,3}, V. Navarro-Compán^{2,3}, C. Diego¹, I. Monjo², L. Nuño², A. Villalva³, D. Peiteado³, D. Pascual-Salcedo², P. Nozal¹, A. Balsa^{2,3}, C. Plasencia^{2,3}. ¹La Paz University Hospital, Immunology, MADRID, Spain; ²IdiPaz. La Paz University Hospital, Immuno-Rheumatology Research Group, MADRID, Spain; ³La Paz University Hospital, Rheumatology, MADRID, Spain

Background: Infliximab (Ifx) has proven effective in treating rheumatoid arthritis (RA) and spondyloarthropathies (SpA), although around 40% of cases fails, mainly due to immunogenicity. Formation of immunocomplexes between antibodies to Ifx (ATI) and Ifx can increase drug clearance, leading to treatment failure. Standard ELISA assays which are drug -sensitive are frequently used, being able to detect only free ATI. Interest in drug-tolerant assays to measure total ATI (free and complexed) is increasing.

Objectives: To compare the development of ATI using both drug-tolerant and drug-sensitive assays at early stages of Ifx therapy. To analyse the relationship of ATI detected by both assays with the drop-out of treatment.

Methods: This is a prospective observational study including 45 patients with RA and 61 with axial-SpA treated with standard doses of Ifx (3mg/kg and 5mg/kg, respectively) enrolled at Biological Therapy Unit of Hospital La Paz. Serum samples were obtained at 2, 6, 12 and 22 weeks (W) after Ifx initiation. The data about discontinuation for inefficacy was obtained from the database. ATI presence was evaluated by a drug-sensitive in-house two-site (bridging) ELISA (bELISA) and a drug-tolerant commercial ELISA assay (Immudiagnostik®IDK). All comparisons were performed throughout non-parametrical test. In SpA group, due to the low number of ATI+ patients at W12 by bELISA the statistical analysis to compare both assays were not performed.

Results: ATI detection by both assays at early stages (≤ 22 W) of treatment is shown in Table 1a. ATI were always detected earlier by IDK than bELISA and also in RA than in SpA patients probably reflecting the effect of lower Ifx doses. Three out of 106 (3%) vs 0 (0%) patients had ATI at W 2 and 62 (58%) vs 20 (18%) patients at W22, by IDK and bELISA, respectively.

Table 1.

	W2		W6		W12		W22	
	AR	SpA	AR	SpA	AR	SpA	AR	SpA
<i>a) ATI+ patients (n, %) at early stages</i>								
bELISA	0	0	3(7%)	0	10(22%)	1(2%)	13(29%)	7(12%)
IDK	1(2%)	2(3%)	7(16%)	2(3%)	16(36%)	16(26%)	28(62%)	34(56%)
<i>b) Patients who discontinued (n, %) Ifx therapy considering ATI status at early stages</i>								
bELISA+					9(90%)*	1(100%)*	12(92%)	4(57%)
bELISA-					23(66%)	22(37%)	20(63%)	19(35%)
IDK+					15(94%)*	7(44%)	24(86%)	13(38%)
IDK-					17(59%)	11(24%)	13(77%)	10(27%)

*p<0.05 comparing between ATI+ vs ATI- in each assay.

Once ATIs appeared, regardless both methods, they persisted throughout the follow-up, indicating that immunogenicity was not transient.

At W22, only 13/28 (46%) and 7/34 (21%) patients with ATI detected by IDK were also positive by bELISA in RA and SpA, respectively.

ATI levels by IDK were higher in ATI+ by bELISA than in ATI- patients at early stages: ATI levels by IDK at W12: 91[74-348] ng/ml ATI+ vs 21.7[15-59.5] ng/ml ATI- (p<0.01) and at W22: 132 [89-372] ng/ml ATI+ vs 23[13-66] ng/ml ATI- (p<0.001). However, only in 4% (2/45) patients with RA and in 13% (8/61) patients with SpA the detection by IDK was earlier than by bELISA at W12.

Free IFX in serum was not detected in bELISA ATI+ patients. In IDK ATI+ patients low circulating Ifx levels were present as compare to ATI- since W6 to the end of follow-up (p<0.01).

More ATI+ patients dropped out Ifx at W12 and W22 regardless de assay (Table 1.b), being statistically significant for both assays in patients with RA and only for bELISA in patients with SpA.

Conclusion: ATI measured by a drug-tolerant assay are always detected earlier than ATI detected by bELISA, indicating that immunogenicity, at least with

Ifx, is usually an early event. High levels of ATI by IDK are associated with an earlier detection by bELISA in case of RA patients. ATI detected only by drug tolerant assays are associated with low levels of circulating Ifx but not with a complete drug neutralization and may do not have clinical relevance compared to ATI detected by bELISA. Many patients have low levels of ATI which can only be detected by drug tolerant assays after long-term of follow-up.

The reasons why ATI levels rise rapidly in some patients while in others remain low are currently unknown but may be relevant if the clinical effect of immunogenicity is to be minimized.

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POS0618

PERSISTENCE OF REMISSION AFTER TAPERING OF GOLIMUMAB IN INFLAMMATORY JOINT DISEASE (IJD)

A. Damiani¹, F. Bartoli¹, V. Gori¹, S. Bellando-Randone¹, G. Fiori¹, M. Matucci-Cerinic¹, S. Guiducci¹. ¹University of Florence, Rheumatology Unit, Firenze, Italy

Background: In refractory IJD, remission may be obtained with anti-TNF α drugs and other biological disease modifying anti-rheumatic drugs (bDMARDs). The last EULAR recommendations suggest tapering of bDMARD when remission persists¹. However, best timing and modality of tapering are uncertain and specific knowledge on patients' characteristics associated to a better outcome is still lacking.

Objectives: To evaluate the persistency of remission after increasing the interval between injections of Golimumab in a group of patients affected by rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS) and juvenile idiopathic arthritis (JIA) and to identify any variables associated to disease flare after tapering.

Methods: Between 2011 and July 2020, 80 patients affected by RA, PsA, AS and JIA treated with Golimumab were enrolled. Their demographic and clinical data, including inflammation (ESR and CRP) and clinimetric indices (DAS28 or BASDAI), were collected at baseline and during the follow up visit (T1). In 22/80 patients that reached clinical remission at T1, the time between Golimumab injections has been prolonged (mean time between injection: 43.7 days); ESR and CRP, DAS28/BASDAI, and time since the start of the tapering (weeks) were evaluated in the next control visit (T2).

Results: 80 patients were enrolled (32 male, mean age 50.6 years $\pm$ 13.91), 34 AS, 33 PsA, 9 RA and 4 JIA. At baseline they have an active disease with a DAS 28 of 4.74 $\pm$ 0.85 and a BASDAI of 5.23 $\pm$ 1.31. At T1, 60/80 patients were in remission (75%), with a mean DAS 28 of 1.84 $\pm$ 0.6 and an average BASDAI of 1.32 $\pm$ 0.6, and 22/60 patients started drug tapering. At T2, 20/22 patients (91%) were in remission, (DAS 28 1.9 $\pm$ 0.49, BASDAI of 0.8 $\pm$ 0.67). A significantly higher BASDAI was observed at T1, even though in the range of absence of disease activity (2.2, $\pm$ 0.28 vs 0.58, $\pm$ 0.47; p < 0.001) in patients who, after extending the therapeutic interval (T1) were no longer in remission at T2. Patients with a flare of disease activity (2/22) were taken back to the 28 days window of Golimumab with a prompt recovery of disease remission. Out of the 38 patients maintained at the standard dose, 4 experienced a disease flare with necessity to switch or swope bDMARD, with a retention rate in this group of 90%. Difference of retention rate between patients on standard vs reduced dose was not statistically significant.

Conclusion: Tapering of Golimumab was successful in 91% of the cases without flare. Moreover, the prolongation of the increase of the treatment window provided the same result as that obtained in patients that continued in the standard time window. This evidence suggests that the extension of the gap between Golimumab administrations may be feasible and safely applied in practice.

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