For Naïve group, 50% (52/104) of patients had at least one positive anti-drug antibody result and it is consistent to other published study [2].
Overall safety summarized as the percentage of patients with at least one treatment emergent AE (TEAE) was similar or lower after switching to CT-P13 (Table 2). No cases of active tuberculosis were reported.

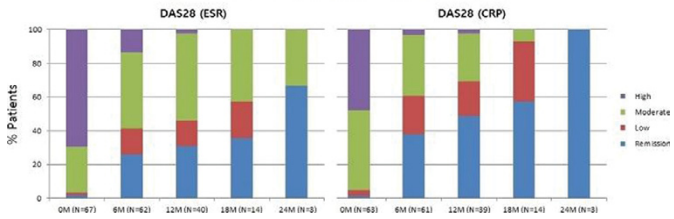
Table 1. DAS28 in CT-P13 Naïve group over 24 months

		Baseline	6 months	12 months	18 months	24 months
DAS28 (ESR)	n	67	62	40	14	3
	Mean	5.78	3.61	3.30	3.01	2.42
	SD	1.14	1.40	1.22	1.03	0.74
DAS28 (CRP)	n	63	61	39	14	3
	Mean	5.06	2.97	2.59	2.35	1.81
	SD	1.19	1.21	1.06	0.69	0.63

Table 2. Safety results in CT-P13 Naïve and Switching group

	Naïve group	Switching group
TEAEs	80.8% (84/104)	66.7% (14/21)
Related TEAEs	31.7% (33/104)	28.6% (6/21)
Infection and Infestation	42.3% (44/104)	33.3% (7/21)

Figure 1. Disease Activity by DAS28 in CT-P13 Naïve group



Conclusions: The overall safety profile revealed that CT-P13 is well-tolerated in patients with RA and remission rate for 24 months also showed that CT-P13 is efficacious under real world practice.
References:
[1] Glintborg et al. ACR 2016.
[2] Krintel et al. Rheumatology 2013.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2413

AB0393 ADVERSE SKIN REACTIONS IN RHEUMATOID ARTHRITIS PATIENTS RECIEVING TUMOR NECROSIS FACTOR ALPHA INHIBITOR – AN ANALYSIS OF DATA FROM THE SLOVENIAN BIOLOGICAL REGISTRY

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Background: Paradoxical skin reactions (PSR) are defined as a new onset or worsening of skin conditions during treatment with tumour necrosis factor alpha (TNF-α) inhibitors that generally improve or respond to this therapy. The list of PSR is growing. The most commonly reported are psoriasiform skin eruptions.
Objectives: To evaluate the frequency of PSR in the group of rheumatoid arthritis (RA) patients treated with TNF-α inhibitor at the time of development of skin eruption.
Methods: We conducted the analysis of the data from the mandatory Slovenian national registry of patients treated with bDMARDs (BioRx.si) which includes spontaneous adverse reaction reports between 01.01.2008–31.05.2016. The analyses were limited to patients with RA.
Results: During the observation period, 1,046 RA (82% female; median (IQR) age at initiation of TNF-α inhibitors 56 (49–63) years) patients treated with TNF-α inhibitors for 3,140 person years. We identified 14 cases with PSR (71% female, median age (IQR) 45 (53–62)). There were 6 PSR cases on adalimumab, 4 on etanercept, 3 on certolizumab – pegol, and 1 on infliximab. 10 patients developed psoriatic/psoriasiform eruptions, 2 patient leucocytoclastic vasculitis, one had lichen planus, and one undifferentiated skin changes. The incidence rate of new onset of psoriasis in RA patients treated with TNF-α inhibitors was estimated at 3.2 cases/1000 patient-years (95% CI 2.58 to 3.82). The incidence rate of leucocytolastic vasculitis was 0.64/1000 person-years (95% CI 0.36 to 0.92), and of lichen planus 0.32/1000 person-years (95% CI 0.12 to 0.52).
Conclusions: The most commonly reported PSR in RA patients treated with TNF-α inhibitor was psoriasiorm PSR, which is in line with published data.
Disclosure of Interest: None declared
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AB0394 TAPERING TNF INHIBITORS IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE STUDY

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Background: Increasing evidence suggests the feasibility of biologic DMARD tapering in RA patients after achieving and maintaining good control of disease activity. Current guidelines on RA treatment also recommend tapering of biologic and non-biologic DMARDs for patients in remission. Data on biologic DMARD tapering reflecting real life settings are limited.
Objectives: To collect information on biologic DMARD tapering and its outcome in RA patients who are followed-up in a rheumatology outpatient clinic.
Methods: In this retrospective study we used the hospital administrative database to identify patients with a diagnosis of RA and a first time prescription of a biologic DMARD that was specifically limited to one of the 3 TNF inhibitors (etanercept, adalimumab, infliximab) between January 2012 and the end of December 2013. Demographics and information regarding treatment and outcome were taken from the medical charts.
Results: Of the 125 patients identified at the database search, 104 were belonging to our clinic and had available follow-up data until June 2016. Seventy-nine of them were women and 25 were men. Their mean age was 47.7±13 SD years and their mean disease duration was 7.4±6.9 SD years. 60% were prescribed etanercept, 23% adalimumab and 17% infliximab. After a mean duration of 14.0±7.6 SD months a dose reduction of TNF inhibitors was made in 44 patients (42%). This was in the form of spacing in 39 patients (Etanercept =16, Infliximab =14, Adalimumab =9) and dose tapering in 5 (all Etanercept). All of these were due to good clinical response except for 1 patient's own request for fear from adverse effects. Following dose reduction increased disease activity was seen in 16 patients (36%) mandating restoration to original dose within a mean of 8.8±9.7 SD months with good response. Twenty-eight patients (64%) preserved their good clinical response during a mean follow-up of 46.1±6.3 SD months which enabled further dose reductions in 20 patients. There was also reductions in the mean number of synthetic DMARD's (1.4±0.8 SD at the initiation of TNF inhibitors and 0.7±0.8 SD at the end of follow-up) and in the percentage of patients using steroids (78% to 33%). At the end of the follow-up, among the whole group of 104 patients, only 73 (70%) were using biologics (TNF inhibitors =49, non-TNF biologics =24). The reasons for stopping biologics in the remaining 31 patients were ongoing remission (16 patients), pregnancy (1 patient), non-compliance (4 patients), injection site reactions (3 patients), fear from adverse events (1 patient), deciding to try complementary medicine (1 patient) and other issues such as losing insurance and family issues (5 patients).
Conclusions: Tapering of TNF inhibitors was possible in 40% of RA patients during their routine follow-up. Half of the patients maintained good clinical response after tapering allowing further dose reductions in one third.
Disclosure of Interest: None declared
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Rheumatoid arthritis - other biologic treatment

AB0395 SUBCUTANEOUS TOCILIZUMAB AS MONOTHERAPY OR IN COMBINATION WITH A CSDMARD IN PATIENTS WITH RHEUMATOID ARTHRITIS: 24 WEEKS RESULTS OF THE FRENCH PHASE IIIB STUDY, "TOSCA"

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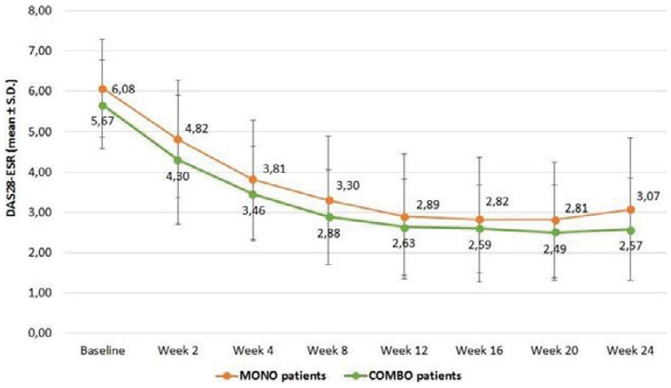
Background: After the two global pivotal studies, which evaluated the safety and efficacy of subcutaneous tocilizumab (TCZ-SC) in combination (combo) with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), it was important to understand the efficacy and safety profile of TCZ-SC both as monotherapy (mono) and in combo with csDMARDs in patients (pts) managed in conditions less strict than those of pivotal clinical trials.
Objectives: To evaluate the efficacy and safety of TCZ-SC 162 mg once weekly (qw) as mono and in combo with csDMARDs over 24 weeks in adult pts with moderate to severe RA. The primary efficacy criterion was the change in DAS28-ESR from baseline to week 24 (W24).
Methods: TOSCA is a national, multicenter, open-label phase IIIb study, part of the international umbrella study (TOZURA). It aimed to enroll TCZ-naïve pts who were csdMARDs inadequate responders (IR) and/or biological DMARD-IR. Pts received TCZ-SC 162 mg qw for 24 weeks, administered at the investigator's discretion as mono or in combo with a csDMARD. Stable oral corticosteroids (CCS), ≤10 mg/day prednisone or equivalent (eq.pred), were allowed.

Results: The baseline characteristics of the 139 included patients were: mean age 57.3 years (±13.8), 74.1% female, mean RA disease duration 10.8 years (±9.2), immunopositivity 85.5%, structural joint damage 65.6%, mean DAS28 5.8 (±1.1). 52.5% of patients were bDMARD-IR. TCZ-SC was initiated in mono TCZ in 30.9% of pts and in combo in 69.1% (79.1% MTX). Oral CCS were used by 56.8% of pts (mean 7.4 mg/d/eq.pred.±2.7). In comparison with combo pts, the mono pts were older (58.7 vs 56.7 years), with a higher mean DAS28 (6.1 vs 5.7), a longer disease duration (11.5 vs 10.6 years), and a higher CCS mean dose (8.3 vs 6.9 mg/d/eq.pred.). At W24, the mean DAS28 score variation vs baseline was -3.1 overall ($p<0.0001$); -3.0 in mono TCZ vs -3.1 in combo TCZ ($p=0.76$) (Fig.). The proportion of pts who achieved DAS28 remission was 51.1% (41.9% in mono vs 55.2% in combo ($p=0.14$)). CDAI remission, which does not include acute phase reactants, was achieved in 17% pts, 16% in mono vs 17% in combo ($p=0.95$). At W24, 27.9% of pts receiving >5 mg CCS at baseline decreased the daily dose ≤5 mg/d/eq.pred. (30.1% in mono TCZ and 26.7% in combo). Out of the 23 pts (16.5%) who withdrew, 13.0% did so for lack of efficacy and 52.1% for safety reasons; one death occurred following a septic shock after surgery for gastric volvulus, not related to TCZ. At W24 95.7% of patients had experienced at least one adverse event (AE) and 10.1% at least one serious AE with similar rates between groups.



Conclusions: TCZ-SC demonstrated at 6 months comparable efficacy, safety and steroid sparing results in mono- and combo therapy consistent with the known profile of TCZ-IV.

Disclosure of Interest: B. Fautrel: None declared, E. Senbel: None declared, O. Vittecoq: None declared, S. Rist: None declared, B. Combe: None declared, T. Schaeverbeke: None declared, F. Lioté: None declared, R.-M. Flipo: None declared, C. Baffie Employee of: Altizem on behalf of Roche, D. Pau Employee of: Roche, E. Condé Da Silva Fraga Employee of: Roche, A. Pinta Employee of: Roche, P. Gaudin: None declared

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AB0396 TOCILIZUMAB I.V. EFFECTIVENESS IN RA PATIENTS IS INDEPENDENT OF SMOKING STATUS

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Background: Cigarette smoking is considered an established risk factor for the development of rheumatoid arthritis (RA) and for poor response in RA patients to treatment with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and with anti-tumor necrosis factor (anti-TNF) agents [1,2].

Objectives: This interim analysis of the German non-interventional study ICHIBAN (NCT01194401) assessed the effectiveness and safety of intravenously administered Tocilizumab (TCZ i.v.) with respect to patients' smoking status (smoker, ex-smoker, non-smoker).

Methods: Since 2010 the ICHIBAN study collects clinical data of the routine use of TCZ i.v. in RA patients. The observation period for each patient is up to two years. At the due date of the current interim analysis (Dec 10, 2015) 2999 patients were enrolled. 902 patients have completed the maximal 104 weeks observation period (Group W104). Patients were subgrouped according to their smoking status at baseline (BL).

Results: At BL the subgroups showed the following distribution: smokers 19.0%, non-smokers 52.5%, and ex-smokers 17.0%. The mean TCZ i.v. treatment duration was 1.7, 1.8, and 1.6 years, respectively, for the three groups.

In comparison to non-smokers and ex-smokers, smokers comprised a higher percentage of male patients, were younger, and showed shorter disease duration. Smokers showed slightly lower overall comorbidity rates, while COPD was observed almost three times more among smokers (3.5%) and ex-smokers (3.9%) than in non-smokers (1.3%). Concomitant use of csDMARDs and glucocorticoids (GC) was more frequent among smokers.

DAS28-ESR disease activity at BL was similar between the 3 subgroups. After 2 years TCZ i.v. therapy, disease activity was comparably decreased in all 3 groups. The mean reduction from BL in DAS28-ESR was 2.6 (smokers), 2.8 (non-smokers), and 2.5 (ex-smokers). At last visit, DAS28-ESR remission (<2.6) was reached by 48.0%, 52.3%, and 51.6% of patients, respectively The similar effectiveness of TCZ i.v. was also shown by patient reported outcomes via visual analogue scales (VAS).

Regarding safety, smokers showed higher event rates of adverse events (AE), serious adverse events (SAE), infections, and serious infections [Tab. 1]

Table 1 Effectiveness and safety of TCZ i.v. in RA patients

		W104 (Total)	Smokers	Non-smokers	Ex-smokers
Baseline characteristics, % (n)		100.0 (902)	19.0 (171)*	52.5 (474)*	17.0 (153)*
Sex (male), % (n)		23.8 (215)	40.9 (70)	15.8 (75)	33.3 (51)
Age [years], mean ± SD		55.7 ± 12.4	51.8 ± 10.1	56.8 ± 13.6	56.6 ± 11.4
Duration of RA [years], median		8.0	6.0	8.0	8.0
Comedication, % (n)					
• DMARDs		42.6 (384)	49.7 (85)	41.4 (196)	37.9 (58)
• GC		61.5 (555)	68.4 (117)	59.7 (283)	56.2 (86)
Comorbidities, % (n)		72.5 (654)	68.4 (117)	72.4 (343)	78.4 (120)
Effectiveness					
DAS28-ESR					
• Week 0 (Baseline), mean ± SD		5.5 ± 1.1	5.5 ± 1.1	5.5 ± 1.1	5.3 ± 1.0
• Last visit under TCZ, mean ± SD		2.7 ± 1.5	2.9 ± 1.7	2.7 ± 1.5	2.8 ± 1.5
• Change from BL, mean ± SD		-2.7 ± 1.6	-2.6 ± 1.7	-2.8 ± 1.7	-2.5 ± 1.5
• Remission (< 2.6), % (n)		51.9 (468)	48.0 (82)	52.3 (248)	51.6 (79)
VAS [mm], median (Q1, Q3)					
• Exhaustion/Tiredness	(Baseline)	60.0 (36, 79)	62.0 (31, 80)	59.0 (40, 78)	55.0 (34, 75)
•	(Last visit)	37.0 (14, 60)	39.0 (13, 62)	35.0 (15, 60)	40.5 (12, 57)
• Intensity of pain	(Baseline)	65.0 (45, 79)	67.0 (42, 80)	63.0 (45, 77)	62.0 (46, 78)
•	(Last visit)	30.0 (13, 56)	32.0 (16, 58)	30.0 (11, 53)	38.5 (15, 60)
• Sleep disturbances	(Baseline)	50.0 (21, 74)	48.0 (15, 80)	45.0 (21, 72)	50.0 (25, 72)
•	(Last visit)	30.0 (10, 60)	27.0 (5, 57)	28.0 (10, 59)	35.0 (12, 62)
Safety (event rate per 100 patient years)					
Adverse events (AEs)		80.1	99.0	74.6	97.9
Serious adverse events (SAEs)		19.4	30.4	15.7	22.2
Infections (AEs) **		21.8	29.4	20.5	26.3
Infections (SAEs) **		2.9	5.2	2.0	2.4
Discontinuations due to AEs		2.9	3.5	2.2	5.7

SD: Standard deviation; VAS: Visual Analogue Scale; Q1, Q3 = 1st / 3rd quartile

* Please note, that for 104 patients (11.5%) the smoking status is unknown

** Infections: All AEs/SAEs with a MedDRA Preferred Term indicating an infection

Conclusions: TCZ i.v. treatment over two years resulted in improvements of all disease activity parameters. Contrary to csDMARDs and TNF-blockers, the results show that smokers benefit from TCZ i.v. to the same extent as non-smokers and ex-smokers. The similar effectiveness of TCZ i.v. was confirmed by distinctly improved patient reported outcomes (PROs) in all subgroups. On the other hand, smoking seems to coincide with a higher rate of adverse events and an increased risk of infections. However, due to differences in baseline characteristics between the subgroups, this has to be interpreted with caution.

References:

[1] Chang K, et al. Int J Mol Sci. 2014 Dec 3;15(12):22279–95.

[2] Theander E, et al. EULAR 2015: FRI0163.

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