Table. Peripheral blood cell counts for each week.

	week	tofacitinib			baricitinib			
		LDA	p	not LDA	LDA	p	not LDA	p
White Blood Cells [μl]	0	6821 ± 2402		6041 ± 2612	7994 ± 4309		7886 ± 2513	
	4	6247 ± 1905	.254	6465 ± 2440	.344	6706 ± 2499	.059	7143 ± 1526.363
	12	6480 ± 1949	.497	5871 ± 2070	.217	6470 ± 2867	.031	7383 ± 2963.356
	24	6733 ± 2297	.858	6450 ± 3001	.428	6418 ± 2875	.024	6833 ± 1021.454
Neutrophils [μl]	0	4888 ± 2399		3982 ± 2300	6221 ± 4085		6221 ± 4085	
	4	4243 ± 1655	.210	4298 ± 2100	.461	4548 ± 2578	.015	5923 ± 2716.294
	12	4261 ± 1843	.324	3617 ± 1869	.236	4542 ± 3062	.019	5429 ± 3055.311
	24	4487 ± 2243	.657	4547 ± 2847	.190	4225 ± 2900	.008	4474 ± 1396.207
Lymphocytes [μl]	0	1419 ± 651		1305 ± 489	1370 ± 416		1395 ± 485	
	4	1515 ± 544	.357	1502 ± 514	.039	1730 ± 659	.013	1530 ± 652.484
	12	1537 ± 555	.523	1327 ± 664	.996	1569 ± 572	.011	1453 ± 401.832
	24	1511 ± 598	.697	1143 ± 378	.092	1792 ± 699	.011	1836 ± 710.109
Platelets [10 ⁹ /μl]	0	26.9 ± 9.1		23.7 ± 6.6	30.3 ± 11.2		26.9 ± 7.4	
	4	25.5 ± 8.9	.291	23.8 ± 6.6	.940	30.5 ± 4.6	.940	27.3 ± 10.8.798
	12	24.7 ± 7.4	.261	25.6 ± 7.5	.209	33.1 ± 8.3	.209	27.0 ± 9.3.905
	24	26.3 ± 8.1	.930	23.3 ± 6.1	.961	33.4 ± 6.9	.961	33.0 ± 4.4.063

Data are mean ± standard deviation. LDA: patients achieved SDAI LDA at week 24. not LDA: patients did not achieve SDAI LDA at week 24. Shown *p* values were calculated by t-test compared to week 0.

Disclosure of Interests: None declared

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AB0359 TNF ALFA THERAPY AND RADIOSYNOVIORTHESIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The treatment of patients with rheumatoid arthritis (RA) has been spectacularly changed since the 1950's. Introduction of the steroid compounds and their local application, the chemical and radionuclide synovectomy, surgical synovectomy, use of non steroid drugs, the basic treatment and the spread of the biological therapy are the most important steps. Introduction of the biological therapy has changed the quality of life for these patients.

Objectives: During biological therapy sometimes 1 or 2 joints could be affected by inflammation. In this cases always the question is how to solve the problem. Change of the biological or basic therapy, use surgical synovectomy or radiosynovectomy (RSO)?

Methods: In our reumatological department 2100 patients with RA were treated with biological therapy between 2002 and 2018. In 100 patients we applied RSO because of the inflammation of the knee joint during biological therapy. We made a long term follow-up in 82 patient. All participants provided written informed consent. 82 participants inflammatory knee joint disease was diagnosed on the basis of the American College of Rheumatology. 70 of 82 patients with rheumatoid arthritis were seropositive, 12 seronegative. Steinbrocker functional stadium II was observed in 72, stadium III in 10. Mean age of 18 male and 76 female patients was 51.4 years (range 24-79) years. In 42 patients the right knee, in 40 the left knee was treated by radiosynovectomy. Mean duration of disease was 8.3 years (range 0.5-25), of synovitis (6.3month (range 3-8) Mean number of punctions of the treated joint prior to radiosynovectomy was 4,2 per patient and of steroid administrations prior to radiosynovectomy 3,0. In 15 patients a systemic steroid therapy has been performed.

Results: During the study period, inflammation decreased. In the first 3 years excellent and good results were recorded in 81,2%. 3 years after radiosynoviorthesis 82.2% of patients did not need another puncture.

Before the knee inflammation patients were in complete remission which status has been achieved after RSO as well. DAS: 2,4+-0,4.

Conclusion:

1. RSO is an effective method to treat the inflammation of the knees.
2. The RSO performed during biological therapy is as effective as in the case of patients without biological therapy.
3. In case of a successful RSO there is no need for biological or basic therapy neither for surgical synovectomy.
4. However an intraarticular injection has a low risk for infection it is recommended to avoid the biological therapy during the RSO.

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AB0360 EFFICACY AND SAFETY OF THE PROSTAGLANDIN EP4 RECEPTOR ANTAGONIST CR6086 ADDED TO METHOTREXATE IN DMARD-NAÏVE EARLY RA PATIENTS: A PHASE 2 RANDOMIZED CONTROLLED TRIAL

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Background: MTX is the first line treatment in early RA. There is robust evidence from cohort studies, but less from RCTs, that a "window of opportunity" exists over 12-16 weeks symptom duration. CR6086 is a selective prostaglandin EP4 receptor antagonist, with an immunomodulatory profile.

Objectives: To test efficacy and safety of CR6086 added to MTX in early RA, DMARD-naïve patients.

Methods: Patients with RA (ACR/EULAR 2010 criteria), < 1 year from symptom onset and naïve to DMARDs were randomized to oral CR6086 30, 90, 180mg, or placebo bid and oral MTX (20mg weekly) for 13 weeks (NCT03163966). Primary endpoint was the ACR20 response rate: 240 patients were needed to detect a difference among groups, with 50% responders on placebo and 70% on the 90mg CR6086 target dose. Pairwise comparisons of proportions were performed, with nonresponder imputation for withdrawals. A subgroup of patients underwent dynamic contrast-enhanced (DCE) MRI for quantification of synovitis at MCP and wrist joints, evaluated as DEMRIQ-ME and DEMRIQ-vol.

Results: The ITT population included all 244 randomized patients receiving at least one dose of study drugs (59 CR6086 30mg/MTX, 60 CR6086 90mg/MTX, 63 CR6086 180mg/MTX, 62 placebo/MTX). Safety was good with no increased rate of infections or other disorders; however, there were more minor upper GI adverse events (AEs) with CR6086, and increased dropouts due to AEs with the 180mg dose (9/63, 14.3% vs 1.7-3.4% in other groups). There were more ACR20 responders with MTX monotherapy than predicted (59.7%) and thus the 10.3% difference with the 90mg target dose (70.0%) was not significant. The low 30mg dose was no better than placebo (55.9%), while the high 180mg dose did not provide additional benefit compared with 90mg (74.0% net of dropouts). CR6086 90mg and 180mg induced a significant improvement in MRI, compared with placebo (Fig. 1). In a post-hoc analysis in patients < 6 months from symptom onset (ACR definition of early RA: 98/244, 40.2%), MTX monotherapy exerted a large 76% ACR20 response rate that precluded potentiation. Conversely, in patients of 6-12 months disease duration (146/244, 59.8%) ACR20 responders were 48.6% with MTX monotherapy vs 68.4% with 90mg, i.e. a 19.8% difference as postulated, with proportional differences in secondary endpoints (Tab. 1).

Conclusion: There was no benefit demonstrated for CR6086 added to MTX in the study cohort as a whole. However, in a post-hoc analysis, enhanced responses were observed with CR6086 90mg bid added to MTX in patients >6 months disease duration. This generated the hypothesis that addition of CR6086 90mg bid may benefit in RA patients initiating MTX after the window of opportunity, to be tested in further studies.

Table 1. ITT outcomes at week 13

	Symptom onset <12 months (principal analysis)		Symptom onset 6-12 months (post-hoc analysis)*	
	Placebo +MTX (N=62)	CR6086 90mg +MTX (N=60)	Placebo +MTX (N=37)	CR6086 90mg +MTX (N=38)
ACR20, %	59.7%	70.0%	48.6%	68.4%
ACR50, %	33.9%	38.3%	29.7%	39.5%
ACR70, %	17.7%	23.3%	10.8%	28.9%
DAS28 (CRP) <2.6, %	12.9%	20.0%	8.1%	18.4%
CDAI ≤2.8, %	8.1%	11.7%	5.4%	15.8%
SDAI ≤3.3, %	6.5%	10.0%	2.7%	15.8%
Boolean-based remission, %	6.5%	6.7%	2.7%	10.5%

*In patients with symptom onset <6 months, MTX monotherapy exerted a large 76% ACR20 response, and correspondingly high secondary efficacy parameters, precluding potentiation in this subset

Figure 1. Change in MRI (DEMRIQ-ME[®]) after 13 weeks

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AB0361

EFFICACY AND SAFETY OF BARICITINIB (BARI) IN RHEUMATOID ARTHRITIS(RA): CLINICAL AND ULTRASOUND EVALUATION IN REAL LIFE

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Background: Remission or low disease activity (LDA) are the ultimate goals of both conventional anti-rheumatic drugs (csDMARD) and biologic disease-modifying anti-rheumatic drugs (bDMARD) in treating RA. Janus Kinase (JAK) inhibitors are nowadays part of tsDMARDs, with BARI as an oral selective JAK1-2 inhibitor. Ultrasound (US) is a valuable imaging tool for detecting inflammatory joint changes and monitoring RA patients. The US7 score (US7) is a semiquantitative score including grayscale (GS) and power Doppler (PD) measurements of synovitis and tenosynovitis in 7 joints of the clinically dominant hand and foot.

Objectives: to evaluate real life efficacy and safety of BARI 4mg in RA patients using clinical, clinimetric and US evaluation.

Methods: adult RA patients starting BARI were eligible. DAS28ESR, CDAI, SDAI, painVAS, HAQ, COCHIN, laboratory parameters and US7 were performed/collected at baseline (BL) and after 3 and 6 months. Adverse events (AE) and concomitant medications were recorded. Responder/non responder status was determined using DAS28ESR improvement according to the EULAR Response Criteria at 3 months. Moreover, SDAI clinical remission or LDA (remission: SDAI≤3.3; LDA:3.3<SDAI≤11) were calculated at 3 and 6 months.

Results: 43 patients (12 csDMARD and 31 bDMARD failure) were enrolled, with 30 patients starting BARI in combination with a csDMARDs. BL painVAS was 68±23mm and disease activity was moderate to severe according to DAS28VES, CDAI and SDAI. BARI determined a significant improvement of every disease activity composite score and US7 components, except tendon PD; steroid daily dosage was significantly reduced.

28 patients were considered Responders at 3 months: responders used to have higher disease activity levels and synovitis scores at baseline.

Interestingly, painVAS and steroid dosage significantly decreased both in responders and non-responders, achieving similar value at 6 months. Non-responders showed both synovial and tendon involvement relapse at 6 months, with significantly higher PD score compared to responders. Remission was reached by 12.8% patients at 3 months and 21.6% at 6 months, while LDA patients were respectively 53.8% and 51.3%; combination with csDMARD was the only factor positively associated with remission/LDA at 3 months.

The percentage of dropped-out patients due to AE was aligned with literature data (5% in 6 months) whereas the percentage of Herpes Zoster Virus (HZV) infections was higher (4.6% in 6 months in our population vs 4.3% in 1 year in RCTs). Corticosteroid dosage was directly associated with AE development at 6 months.

Conclusion: Real life data confirmed BARI RCTs efficacy and safety data. Non responders showed both synovial and tendon PD disease relapse, despite painVAS and steroid reduction were comparable to responders. In our population, HZV infection prevalence was higher than in RCTs and corticosteroid dosage was positively associated with AE development at 6 months.

	BL		3M		p value	6M		p value
	R	NR	R	NR		R	NR	
painVAS	67,88±23,37	58,18±22,72	30,19±23,52	45,64±25,48	p=0.0040	30,19±20,42	29,73±22,15	p=0.2105
Daily prednisone equivalent	5,97±5,57	5,45±4,30	2,96±3,02	3,95±3,63	p=0.2248	1,63±2,10	3,03±3,59	p=0.1247
GSS	8,50±5,25	7,00±3,81	3,69±3,63	2,33±2,45	p=0.9334	3,56±3,01	4,22±2,64	p=0.2452
GST	2,88±2,33	3,11±2,09	0,88±0,89	1,56±1,59	p=0.6501	1,00±1,37	2,78±1,72	p=0.0831
PDS	8,00±7,11	3,33±3,46	3,00±3,48	2,44±3,36	p=0.0066	3,25±3,13	5,00±4,56	p=0.0006
PDT	2,81±2,46	2,44±3,36	0,88±1,54	1,33±1,50	p=0.44990	1,06±1,53	3,78±3,19	p=0.0156
Erosions	1,25±2,05	0,44±0,73	1,50±2,03	0,44±0,73	p=0.0736	1,31±2,09	1,11±1,27	p=0.0902