attained DAS-28 LDA at least once up to one year was 67 (92%, 80% to 97%) and the number of patients attaining DAS-28 and Boolean remission were 31 (50%, 34% to 61%) and 12 (20%, 9% to 30%) respectively. Median time to DAS-28 LDA was 16 weeks (Figure 1). Cox regression analyses did not show any sufficiently precise association of remission or LDA with age, gender, seropositivity, disease duration, concomitant DMARD use and number of previous bDMARDs. Increasing number of previous bDMARDs was associated with poor baricitinib survival (HR=1.5, 95%CI 1.1 to 2.2) while this association was not robust to adjustment for baseline disease activity. Favorable changes were observed in tender and swollen joint counts, pain-VAS, patient and physician disease assessment scores, RAID, FACIT and the acute phase response.

Conclusion: In this prospective observational study, we observed high rates of LDA and DAS-28 remission and significant improvements in disease activity and patient reported outcome measurements over time.

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Table 1

Age, yr, mean (SD)	57.8 (12.1)
Sex, n(%)	Male 23 (27.1) Female 62 (72.9)
Disease duration, yr, mean (SD)	8.5 (8.2)
RF status, n(%)	Positive 69 (81.2)
ACPA status, n(%)	Positive 66 (77.6)
anti-CCP status, n(%)	Positive 45 (52.9)
Follow up, weeks, mean (SD)	49.3 (28.9)
Baricitinib use	Monotherapy 51 (60.0) Combination 34 (40.0)
TJC (78), mean (SD)	6.6 (6.6)
SJC (76), mean (SD)	4.3 (5.5)
ESR, mm/h, mean (SD)	20.5 (16.4)
CRP, mg/L, mean (SD)	11.7 (12.7)
DAS-28, mean (SD)	4.4 (2.1)
HAQ-DI, mean (SD)	1.2 (0.7)
No. of previous csDMARDs	0 1 (1.2) 1 27 (31.8) 2 31 (36.5) 3 17 (20.0) 4 8 (9.4) 5 1 (1.2)
No. of previous bDMARDs	0 28 (32.9) 1 16 (18.8) 2 19 (22.4) 3 8 (9.4) 4 8 (9.4) 5 6 (7.1)

Figure 1

Figure 1. Cumulative probability of low disease activity or remission under treatment with baricitinib.

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AB0331

EFFICACY, RETENTION RATE AND PREDICTORS OF TOFACITINIB EFFICACY AND RETENTION IN RHEUMATOID ARTHRITIS PATIENTS: HUR-BIO REAL-LIFE EXPERIENCE

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Background: Tofacitinib (TOF) is an oral Janus Kinase (JAK) inhibitor and is indicated in the treatment of rheumatoid arthritis (RA). Several interventional or observational studies demonstrated its safety and efficacy, however, its real-life retention rate and related factors need to be elucidated further and its efficacy needs to be approved in real-life.

Objectives: To assess the real-life efficacy, retention rate and related factors of both parameter in rheumatoid arthritis patients under tofacitinib.

Methods: We analyzed all RA patients registered to HURBIO database who received at least 1 dose of tofacitinib (*for drug retention*) and who had at least 1

control visit under tofacitinib (*for efficacy*). Drug retention rates were calculated using the Kaplan-Meier method and predictors of drug retention were determined by Cox proportional hazard model. Patients were grouped as "responder" or "non-responders according" to DAS28 at last control visit: DAS28-CRP≤3.2: "Responders"; DAS28-CRP>3.2: "Non-responders". Predictors of response (DAS28-CRP≤3.2 at last visit) were determined by logistic regression analysis. Reasons for switching and discontinuation were also determined.

Results: For drug retention; a total of 247 (210 (85%) female) patients were recruited. Mean age was 53.1±12.6 years. Mean disease duration was 11.3±8.0 years. Rheumatoid factor and anti-CCP antibodies were positive in 160/240 (66.7%) and 135/207 (65.2%) patients, respectively. Combination with DMARDs was used in 83.3% of patients. 55.5% of patients was biologic-naïve. Median follow-up while receiving tofacitinib was 10.2 (IQR:4.0-24.2) months. One-year crude retention rate was 64%. Median duration of drug retention was 24.8 months. Predictors of good tofacitinib retention were (in multivariate analysis): *living in Ankara (where our center is located)* (HR 1.43 (0.96-2.14); 95% CI) and *BMI> 25* (HR 1.46 (0.97-2.29); 95% CI).

For efficacy; a total of 204 (174 (85.4%) female) patients were recruited. Mean age was 53.2±12.5 years. Mean disease duration was 11.5±8.1 years. Rheumatoid factor and anti-CCP antibodies were positive in 135/198 (68.1%) and 115/171 (67.2%) patients, respectively. Detailed demographic and clinical characteristics of participants were given in table 1. Median follow-up while receiving tofacitinib was 11.6 (IQR:5.2-26.2) months. DAS28-CRP levels at baseline and last visit were 4.8 (IQR:3.9-5.4) and 3.3 (IQR:2.5-4.6), respectively (p<0.001). At last visit, 19.6% of patients was in low-disease activity (2.6≤DAS28-CRP≤3.2), 26.0% of patients was in remission (DAS28-CRP<2.6). Predictors of good response to tofacitinib were (in multivariate analysis, adjusted for follow-up duration under tofacitinib): *biologic-naïve* (aOR 2.38 (1.30-4.34); 95% CI) and *RF negativity* (aOR 2.12 (1.13-3.95); 95% CI).

The most common cause of drug discontinuation was primary failure (in 36/108 patients, 33.4%).

Conclusion: Tofacitinib seems an effective treatment option for rheumatoid arthritis. Relationship between seronegativity and good response to tofacitinib needs to be elucidated. Also, Clinicians should keep in their mind that in addition to patient characteristics, socioeconomic factors may influence the adherence to the treatment.

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AB0332

IMMUNOSUPPRESSIVE AND IMMUNOMODULATING AGENTS IN RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW OF CLINICAL TRIALS AND THEIR CURRENT DEVELOPMENT STAGE

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Background: Rheumatoid arthritis (RA) is the most frequent chronic inflammatory diseases with an incidence of 0.5% to 1%. Therapeutic arsenal of RA has continuously expanded in recent years with the recent therapeutic progress with the arrival of conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), biological (bDMARDs) and targeted synthetic (tsDMARDs), JAK inhibitors. However, there are still some unmet needs for patients who do not achieve remission and who continue to worsen despite treatments. Of note, only approximately 40% of patients are ACR70 responders, in most randomized controlled trials. For these patients, finding new therapeutic avenues is challenging.

Objectives: The objective of our study was to analyze the whole pipeline of immunosuppressive and immunomodulating drugs evaluated in RA and describe their mechanisms of action and stage of clinical development.

Methods: We conducted a systematic review of all drug therapies in clinical development in RA in 17 databases of international clinical trials. Inclusion criterion: study from one of the databases using the keywords "Rheumatoid arthritis" (search date: June 1, 2019). Exclusion criteria: non-drug trials, trials not related to RA or duplicates. We also excluded dietary regimen or supplementations, cellular therapies, NSAIDs, glucocorticoids or their derivatives and non-immunosuppressive or non-immunomodulating drugs. For each csDMARD, bDMARD and tsDMARD, we considered the study at the most advanced stage. For bDMARDs, we did not take into account biosimilars.

Results: The research identified 4652 trials, of which 242 for 243 molecules met the inclusion and exclusion criteria. The developed molecules belong to csDMARDs (n=21), bDMARDs (n=117), tsDMARDs (n=105).

Among the 21 csDMARDs molecules: 8 (38%) has been withdrawn, 4 (19%) are already labelled in RA (hydroxychloroquine, leflunomide, methotrexate and sulfasalazine) and 9 (43%) are in development: 1 (11%) is in phase I/II, 5 (56%) in phase II, 3 (33%) in phase IV.

Among the 117 bDMARDs molecules: 69 (59%) has been withdrawn, 9 (8%) are labeled in RA (abatacept, adalimumab, anakinra, certolizumab, etanercept, golimumab, infliximab, rituximab, sarilumab, tocilizumab) and 39 (33%) are in development: 9 (23%) in phase I, 3 (8%) in phase I/II, 21 (54%) in phase II, 5 (12%) are in phase III, 1 (3%) in phase IV. bDMARDs currently under development target B cells (n=4), T cells (n=2), T/B cells costimulation (n=2), TNF alpha (n=2), Interleukine 1 or his receptor (n=3), Interleukine 6 or his receptor (n=7), Interleukine 17 (n=4), Interleukine 23 (n=1), GM-CSF (n=1), other cytokines or chemokines (n=5), integrins or adhesion proteins (n=3), interferon receptor (n=1) and various other targets (n=4).

Among the 105 tsDMARDs molecules: 64 (61%) has been withdrawn, 6 (6%) JAK inhibitors, have just been or will probably soon be labelled (baricitinib, filgotinib, peficitinib, tofacitinib and upadacitinib), 35 (33%) are in development: 8 (24%) in phase I, 26 (74%) in phase II, 1 (3%) in phase III and. tsDMARDs currently under development target tyrosine kinase (n=12), janus kinase (JAK) (n=3), sphingosine phostate (n=3), PI3K pathway (n=1), phosphodiesterase-4 (n=3) B cells signaling pathways (n=3) and various other targets (n=10).

Conclusion: A total of 242 therapeutic trials involving 243 molecules have been or are being evaluated in RA. This development does not always lead to new treatments since 141 (58%) have already been withdrawn. Hopefully, some of the currently evaluated drugs will contribute to improve the therapeutic management of RA patients, requiring a greater personalization of therapeutic strategies, both in the choice of molecules and their place in therapeutic sequences.

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AB0333

CLINICAL AND ULTRASONOGRAPHIC RESPONSE TO SUBCUTANEOUS METHOTREXATE IN EARLY RHEUMATOID ARTHRITIS. PRELIMINARY RESULTS.

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Background: Metotrexate (MTX) is usually the first line therapy for Rheumatoid Arthritis (RA) because of its favorable efficacy-toxicity ratio. However the exact mechanism and treatment response time in both a clinical and ultrasonographic setting are still uncertain.

Objectives: To describe the clinical and ultrasound response to MTX during the first 6 months of treatment in early RA patients who started subcutaneous methotrexate as the first disease-modifying drug (DMARD).

Methods: Ongoing prospective cohort of patients with early RA (ACR-EULAR 2010 criteria), over 18 years and starting MTX-SC. Patients had a clinical and ultrasonographic evaluation at baseline, 1, 3 and 6 months. We collected demographic data, C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], rheumatoid factor [RF], anti-citrullinated protein antibody [ACPA], inflammatory activity indexes (DAS28esr and DAS28crp) and EULAR's response to treatment (delta value of -1.2 in DAS28 scores). Joints explored with ultrasound were elbows and wrists (radio-carpal and inter-carpal joint) counted as a single joint, 1st-5th metacarpophalangeal (MCP), proximal interphalangeal (IP), knees, tibio-talar and subtalar joints and 2nd-5th metatarsophalangeal (MTF) joints. Bone erosions were evaluated in 2nd and 5th MCP, styloid, distal ulna and 5th MTF. Synovitis was graduated semi-quantitatively from 0 to 3 (OMERACT) and calculated on B mode and Doppler.

Results: 35 patients were included (mean age 61.2 years, 65.7% women) with a median of 0.8 (+/-8) months delay to diagnosis. 34 patients (97.1%) started 15mg MTX-SC/weekly. A higher DAS28esr was found in baseline data for the group that had a response by month 1 (DAS28esr baseline 5.5 vs 4.2 p=0.01), no other significant differences were found. During the first month, a significant response was achieved in 13 (41%) patients and remission in 11 (35%) (Table 1). 17 patients have 6th month data. 11 (64.7%) have achieved EULAR response compared to baseline (P=0.0005) out of which 7 (54.5%) had already reached it by month 1. A difference in MTX dose (month1 14.8 vs month6 17.1 p=0.003) was found between month 1 and 6, with no differences in disease activity. In the ultrasonographic baseline data; 8 patients (22.9%) had erosions, with a mean of 2.75 erosions/patient (22 of the 280 locations). During the follow up the global rating lowered,

with no differences in B mode but significant differences in Doppler at the 6 month mark (Table 2). As of this report, 10 patients (28.5%) had stopped MTX treatment due to lack on response or adverse effects and 8 (22.9%) are waiting 6th month evaluation.

Table 1. Baseline vs month 1

	Baseline	Month 1	P Value
EULAR response	0	13 (41)	0.00005
MTX Dose mg (SD)	14.8 (+/-0.8)	14.8 (+/-1.6)	1
Prednisone Dose mg(SD)	5.9 (+/-6.5)	2.9 (+/-3)	0.02
DAS28crp (SD)	4.3 (+/-1.5)	3.4 (+/-1.4)	0.02
DAS28esr (SD)	(4.8 (+/-1.5)	3.7 (+/-1.4)	0.006
Remission (DAS28<1.2)	3(9.6)	11(35.5)	0.04

Table 2. Ultrasound synovitis global rating.

	Baseline N=35	1 month N=31	3 months N=25	6 months N=17
B Mode: Median (interquartile range)	8 (3.5-12)	8 (3-12.5)	6 (4-11)	5 (2-11) p 0,16
Doppler Mode: Median (interquartile range)	2 (0.5-6)	2 (0-6)	2 (0-6)	0 (0-2) p 0,005

Conclusion: In this cohort half of the patients that responded to treatment had achieved this by month 1. A higher baseline inflammatory profile was related to the response. Little difference is found between month 1 and 6 on clinical data, however ultrasonographic results suggest that at least 6 months are needed for Doppler improvement. Perhaps MTX has a faster effect over joint pain and lowers DAS28 scores requiring longer to completely suppress inflammatory activity.

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AB0334

COST-EFFECTIVENESS OF JAK INHIBITORS IN RHEUMATOID ARTHRITIS IN THE REAL WORLD PRACTICE

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Background: The Janus Kinase (JAK) inhibitors Baricitinib (BAR) and Tofacitinib (TOF), both in monotherapy or in combination with methotrexate, are indicated for moderate to severe active rheumatoid arthritis (RA) with inadequate response to conventional synthetic disease modifying anti-rheumatic drugs (csDMARD). Data about cost-effectiveness in a real-world setting are still scarce.

Objectives: To assess the cost-effectiveness (C-E) of BAR and TOF in patients with RA in usual clinical practice.

Methods: Retrospective observational study of adult RA patients who started BAR and TOF between September 2017 and December 2019, in a university hospital. Data were collected from the electronic medical records and the Dominion® External Patient Dispensing program. Demographic, clinical and laboratory parameters [erythrocyte sedimentation rate (ESR), C reactive protein (CRP), Rheumatoid factor (RF), anti-citrullinated peptide antibodies (ACPA)], concomitant csDMARD, previous biological (b) DMARD, DAS28-ESR activity score items, and treatment duration were registered. DAS28-ESR remission or low disease activity (LDA) were used as the effectiveness measure to estimate C-E. The official Spanish prices were considered to calculate the costs of the treatments. Statistical analysis was performed with SPSS v.15 program. Descriptive statistics are shown in proportions, medians and interquartile ranges (IQR).