

Supplementary file

Methods: Study selection

Title and abstract review of the main search as well as data extraction was done independently by two of the authors (KC and SE). Discrepancies were resolved by discussion.

Glucocorticoids in RA

A systematic literature search was performed in PUBMED Medline, EMBASE and Cochrane library databases between January 2013 and February 2016, using the followings key-words for articles in English: rheumatoid arthritis, Glucocorticoids, Prednisone, Prednisolone. Additional studies were identified by hand searching reference lists and abstracts presented at the American College of Rheumatology 2013-2015 and European League Against Rheumatism from 2013 to 2015. The trials were initially selected on the basis of their titles and abstract, then on the full texts.

csDMARDs in RA

Literature published on the following csDMARDs, given in monotherapy and in combination, was examined: methotrexate, leflunomide, sulfasalazine, hydroxychloroquine, intramuscular gold, auranofin, azathioprine, cyclosporine, minocycline, D-penicillamin, cyclophosphamide, chlorambucil, mycophenolate, tacrolimus. A systematic literature search was performed in PUBMED Medline, EMBASE and Cochrane library databases using the following key-words for articles in English: rheumatoid arthritis, name of drug or combination. Additional studies were identified by hand searching reference lists and abstracts presented at the American College of Rheumatology 2013-2015 and European League Against Rheumatism from 2013 to 2015. Concerning the efficacy of MTX in monotherapy versus in combination, we included RCTs comparing in adult RA, MTX monotherapy to MTX in combination with another csDMARD without glucocorticoid differences.

tsDMARDs in RA

A systematic literature search was performed in PUBMED Medline, EMBASE and Cochrane library databases after January 2013 using the followings key-words for articles in English: rheumatoid arthritis, tofacitinib, Jak inhibitor, baricitinib, CP-690,550, LY3009104. Additional studies were identified by hand searching reference lists and abstracts presented at the American College of Rheumatology 2013-2015 and European League Against

Rheumatism from 2013 to 2015. The trials were initially selected on the basis of their titles and abstract, then on the full texts.

Figure A: Literature search strategy for all RCTs reporting the efficacy and safety of addition of GCs in RA

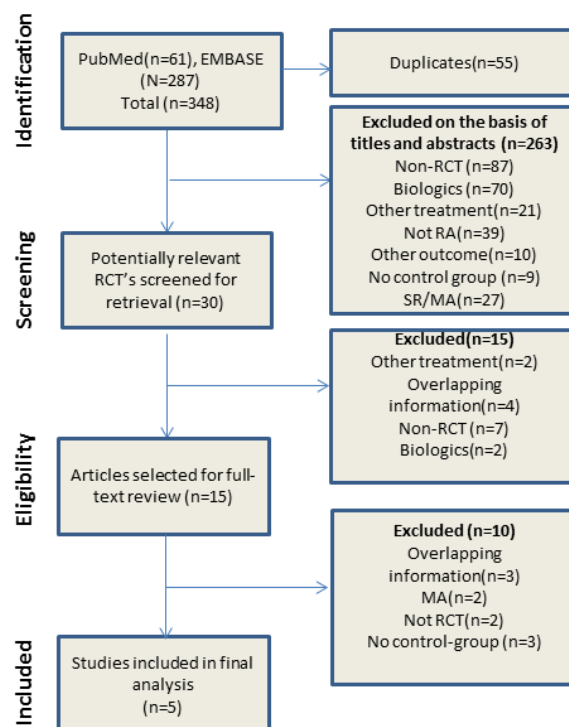


Figure B: Literature search strategy for all RCTs reporting the efficacy and safety of MTX monotherapy versus MTX in combination with other csDMARD

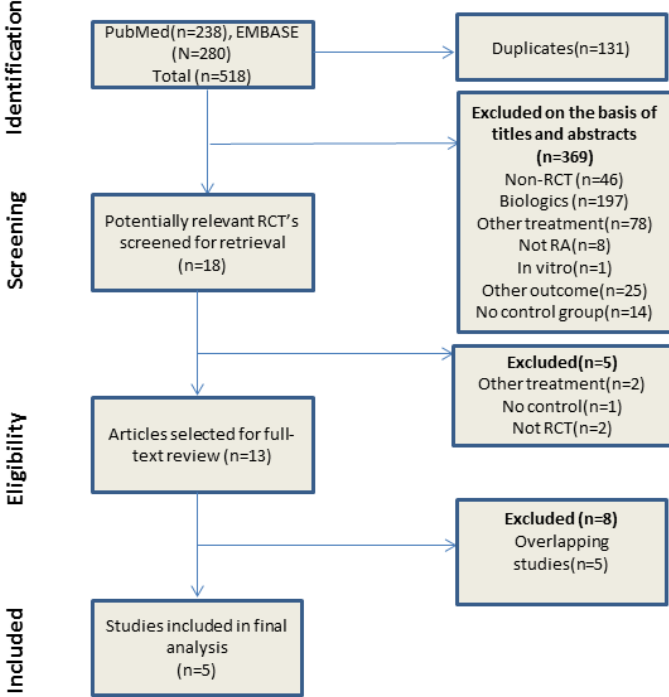
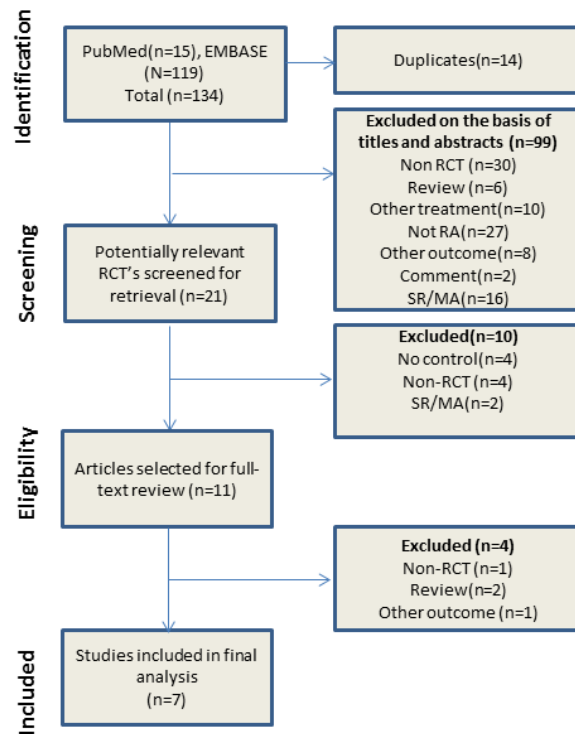


Figure C: Literature search strategy for all RCTs reporting the efficacy and safety of tofacitinib



Data collection

Efficacy was assessed by the change in signs and symptoms (swollen and tender joint count, Disease Activity Score, ACR 20/50/70 response rates, pain, patient and physician global assessment, acute phase reactants ESR and CRP) or disability status (by the health assessment questionnaire (HAQ or MHAQ)) between baseline and week 12, week 24, week 52 and week 104 when available, and by the change in radiographic joint damage (according to total Sharp score, Sharp modified by Van der Heijde, Larsen score) between baseline and week 52 and week 104 when available in both groups.

Two investigators collected the data, using a predetermined form. The following methodological features were collected: blinding, intent-to-treat-analysis or not, number of participants who completed the follow-up. The evaluation of the validity of the included studies was done using the Cochrane Collaboration's tool for assessing risk of bias. For each trial, demographic characteristics (sex, mean age), RA duration, background treatment, type

of glucocorticoids (with doses), type of DMARD (with doses), type of comparator, and duration of follow-up were collected.

Supplementary table 1. Randomised controlled trials comparing the efficacy of methotrexate monotherapy with csDMARD combination.

	Study design	ROB	N. patients	Disease duration	Outcome	MTX monotherapy arm	csDMARD combination arm	p-value
tREACH (1y)	superiority	High	281	1 year	AUC for DAS	25.6±8.4	23.2±8.3	0.0497
					AUC for HAQ	6.9±5.4	8.6±5.9	0.052
					DAS status	3.4±1.1	3.4±1.0	NS
					HAQ status	1.0±0.6	1.1±0.7	NS
					radiographic progression*	1 (0-3)	1 (0-3.5)	NS
CareRA	superiority	High	290	16 weeks	DAS28(CRP) <2.6	73.5%	~ 70%	NS

ROB = Risk of Bias; MTX = Methotrexate; csDMARDs = conventional synthetic Disease Modifying Anti-rheumatic Drugs; AUC = Area Under the Curve; DAS = Disease Activity Score; HAQ = Health Assessment Questionnaire; CRP = C-reactive protein; NS = non-significant

* Radiographic progression was measured with the modified Sharp–van der Heijde score (SHS)