Electronic Supplementary Material #2

The impact of biologics and tofacitinib on cardiovascular risk factors and outcomes in patients with rheumatic disease: a systematic literature review

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Table 1. Summary of study characteristics assessing CV risk in RA

Characteristic	**boDMARD**									**tsDMARD**
	ABA	**ADA**	**CZP**	**ETN**	**GLM**	**INF**	**RTX**	**SEC**	**TCZ**	**TOFA**
Study type, n										
RCT	1 [16]	4 [26, 27, 29, 30, 32]	1 [42, 43]	3 [27, 30, 44]	1 [53]	2 [56-58]		1 [77, 78]	10 [16, 26, 27, 30, 32, 79-82, 84, 85, 92]	9 [29, 83, 93-101]
PC	2 [17, 18]	5 [33-37]		5 [35, 45-48]		13 [35, 54, 55, 59-69]	6 [17, 71-75]		7 [17, 37, 72, 86-89]	
RC	5 [19-24, 85]	5 [19, 24, 38-41]		5 [19, 38, 49-52]		5 [19, 38, 49, 51, 70]	4 [19-21, 23, 25, 28, 31, 76]		6 [20-25, 90, 91]	
Treatment Duration, w	12–72	16–624	52 (+48)	16–525	104	6–156	12–572	16	12–156	6–104

Patients enrolled, n	32–27,082	32–15,554	982	32–15,554	1884	38–15,554	33–27,082	237	32–68,447	69–956

Blank shaded cells indicate that there were no studies in this category for that drug.

ABA abatacept, *ADA* adalimumab, *boDMARD* biological originator disease-modifying anti-rheumatic drug, *CV* cardiovascular, *CZP* certolizumab pegol, *ETN* etanercept, *GLM* golimumab, *INF* infliximab, *PC* prospective cohort study, *RA* rheumatoid arthritis, *RC* retrospective cohort study, *RCT* randomized clinical trial, *RTX* rituximab, *SEC* secukinumab, *TCZ* tocilizumab, *TOFA* tofacitinib, *tsDMARD* targeted synthetic disease-modifying anti-rheumatic drug

Table 2. Baseline characteristics of patients with RA

Baseline data	boDMARD									tsDMARD
	ABA	**ADA**	**CZP**	**ETN**	**GLM**	**INF**	**RTX**	**SEC**	**TCZ**	**TOFA**
Number of studies										
RCT	1	5	1	3	1	2	0	1	10	9
nRCT	7	10	0	10	0	18	10	0	13	0
Age, yrs										
RCT	NR	52.5–63.0	51.4–52.4	59.3–61.0	NR	51.6–53.0	NA	NR	49.3–62.0	47.9–53.0
nRCT	55.9–58.4	51.0–58.4	NA	40.0–57.0	NA	38.0–62.7	49.0–60.9	NA	52.0–62.8	NA
Female, %										
RCT	NR	79.4–85.7	82.4–83.9	72.2–85.7	NR	71.0–95.0	NA	NR	73.0–86.4	76.7–90.0
nRCT	75.9–100	72.7–88.2	NA	70.0–100	NA	40.8–100	71.0–100	NA	75.9–87.0	NA

Disease duration, yrs										
RCT	NR	0.8–8.1	6.1–6.2	0.9–10.1	NR	0.4–1.0	NA	NR	0.8–9.8	2.7–11.0
nRCT	6.2–14.6	0.3–14.6	NA	1.0–15.2	NA	1.2–14.3	7.1–17.6	NA	6.2–14.6	NA
CRP, mg/dL										
RCT	NR	25.0–175.0	140.0–160.0	26.7	NR	13.7–23.6	NA	NR	0.9–320.0	22.3–356.0
nRCT	112	12.0–19.0	NA	20.1–80.0	NA	2.2–29.8	15.0–96.0	NA	3.1–181.0	NA
ESR, mm/h										
RCT	NR	37.0–48.5	42.5–45.0	39.0	NR	55.0–65.0	NA	NR	38.0–50.5	50.5–56.0
nRCT	32.6	17.0–40.0	NA	23.0	NA	30.7–41.0	23.0–47.1	NA	41.4–64.0	NA
DAS28										
RCT	NR	5.3–6.8	6.9–7.0	5.2	NR	4.6–5.1	NA	NR	5.2–6.8	5.6–6.5
nRCT	5.1–5.9	5.1–6.5	NA	4.1–6.6	NA	4.6–6.6	3.7–6.6	NA	4.6–5.3	NA

History of CV risk/event, %										
RCT	0.0	0.0–77.2	NR	0.0–83.5	NR	0.0–30.0	NA	NR	0.0–77.2	1.8–11.5
nRCT	8.0–45.0	0.0–45.0	NA	0.0–59.0	NA	0.0–47.8	0.0–57.0	NA	0.0–45.0	NA
Prior csDMARDs, %										
RCT	100	0.0–55.9	100	0.0	NR	0.0–100	NA	100	0.0–100	37.0–100
nRCT	100	38.2–100	NA	0.0–100	NA	10.0–100	78.8–100	NA	100	NA
Prior boDMARD, %										
RCT	100	0.0–7.8	NR	0.0	NR	0.0	NA	NR	0.0–100	1.0–19.7
nRCT	64.1–100	100	NA	0.0–100	NA	100	64.1–100	NA	51.0–72.0	NA

ABA abatacept, *ADA* adalimumab, *boDMARD* biological originator disease-modifying anti-rheumatic drug, *CRP* C-reactive protein, *csDMARD* conventional synthetic disease-modifying anti-rheumatic drug, *CV* cardiovascular, *CZP* certolizumab pegol, *DAS28* disease activity score based on 28 joints, *ESR* erythrocyte sedimentation rate, *ETN* etanercept, *GLM* golimumab, *INF* infliximab, *NA* not applicable, *NR* not reported, *nRCT* not randomized clinical trial, *RA* rheumatoid arthritis, *RCT* randomized clinical trial, *RTX*

rituximab, *SEC* secukinumab, *TCZ* tocilizumab, *TOFA* tofacitinib, *tsDMARD* targeted synthetic disease-modifying anti-rheumatic drug

Table 3. Summary of study characteristics assessing CV risk in PsA

Characteristic	**boDMARD**				
	ADA	**ETN**	**INF**	**SEC**	**UST**
Study type, n					
RCT		1 [105]		1 [103, 104]	1 [102]
PC		1 [106]	1 [62]		
RC	2 [41, 107]	1 [107]			
Treatment duration, w	104–624	12–260	26	52	108
Patients enrolled, n	210–16,842	84–210	60	606	615

Blank shaded cells indicate that there were no studies in this category for that drug.

ADA adalimumab, *boDMARD* biological originator disease-modifying anti-rheumatic drug, *CV* cardiovascular, *ETN* etanercept, *INF* infliximab, *PC* prospective cohort study, *PsA* psoriatic arthritis *RC* retrospective cohort study, *RCT* randomized clinical trial, *SEC* secukinumab, *UST* ustekinumab

Table 4. Baseline characteristics of patients with PsA

Baseline data	boDMARD					
	ADA	**ETN**	**GLM**	**INF**	**SEC**	**UST**
Number of studies						
RCT	0	0	1	0	1	1
nRCT	2	3	0	1	0	0
Age, yrs						
RCT	NA	NA	NR	NA	48.5–49.6	NR
nRCT	42.6–48.4	42.7–47.1	NA	42.5	NA	NA
Female, %						
RCT	NA	NA	NR	NA	52.5	NR
nRCT	48.6–47.4	29.8–52.0	NA	60.0	NA	NA
Disease duration, yrs						
RCT	NA	NA	NR	NA	NR	NR
nRCT	3.0–14.6	3.1–9.0	NA	0.9	NA	NA
CRP, mg/dL						
RCT	NA	NA	NR	NA	NR	NR
nRCT	NR	13.4	NA	NR	NA	NA
ESR, mm/h						

RCT nRCT	NA NR	NA 21.9	NR NA	NA 41.0	NR NA	NR NA
DAS28 RCT nRCT	NA NR	NA 4.6	NR NA	NA NR	NR NA	NR NA
History of CV risk/event, % RCT nRCT	NA 0.0–62.7	NA 0.0–61.9	NR NA	NA 0.0	NR NA	NR NA
Prior csDMARDs, % RCT nRCT	NA NR	NA 100	NR NA	NA NR	NR NA	NR NA
Prior boDMARD, % RCT nRCT	NA 0.0	NA 0.0	NR NA	NA NR	17.3–19.3NA	NR NA

ADA adalimumab, *boDMARD* biological originator disease-modifying anti-rheumatic drug, *CRP* C-reactive protein, *csDMARD* conventional synthetic disease-modifying anti-rheumatic drug, *CV* cardiovascular, *DAS28* disease activity score based on 28 joints, *ESR* erythrocyte sedimentation rate, *ETN* etanercept, *GLM* golimumab, *INF* infliximab, *NA*

not applicable, *NR* not reported, *nRCT* not randomized clinical trial, *PsA* psoriatic arthritis, *RCT* randomized clinical trial, *SEC* secukinumab, *UST* ustekinumab

Table 5. Summary of study characteristics assessing CV risk in AS

Characteristic	**boDMARD**				
	ADA	**ETN**	**GLM**	**INF**	**SEC**
Study type, n					
RCT			2 [53, 110]		1 [108, 109]
PC		2 [111, 112]		6 [54, 55, 62, 113-115]	
RC	1 [41]				
Treatment duration, w	624	12–24	52–104	7–26	104
Patients enrolled, n	23,458	55–92	41–1884	30–82	371

Blank shaded cells indicate that there were no studies in this category for that drug.

ADA adalimumab, *AS* ankylosing spondylitis, *boDMARD* biological originator disease-modifying anti-rheumatic drug, *CV* cardiovascular, *ETN* etanercept, *GLM* golimumab, *INF* infliximab, *PC* prospective cohort study, *RC* retrospective cohort study, *RCT* randomized clinical trial, *SEC* secukinumab

Table 6. Baseline characteristics of patients with AS

Baseline data	boDMARD				
	ADA	**ETN**	**GLM**	**INF**	**SEC**
Number of studies					
RCT	0	0	2	0	1
nRCT	1	2	0	6	0
Age, yrs					
RCT	NA	NA	34.2–35.6	NA	NR
nRCT	43.1	41.0–43.0	NA	34.3–42.0	NA
Female, %					
RCT	NA	NA	10.0	NA	NR
nRCT	27.5	10.0–35.0	NA	1.5–13.0	NA
Disease duration, yrs					
RCT	NA	NA	8.0–11.0	NA	NR
nRCT	10.9	8.5	NA	1.5–13.0	NA
CRP, mg/dL					
RCT	NA	NA	19.9–23.9	NA	NR
nRCT	NR	11.0–13.0	NA	2.2–36.4	NA
ESR, mm/h	NA	NA	20.0–29.0	NA	NR
RCT	NR	15.0–37.0	NA	26.3–46.2	NA

nRCT					
BASDAI					
RCT	NA	NA	NR	NA	NR
nRCT	NR	4.9–6.0	NA	4.9–7.0	NA
History of CV risk/event, %					
RCT	NA	NA	0.0–40.0	NA	NR
nRCT	NR	0.0–20.0	NA	0.0–43.3	NA
Prior csDMARDs, %					
RCT	NA	NA	0.0	NA	NR
nRCT	NR	NR	NA	100	NA
Prior boDMARD, %					
RCT	NA	NA	NR	NA	NR
nRCT	NR	NR	NA	NR	NA

adalimumab, *AS* ankylosing spondylitis, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *boDMARD* biological originator disease-modifying anti-rheumatic drug, *CRP* C-reactive protein, *csDMARD* conventional synthetic disease-modifying anti-rheumatic drug, *CV* cardiovascular, *ESR* erythrocyte sedimentation rate, *ETN* etanercept, *GLM* golimumab, *INF* infliximab, *NA* not applicable, *NR* not reported, *nRCT* not randomized clinical trial, *RCT* randomized clinical trial, *SEC* secukinumab

Table 7. Summary of study characteristics assessing CV risk in JIA

Characteristic	**boDMARD**		
	ADA	**ETN**	**TCZ**
Study type, n			
RCT			2 [116-119]
PC		1 [120]	
RC	1 [41]	1 [121]	
Treatment duration, w	624	52–572	6–104
Patients enrolled, n	23,458	30–278	92-188

Blank shaded cells indicate that there were no studies in this category for that drug.

ADA adalimumab, *boDMARD* biological originator disease-modifying anti-rheumatic drug, *CV* cardiovascular, *ETN* etanercept, *JIA* juvenile idiopathic arthritis, *PC* prospective cohort study, *RC* retrospective cohort study, *RCT* randomized clinical trial, *TCZ* tocilizumab

Table 8. Baseline characteristics of patients with JIA

Baseline data	boDMARD		
	ADA	**ETN**	**TCZ**
Number of studies			
RCT	0	0	2
nRCT	1	2	1
Age, yrs			
RCT	NA	NA	6.9–13.1
nRCT	11.2	12.3	NR
Female, %			
RCT	NA	NA	71.0–86.0
nRCT	80.2	73.0	NR
Disease duration, yrs			
RCT	NA	NA	3.4–4.7
nRCT	3.9	2.5	NR
CRP, mg/dL			
RCT	NA	NA	218.0–266.0
nRCT	NR	0.9	NR
ESR, mm/h	NA	NA	34.2–36.6
RCT	NR	35.0	NR

nRCT			
History of CV risk/event, %			
RCT	NA	NA	NR
nRCT	NR	NR	NR
Prior csDMARDs, %			
RCT	NA	NA	60.0–76.0
nRCT	NR	100	NR
Prior boDMARD, %			
RCT	NA	NA	18.0–39.0
nRCT	NR	NR	NR

ADA adalimumab, *boDMARD* biological originator disease-modifying anti-rheumatic drug, *CRP* C-reactive protein, *csDMARD* conventional synthetic disease-modifying anti-rheumatic drug, *CV* cardiovascular, *ESR* erythrocyte sedimentation rate, *ETN* etanercept, *NA* not applicable, *NR* not reported, *nRCT* not randomized clinical trial, *RCT* randomized clinical trial, *TCZ* tocilizumab