Relative Efficacy and Safety of Tofacitinib, Baricitinib, Upadacitinib, and Filgotinib in Comparison to Adalimumab in Patients with Active Rheumatoid Arthritis

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Background

- JAK inhibitors have different selectivity for JAKs which may confer different benefit-risk profiles
  - TOF is JAK1/JAK3 and JAK2 selective
  - BARI is JAK1 and JAK2 selective
  - UPA and FIL are both JAK1 selective
- Relative efficacy and safety of the JAK inhibitors remain unclear due to a lack of data from head-to-head comparison trials
- This meta-analysis investigated the relative efficacy and safety of TOF, BARI, UPA, and FIL in comparison to ADA in patients with active RA and an IR to MTX

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Study Design

- 4 RCTs were included in the Bayesian network meta-analysis
  - The analysis included 5451 patients, 3432 efficacy-related and 238 safety-related events
  - Results from different arms were analysed simultaneously
- Relative effects were converted into a probability that a treatment was best, second-best, and so-on, or into a ranking for each treatment called SUCRA
  - A value of 100% for SUCRA was obtained when treatment was the best and a value of 0% was obtained when treatment was the worst
  - League tables were used to organize the summary estimates by ranking the treatments based on their SUCRA value
- Inconsistency was assessed by plotting the posterior mean deviance in the inconsistency model against posterior mean deviance in the consistency model
  - A sensitivity test was performed by comparing the fixed- and random-effects model

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Study Characteristics

Study	Patient Total	Treatment + MTX	No. of patients	ACR20	ACR50	ACR70	SAEs	HZ
ORAL Strategy	762	TOF 5mg	376	275	173	94	27	8
		ADA 40mg	386	274	169	80	24	6
RA BEAM	1005	BARI 4mg	487	360	246	145	23	7
		ADA 40mg	330	219	150	72	6	4
		PBO	188	179	94	39	22	2
SELECT COMPARE	1129	UPA 15mg	651	439	338	226	24	5
		ADA 40mg	327	187	137	75	14	1
		PBO	151	232	136	62	19	3
FINCH 1	1755	FIL 100mg	475	369	250	140	21	2
		FIL 200mg	480	375	278	174	14	2
		ADA 40mg	325	242	171	96	14	2
		PBO	475	281	158	71	20	2

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Odds Ratio of ACR20 Between Different Treatments

BARI 4mg						
1.15 (0.83-1.59)	UPA 15mg					
1.53 (1.01-2.31)	1.33 (0.90-1.98)	TOF 5mg				
1.64 (1.14-2.35)	1.43 (1.02-2.00)	1.07 (0.70-1.64)	FIL 200mg			
1.68 (1.17-2.42)	1.47 (1.05-2.06)	1.10 (0.72-1.69)	1.03 (0.75-1.39)	FIL 100mg		
1.71 (1.31-2.23)	1.49 (1.18-1.89)	1.12 (0.81-1.54)	1.04 (0.78-1.39)	1.01 (0.76-1.35)	ADA 40mg	
4.39 (3.40-5.69)	3.83 (3.09-4.76)	2.88 (2.02-4.13)	2.68 (2.05-3.53)	2.61 (2.00-3.43)	2.58 (2.18-3.05)	PBO

All treatments were administered with MTX. Odds ratios are the first number in each cell and 95% credible intervals are the (ranges in parentheses). OR>1 signifies that the treatment in the top left is better.

BARI and UPA had significantly higher ACR20 response rates than ADA

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Odds Ratio of ACR70 Between Different Treatments

UPA 15mg						
1.12 (0.77-1.63)	**BARI 4mg**					
1.43 (1.00-2.04)	1.27 (0.87-1.87)	**FIL 200mg**				
1.43 (0.93-2.20)	1.28 (0.81-2.02)	1.00 (0.65-1.55)	**TOF 5mg**			
1.82 (1.40-2.37)	1.63 (1.20-2.18)	1.27 (0.97-1.68)	1.28 (0.90-1.79)	**ADA 40mg**		
1.94 (1.36-2.79)	1.74 (1.18-2.57)	1.36 (1.04-1.78)	1.36 (0.87-2.12)	1.07 (0.81-1.42)	**FIL 100mg**	
4.98 (3.28-6.51)	4.45 (3.27-6.09)	3.49 (2.64-4.63)	3.50 (2.33-5.24)	2.74 (2.22-3.41)	2.56 (1.92-3.42)	**PBO**

All treatments were administered with MTX. Odds ratios are the first number in each cell and 95% credible intervals are the (ranges in parentheses).
OR>1 signifies that the treatment in the top left is better.

UPA and BARI had significantly higher ACR70 response rates than ADA

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Discussion

- BARI 4mg and UPA 15mg were the most effective treatments for MTX IR patients with active RA based on ACR response rates
  - BARI and UPA had significantly higher ACR20/70 response rates than ADA 40mg
  - TOF 5mg and FIL 200mg had comparable ACR20/70 response rates to ADA 40mg
- There were no statistically significant differences between JAK inhibitors and placebo in terms of SAEs and HZ
- Study limitations include:
  - A short duration which was insufficient to judge all the important safety issues
  - Indirect comparison calibration relied on comparisons to PBO and ADA
  - Treatment rankings derived from network meta-analyses have a substantial degree of imprecision and interpreting such rankings requires caution

All treatments were administered with MTX.

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