

THE LANCET

Rheumatology

Supplementary appendix

This appendix formed part of the original submission. We post it as supplied by the authors.

Supplement to: Mehta P, Sanchez E, Moraitis E, et al. Influenza vaccination and interruption of methotrexate in adult patients in the COVID-19 era: an ongoing dilemma. *Lancet Rheumatol* 2020; published online Nov 10. [https://doi.org/10.1016/S2665-9913\(20\)30392-1](https://doi.org/10.1016/S2665-9913(20)30392-1).

Study Reference	Study 1: NCT02748785 ¹ Park et al., 2017;				Study 2: NCT02897011 ² Park et al., 2018	
MTX randomisation groups in relation to influenza vaccination	MTX continue Group 1	MTX hold 4 weeks before Group 2	MTX hold 2 weeks before & after Group 3	MTX hold 4 weeks after Group 4	MTX continue	MTX hold 2 weeks after
Study design	Prospective randomised parallel-group single-centre study, patients with RA on stable dose of MTX were randomly assigned at a ratio of 1:1:1:1.				Prospective randomised parallel-group multicentre study, patients with RA on stable dose of MTX were randomly assigned at a ratio of 1:1	
Influenza vaccine	Seasonal trivalent influenza vaccine, containing A (H1N1), A(H3N2) and B (Yamagata)				Seasonal quadrivalent influenza vaccine, containing four antigens: A(H1N1), (H3N2), B (Yamagata) and B (Victoria)	
Satisfactory vaccination response definition	≥4-fold increase in HI antibody titre at 4 weeks after vaccination, relative to the baseline, in ≥1 influenza vaccine antigens				≥4-fold increase in HI antibody titre at 4 weeks after vaccination relative to the baseline, in ≥2 influenza vaccine antigens	
RA flare definition	Increase in DAS28 of >1.2 (or >0.6 if the baseline DAS28 was ≥3.2)					
n=	54	44	49	52	156	160
% achieving satisfactory vaccine responses; P value compared to MTX continue	31.5 (N/A)	22.7 (p=0.334)	*51.0 (p=0.044)	46.2 (p=0.121)	54.5 (N/A)	*75.5 (p<0.001)
% RA flares at any time ≤20 weeks	24.1	34.1	38.8	21.2	5.1	10.6

Table Summary of evidence for interrupting methotrexate on antibody responses to influenza vaccination and RA flares

*indicates statistical significance reached vs MTX continuation. MTX, methotrexate; RA, rheumatoid arthritis; HI, haemagglutination inhibition; DAS28, disease activity score (28); N/A Not applicable

References:

1. Park JK, Lee MA, Lee EY, et al. Effect of methotrexate discontinuation on efficacy of seasonal influenza vaccination in patients with rheumatoid arthritis: a randomised clinical trial. *Annals of the rheumatic diseases* 2017; **76**(9): 1559-65.
2. Park JK, Lee YJ, Shin K, et al. Impact of temporary methotrexate discontinuation for 2 weeks on immunogenicity of seasonal influenza vaccination in patients with rheumatoid arthritis: a randomised clinical trial. *Annals of the rheumatic diseases* 2018; **77**(6): 898-904.