Imaging and Histological Changes to Tocilizumab in Patients with Moderate to Severe RA: A Single Centre Randomised Double-Blind Pacebo-Controlled Study

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Background

- Tocilizumab (TCZ) is a well-established biologic therapy in the treatment of rheumatoid arthritis (RA)
- There is limited data on imaging and synovial tissue histology changes

Aim

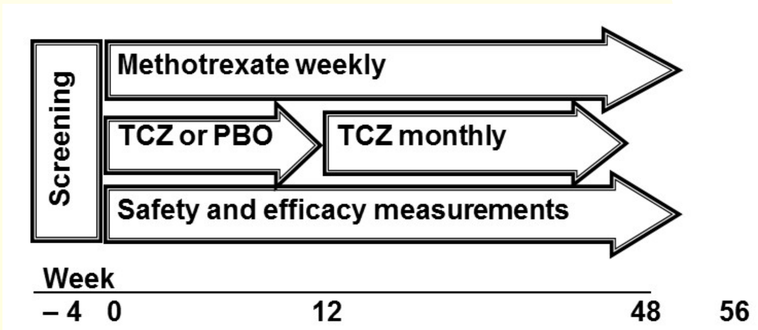
To evaluate level of response to TCZ as defined by power Doppler (PD) ultrasound (US) and synovial tissue histology changes.

Patients and methods

Main inclusion Criteria:

- Patients with RA
- Inefficacy to minimum one DMARD +/- TNFi, with DAS28 ≥ 3.2
- knee synovitis amenable to synovial biopsy

Study design



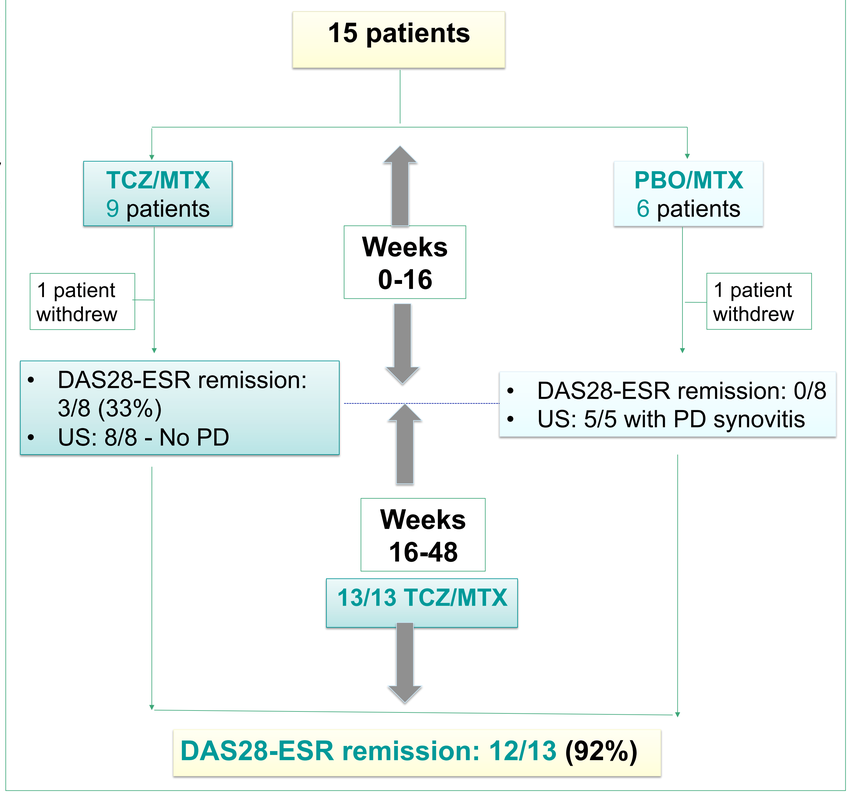
- Phase 1 week 0-12: Randomised, blinded, PBO-controlled study: TCZ/MTX vs PBO/MTX
- Phase 2: Week 16-48: Open-label TCZ/MTX

Assessments

- Clinical assessment weeks 0, 12, 24, 48
- US dominant MCPs & wrist weeks 0 & 12
- US-guided synovial biopsy of knee at weeks 0 & 12; 48 (biopsy optional) with preliminary results reporting change in synovitis score weeks 0-12

Results (Patient flow, Clinical and Ultrasound data)

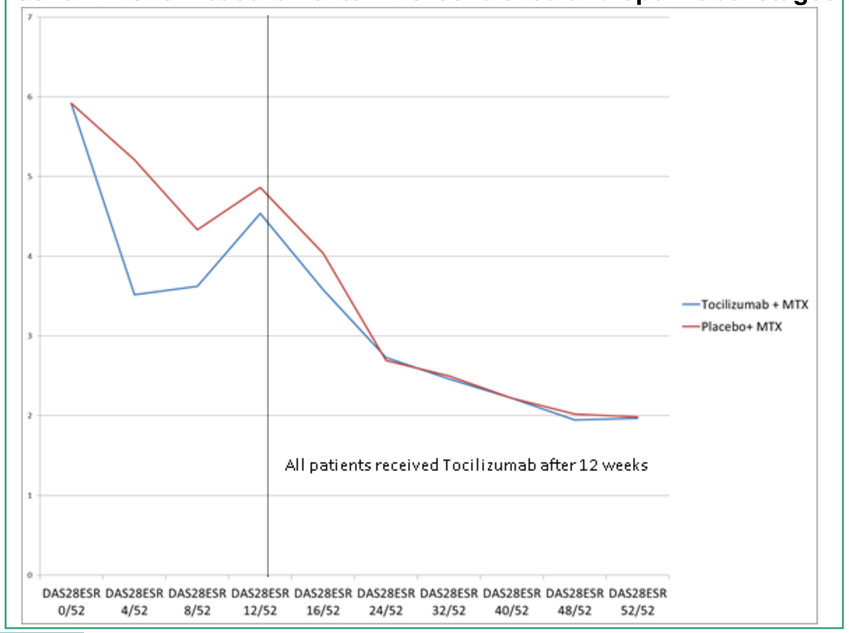
- 15 patients recruited: 12 (80%) female



Results: Week 0-12 histology

- Data in n=13 (21/26 samples (80%) samples useable)
- Median(IQR) total synovitis score at week 0 vs 12:
  - TCZ/MTX: 3(2.75, 4.25) vs 3(2.5,4)
  - PBO/MTX: 6,(4,7) vs 6(4,6)
- Week 0 total synovitis score did not predict early or late response.

Serial DAS28 measurements PBO-controlled and open-label stages



Results: Week 0-12 Ultrasound MCPs-wrist (dominant hand)

Treatment arm		Hand and wrist US							
		GS total score		No. of joints with abnormal GS		PD total score		No. of joints with abnormal PD	
		0 m	3m	0 m	3m	0 m	3m	0 m	3m
TCZ/MTX	Median (IQR)	10.0 (6.5-12)	5.0 (3.5-12)	6.0 (4.5-7)	4.0 (3.5-6.5)	3.0 (2.5-9)	5.0 (0-5)	2.0 (1.5-4)	2.0 (0-5.5)
PBO/MTX	Median (IQR)	9 (7-15.5)	12.5 (10-16.8)	6.5 (4.5-8)	7.5 (3-8)	6.5 (9-14)	7.5 (1-11)	3.0 (4.5-8)	4.0 (6-8)

Conclusion

- TCZ/MTX was associated with significant clinical and US imaging improvement compared to PBO/MTX.
- An absence of change in synoviis score with TCZ/MTX implies a different mechanism for response compared to observations following other anti-cytokine therapies such as TNFi.
- Further histochemistry analysis and investigation should clarify these findings and may identify indicators of response on a tissue level.