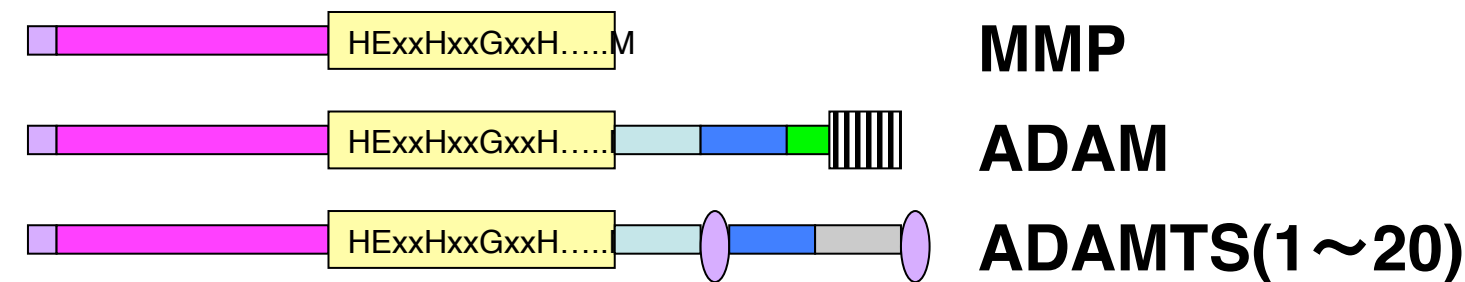


ADAMTS5, which has negative correlation with IL-6, is a biomarker for the efficacy prediction of tocilizumab in rheumatoid arthritis

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PURPOSE



- Signal peptide
- Catalytic domain
- Disintegrin-like domain
- TSR
- TM region

We have previously (2009ACR, 2010ACR) reported that the efficacy of biologics, infliximab and adalimumab can be predictable using baseline blood a disintegrin and metalloproteinase with thrombospondin motifs 5 (ADAMTS5) mRNA level. In this study presented here, we investigated whether the efficacy of tocilizumab (TCZ) for the treatment of RA can be predicted by the baseline blood ADAMTS5 mRNA level because recently IL-6 has been reported to suppress ADAMTS5 expression.

METHODS

- 1) Patients: 54 RA patients who received TCZ
- 2) Patient assessment
TCZ-treated patients were assessed before TCZ treatment and after 12 weeks for DAS28 and HAQ, and were categorized according to the EULAR response criteria and EULAR remission criteria.
- 3) Quantification of ADAMTS5 mRNA
Peripheral blood samples were collected at baseline and ADAMTS5 mRNA was quantified using real-time PCR (BiologicMate®). Baseline IL-6 mRNA was also estimated using real-time PCR.

PATIENT BACKGROUND

number of patients	54
Age (y/o)	62.3 ± 12.4
Disease duration (months)	153 ± 131
DAS28(0w)	5.40 ± 1.16
HAQ(0w)	1.60 ± 0.78
Prednisolone (mg/day)	4.43 ± 3.86
MTX (mg/week)	3.58 ± 3.76

RESULTS

EFFECTIVENESS OF TCZ

	TCZ (n=54)	
	0w	12w
EULAR Response, %(no)		
Good		42.6% (23)
Moderate		35.2% (19)
None		22.2% (12)
Remission, %(no)		24.0% (13)
DAS28	5.40 ± 1.16	3.75 ± 1.51
HAQ	1.60 ± 0.78	1.48 ± 0.90

Increased expression of the baseline ADAMTS5 mRNA in the responders of TCZ

	R (n=42)	NR (n=12)	p-value
ADAMTS5 ($\times 10^{-4}$) (0w)	2.85 ± 2.37	1.56 ± 0.81	0.049
Age	60.5 ± 12.5	69.1 ± 9.6	0.089
Disease duration, months	154 ± 139	147 ± 98	0.882
IL-6 ($\times 10^{-3}$)(0w)	0.24 ± 0.26	0.11 ± 0.11	0.126
MTX, mg/week	3.58 ± 3.95	3.60 ± 3.24	0.986
Prednisolone, (0w), mg/day	4.30 ± 4.22	4.89 ± 2.20	0.692
DAS28 (0w)	5.35 ± 1.21	5.56 ± 0.93	0.597
HAQ (0w)	1.61 ± 0.81	1.56 ± 0.76	0.875

R: Responder, NR: Non responder

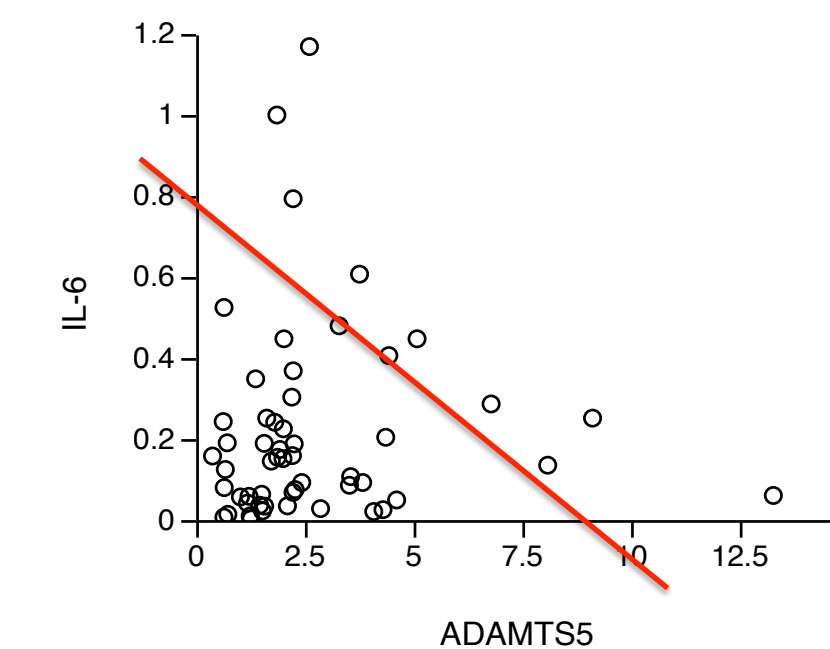
Cut-off value of ADAMTS5 mRNA for predicting the clinical remission (DAS28<2.6) by TCZ

	Cut-Off value	AUC(%)
TCZ	1.6×10^{-4}	0.750 for Remission at 12 wks

Baseline ADAMTS5 mRNA is independent of the patient background

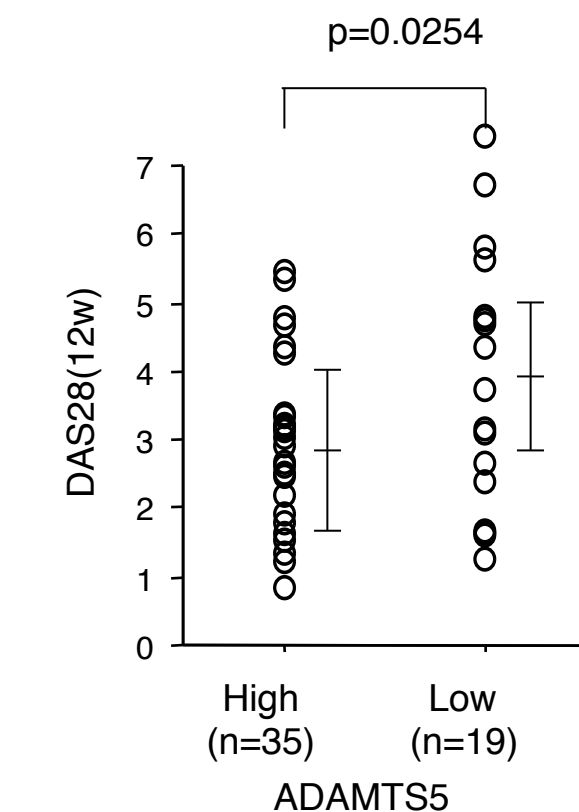
	ADAMTS5		p-value
	High (n=35)	Low (n=19)	
Age	60.8 ± 11.7	65.5 ± 15.4	0.353
Disease duration, months	173 ± 145	98 ± 71	0.078
MTX, mg/week	3.57 ± 3.86	3.45 ± 3.48	0.435
Prednisolone, (0w), mg/day	4.30 ± 4.24	5.30 ± 2.63	0.933
DAS28 (0w)	5.29 ± 1.18	5.62 ± 1.11	0.319
HAQ (0w)	1.58 ± 0.71	1.67 ± 1.01	0.765

ADAMTS5 is inversely related to IL-6



CONCLUSION

The baseline ADAMTS5 level, which might be related to the baseline IL-6, is a candidate biomarker for the prediction of the response to TCZ in RA patients.



DAS28 at 12 weeks' treatment with TCZ was decreased in the High-ADAMTS5

Prediction of the efficacy of TCZ using baseline ADAMTS5

TCZ: by high ($> 1.60 \times 10^{-4}$) ADAMTS5

Remission (12w)	
Accuracy(%)	75.0
PPV (%)	45.7
NPV (%)	94.7

Tocilizumab

