

RA33 Antibodies

New data on a (not really new) marker linked to CCP-negative RA with a mild prognosis

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Disclosure

Collaboration with PhaDia (Thermo Fisher)

Development of an assay for determination of autoantibodies to hnRNP-A2 (RA33).

PhaDia did not and does not pay any consultant fees or honoraria to Dr Guenter Steiner or to Dr Josef Smolen.

PhaDia partially covered travel expenses of Dr Steiner for the ACR Meeting 2010 and travel expenses related to Dr Steiner's activities in the Austrian EASI group.

RA Diagnostics 2011

Questions & Challenges

- **The “seronegative“ patient**

Is there more than RF & ACPA?

- **Prognostic markers**

Disease activity

Disease outcome

Response to therapy

- **Pre-disease diagnostics**

Identificaton of healthy persons at risk for developing RA

Treatment immediately at (or even before?) disease onset

RF and ACPA

Reliable and highly appreciated markers for RA

Antibody	Sensitivity established RA	Sensitivity early RA	Specificity
RF	70-80%	45-55%	70-96%
ACPA	70-80%	45-55%	92-99%

Nobody is perfect!

Problem 1: Prevalence of RF and ACPA in early disease

Problem 2: Overlap RF-ACPA

Problem 3: Moderate specificity of low titer RF

ACPA and RF in very early arthritis

Nell et al, Ann Rheum Dis 2005

Disease duration <3 months

200 patients included

Final diagnosis: 102 RA, 98 non-RA

	RA %	Non-RA %	PPV %
RF (<50 U/ml)	10	7	59
RF50 (\geq50 U/ml)	45	4	92
ACPA (CCP)	41	2	96

RF50 and/or ACPA in 58% of patients

Autoantibodies in very early RA

RF, ACPA, anti-RA33

Nell et al, Ann Rheum Dis 2005

	Sensitivity %	Specificity %	PPV %
RF50 (>50 U/ml)	45	96	92
ACPA (CCP2)	41	98	96
Anti-RA33 (hnRNP-A2)	28	90	74

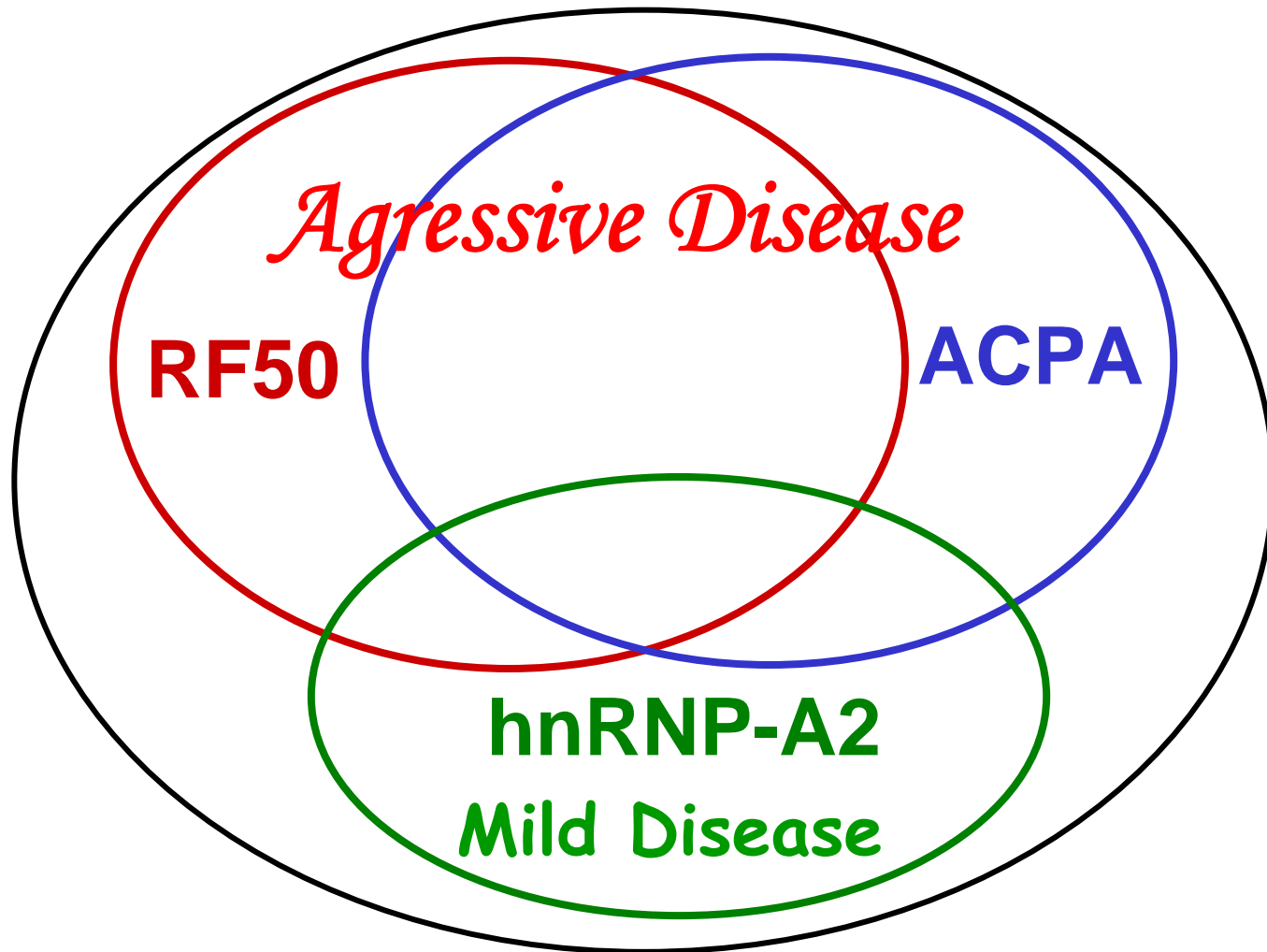
RF50 and/or ACPA and/or anti-RA33 in 70% of patients

Prognostic value of autoantibodies for erosive disease

	Erosive n=36	Non-erosive n=30	P (Pearson Chi Square)	PPV %
RF50	21	6	p=0.002	78%
ACPA	22	3	p<0.001	88%
Anti-RA33	11	7	p=n.s.	61%
Anti-RA33 only	2	9	p<0.05	18%

RF, ACPA & anti-hnRNP-A2 in early RA

Nell et al, Ann Rheum Dis 2005



EliA™ for quantification of anti-RA33



EliA™ for quantification of anti-RA33

serum bank data

Diagnosis	n	positive	percentage
RA (early)	80	16	20%
RA (late)	85	11	13%
SLE	20	3	15%
Other CTDs	37	0	0%
Reactive arthritis	20	0	0%
Psoriatic arthritis	20	0	0%
Osteoarthritis	30	1*(CCP+)	3%
Healthy subjects	100	3	3%
Sensitivity			20%
Specificity			97%

The SAVE Trial

Stop Arthritis Very Early

Machold et al., ARD 2010;69:495-502

Multicenter study

involving 383 patients with early arthritis from 25 centers

Inclusion criteria

Arthritis of ≥ 1 joint

Disease duration of ≤ 16 weeks

Intervention

120 mg Methylprednisolone i.m. at day 0 or placebo=saline (in addition to NSAID/coxib)

Primary target/outcome: Remission

Defined as:

- no swollen joints and ≤ 2 tender joints

and 2 out of the 3 following:

- CRP within the normal range
- patient global assessment of disease activity of < 1 cm on a 10 cm visual analogue scale
- pain < 1 cm on a 10 cm visual analogue scale

At 3 and 12 months from baseline without DMARD therapy

Observation over 52 weeks (2, 12, 52 week-visits)

Diagnoses after 12 months

Diagnosis	n
Rheumatoid arthritis	132
Undifferentiated arthritis	62
Reactive arthritis	21
Osteoarthritis	17
Other arthritides	23
SLE & CTD	9
Remission	27
No diagnosis	34
Total	325

Antibodies at baseline

Diagnosis	0	RF	CCP	RA33
RA	132	72	72	20
UDA	62	3	3	6
REA	21	1	0	0
OA	17	0	0	0
Other arthritides	21	2	0	1
SLE & CTD	9	2	1	2
Remission	27	2	1	1
No diagnosis	34	5	2	1
Sensitivity		55%	55%	15%
Specificity		92%	96%	91%

Summary & Preliminary Conclusions

- The RA33 EliA prototype allows to measure levels of anti-RA33 antibodies in a highly reproducible manner.
- Anti-RA33 antibodies are present in 15-20% of patients with early onset RA and also in approximately 10% of patients with a 1 year diagnosis of UDA.
- Anti-RA33 is the only antibody in approximately 10% of early RA patients.
- Anti-RA33 may be a marker for a subset of polyarthritis (RA) patients with mild disease and a favourable prognosis showing a good response to NSAID or DMARD treatment.

The RA33 syndrome - does it exist?

Autoantibodies in Early Arthritis

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