Biologics increase the chance of remission by two. Results from the German biologics register

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RABBIT

www.biologika-register.de

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Background

The German prospective cohort study RABBIT (German acronym for: **r**heumatoid **a**rthritis – o**b**servation of **bi**ologic **t**herapy) was established in May 2001 to investigate the long-term safety, effectiveness and costs of biologic therapies in comparison to conventional disease modifying anti-rheumatic drugs (DMARD) in rheumatoid arthritis (RA).

Objective

To investigate the frequency of remission at 12 months according to the DAS28 or modified ARA criteria in patients treated with either biologics or conventional DMARDs .

Patients and Methods

Patients

- RA patients enrolled into the German biologics register RABBIT
- new prescription of etanercept, adalimumab, infliximab, or anakinra at study entry
- new prescription of a DMARD after at least two DMARD failures including MTX (control group)

Assessments at baseline, 3, 6 12 months

- 28 joint counts of tender (TJC) and swollen joints (SJC)
- CRP, ESR
- functional capacity (Funktionsfragebogen Hannover, FFbH)
- treatment (DMARD and/or biologic therapy, glucocorticoids)
- no. of treatment failures (at baseline)

Endpoints

- Remission according to the DAS28 (DAS28< 2.6)
- Remission according to the following modification of the ARA criteria: fulfilment of 4 out of 5 criteria at one point in time:
  0 TJC, 0 SJC, ESR<30mm/h (males: <20mm/h), morning stiffness < 15 min, pain <=1 at 0 to 10 scale

Statistical analysis

- Propensity score methods were applied to adjust for confounding by indication. Age, gender, number of DMARD failures, DAS28, ESR, FFbH, and as additional markers of disease severity osteoporosis and previous treatment with cyclosporin A were used for propensity score modelling.
- Multivariate logistic regression was applied to calculate adjusted odds ratios (OR) of remission.
- In a second approach the propensity score was used to match cases and controls directly.

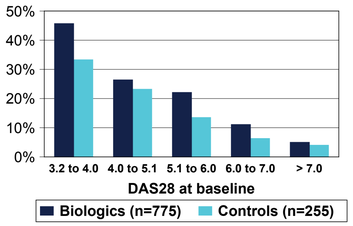
Results

A total of 1,083 patients who were enrolled between May 2001 and December 2003, fulfilled the inclusion criteria. As expected, the patients in the biologics groups had significantly more active disease and more previous DMARD failures (Tab. 1). Therefore, propensity score methods were applied to adjust for confounding by indication.

Tab. 1: Patient characteristics

	Biologics	Controls
n	818	265
Age, mean	53.7	57.4
Disease duration (median, years)	10	9
Swollen joint count (0-28)	10.5	8.2
CRP (mg/L), median	18	12
DAS 28, mean	6.1	5.5
FFbH (mean % of full function)	53.1	61.4
No. Previous DMARDs, mean	4.0	2.8
Comorbidity (%)	70.0	72.8
Osteoporosis (%)	28.6	18.5

Fig. 1: DAS28 remission at 12 months in %



High remission rates (DAS28 remission 30.6%, ARA remission 16.9% were observed in biologics patients with a moderate disease activity (DAS28: 3.2 to 5.1, see Fig. 1) at start of treatment. These rates decreased to 8.5% in patients with DAS28 > 6. The overall rates for DAS28 (ARA) remission were 16.6%, 13.2% respectively.
There was a significant association between the propensity score and the remission status indicating that patients receiving biologics had a lower a-priori chance of remission than control patients.
Taking risk factors of remission simulataneously into account we found that biologics increase the chance of both types of remission by two (Tab. 2).

Tab. 2: Adjusted Odds ratios (OR) of remission at 12 months (results of a multivariate logistic regression analysis)

	DAS28 remission		ARA remission	
	OR	95%CI	OR	95%CI
Age /10 years	0.74	0.62-0.87	0.72	0.61-0.85
Propensity score /0.1 units	0.89	0.80-0.99	0.84	0.75-0.94
DAS28	0.46	0.35-0.61		
Tender joint count	1.05	1.01-1.09		
FFbH (% of full function)/10 units			1.13	1.03-1.25
Osteoporosis	0.51	0.30-0.87		
Anti-TNF agents versus controls	1.97	1.20-3.21	2.09	1.22-3.59

These results were confirmed by a matched pairs analysis (Tab. 4).

Sustained remission

Sustained DAS28 or ARA remission over a six months period was achieved in less than 10% of the patients. Only 74/133 patients (56%) who were in DAS28 remission at six months fulfilled the criteria at 12 months too (ARA remission: 44/102 43%). The number of previous DMARD failures was identified as risk factor of an increase in the DAS28 to moderate or high disease activity.

Tab. 4: Patients' characteristics and remission rates (12 months) of machted pairs (difference in propensity score of pairs <0.05 units)

	Biologics	Controls	p
n	193	193	
At baseline (means (SD))			
Age	54.7 (12.1)	55.9 (10.3)	0.50
Swollen joint count	8.7 (6.1)	8.8 (5.5)	0.59
DAS28	6.1 (1.1)	6.1 (1.1)	0.54
no. previous DMARDs	3.1 (1.1)	3.0 (1.0)	0.74
At 12 months			
DAS28 remission n (%)	48 (24.9)	24 (12.4)	0.004
ARA remission n (%)	31 (16.1)	16 (8.3)	0.036

Conclusion:

Biologics increase the chance of remission by two. However, temporary of even sustained remission remain ambitious aims which are achieved in a minority of patients only.

Disclosure:

Supported by a joint, unconditional grant from Wyeth Pharma GmbH, essex pharma GmbH, Amgen GmbH and Abbott GmbH & Co. KG.

Acknowledegment

The authors wish to thank those rheumatologists who enrolled at least 25 patients each:
M Stoyanova-Scholz, Duisburg; K Babinsky, Halle; S Wassenberg and G Herborn, Ratingen; A Kapelle, Hoyerswerda; T Klopsch Neubrandenburg; U von Hinüber and W Demary, Hildesheim; R Dockhorn, Weener; K Rockwitz, Goslar; A Bussman, Geilenkirchen; K Richter, Dresden; C Richter, Stuttgart; A Gräßler, Pirna; B Krummel-Lorenz, Frankfurt/Main; E Wilden, Cologne; E Edelmann, Bad Aibling; T Karger, Cologne; C Kneitz, Würzburg; Grünke, Erlangen; L Meier, Hofheim; W Ochs, Bayreuth; S Schewe, Munich; H Sörensen, Berlin; V Petersen, Hamburg; P Herzer, Munich; M Bohl-Bühler, Brandenburg; H Tremel, Hamburg; W Liman, Hagen; K Krüger, Munich; H Kellner, Munich; C Stille, Hannover; A Gause, Elmshorn; M Zänker, Eberswalde; R Haux, Berlin; K Alliger, Zwiesel; A Teipel, Leverkusen; K Karberg, Berlin; K Gräfenstein, Treuenbrietzen; C Eisterhues, Braunschweig; D Pick, Grafschaft Holzweiler; B Hellmich, Lübeck/Bad Bramstedt; J Gutfleisch, Biberach; T Grebe, Attendorn; U Lange, Bad Nauheim; T Dexel, Munich; W Biewer, Saarbrücken; M Schneider Düsseldorf.