Long Term Observation of Biologics in Germany – Which Patients Are Treated with Biologic Compounds?

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Introduction

The efficacy of etanercept, infliximab, anakinra and adalimumab has been proven in randomised clinical trials in patients with active rheumatoid arthritis (RA), in particular in patients not responding to conventional disease modifying antirheumatic drugs (DMARDs). Nevertheless, the percentage of patients with rheumatoid arthritis treated with biologic compounds is limited especially due to financial restrictions. Therefore, we used data from the German biologics register (RABBIT) to investigate which patients are likely to receive this kind of treatment.

Patients and Methods

Since May 2001, patients with RA and a new prescription of etanercept, infliximab, anakinra (since January 2003) or adalimumab (since September 2003) as well as control patients have been consecutively enrolled into the German biologics register (RABBIT). For better comparability with the patients on biologics, the control group consists of patients with RA who had a change in their DMARD therapies (no first prescription). The patients will be followed-up for five years. 172 rheumatological units (private practices and outpatient departments of hospitals) from all parts of Germany participate. Data are shown for patients enrolled until March 2004.

Additional comparison data are available for more than 11.000 RA patients per year from the National Database of the German Arthritis Centres (NDB) that registers outpatients treated by German rheumatologists.

Logistic regression was applied to investigate the contribution of different predictors of biologic therapy simultaneously.

The results of the multivariate logistic regression analysis are shown as estimated likelihoods (propensity scores) of being treated with biologics.

Results

As of March 2004, 2084 patients with RA had been registered in the RABBIT database.

Table 1 shows the demographic and clinical characteristics of the cases, controls, and the patients in the National Database (NDB). In patients who had just started on the biologic therapy, the disease was more active and severe than in patients from the control group ($p<0.01$, in all parameters shown in tab. 1). However, in patients in the control group the disease was significantly more active than in the average RA patient in the NDB. There was no difference in age, disease activity, severity or disability among the groups treated with biologics.

Tab. 1: Patient characteristics in RABBIT and in the National Database (NDB)

Patients enrolled till March 2004	Etaner-cept	Inflixi-mab	Anakin-ra	Adali-mumab	Con-trols	NDB[1]
N	633	399	80	221	751	11,742
Women (%)	77.9	71.4	75.0	81.9	81.4	77.0
Age	53.4	53.3	54.9	55.1	56.4	59.7
% Employed (age < 60)	54.1	48.5	31.9	48.8	57.3	52.1
DAS28	6.0	6.0	6.0	5.8	5.3	4.0
Swollen joints (0-28)	10.0	10.4	9.9	9.5	7.5	3.3
CRP mg/L (median)	19.0	20.0	21.0	16.0	10.0	12.0
Pain	6.6	6.7	6.5	6.7	5.9	4.6
FFbH (mean % of full function)	53.9	54.3	50.4	53.4	64.5	67.8
No. of previous DMARDs	4.0	3.9	4.6	4.0	2.1	n.a.

Values are means if not otherwise specified.

Most of the patients in the biologics groups were previously treated with methotrexate (MTX), or leflunomide; further, a high percentage was treated with azathioprine, cyclosporine A or biologics (tab. 2). These percentages are distinctly lower in the control group. A rather high percentage of patients under adalimumab or anakinra was previously treated with biologics. This can only partly be explained by their more recent registration date.

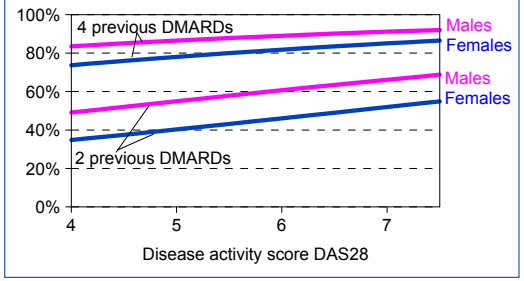
Tab. 2: Percentage of patients previously treated with DMARDs

	Etaner-cept	Infliximab	Anakin-ra	Adalimu-mab	Controls
Methotrexate	90.8	91.9	80.0	87.7	69.6
Leflunomide	71.8	67.0	76.3	69.1	13.1
I.m. gold	35.8	35.3	52.5	37.3	25.7
Antimalarials	45.5	44.1	55.0	50.9	30.6
Sulfasalazine	62.4	61.5	63.8	61.4	44.1
Azathioprine	19.5	18.1	28.8	10.5	5.4
Cyclosporine A	19.5	17.4	22.5	10.5	2.8
Other DMARDs	39.9	34.3	48.8	31.4	13.7
Biologics	10.1	17.1	27.5	45.0	2.9

Before study entry 45% of the cases were treated with leflunomide (alone (20%), in combination with MTX (17%), other DMARDs (3%)), 57% with MTX, and 5% with biologics. In the control group these percentages are 10%, 57%, and 2%.

Age, sex, number of previous DMARDs, disease activity score (DAS28), disability and ESR are highly significant predictors of a biologic therapy (multivariate logistic regression). As expected, the estimated probability of being treated with biologics increases with increasing DAS28 (see Fig. 1 below) (OR=1.3). In addition the number of DMARDs applied previously is an even stronger predictor (OR= 2.3).

Fig. 1: Likelihood of being treated with biologics in % Estimated by multivariate logistic regression



Conclusion:

As expected, patients in Germany receiving biologics are more severely ill than patients receiving conventional DMARDs. A high disease activity, poor functional status and a high number of previous treatment failures with conventional DMARDs are highly predictive for treatment with biologics.

Disclosure:

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