Initiation of biologic treatment over the past 15 years reflects changes in treatment strategies:
results from the prospective cohort of the German biologics register RABBIT

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Background & Objectives

After the approval of the first biologic (b) DMARDs for the treatment of rheumatoid arthritis (RA) in 2001, these substances were preferentially used in patients with severe disease. Today, increasingly patients with moderate disease or co-morbidities are treated with biologics, leading to changes in patient case mix.

We aimed to examine which clinical parameters influence the decision of rheumatologists to start the 1st bDMARD treatment in patients with RA and how these factors changed over the past 15 years.

Patients & Methods

We used data of the German biologics register RABBIT. Until April 2015, 13,568 RA patients were enrolled. For this analysis we considered 9,513 patients being biologic-naïve at enrolment. They were stratified according to their year of inclusion in RABBIT.

We applied a machine learning method of model-based boosting to select clinical parameters which have a relevant impact on treatment decisions in each of the three episodes and compared the results with multiple logistic regression models.

Conclusions

The new treatment guidelines recommend earlier use of bDMARDs already in patients with moderate disease. This change in treatment strategy is reflected in our database.

Growing knowledge and experience with bDMARDs increasingly allows rheumatologists to treat also patients with serious comorbidities like heart failure.

Results

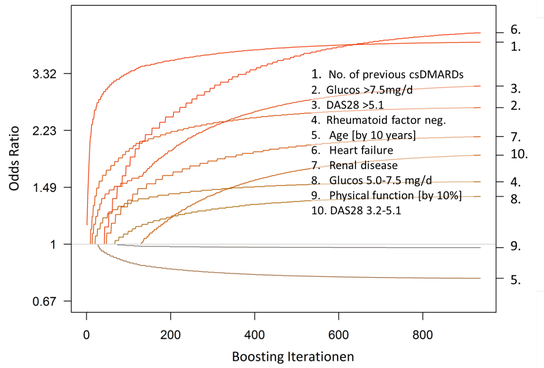
Baseline characteristics of patients changed with enrolment period (Table 1). The proportion of patients included at onset of a bDMARD was consistently between 60 and 62%. Of those, the quota of TNFi decreased over time from 94% in 2001-03 to 83% in 2009-15.

Compared to patients on a new csDMARD therapy, those starting a bDMARD presented with higher DAS28 at inclusion (6.0 vs. 5.4 in 2001-03 | 5.6 vs. 4.8 in 2004-06 | 5.0 vs. 4.5 in 2009-15) and they received higher glucocorticoid doses (7.0 mg/d vs. 4.8 mg/d | 6.4 vs. 4.5 | 5.3 vs. 3.2). Comorbid conditions like chronic renal and liver diseases, heart failure and osteoporosis were more prevalent in bDMARD starters.

Treatment decision

The likelihood to receive a 1st bDMARD increased with prior csDMARD failures, higher DAS28 and glucocorticoid dosage independent of enrolment year (Table 2, data of 2004-06 not shown). In contrast, higher age and better physical function diminished the chance.

Boosting model for starting the 1st bDMARD in 2009-2015



The figure shows the sequence of variables included in the model. The earlier a variable is included (reading from left, see rank list), the more it is relevant to model improvement.

Table 1: Baseline characteristics of bDMARD-naïve patients recruited in RABBIT stratified by year of inclusion

Enrolment period	2001-2003		2004-2006		2009-2015	
Enrolment therapy	csDMARD	bDMARD	csDMARD	bDMARD	csDMARD	bDMARD
N	701	1,080	1,067	1,714	2,011	2,940
Disease duration, years	9.3 (8.7)	11.9 (9.4)	8.3 (8.8)	11.2 (9.4)	6.5 (7.4)	9.1 (8.4)
Gender, female, N(%)	567 (80.9)	813 (75.3)	826 (77.4)	1351 (78.8)	1489 (74.0)	2198 (74.8)
Age, years	56.6 (11.3)	53.8 (12.5)	56.0 (11.5)	53.9 (12.3)	58.8 (12.8)	56.8 (12.7)
Rheumatoid factor pos, N(%)	522 (74.5)	871 (80.6)	752 (70.5)	1379 (80.5)	1139 (56.8)	2040 (70.6)
No. of previous csDMARDs	2.0 (1.1)	3.6 (1.5)	1.7 (0.9)	3.1 (1.2)	1.3 (0.6)	2.2 (1.0)

Numbers are means (SD) unless otherwise specified.

Table 2: Odds ratios of logistic regression vs. boosting to receive the 1st bDMARD

Enrolment period		2001-2003		2009-2015	
Odds ratio		LogReg (95%CI)	Boosting	LogReg (95%CI)	Boosting
Intercept		0.70 (0.19-2.60)	0.60	0.19 (0.10-0.37)	0.11
Sex (males vs. females)		2.04 (1.52-2.74)	2.01	1.17 (1.00-1.37)	
Age (by 10 years increase)		0.66 (0.59-0.74)	0.69	0.78 (0.73-0.82)	0.79
Rheumatoid factor (neg vs. pos)		1.15 (0.86-1.54)		1.55 (1.34-1.78)	1.55
No. of previous csDMARDs		2.61 (2.34-2.90)	2.57	4.20 (3.79-4.66)	4.14
Renal disease (yes vs. no)		2.78 (1.26-6.17)		2.14 (1.43-3.19)	2.13
Heart failure (yes vs. no)		1.68 (0.75-3.77)		4.56 (2.16-9.59)	4.41
GC (<5 mg/d Ref.)	5.0-7.5 mg/d	1.13 (0.83-1.53)	1.09	1.42 (1.21-1.65)	1.40
	>7.5 mg/d	2.08 (1.55-2.78)	2.04	2.60 (2.16-3.12)	2.61
DAS28 (<3.2 Ref.)	3.2-5.1	1.35 (0.57-3.15)		1.95 (1.55-2.46)	1.87
	>5.1	2.32 (0.99-5.44)	1.70	3.22 (2.51-4.13)	3.03
Fatigue		1.03 (0.98-1.09)	1.03	0.99 (0.96-1.03)	
Pain		0.97 (0.90-1.04)	0.98	0.98 (0.95-1.02)	
Improved physical function (by 10%)		0.87 (0.81-0.93)	0.87	0.96 (0.92-1.00)	0.98

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