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Letter to the Editor

Repeated switches between reference product etanercept and biosimilar do not affect disease activity or retention rate of etanercept over 24 months – a cohort study with historical controls



As highlighted in a recent editorial in this journal [1], the issue of the effects of multiple switches between a reference biologic and biosimilar on disease activity and retention rate has not been addressed in clinical trials. Consensus-based recommendations for the use of biosimilars in rheumatology were published in 2018 [2] and stressed that multiple switching should be assessed in registries. We have evaluated the effects of switching from reference product etanercept (RPE) to the biosimilar SB4 and 18 months later reswitching to RPE, in a cohort of 143 patients at an outpatient rheumatology center in Sweden, using data from the Swedish Rheumatology Quality Register. A reswitch at 18 months was performed for economical reasons as the price of RPE had then been reduced. It was allowed to reswitch to RPE before the planned reswitch at 18 months, at the request of the patient or if medically indicated. Retention rates of the biosimilar and of etanercept (RPE or biosimilar) were compared to the retention rate of RPE in a historical cohort from the same clinical setting, using Kaplan–Meier curves.

Baseline characteristics of the patients are described in Table 1.

The retention rate of the biosimilar at 6 and 12 months was 90% and 78% (Fig. 1). The 6-month retention rate was identical to that reported in a Dutch cohort study where patients were switched from RPE to biosimilar [3]. The 12-month retention rate in our cohort is in line with a report from the DANBIO registry where the

Table 1

Baseline characteristics of patients in the switching cohort and in the historical cohort

Variable	Switching cohort, N = 143	Historical cohort, N = 97	P
Female, N (%)	87 (61)	63 (65)	0.52
Age, mean (SD)	56.5 (15.6)	57.1 (14.8)	0.76
Duration of etanercept therapy (years) median (IQR)	1.6 (6)	4.6 (5)	<0.0001
Disease duration (years) median (IQR)	16 (21)	19 (15)	0.12
Concomitant use of csDMARD	69 (48)	55 (57)	0.20
DAS28-CRP, mean (SD)	2.57 (1.17)	2.35 (0.82)	0.15
Diagnosis			
Rheumatoid arthritis, n (%)	75 (52)	62 (64)	0.43
Psoriatic Arthritis, n (%)	26 (18)	14 (14)	
Ankylosing spondylitis, n (%)	12 (8)	6 (6)	
Spondyloarthritis, n (%)	12 (8)	4 (4)	
Other, n (%)	18 (13)	11 (11)	

SD: standard deviation; IQR: interquartile range; csDMARD: conventional synthetic disease-modifying antirheumatic drug; hs-CRP: high-sensitive c-reactive protein; DAS28-CRP: disease activity score 28 using c-reactive protein. *t*-test or Wilcoxon test was used to test significances of differences between cohorts for continuous variables, χ^2 test was used for categorical variables.

retention rate of biosimilar etanercept 12 months after switch from RPE was 83% [4]. In our cohort, the retention rate of the biosimilar then dropped to 69% at 18 months (Fig. 1), which was significantly lower than the retention rate of RPE in our historical cohort

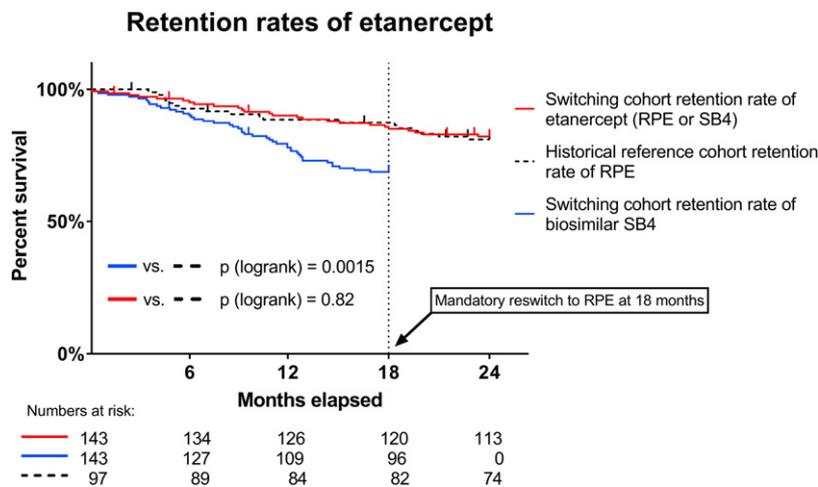


Fig. 1. Kaplan–Meier curves showing i) blue line - the retention rate of SB4 up to the reswitch to RPE at 18 months ii) red line - the retention rate of etanercept (RPE or SB4) in the switching cohort up to 24 months and iii) broken black line - the retention rate of RPE in the historical cohort. Subjects that discontinued therapy because of remission or pregnancy were censored and are indicated with tick marks on the curves at the time of censoring. RPE: reference product etanercept.

($P=0.0015$). The main explanation was patients' preference for RPE, as 19 of 143 patients reswitched to RPE at their own request, before all patients were reswitched at 18 months, without any objective signs of disease worsening. For 3 of the 19 patients, problems using the biosimilar device led to premature reswitch to RPE but for the other patients we were not able to further explore the reasons behind the preference for RPE, due to the register nature of the study.

This finding of patients' acceptance for the biosimilar decreasing over time was also made by Scherlinger et al in their study of patients that switched from originator infliximab to biosimilar [5].

At the end of follow-up, 6 months after reswitch to RPE had been performed, the retention rate of etanercept was 83% in the multiswitching cohort, compared to a retention rate of 81% in the historical cohort ($P=0.82$) (Fig. 1). Disease activity was stable over time in both cohorts (data not shown, available upon request from the corresponding author).

In conclusion, our findings provide reassuring evidence that in a clinical setting repeated switches between RPE and biosimilar do not influence disease activity or retention rate of etanercept over a timespan of two years.

Disclosure of interest

The authors declare that they have no competing interest.

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