Outcome in patients with rheumatoid arthritis switching TNF-α antagonists: a single center, observational study over an 8-year period

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Switching from one anti-TNF-α agent to another could represent an option in rheumatoid arthritis (RA) patients who fail or are intolerant to the first treatment (1).

In this ongoing, longitudinal, observational study, we collected data of patients starting biological treatments since 2000. The present analysis is restricted to RA patients who switched to another anti-TNF-α due to lack of efficacy (LaE), loss of efficacy (LoE), or adverse events (AEs).

Each patient was evaluated at baseline before starting anti-TNF-α, every 3 months, and at the last administration of the drug, as previously described (2). The clinical response (none, moderate, good) was evaluated according to the EULAR criteria (3); clinical remission (DAS28 <2.6) and low disease activity (DAS28 ≤3.2) were also calculated (4).

A total of 395 anti-TNF-α-naïve RA patients has been registered, 253 (64.1%) started etanercept, 115 (29.1%) adalimumab, and 27 (6.8%) infliximab. Thirty-seven patients (mean age 50 years, range 17-78; mean disease duration 8.5 years, range 3-22) switched to another anti-TNF-α: 35.1% for LaE, 40.5% for LoE, and 24.3% for AEs.

During the follow-up (mean 16.3 months, range 3-47) 12 patients discontinued the second anti-TNF-α, 7 for LaE, 4 for LoE, and 1 for AE. Mean treatment duration with the second anti-TNF-α was longer in patients switching for LoE (18.5 months, range 3-38) and AEs (19.1 months, range 4-28) than in those for LaE (11.0 months, range 3-47) (p<0.05). Figure 1 shows the proportion of patients achieving remission, low disease activity, good and moderate/good EULAR responses at last observation with the first drug, at baseline before the second and 3 months after switching from etanercept to adalimumab (Top panel) and from adalimumab to etanercept (Bottom panel).

Of the 22 switchers from etanercept to adalimumab, 36.4% changed for LaE, 50% for LoE, and 13.6% for AEs. The mean duration of adalimumab was longer than the previous etanercept (16.4 *vs*. 12.6 months, NS). Ten of the 22 switchers discontinued the second anti-TNF-α after a mean of 7.4 months (range 3-22): 5 for LaE, 4 for LoE, and 1 for AE (hypertension, also experienced with etanercept).

Twelve patients switched from adalimumab to etanercept: 41.7% for LaE, 16.6% for LoE, and 41.7% for AEs. The mean duration of etanercept was significantly longer than the previous adalimumab (14.2 *vs*. 8.8 months, p<0.05). Two out of 12 switchers discontinued adalimumab for LaE after 3 and 5 months.

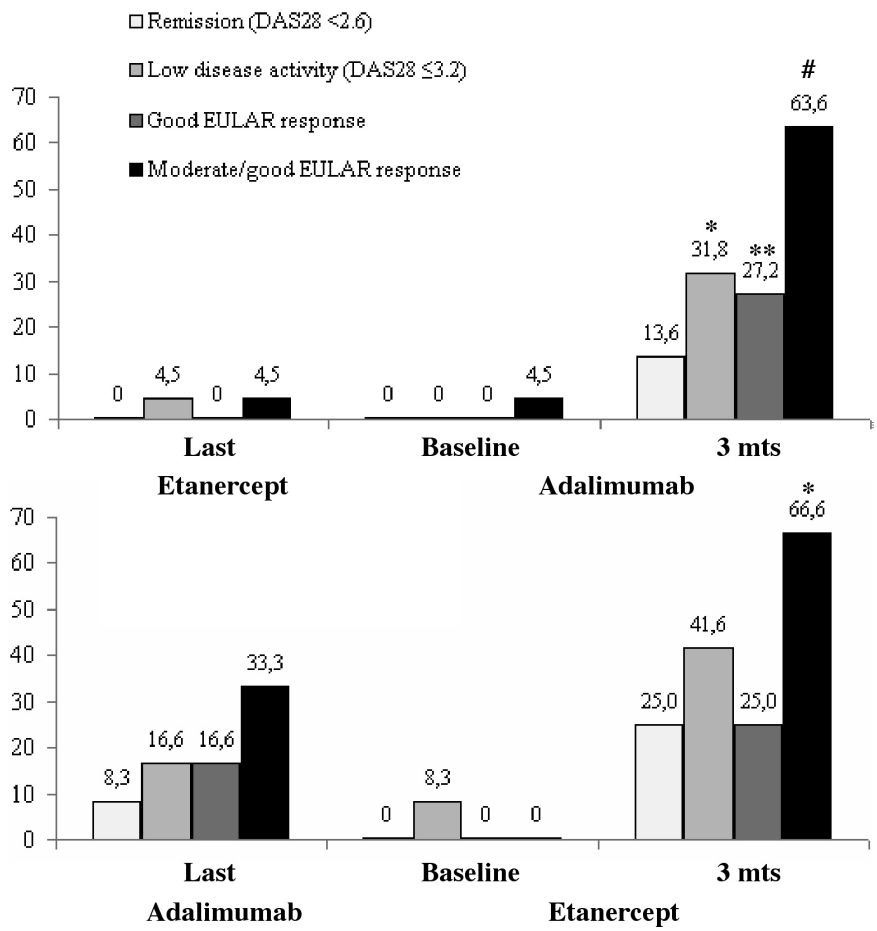

Fig. 1. **(Top)** Proportion of patients who switched from etanercept to adalimumab (n=22, mean age 51.6 years, range 17-78; mean disease duration 8.4 years, range 3-22) achieving remission (as defined by DAS28), low disease activity, good and moderate/good EULAR response at last observation with etanercept, at baseline before adalimumab, and after 3 months of adalimumab treatment. *p<0.01, **p<0.05, $^{\#}p$<0.0001 *vs*. baseline before adalimumab treatment. **(Bottom)** Proportion of patients who switched from adalimumab to etanercept (n=12, mean age 45.1 years, range 33-64; mean disease duration 8.5 years, range 3-17) achieving remission, low disease activity, good and moderate/good EULAR response at last observation with adalimumab, at baseline before etanercept, and after 3 months of etanercept treatment. *p<0.01 *vs*. baseline before etanercept treatment.

Three patients started etanercept following infliximab failure (2 for LoE and 1 for AE): after 3 months only one reached a moderate/good EULAR response. The mean duration of etanercept was longer than the previous infliximab (23.7 *vs*. 18 months, NS).

The findings of this study confirm that the failure of a first anti-TNF-α does not preclude the response to another and the probability of achieving a response after the switching is higher when LoE or AEs cause the discontinuation, in agreement with some of the published reports (5, 6). Indeed, in a recent study the response to a second anti-TNF-α was irrespective of the reason for switching, although a better outcome was observed in patients who changed for LaE (7).

In our patients, the mean treatment duration with the second anti-TNF-α was significantly longer than with the first one, in agreement with the Danish register (8). In contrast, the Spanish register showed a reduction in the survival of the second anti-TNF-α, albeit longer in patients switching to AEs (9).

In conclusion, our data support the possibility of trying another anti-TNF-α in RA patients failing the first-place treatment for LoE or AEs, while, in case of LaE, different biological drugs, such as rituximab and abatacept, might offer a greater chance of therapeutic success.

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