The main reason for discontinuation of secukinumab is loss of efficacy: secondary non-responders with 94 events. Primary non-responders were responsible for discontinuation in 28 events. Nine adverse events were also recorded as reason for discontinuation (Figure 2).

Similarly with other treatments, adverse events to secukinumab which are responsible for the treatment discontinuation are more frequent in the first 6 months of exposure; subsequently, the curve flattens. A relative similar behaviour is seen for primary non-responder patients. By contrast, secondary loss of efficacy appears late in time.

The effectiveness measures for secukinumab interventions at 6 months and 12 months of treatment used were BASDAI and disease activity score (ASDAS). From the literature, it is known that a level of BASDAI > 4 reflects active disease. Because for BASDAI a clear cut-off value for inactive disease has not been validated, we used a cut-off value of 2 for inactive disease (in line with the one used in the EuroSpA study); a level of BASDAI between 2 and 4 corresponded in our analysis with low disease activity. For ASDAS, we have used the ASAS cut-off levels: inactive disease for ASDAS<1.3 and low disease activity for ASDAS < 2.1 (11).

Table 3 displays the efficacy parameters for the entire secukinumab cohort, and compares groups based on previous exposure to bDMARDs.

Overall, at a cohort level, regardless of the score used to define efficacy, there is an improvement of BASDAI and ASDAS from 6 months to 12 months of treatment with secukinumab. At 6 months, the mean BASDAI corresponds to low disease activity, whereas mean ASDAS level stays in the high disease activity category; at 12 months, BASDAI drops to inactive disease state and ASDAS level decreased to low disease activity.

There are no major differences between different clinical scenarios related to previous bDMARDs exposure for BASDAI-6 months and BASDAI-12 months, except for BASDAI-6 months for biologic naïve patients (43% - significantly lower compared to 62% for the other groups). However when using ASDAS, biologic naïve patients have a significantly better treatment response to secukinumab at 6 months and at 12 months, being at low disease activity state from 6 months onwards. Patients previously exposed to biologics have a better response when a lower number of prior biologics were used: patients who received only 1 biologic before secukinumab reach low disease activity state at 12 months, whereas patients who received 2 or more biologic drugs stay in high disease activity even at 12 months.

Figure 3 and figure 4 display disease activity state after 6 months and after 12 months of treatment with secukinumab, with comparison between the 3 groups.

There were no differences between groups according to age and disease duration related to efficacy parameters.

DISCUSSION

The randomized controlled trials (RCT) are the gold standard for assessing the efficacy of pharmacological treatments and other interventions (12). Results from RCTs may, however, lack external validity (13) due to their highly standardized design, strict inclusion and exclusion criteria, and fixed treatment regimens that may often be at odds with real world conditions (14,15). Patient characteristics may differ between RCTs and observational studies (registry data) and may modify treatment effects (16).

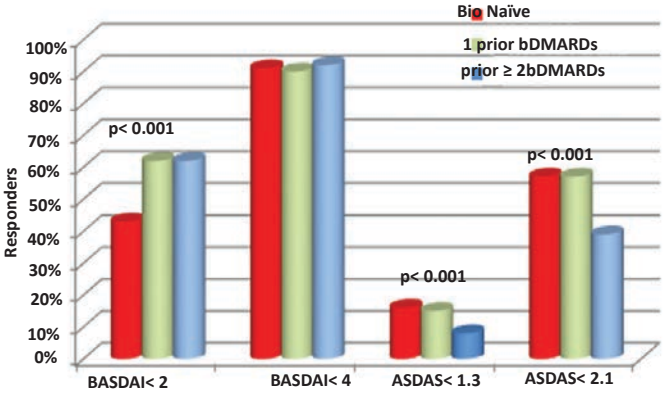

FIGURE 3. *Disease state after 6 months of treatment with secukinumab compared across previous exposure bDMARDs*

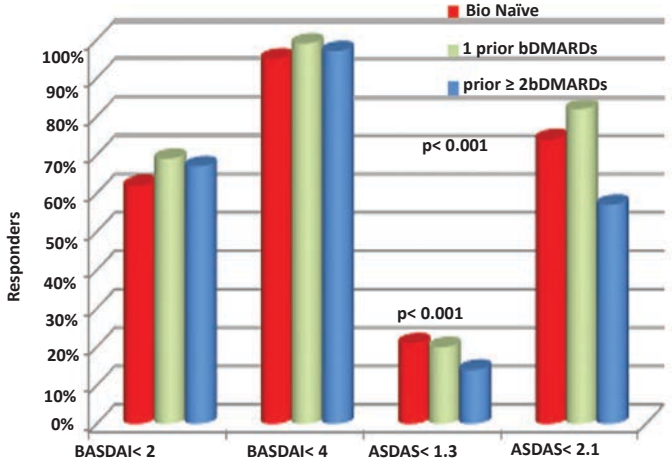

FIGURE 4. *Disease state after 12 months of treatment with secukinumab compared across previous exposure bDMARDs*