**“Persistence in treatment with TNF-alpha inhibitors in Spondyloarthritis: comparison between original and biosimilar drugs - a pilot study”**

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**Abstract**

**Introduction**: Biosimilars have demonstrated comparable efficacy, safety and immunogenicity to original drugs in randomized clinical trials, with subsequent extrapolation of their therapeutic indications to those of the original drug1,2,3. Some studies with real-world data supporting this biosimilarity have been published4,5,6. However, long-term data of their use in Spondyloarthritis (SpA) is still scarce.

**Objectives**: To compare effectiveness and safety of original TNF-alpha inhibitors (iTNF) and biosimilars in bDMARD-naïve patients diagnosed with SpA, measured by persistence rates (PR) over 3 years of follow-up; to compare disease activity and response rates after 6, 12 and 24 months; to investigate the frequency and reasons for discontinuation comparing the rates of adverse events (AEs).

**Methods**: A retrospective observational study of patients followed at the Rheumatology Unit of ULS Viseu Dão-Lafões, using data collected prospectively from The Rheumatic Diseases Portuguese Registry (Reuma.pt) was performed, including patients with: age ≥18 years old; diagnosis of SpA (axial or peripheral) and bDMARD-naïve, who initiated treatment with Humira®, Enbrel®, Simponi®, Imraldi®, Hyrimoz® or Benepali®, between January 2010 and May 2022. Kaplan-Meyer and Cox regression were used to calculate the PR in treatment. Disease activity mean and standard deviation at 6, 12 and 24 months of treatment were compared. Causes for therapy discontinuation were summarized using descriptive statistics. Statistical significance was assumed for p-values <0.05.

**Results**: A total of 127 patients were included, 83 under original iTNF and 44 under biosimilar iTNF. The majority had radiographic axial SpA (56.6% under original iTNF, 59.1% under biosimilar iTNF) and were HLA-B27 positive (65.1% under original iTNF, 68.2% under biosimilar iTNF). PR at 3-years was significantly higher under original iTNF (61.4%) (figure 1), with an average drug use time of 27.2 months; compared to 33.3% under biosimilar iTNF, with an average drug use time of 23.7 months (p=0.012). The main cause of discontinuation was secondary failure, with a higher proportion observed under biosimilar iTNF (52.8% vs 18.1%, p<0.01). No differences were found regarding primary failure or the rate of AEs.

The most commonly reported AEs were infections, skin reactions at the injection site and paradoxical psoriasis. The cumulative risk of AEs was higher under original iTNF (15.7% vs. 8.3%), although not statistically significant (p=0.282).

The proportion of subjects in remission or low disease activity was greater under original iTNF at 6 months, with statistically significant differences in BASDAI (p=0.024), BASFI (p=0.02), ASDAS-PCR (p=0.031) and BASDAI response (p=0.048). However, this difference was not consistently reproduced at 12 and 24 months, except for BASFI at 12 months (p=0.015) and ASDAS-PCR at 24 months (p=0.020) (table 1).

**Conclusions**: Our results suggest greater efficacy of the original iTNF, with no differences in the safety profile, compared to biosimilars. However, the number of missing data and the sample size were a limitation of the study, which limits the extrapolation of our conclusions. Further studies with a larger sample size are needed to confirm these results, as they could have important implications for clinical practice.