AB0401

SWITCH FROM ETANERCEPT ORIGINATOR TO ETANERCEPT BIOSIMILAR: DATA FROM REAL LIFE

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Background: Biosimilars of antiTNF- α are now available for the treatment of arthritis. There are a lot of data about maintenance of clinical efficacy after switching from originator to biosimilar but also reports about flares and adverse events (AE). Controversies still exist due to ethical and economic reasons. We describe the disease activity trend after switching from etanercept originator (oETA) to its biosimilar (bETA) in a population of Turin, Piedmont, Italy. In this region switch to biosimilar is mandatory by law except in case of patients with history of allergy, off-label, psychological reasons, active disease that required different treatment.

Objectives: To evaluate the disease activity trend before and after switch from oETA to bETA.

Methods: We switched 82 patients (M/F 33/49, mean age 59.65 $\pm$ 11.5, duration of disease 17.56 $\pm$ 10.3 years) in stable state of disease from oETA to bETA; 49 patients affected by RA, 24 by PsA, 10 by AS. The mean of duration of oETA and bETA treatment was respectively 129.2 and 6.2 months. We evaluated VAS-pain, Global-Health, CRP, number of swollen and tender joints, DAS28 for RA, DAPSA for PsA, HAQ and HAQ-S, BASDAI for AS patients.

Results: Differences of variables between oETA and bETA are summarized in table1.

We didn't find any significant difference between oETA and bETA in order to efficacy. However 8 patients, 5 RA and 4 PsA(9.75%) discontinued bETA because arthritis flare(7) or AE(1).

Conclusion: Data about maintenance of efficacy and percentage of discontinuation were similar to the literature. We didn't find significant differences on efficacy after switching from originator to biosimilar.

However, considering the rate of flares and AE, further strong studies are required.

Treatment	DAS28 RA	HAQ RA	DAPSA PsA	HAQ PsA	BASDAI SA	HAQ-S SA
oETA	2.61 ($\pm$ 0.92)	0.85 ($\pm$ 0.52)	8.15 ($\pm$ 5.6)	0.88 (0.6)	2.88 ($\pm$ 2.6)	0.85 ($\pm$ 0.42)
bETA	2.68 ($\pm$ 1.21)	0.92 ($\pm$ 0.7)	11.66 ($\pm$ 9.63)	0.9 ($\pm$ 0.69)	2.7 ($\pm$ 2.16)	0.58 ($\pm$ 0.26)

Tab. 1 The analysis of variables between Etanercept originator (oETA) and Etanercept biosimilar (bETA)

REFERENCES

- [1] Jørgensen, K. K. et al. Lancet 2017 Jun 10;389(10086):2304-2316.
- [2] Kay J and KL Winthrop Nat Rev Rheumatol 2017 Jul;13(7):391-392.
- [3] Toussiot E, Marotte H. RMD Open 2017;3:e000492.

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AB0402

MEASURING PATIENT EXPERIENCE OF SWITCHING BIOLOGIC TREATMENT – A SYSTEMATIC LITERATURE REVIEW

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Background: Biologics have transformed the treatment of inflammatory arthritis (IA). However, the complexity of disease management has increased with the introduction of biosimilars and novel treatments. Hence, patient experience and satisfaction has become increasingly important in treatment individualization.

Objectives: Firstly, to assess to what extent IA patient experience of switching biologics is measured in the literature; secondly, to summarize patient-reported outcomes (PROs) as well as medical/non-medical reasons associated with switching.

Methods: A systematic literature review (SLR) was performed in accordance with PRISMA guidelines. EMBASE and MEDLINE were searched for relevant publications from 2013 to present day, together with relevant conference abstracts from 2018 (ACR-ARHP, EULAR, and ISPOR). Studies published in English including either a) patient-reported outcomes (PROs) associated with switching biologics, or b) reasons for switching and/or discontinuing biologics treatment as noted by health care professionals and/or

patients were included. The scope was limited to European and North American populations. While the initial search included patient populations with ulcerative colitis in addition to IA patients, results presented within this abstract focus on IA populations only.

Results: After initial screening of 1781 abstracts, sixty-eight studies including IA patients were identified for inclusion in the analysis. Of the remaining studies, 39/68 (57%) included ≥ 1 treatment switch. The majority of studies were conducted in Europe (36/39; 92%), with the proportion of female patients ranging between 12-90%. Thirteen studies (18%) included at least one PRO, 4 of which only recorded PROs prior to switch (6%). The most commonly reported PRO was PGA/VAS, followed by HAQ and questions asking patients to rank their switching experience using various pre-defined categories (Figure 1). While the most common reasons for discontinuing treatment, which may or may not include switching, was provided in 33 studies (loss of efficacy and safety), reasons strictly for switching are infrequently reported.

Conclusion: Patient satisfaction is important, as it has been linked to clinical safety, treatment effectiveness, and adherence (Doyle et al., 2013). However, this SLR highlights a notable lack of information regarding patient-reported experience of switching biologic treatment. The PROs reported in a minority of studies encompass several regions related to patient well-being – such as pain, fatigue, etc. – but provides very limited information on the experience of switching. Hence, to improve disease management and treatment individualization, further research is required.

REFERENCE

- [1] Doyle, et al. A systematic review of evidence on the links between patient experience and clinical safety and effectiveness. BMJ Open, 2013.

Figure 1

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AB0403

PREDICTORS OF PERSISTENCE OF BIOLOGIC DRUG STEP-DOWN STRATEGIES IN INFLAMMATORY ARTHRITIS: A LONGITUDINAL STUDY IN CLINICAL PRACTICE WITH A LONG FOLLOW-UP

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Background: Recommendations for the management of Rheumatoid Arthritis (RA) and spondyloarthritis (SpA) with bDMARD include dose-tapering

as an adequate option for patients on persistent remission. Although data regarding these strategies has increased in recent years, there is scarce evidence about their long-term effect.

Objectives: Our aim was to analyze the persistence of bDMARD dose-reduction in clinical practice and evaluate its predictors in patients with RA and SpA

Methods: Retrospective longitudinal study from 2006 to 2018. From a cohort of 153 patients with chronic inflammatory arthritis treated with bDMARD (TNF inhibitors, rituximab, tocilizumab, and abatacept) we recruited those with RA and SpA receiving reduced-dose regimens.¹ Variables analyzed were: persistence of bDMARD dose-reduction, predictors of this persistence reported in the literature such as treatment with glucocorticoids (GC) or conventional synthetic DMARD (csDMARD), disease activity and duration of disease at dose-reduction as well as demographic and other clinical features.

A Cox proportional hazards model was used to identify factors associated with persistence on reduced-doses during the study period.

Results: 56 patients (RA:33; SpA:23) on tapered bDMARD (etanercept 51.8%, adalimumab 32.1%, Infliximab 3.6% and tocilizumab 12.5%) at study entry were included. Their clinical and laboratory features are shown in table 1.

After a mean follow-up on tapered-dose of 4.4 years (range 0.35-8.72), 42.9% of subjects overall remained on reduced doses (RA: 36.4%; SpA: 52.2%). (Fig. 1)

From those who required discontinuation of the step-down regimen, 16 (48.4%) achieved the therapeutic objective and 7 (22.6%) failed after returning to standard dose respectively.

bDMARD were discontinued in 4 (12.9%) patients due to sustained disease remission (RA=3; SpA=1), 3 (9.7%) due to adverse events and 2 (6.4%) due to other reasons. No significant differences in the variables analyzed were found between patients continuing vs discontinuing reduced-dose regimens.

After adjusting for age, sex, diagnosis and disease duration, the concurrent use of GC at the time of dose-reduction was an independent predictor of discontinuation of the step-down regimen [aHR 3.6 (1.4 – 9.3)]

Conclusion: A significant proportion of patients with RA and SpA (36.4% and 52.2% respectively) can be maintained with reduced doses of bDMARD after a long-term follow-up.

Concurrent use of GC at the time of dose-reduction was found an independent predictor of discontinuation of the step-down regimen.

REFERENCES

- [1] Inciarte-Mundo J, et al. *Reumatol Clin.* 2014;10(1):10–16

Table 1. Demographic and clinical features at bDMARD dose-reduction.

	Total n: 56	Continue tapered bDMARD n: 24	Withdrawn tapered bDMARD n:32
Age	52.3 ± 14.3	54 ±13.9	51.1 ± 14.7
Female	32 (57.1%)	10 (41.7%)	22 (68.8%)
Ever-smokers	25%	23.8%	26.1%
Diagnostics	33	12 (36.4%)	21 (63.6%)
RA	23	12 (52.2%)	11 (47.8%)
SpA			
Mean disease duration	14.4 ± 6.8	18.5±7.9	12.1 ± 4.9
RA	13.9 ± 6.3	13.9 ± 7.53	14 ± 5
SpA	6.3		
Disease activity	2.3 ± 0.5	2.3 ± 0.3	2.3 ± 0.6
RA (DAS28)	1.6 ± 1.7	1.7 ± 1.8	1.5 ± 1.7
AS (BASDAI)			
Antibody Status	28 (85%)	9 (75%)	19 (90.5%)
(RA)	29 (88%)	9 (75%)	20 (95.2%)
RF			
ACPA			
Erosive disease (RA)	24/33	9/12	15/21
bDMARD Naive	28 (85%)	11(91.7%)	17(81%)
RA	17	9 (75%)	8 (72.7%)
SpA	(73.9%)		
Concomitant csDMARD	19 (57.6%)	7(58.3%)	12(55%)
RA	5(21.7%)	1(8.3%)	4(36.3%)
SpA			
Concomitant GC	8(24.2%)	2(16.7%)	6(28.6%)
RA	2(9%)	0	2(18.2%)
SpA

Figure 1. Survival curve for persistence on tapered-dose strategy. Data are proportion (solid line) and 95 CI (coloured area)

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AB0404 VALIDATION OF A THERAPEUTIC DRUG MONITORING TEST TO MEASURE THE ADALIMUMAB BIOSIMILAR SB5 IN COMPARISON WITH THE REFERENCE ADALIMUMAB

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Background: Validation of therapeutic drug monitoring (TDM) tests is an essential requirement for using these tools to help assess reasons for non-response. The arrival of biosimilars has prompted a need to validate that existing TDM tests are suitable to determine drug levels for all versions of a given molecule. The adalimumab (ADL) biosimilar SB5 (Biogen) was authorised by the European Commission in August 2017, and has recently become available for prescription in several European countries. Promonitor[®]-ADL test is routinely used to monitor IBD patients treated with ADL.

Objectives: In this study we validated the suitability and performance of Promonitor-ADL CE-marked TDM test for quantifying SB5 serum concentrations in comparison to reference adalimumab (Abbvie).

Methods: The study evaluated imprecision and bias applied to the reference ADL and SB5 biosimilar. The validation study was in line with the design requirements established in the Clinical & Laboratory Standards Institute (CLSI) guideline EP10-A3 for the determination of imprecision and bias. Imprecision was evaluated using three replicates of five human serum sample matrices representative of clinically relevant ADL concentrations and spanning the measurement range of Promonitor-ADL.¹ Validations were ran on one instrument with one kit lot by one operator over six non-consecutive operating days and one run per testing day, with an acceptance criterium of CV%≤20%. The Lower Limit of Quantification (LLOQ) of Promonitor-ADL was determined according to CLSI guideline EP17-A2.

Results: The imprecision of Promonitor-ADL was calculated by estimating the components of variance due to within-run and between-day factors meet the accuracy goals proposed at all concentration levels of SB5 vs the reference adalimumab (CV% between 5% and 12%). The assessment of accuracy showed that Promonitor-ADL equally measures the active moiety of the reference adalimumab or the adalimumab biosimilar SB5. The test is able to quantify SB5 in the measurement range of 0.9 to 10.9 mg/mL with a bias estimate of -0.124 (1%) to 0.897 (10%) mg/mL and an overall imprecision of 5% to 11%. The measurement range includes the recommended clinical decision points. LLOQ of the test to determine ADL was determined to be 0.36 mg/mL.

Conclusion: This study demonstrates that Promonitor-ADL test can measure either the reference ADL drug or the adalimumab biosimilar SB5 with equivalent sensitivity, precision and accuracy.

REFERENCES

- [1] Feuerstein, et al 2017. *Gastroenterology* 153: 827–834 AGA Institute Guideline on Therapeutic Drug Monitoring in IBD.