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SAT0201 REAL WORLD EVIDENCE ON SWITCHING BETWEEN ETANERCEPT AND ITS BIOSIMILAR IN RHEUMATIC DISEASES

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Background: Etanercept (Etn) is a biologic agent (BA) that has been proved to be successful in the treatment of rheumatic diseases, by acting as tumour necrosis factor inhibitor, but it is costly. In February 2016, the first etanercept biosimilar (EtnBS) was launched in Germany as a relatively cheaper alternative.

Objectives: In a recent study using the German Longitudinal Prescriptions database IQVIA® (LRx) we showed that despite many patients (approximately 50%) were moved from EtnBA to EtnBS treatment over the year following its launch, some (10%) switched back to the original product after few months¹. As new data are available from the database, the objective of this second analysis was to evaluate switching-back dynamics over longer follow-up durations.

Methods: The German LRx covers prescription data from January 2008, representing approximately 60% of the German statutory health insurance market. The study period was from February 2016, date of EtnBS launch in Germany, to August 2017 (last available data). Patients receiving first EtnBS prescription (index date) during the study period were retrospectively identified and separated into two groups based on treatment received in the 12 months prior to index date: treatment-naïve patients (no prior biologic treatment) and patients previously treated with EtnBA or other anti-TNF biologics. For the latter group, the cumulative proportion of patients switching back from EtnBS to EtnBA and the median time to the switch-back were evaluated over 3 time periods corresponding to dates of new data availability within the data source: February 2016-September 2016 (1), February 2016-March 2017 (2), and February 2016-August 2017 (3). The results were compared using the chi square test with significance set at p<0.05. Data on the market share for biologic agents and their biosimilars in rheumatic diseases are also shown on a monthly basis, between January 2015 and August 2017.

Results: A total of 707, 1,607 and 2,229 patients were identified who received prior EtnBA treatment before switching to EtnBS in time periods 1, 2 and 3 respectively. Of these patients, the proportion of those who switched back to EtnBA significantly (p<0.05) increased over time: 53 (7%) in time period 1, 153 (10%) in time period 2 and 320 (14%) in time period 3. Patients generally switched back to the biologic agent within 3–4 months of starting EtnBS treatment. The use of EtnBS by rheumatologists has constantly grown since February 2016, with a market share of 6% in Dec 2016 increased to 12% in August 2017.

Conclusions: This study confirmed previous findings on switching dynamics between EtnBA and its biosimilar. In addition, the study shows that despite a constant increase in the use of EtnBS since its launch, from September 2016 to August 2017, the proportion of patients who switch back to EtnBA after 3–4 months of initiating EtnBS has doubled.

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SAT0202 COMPARISON OF THE BIOAVAILABILITY OF A SINGLE DOSE OF CERTOLIZUMAB PEGOL INJECTED BY PRE-FILLED SYRINGE OR BY ELECTRO-MECHANICAL AUTO-INJECTION E-DEVICE: A PHASE 1, OPEN-LABEL, RANDOMISED, PARALLEL GROUP, SINGLE-CENTRE BIOEQUIVALENCE STUDY

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Background: When administered subcutaneously (SC) using a pre-filled syringe (PFS), the anti-TNF certolizumab pegol (CZP) has a half-life of ~14 days and has shown good bioavailability (~80%) at all tested doses in healthy volunteers and patients with rheumatoid arthritis.^{1,2} A reusable electro-mechanical auto-injection device (e-Device), ava[®], was recently approved in the EU,¹ providing an alternative SC-delivered CZP option in addition to the PFS and autoinjector device (AutoClicks[®]).^{1,3}

Objectives: To determine if a single 200 mg CZP dose is bioequivalent when delivered SC by PFS or e-Device, and to assess the safety and tolerability of both administration methods.

Methods: NCT02806219 was a phase 1, open-label, randomized, parallel group, single-center bioequivalence study. Healthy volunteers were randomized 1:1 to receive CZP via either the PFS or e-Device. Primary outcomes were assessed using the pharmacokinetic per-protocol set (PK-PPS): maximum CZP plasma concentration (C_{max}), area under the plasma concentration vs time curve (AUC), and AUC from baseline (BL) to final data point (AUC_(0-t)). At BL (Day 1), volunteers received a single 200 mg CZP dose. CZP plasma concentrations were measured on Day 1 prior to CZP administration, at 12 hours (h) post-dose, and on Days 2–7, 10, 14, 21, 28, 42, 56, and 70. Safety and tolerability were assessed using the safety set (all receiving a CZP dose) via reported treatment-emergent adverse events (TEAEs), serious AEs, and adverse device events (ADEs: AEs considered by the investigator to be related to/caused by the device). An injection site pain visual analog scale (VAS; 0–100 mm) was completed immediately post-injection (0 h) and 1 h post-injection.

Results: 100 healthy volunteers were randomized to receive CZP either via PFS (n=50) or e-Device (n=50). The mean plasma CZP concentration vs time profiles for the e-Device and PFS were comparable. Point estimates and 90% confidence intervals (CIs) for test/reference geometric mean ratios in C_{max} and AUC were contained within bioequivalence limits of 80–125% (table 1). Both administration methods were equally well tolerated; all reported TEAEs were mild or moderate, with no ADEs or injection site reaction TEAEs. Mean VAS pain scores were low at 0 h (PFS: 10.7 [SD 14.3], e-Device: 18.0 [24.4]) and 1 h (1.4 [2.9] vs 2.7 [7.0]).

Table 1 Results of the bioequivalence analysis comparing the PFS and e-Device

	Reference	Test		Test/Reference		ANCOVA CV (%)
		CZP 200mg PFS	CZP 200mg e-Device	Point estimate	90% CI	
	n	Geometric LS Mean (95% CI)	Geometric LS Mean (95% CI)			
C _{max} (µg/mL)	48	28.8 (27.1, 30.5)	28.7 (27.1, 30.4)	1.00	0.93, 1.07	20.8
AUC _(0-t) (µg·d/mL)	47	670.8 (623.7, 721.5)	668.7 (623.1, 717.7)	1.00	0.92, 1.09	25.6
AUC (µg·d/mL)	45	701.8 (653.3, 754.0)	688.6 (643.0, 737.6)	0.98	0.90, 1.07	24.6

PK-PPS: analysis of covariance; AUC: area under the curve; AUC_(0-t): AUC from baseline to final data point; CI: confidence interval; C_{max}: maximum plasma concentration; CV: coefficient of variation; d: day; CZP: certolizumab pegol; LS: least squares; PFS: pre-filled syringe; PK-PPS: pharmacokinetic per-protocol set.

Conclusions: CZP 200 mg doses were bioequivalent whether administered by PFS or e-Device. The SC-delivered CZP injections were well tolerated in healthy volunteers when using either method.

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