Persistence in Rheumatoid Arthritis Patients on Biosimilar and Bio-Originator Etanercept: A Pooled Analysis of Pan-Canadian Cohorts

Cristiano S Moura[1], Denis Choquette[2], Louis Coupal[2], Orit Schieir[3], Vivian P Bykerk[4,5], Marie-France Valois[1], Gilles Boire[6], Walter P. Maksymowych[7], Sasha Bernatsky[1], on behalf of CATCH, RHUMADATA, RAPPORT, and EUPA investigators

[1]McGill University, Canada, [2]Institut de Rhumatologie de Montréal, Canada, [3]University of Toronto, Canada, [4]Mount Sinai Hospital, Canada, [5]Hospital for Special Surgery, USA, [6]University of Sherbrooke, Canada, [7]University of Alberta, Canada

Background

- Biosimilar etanercept (ETA-B) was recently introduced in Canada but real-world data descriptions of drug persistence (and comparisons with the originator product, ETA-O) are still scarce.

Objectives

- To describe the recent use of etanercept biosimilar and to compare therapy persistence with its originator biologic medication in patients with rheumatoid arthritis (RA).

Methods

- We used data from four ongoing, prospective cohorts in Canada:
  - Canadian Early Arthritis Cohort (CATCH);
  - Rheumatoid Arthritis Pharmacovigilance Program and Outcomes Research in Therapeutics (RAPPORT);
  - Early Undifferentiated Polyarthritis (EUPA) cohort,
  - RHUMADATA® registry.
- We studied biologic-naïve and biologic-experienced RA adults initiating ETA-B or ETA-O between Jan. 2015 and Oct. 2019.
  - Switchers from ETA-O to ETA-B (or vice-versa) were included.
- We assessed persistence of therapy in the first 12 or 24 months, measured as time from therapy initiation (time zero) to discontinuation.
  - Individuals switching between products could contribute further person-time to the new exposure category.
- Multivariable Cox regression models were performed with each cohort dataset separately, following a common protocol.
  - Model variables included age, sex, comorbidity, past biologic use, and disease duration.
- After testing for between-study heterogeneity, cohort-estimated hazard ratios (HR) were pooled using random effects meta-analysis.

Results

- We identified 262 episodes of etanercept use (118 ETA-B and 144 ETA-O) from 250 RA patients.
- Sex, age, and other baseline characteristics across the four cohorts are shown in Table 1.
- In the pooled analysis, the adjusted HR for discontinuation at 12 months comparing ETA-B to ETA-O was 0.82 (95% CI: 0.42-1.60, Figure 1).
- In the pooled analysis for therapy discontinuation at 24 months, the adjusted HR was 0.51 (95% confidence interval, CI: 0.26-0.98, Figure 2).

Table 1 – Characteristics of studied patients according to their treatment episodes, biosimilar etanercept (ETA-B) or bio-originator etanercept (ETA-O).

Characteristic	EUPA		RAPPORT		RHUMADATA		CATCH	
	ETA-B	ETA-O	ETA-B	ETA-O	ETA-B	ETA-O	ETA-B	ETA-O
	N=19	N=27	N=32	N=30	N=39	N=52	N=28	N=35
Female sex, (%)	12 (63)	18 (67)	20 (63)	22 (73)	28 (72)	38 (73)	20 (71)	27 (77)
Mean age in years[1], SD	59 (13)	59 (16)	51 (15)	54 (15)	59 (15)	54 (15)	55 (12)	51 (13)
Current smoker, (%)	3 (17)	5 (21)	9 (32)	5 (19)	8 (21)	9 (17)	5 (18)	8 (23)
Cardiovascular disease, (%)	0 (0)	0 (0)	1 (3.1)	1 (3.3)	8 (21)	2 (4)	NA	NA
Diabetes, (%)	0 (0)	0 (0)	4 (12.5)	1 (3.3)	2 (5)	3 (6)	NA	NA
Hypertension, (%)	NA	NA	5 (15.6)	4 (13.3)	14 (36)	22 (42)	NA	NA
RA duration in years[1], SD	2.1 (2.5)	7.0 (12.5)	8.0 (6)	11.6 (15)	11.6 (11.7)	8.6 (9.0)	4.4 (3.5)	2.7 (2.6)
DAS28[1]	1.7 (NA)	4.3 (2.8)	5.9 (1.0)	5.6 (1.1)	4.1 (2.1)	4.2 (1.2)	4.0 (1.8) 23	4.3 (1.8)
SDAI[1]	13 (14)	44 (5)	NA	NA	21 (15)	23 (8)	(14)	25 (16)
Use of medications, N(%)								
Oral steroids	15 (79)	17 (63)	6 (19)	4 (13)	29 (74)	31 (60)	9 (32)	13 (37)
Past Biologic DMARDs used	8 (42)	6 (22)	2 (6)	0 (0)	21 (54)	20 (38)	19 (68)	21 (60)
Non-biologic DMARD	19 (100)	27 (100)	30 (94)	26 (87)	32 (82)	23(44)	25 (89)	33 (94)

[1] At time zero or at the closest date before time zero. SD=standard deviation

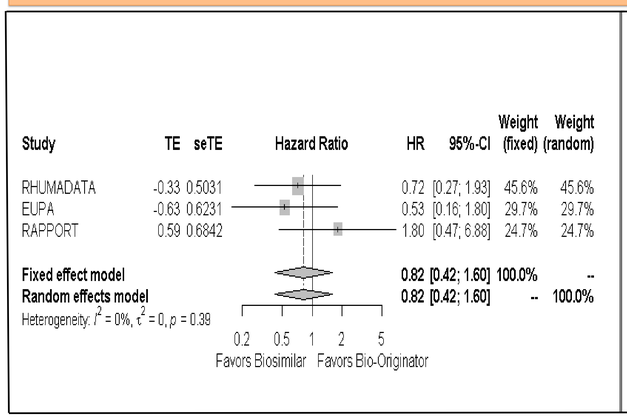

Figure 1 - Pooled adjusted Hazard Ratio [95% confidence interval (CI)] of discontinuation at 12 months for biosimilar versus bio-originator adjusted by sex, age, comorbidity, past biologic use, and disease duration.

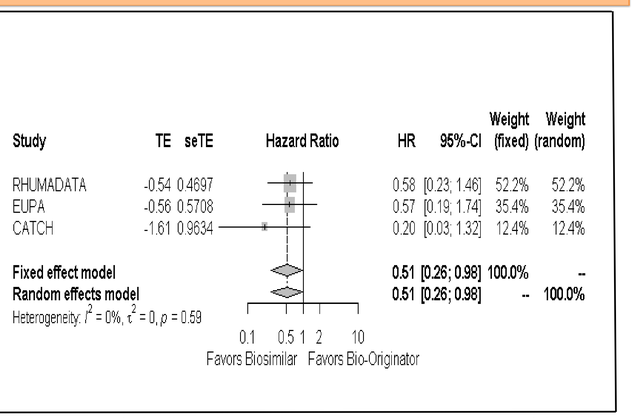

Figure 2 - Pooled adjusted Hazard Ratio [95% confidence interval (CI)] of discontinuation at 24 months for biosimilar versus bio-originator adjusted by sex, age, comorbidity, past biologic use, and disease duration.

Conclusion

- Given the wide confidence intervals around our estimates, we were unable to establish clear differences in persistence with ETA-B versus ETA-O.
- We must also acknowledge that some of the observed associations may be related to residual confounding
  - E.g. disease activity, time-dependent effects of concomitant drugs) and/or survivorship bias (in patients transitioning from ETA-O to ETA-B).
- Still, our study hints that in the real world, bio-originators may indeed be associated with similar or even better drug persistence.

Participating cohorts

CATCH — INSTITUT de RHUMATOLOGIE de MONTRÉAL

EUPA — Early Undifferentiated Polyarthritis cohort

RAPPORT — Rheumatoid Arthritis Pharmacovigilance Program and Outcomes Research in Therapeutics

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CATCH, RAPPORT, RHUMADATA, and EUPA Investigators*

Drs. M. Baron, L. Bessette, G. Boire, V. Bykerk, I. Colmegna, S. Fallavollita, D. Haaland, B. Haraoui, G. Hazlewood, C. Hitchon, S. Jamal, R. Joshi, E. Keystone, B Nair, P. Panopoulos, J. Pope, L. Rubin, C. Thorne, E. Villeneuve, M. Zummer, Nathalie Carrier, Patrick Liang, and Sophie Roux.