Significative increased risk of major adverse cardiovascular events related to baricitinib use in patients with Rheumatoid Arthritis compared to patients with TNFi – SNDS results

ABSTRACT

BACKGROUND

An international **post-authorization safety study** using real-world data was set up to assess the **safety profile of baricitinib** for the treatment of **rheumatoid arthritis (RA).** Results issued from the **French nationwide healthcare database (SNDS)** are presented here.

OBJECTIVES

To **compare the risk of** :

- Venous thromboembolism, **VTE**
- Major adverse cardiovascular events, **MACE**
- Serious infection, **SI**

between **RA patients** treated with **baricitinib** and similar patients treated with **tumor necrosis factor inhibitors (TNFi**).

METHODS

- Comparative cohort study conducted in the **SNDS between 2017 and 2019:**
  - including all French **patients aged 18 years or older with RA initiating baricitinib or TNFi** (index date, ID) with a history period of at least 180 days
  - excluding patients with an occurrence of the outcome of interest within 180 days prior ID, with tofacinitib dispensing within 180 days prior ID and concomitant dispensing of ≥2 bMARD at ID
  - without concomitant use of anticoagulant at ID (VTE and MACE cohorts only).
- One cohort for each event of interest: **VTE**, **MACE**, and **SI**
- For each cohort, one **propensity score (PS) model** was generated, relying on history of relevant comorbidities, previous use of conventional RA treatments, and advanced treatment lines.
- **Matching:** new users of baricitinib were **1:1 matched** on propensity score with patients starting a new TNFi line.
- **Incidence rate** and 95% confidence interval (95%CI) of each outcome estimated in the baricitinib and TNFi-matched cohorts. The incidence rate ratios (IRRs) and 95%CI were estimated using a modified Poisson regression model.

RESULTS

- Of the eligible baricitinib-treated patients, were matched with TNFi-treated patients:
  - 2 859 patients in VTE cohort, contributing respectively to 1 855 and 1 923 person-years (PY) of baricitinib and TNFi exposure,
  - 2 864 patients in MACE cohort, contributing to 1 848 and 1 896 PY of baricitinib and TNFi exposure,
  - 2 979 patients in SI cohort contributing to 1 920 and 1 994 PY baricitinib and TNFi exposure.
- During follow-up:
  - 33 patients experienced VTE (20 with baricitinib),
  - 36 experienced MACE (25 baricitinib),
  - 72 experienced SI (36 baricitinib).
- Incidence rates in baricitinib and TNFi-treated patients were respectively:
  - 1.1 (95% CI [0.7 to 1.7]) and 0.7 [0.4 to 1.2] VTE per 100 PY,
  - 1.4 [0.9 to 2.0] and 0.6 [0.3 to 1.0] MACE per 100 PY,
  - 1.9 [1.3 to 2.6] and 1.8 [1.3 to 2.5] SI per 100 PY.
- Overall IRRs comparing baricitinib *vs* TNFi treatment were 1.59 [0.79 to 3.21] for VTE, 2.33 [1.15 to 4.74] for MACE, and 1.04 [0.65 to 1.65] for SI.

CONCLUSION

French results suggest a **significative increased risk of MACE** related to **baricitinib use** in patients with RA compared to patients with TNFi. Baricitinib has been available in France since 2017, thus, these **analyses** are **only based on the first years of marketing** where treated patients are often refractory to previous lines of treatment. **These results must be interpreted in the light of those from the other countries participating to this study to build a robust baricitinib safety profile.**

Disclosure

Study carried out in partnership with Aetion Inc., financed by Eli Lilly and Company, and supervised by a scientific committee of independent experts in accordance with the ENCePP code of conduct.

Comparative safety of baricitinib versus TNFi in Rheumatoid Arthritis management in the French population: a propensity score-matched cohort study

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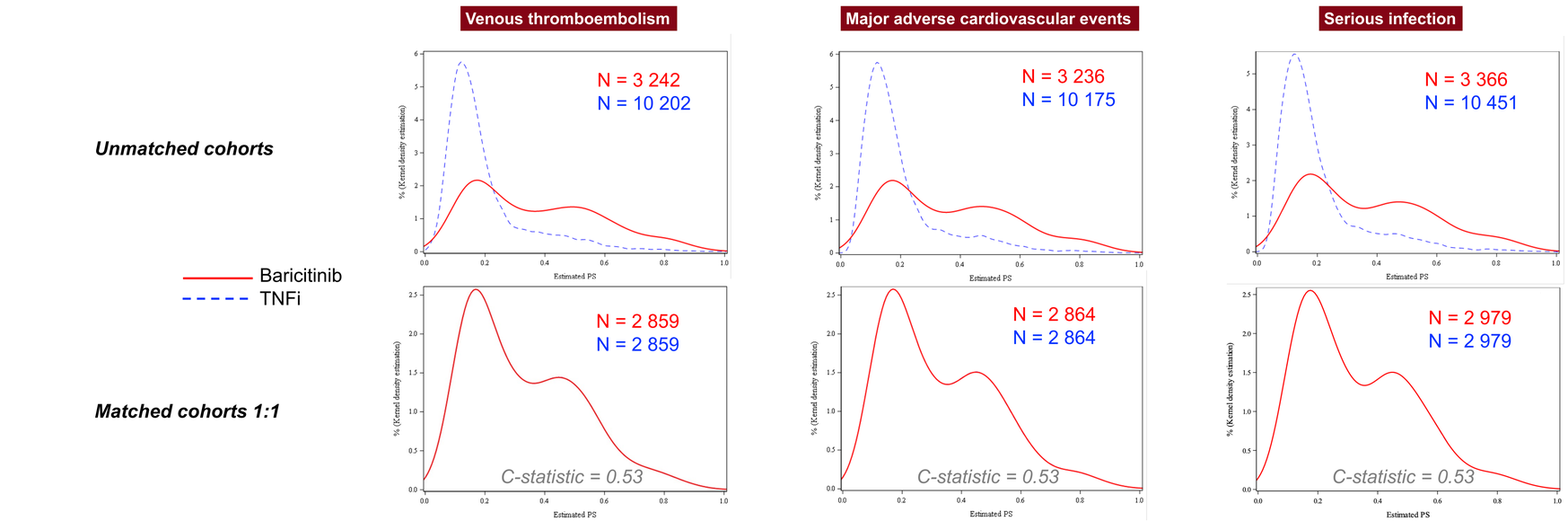

Figure 1. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched and matched cohorts, matching ratio 1:1 on PS ± 0.01

Table 2. Crude incidenc e rates of outcomes VTE, MACE and SI in matched cohorts [SNDS]

Matched cohorts (1:1)	Venous thromboembolism			Major adverse cardiovascular events			Serious infection		
	Baricitinib n = 2 859	TNFi n = 2 859	Total n = 5 718	Baricitinib n = 2 864	TNFi n = 2 864	Total n = 5 728	Baricitinib n = 2 979	TNFi n = 2 979	Total n = 5 958
Exposure, in PY	1 855	1 923	3 778	1 848	1 896	3 744	1 920	1 994	3914
Outcome, N	**20**	**13**	**33**	**25**	**11**	**36**	**36**	**36**	**72**
Median time to 1st occurrence of the outcome, in days (SD)	227.0 (165.4)	181.4 (156.3)	209.0 (161.0)	215.8 (179.6)	226.1 (176.9)	218.9 (176.3)	206.4 (188.4)	155.2 (169.8)	180.8 (179.9)
Median	204.0	113.0	168.0	171.0	174.0	172.5	127.0	100.0	114.5
[Min; Max]	[17.0;632.0]	[28.0;555.0]	[17.0;632.0]	[4.0;710.0]	[1.0;522.0]	[1.0;710.0]	[6.0;629.0]	[1.0;743.0]	[1.0;743.0]

PY: Person-Years; SD: Standard deviation; TNFi: tumor necrosis factor inhibitor.

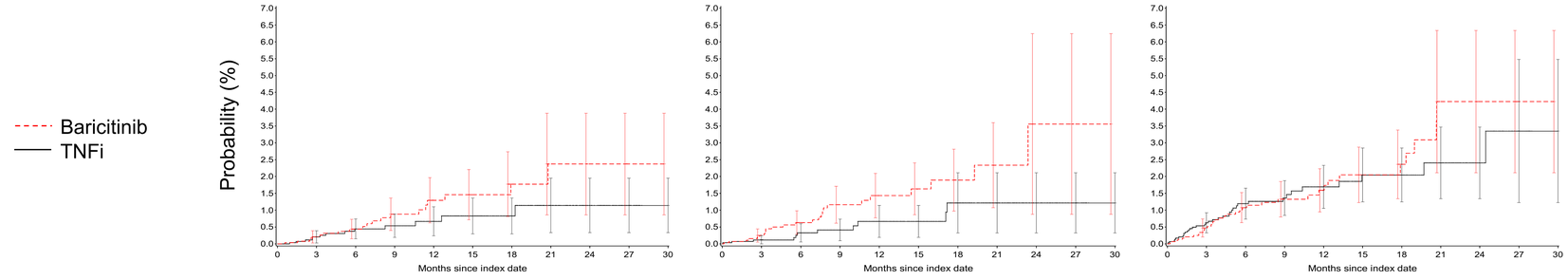

Figure 2. (1 - Kaplan-Meier) curves for outcomes, matched cohorts

Table 3. Incidence rate ratios of VTE, MACE and SI in matched cohorts [SNDS]

Matched cohorts (1:1)	Venous thromboembolism N Bari / TNFi = 2 859 / 2 859		Major adverse cardiovascular events N Bari / TNFi = 2 864 / 2 864		Serious infection N Bari / TNFi = 2 979 / 2 979	
IR Baricitinib [95%CI] *(/100 PY)*	1.08	[0.70 ; 1.67]	1.35	[0.92 ; 2.00]	1.87	[1.36 ; 2.59]
IR TNFi [95%CI] *(/100 PY)*	0.68	[0.39 ; 1.16]	0.58	[0.32 ; 1.05]	1.81	[1.31 ; 2.50]
IRR [95%CI]	**1.59**	**[0.79 ; 3.21]**	**2.33**	**[1.15 ; 4.74]**	**1.04**	**[0.65 ; 1.65]**

PY: Person-Years; CI: confidence interval; TNFi: tumor necrosis factor inhibitor; IR: Incidence Rate; IRR: Incidence Rate Ratio *(Baricitinib / TNFi)*

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