OP0247 AN IMPROVED MATRIX TO PREDICT RAPID RADIOGRAPHIC PROGRESSION OF EARLY RHEUMATOID ARTHRITIS PATIENTS: POOLED ANALYSES FROM SEVERAL DATABASES

A. Vanier[1], J. Smolen[2], C. Allaart[3], R. Van Vollenhoven[4], P. Verschueren[5], N. Vastesaeger[6], S. Saevarsdottir[4], K. Visser[3], D. Aletaha[2], B. Combe[7], B. Fautrel[1]. *[1]UPMC Univ Paris 6 and AP-HP Pitié-Salpêtrière Hospital, Paris, France; [2]University of Vienna, Vienna, Austria; [3]Leiden University Medical Centre, Leiden, Netherlands; [4]Karolinska Institute, Stockholm, Sweden; [5]Leuven University, Leuven, Belgium; [6]Merck Sharp and Dohme, Lucerne, Switzerland; [7]Université de Montpellier 1, Montpellier, France*

Background: In early rheumatoid arthritis (RA), some patients exhibit rapid radiographic progression (RRP) after one year, associated with poor functional prognosis. Identifying at the time of diagnosis the characteristics predictive of RRP is of importance. Several matrices predicting this risk have been proposed over the last years. They were limited somewhat in terms of precision or were built using specific populations.
Objectives: To develop a matrix to predict RRP with better precision and generalizability by pooling databases from various studies.
Methods: The study is based on the pooling of individual data from cohorts (ESPOIR and Leuven) and clinical trials (BeSt, SWEFOT and ASPIRE). Included patients were adult DMARD-naïve patients with recent suspected or confirmed diagnosis of active RA for which the first therapeutic strategy after inclusion was to prescribe MTX or leflunomide in monotherapy for at least 3 months. The main outcome was the presence after one year of RRP defined as an increase in modified Sharp score (vSHS) of at least 5 points between baseline and year one. Baseline characteristics were compared by the presence of RRP to search for predictors. A logistic regression model to predict RRP was built. The best model was selected by 10-fold stratified cross-validation by maximizing the Area Under the Curve (AUC). Calibration and discriminatory power of the model were assessed. Model parameters were extracted to estimate the probability of a RRP for each combination of level of baseline characteristics.
Results: The data of 1306 patients were pooled. After one year, 236 exhibited RRP (20.6%, $CI_{95\%}$ [18.2–22.9], mean probability of RRP of 0.21). Model of prediction of RRP included as baseline characteristics Rheumatoid Factor (RF) positivity (OR=2.1 $CI_{95\%}$ [1.5–3.0]; p<0.001), erosive disease on X-rays (OR=2.3 $CI_{95\%}$ [1.7–3.2]; p<0.001), CRP>30mg/l (OR=2.1 $CI_{95\%}$ [1.5–3.0]; p<0.001), number of swollen joints>10 (OR=1.5 $CI_{95\%}$ [1.01–2.2]; p=0.048). Model calibration was good (Hosmer and Lemeshow test: p=0.79). AUC was 0.68. The matrix proposes estimated RRP probability for 36 combinations of level of baseline characteristics. Its range goes from patients with a 4.1 fold lower risk of RRP compared to average risk (probability of 0.05 $CI_{95\%}$ [0.03–0.08], patient with CRP <10mg/l, without RF, without erosive disease on X-ray, with <6 swollen joints), to patients with a 2.3 fold higher risk than average (probability of 0.47 $CI_{95\%}$ [0.39–0.55], patient with CRP >30, with RF, with erosive disease on X-ray, with >10 swollen joints).

		Absence of typical RA erosion on radiographs			Presence of typical RA erosions on radiographs		
		SJC < 6	6 ≤ SJC < 10	SJC ≥ 10	SJC < 6	6 ≤ SJC < 10	SJC ≥ 10
RF positivity	CRP ≥ 30	0.21 [0.14 ; 0.29]	0.21 [0.15 ; 0.29]	0.28 [0.21 ; 0.36]	0.37 [0.28 ; 0.47]	0.38 [0.29 ; 0.48]	0.47 [0.39 ; 0.55]
	10 ≤ CRP < 30	0.13 [0.08 ; 0.18]	0.13 [0.08 ; 0.19]	0.18 [0.12 ; 0.24]	0.25 [0.17 ; 0.33]	0.25 [0.18 ; 0.33]	0.33 [0.25 ; 0.41]
	CRP < 10	0.11 [0.07 ; 0.15]	0.11 [0.08 ; 0.15]	0.15 [0.11 ; 0.20]	0.22 [0.16 ; 0.28]	0.22 [0.17 ; 0.28]	0.29 [0.22 ; 0.36]
RF negativity	CRP ≥ 30	0.11 [0.07 ; 0.17]	0.11 [0.07 ; 0.17]	0.15 [0.10 ; 0.21]	0.22 [0.14 ; 0.31]	0.22 [0.15 ; 0.31]	0.29 [0.22 ; 0.37]
	10 ≤ CRP < 30	0.06 [0.04 ; 0.10]	0.07 [0.04 ; 0.10]	0.09 [0.06 ; 0.13]	0.13 [0.08 ; 0.19]	0.14 [0.09 ; 0.20]	0.18 [0.13 ; 0.25]
	CRP < 10	0.05 [0.03 ; 0.08]	0.06 [0.03 ; 0.08]	0.08 [0.05 ; 0.11]	0.11 [0.07 ; 0.16]	0.12 [0.08 ; 0.17]	0.16 [0.11 ; 0.22]

Conclusions: A matrix proposing RRP probability at one year with better precision (i.e. narrower $CI_{95\%}$than those previously published) in early RA for various combinations of levels of a few common baseline characteristics has been built using several databases. However, discriminating power is not ideal. Further investigations will be needed to fully explore the potential complexity of predicting RRP in early RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4752

OP0248 SERIOUS INFECTION AND ASSOCIATED RISK FACTORS IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS TREATED WITH BARICITINIB

K.L. Winthrop[1], M.C. Genovese[2], M. Harigai[3], L. Chen[4], C.L. Dickson[4], D.L. Hyslop[4], A. Nishikawa[5], J.D. Bradley[4], M. Dougados[6]. *[1]Oregon Health and Science Univ., Portland; [2]Stanford Univ., Palo Alto, United States; [3]Tokyo Women's Medical Univ., Tokyo, Japan; [4]Eli Lilly and Company, Indianapolis, United States; [5]Lilly Japan, K.K., Kobe, Japan; [6]Paris-Descartes Univ., Paris, France*

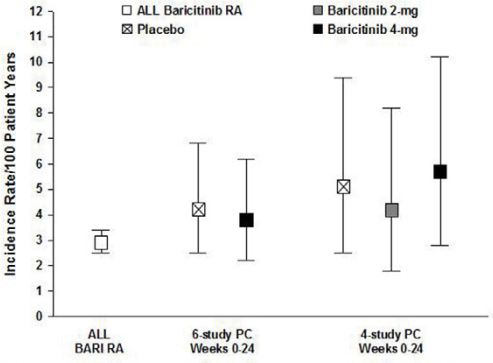
Background: Baricitinib (BARI) is an oral Janus Kinase (JAK)1/JAK2 inhibitor in development for patients (pts) with active rheumatoid arthritis (RA). Compared to the general population, RA pts have an increased rate of serious infection events (SIE) due to disease state and concomitant therapies.[1]
Objectives: To evaluate the incidence rate (IR) of SIE and associated risk factors in BARI-treated pts with active RA across 8 completed studies (4 Ph3, 3 Ph2, 1 Ph1) and 1 ongoing long-term extension (LTE) study.
Methods: The ALL BARI RA analysis set included pts exposed to any BARI dose, with exposure up to 5 years (yrs) (Phase [Ph] 1–3 and LTE studies); the comparison with placebo (PBO) was based on 6 studies (Ph 2–3) with BARI 4 mg once daily (QD) and PBO arms up to Week (Wk) 24; dose response assessment was based on 4 studies (Ph 2–3) with both BARI 2 and 4 mg QD arms up to Wk 24. An extensive list of potential risk factors for SIE was investigated in the ALL BARI RA set using Cox models; SIE risk factors among BARI-treated pts are reported (Table).
Results:
The most frequent SIE observed in the ALL BARI RA set (N=3492; 5133 pt-yrs (PY) of exposure [PYE] were pneumonia, herpes zoster, urinary tract infection, and cellulitis (all <1%), and 2 patients with SIE died (IR=0.04/100 PY). In the ALL BARI RA set, SIE were reported in 150 pts (IR=2.9/100 PY). During 0–24 Wks, similar SIE rates were observed in BARI 4 mg (N=997; 417 PYE) and PBO (N=1070; 403 PYE) groups in the 6-study set, and between BARI 2 mg (N=479; 192 PYE) and 4 mg (N=479; 194 PYE) dose groups in the 4-study set (Figure). Prior biologic use, advancing age, region of Asia (excluding Japan), non-normal body mass index (BMI), and corticosteroid use were identified as independent factors for SIE in the ALL BARI RA set (Table). Among these SIE risk factors, none significantly differed between BARI 4 mg and PBO in the 6-study dataset (data not shown).

Table 1. Hazard Ratio and 95% CI for Serious Infection in the ALL BARI RA Analysis Set

Clinical Factor	Univariate HR [95% CI]	Multivariate HR [95% CI]
Line of therapy (bDMARD-IR vs. csDMARD-IR)	1.6 [1.1, 2.3]	1.5 [1.0, 2.3]
Age (65+ vs. 18–64 yrs)[a]	2.2 [1.6, 3.2]	2.5 [1.8, 3.6]
Region (Asia [excluding Japan] vs. US/Canada)	2.4 [1.3, 4.4]	2.7 [1.4, 5.2]
BMI (kg/m^2) (vs. normal [18–24])[a]		
Underweight (<18)	3.4 [1.7, 7.0]	3.1 [1.5, 6.4]
Overweight (25–29)	1.6 [1.0, 2.4]	1.8 [1.1, 2.7]
Obese (≥30)	1.4 [0.9, 2.2]	1.8 [1.1, 2.9]
RA duration (10+ vs. 0–4 yrs)[a]	1.7 [1.1, 2.6]	–
DAS28-hsCRP (for every one unit increase)[a]	1.1 [1.0, 1.3]	–
HAQ-DI (≥1.5 vs. <1.5)[a]	1.5 [1.1, 2.1]	–
Corticosteroid dose (mg/day)[a]		
0.1–4.9 vs. none	2.2 [1.3, 3.7]	2.3 [1.4, 3.9]
5+ vs. none	1.7 [1.2, 2.5]	1.9 [1.3, 2.7]

[a]Data at baseline. Abbreviations: CI, confidence interval; HR, hazard ratio.

Figure. Serious Infection Incidence Rate and 95% CI by Analysis Set



	ALL BARI RA	6-study PC Weeks 0-24		4-study PC Weeks 0-24		
IR/100 Patient Years	2.9	4.2	3.8	5.1	4.2	5.7
All Patients	3492	1070	997	551	479	479
With Events	150	17	16	10	8	11
Patient Years	5133	403	417	195	192	194

Abbreviations: CI=confidence interval; IR=incidence rate; PC=placebo controlled; RA=rheumatoid arthritis

Conclusions: SIE incidence was similar between BARI- and PBO-treated RA pts. SIE risk factors include concomitant corticosteroids, prior biologics, non-normal BMI, Asian region of enrollment, and advancing age.
References:
[1] Listing J et al. Rheumatology. 2013;52:53–61.
Disclosure of Interest: K. Winthrop Grant/research support from: Pfizer, BMS, Consultant for: Pfizer, UCB, Abbvie, Eli Lilly and Company, Amgen, BMS, M. Genovese Grant/research support from: Eli Lilly and Company, Abbvie, Astellas, Galapagos, Pfizer, Vertex, Crescendo Bioscience, Consultant for: Eli Lilly and Company, Abbvie, Astellas, Galapagos, Pfizer, Vertex, Crescendo Bioscience, M. Harigai Grant/research support from: Bristol-Myers Squibb KK, Eisai Co Ltd, Ono Pharma, Takeda Pharma Ltd, Consultant for: Eli Lilly and Company, L. Chen Employee of: Eli Lilly and Company, C. Dickson Employee of: Eli Lilly and Company, D. Hyslop Employee of: Eli Lilly and Company, A. Nishikawa Employee of: Eli Lilly Japan K.K., J. Bradley Employee of: Eli Lilly and Company, M. Dougados Grant/research support from: Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS, Consultant for: Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS
DOI: 10.1136/annrheumdis-2017-eular.1312