Patient Disease Trajectories in Baricitinib 2-mg-Treated Patients with Rheumatoid Arthritis and Inadequate Response to Biologic DMARDs

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BACKGROUND

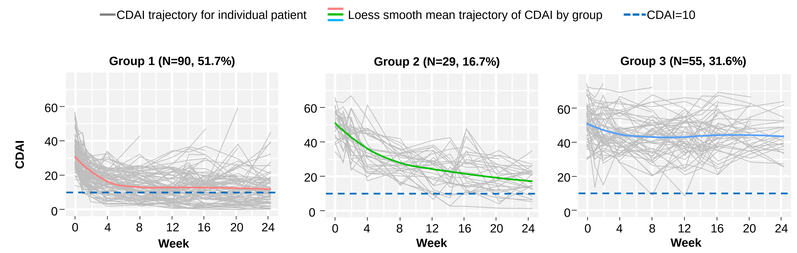
- Baricitinib, a selective Janus kinase 1 and 2 inhibitor, is approved in more than 60 countries for the treatment of moderately-to-severely active rheumatoid arthritis (RA)
- In the Phase 3 RA-BEACON (NCT01721044) trial, baricitinib 2-mg demonstrated clinical efficacy in patients with RA who were inadequate responders to biologic disease-modifying antirheumatic drugs (bDMARDs)[1]
- It is important to understand if patients have different disease response patterns and how these patterns relate to baseline characteristics, clinical measures, and patient outcomes

OBJECTIVES

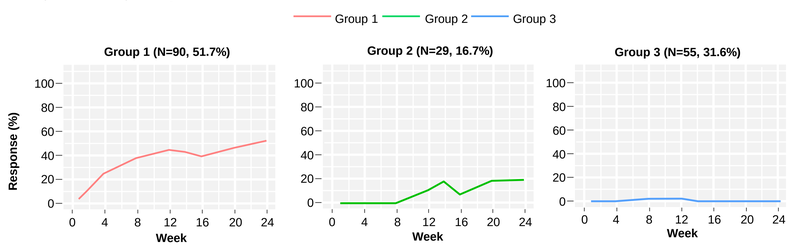
- To identify patients' response patterns after receiving baricitinib 2-mg over 24 weeks in RA-BEACON
- To examine the associated baseline characteristics and clinical disease measures within each response pattern group

KEY RESULTS

Patients were Classified Into 3 Subgroups by GMM Based on Their CDAI Response Patterns



LDA (CDAI ≤10) Response Rate Over Time



- Groups 1 and 2 had a rapid rate of CDAI improvement

Summary of CDAI Values for the 3 Groups Identified

Week	Group	Mean (SD)	ΔCDAI (%)[a]
0	1	33.9 (9.0)	-
	2	51.3 (8.1)	-
	3	52.2 (11.0)	-
4	1	16.1 (7.5)	-17.8 (52.6)
	2	35.0 (11.3)	-16.3 (31.7)
	3	45.2 (10.5)	-7.0 (13.4)
12	1	12.0 (7.7)	-21.8 (64.4)
	2	24.6 (9.9)	-26.7 (52.0)
	3	43.4 (12.2)	-8.8 (17.0)
24	1	11.8 (9.4)	-22.1 (65.3)
	2	17.3 (8.0)	-34.0 (66.3)
	3	42.6 (10.6)	-9.6 (18.3)

[a] Based on the group mean change from baseline

- Group 1 had the lowest baseline CDAI, achieved 53% improvement in group mean of CDAI at Week 4 (change from baseline, ΔCDAI -18), 64% improvement at Week 12 (ΔCDAI -22), and maintained similar improvement through 24 weeks
- Group 2 had higher baseline CDAI than Group 1, achieved 32% improvement in mean CDAI at Week 4 (ΔCDAI -16) with greater improvement at Week 12 (52%, ΔCDAI -27) and Week 24 (66%, ΔCDAI -34)
- Group 3 had a baseline CDAI similar to Group 2, but had smaller improvement, achieving 18% improvement in CDAI (ΔCDAI -10) at Week 24

Baseline Characteristics

	Group 1 (N=90)	Group 2 (N=29)	Group 3 (N=55)
Age, years	54.1 (11.6)	59.9 (11.1)	54.2 (9.6)
Male, n (%)	19 (21.1)	6 (20.7)	12 (21.8)
BMI, kg/m²	31.0 (7.6)	31.4 (7.9)	30.2 (8.4)
RF positive, n (%)	69 (76.7)	22 (75.9)	37 (67.3)
ACPA positive, n (%)	66 (73.3)	23 (79.3)	35 (63.6)
hsCRP, mg/L	18.7 (22.3)	18.8 (18.6)	22.3 (24.7)
ESR, mm/h	40.8 (23.2)	43.8 (18.0)	51.4 (25.3)
Duration of RA, years	13.4 (7.5)	15.8 (8.5)	13.1 (8.6)
≥3 bDMARD use	23 (25.6)	7 (24.1)	20 (36.4)
TJC28	12.4 (5.2)	20.8 (3.8)	21.7 (5.5)
SJC28	8.9 (3.9)	16.3 (4.8)	16.0 (6.2)
PGA	62.0 (17.6)	69.9 (13.9)	73.4 (14.9)
PatGA	62.5 (20.5)	71.8 (14.1)	73.2 (17.7)
Pain VAS	57.2 (22.9)	64.9 (20.5)	69.5 (17.3)
HAQ-DI	1.5 (0.5)	1.7 (0.6)	2.0 (0.5)
DAS28-hsCRP	5.5 (0.7)	6.6 (0.6)	6.6 (0.8)

Data are mean (standard deviation) unless stated otherwise

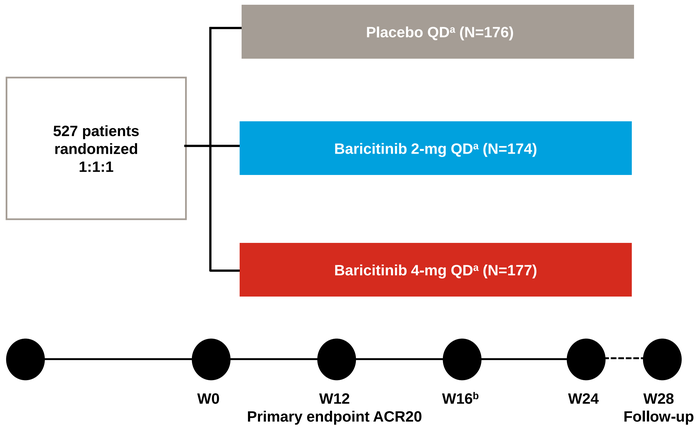
- Compared to Groups 1 and 2:
  - Group 3 had numerically more pain and worse physical function (HAQ-DI) at baseline, and a larger proportion of patients who had used ≥3 bDMARDs
  - Group 3 had a numerically lower proportion of ACPA positive or RF positive patients
  - Groups 3 had numerically higher baseline ESR and CRP

CONCLUSIONS

- There were 3 response patterns to baricitinib 2-mg treatment in the RA-BEACON trial
- The majority of baricitinib 2-mg-treated patients achieved a good response (Groups 1 and 2, 68%) with at least 50% improvement in CDAI by Week 12
  - Response was observed as early as Week 4 and was maintained or continued to improve in these groups through Week 24
- Patients who were less responsive (Group 3) tended to be more treatment experienced with greater pain and worse physical function at baseline
- Strengths: Prospectively collected data with minimal missing information
  - The data help us understand trajectories of response for baricitinib 2-mg
- Limitation: The generalizability of data collected from randomized clinical trials of patients with moderately to severely active and refractory RA to usual practice is unknown

METHODS

Study Design, RA-BEACON

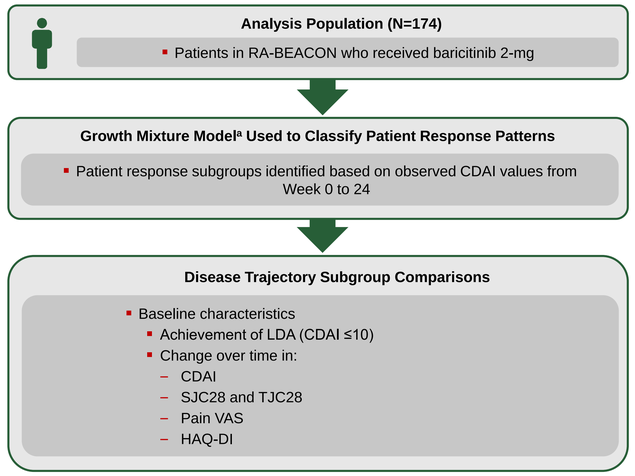


[a] Concomitant treatment with stable doses of csDMARDs, NSAIDs, analgesic agents, glucocorticoids (≤10 mg of prednisone or the equivalent per day), or a combination of these drugs was permitted
[b] At Week 16, patients whose tender and swollen joint counts at baseline were reduced by <20% at both Week 14 and Week 16 were given rescue treatment (baricitinib 4-mg daily)

Key Eligibility Criteria

- Adults with moderately to severely active RA
  - ≥6 tender joints of 68 joints examined
  - ≥6 swollen joints of 66 joints examined
  - High-sensitivity C-reactive protein ≥3 mg/L
- Inadequate response or intolerance to ≥1 tumor necrosis factor inhibitor
- ≥8 weeks stable background conventional synthetic DMARD

Analyses



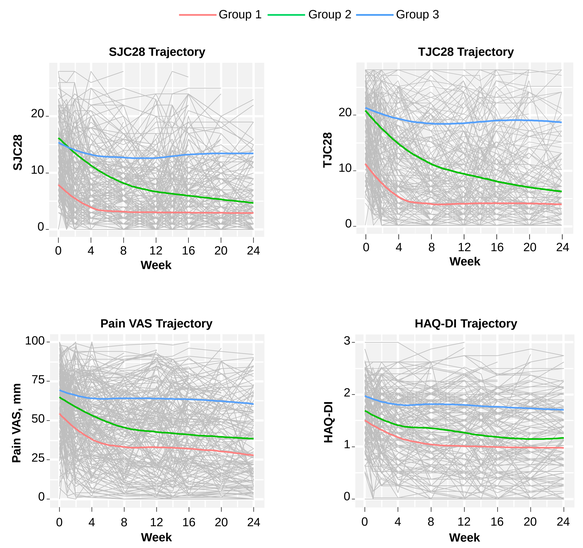
[a] A novel latent class mixed model used to classify the longitudinal disease patterns instead of predefining a clinical responder at a specific time point

Application of Growth Mixture Model (GMM)[2]

- Analysis strategy: Different from a responder analysis defined at a certain time point (for example, Clinical Disease Activity Index [CDAI] low disease activity responder at Week 24)
- Analysis specifications:
  - Baricitinib 2-mg only
  - CDAI observed data from Week 0 to 24 or up to rescue
    - No data imputation after rescue or discontinuation
  - The number of subgroups can be determined based on a data-driven method (such as Bayesian information criterion)
  - Comparisons are descriptive
    - No formal statistical comparisons were made

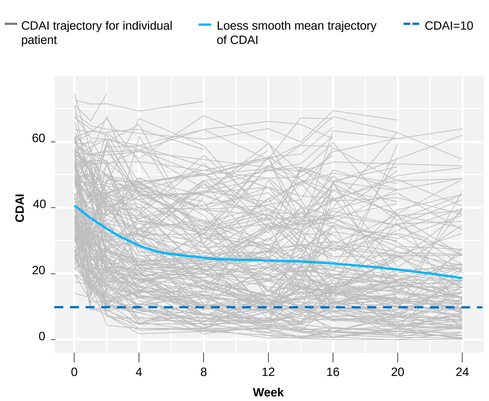
RESULTS

Trajectories of Subgroups for SJC28, TJC28, Pain VAS, and HAQ-DI Over Time



- The distributions of SJC28, TJC28, pain VAS, and HAQ-DI within each response pattern showed similar trajectories as the corresponding group CDAI trajectory

Baricitinib 2-mg Patient Trajectory: CDAI Response Over Time (All Patients)



DISCLOSURES

- **M. C. Genovese** has received grant/research support and is a consultant for: AbbVie, Eli Lilly and Company, Galapagos, and Pfizer; **M. Weinblatt** has been a consultant and/or has received research support from: AbbVie, Amgen, BMS, Corrona, Crescendo Bioscience, Eli Lilly and Company, Gilead, GlaxoSmithKline, Lycera, Merck, Novartis, Pfizer, Roche, Samsung, Sanofi/Regeneron, and SetPoint; **J. Wu**, **B. Jia**, **A. Quebe**, **L. Sun**, **Y-F. Chen**, **C. Helt**, **A. K. Bacani**, and **P. Reis** are employees and shareholders of Eli Lilly and Company; **J. Pope** has received research grants from: Bayer, BMS, Merck, Pfizer, Roche, and UCB, and received honoraria from: AbbVie, Actelion, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, and UCB
- This study was sponsored by Eli Lilly and Company, under license from Incyte Corporation. Medical writing assistance was provided by Samantha Forster, PhD, CMPP, of ProScribe – Envision Pharma Group, and was funded by Eli Lilly and Company
- This study was and previously presented at American College of Rheumatology (ACR); Atlanta, USA; November 8-13, 2019

ABBREVIATIONS

ACPA=anti-citrullinated protein antibody; ACR20=American College of Rheumatology ≥20% response; bDMARD=biologic disease-modifying antirheumatic drugs; BMI=body mass index; CDAI=Clinical Disease Activity Index; csDMARD=conventional synthetic disease-modifying antirheumatic drug; DAS28=Disease Activity Score 28-joint count; ESR=erythrocyte sedimentation rate; GMM=growth mixture model; HAQ-DI=Health Assessment Questionnaire-Disability Index; hsCRP=high-sensitivity C-reactive protein; LDA=low disease activity; Loess=locally estimated scatterplot smoothing; NSAID=nonsteroidal anti-inflammatory drug; PatGA=Patient's Global Assessment of disease activity; PGA=Physician's Global Assessment of disease activity; QD=once daily; RA=rheumatoid arthritis; RF=rheumatoid factor; SD=standard deviation; SJC28=swollen joint count of 28 joints examined; TJC28=tender joint count of 28 joints examined; VAS=visual analog scale; W=Week

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2. Proust-Lima C, et al. *J Stat Softw.* 2016;78;doi:10.18637/jss.v078.i02.

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