Impact of Disease History on the Efficacy of Ritlecitinib (PF-06651600) in Patients With Alopecia Areata: Post Hoc Analysis of the ALLEGRO Phase 2b/3 Study

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BACKGROUND

- Alopecia areata (AA) is an autoimmune disease with an underlying immuno-inflammatory pathogenesis and is characterized by non scarring hair loss ranging from small bald patches to complete loss of scalp, face, and/or body hair[1]
- Ritlecitinib, an oral JAK3/TEC inhibitor, demonstrated efficacy and safety in patients aged ≥12 years with AA in the ALLEGRO phase 2b/3 study (NCT03732807)[2]
- Disease history, including disease duration and/or episode duration, has been associated with severity, prognosis, and treatment efficacy in AA[3-5]

OBJECTIVE

- This post hoc analysis aimed to assess the impact of disease duration and duration of current AA episode on response to ritlecitinib
- Descriptive analyses were further conducted to analyze the contribution of current episode duration on response to ritlecitinib

METHODS

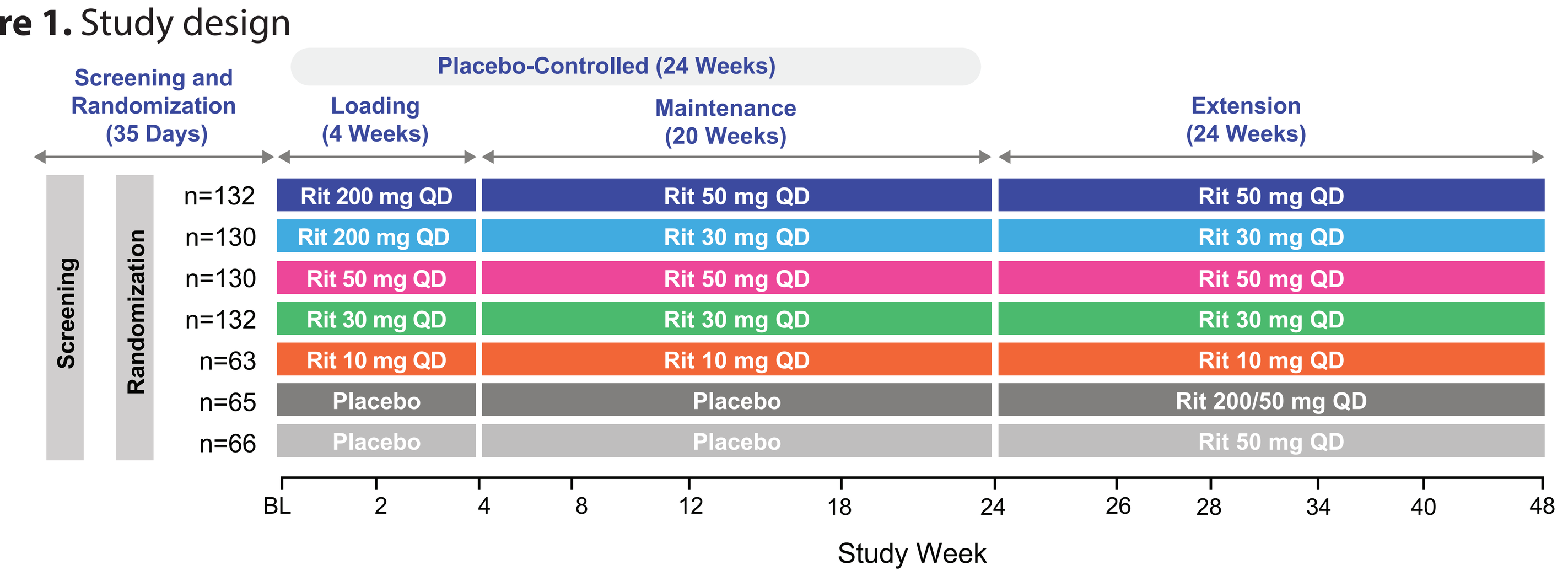
Study design

- The ALLEGRO phase 2b/3 trial was an international, randomized, double-blind, placebo-controlled, combined dose-ranging and pivotal phase 2b/3 study (**Figure 1**)
- Patients received daily ritlecitinib (with or without a 200-mg loading dose in the first 4 weeks): 200/50, 200/30, 50, 30, or 10 mg (10 mg assessed for dose ranging only), or placebo for 24 weeks
- During the 24-week extension, ritlecitinib groups continued on the 50-, 30-, or 10-mg maintenance doses, and patients initially assigned to placebo switched to ritlecitinib 200/50 or 50 mg daily

Key eligibility criteria

- Patients were ≥12 years of age with a diagnosis of AA and ≥50% scalp hair loss, including patients with alopecia totalis (AT) and alopecia universalis (AU), and a current AA episode duration of 6 months to 10 years

Figure 1. Study design



Screening and Randomization (35 Days)
Placebo-Controlled (24 Weeks)
Loading (4 Weeks)
Maintenance (20 Weeks)
Extension (24 Weeks)
Screening
Randomization
n=132
n=130
n=130
n=132
n=63
n=65
n=66
Rit 200 mg QD
Rit 50 mg QD
Rit 200 mg QD
Rit 30 mg QD
Rit 50 mg QD
Rit 30 mg QD
Rit 10 mg QD
Placebo
Rit 200/50 mg QD
BL
2
4
8
12
18
24
26
28
34
40
48
Study Week

BL, Baseline; QD, once daily; Rit, ritlecitinib.

Outcomes and statistical analysis

- In this post hoc analysis, multivariable logistic regression with 2 different variable selection methods was used to evaluate the effect of ritlecitinib (vs placebo), baseline disease duration, and current AA episode duration (both <1 year vs ≥1 year) on response based on Severity of Alopecia Tool (SALT) score ≤20 (≤20% scalp without hair) at Week 24, while controlling for other covariates
  - Covariates listed below were included in the models to evaluate the independent effect of disease and episode duration:
    - Age (continuous)
    - Sex (male vs female)
    - Race (White vs Other; Asian vs Other)
    - Body mass index (BMI; continuous)
    - Current episode duration (<1 year vs ≥1 year)
    - Disease duration (<1 year vs ≥1 year)
    - Extent of AA (AT/AU vs non-AT/AU)
    - Prior pharmacological treatment for AA (yes or no)
    - Eyelash hair loss at baseline (continuous)
    - Eyebrow hair loss at baseline (continuous)
    - Active shedding (yes vs no)
    - Treatment arm (ritlecitinib vs placebo; excluding 10-mg group)
- The 2 multivariable logistic regression models included in this analysis were:
  - **All variables model:** considered all covariates listed above to adjust for the variables of interest
  - **Stepwise model:** a stepwise approach was taken for additional sensitivity analysis; nonsignificant covariates were excluded from this model to increase precision for the independent variables of interest
  - Odds ratios (ORs) and 95% CIs were reported for both logistic regression models
- An additional descriptive subgroup analysis assessed the proportions of patients with response based on SALT score ≤20 at Week 48 by episode duration <1 or ≥1 year for active ritlecitinib treatment arms (200/50, 200/30, 50, and 30 mg)

RESULTS

- At baseline, mean (range) duration of disease since initial diagnosis was 10.06 (0.04-60.11) years and duration of current AA episode was 3.35 (0.02-9.97) years; most patients had disease and episode duration ≥1 year (**Table 1**)

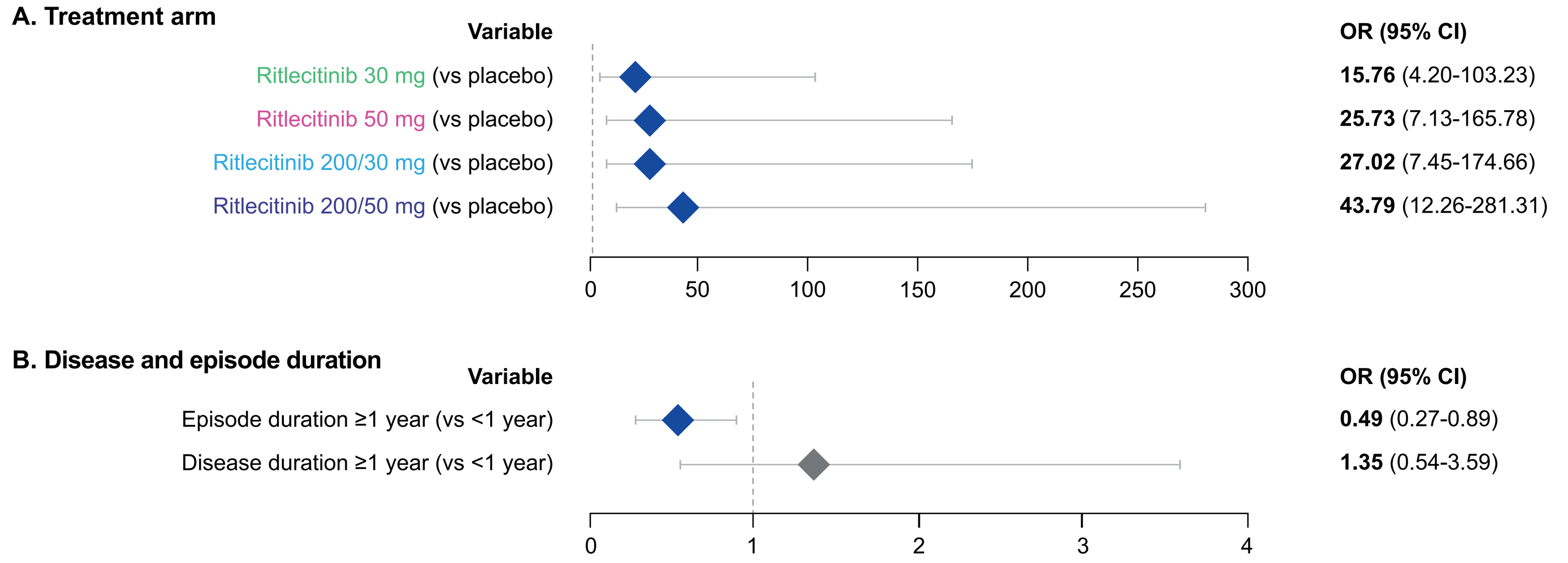
Table 1. Baseline characteristics

	Ritlecitinib QD					
	200/50 mg (n=132)	200/30 mg (n=130)	50 mg (n=130)	30 mg (n=132)	10 mg (n=63)	Placebo* (n=131)
Age						
Mean (SD), years	34.5 (15.0)	33.7 (13.8)	32.4 (13.4)	33.7 (14.8)	34.3 (13.9)	34.0 (15.0)
12-17 years, n (%)	20 (15.2)	19 (14.6)	18 (13.8)	20 (15.2)	9 (14.3)	19 (14.5)
≥18 years, n (%)	112 (84.8)	111 (85.4)	112 (86.2)	112 (84.8)	54 (85.7)	112 (85.5)
Female, n (%)	81 (61.4)	85 (65.4)	71 (54.6)	80 (60.6)	43 (68.3)	86 (65.6)
Race, n (%)						
White	92 (69.7)	90 (69.2)	79 (60.8)	91 (68.9)	42 (66.7)	94 (71.8)
BMI, mean (SD), kg/m²	25.2 (4.9)	25.2 (5.3)	24.7 (5.0)	24.9 (4.7)	24.5 (5.6)	25.0 (6.2)
AT/AU, n (%)	60 (45.5)	60 (46.2)	60 (46.2)	61 (46.2)	29 (46.0)	60 (45.8)
Baseline SALT score, mean (SD)						
All patients	90.3 (15.1)	90.5 (14.3)	90.3 (14.7)	90.0 (15.1)	88.3 (16.9)	93.0 (11.5)
Non-AT/AU†	82.2 (16.5)	82.4 (15.4)	82.0 (15.9)	81.5 (16.27)	78.3 (17.6)	87.0 (12.9)
Duration of current AA episode						
Mean (SD), years	3.4 (2.93)	3.4 (2.89)	3.2 (2.67)	3.6 (2.82)	3.3 (2.65)	3.2 (2.65)
<1 year, n (%)	32 (24.4)	28 (21.7)	30 (23.1)	26 (19.7)	16 (25.8)	31 (23.7)
≥1 year, n (%)	99 (75.6)	101 (78.3)	100 (76.9)	106 (80.3)	46 (74.2)	100 (76.3)
Duration of disease since initial diagnosis						
Mean (SD), years	9.9 (10.8)	11.6 (11.7)	8.7 (8.7)	8.8 (8.9)	10.8 (10.7)	11.0 (11.8)
<1 year, n (%)	10 (7.6)	10 (7.8)	14 (10.8)	10 (7.6)	5 (8.1)	14 (10.7)
≥1 year, n (%)	121 (91.2)	119 (92.2)	116 (89.2)	122 (92.4)	57 (91.9)	117 (89.3)
Any prior pharmacological treatment for AA, n (%)	91 (68.9)	78 (60.0)	100 (76.9)	91 (68.9)	44 (69.8)	95 (72.5)

AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis; BMI, body mass index; QD, once daily; SALT, Severity of Alopecia Tool.
*Placebo for 24 weeks and then switched to ritlecitinib 200/50 mg or 50 mg.
†Participants in the AT/AU category had a SALT score of 100 (complete scalp hair loss) at baseline.

- Irrespective of the modeling approach taken, all active ritlecitinib regimens were significantly positively associated with SALT score ≤20 response vs placebo at Week 24 (**Figures 2 and 3**)
- While disease duration was not significantly associated with SALT score ≤20 response at Week 24 (**Figure 2**), shorter episode duration (<1 year) was significantly positively associated with SALT score ≤20 response, irrespective of the model used (**Figure 3**)

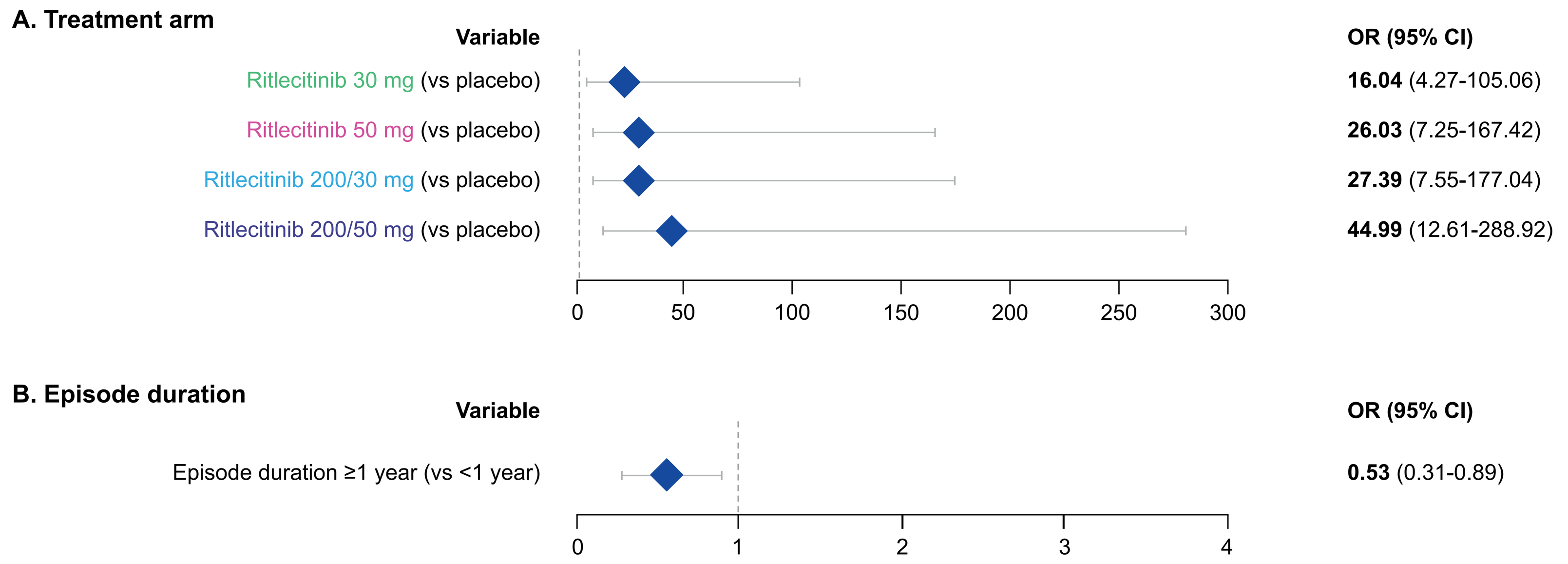
Figure 2. Odds ratios for SALT score ≤20 response at Week 24 based on (A) ritlecitinib dose vs placebo and (B) disease and episode duration (<1 vs ≥1 year) in the all variables model*



A. Treatment arm
Variable
OR (95% CI)
Ritlecitinib 30 mg (vs placebo)
15.76 (4.20-103.23)
Ritlecitinib 50 mg (vs placebo)
25.73 (7.13-165.78)
Ritlecitinib 200/30 mg (vs placebo)
27.02 (7.45-174.66)
Ritlecitinib 200/50 mg (vs placebo)
43.79 (12.26-281.31)
0
50
100
150
200
250
300
B. Disease and episode duration
Variable
OR (95% CI)
Episode duration ≥1 year (vs <1 year)
0.49 (0.27-0.89)
Disease duration ≥1 year (vs <1 year)
1.35 (0.54-3.59)
0
1
2
3
4

AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis; OR, odds ratio; SALT, Severity of Alopecia Tool.
*Blue markers indicate independent covariates of interest that were significant in the all variables model. Covariates that were not significant are shown in grey. Other significant covariates (not shown) included sex (male vs female) and extent of AA (AT/AU vs non-AT/AU).

Figure 3. Odds ratios for SALT score ≤20 response at Week 24 based on (A) ritlecitinib dose vs placebo and (B) disease and episode duration (<1 vs ≥1 year) in the stepwise model*

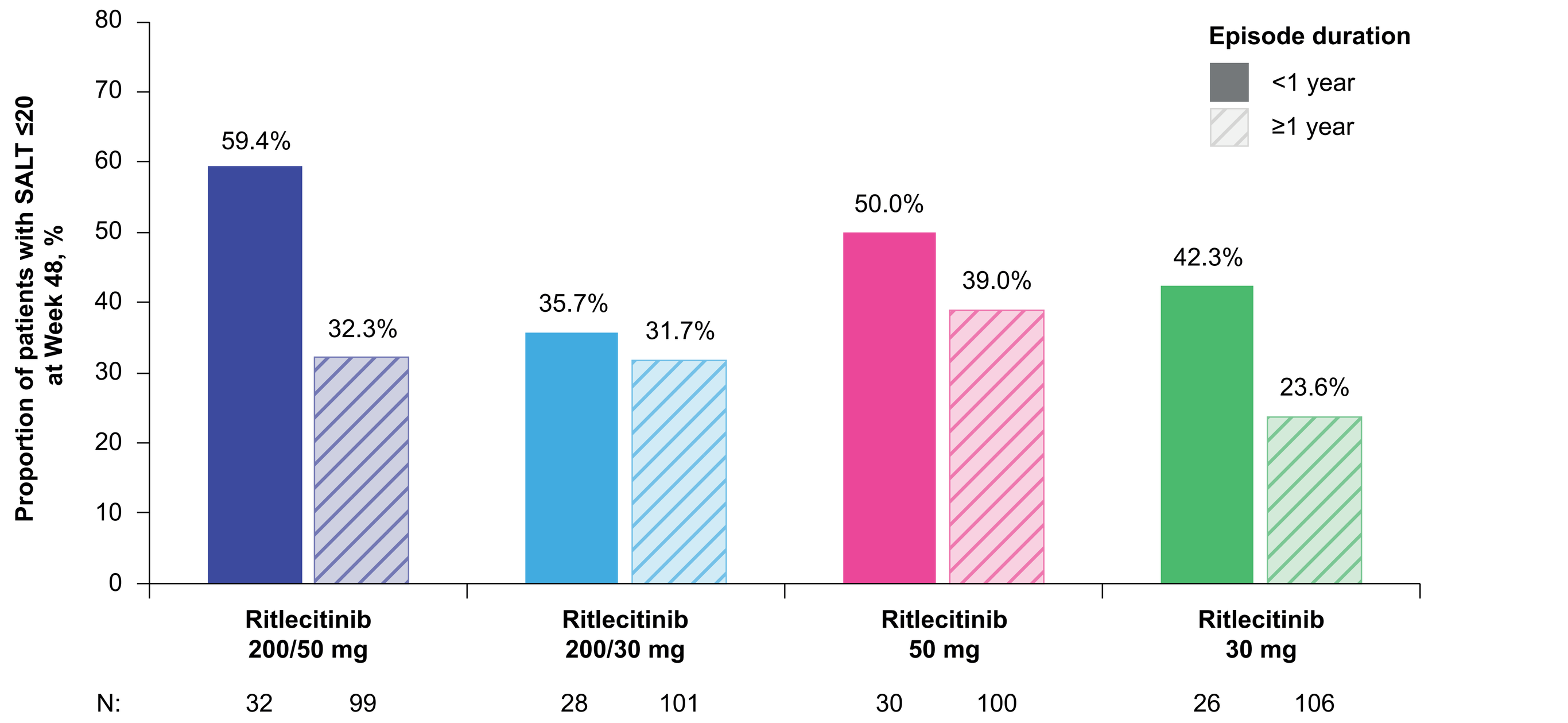


A. Treatment arm
Variable
OR (95% CI)
Ritlecitinib 30 mg (vs placebo)
16.04 (4.27-105.06)
Ritlecitinib 50 mg (vs placebo)
26.03 (7.25-167.42)
Ritlecitinib 200/30 mg (vs placebo)
27.39 (7.55-177.04)
Ritlecitinib 200/50 mg (vs placebo)
44.99 (12.61-288.92)
0
50
100
150
200
250
300
B. Episode duration
Variable
OR (95% CI)
Episode duration ≥1 year (vs <1 year)
0.53 (0.31-0.89)
0
1
2
3
4

AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis; OR, odds ratio; SALT, Severity of Alopecia Tool.
*Blue markers indicate independent covariates of interest that were significant in the stepwise model. Other significant covariates (not shown) included sex (male vs female), extent of AA (AT/AU vs non-AT/AU), and eyebrow hair loss at baseline. Disease duration (<1 year vs ≥1 year) was excluded from the stepwise model.

- While across active ritlecitinib doses (200/50, 200/30, 50, or 30 mg), a substantial proportion of patients with episode duration ≥1 year were SALT score ≤20 responders at Week 48, the proportion of patients with SALT score ≤20 response was numerically higher in those with episode duration <1 year (**Figure 4**)

Figure 4. Proportion of patients with SALT score ≤20 response at Week 48 by current AA episode duration <1 or ≥1 year



AA, alopecia areata; SALT, Severity of Alopecia Tool.

LIMITATIONS

- One-year thresholds for disease and episode duration were selected based on clinical relevance but were not used to stratify patients at enrollment; results may differ based on different thresholds for disease and episode duration treatment

CONCLUSIONS

- Treatment with ritlecitinib results in an increased likelihood of treatment response regardless of disease duration or duration of AA episode
- However, episode duration was independently associated with a reduced likelihood of SALT score ≤20 response, suggesting that while ritlecitinib is efficacious in AA regardless of disease duration, there is a potential benefit of initiating ritlecitinib therapy early in the course of an AA episode
- Further studies are needed to better understand the impact of disease history on clinical efficacy of AA treatments

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DISCLOSURES

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