Efficacy of Ritlecitinib (PF-06651600) in Patients With Alopecia Totalis and Alopecia Universalis: Post Hoc Analysis of the ALLEGRO Phase 2b/3 Study

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BACKGROUND

- Alopecia areata (AA) is an autoimmune disease that has an underlying immuno-inflammatory pathogenesis and is characterized by nonscarring hair loss ranging from small patches to complete scalp, face, and/or body hair loss[1]
- Spontaneous hair regrowth can occur in AA; however, it is unlikely to occur in extensive forms of AA, including alopecia totalis (AT; complete loss of scalp hair) and alopecia universalis (AU; complete loss of scalp, face, and body hair)[2]
- The Severity of Alopecia Tool (SALT) assesses the extent of scalp hair loss with scores ranging from 0 (no scalp hair loss) to 100 (complete scalp hair loss); patients with AT and AU have a SALT score of 100[3]
- Ritlecitinib, an oral JAK3/TEC inhibitor, demonstrated efficacy and safety in patients aged ≥12 years with AA in the ALLEGRO phase 2b/3 trial (NCT03732807)[4]

OBJECTIVE

- To evaluate the efficacy of ritlecitinib at Weeks 24 and 48 in patients with AT and AU in the ALLEGRO phase 2b/3 study

METHODS

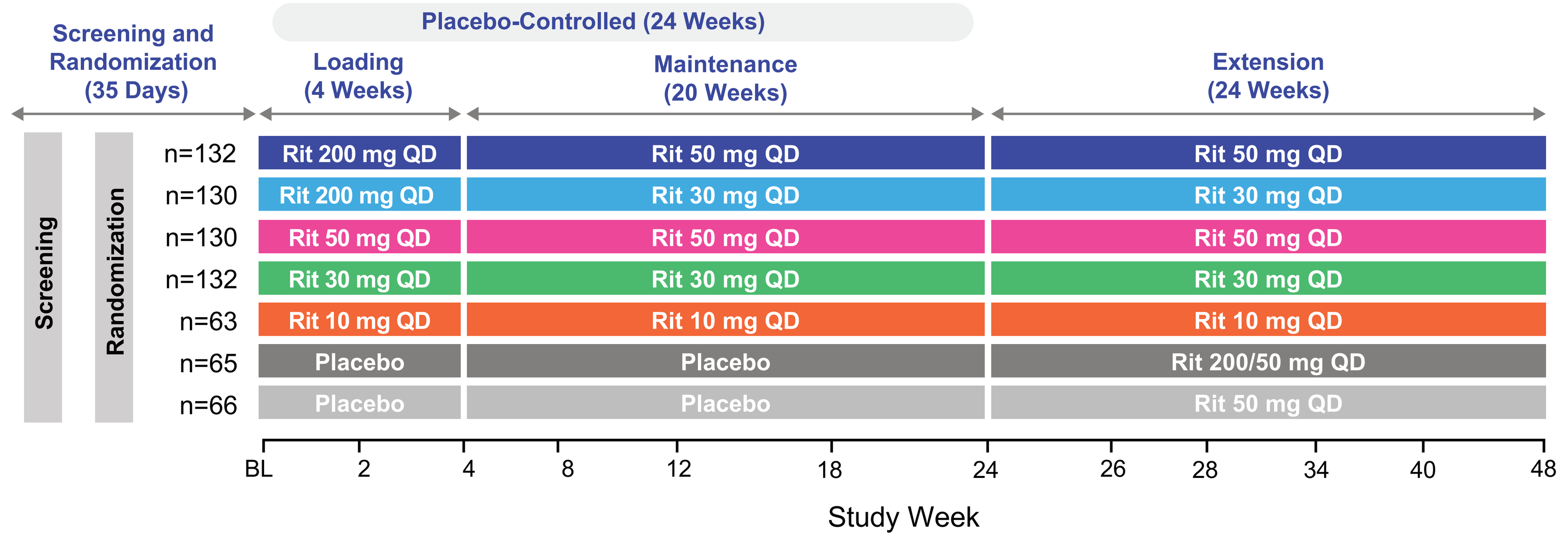
Study design

- 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 once daily ritlecitinib (± a 4-week 200-mg daily loading dose): 200/50 mg, 200/30 mg, 50 mg, 30 mg, 10 mg (10 mg assessed for dose ranging only), or placebo for 24 weeks
- During the 24-week extension, ritlecitinib groups continued receiving their 50, 30, or 10 mg maintenance doses, and patients initially assigned to placebo switched to 200/50 or 50 mg daily

Key eligibility criteria

- Patients aged ≥12 years with a diagnosis of AA and ≥50% scalp hair loss, including those with AT and 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 50 mg QD
Rit 200 mg QD
Rit 30 mg QD
Rit 30 mg QD
Rit 50 mg QD
Rit 50 mg QD
Rit 50 mg QD
Rit 30 mg QD
Rit 30 mg QD
Rit 30 mg QD
Rit 10 mg QD
Rit 10 mg QD
Rit 10 mg QD
Placebo
Placebo
Rit 200/50 mg QD
Placebo
Placebo
Rit 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

- This study assessed the proportion of patients in each subgroup with response based on a SALT score of ≤20 (≤20% scalp without hair) and a Patient Global Impression of Change (PGI-C) response of "moderately improved" or "greatly improved" at Weeks 24 and 48
  - **PGI-C** is a self-reported, single-item scale on which patients rate the improvement or worsening of AA compared with AA at the start of the study, using a scale of 7 responses ranging from "greatly improved" to "greatly worsened"

Statistical analysis

- In this post hoc analysis, patients were stratified by type of AA at baseline and were divided into 4 subgroups: AT/AU, AT, AU, and non-AT/non-AU
  - The AT/AU subgroup comprised all patients with a SALT score of 100 (complete scalp hair loss) at baseline
  - Patients in the AT or AU groups had a SALT score of 100 at baseline and a clinical diagnosis of AT or AU, respectively, by the investigator
- Descriptive analyses were used to evaluate the proportion of patients with SALT ≤20 and PGI-C response by AT/AU status
- 95% CIs were calculated based on normal approximation

RESULTS

- Of the 718 patients randomized, 151 (21%) had AT and 147 (20%) had AU; patients with AT and AU were evenly distributed across treatment groups (**Table 1**)

Table 1. Baseline characteristics

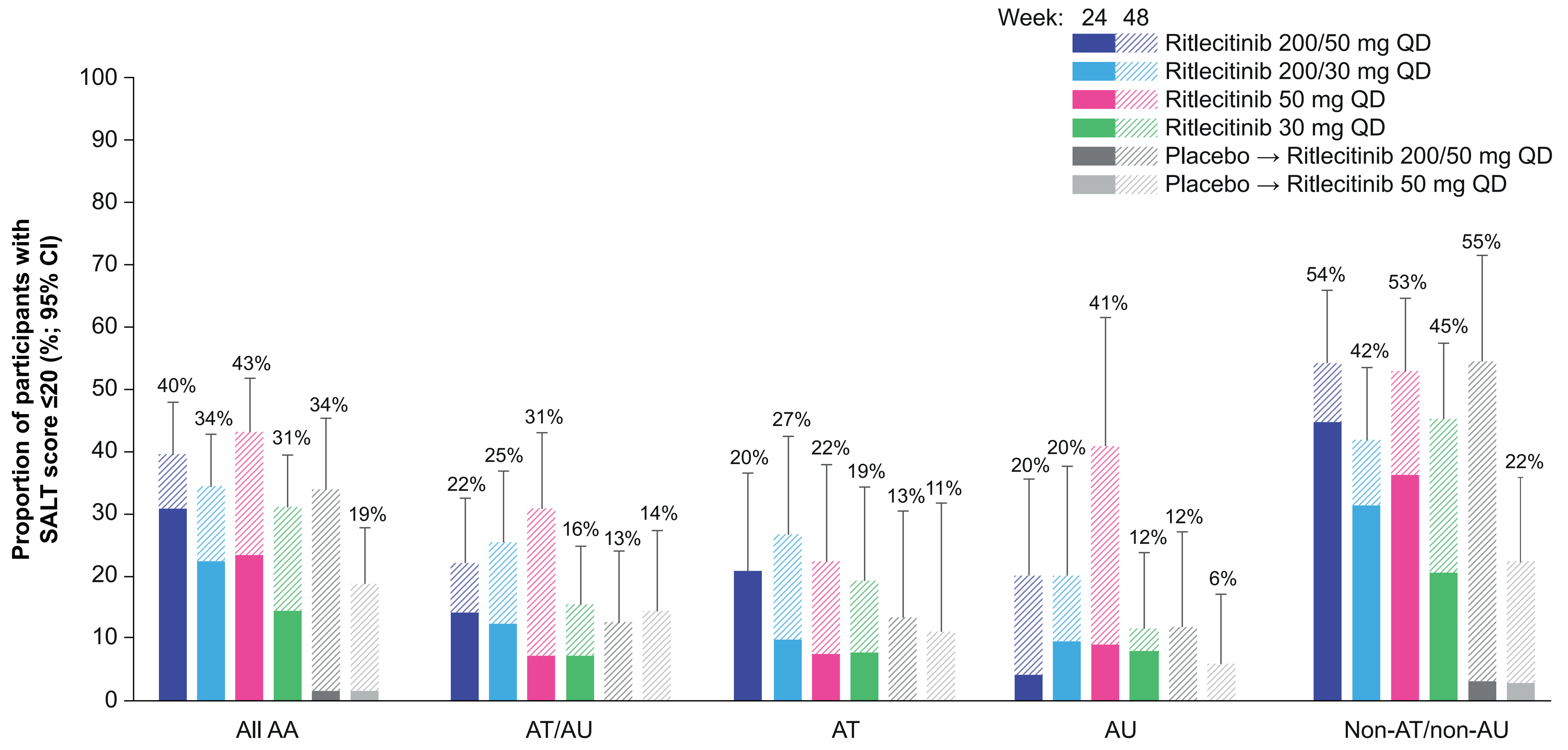
	Ritlecitinib QD					
	200/50 mg (n=132)	**200/30 mg (n=130)**	**50 mg (n=130)**	**30 mg (n=132)**	**10 mg (n=63)**	**Placebo* (n=131)**
Age						
Mean (SD), years	34.5 (15.0)	33.7 (13.8)	32.4 (13.4)	33.7 (14.8)	34.3 (13.9)	34.0 (15.0)
12-17 years, n (%)	20 (15.2)	19 (14.6)	18 (13.8)	20 (15.2)	9 (14.3)	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)
White, n (%)	92 (69.7)	90 (69.2)	79 (60.8)	91 (68.9)	42 (66.7)	94 (71.8)
Type of AA, n (%)						
AT/AU†	60 (45.5)	60 (46.2)	60 (46.2)	61 (46.2)	29 (46.0)	60 (45.8)
AT‡	25 (18.9)	34 (26.2)	30 (23.1)	26 (19.7)	12 (19.0)	24 (18.3)
AU‡	26 (19.7)	21 (16.1)	24 (18.5)	29 (22.0)	13 (20.6)	34 (26.0)
Non-AT/non-AU	72 (54.5)	70 (53.8)	70 (53.8)	71 (53.8)	34 (54.0)	71 (54.2)
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/non-AU†	82.2 (16.5)	82.4 (15.4)	82.0 (15.9)	81.5 (16.3)	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)

AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis; QD, once daily; SALT, Severity of Alopecia Tool.
*Patients received placebo for 24 weeks and then switched to ritlecitinib 200/50 mg or 50 mg QD.
†All patients in the AT/AU category had a SALT score of 100 at baseline. This subgroup includes patients who had received a clinical diagnosis of AT or AU plus those with a baseline SALT score of 100 without a clinical diagnosis of AT or AU.
‡Patients in the AT or AU category had a SALT score of 100 at baseline and received a clinical diagnosis of AT or AU, respectively, by the investigator. Patients with AT or AU were included in the AT/AU category.

Efficacy by AT/AU status at Weeks 24 and 48

- In all AA subgroups, SALT ≤20 response rates generally increased between Weeks 24 and 48 (**Figure 2**)
  - Across all ritlecitinib treatment groups (200/50 mg, 200/30 mg, 50 mg, 30 mg), SALT ≤20 response rates were highest in the non-AT/non-AU group at Weeks 24 and 48
  - Placebo response rates were low across all subgroups at Week 24; a substantial proportion of patients who switched to ritlecitinib 200/50 or 50 mg had a SALT ≤20 response by Week 48
  - At Week 48, the proportion of patients with a SALT ≤20 response was generally similar across the AT/AU, AT, and AU subgroups
- Higher proportions of patients with non-AT/non-AU had a PGI-C response of "moderately improved" or "greatly improved" in all treatment groups vs patients with AT/AU, AT, or AU at Week 24, and response rates generally improved through Week 48 (**Figure 3**)
  - At Week 48, up to 49%, 50%, and 64% of patients had a PGI-C response in the AT/AU, AT, and AU subgroups, respectively, vs up to 73% in the non-AT/non-AU subgroup

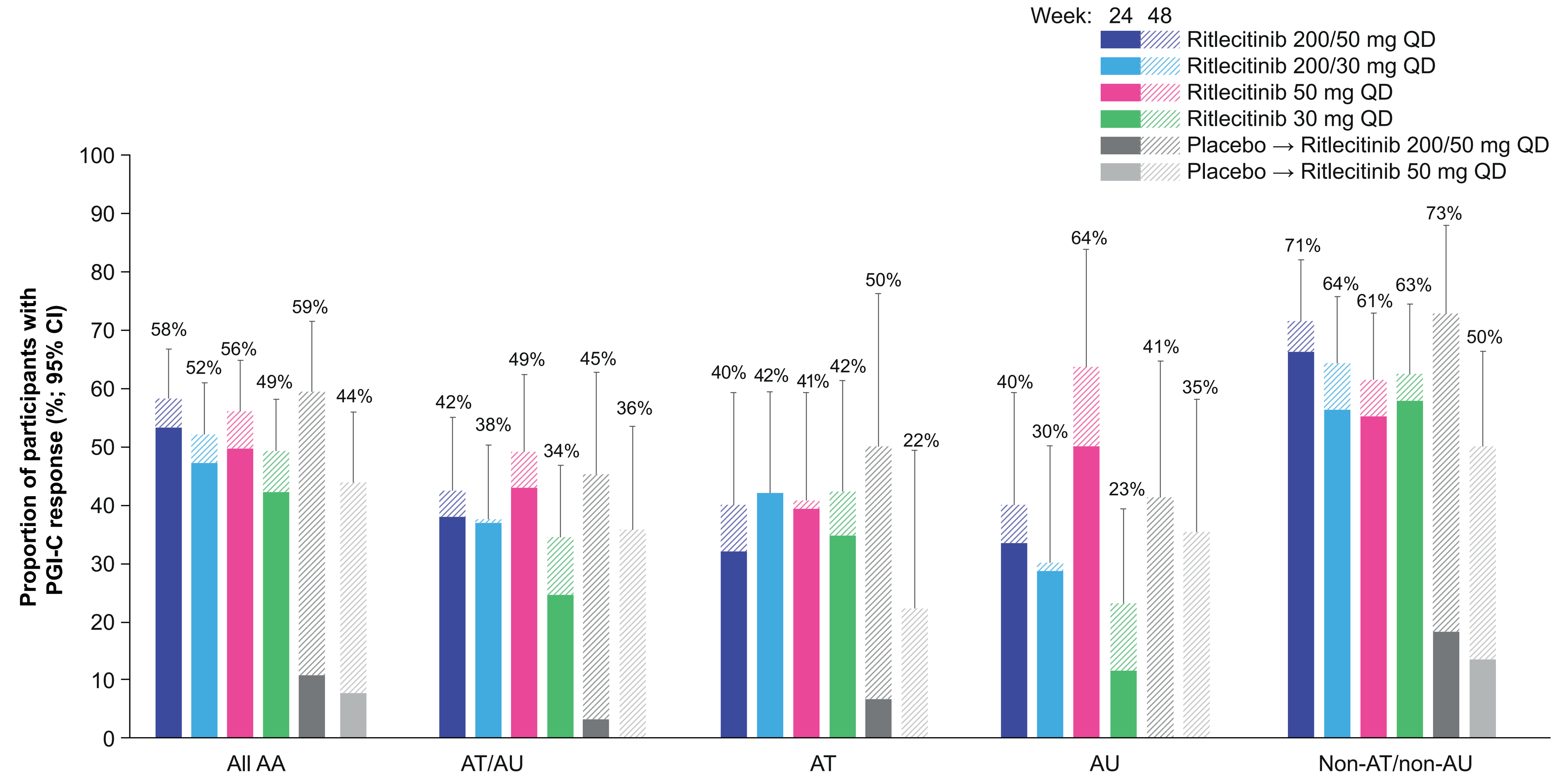
Figure 2. Response based on SALT ≤20 at Weeks 24 and 48 by AT/AU status



Week: 24 48
Ritlecitinib 200/50 mg QD
Ritlecitinib 200/30 mg QD
Ritlecitinib 50 mg QD
Ritlecitinib 30 mg QD
Placebo → Ritlecitinib 200/50 mg QD
Placebo → Ritlecitinib 50 mg QD
Proportion of participants with SALT score ≤20 (%; 95% CI)
100
90
80
70
60
50
40
30
20
10
0
40%
34%
43%
31%
34%
19%
22%
25%
31%
16%
13%
14%
20%
27%
22%
19%
13%
11%
20%
20%
41%
12%
12%
6%
54%
42%
53%
45%
55%
22%
All AA
AT/AU
AT
AU
Non-AT/non-AU

AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis; QD, once daily; SALT, Severity of Alopecia Tool. Percentages and error bars (95% CIs) are shown for SALT ≤20 response at Week 48.

Figure 3. Response based on PGI-C score* at Weeks 24 and 48 by AT/AU status



Week: 24 48
Ritlecitinib 200/50 mg QD
Ritlecitinib 200/30 mg QD
Ritlecitinib 50 mg QD
Ritlecitinib 30 mg QD
Placebo → Ritlecitinib 200/50 mg QD
Placebo → Ritlecitinib 50 mg QD
Proportion of participants with PGI-C response (%; 95% CI)
100
90
80
70
60
50
40
30
20
10
0
58%
52%
56%
49%
59%
44%
42%
38%
49%
34%
45%
36%
40%
42%
41%
42%
50%
22%
40%
30%
64%
23%
41%
35%
71%
64%
61%
63%
73%
50%
All AA
AT/AU
AT
AU
Non-AT/non-AU

AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis; PGI-C, Patient Global Impression of Change; QD, once daily.
*PGI-C response was defined as "moderately improved" or "greatly improved". Percentages and error bars (95% CIs) are shown for PGI-C response at Week 48.

CONCLUSIONS

- Ritlecitinib demonstrated clinical and patient-reported efficacy across all AA subgroups, including in patients with more extensive forms of AA (AT and AU)
- Higher SALT ≤20 response rates were observed in patients with less extensive AA (non-AT/non-AU) than in patients with AT/AU, AT, or AU over 48 weeks of ritlecitinib treatment
- While SALT ≤20 responses were lower in patients with AT/AU compared to those without AT/AU, a substantial proportion of patients with AT/AU still reported moderate or great improvement in their AA while receiving ritlecitinib, suggesting that many patients experienced meaningful benefit without achieving SALT ≤20 response

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DISCLOSURES

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