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Using Patient Preference to Inform Ritlecitinib Dose Selection for Alopecia Areata Treatment

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BACKGROUND

- Alopecia areata (AA) is an autoimmune disease that has an immuno-inflammatory pathogenesis and is characterized by nonscarring hair loss ranging from small bald patches to complete loss of scalp, face, and/or body hair[1]
- Recent evidence demonstrates that treatment with JAK inhibitors can lead to substantial hair regrowth in patients with AA, which can significantly improve patients' quality of life[2]
  - Baricitinib, a JAK1/2 inhibitor was recently approved to treat adults with severe AA
  - Ritlecitinib is an oral JAK3/TEC inhibitor that demonstrated efficacy and safety in the ALLEGRO phase 2b/3 randomized controlled trial[3]
- JAK inhibitors carry identified risks (such as serious infections, malignancies, and thrombosis)[4]

OBJECTIVE

- To compare benefit-risk profiles of two doses of ritlecitinib (50 mg vs. 30 mg once-daily [QD]), integrating patient preferences and clinical efficacy estimates for ritlecitinib in AA

METHODS

- A discrete-choice experiment (DCE) elicited preferences for benefit and safety attributes of systemic AA treatments (**Table 1**)
  - Benefits included probabilities of achieving:
    - ≥80% scalp hair coverage (Severity of Alopecia Tool [SALT] score ≤20)
    - Moderate to normal eyebrows
    - Moderate to normal eyelashes
  - Risks included 3-year probabilities of:
    - Serious infection
    - Cancer (including non-melanoma skin cancer)
    - Blood clots

Table 1. DCE attributes

Attribute	Patient-Facing Description	Corresponding Clinical Trial Endpoint
Hair on most or all your scalp	The chance of getting most or all your scalp hair (80% to 100% of your scalp hair) after 24 weeks on treatment	Absolute Severity of Alopecia Tool (SALT) score of ≤20 (indicating hair regrowth on ≥80% of the scalp)
Eyebrows	The chance of getting moderate (mildly decreased density and/or short gaps in the eyebrows) or normal eyebrows after 24 weeks on treatment	≥2-grade improvement from baseline or absolute score of 3 in the Eyebrow Assessment (EBA) among those with an abnormal baseline score The EBA is a 4-point scale where 0 = no eyebrow hair, 1 = minimal eyebrow hair, 2 = moderate eyebrow hair, and 3 = normal eyebrow hair
Eyelashes	The chance of getting moderate (mildly decreased density and/or short gaps in the eyelashes) or normal eyelashes after 24 weeks on treatment	≥2-grade improvement from baseline or absolute score of 3 in the Eyelash Assessment (ELA) among those with an abnormal baseline score The ELA is a 4-point scale where 0 = no eyelash hair, 1 = minimal eyelash hair, 2 = moderate eyelash hair, and 3 = normal eyelash hair
Risk of serious infections during 3 years of treatment	A serious infection means that you may have to stay in hospital for treatment of the infection and/or receive treatment through an injection. The serious infection may potentially be life-threatening. You may need to temporarily (until the infection has cleared) or permanently stop your treatment for alopecia areata. Examples of such infections may include lung infection, shingles, urinary tract infection etc.	-
Risk of cancer during 3 years of treatment	Cancer typically requires chemotherapy or surgery, and some cancers can be life-threatening. Some cancers can be treated or cured with treatment while others may not be treatable. You may need to temporarily or permanently stop your treatment for alopecia areata.	-
Risk of blood clots during 3 years of treatment	Blood clots require treatment with blood thinning medication, may require you to stay in hospital for treatment, and in some cases may potentially be life threatening. You may need to temporarily or permanently stop your treatment for alopecia areata.	-

DCE, discrete choice experiment.

- Preference estimates were used to calculate the maximum acceptable risk (MAR) that patients would accept for expected increases in benefit from choosing a higher dose of ritlecitinib over a lower dose
  - The MAR for a given 3-year risk is the percentage-point increase in that individual risk that will yield a utility loss that will exactly offset the utility gain from the increased benefit achieved by switching from ritlecitinib 30 mg QD to 50 mg QD, assuming that all other risks remain unchanged
- MARs were calculated separately for each risk and jointly for all possible combinations of risks
- Ritlecitinib efficacy benefits were calculated using clinical data from the ALLEGRO-2b/3 clinical trial[3]
  - The proportions of patients in the trial who received ritlecitinib 50 mg QD or 30 mg QD and achieved the endpoints listed in **Table 1** at Week 24 were calculated

RESULTS

- The preference survey was administered to adult patients (n=201) with physician confirmation of ≥50% scalp hair loss due to AA in the United States (n=62) and Europe (United Kingdom [n=22], France [n=3], Germany [n=30], Spain [n=25], Italy [n=59])
- The observed efficacy benefit of ritlecitinib 50 mg QD exceeded the efficacy benefit of 30 mg QD (**Table 2**)

Table 2. Ritlecitinib effects in ALLEGRO phase 2b/3 trial

Benefit	Ritlecitinib 50 mg QD	Ritlecitinib 30 mg QD
Response based on SALT score ≤20 at Week 24, n/N (%)	29/124 (23.4)	17/119 (14.3)
EBA response at Week 24, n/N (%)	29/100 (29.0)	17/102 (16.7)
ELA response at Week 24, n/N (%)	26/90 (28.9)	24/92 (26.1)

EBA, eyebrow assessment; ELA, eyelash assessment; QD, once daily; SALT, Severity of Alopecia Tool.

- In exchange for the expected benefits of increasing ritlecitinib dose from 30 mg QD to 50 mg QD, respondents were willing to accept statistically significant increases in risk (**Table 3**)

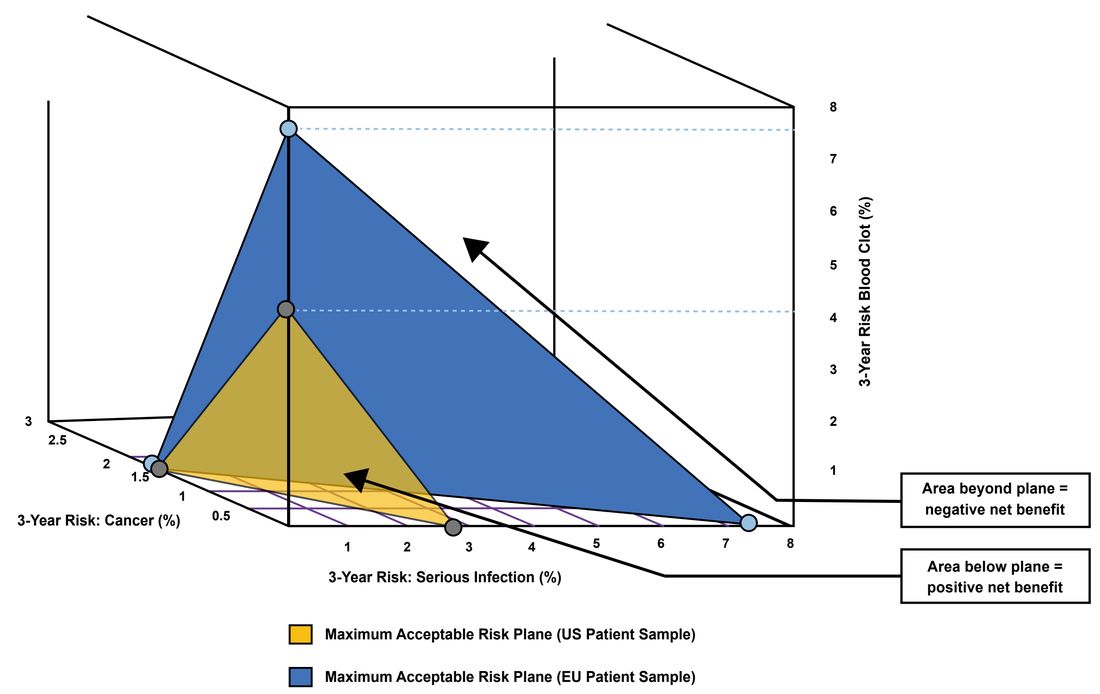
Table 3. MAR in exchange for the increase in efficacy benefit achieved by increasing ritlecitinib dose from 30 to 50 mg QD

3-Year Risk	Overall Sample MAR (95% CI)	US Sample MAR (95% CI)	EU Sample MAR (95% CI)
Serious infection	3.88 (3.04, 5.14)	2.80 (2.03, 3.95)	7.29 (4.89, 13.06)
Cancer	1.63 (1.23, 2.25)	1.60 (1.04, 2.77)	1.71 (1.28, 2.46)
Blood clot	5.30 (4.04, 7.52)	4.26 (2.97, 6.79)	7.61 (5.23, 13.87)

MAR, maximum acceptable risk; QD, once daily.

- On average, US patients appeared less tolerant of 3-year blood clot risks and 3-year serious infection risks than patients in the EU. Risk tolerance for the 3-year risk of cancer was similar between patients in the US and patients in the EU
- The combinations of these 3 risks (ie, a simultaneous increase in all 3 risks) that would be acceptable to patients in the EU and patients in the US are shown in **Figure 1**
  - Because the marginal disutility of each percentage-point increase in risk is constant in the model:
    - The marginal rate of substitution between two risks is constant and can be represented as a straight line
      - Example: for each 1-percentage-point reduction in the 3-year risk of blood clot, patients in the overall sample would be willing to accept a 0.73 percentage-point increase in the risk of serious infection
    - The plane representing all combinations of increases in the three risks that will exactly offset the benefit of 50 mg QD over 30 mg QD is a flat surface
      - Example: for each 1-percentage-point reduction in the 3-year risk of serious infection, patients in the overall sample would be willing to accept **both** a 0.21 percentage-point increase in the 3-year risk of cancer and a 0.68 percentage-point increase in the 3-year risk of blood clot
  - For both the EU sample and the less risk-tolerant US sample, tolerance of any combination of 3-year risks that patients would accept for the increase in benefit of ritlecitinib 50 mg QD over 30 mg QD is relatively high and expected to exceed the difference in these risks between the two doses. Therefore, the net benefit of the 50 mg QD dose is likely to exceed the net benefit of the 30 mg QD dose

Figure 1. Maximum acceptable combinations of 3 risks in exchange for the increase in efficacy benefits by switching from ritlecitinib 30 mg QD to 50 mg QD for US patients (yellow surface) and EU patients (blue surface)



CONCLUSIONS

- Ritlecitinib 50 mg QD and 30 mg QD have both been shown to be efficacious in treating patients with AA
- Adult patients with AA are willing to accept hypothetical increases in safety risks of serious infection, malignancy, and thromboembolism with a higher dose of ritlecitinib (50 mg QD over 30 mg QD) for increased probabilities of hair regrowth on the scalp, eyebrows, and eyelashes
- The absolute percent increase in risk that patients are willing to tolerate in exchange for the increase in benefit associated with increasing ritlecitinib dose from 30 mg QD to 50 mg QD is likely greater than any increase in actual risk between the two doses
- This study demonstrates the utility of patient preference data in informing optimal dose selection for an AA treatment

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DISCLOSURES

Brett Hauber, Jonathan Mauer, Ernest Law, Edward Whalen, Dalia Wajsbrot, Samuel Zwillich, and Robert Wolk are employees of and hold stock or stock options in Pfizer, Inc. Chiara Whichello, Myrto Trapali, and Nicolas Krucien are employees of Evidera which received funding from Pfizer to conduct this study. Tommi Tervonen was an employee of Evidera at the time of this study.

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