Title

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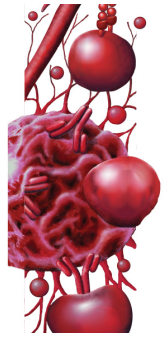

A plain language summary on ritlecitinib treatment for adults and adolescents with alopecia areata

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Summary

What is this summary about?

This is a summary of the results of the ALLEGRO phase 2b/3 clinical trial, originally published in *The Lancet*. ALLEGRO-2b/3 looked at how well and safely the study medicine, ritlecitinib, works in treating people with alopecia areata ('AA' for short).

The immune system protects your body from outside invaders such as bacteria and viruses. AA is an autoimmune disease, meaning a disease in which one's immune system attacks healthy cells of the body by mistake. In AA, the immune system attacks hair follicles, causing hair to fall out.

AA causes hair loss ranging from small bald patches to complete hair loss on the scalp, face, and/or body.

Ritlecitinib is a medicine taken as a pill every day, by mouth, that is approved for the treatment of severe AA. It blocks processes that are known to play a role in causing hair loss in patients with AA.

How to say (double click to play sound)...

- **Ritlecitinib:** rit-leh'-sih-tih-nib
- **Alopecia areata:** a-luh-pee-shuh eh-ree-ay-tuh

What were the results of the study?

Adults and adolescents (12 years and older) took part in the ALLEGRO-2b/3 study. They either took ritlecitinib for 48 weeks or took a placebo (a pill with no medicine) for 24 weeks. Participants taking placebo later switched to taking ritlecitinib for 24 weeks. The study showed that participants taking ritlecitinib had more hair regrowth on their scalp after 24 weeks than those taking the placebo. Hair regrowth was also seen on the eyebrows and eyelashes in participants taking ritlecitinib. Hair regrowth continued to improve to week 48 with continued ritlecitinib treatment. In addition, more participants taking ritlecitinib reported that their AA had 'moderately' or 'greatly' improved after 24 weeks than those taking the placebo. Similar numbers of participants taking ritlecitinib or placebo had side effects after 24 weeks. Most side effects were mild or moderate.

What do the results of the study mean?

Ritlecitinib was an effective and well-tolerated treatment over 48 weeks for people with AA.

Where can I find the original article on which this summary is based?

You can read the original article published in *The Lancet*: https://doi.org/10.1016/S0140-6736(23)00222-2

Who sponsored this study?

The study and this summary were funded by Pfizer Inc.

Future Medicine part of fsg

Who is this article for?

This summary is by the authors of the original article to help patients with alopecia areata, caregivers, patient advocates, and healthcare professionals understand the results of the ALLEGRO-2b/3 clinical trial.

What is alopecia areata?

- Alopecia areata ('AA' for short) is an autoimmune disease in which a person experiences hair loss ranging from small patches of hair loss to complete scalp, face, and/or body hair loss
- AA can affect adults and children of all ages, races, and sexes
- AA affects about 2% of people (2 in every 100 people) around the world
- Hair loss due to AA can have a large impact on quality of life, including an emotional burden

What is ritlecitinib?

- Ritlecitinib is a medicine that blocks processes that are known to play a role in causing hair loss in people with AA. Ritlecitinib is taken every day by mouth in the form of a tablet (pill)
- Ritlecitinib is approved in the United States and Japan for the treatment of severe AA

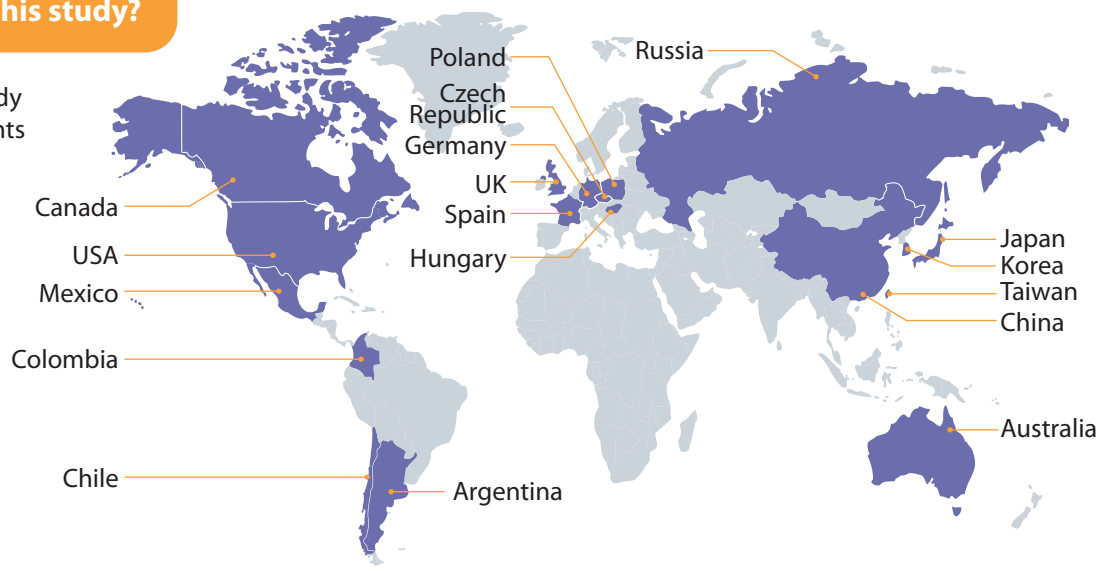
What was the study designed to look at?

The ALLEGRO-2b/3 clinical study was designed to look at how well and how safely different doses of ritlecitinib work in people with AA.
Specifically, the researchers wanted to know:

? Does ritlecitinib treatment cause hair to regrow in people with AA?

Who took part in this study?

The ALLEGRO-2b/3 study included 718 participants from 18 countries.



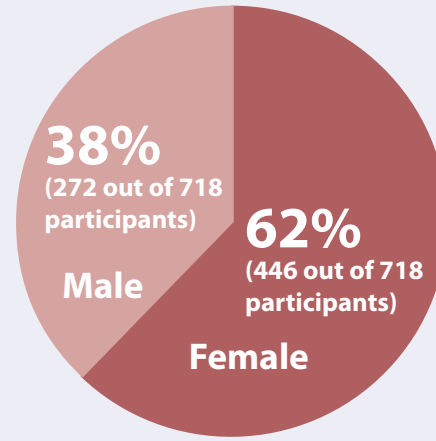
Participants who took part in the study:

- ✓ Were 12 years of age or older
- ✓ Had at least 50% (half) of their scalp hair lost due to AA
- ✓ Did not see any hair regrowth for at least the past 6 months

Patients with AA could not take part in the study if they:

- ✕ Had other causes of hair loss not due to AA
- ✕ Had a history of certain infections or cancers

Sex



Age

85% Ages 18+
(613 out of 718 participants)

15% Ages 12–17
(105 out of 718 participants)

Race

68% White
(488 out of 718 participants)

4% Black or African American
(27 out of 718 participants)

26% Asian
(186 out of 718 participants)

2% Other or not reported
(17 out of 718 participants)

Time with disease

Average time since alopecia areata diagnosis:
10 years

Currently experiencing hair loss for an average of:
3 years

Location of hair loss

83% (596 out of 718 participants)
Had hair loss on the eyebrows

74% (533 out of 718 participants)
Had hair loss on the eyelashes

46% (330 out of 718 participants)
Had no scalp hair (alopecia totalis) or no scalp, face, and body hair (alopecia universalis)

54% (388 out of 718 participants)
Had some scalp hair

How was the study carried out?

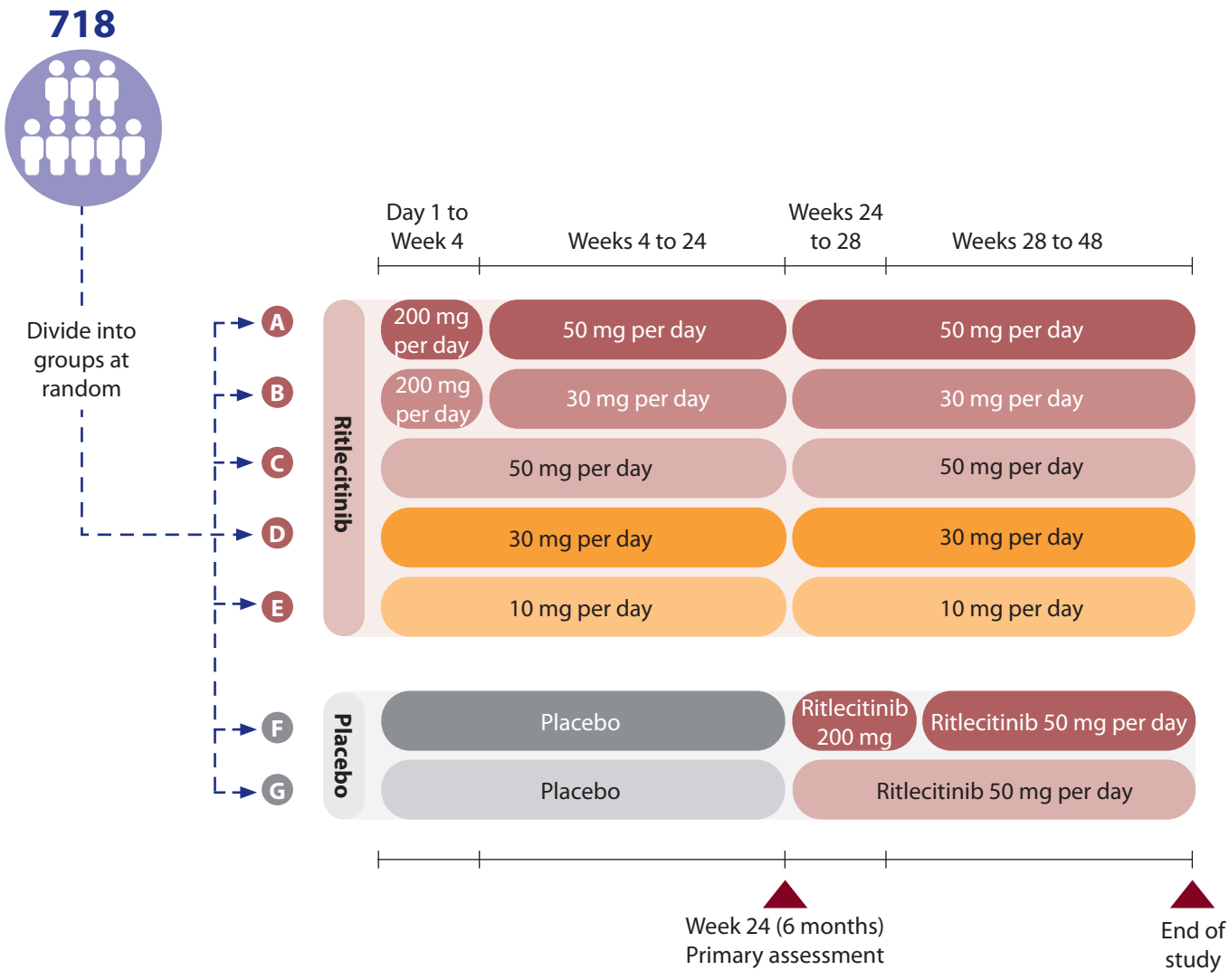
ALLEGRO-2b/3 was a **phase 2b/3, randomized**, **double-blind**, **placebo-controlled** trial.

Phase 2b/3: As a Phase 2b/3 trial, the current clinical trial looked at different doses of ritlecitinib in a large group of patients. A previous Phase 2a clinical trial in a smaller number of patients with AA had also studied the effectiveness of ritlecitinib at regrowing hair and its safety.

Randomized: Participants were randomly assigned to one of seven treatment groups.

Double-blind: Neither the participants nor the study researchers knew which treatment or dose a participant was taking.

Placebo-controlled: Some participants took a placebo. This pill looked like the study treatment (ritlecitinib) but did not have any medication in it.



How was the effect of ritlecitinib measured?

The effect of ritlecitinib on the amount of hair loss was measured on the scalp:

- The Severity of Alopecia Tool (SALT) is a scale used by doctors to measure the amount of scalp hair loss. SALT scores range from 0 (no hair loss on the scalp) to 100 (total loss of scalp hair)
- Doctors looked at how many participants achieved 20% or less scalp hair loss (SALT score of 20 or less), meaning that 80% or more of the scalp had hair
- Doctors looked at how many participants achieved 10% or less scalp hair loss (SALT score of 10 or less), meaning that 90% or more of the scalp had hair

The effect of ritlecitinib on the amount of eyebrow and eyelash hair loss was also measured:

- The eyebrow assessment (EBA) is a scale used by doctors to measure the amount of eyebrow hair loss. EBA scores range from 0 (no eyebrow hair) to 3 (normal eyebrow hair)
- The eyelash assessment (ELA) is a scale used by doctors to measure the amount of eyelash hair loss. ELA scores range from 0 (no eyelash hair) to 3 (normal eyelash hair)
- Doctors looked at how many participants achieved regrowth of eyebrow and eyelash hair, defined as 2-point improvement in EBA or ELA score or EBA or ELA score of 3 (normal)

Participants answered a questionnaire that asked about their AA since the start of the study.
The options to choose from were:

Greatly improved **Moderately improved**

Slightly improved **Not changed** **Slightly worsened**

Moderately worsened **Greatly worsened**

The researchers looked at how many participants reported that their disease had 'moderately' or 'greatly' improved from the start of the study.

What were the overall results of the ALLEGRO-2b/3 study?

1 How well did ritlecitinib work in treating scalp hair loss?

The percentages of participants who achieved 20% or less scalp hair loss (SALT score of 20 or less), meaning 80% of the scalp had hair, by week 24 were:

Participants with SALT score of 20 or less at week 24

Group A: ritecitinib 200/50 mg

Group B: ritecitinib 200/30 mg

Group C: ritecitinib 50 mg

Group D: ritecitinib 30 mg

Group E: ritecitinib 10 mg

Groups F & G combined: placebo

These percentages increased for the next 24 weeks (to week 48) in participants continuing or switching to ritlecitinib:

Participants with SALT score of 20 or less at week 48

Group A: ritecitinib 200/50 mg

Group B: ritecitinib 200/30 mg

Group C: ritecitinib 50 mg

Group D: ritecitinib 30 mg

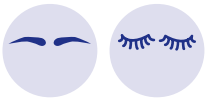
Group E: ritecitinib 10 mg

Group F: placebo switch to ritecitinib 200/50 mg

Group G: placebo switch to ritecitinib 50 mg

By week 24, the percentages of participants who achieved 10% or less scalp hair loss (SALT score of 10 or less), meaning that 90% or more of the scalp had hair, were also higher in those taking ritlecitinib than those taking placebo. These percentages also continued to increase for the next 24 (to week 48) weeks in participants taking ritlecitinib.

2 How well did ritlecitinib work in treating hair loss of the eyebrows and/or eyelashes?



The number of participants who achieved regrowth of eyebrow and eyelash hair increased over 48 weeks in the ritlecitinib 200/50 mg, 200/30 mg, 50 mg, or 30 mg groups (groups A, B, C, and D).

3 Did participants report that their AA had improved?

The percentages of participants who said that their disease had moderately or greatly improved at week 24 were:

Participants with moderate or great improvement at week 24

Group A: ritecitinib 200/50 mg

Group B: ritecitinib 200/30 mg

Group C: ritecitinib 50 mg

Group D: ritecitinib 30 mg

Group E: ritecitinib 10 mg

Groups F & G combined: placebo

These percentages increased for the next 24 weeks (to week 48) in participants continuing or switching to ritlecitinib:

Participants with moderate or great improvement at week 48

Group A: ritecitinib 200/50 mg

Group B: ritecitinib 200/30 mg

Group C: ritecitinib 50 mg

Group D: ritecitinib 30 mg

Group E: ritecitinib 10 mg

Group F: placebo switch to ritecitinib 200/50 mg

Group G: placebo switch to ritecitinib 50 mg

What side effects were seen?

- Medical problems that happen during the study are called adverse events
- Adverse events may or may not be caused by the treatment in the study

The percentages of participants with adverse events in each treatment group during the first 24 weeks of the study are shown in the table below:

Ritlecitinib dose	Ritlecitinib for 24 weeks					Placebo for 24 weeks
	200/50 mg	200/30 mg	50 mg	30 mg	10 mg	
Group	A	B	C	D	E	F & G combined
Number of participants	131	129	130	132	62	131
Any adverse event	73% (96 out of 131 participants)	71% (91 out of 129 participants)	75% (98 out of 130 participants)	73% (96 out of 132 participants)	69% (43 out of 62 participants)	71% (93 out of 131 participants)
Upper respiratory tract infection	12% (16 out of 131 participants)	8% (10 out of 129 participants)	6% (8 out of 130 participants)	8% (11 out of 132 participants)	3% (2 out of 62 participants)	8% (10 out of 131 participants)
Common cold (naso-pharyngitis)	11% (15 out of 131 participants)	14% (18 out of 129 participants)	10% (13 out of 130 participants)	12% (16 out of 132 participants)	10% (6 out of 62 participants)	6% (8 out of 131 participants)
Headache	8% (11 out of 131 participants)	8% (10 out of 129 participants)	9% (12 out of 130 participants)	15% (20 out of 132 participants)	18% (11 out of 62 participants)	8% (11 out of 131 participants)

During the entire 48 weeks of the study, the most common adverse events were:

Headache

Common cold (nasopharyngitis)

Nausea (feel like throwing up)

Upper respiratory tract infection

Acne (pimples)

The percentages of participants with these adverse events in each treatment group are shown in the next table:

	Ritlecitinib for 48 weeks					Placebo for 24 weeks, then switch to ritlecitinib for 24 weeks	
Ritlecitinib dose	**200/50 mg**	**200/30 mg**	**50 mg**	**30 mg**	**10 mg**	**200/50 mg**	**50 mg**
Group	A	B	C	D	E	F	G
Number of participants	131	129	130	132	62	65	66
Headache	13% (17 out of 131 participants)	11% (14 out of 129 participants)	12% (16 out of 130 participants)	18% (24 out of 132 participants)	19% (12 out of 62 participants)	12% (8 out of 65 participants)	12% (8 out of 66 participants)
Common cold (naso-pharyngitis)	15% (19 out of 131 participants)	16% (21 out of 129 participants)	14% (18 out of 130 participants)	16% (21 out of 132 participants)	11% (7 out of 62 participants)	11% (7 out of 65 participants)	6% (4 out of 66 participants)
Upper respiratory tract infection	14% (18 out of 131 participants)	9% (12 out of 129 participants)	8% (11 out of 130 participants)	12% (16 out of 132 participants)	3% (2 out of 62 participants)	11% (7 out of 65 participants)	9% (6 out of 66 participants)
Nausea	8% (11 out of 131 participants)	2% (3 out of 129 participants)	2% (3 out of 130 participants)	9% (12 out of 132 participants)	5% (3 out of 62 participants)	12% (8 out of 65 participants)	2% (1 out of 66 participant)
Acne	5% (6 out of 131 participants)	8% (10 out of 129 participants)	9% (12 out of 130 participants)	9% (12 out of 132 participants)	5% (3 out of 62 participants)	8% (5 out of 65 participants)	12% (8 out of 66 participants)

Were there any serious adverse events?

Adverse events are considered serious when they are life threatening, need hospital care, or cause lasting problems. They may or may not have been caused by the study treatment.

14 out of 715 participants (2%) had serious adverse events during the 48 weeks of the study.

- In the ritlecitinib 200/50 mg group, 4 out of 131 participants (3%) experienced a serious adverse event:
  - Inflammation of the appendix (appendicitis)
  - Infection of the lung tissue (empyema) and overactive toxic response to an infection (sepsis)
  - Breast cancer
  - Miscarriage

- In the ritlecitinib 200/30 mg group, 2 out of 129 participants (2%) experienced:
  - Inflammation of the appendix (appendicitis)
  - Chemical poisoning and suicidal behavior

- In the ritlecitinib 50 mg group, 2 out of 130 participants (2%) experienced:
  - Breast cancer
  - Blockage in an artery in the lungs (pulmonary embolism)

- In the ritlecitinib 30 mg group, 1 out of 132 participants (1%) experienced:
  - Infection or inflammation of pouches that form in the intestines (diverticulitis)

- In the ritlecitinib 10 mg group, 2 out of 62 participants (3%) experienced:
  - Suicidal behavior
  - Inflammatory condition of the skin (eczema)

- 3 out of 131 participants (2%) taking placebo (during the first 24 weeks of the study) experienced:
  - Miscarriage
  - A condition in which a person experiences blindness, paralysis, or other nervous system (neurologic) symptoms that cannot be explained by illness of injury (conversion disorder)
  - Heavy period

No participants died during the study.

What do the results of this study mean?

- This study included participants aged 12 years and older with AA and at least half of their scalp hair lost. 330 out of 715 participants (46%) had total loss of scalp hair at the start of the study
- By week 24, participants taking ritlecitinib 200/50 mg, 200/30 mg, 50 mg, or 30 mg were more likely to have at least 80% or 90% of their scalp covered with hair than participants taking the placebo
- By week 24, participants taking ritlecitinib 200/50 mg, 200/30 mg, 50 mg, or 30 mg were more likely to report moderate or great improvement in their AA since the beginning of the study than participants taking the placebo
- The numbers of participants taking ritlecitinib who had hair regrowth on the scalp, eyebrows, and eyelashes continued to increase over the 48 weeks of the study
- During the entire 48 weeks of the study, serious side effects occurred in 2% of participants
- The most common side effects were nasopharyngitis (common cold), upper respiratory tract infection, nausea, and acne
- Ritlecitinib was an effective and well-tolerated treatment over 48 weeks for people with AA
- After completing the trial, patients could enter the ongoing open-label ALLEGRO-LT trial in which they received ritlecitinib 50 mg once daily

The results of this study may differ from those of other studies. Researchers should make treatment decisions based on all available evidence and not just on the results of a single study.

Where can readers find more information on this study?

Original article
The original article "Efficacy and safety of ritlecitinib in adults and adolescents with alopecia areata: a randomized, double-blind, multicentre phase 2b/3 trial" was published in *The Lancet* in April 2023 and can be found here: https://doi.org/10.1016/S0140-6736(23)00222-2

Trial registration site
You can read more about the phase 2b/3 ALLEGRO study at the following study registration website:
https://clinicaltrials.gov/ct2/show/NCT03732807

For more information on clinical studies in general, please visit:
https://www.clinicaltrials.gov/ct2/about-studies/learn

Educational resources
For more information about alopecia areata, please visit: https://www.understandalopeciaareata.com/

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Financial & competing interests disclosure

A full list of disclosures of the authors can be found in the original article.