

JAK inhibitors for Alopecia Areata

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Disclosures

I have received honoraria and/or consulting fees from:

Abbvie, AltruBio Inc, Amirall, AnaptysBio, Arena Pharmaceuticals, Aslan Pharmaceuticals, Bristol Meyers Squibb, Concert Pharmaceuticals Inc, Equillium, Horizon Therapeutics, Eli Lilly and Company, Incyte Corp, Janssen Pharmaceuticals, LEO Pharma, Merck, Otsuka/Visterra Inc, Pfizer Inc, Q32 Bio Inc, Regeneron, Sanofi Genzyme, Sun Pharmaceutical, TWi Biotechnology Inc, and Ventyx Biosciences Inc.

I am or have been a clinical trial investigator for:

AnaptysBio, Arena Pharmaceuticals, Aslan Pharma, Bristol Meyers Squibb, Concert Pharmaceuticals Inc, Eli Lilly and Company, NIH, Pfizer Inc

I have been on speaker bureaus for:

Abbvie, Incyte, Eli Lilly, Pfizer, Regeneron, Sanofi Genzyme

Results of JAK Inhibitor Treatment of AA

Before and After Treatment With JAK Inhibitor



Photos courtesy of Brett King, MD, PhD.

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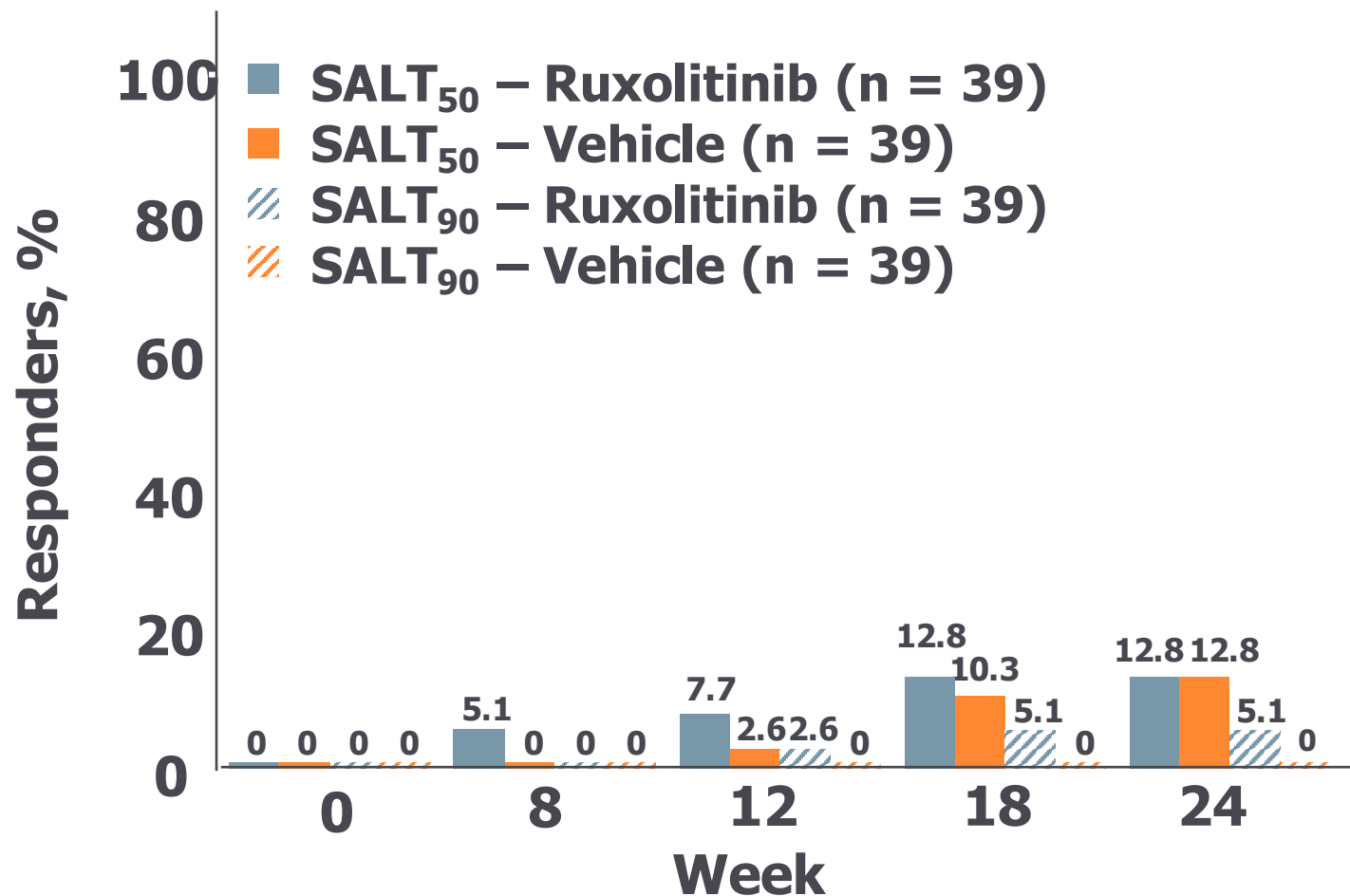
Randomized Controlled Trials of JAK Inhibitors for AA

Randomized Controlled Trials of JAK Inhibitors for AA

- Topical ruxolitinib 1.5% cream^[a]
- Topical delgocitinib ointment^[f]
- Ritlecitinib^[b]
- Baricitinib^[c,d]
- Deuruxolitinib (CTP-543)^[e]

a. Olsen EA, et al. J Am Acad Dermatol. 2020;82:412-419; b. ClinicalTrials.gov. Accessed April 12, 2022. <https://clinicaltrials.gov/ct2/show/NCT03732807>;
c. ClinicalTrials.gov. Accessed April 12, 2022. <https://clinicaltrials.gov/ct2/show/NCT03570749>; d. King B, et al. J Am Acad Dermatol. 2021;85:847-853; e.
ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT04518995>; f. Mikhaylov D, et al. Arch Dermatol Res. 2022 [Epub ahead of print]

Ruxolitinib 1.5% Cream: Phase 2 Data



Ruxolitinib 1.5% cream was ineffective for the treatment of AA

- Delgocitinib ointment was ineffective in a RCT
- Tofacitinib ointment was ineffective in an open-label trial
- **Topical JAK inhibitors are ineffective for treatment of AA**

* SALT50 = 50% improvement from baseline SALT score; SALT90 = 90% improvement from baseline SALT score; RCT = randomized controlled trial
Olsen EA, et al. J Am Acad Dermatol. 2020;82:412-419.

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Baricitinib: Phase 3 Data in Adults

FDA NEWS RELEASE

FDA Approves First Systemic Treatment for Alopecia Areata



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For Immediate Release: June 13, 2022

Baricitinib is a prescription medication that is a Janus kinase (JAK) inhibitor, and is used to treat **adults** with severe alopecia areata.

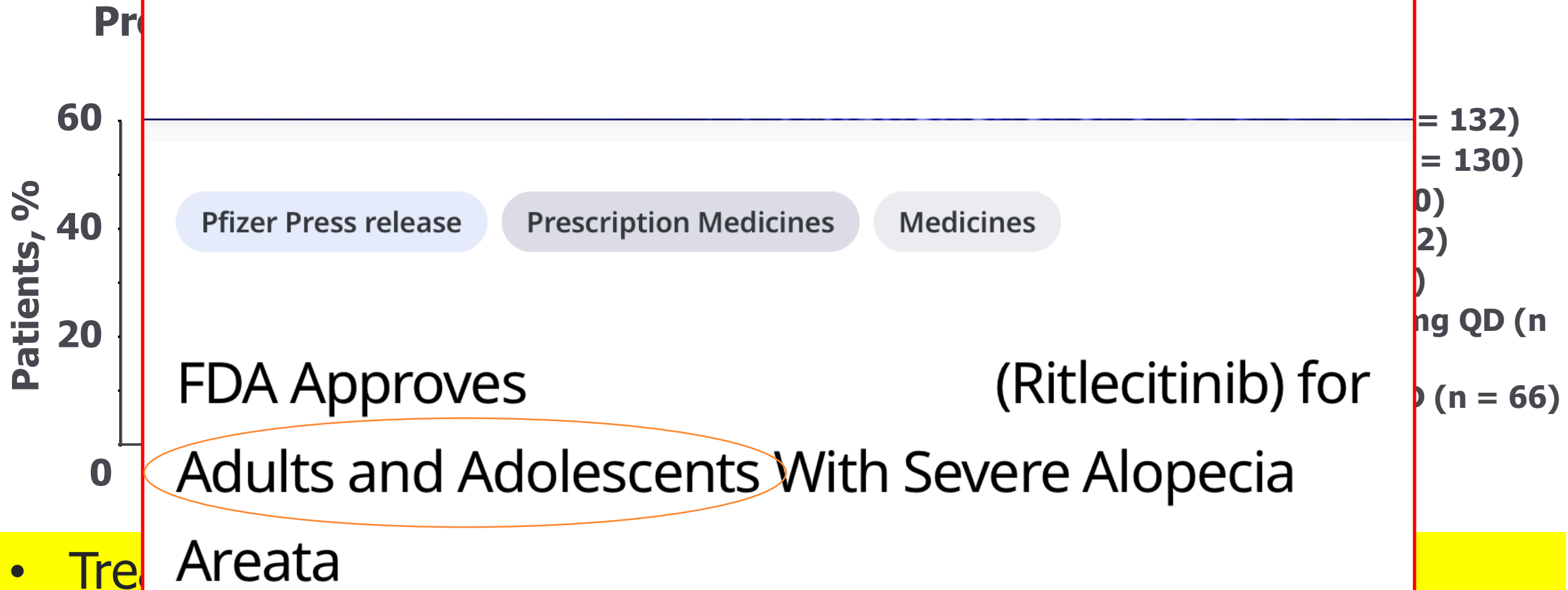
^aCIs are constructed using the wilson method, without continuity correction.

BARI = baricitinib; CI = confidence interval; PBO = placebo; SALT = Severity of Alopecia Tool.

Kwon O, et al. Presented at: AAD Annual Meeting; March 25-29, 2022; Boston, MA. Late-breaking abstract SO26.

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Ritlecitinib: Phase 3 Data in Adolescents and Adults



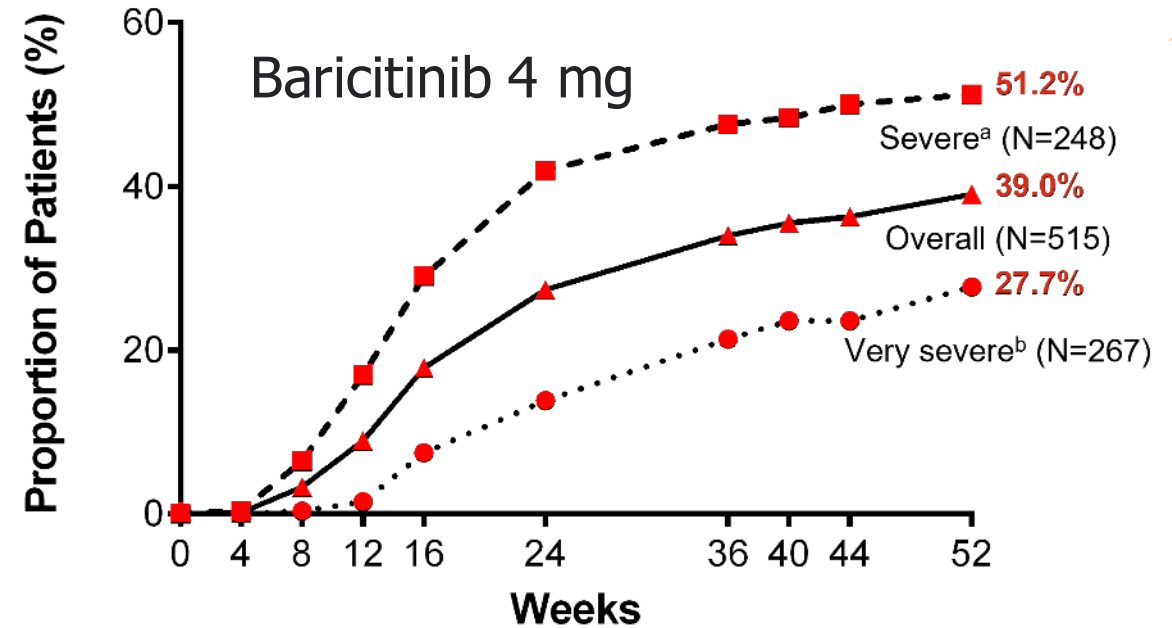
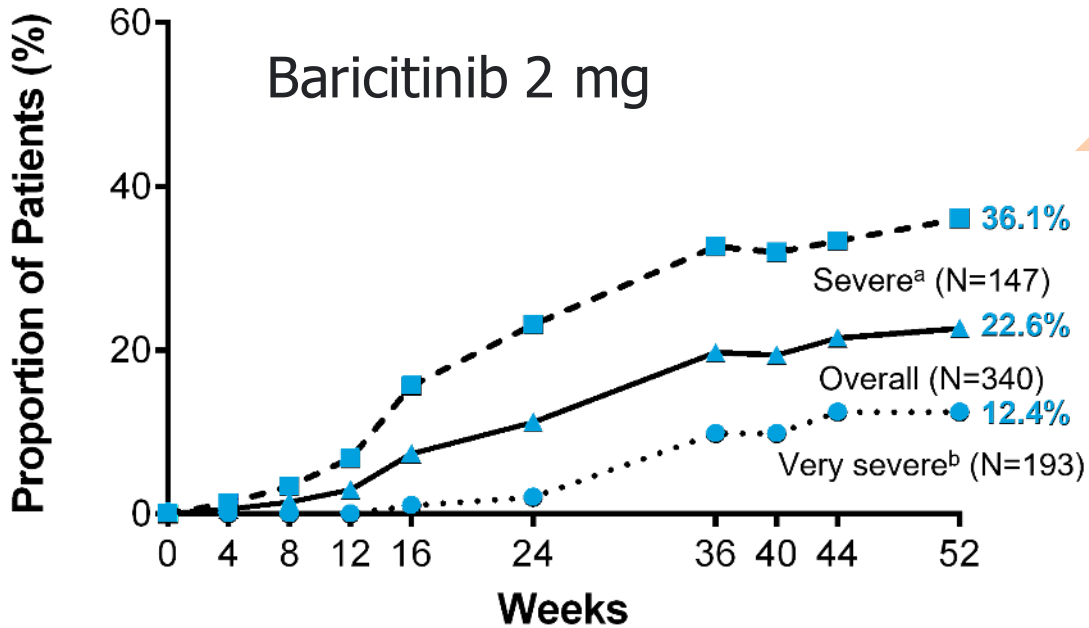
*Statistically significant
King B, et al. Pres

Optimizing Treatment with JAK Inhibitors

Factors That Increase Treatment Effectiveness: Having Hair at The Start of Treatment

Treatment response increases when there is hair present at the time of treatment initiation

Proportion of patients achieving SALT Score ≤ 20

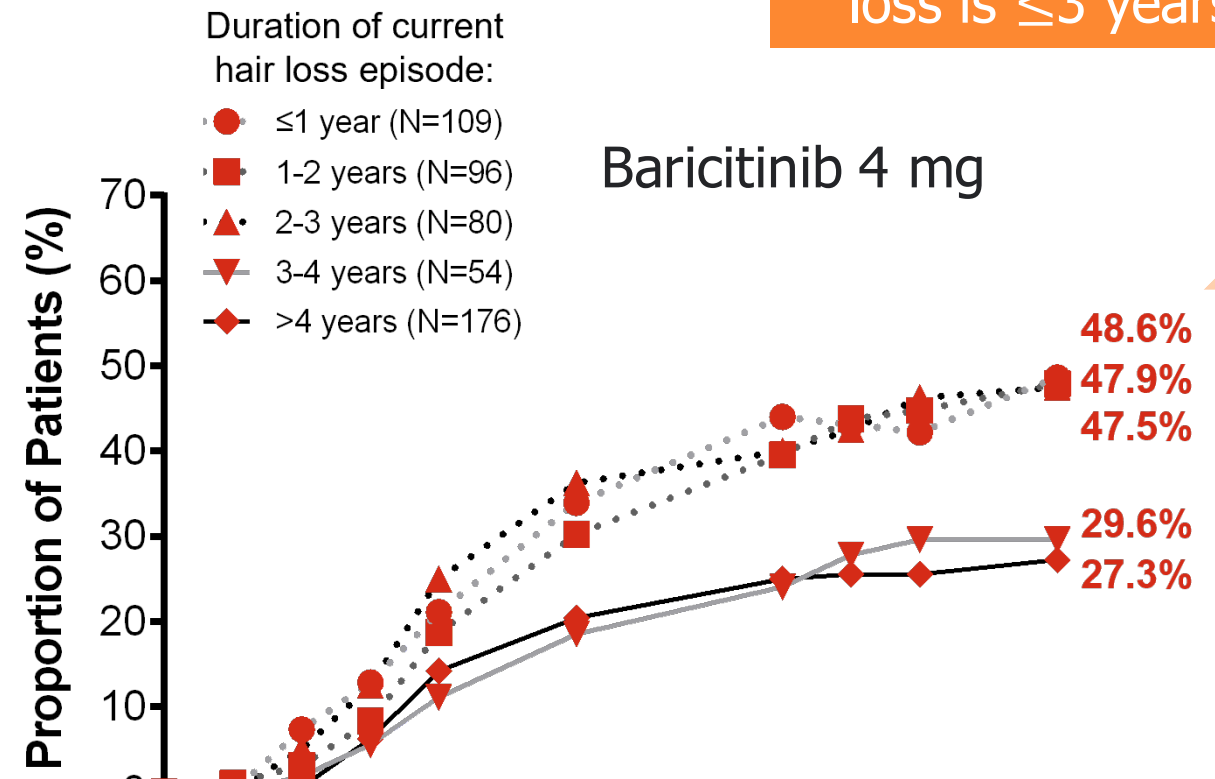
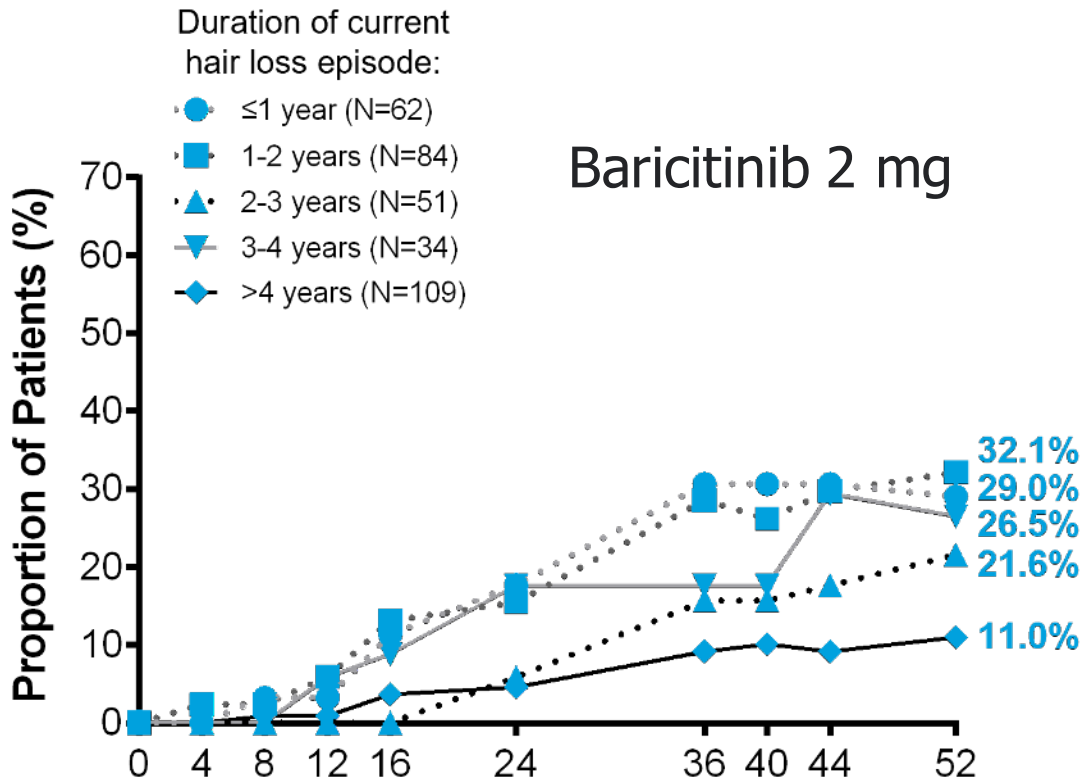


- Treatment is more effective in patients before total scalp hair loss occurs
- Initiate treatment with the higher dose of Olumiant (4 mg) when there is very severe scalp hair loss

Factors That Increase Treatment Effectiveness: Duration of Current Episode of Severe Scalp Hair Loss

Treatment response increases when current episode of severe scalp hair loss is ≤ 3 years

Proportion of patients achieving SALT Score ≤ 20

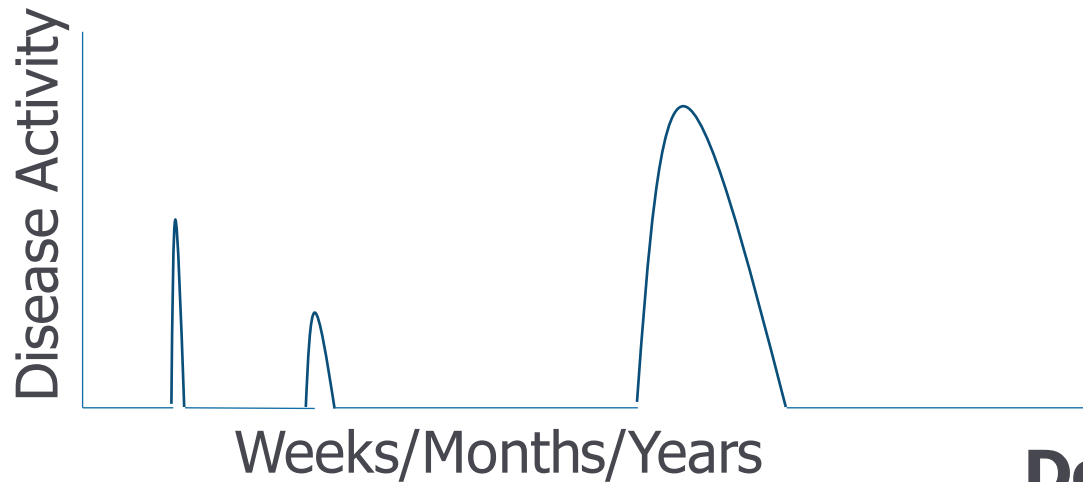


- Treatment is more effective when initiated early in severe scalp hair loss episode

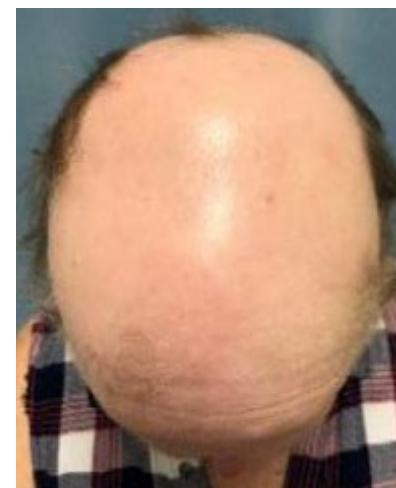
“What happens if I do nothing? Will my hair grow back on its own?”

The Natural History of Alopecia Areata

AA is said to wax and wane, with *unpredictable* periods of relapse and remission

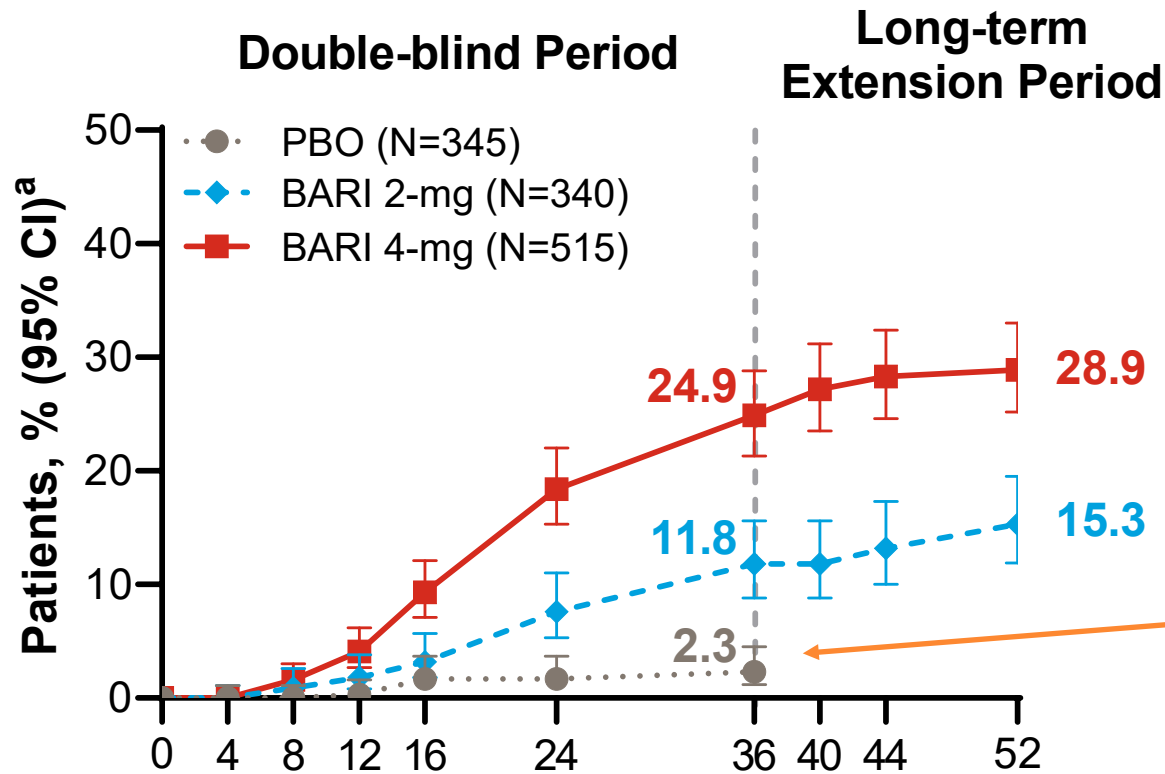


Does severe AA wax and wane?



What is the Rate of Spontaneous Remission of Severe AA?

Proportion of patients achieving SALT score ≤ 10



2.3% of patients with severe AA experience spontaneous remission over 36 weeks

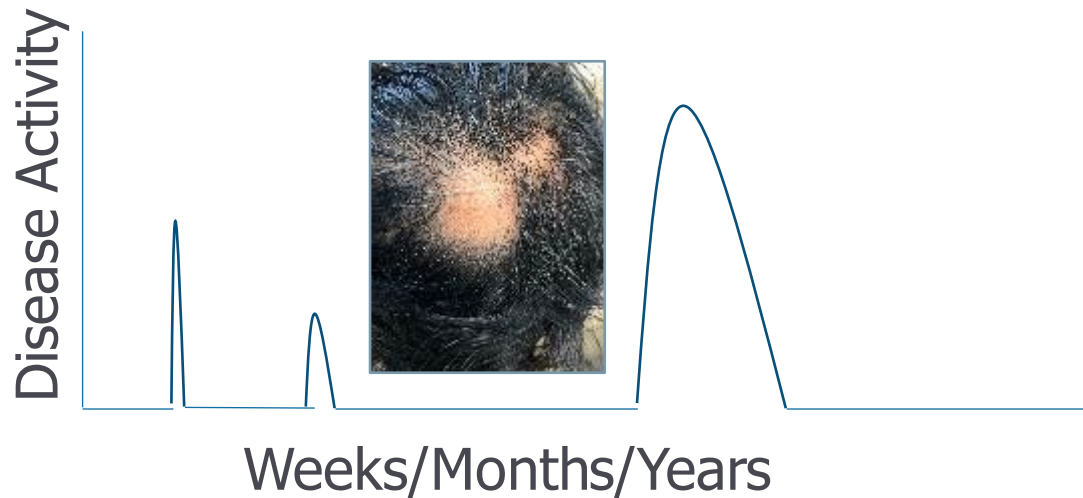
- Spontaneous remission is rare with severe AA

BARI = baricitinib; CI = confidence interval; PBO = placebo; SALT = Severity of Alopecia Tool.

Kwon O, et al. Presented at: AAD Annual Meeting; March 25-29, 2022; Boston, MA. Late-breaking abstract SO26.

The Natural History of Alopecia Areata

In cases of *limited hair loss*, spontaneous remission is not uncommon, though many patients will have **unpredictable**, relapsing and remitting disease



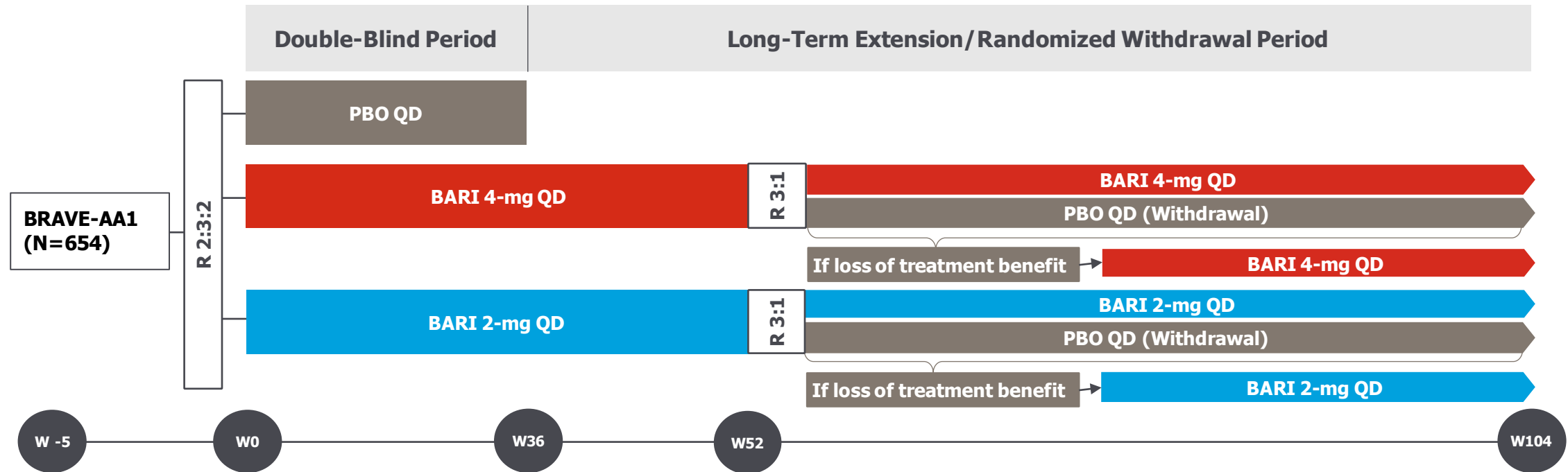
In cases of *moderate to severe hair loss*, hair loss is **chronic** and **spontaneous remission is extremely unlikely**



When can Treatment be Stopped in Severe AA Patients?

What Happens When Baricitinib is Stopped?

Study Design: BRAVE-AA1

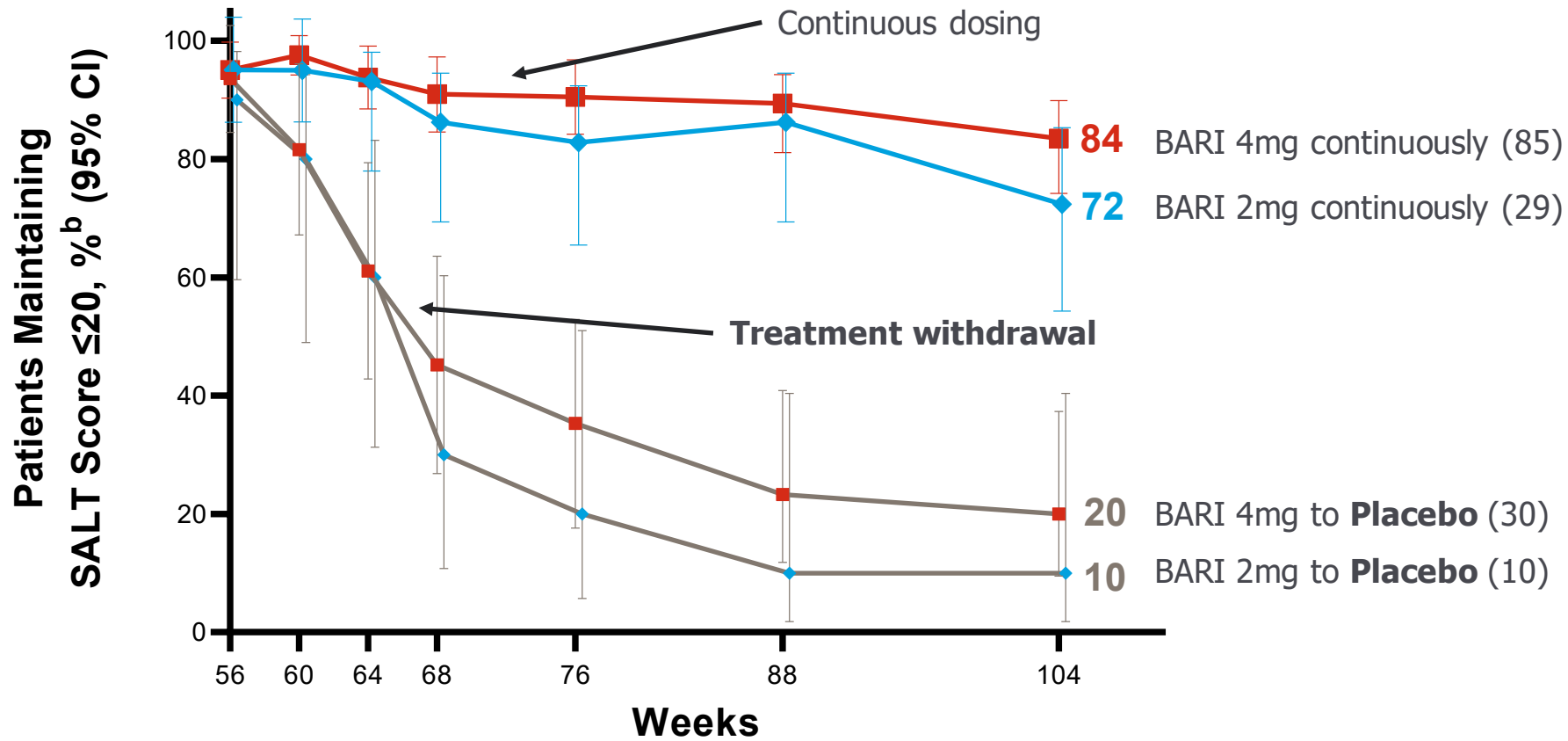


BARI = baricitinib
King B, et al. World Congress of Dermatology 2023, P2430. Sponsored by Eli Lilly and Company

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What Happens When Baricitinib is Stopped?

Proportion of patients achieving SALT Score ≤ 20

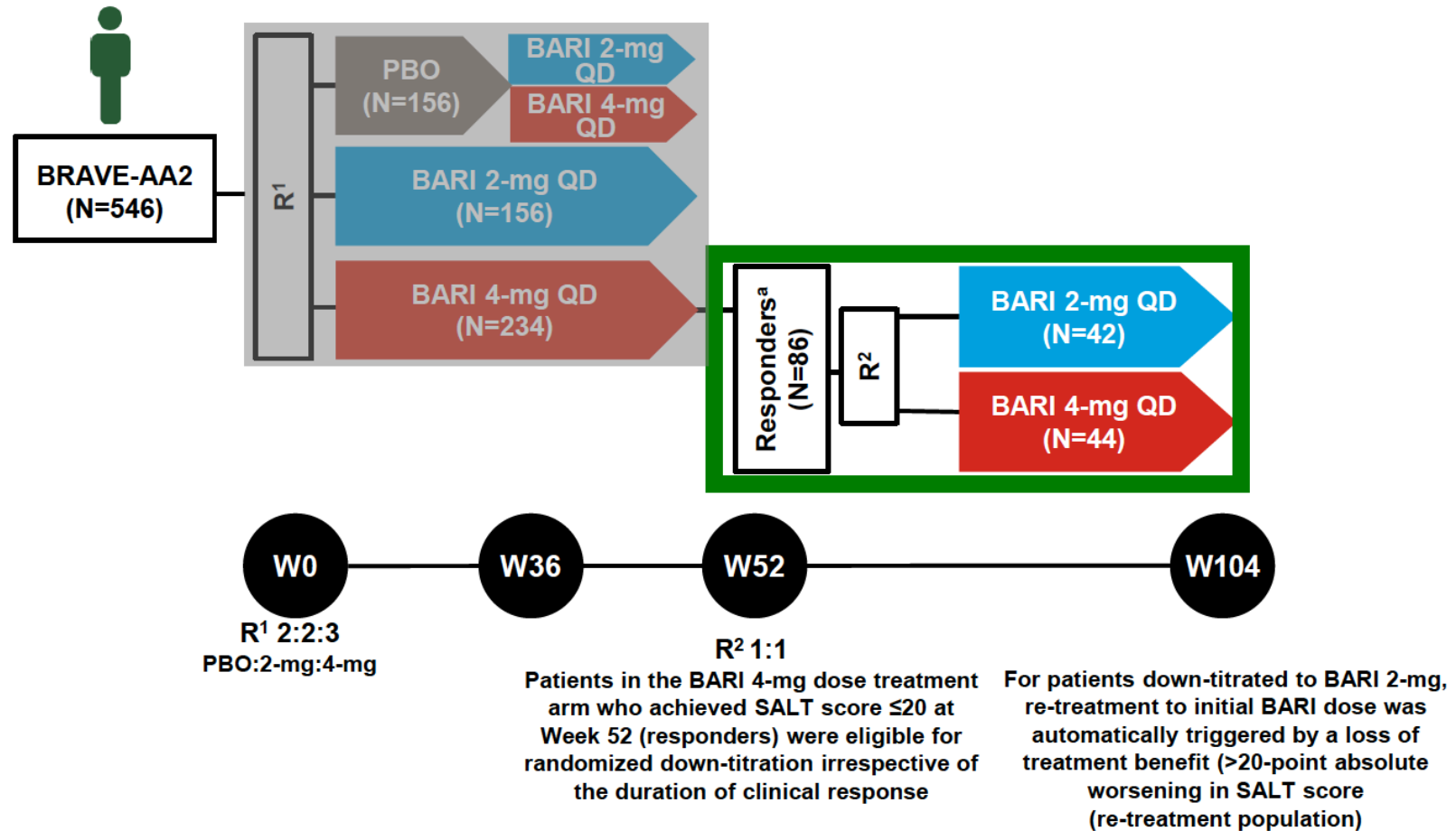


- Stopping treatment will lead to disease flare in the vast majority of patients
- Disease flare occurs *weeks to months* after stopping treatment and can be *fast and extreme*
- Regrowth of hair after resuming treatment takes months and *may not happen at all*

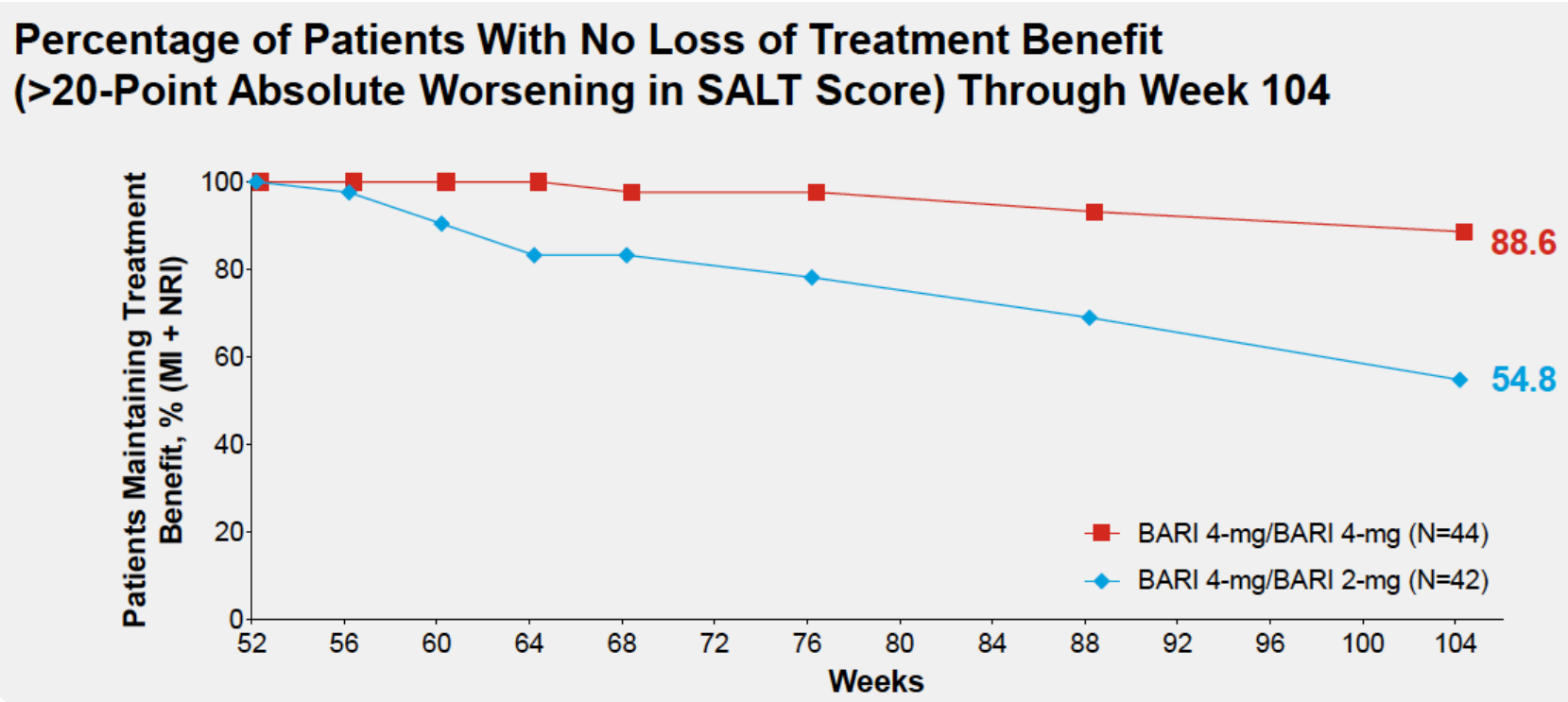
Tapering the Dose of JAK Inhibitor

Tapering the Dose of Baricitinib

Study Design: BRAVE-AA2 Down-Titration Arm



What Happens When Baricitinib is Tapered From 4mg to 2mg **ABRUPTLY**?



- **ABRUPT BIG DOSE DECREASES** will lead to disease flare in many patients
- Disease flare occurs *weeks to months* after **ABRUPT BIG DOSE DECREASES** and can be *fast and extreme*
- Regrowth of hair after resuming prior dose of JAK inhibitor takes months

Managing JAK Inhibitor Treatment Long-Term

What to do With JAK Inhibitor Treatment After Hair Regrowth?

- **After regrowth, continue the dose that the patient is taking...**

YOU DO NOT HAVE TO TAPER!

- **After regrowth, if you decide to taper the dose of JAK inhibitor...**

Make **SMALL CHANGES/DECREASES IN THE DOSE and continue the smaller dose for at least 4 months before considering another small dose decrease**

Conclusions

- AA is an autoimmune disease with a genetic predisposition
- There is no data to support use of topical JAK inhibitors for AA
- The oral JAK inhibitor baricitinib has been approved for adults with severe AA
- The oral JAK inhibitor ritlecitinib has been approved for adults and adolescents with severe AA
- Treatment is more effective before there is very severe scalp hair loss
- Treatment response decreases as the duration of current episode of severe AA increases
- Spontaneous remission is rare for people with severe AA and *stopping* treatment leads to disease flare in the vast majority of patients
- When decreasing the dose of JAK inhibitor, *taper the dose gradually* over many months