Kyowa Kirin Co., Ltd.

Rocatinlimab Update Phase 3 Study: ROCKET ASCEND Topline Data

September 9, 2025

Event Summary

[Event Name]	Rocatinlimab Update Phase 3 Study: ROCKET ASCEND Topline Data	
[Date]	September 9, 2025	
[Number of Speakers]	2	
	Abdul Mullick	Representative Director, President & Chief Operating Officer
	Takeyoshi Yamashita	Director, Executive Vice President and Chief Medical Officer

Presentation

Moderator: Thank you for joining us today for an online briefing on the interim analysis top-line data from the ASCEND study, an international Phase 3 Study ROCKET program of Rocatinlimab in adult patients with moderate to severe atopic dermatitis, which was released today at 8:30 AM.

Please note the following prior to the briefing. We will keep the names and company names of all participants for a certain period of time as a list of participants. Please understand this in advance.

Please note that the content of this presentation will be available on-demand and as a transcript on our website, so please be aware of this before speaking.

The information presented today contains forward-looking statements. Please note that there is uncertainty due to various risks.

Today's speakers and Q&A session will be Abdul Mullick, President and COO, and Takemi Yamashita, Executive Vice President and CMO.

Today's online meeting is scheduled for a maximum of 60 minutes. First, we will give you an overview and then take your questions. Please download the documents from our IR website.

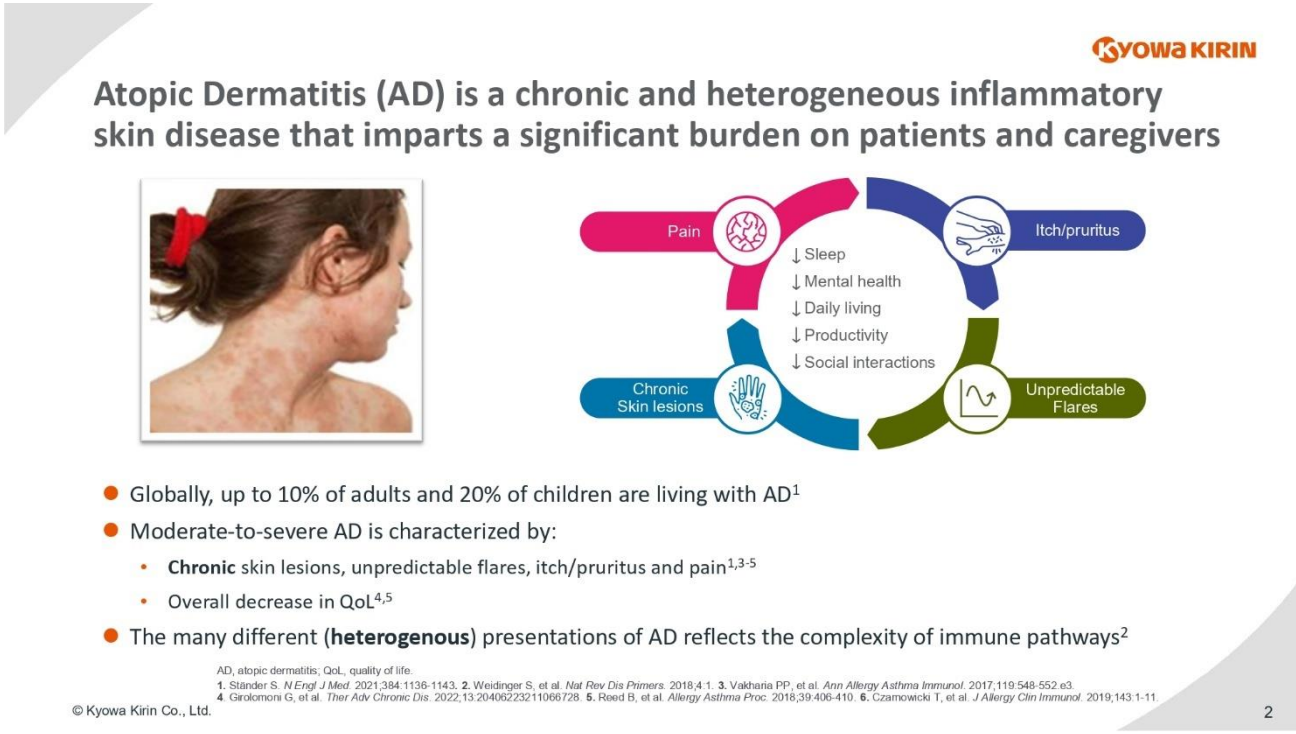
Let us begin with an overview. Abdul, thank you very much for your time.

Mullick*: Good morning, everyone. I am Mullick, President COO of Kyowa Kirin. I am very pleased to be here today with Chief Medical Officer Yamashita.

Today, I am very proud to present the interim analysis top-line data from the ASCEND study, an international Phase 3 Study ROCKET program of Rocatinlimab in adults with moderate to severe atopic dermatitis.

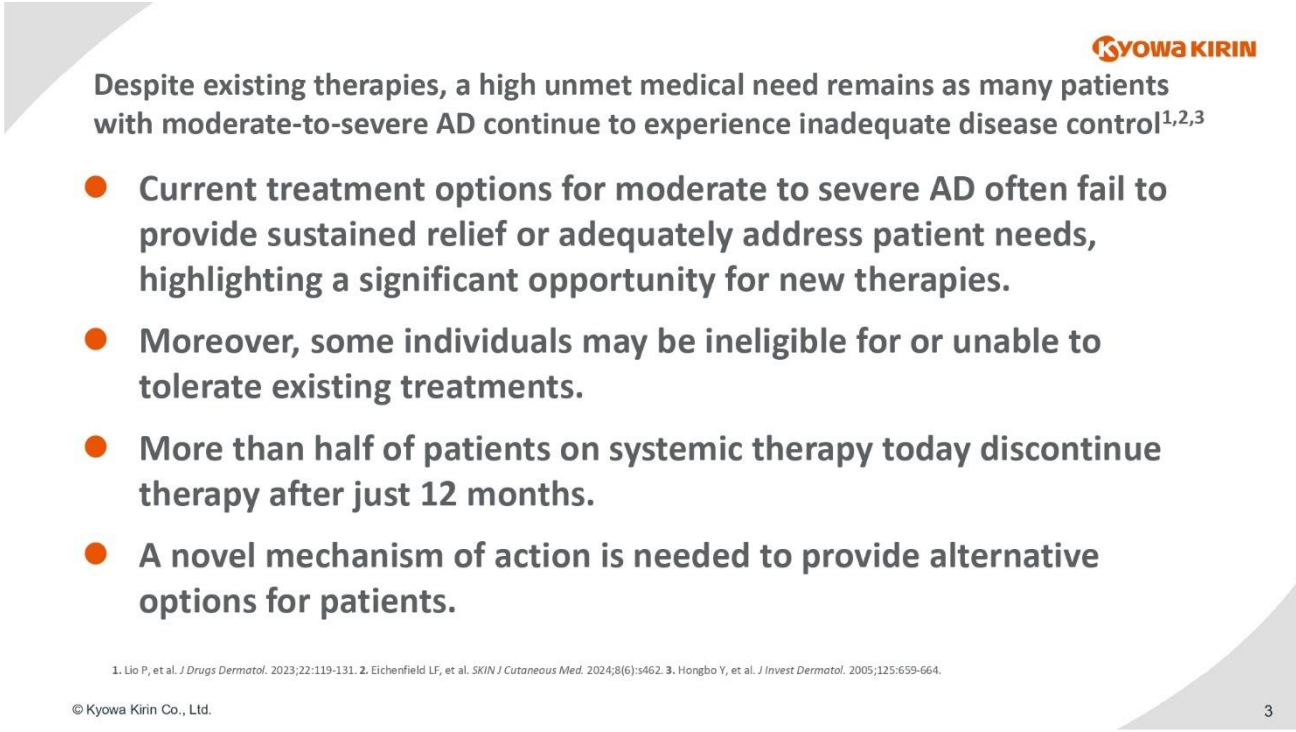
We are setting this time with two major goals. We have conducted a two-year study evaluating first the long-term safety and then the long-term efficacy of the product. And not just patients, and not just health care providers, but there are a number of issues in our daily experience with atopic dermatitis, therefore, I would like to share some with you in this meeting,

First, let me tell you that there are great unmet needs. And we will give you further top-line data. We will share only the topline data today to see what we have found out in the interim analysis. Both companies will work hard to present more detailed results at various conferences and in professional journals.



I would like to start explaining. Atopic dermatitis is a multi-pathogenic condition. Symptoms may appear in various forms. Dry skin and itching and pain may also occur. Patients scratch because they itch, thereby causing thickening. It is not simply an inflammation of the skin. Very diverse. It is very much about immune pathways.

It affects not only the skin, but also sleep, mental health, and daily life. Alternatively, it can also affect social life. A very large burden is placed on patients with atopic dermatitis. It is also characterized by recurring symptoms.

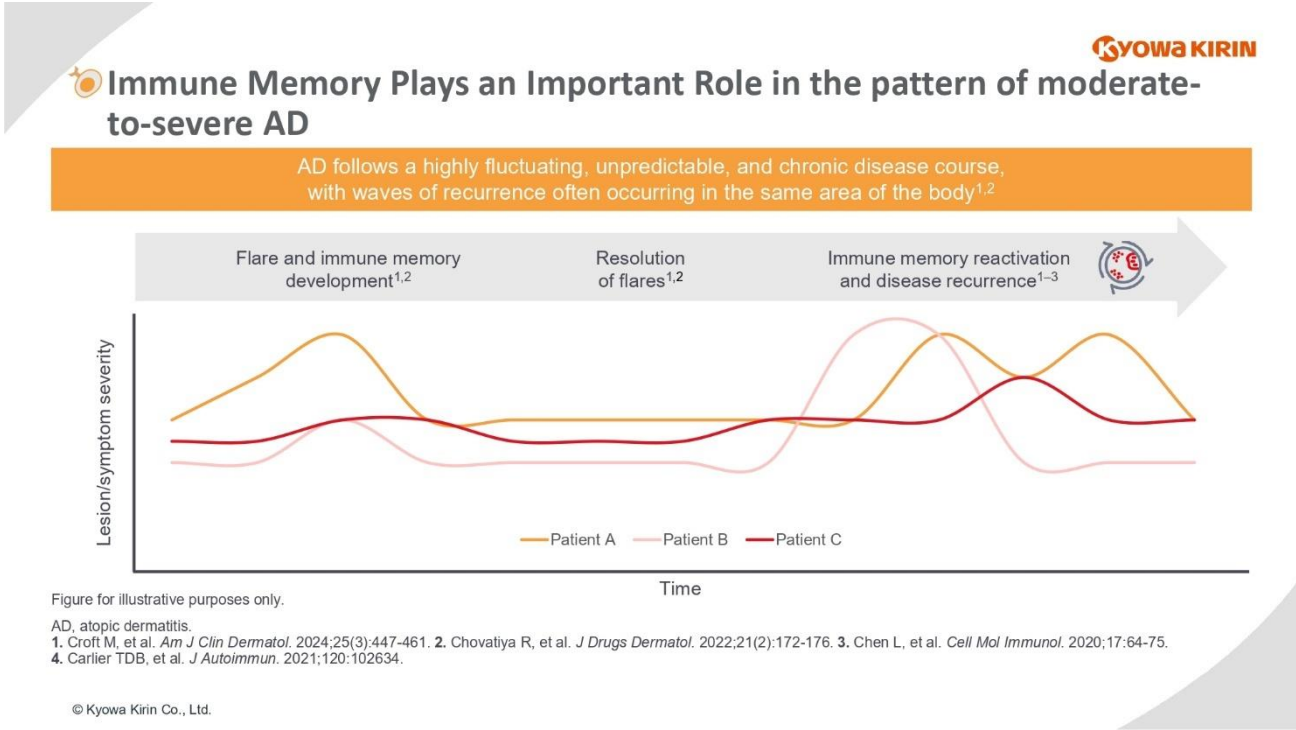


So far, there has been an evolution in the management of atopic dermatitis. However, patients with moderate and severe disease cannot adequately control their symptoms. For example, some may not be eligible or tolerate existing drug use.

A survey was recently conducted and more than half of patients receiving systemic therapy discontinue treatment within 12 months. So, there is a strong demand for a therapeutic agent with a novel mechanism of action that address significant unmet needs.

Ideally, we need a drug that approaches the root cause and, unlike existing drugs, approaches the downstream of the cytokine pathway.

Atopic dermatitis is a chronic disease. It does not simply mean that symptoms will flare up or recur. Immune memory is relevant.

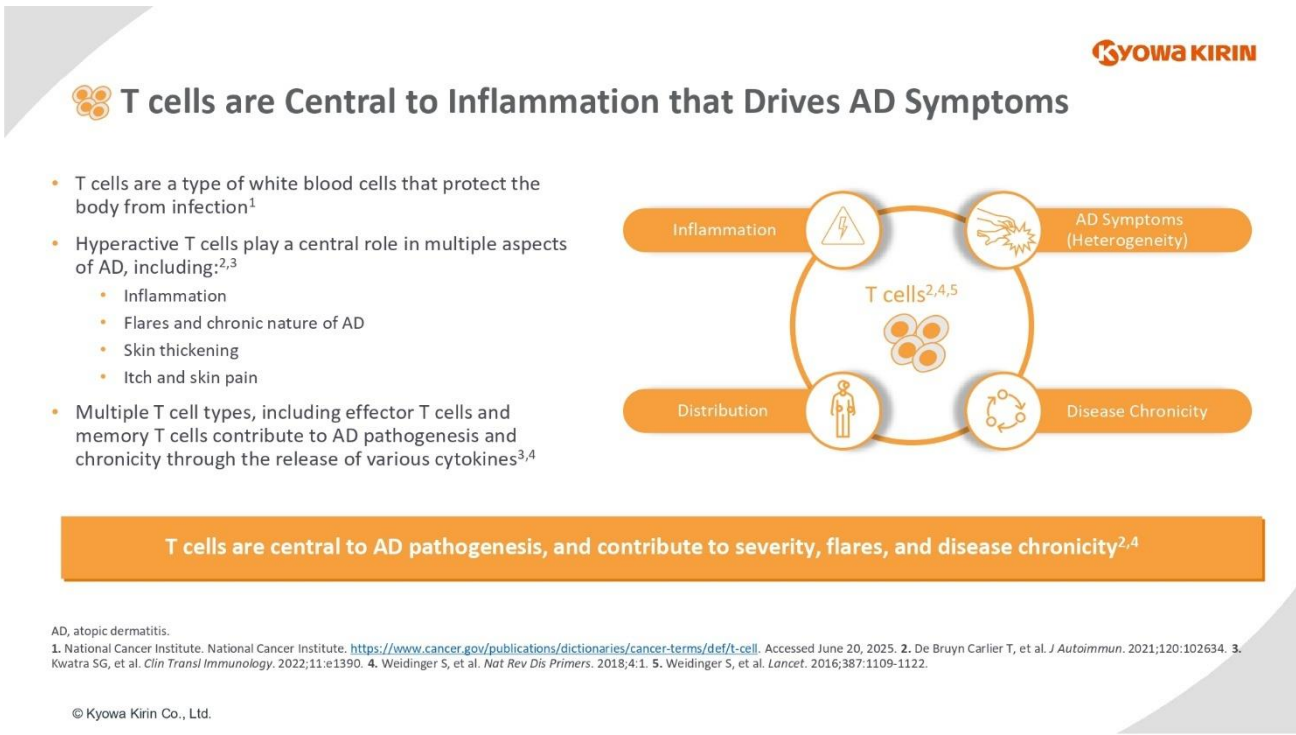


See this graph. As shown here, the symptoms fluctuate significantly between worsening and improvement. Flare up again, flares improve, and by directly targeting immune memory, meaningful improvement can be achieved in this chronic condition.

Right now, there are no drugs that directly approach the root cause of this disease. This has created a huge gap. In addition, to reduce the physical and emotional burden, we considered lengthening the dosing intervals. There is a huge unmet need for patients with moderate and severe disease.

Now I would like to hand over to Mr. Yamashita.

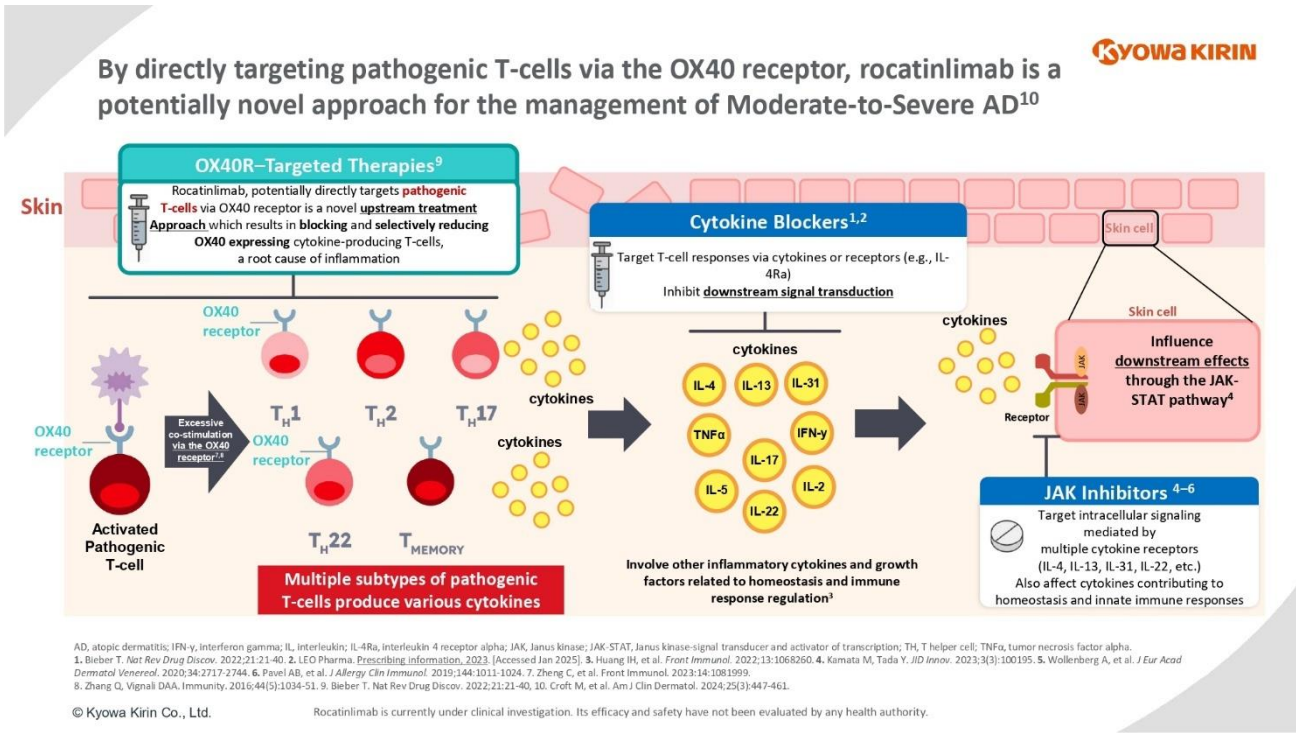
Yamashita: I would like to introduce T-cell balance, the novel mechanism of Rocatinlimab for atopic dermatitis.



T cells are a type of white blood cell that protects the body from infection and play a central role in the immune responses. In atopic dermatitis, these T cells are over-activated and involved in the disease process. Specific symptoms include persistent inflammation, flare-ups, chronicity, skin thickening, itching and skin pain.

These symptoms are caused by cytokines released by several types of T cells, including effector T cells and memory T cells, which promote the severity and prolongation of symptoms.

In other words, T cells are the central players in the pathogenesis of atopic dermatitis, and their activity determines the intensity of symptoms, frequency of flare-ups, and duration of disease. This understanding is a critical foundation for the development of new T cell-targeted treatments.



AD, atopic dermatitis; IFN-γ, interferon gamma; IL, interleukin; IL-4Rα, interleukin 4 receptor alpha; JAK, Janus kinase; JAK-STAT, Janus kinase-signal transducer and activator of transcription; TH, T helper cell; TNFα, tumor necrosis factor alpha.

1. Bieber T. *Nat Rev Drug Discov.* 2022;21:21-40. **2.** LEO Pharma. Prescribing information, 2023. [Accessed Jan 2025]. **3.** Huang IH, et al. *Front Immunol.* 2022;13:1068260. **4.** Kamata M, Tada Y. *JID Innov.* 2023;3(3):100195. **5.** Wollenberg A, et al. *J Eur Acad Dermatol Venereol.* 2020;34:2717-2744. **6.** Pavel AB, et al. *J Allergy Clin Immunol.* 2019;144:1011-1024. 7. Zheng C, et al. Front Immunol. 2023:14:1081999.
8. Zhang Q, Vignali DAA. Immunity. 2016;44(5):1034-51. 9. Bieber T. Nat Rev Drug Discov. 2022;21:21-40, 10. Croft M, et al. Am J Clin Dermatol. 2024;25(3):447-461.

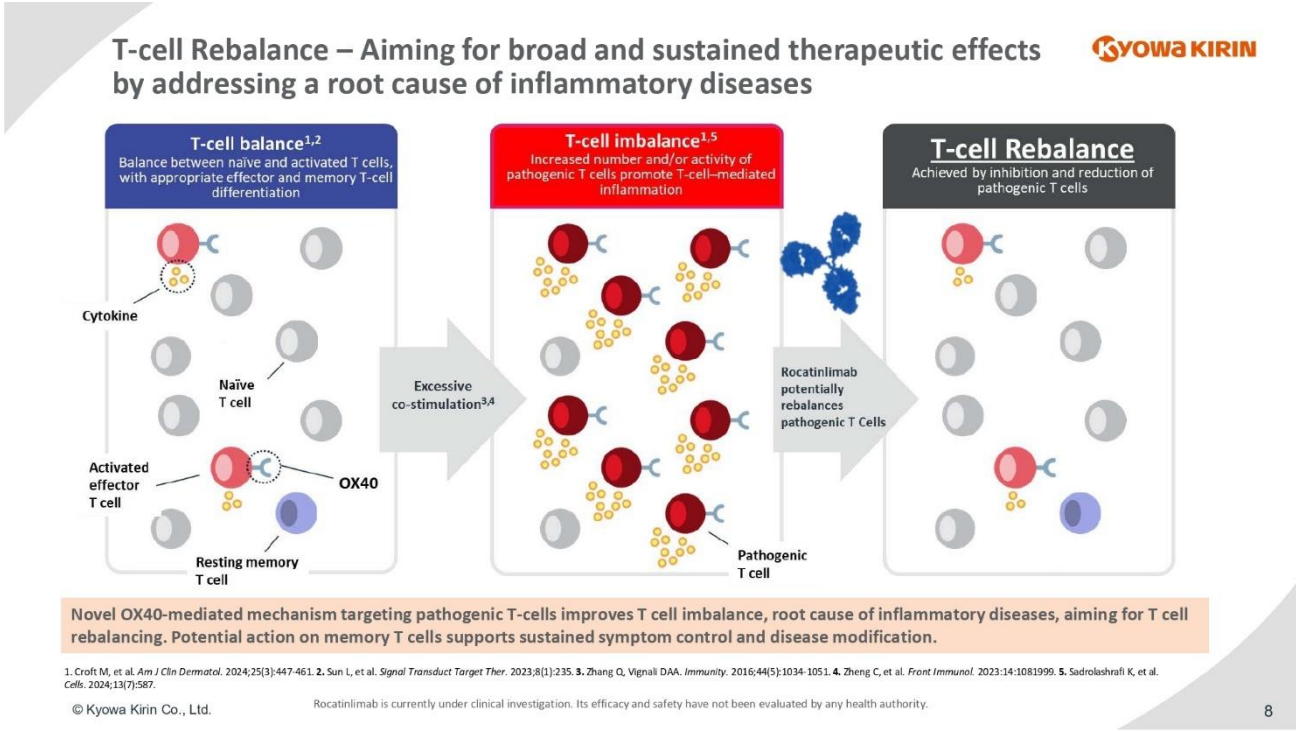
Rocatinlimab is currently under clinical investigation. Its efficacy and safety have not been evaluated by any health authority.

This slide shows current therapies for moderate to severe atopic dermatitis and the positioning of Rocatinlimab, which targets OX40.

The T cells I mentioned earlier are activated and cytokines are released from them. This variety of cytokines is where inflammation occurs in the skin tissue, causing atopic dermatitis.

There are JAK inhibitors that suppress this reaction locally in the skin, and there are antibody drugs and biologics that are currently positioned in the category of cytokine blockers that block a variety of cytokines.

Rocatinlimab targets OX40 to suppress T cells that release various cytokines. Rocatinlimab is known to suppress not only these activated T cells, but also the memory T cells that remember the disease, which is T memory on the lower right and left.



T cells are usually mostly inactive, as shown on the left, among which there are some, activated T cells to respond to various stimuli. When these T cells are activated, OX40 comes to the surface, and this is where Rocatinlimab targets.

There are also memory T cells that remember the symptomatic response I mentioned earlier, and this is where the inflammatory flare that was introduced by Mr. Abdul comes into play.

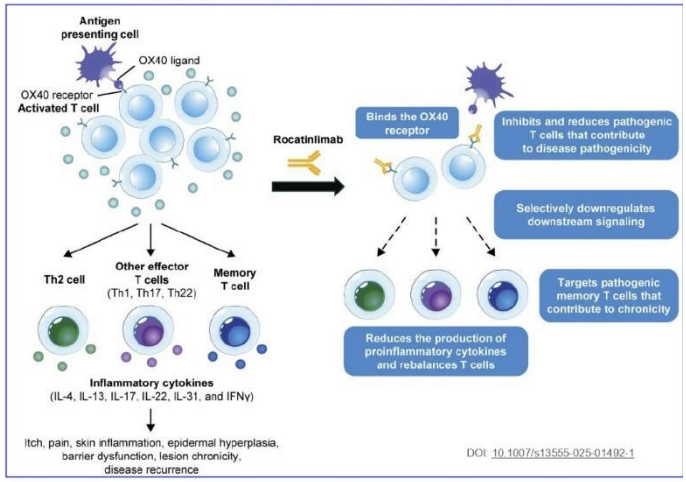
In fact, patients with moderate or severe atopic dermatitis have an abnormal increase in these activated T cells and an abnormal state in which many of the cytokines I just described are released.

These activated T cells express OX40, and Rocatinlimab targets and suppresses these activated T cells, resulting in returning to the state shown in the right side. The return of the left side to the normal state are called “T-cell Rebalance”.

Peer-Reviewed article just published: Rocatinlimab as a novel T-cell rebalancing therapy

- *Journal: Dermatology and Therapy* (September 2025)
- *Title:* ***Rocatinlimab: A Novel T-Cell Rebalancing Therapy Targeting the OX40 Receptor in Atopic Dermatitis***
- **Authors:** Emma Guttman-Yassky, Eric Simpson, Ehsanollah Esfandiari, Hirotaka Mano, Jillian Bauer, Prista Charuworn, Kenji Kabashima
- **Key Summary points:**
  - *There is an unmet need for novel treatments for moderate-to-severe atopic dermatitis that offer* ***longer dosing intervals and provide durable responses off therapy****.*
  - ***T-cell imbalance*** *is a root cause of atopic dermatitis.*
  - *Rocatinlimab (AMG 451/KHK4083) is a* ***first-in-class T-cell rebalancing therapy*** *that inhibits and reduces pathogenic T cells by targeting the OX40 receptor.*
  - *To date, rocatinlimab demonstrated strong efficacy, favorable safety, and durable response on and off therapy in treating moderate-to-severe atopic dermatitis.*

Rocatinlimab Mechanism of Action



Rocatinlimab is currently under clinical investigation. Its efficacy and safety have not been evaluated by any health authority.

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KYOWA KIRIN

This is a more scientific explanation of what I have just presented, which I will not explain, but which was made into a paper on September 6.

The concept of T-cell rebalancing is thus now an accepted concept in peer review articles.

KYOWA KIRIN

Phase 3 ROCKET Program Results to date and new study results

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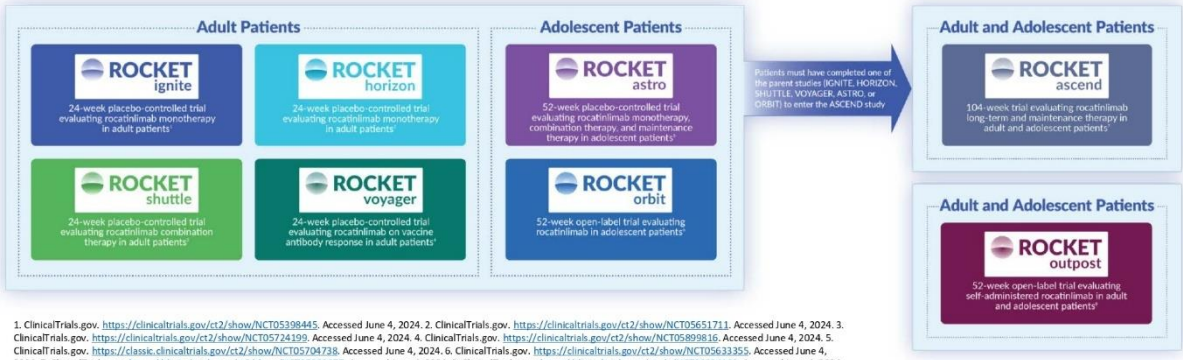
Next, we introduce the ROCKET program.

Rocatinlimab – Phase 3 the ROCKET Program

- Composed of eight global studies enrolling adult and adolescent moderate to severe AD patients
- To date, over 3,300 patients have been enrolled with seven studies having completed enrollment
- Studies were designed to examine long-term sustained efficacy and safety



1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05398445. Accessed June 4, 2024. 2. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05651711. Accessed June 4, 2024. 3. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05724199. Accessed June 4, 2024. 4. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05899816. Accessed June 4, 2024. 5. ClinicalTrials.gov. https://classic.clinicaltrials.gov/ct2/show/NCT05704738. Accessed June 4, 2024. 6. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05633355. Accessed June 4, 2024. 7. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05882877. Accessed June 4, 2024. 8. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06224192. Accessed June 4, 2024.

The entire ROCKET program consists of eight Phase 3 studies, and the ASCEND study, which we present today, is a study design in which patients from the original six studies who have completed them are further enrolled and evaluated on an ongoing basis.

Topline Data: ROCKET IGNITE, SHUTTLE, VOYAGER

https://ir.kyowakirin.com/en/news/news-303296477782016180 8/main/00/link/e20250308.pdf

ROCKET ignite — 24-week placebo-controlled trial evaluating rocatinlimab monotherapy in adult patients

Monotherapy

Primary Endpoint*	rocatinlimab Higher Dose (Week 24)		rocatinlimab Lower Dose (Week 24)	
	%	Difference from placebo (p-value)	%	Difference from placebo (p-value)
EASI-75	42.3	29.5 (p<0.001)	36.3	23.4 (p<0.001)
vIGA-AD 0/1	23.6	14.9 (p<0.001)	19.1	10.3 (p=0.002)
rIGA-0/1	22.7	14.4 (p<0.001)	16.3	8.0 (p=0.01)

ROCKET shuttle — 24-week placebo-controlled trial evaluating rocatinlimab combination therapy in adult patients

Combination with TCS/TCI

Primary Endpoint*	rocatinlimab Higher Dose (Week 24)		rocatinlimab Lower Dose (Week 24)	
	%	Difference from placebo (p-value)	%	Difference from placebo (p-value)
EASI-75	52.3	28.7 (p<0.001)	54.1	30.4 (p<0.001)
vIGA-AD 0/1	26.1	13.8 (p<0.001)	25.8	13.5 (p<0.001)
rIGA-0/1	23.3	11.5 (p<0.001)	22.7	10.9 (p=0.002)

ROCKET voyager — 24-week placebo-controlled trial evaluating rocatinlimab on vaccine antibody response in adult patients[4]

Responses to vaccinations

Demonstrated that rocatinlimab does not interfere with responses to tetanus and meningococcal vaccinations.

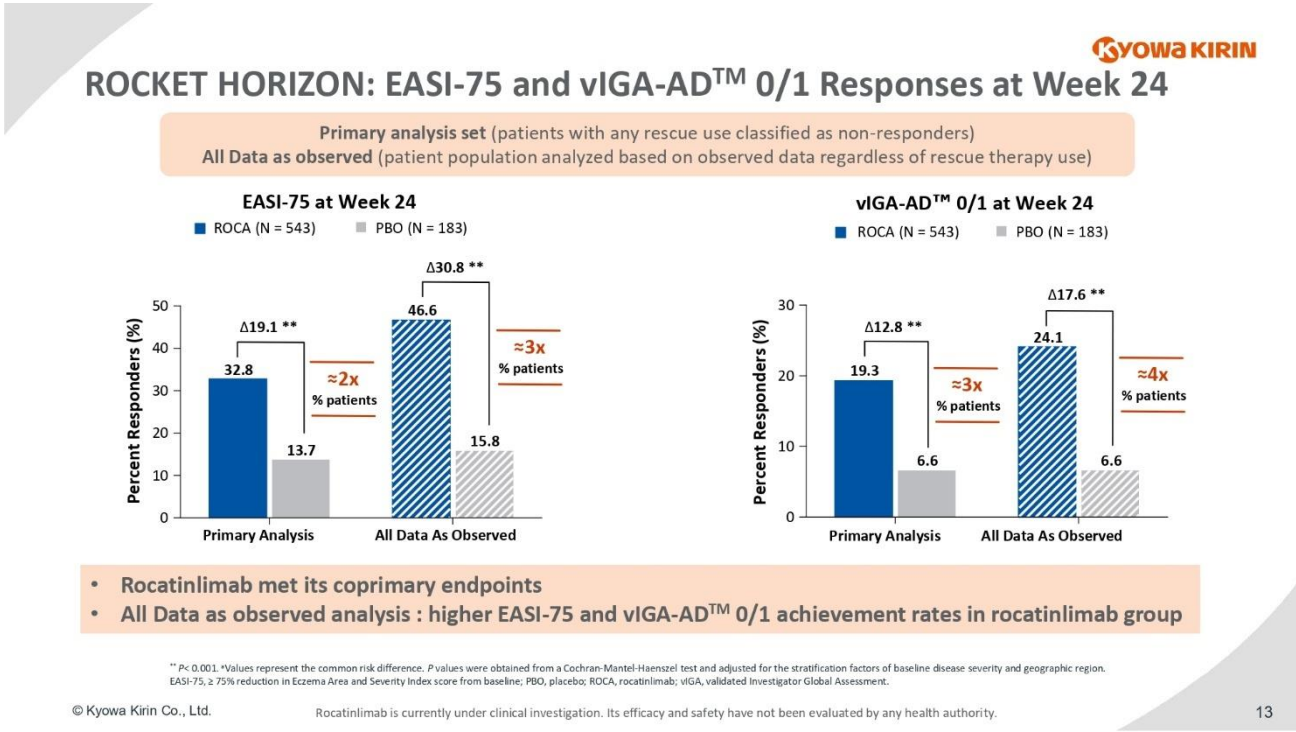
*In the US, revised Investigator Global Assessment (rIGA) replaces vIGA as co-primary endpoint

Rocatinlimab is currently under clinical investigation. Its efficacy and safety have not been evaluated by any health authority.

This will be a reminder, but the results of the study that we have disclosed so far, ROCKET IGNITE is a single agent study. We have also presented the results of studies on ROCKET SHUTTLE when used in combination with topical agents.

IGNITE was tested at two doses, 150 mg and 300 mg. In the topical application studies, a trend toward higher efficacy was observed.

At the bottom of the list is responses to vaccinations, which confirms that Rocatinlimab has no particular effect on the process of disrupting the effects of vaccines.

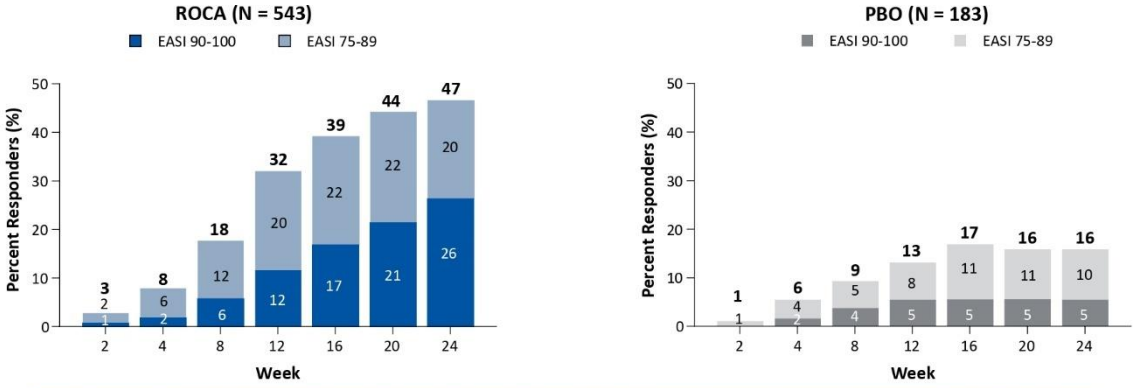


The ROCKET HORIZON and IGNITE studies are single agent studies. In our protocol, all such patients who use concomitant medications during the course of the treatment are considered as non-responders. This is the data that we call the “Primary Analysis”.

We continued to observe these individuals to determine whether the treatment was effective or not, which is what “All Data as Observed” refers to. As mentioned earlier, when we included cases where the treatment was used in combination to some extent, we observed that the effectiveness was higher.

ROCKET HORIZON: EASI 75-89 and EASI 90-100 at Week 24

All Data as observed (patient population analyzed based on observed data regardless of rescue therapy use)



Rocatinlimab-treated patients showed a continuous increase in deep remission (EASI 90–100) rates

Values above bars indicate the percent of patients that were EASI-75 responders.
EASI, Eczema Area and Severity Index; EASI-75, ≥ 75% reduction in Eczema Area and Severity Index score from baseline; EASI 75-89, ≥ 75% to ≤ 89% reduction in EASI score from baseline; EASI 90-100, ≥ 90% to ≤ 100% reduction in EASI score from baseline; PBO, placebo; ROCA, rocatinlimab.

Rocatinlimab is currently under clinical investigation. Its efficacy and safety have not been evaluated by any health authority.

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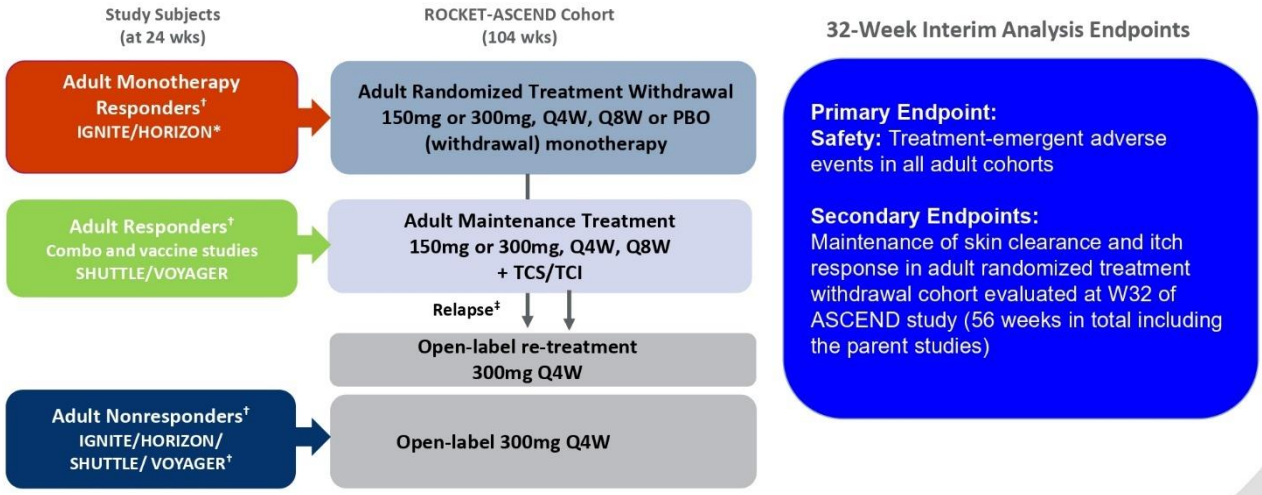
In addition, data from the HORIZON study looking at efficacy over time showed that the rate of achievement of EASI 75 increased toward 24 weeks. In addition, we have previously shown that patients who achieve a more effective EASI 90 have a linear increase at 24 weeks. These data have been disclosed so far.

ROCKET-ASCEND TRIAL DESIGN: ADULT COHORTS[1]



*Additional data will be generated in adolescents including Q4W maintenance, Q8W extension (not shown). †Responders are defined as achieving EASI-75 and/or vIGA 0/1 at Wk 24 without the use of rescue therapy. ‡Relapse defined as loss of at least 50% of improvement in EASI response at Wk 24 of parent study from parent study baseline, or initiation of rescue therapy for AD.
AD, atopic dermatitis; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; TCI, topical calcineurin inhibitor; TCS, topical corticosteroid; Wk, Week
1. Guttman-Yassky E, et al. [Published online ahead of print February 26, 2025]. *Immunotherapy*.

Rocatinlimab is currently under clinical investigation. Its efficacy and safety have not been evaluated by any health authority.

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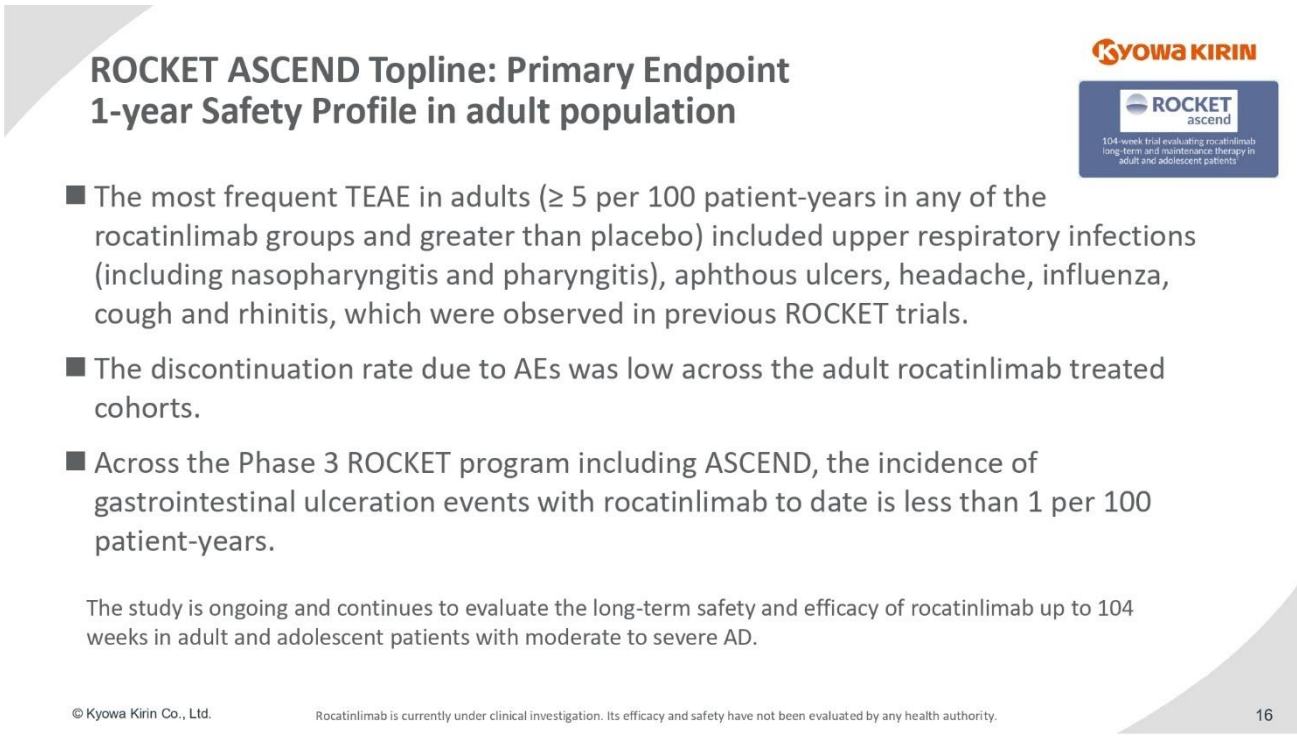
Continuing on, here is today's ASCEND study. The ROCKET ASCEND study, as I mentioned earlier, is in the process of further ongoing evaluation from the studies we have been conducting.

As you can see on the left side, there are patients who were responders in the monotherapy IGNITE and HORIZON studies, patients who were effective in the SHUTTLE combination study, patients who were effective in VOYAGER, and patients who were non-responders, and for these patients, the open-label dosing was used.

The primary endpoint is an assessment of the overall safety of such studies. The secondary endpoints that we will discuss in this and later sections are those that look at the maintenance of those who have been monotherapy.



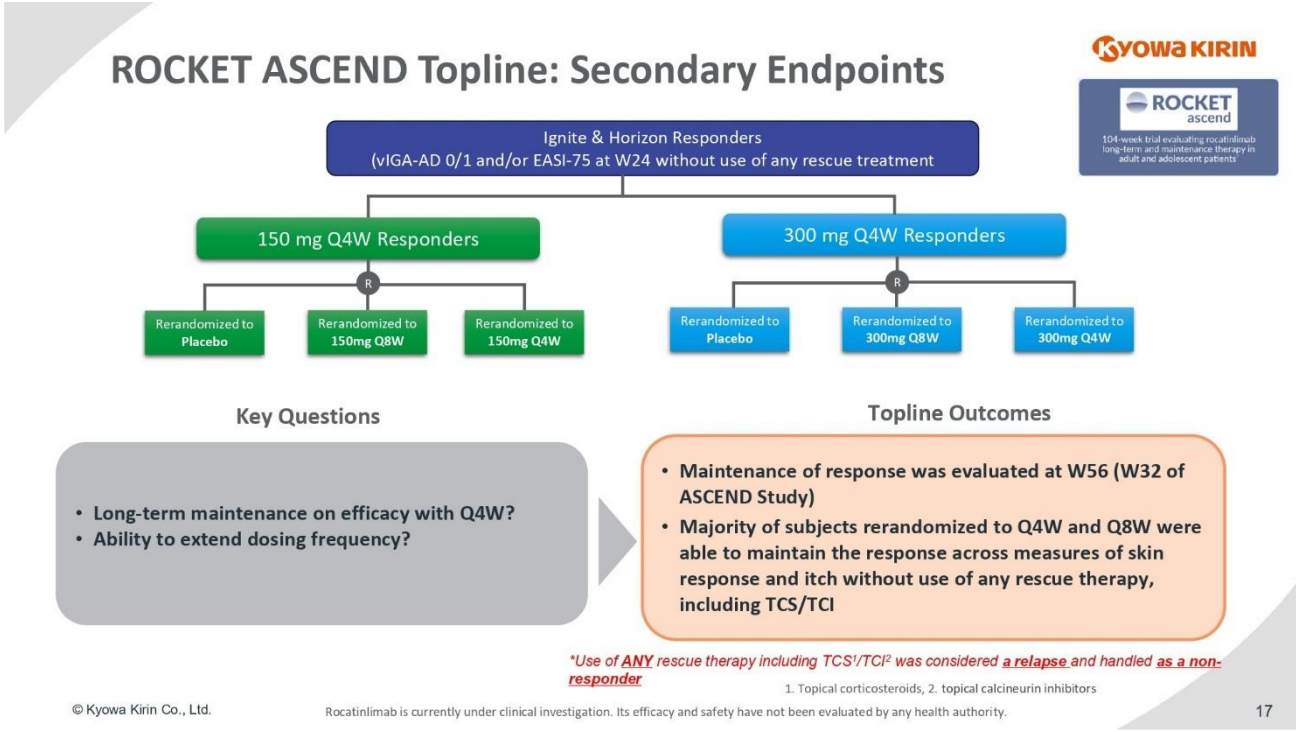
First, let us introduce the safety profile of the primary endpoint. The parent trial was 24 weeks and then 32 weeks of data were obtained for this study.

We have obtained a safety profile for approximately one year, and in the adult Rocatinlimab group, TEAEs with a frequency of at least 5 per 100 patients per year and more frequent than placebo included upper respiratory tract infections, aphthous ulcers, headache, influenza, cough, and rhinitis.

These are similar to those that have been confirmed in previous studies. In addition, the discontinuation rate due to adverse events was remarkably low.

In addition, throughout the ROCKET program, including ASCEND, some events of peptic ulceration with Rocatinlimab were seen, but the incidence was less than 1 event per 100 patients per year.

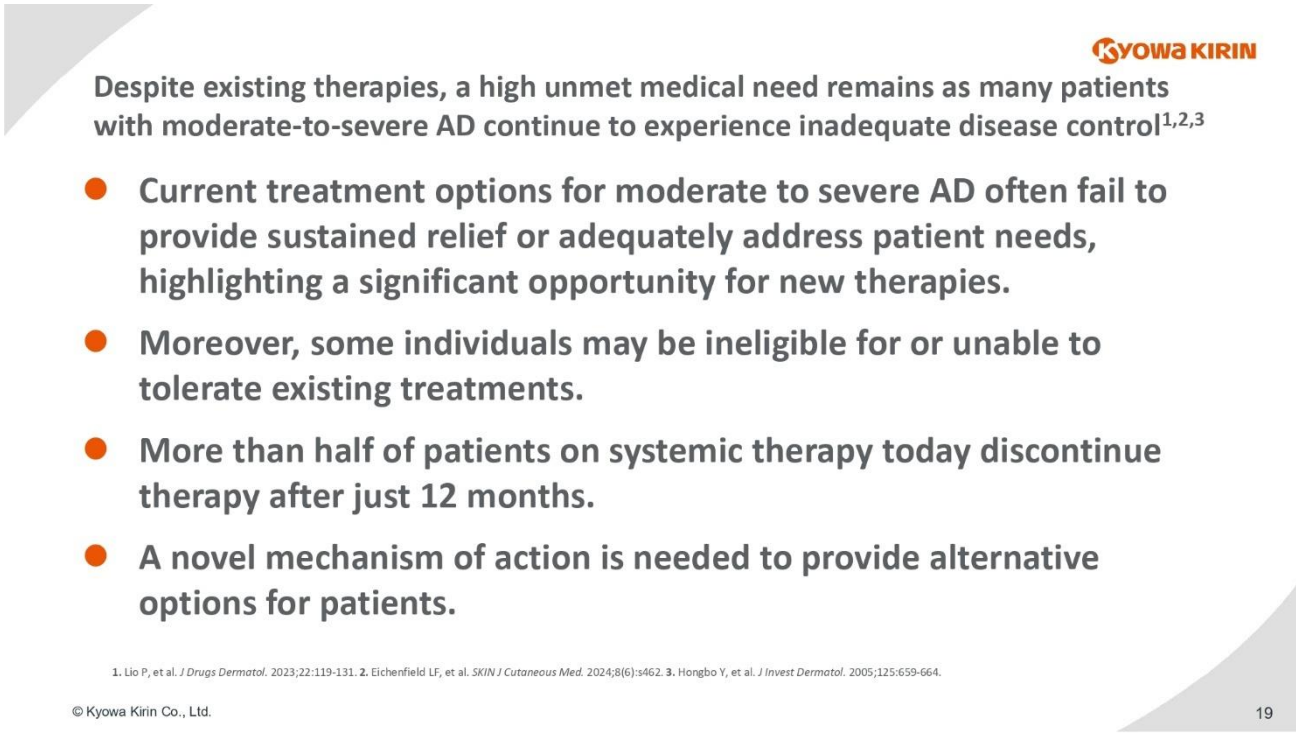
The ASCEND study is being presented at 32 weeks, and we will continue to obtain safety data over a total of 128 weeks and up to that point. We plan to include those data and establish a safety profile.



Next, we introduce secondary endpoints. The secondary endpoints in this study are to determine whether patients who have shown efficacy in the single agent IGNITE and HORIZON studies will continue to benefit from the treatment.

Patients who benefited from these two studies included those on 150 mg or 300 mg. In each case, the patients were assigned to either the placebo group, the Q8W group, or the Q4W group with different treatment intervals, and the study has just continued. We have just evaluated them as such at 24 and 32 weeks this time, for a total of 56 weeks.

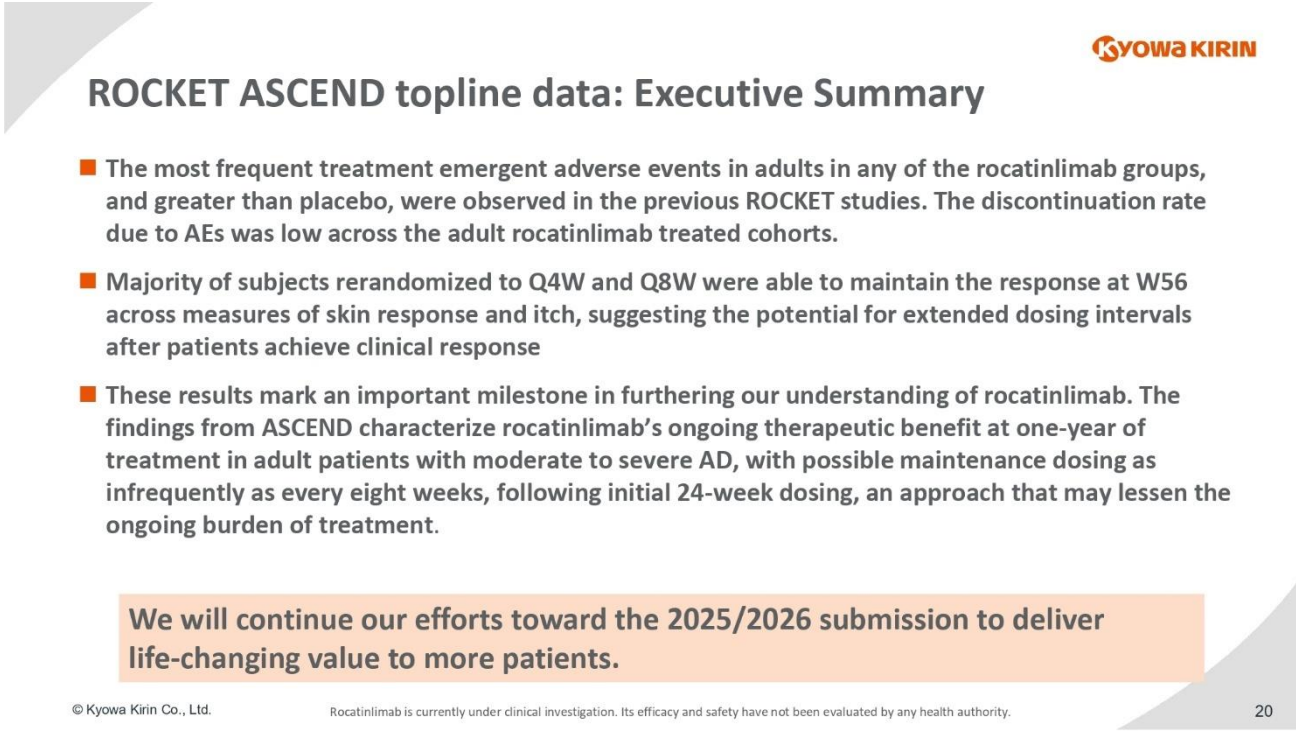
In this study, as I mentioned earlier with IGNITE and HORIZON, we are doing such a rigorous evaluation that if we add a little rescue therapy or different treatment in the middle, we will remove all of them.



Mullick*: Now I would like to summarize.

First, here are the slides I presented at the beginning of today's presentation. The reasons for introducing it again are, first, that atopic dermatitis affects a large number of people worldwide, but existing treatments have not yet achieved adequate disease control.

More importantly, control of this disease as a chronic condition is a major challenge for patients, and therapists.



This is the last slide of today's summary of top-line data. First, with respect to safety, similar to previously published results, the majority of patients who were re-randomized to Q4W or Q8W were still able to maintain a response at Week 56 on the assessment endpoint of skin symptoms.

And a subset of patients, the effect was maintained for 32 weeks. This is true for randomized or placebo. And we know that Rocatinlimab is the one that provides an excess treatment option.

Based on this study, we will steadily move forward with efforts to deliver life-changing value to more patients with the aim of submitting applications in 2025/2026.

That is all.

Question & Answer

Moderator [M]: Now I would like to move on to the question-and-answer session.

Yamaguchi [Q]: Regarding the top-line results for the secondary endpoints, it seems like the comments are not quite specific, and I'm a bit unclear on the interpretation.

First of all, in the key question, I'm not sure how to interpret whether the monotherapy maintenance—whether it's Q4W, Q8W, or placebo—actually achieved EASI 75 or EASI 90. Does the conclusion ultimately state that it is achieved?

Yamashita [A]: As I mentioned earlier, this study is an analysis focusing on patients who showed a response. Patients were assigned to three groups—placebo, Q4W, and Q8W—and a certain level of maintenance was observed in each group. Since the patients are diverse, it is still unclear how much can be concluded based on this data alone, but we have obtained data indicating that the response is being maintained.

Yamaguchi [Q]: Understood. Well, it means that although there are some fluctuations, the data show that maintenance is being achieved. I believe detailed measures like EASI scores will only be presented at congress meeting.

Yamashita [A]: Well, Regarding the degree of efficacy and such, we would like to disclose these results only after proper scientific evaluation. So, this time, we are only discussing very qualitative aspects. Naturally, based on the data to date, patients who are responding well to Q4W can be maintained at a very strong level for about a year, as expected, if Q4W is continued, and I think that Q8W, in which the frequency of administration is reduced, can also be maintained in a very good way.

Furthermore, even among those switched to placebo, there are populations where efficacy appears to be maintained even without further treatment.

I would like to present the details with solid data and evaluation, as I mentioned earlier.

Yamaguchi [Q]: Second. This means that you are looking at the data and we are not looking at the data and in the question-and-answer session, so some things are difficult to understand.

I think range that was originally expected for your company and for Yamashita-san: if it were an actual drug, it would be gradually effective, and if it were a placebo, it would go down a little, but still be fairly well maintained. How did your expectations compare with those of you, Yamashita-san or the team?

Yamashita [A]: In terms of my personal expectations, I think we are getting promising results. We have also been talking about the possibility of something like disease modification happening with the Phase 2 data. I think we are seeing some of those effects.

On the other hand, the data suggest that Rocatinlimab is a drug that can provide benefits to patients with very complicated treatment histories, with varying degrees of disease progression, and with considerable individual differences.

Yamaguchi [M]: I understand. That's all from me. Thank you very much.

Ueda [Q]: As my first point, I would like to ask a follow-up question regarding your current question.

In that case, I believe the efficacy has not yet plateaued at 24 weeks. In this data, while there is mention of the possibility of maintenance dosing at 4-week and 8-week intervals, I don't see much specific reference to off-treatment periods on the slides.

Could you please follow up on how we should interpret this aspect?

Yamashita [A]: Regarding whether the initial treatment effect continues to increase steadily, this analysis focuses on patients who demonstrated treatment efficacy at week 24. Therefore, patients who had insufficient treatment efficacy at week 24 but later achieved the endpoint were not included in this count.

Thus, the results are based on a study of how well patients who are achieving treatment maintain it. Therefore, regarding the first question, it is not within the scope of this disclosure.

However, the ASCEND study as a whole does not set this as an endpoint in this protocol, but I believe we will be able to present such data in future analyses.

In such a situation, as I mentioned earlier, we are obtaining data that suggests maintenance in each of these areas.

Ueda [Q]: How should I interpret the part about off-treatment?

Yamashita [A]: Regarding off-treatment we have confirmed this from data of patients assigned to placebo. When evaluating these patients based on efficacy criteria, treatment effect does not suddenly drop off; rather, there are various cases where it is very well maintained or somewhat diminished.

As I mentioned earlier, in this context, the content suggests that it may be quite possible for some patients to take a break from the medication.

Ueda [Q]: The second point, which I believe is also related to the future development plan, is it correct to understand that if we apply with the current data, the drug would be administered once every 4 weeks for the first 6 months, and then once every 8 weeks or with off-treatment periods, or is that how it would be used?

In addition, I would like to know if you are also considering a study in which the dosing interval would be extended from the beginning, for example, to once every 8 or 12 weeks.

Yamashita [A]: At this point, we do not have any firm plan, and we will probably obtain a variety of data from this and future analyses.

However, regarding approval, this is a matter of discussion between the FDA and the regulatory authorities, and we would like to proceed with discussions with the authorities on how the label can first be approved in a properly controlled study.

Therefore, we are not at the stage of disclosing that we will conduct additional studies at this time, as we must first analyze this study thoroughly.

Ueda [M]: Yes, sir. Thank you very much. That's all from me.

Hashiguchi [Q]: The first question is what was the difference between Q4W and Q8W? In your earlier explanation, you said that Q4W was maintained fairly well and Q8W was maintained in good shape, which I felt was a slightly different expression.

If we evaluate simply by the degree to which efficacy is maintained, Q4W is better, but if we let the patient choose according to the patient's condition, convenience, and the degree to which the frequency of administration is important, we can present both options. I would like to confirm whether it is correct to say that the data was such that your company can offer either option.

Yamashita [A]: As mentioned earlier, the patient backgrounds in each group may vary significantly based on this data. Additionally, determining how to evaluate the actual duration of efficacy presents challenges. Given these factors, I believe it's difficult to definitively state whether a difference exists or not in this instance.

I would like to refrain from commenting on the specifics of that area at this time, but I think Q8W is also a very good result.

Hashiguchi [Q]: The second point is to confirm how far you have come in this analysis and when and how you might be able to disclose the analysis after this.

I'm looking at page 26 of the Q2 earnings presentation slides, and there are six key questions there, and in this case, you saw a response in the parent study, and you examined three key questions in the randomized patients.

Regarding the three key questions about patients who flared up again or who did not respond in the parent study, is it correct to understand that these were not verified in this study?

Yamashita [A]: What we are presenting here is exactly the primary endpoint on the protocol of the ASCEND study, and the safety part set for the secondary endpoint is very much the main objective of this study, and we are disclosing that.

The effectiveness section was set as a secondary endpoint only in a very localized area, so that is the only disclosure this time.

However, the study as a whole will be structured in such a way that data will be obtained on the follow-up of patients who were administered the combination drug and on the follow-up of patients who were initially in the non-responder group, but such analysis has not yet been conducted. We are about to disclose first only what we have stipulated in this protocol.

The timing of disclosure will be exploratory analysis, which is not specified in the protocol, as the various data I mentioned earlier will be obtained in the future. I think it's necessary to examine whether such things have significant evidence to support them, among other factors.

In that sense, I think it would be good to introduce these things to the world, incorporating peer review mechanisms like academic conferences and papers.

Hashiguchi [Q]: So, the pre-defined analysis has already been completed at least for this 56-week period, and only exploratory analysis remains after this time?

Yamashita [A]: Yes, that's right. Only the primary and secondary endpoints were introduced at this time.

Hashiguchi [M]: I understand. Thank you very much.

Sakai [Q]: How does your company follow up on the patients who ended up on placebo?

In other words, the fact that the efficacy persists—whether in this Q4W, 150, or 300—means that the patient was properly treated. By switching the patient to placebo, his T cells will be effectively controlled.

Please tell us how you are analyzing this area, or rather, how you are understanding the situation.

Yamashita [A]: In this case, we are looking at EASI and IGA as specified in the protocol, as well as itching, but that is what the protocol says to look for, and we have no further information to disclose at this time.

Sakai [Q]: Is it my understanding that your company is aware of the situation of the patients, but has not disclosed it?

Yamashita [A]: As for data, the protocol is to move to open label administration this time when patients flare up again, so I believe the data exists showing how long it was maintained and what the circumstances were.

Sakai [Q]: Some patients have flared up again?

Yamashita [A]: We have not seen the data this time. We're starting by introducing only the truly top-tier information this time.

Sakai [Q]: So, this is the second question, is it correct to understand that the possibility of discontinuing medication has not yet been conclusively demonstrated by clinical study data?

Yamashita [A]: I believe that the patients assigned to the placebo in this case will start counting as taking a break off the drug from that point on. In this case, the patients were followed up to 32 weeks, and some consistently did not require administration, while others did require it. For those requiring administration, as mentioned earlier, if they were non-responders—since this is a blinded study, they would be evaluated as non-responders—they would then receive open-label treatment.

Sakai [Q]: So, the point is that if it is not effective, you will move to open label, is that right? So, we will know the number of those patients, of course.

Yamashita [A]: Yes, that's right. In both groups, if there is no effect, we will move to open label, so we are in a situation where we cannot know how much came from placebo and how much came from any group without detailed analysis.

Sakai [Q]: Am I correct in understanding that this will be disclosed in the future analysis?

Yamashita [A]: It may be in the form of a breakdown of the open label results, and I think we are still discussing that, but I think we are supposed to have a variety of data at hand.

Sakai [M]: I understand. Thank you very much.

Mullick [A]*: I would like to make one additional point. One of the criteria for flare-ups is the use of rescue therapy, a very strict requirement. In looking at this effect, the use of steroids, etc., is also considered a flare-up and is treated as an open label, so very strict criteria are used.

We are also looking at the use of rescue therapy as a patient cohort, so we are looking at results in that context. Thank you very much.

Wada [Q]: First, I understand that your company plans to apply with these top line results, but am I correct in assuming that the timing of the application will remain the same? With the data announced this time, is the plan to proceed with the application alongside HORIZON and IGNITE? Could you please tell me the timing of the application?

Yamashita [A]: There is no change from what we have been disclosing.

Wada [Q]: Also, in the unmet need section of the premise, on page three, it says that more than half of the patients receiving systemic therapy discontinue treatment within 12 months, what are the reason for discontinuation of systemic therapy as a clinical unmet need?

I would also like to know how your company's Rocatinlimab is positioned to address this issue.

Mullick [A]*: In this market, there are two things first. One point, this is a chronic disease. Patients have to be treated all the time, they have to take drugs, some of them, for example, have no more chronic episodes, and then they stop the drugs, which may cause them to flare up and have to start the drugs again.

Second, the response may stop in many patients. The doctor, and the patient look for other treatments, and all the current treatments occur downstream. Therefore, we need a new mechanism of action that works in a different way.

A significant number of patients suffer from atopic dermatitis. The number is 60 million or 70 million in the US. And those who are receiving state-of-the-art treatment today are relatively few, when you consider the various factors combined, on the part of patients who have this unmet need.

On the other hand, we believe that patients need to move away from conventional treatment to more advanced treatments. This is a very exciting and prospective area. That is why we are growing so much.

Wada [Q]: Is it correct to assume that what you are referring to as systemic therapy is cytokine therapy? I'd like to know the exact percentage related to steroid use, specifically whether this indicates over half of patients receiving systemic therapy are included. I would appreciate further details on this.

Yamashita [A]: I think systemic therapy, generally speaking, includes systemic therapy with steroids and immunosuppressants. The premise of our clinical study is that the patients are those who have received systemic therapy.

Therefore, I am not sure if the population here is exactly the same as the patients in our clinical studies, and I suspect that this information may have changed little by little depending on when the data was obtained.

Wada [Q]: One last point, you mentioned doses of 150 and 300. Previously, studies like IGNITE referred to high dose and low dose. Is it correct to understand that the low dose is now specified as 150 and the high dose as 300?

Yamashita [A]: Yes. We have been making such disclosures since the previous place.

Wada [M]: I remember that. I understand. Thank you very much.

Muraoka [Q]: It's extremely difficult—my mind simply can't keep up with organizing all this information full of gaps. I think you mentioned the placebo group where the patients who could take a break from the drugs or off-treatment, and you mentioned that some patients were able to maintain, and some were not able to maintain.

Is it possible to predict to some extent which patients will or will not maintain their effectiveness after stopping this treatment? If you don't understand how things change under these conditions, then when this drug comes out, I think doctors won't know whether they should stop giving it to this patient or not.

Is there any such analysis, even if the results cannot be said today, and do we know to some extent what the predictors are?

Yamashita [A]: At this point, such analysis has not progressed at all, and we only have data on the overall rounded state.

As you mentioned, and as I stated earlier, patients are highly diverse and may have different treatment backgrounds. Therefore, with over 3,000 patients enrolled in this study, I hope we can perform various analyses within a scope that allows us to secure a sufficient number of cases for proper stratification.

However, we have not yet collected such data at this time.

Muraoka [Q]: Do you have an image in your mind that this is probably the kind of predictor?

Yamashita [A]: Patients who have become highly resistant to prior treatments—while it depends on the specific treatments they received—likely fall into two categories: those with a particularly severe refractory condition, and those who, relatively speaking, haven't yet undergone a wide range of treatments in their treatments journey.

Also, I think there are many factors, such as different depths of disease in individuals to begin with. There are patients for whom it does not work to begin with, so I think it is very important to take a close look at such factors.

What we are very encouraged about this time is that the fundamental premise for all these studies is that patients have received prior treatment, still have symptoms, and have failed previous therapies. Within that premise, as we further subdivide the cases, we hope to clearly identify which patients Rocatinlimab can benefit.

It is difficult to say simply about such patients, and there may be many different cases, but I predict that Rocatinlimab will be a very effective treatment tool for a certain degree of population.

Muraoka [Q]: One of the things what you are saying now is that for patients with dupilumab failure, we might see some who could potentially achieve off drug with Rocatinlimab, correct?

Yamashita [A]: My expectation is that if we can show the efficacy of such biologics and JAK kinase inhibitors in patients who are no longer responding to such treatments, it would be a very useful drug for patients.

Given that capability, it stands to reason that some patients in this study entered without prior exposure to dupilumab or JAK inhibitors, receiving only systemic therapy—specifically, other systemic therapies. We've also collected data on moderate-to-severe first-line cases, so I'm hopeful we can thoroughly evaluate the effective aspects of dupilumab alongside these findings.

Naturally, we also expect the points you asked about.

Muraoka [Q]: I understand. I am sure that there will be no announcement at the conference next week, but is it safe to assume that we will be able to hear at conference around next March?

Yamashita [A]: We will need to discuss that in the future, but we would like to focus first on data analysis and then on the application process, so there is a possibility that the timing could be next year, as you mentioned.

Muraoka [Q]: Would it be about the early 2026? I am not trying to limit the time frame, but I am asking how long we have to wait in this limbo.

Yamashita [A]: We are not trying to cause too much frustration, but we are disclosing very limited information because it may be a long time before we can talk about it if we miss this opportunity.

In this context, I think it is important that the exploratory data I mentioned earlier not only be judged by the Company but also evaluated carefully.

Abdul has some comments, and I will hand over to him.

Mullick [A]*: The priority for us is to continue to analyze the data first and prepare for the application. Considerable effort must be devoted here. And in the process, of course, we would like to disclose the data further, including in collaboration with our partners.

Today, the first thing to note is that this data was very encouraging. And supporting what we would like to see in clinical studies, there is an unmet need with respect to this disease, although there are some aspects that we cannot disclose yet.

And we believe that it was very encouraging in this regard to be able to offer better treatment options to our patients.

Muraoka [M]: I understand. Thank you very much.

Mamegano [Q]: I would like to know from you regarding the evaluation of the secondary endpoints. Congratulations on the very good news that the effect was maintained this time with Q4W and Q8W.

However, I am a little confused as to what was being maintained. Was there a solid statistical evaluation? Or, for example, I think many patients were maintained, but I wonder if some of them were dropped out.

I'm not sure if you can disclose what exactly was being maintained or how it was being maintained, but could you tell me?

Also, I believe randomization was used, but I am curious whether this analysis will clearly shows which is better, Q4W or Q8W, or placebo, or something like that.

This is because I recall you mentioned including the ASCEND study in the application package, so I was thinking that perhaps you had some kind of labeling in mind when you included this part. I would appreciate it if you could tell me more about this.

Yamashita [A]: Firstly, there are certain evaluation items where maintenance is assessed. We evaluate the maintenance of scores such as EASI and an IGA. We are also taking data on whether each patient in each group maintains that score at the designated survey point, and we are looking at the trends, so this is not a discussion about statistical significance. The data represent the percentage of patients maintaining the scores at each time point.

Also, I am not a statistician and do not have expertise in this area, but I would naturally consider such comparisons if possible. This time, we are focusing on observing the trends.

Furthermore, once the effectiveness and maintenance of the effect have been confirmed, it seems realistic to consider whether to include an option to extend the dosing interval derived from these data, and if a flare-up occurs again, to revert to the original treatment—such choices appear to be practical treatment strategy. I think the key point will be whether this data can show such a point.

Regarding the application, in the real world, combination therapy is also a topic of discussion. However, I believe the first step is to thoroughly understand what Rocatinlimab is as a drug and clearly define its positioning.

Mamegano [Q]: I think that the application could have been submitted even without the ASCEND study, but is it correct to say that the ASCEND study was worthwhile because the data could be used to negotiate with the FDA regarding the 8-week dosing schedule?

Yamashita [A]: One important point is that accumulate safety information is crucial. As I mentioned earlier, patient backgrounds vary considerably, including different age groups and whether they are receiving concomitant treatments or not. I believe large-scale long-term studies like this are necessary.

Furthermore while it is exploratory as I mentioned before, I believe this study is highly valuable for thoroughly characterizing the potential of Rocatinlimab. We also believe that this could have a significant impact on drug selection.

Mamegano [M]: I understand. Thank you very much.

Moderator [M]: Thank you very much. This is the end of the online information session on the ASCEND study interim analysis and top-line data.

Thank you very much for your participation today. Thank you for your continued support of Kyowa Kirin.

[END]