Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/medical-industry-feature/expanding-treatment-options-for-patients-12-years-of-age-and-older-with-moderate-to-severe-atopic-dermatitis/14923/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

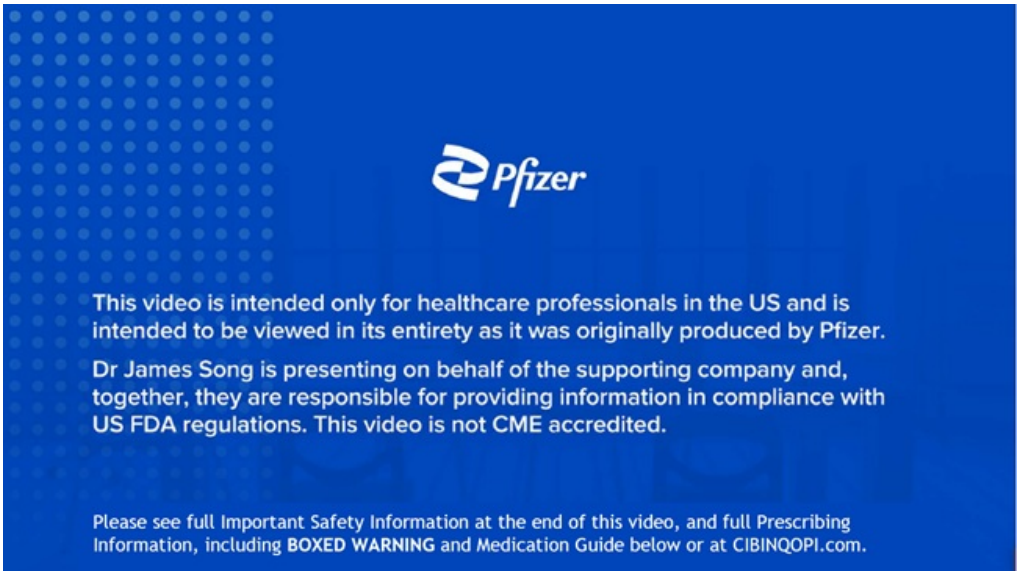
Expanding Treatment Options for Patients 12 Years of Age and Older With Moderate-to-Severe Atopic Dermatitis

FRAME 1:

Hello, my name is Dr James Song and today we'll be discussing expanding atopic dermatitis options for adults and pediatric patients 12 years of age and older with moderate-to-severe atopic dermatitis.

CIBINQO is a once-daily oral treatment for adults and pediatric patients 12 years of age and older with refractory, moderate to severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies is inadvisable.

FRAME 2:



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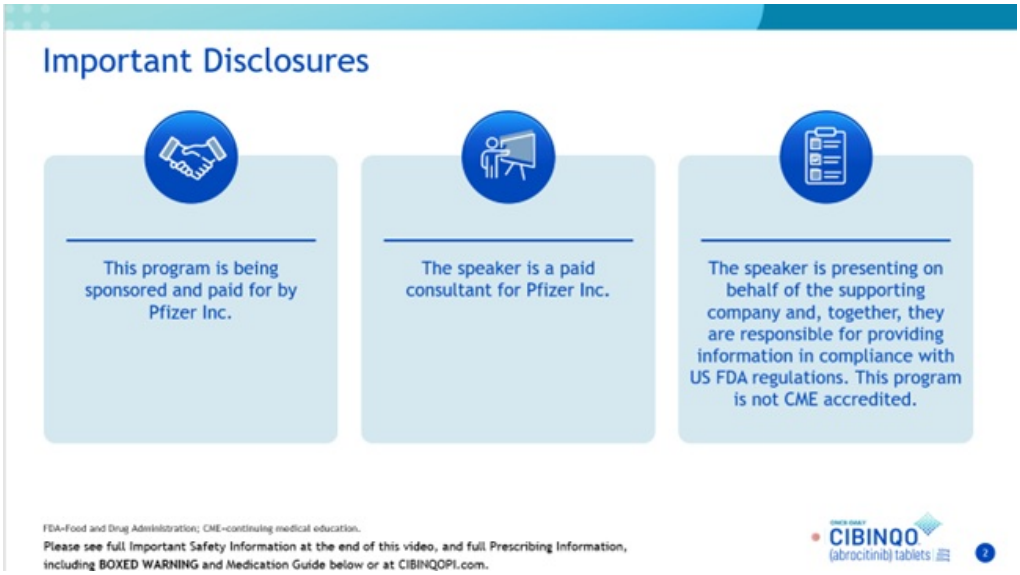


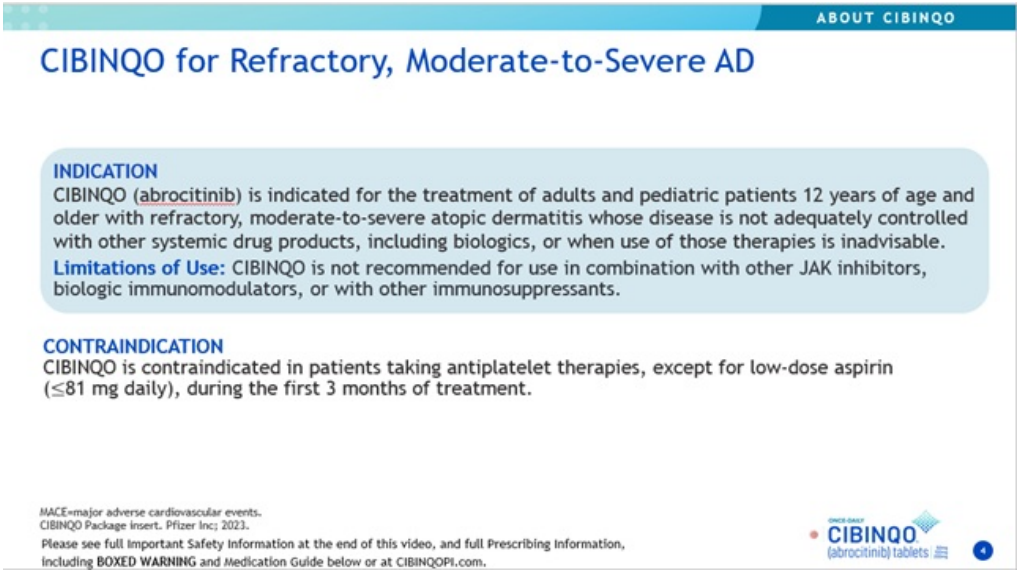
Before we begin, let's review some important disclosures: (1) this program is being sponsored and paid for by Pfizer Inc, (2) I am a paid consultant for Pfizer, and (3) this program is not CME accredited.

FRAME 4:

Today we will be talking about CIBINQO

- An overview of CIBINQO and its mechanism of action
- The efficacy data
- The safety data
- And how to start and monitor your patients who are on CIBINQO

FRAME 5:

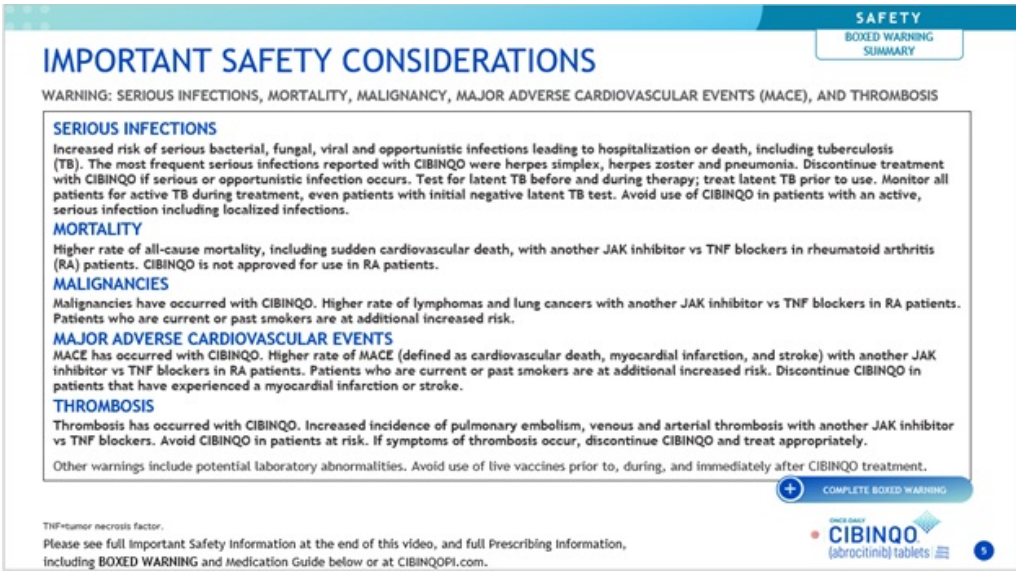


As mentioned earlier, CIBINQO is indicated for patients 12 years of age and older with refractory, moderate-to-severe atopic dermatitis not adequately controlled with other systemics, including biologics.

CIBINQO is not recommended for use in combination with other JAK inhibitors, biologic immunomodulators, or with other immunosuppressants.

CIBINQO is contraindicated in patients taking antiplatelet therapies, except for low-dose aspirin (≤ to 81 mg daily), during the first 3 months of treatment.

FRAME 6:



Please be aware that CIBINQO Prescribing Information includes the following boxed warning:

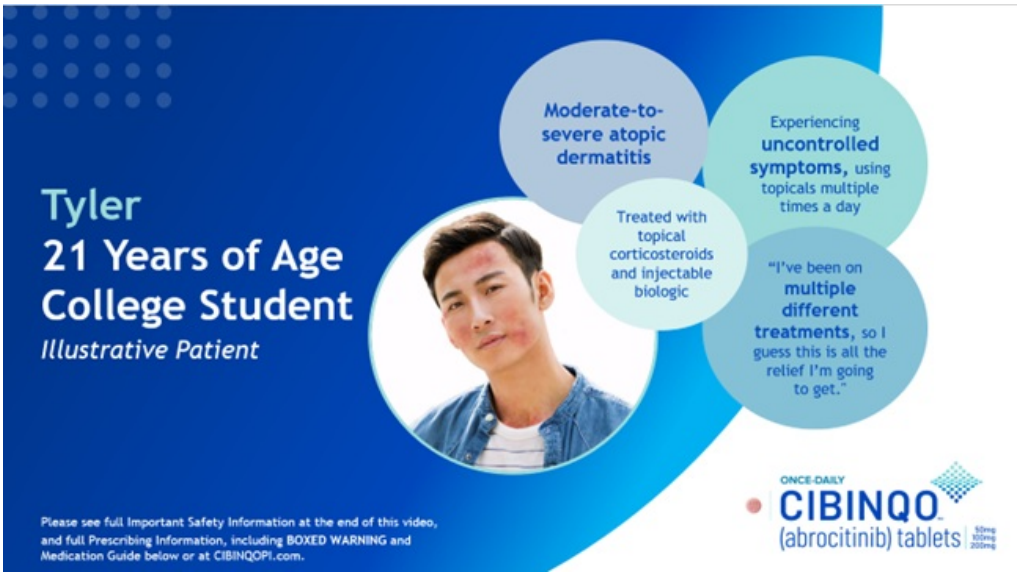
Increased risk of serious bacterial, fungal, viral, and opportunistic infections that may lead to hospitalization or death, including tuberculosis. Avoid use in patients with active serious infection and discontinue treatment if serious or opportunistic infection occurs.

Higher rate of all-cause mortality and MACE (defined as cardiovascular death, myocardial infarction, and stroke) with another JAK inhibitor vs. TNF blockers in rheumatoid arthritis patients. CIBINQO is not approved for use in rheumatoid arthritis.

Malignancies, MACE, and thrombosis have occurred in patients treated with CIBINQO. Higher rate of lymphomas, lung cancers, MACE, pulmonary embolism, venous and arterial thrombosis with another JAK inhibitor vs. TNF blockers. Patients who are current or past smokers are at increased risk. Discontinue if myocardial infarction, stroke, or symptoms of thrombosis occur.

Perform recommended testing, evaluations, and immunizations prior to CIBINQO initiation and monitor patients during treatment. Please see full Prescribing Information for details.

FRAME 7:

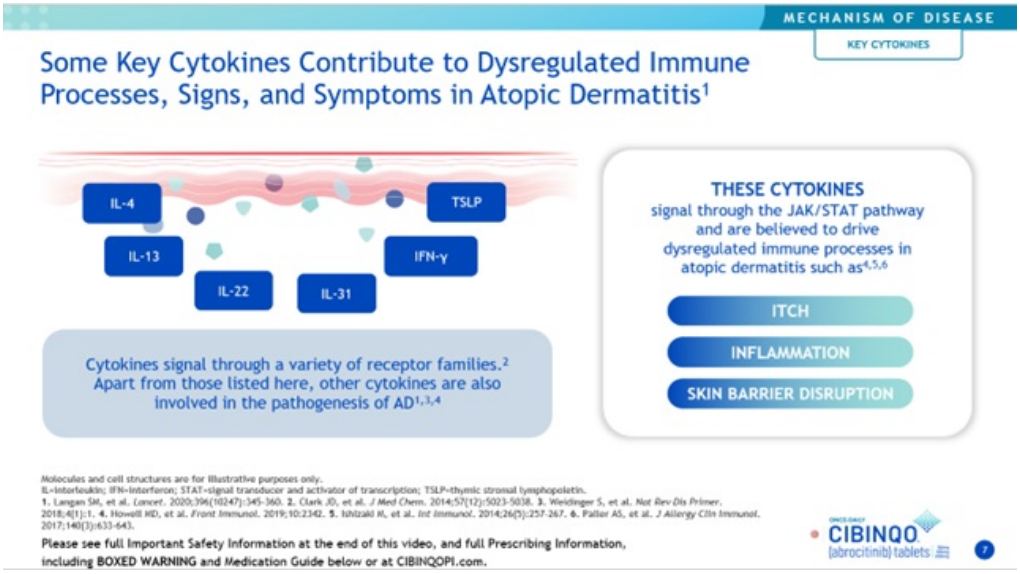


As we go through this presentation, consider a patient type like Tyler, a 21-year-old with moderate-to-severe atopic dermatitis who has been treated with topical corticosteroids and a biologic and is still experiencing uncontrolled symptoms. He feels that he's already doing everything he can to address his AD and worries that this is all the relief he is going to get.

For a patient like Tyler whose current treatment is not adequately controlling his disease, it may be worthwhile to consider a treatment with a different mechanism of action to manage his AD.

Let's look at how a treatment like CIBINQO works.

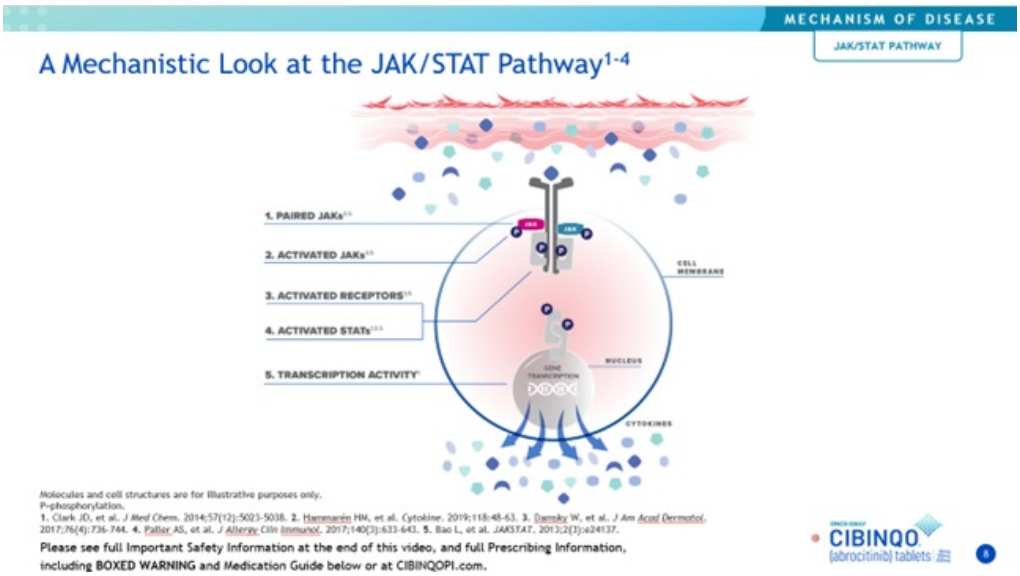
FRAME 8:



These cytokines signal through the JAK/STAT pathway and are believed to drive dysregulated immune processes in atopic dermatitis, such as itch, inflammation, and barrier disruption.[1-3]

Cytokines signal through a variety of receptor families.[4] And apart from those listed here, other cytokines are also involved in the pathogenesis of AD.[1,5,6]

FRAME 9:

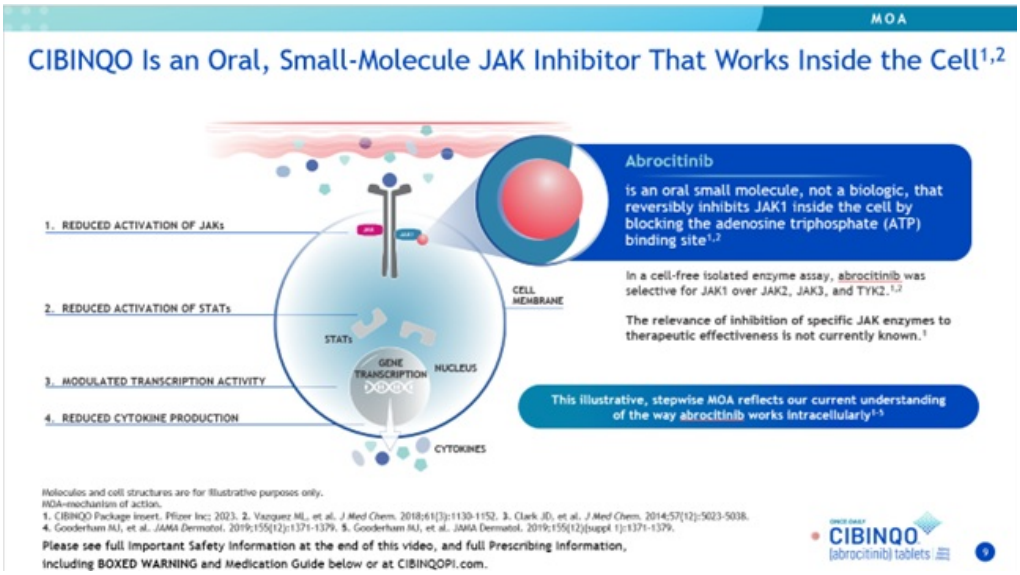


The Janus kinase and signal transducer and activator of transcription (JAK/STAT) pathway plays a role in regulating the signaling of various cytokines and is one of several pathways that influence inflammation.[1-3]

Let's discuss some of the key details and steps of the JAK/STAT pathway:

- First, it is important to note that JAKs are enzymes located inside the cell and become activated when cytokines and other growth factors bind to their receptors at the cell membrane.[2-4]
- When ligands bind to the receptors, it causes JAK pairs to move close to each other. These JAK pairs then phosphorylate and activate each other; this in turn phosphorylates and activates signal transducers and activators of transcription, or STATs.[2-5]
- Activated STATs translocate to the nucleus where they affect the gene transcription of proinflammatory cytokines.[4,5]

FRAME 10:



Now, let's discuss the properties of CIBINQO, or abrocitinib, and how it works inside the cell.

Abrocitinib is an oral, small molecule. It is not a biologic, and it reversibly inhibits JAK1 by blocking the adenosine triphosphate (ATP) binding site.[1]

In lab assays, abrocitinib was selective for JAK1 over JAK2, JAK3, and TYK2; however, the relevance of inhibition of specific JAK enzymes to therapeutic effectiveness is not currently known.[1,2]

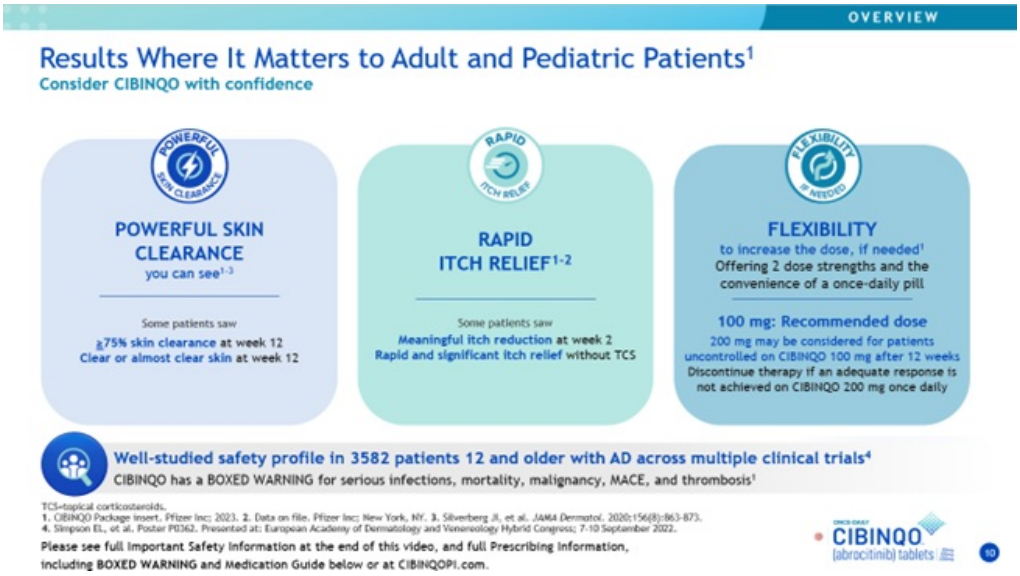
This illustrative, stepwise mechanism of action (MOA) process reflects our current understanding of the way abrocitinib works intracellularly.[1-5]

Abrocitinib is thought to modulate the JAK/STAT signaling pathway at the point of JAK1, thus reducing JAK phosphorylation or activation.[1]

In turn, corresponding STATs may be prevented from phosphorylating or activating and may not dimerize or translocate to the nucleus.[2,3]

And as a result, downstream gene transcription that perpetuates the production of cytokines may be reduced.[1-5]

FRAME 11:



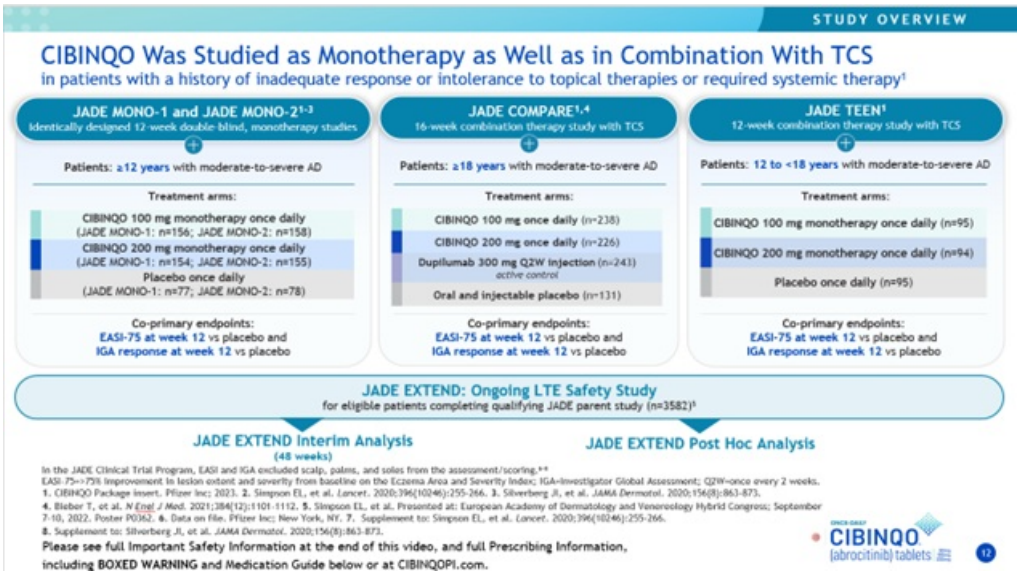
Throughout this presentation we will discuss

- The efficacy of CIBINQO, including powerful skin clearance and rapid itch relief results.[1-3]
- The flexibility to increase the dose of CIBINQO, if needed.[1]
- And the well-studied safety profile of CIBINQO.[4]

FRAME 12:

Let's get into the efficacy of CIBINQO.

FRAME 13:



The JAK1 Atopic Dermatitis Efficacy/Safety (JADE) Program evaluated CIBINQO for the treatment of moderate-to-severe atopic dermatitis (AD). JADE MONO-1, JADE MONO-2, JADE COMPARE, and JADE TEEN were the pivotal trials informing the approval of CIBINQO in adults and adolescents.[1-5]

As a reminder, the approved indication for CIBINQO is in moderate-to-severe AD patients whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies is inadvisable, which differs slightly from the population that was studied.

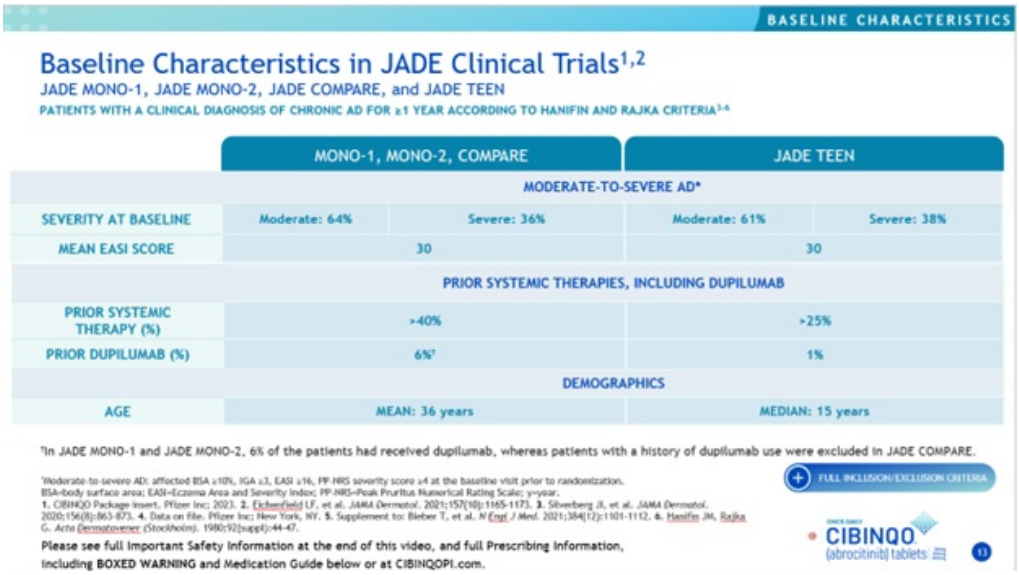
JADE MONO-1 and JADE MONO-2 were identically designed 12-week, phase 3, randomized, double-blind, placebo-controlled trials that studied CIBINQO as monotherapy versus placebo. All patients were aged 12 years or older, with moderate-to-severe AD and a history of inadequate response to topical or systemic therapy. Patients were randomized to receive CIBINQO 100 mg once daily, CIBINQO 200 mg once daily, or placebo for 12 weeks.

JADE COMPARE which was a phase 3, randomized, double-blind, double-dummy, placebo-controlled, parallel-group trial that studied CIBINQO in combination with topical corticosteroids versus placebo. Dupilumab was an active control for all endpoints except PP-NRS4 response at week 2, for which it was compared head-to-head with CIBINQO. The study enrolled patients aged 18 years or older with moderate-to-severe AD and a history of inadequate response to prescription topical or systemic therapy to control their disease. Patients were randomized to receive CIBINQO 100 mg once daily, CIBINQO 200 mg once daily, dupilumab (as per label), or placebo for 16 weeks. Background medicated topical therapy was used in all arms.

JADE TEEN was a phase 3, randomized, double-blind, placebo-controlled trial that studied CIBINQO in combination with topical corticosteroids versus placebo. The study included patients who were aged 12 to 18 years with moderate-to-severe AD. Eligible patients had a prior inadequate response or had received systemic therapy. Patients were randomized to receive CIBINQO 100 mg once daily, CIBINQO 200 mg once daily, or placebo for 12 weeks.

The long-term extension trial (LTE), JADE EXTEND, is an ongoing long-term safety study for eligible patients completing qualifying JADE parent trials, whose primary endpoints include the incidence of safety events and clinical abnormalities. We will review a 48-week interim analysis and a post hoc analysis from this study later in the presentation.

FRAME 14:

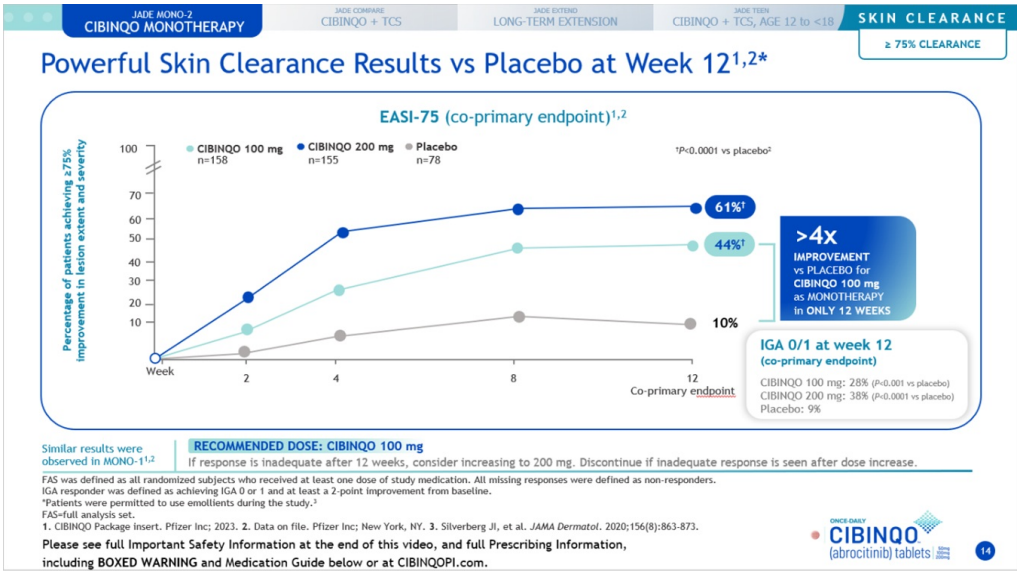


Before we get into the efficacy data, lets first take a look at the baseline characteristics of patients in JADE MONO-1, JADE MONO-2, JADE COMPARE, and JADE TEEN.

Let's begin with JADE MONO-1, JADE MONO-2, AND JADE COMPARE. In these studies 64% of patients had moderate atopic dermatitis, 36% had severe atopic dermatitis, and the mean EASI score was 30. More than 40% of patients had used prior systemic therapy, with 6% having previously used dupilumab. The average age of patients included in these studies was 36 years.

In JADE TEEN, 61% of patients had moderate AD, 38% had severe AD, and the mean EASI score was 30. More than 25% of patients had used prior systemic therapy, with 1% having previously used dupilumab. The median age of patients in JADE TEEN was 15 years.

FRAME 15:



We will now review the efficacy data for the 100 mg and 200 mg doses of CIBINQO in the clinical trials; however, please keep in mind that the recommended dosage of CIBINQO is 100 mg orally, once daily. After 12 weeks, if a patient's response to 100 mg is inadequate you can then consider increasing to 200 mg.

Now, let's look at the 75% skin clearance (EASI 75) results from the monotherapy study. We see that in only 12 weeks, significantly

more patients treated with CIBINQO alone achieved 75% skin clearance versus placebo.[1,2]

44% of patients who received CIBINQO 100 mg and 61% of patients who received CIBINQO 200 mg achieved an EASI-75 response versus just 10% for placebo, reflecting a 4x greater improvement for CIBINQO 100 mg vs. placebo.[1,2]

Besides 75% skin clearance, the other co-primary endpoint of this study was patients who achieved an IGA of clear or almost clear (0/1). We saw that 28% and 38% of patients receiving CIBINQO 100 mg and 200 mg, respectively, achieved an IGA response compared with 9% of patients receiving placebo at week 12.[1,2]

Results were similar for JADE MONO-1[1,2]

FRAME 16:

On the next few slides, we are going to look at some photos of clinical trial patients treated with CIBINQO monotherapy.

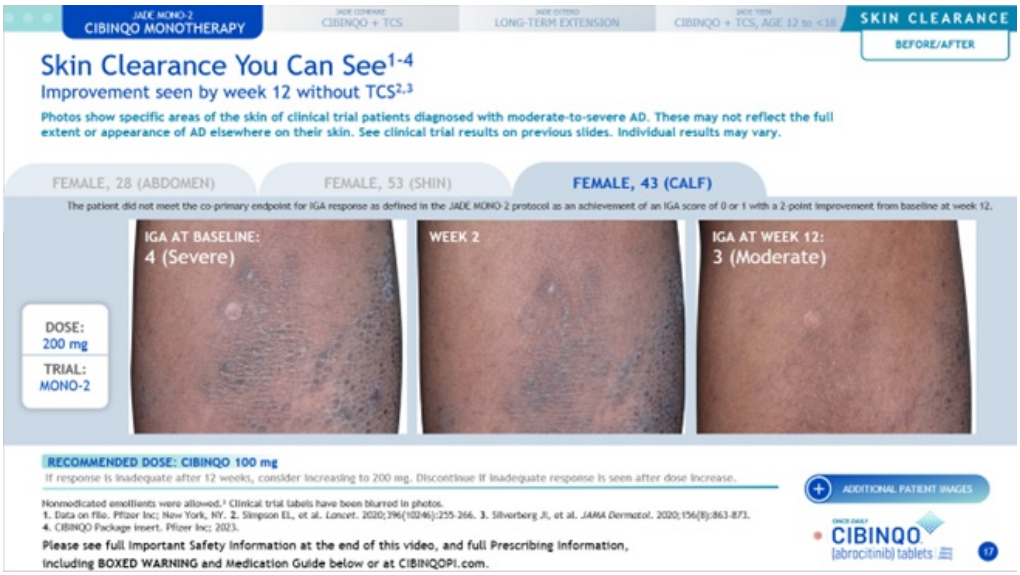
The photos on this slide show a 28-year-old female's abdomen. She had moderate atopic dermatitis, as defined by IGA 3 at baseline, and achieved almost clear skin, as defined by IGA 1, after 12 weeks of treatment with CIBINQO 100 mg.

Not everyone will respond to treatment with CIBINQO. Individual results may vary.

FRAME 17:

These are images of a 53-year-old female's shin. She had moderate atopic dermatitis, as defined by IGA 3 at baseline, and achieved almost clear skin, as defined by IGA 1, after 12 weeks of treatment with CIBINQO 100 mg without topical corticoid steroids.

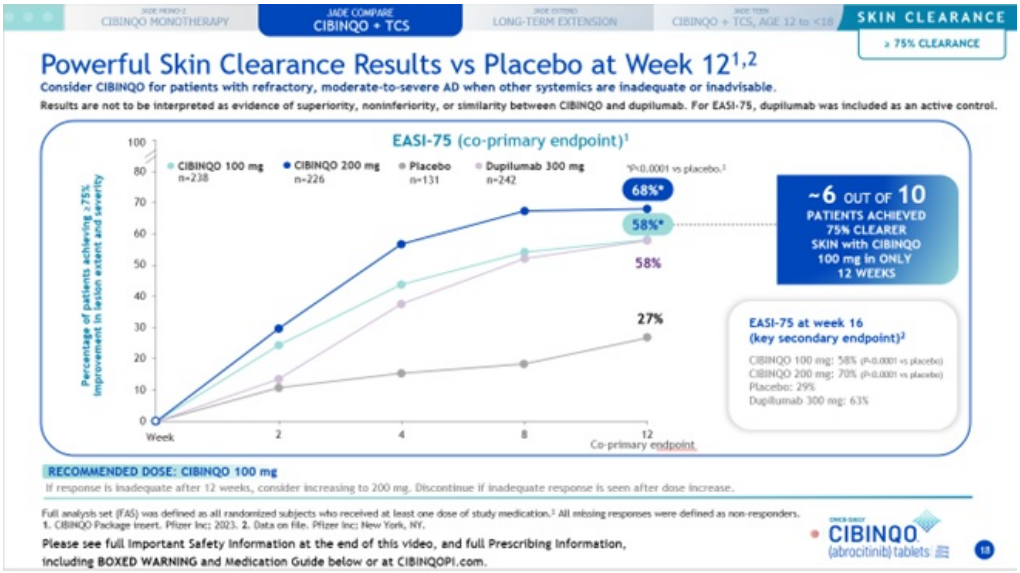
FRAME 18:



On this slide, we are going to look at photos of a 43-year-old female's calf.

This patient had severe AD, as defined by IGA 4 at baseline, and achieved moderate AD, defined by IGA 3 after 12 weeks of treatment with CIBINQO 200 mg once daily.[1] But despite this improvement, the patient did not meet the co-primary endpoint for IGA response as defined in the JADE MONO-2 protocol as an achievement of an IGA score of 0 or 1 with a 2-point improvement from baseline at week 12.

FRAME 19:



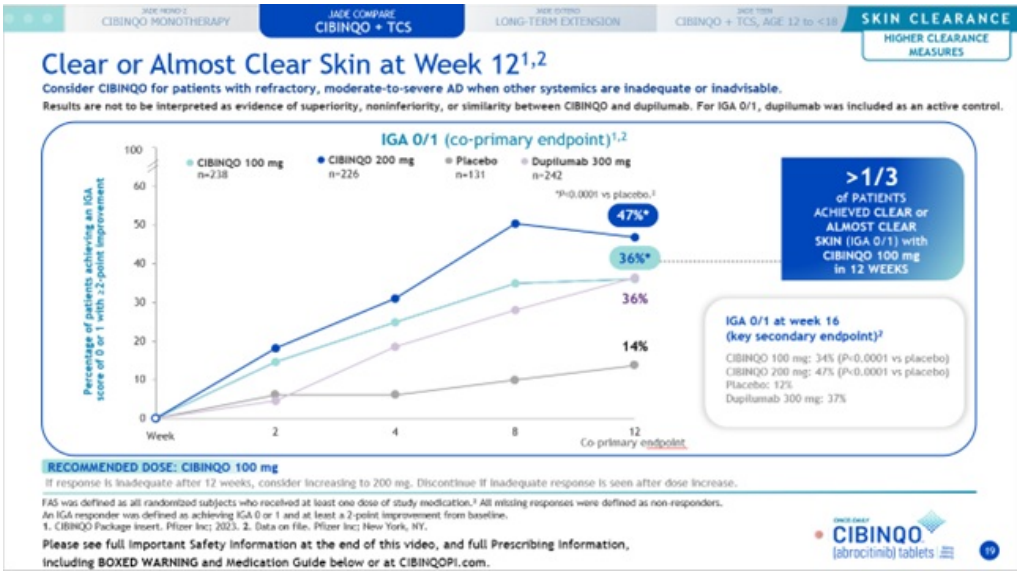
We mentioned previously, that one of the co-primary endpoints in the JADE studies was patients who achieved 75% skin clearance or EASI 75. On this slide, we will discuss that EASI-75 endpoint in patients who received CIBINQO + TCS in the JADE COMPARE study.[1]

Treatment with CIBINQO was associated with powerful skin clearance results at week 12 vs placebo. [1]

For EASI-75 at week 12, 58% of patients receiving 100 mg and 68% of patients receiving 200 mg of patients treated with CIBINQO had achieved a response vs just 27% for placebo with background topical therapy.[1]

For EASI-75 at week 16, the key secondary endpoint, 58% on the 100 mg) and 70% on the 200 mg of patients treated with CIBINQO had achieved a response vs 63% with dupilumab and 29% with placebo.[2]

FRAME 20:



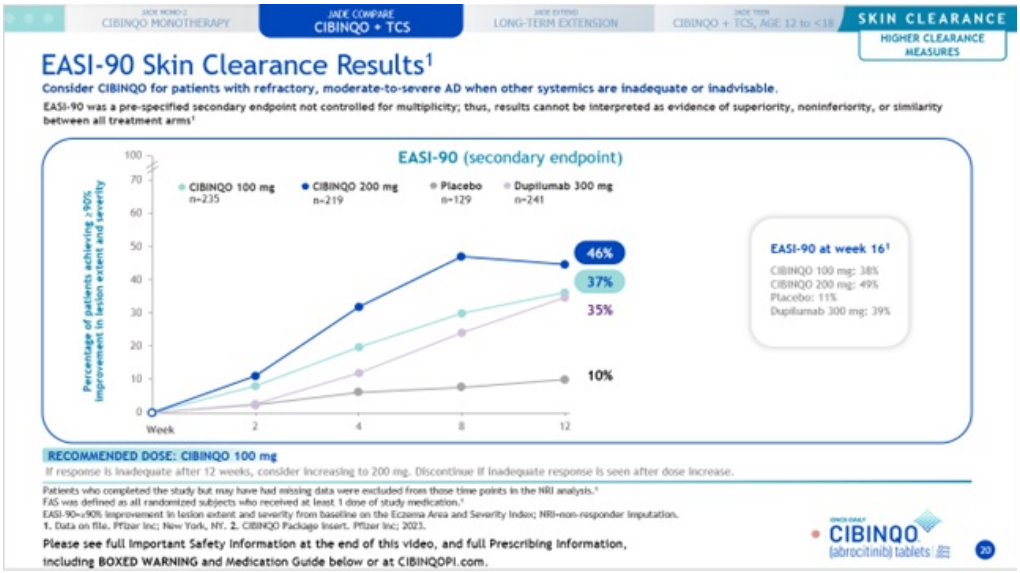
On this slide, we will discuss the other co-primary endpoint among patients who received CIBINQO+topical corticoid steroids, which as mentioned earlier was patients who achieved an IGA of clear or almost clear (0/1).

Treatment with CIBINQO was associated with clear or almost clear skin versus placebo at week 12.[1]

For IGA at week 12, 36% of patients on the 100 mg dose and 47% of patients on the 200 mg dose of patients treated with CIBINQO had achieved a response versus just 14% for placebo with background topical therapy.[1]

A key secondary endpoint of JADE COMPARE was an IGA 0/1 at week 16. For this endpoint, 34% of patients with 100 mg and 47% of patients with 200 mg of patients treated with CIBINQO achieved a response versus 37% with dupilumab and 12% with placebo.[2]

FRAME 21:

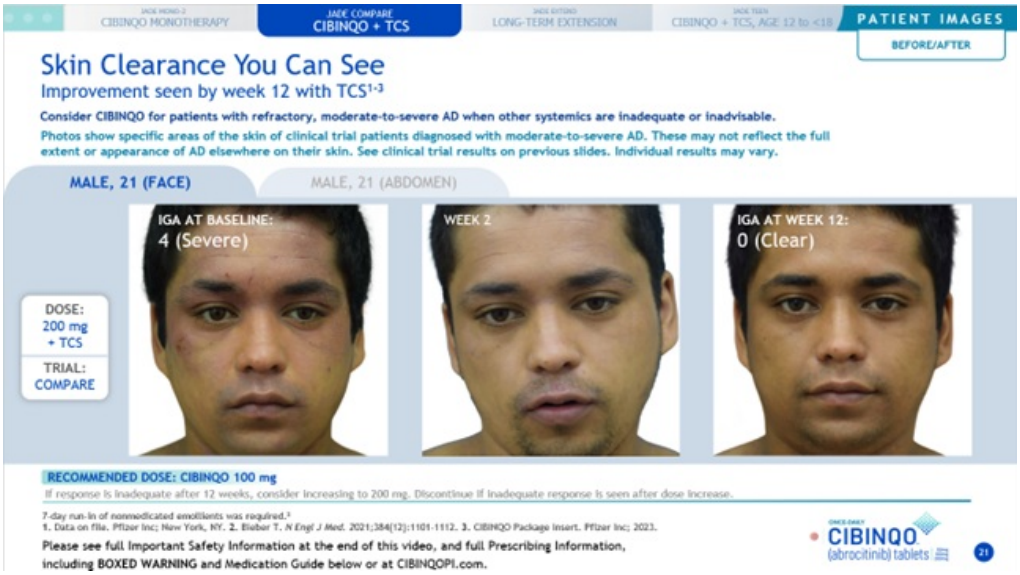


Still focusing on JADE COMPARE, lets now look at the 90% skin clearance or EASI-90 results. EASI-90 was a prespecified secondary endpoint not controlled for multiplicity. Results cannot be interpreted as evidence of superiority, noninferiority, or similarity between all treatment arms.

After 12 weeks of treatment, 37% of patients on the 100 mg dose and 46% of patients on the 200 mg dose of patients treated with CIBINQO had achieved an EASI-90 response as did 35% with dupilumab and 10% with placebo.

For EASI-90 at week 16, 38% of patients with 100 mg and 49% of patients with 200 mg of patients treated with CIBINQO had achieved a response versus 39% with dupilumab and 11% with placebo.

FRAME 22:



On this slide and the next one we will look at photos of one clinical trial patient using CIBINQO in combination with topical corticosteroids in areas including the face and abdomen

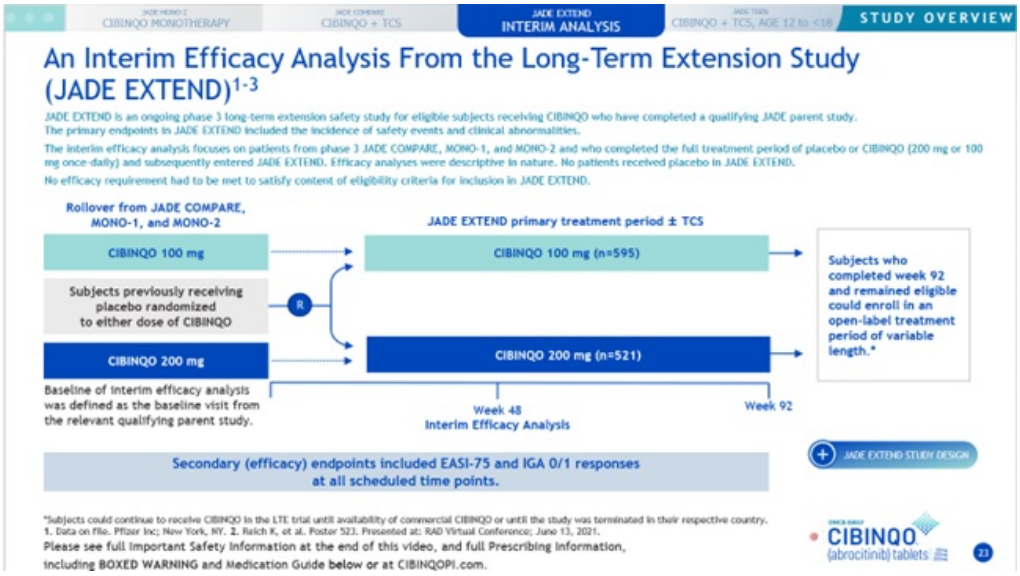
This patient had severe AD, as defined by IGA 4 at baseline, and achieved clear skin, as defined by IGA 0, after 12 weeks of treatment with CIBINQO 200 mg once daily plus topical corticosteroids.[1]

FRAME 23:

This is the abdomen of the same patient discussed on the previous slide.

And as a reminder this patient had severe AD, as defined by IGA 4 at baseline, and achieved clear skin, as defined by IGA 0, after 12 weeks of treatment with CIBINQO 200 mg once daily plus topical corticosteroids.[1]

FRAME 24:



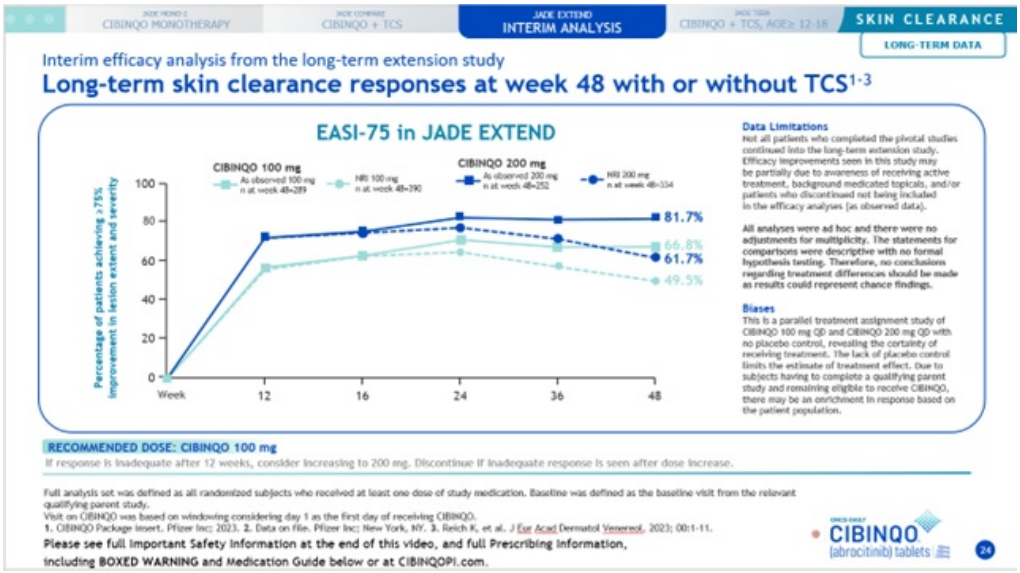
We will now review the design of a 48-week interim efficacy analysis from JADE EXTEND, which is a long-term extension (LTE) safety study evaluating patients taking CIBINQO. The primary endpoints of JADE EXTEND are incidence of safety events and clinical abnormalities, but the secondary endpoints included efficacy as well.

This analysis focuses on patients from the phase 3 JADE COMPARE, MONO-1, and MONO-2 studies who completed the full treatment period with placebo or CIBINQO and subsequently entered JADE EXTEND to receive CIBINQO 100 mg or 200 mg daily.

The secondary efficacy endpoints evaluated in this analysis included EASI-75 response and IGA 0/1 response with ≥2-point improvement at all scheduled time points.

After all the phase 3 data have been reviewed in full, we will then discuss the overall safety profile of CIBINQO, which includes the safety outcomes from JADE EXTEND.

FRAME 25:



On this slide and the next one, we will review the results of the 48-week interim analysis. This was an ad hoc analysis that was descriptive in nature and was not adjusted for multiplicity. As expected, not all patients who completed the pivotal studies continued into the long-term extension study. Also, based on the study population, it is possible that there may be an enrichment in response as well as

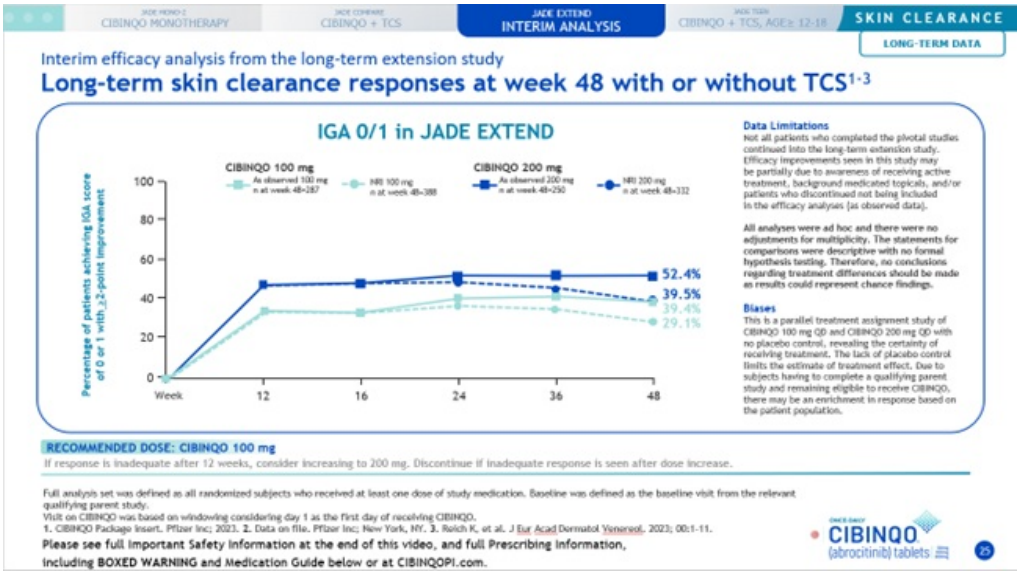
patient awareness of receiving active treatment.

We will be focusing on the 2 secondary efficacy endpoints mentioned on the previous slide: EASI-75 response and IGA 0/1 response. Let's begin by looking at the EASI-75 responses at week 48.

For the observed population, 66.8% of patients taking CIBINQO 100 mg and 81.7% of patients taking CIBINQO 200 mg achieved a response at week 48.

For the population included in the NRI analysis, 49.5% of patients taking CIBINQO 100 mg and 61.7% of patients taking CIBINQO 200 mg achieved a response at week 48.

FRAME 26:

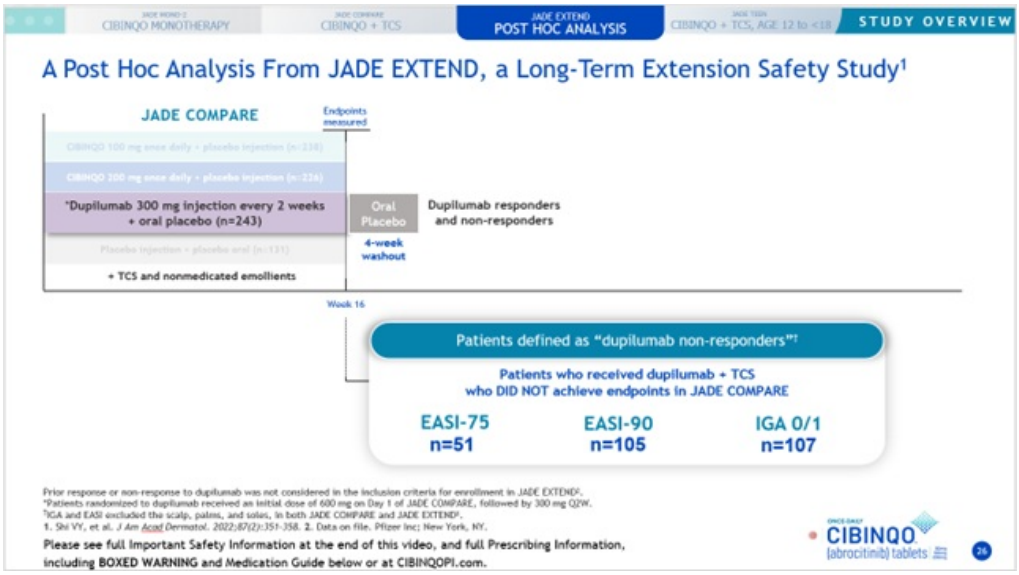


Now, we will discuss IGA 0/1 responses at week 48.

For the observed population, 39.4% of patients taking CIBINQO 100 mg and 52.4% of patients taking CIBINQO 200 mg achieved a response at week 48.

For the population included in the NRI analysis, 29.1% of patients taking CIBINQO 100 mg and 39.5% of patients taking CIBINQO 200 mg achieved a response at week 48.

FRAME 27:



Now, lets discuss an additional data cut from JADE EXTEND: a post hoc analysis of the long-term safety study.

The post hoc analysis, evaluated adults who received dupilumab in JADE COMPARE and then received CIBINQO in JADE EXTEND.

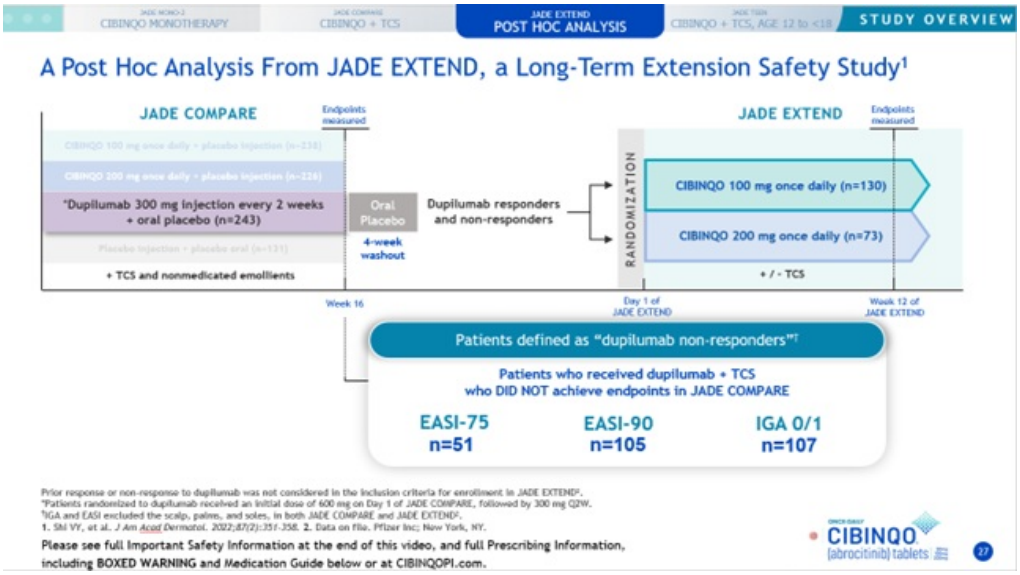
Previously, we reviewed JADE COMPARE. And as you may recall, patients in that study were randomized to receive CIBINQO 100 mg once daily, CIBINQO 200 mg once daily, dupilumab, or placebo for 16 weeks.[1]

At the end of the 16-week washout period, patients receiving dupilumab entered a 4-week washout period and eligible patients could then enter JADE EXTEND.[1]

The patients who had received dupilumab in JADE COMPARE were assessed for their response to treatment in that study and classified as dupilumab “responders” or “non-responders.” Prior dupilumab responders were patients who achieved 1 or more of the following responses IGA of clear or almost clear with a ≥2-grade improvement (IGA 0/1); ≥75% improvement in EASI also referred to as EASI-75; ≥90% improvement in EASI also referred to as EASI-90 at week 16 of JADE COMPARE.[1]

Of note, prior response or non-response to dupilumab was not considered in the inclusion criteria for enrollment in JADE EXTEND. Not all patients who completed the pivotal studies continued into the long-term extension study.[2]

FRAME 28:

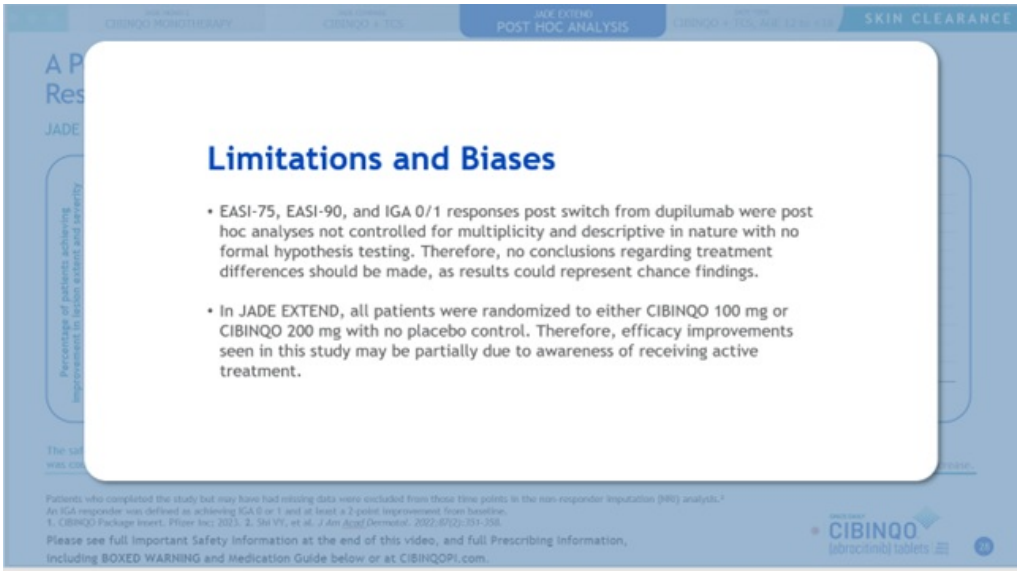


Patients who completed the washout period were then assigned to receive CIBINQO 200 mg or 100 mg once daily. There were no patients on placebo in JADE EXTEND.

This post hoc analysis evaluated the patients from JADE COMPARE taking dupilumab + topical corticosteroids who did not achieve EASI-75, EASI-90, or IGA 0/1 at week 16 and enrolled in JADE EXTEND and completed 12 weeks of treatment with CIBINQO we will refer to these patients as “dupilumab non-responders”.

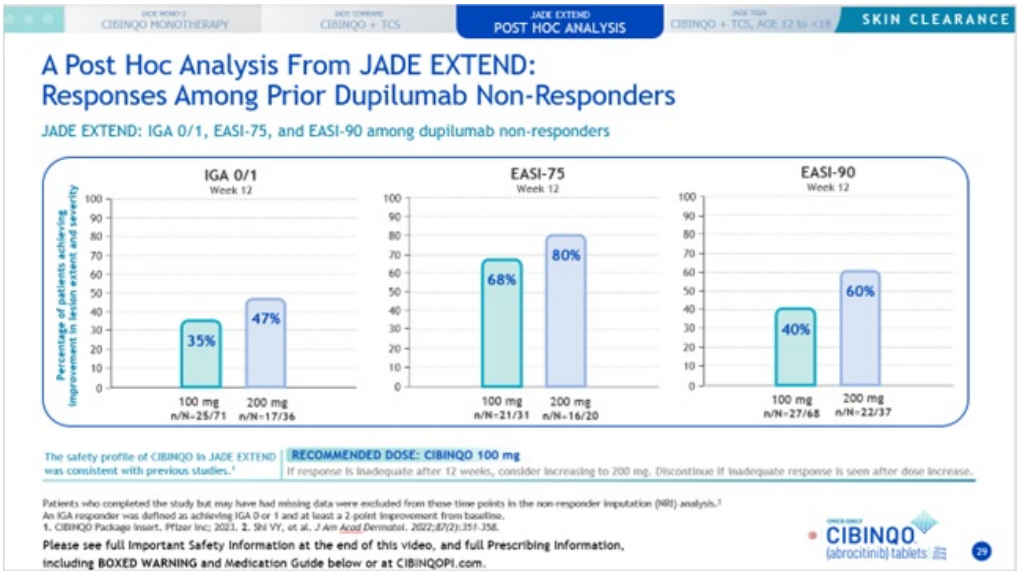
It also evaluated the patients from JADE COMPARE taking dupilumab + topical corticosteroids who did achieve EASI-75, EASI-90, or IGA 0/1 at week 16 and enrolled in JADE EXTEND and completed 12 weeks of treatment with CIBINQO we will refer to these patients as “dupilumab responders”); however, in this presentation, we will specifically look at outcomes for the “dupilumab non-responder” subset.

FRAME 29:



The post-hoc analyses are not controlled for multiplicity and are descriptive in nature, so no conclusions regarding treatment differences should be made.

FRAME 30:



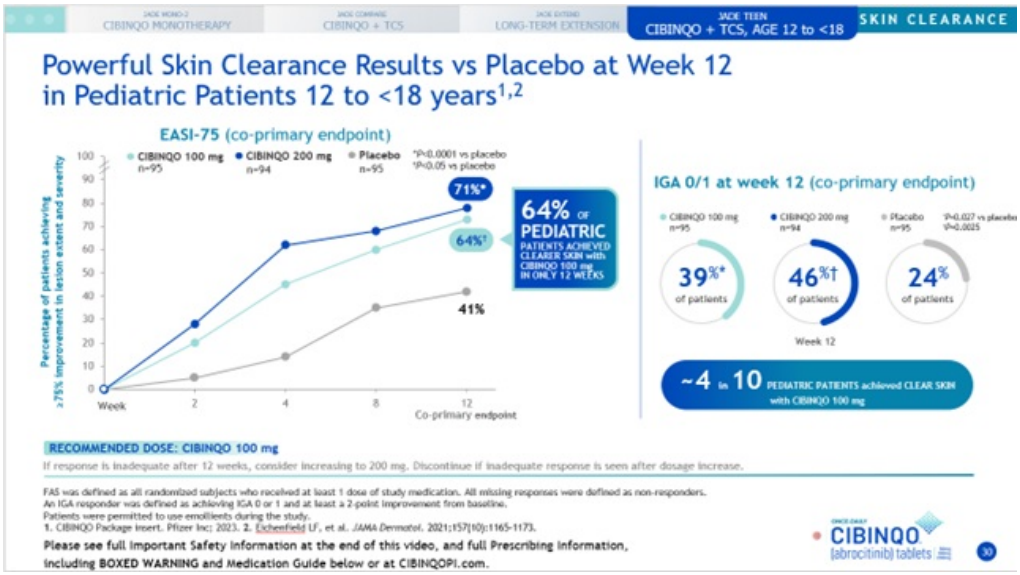
Among prior dupilumab IGA 0/1 non-responders (n=107), 35% taking CIBINQO 100 mg and 47% of dupilumab non-responders taking CIBINQO 200 mg achieved an IGA of 0/1 at week 12 of JADE EXTEND.[1]

Among the patients who did not achieve EASI-75 with dupilumab in JADE COMPARE (n=51), 68% taking CIBINQO 100 mg and 80% of dupilumab non-responders taking CIBINQO 200 mg achieved EASI-75.

And among EASI-90 non-responders (n=105), 40% taking CIBINQO 100 mg and 60% taking CIBINQO 200 mg achieved EASI-90 at week 12 of JADE EXTEND.[1]

The safety profile of CIBINQO in JADE EXTEND was consistent with previous studies.[2]

FRAME 31:

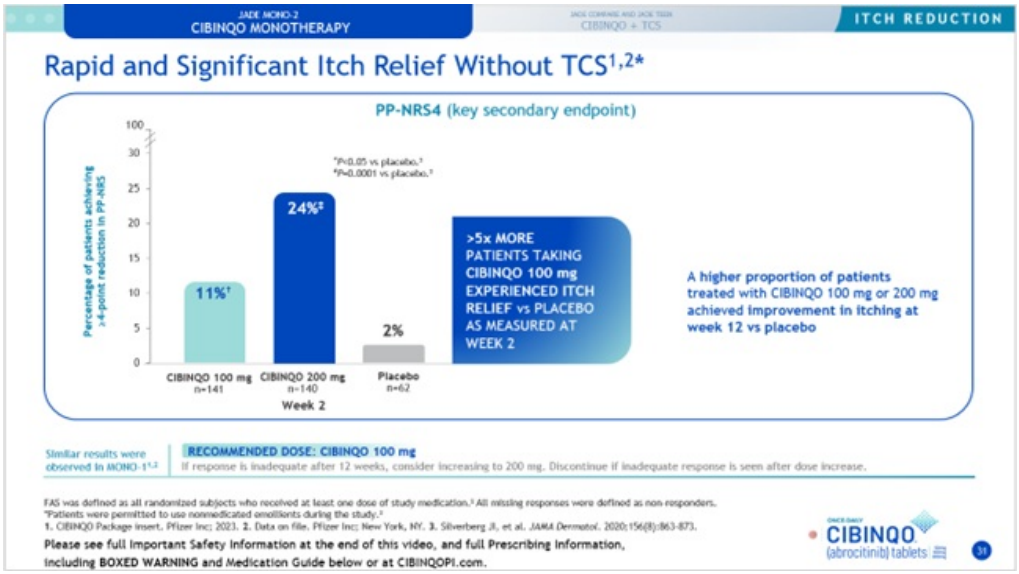


Noting that CIBINQO is approved for use in adolescent patients 12 years of age and older, we will now discuss the skin clearance results from JADE TEEN study, which as a reminder, evaluated CIBINQO + topical corticosteroids against placebo in adolescents who were 12 to less than 18 years old.

The co-primary endpoint of patients achieving 75% skin clearance (EASI-75) was achieved in 64% of patients who received CIBINQO 100 mg and 71% of patients who received CIBINQO 200 mg versus 41% for placebo at week 12.

The other co-primary endpoint of JADE TEEN was patients who achieved an IGA of clear or almost clear (0/1). And we saw that 39% and 46% of patients receiving CIBINQO 100 mg and 200 mg, respectively, achieved an IGA response compared with 24% of patients receiving placebo at week 12.

FRAME 32:



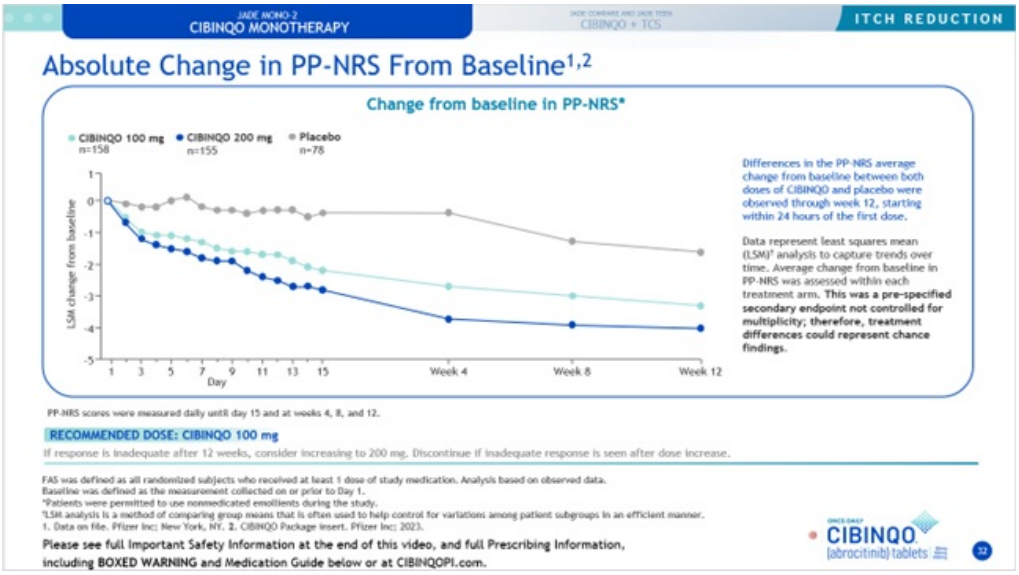
On the previous slides, we reviewed skin clearance data. But now, lets take a look at the itch data, beginning with JADE MONO.

We see that significantly more patients treated with CIBINQO 100 mg (11%) or 200 mg (24%) experienced itch reduction as early as week 2 versus placebo (2%).[1,2]

Which is >5x more patients taking CIBINQO 100 mg versus placebo experienced itch reduction as early as week 2.

A higher proportion of patients in the CIBINQO 100 mg or 200 mg once-daily arm achieved improvement in itch compared with placebo at week 12.[1,2]

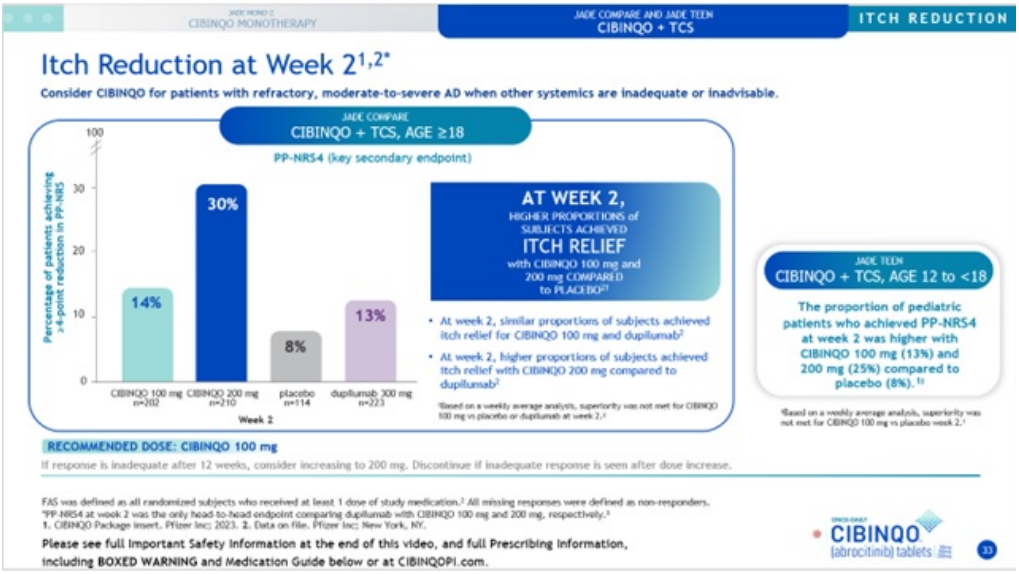
FRAME 33:



Still focusing on itch data from JADE MONO, let's now look at the absolute change from baseline in Peak Pruritus-NRS. This data shows the average change from baseline at each timepoint. Of note, this was a pre-specified secondary endpoint not controlled for multiplicity; and therefore, treatment differences could represent chance findings.

We can see differences in the Peak Pruritus-NRS average change from baseline between both doses of CIBINQO (100 mg and 200 mg) vs placebo through week 12, starting within 24 hours of the first dose.

FRAME 34:



We will now look at the Peak Pruritus-NRS endpoint in patients who received CIBINQO + topical corticosteroids across 2 studies: JADE COMPARE, which enrolled adults only, and JADE TEEN, which enrolled patients 12 to less than 18 years of age.

In JADE COMPARE, at week 2, higher proportions of patients achieved itch relief which we define as a ≥4 - point reduction in Peak Pruritus-NRS with CIBINQO 100mg and 200 mg compared to placebo.[1,2]

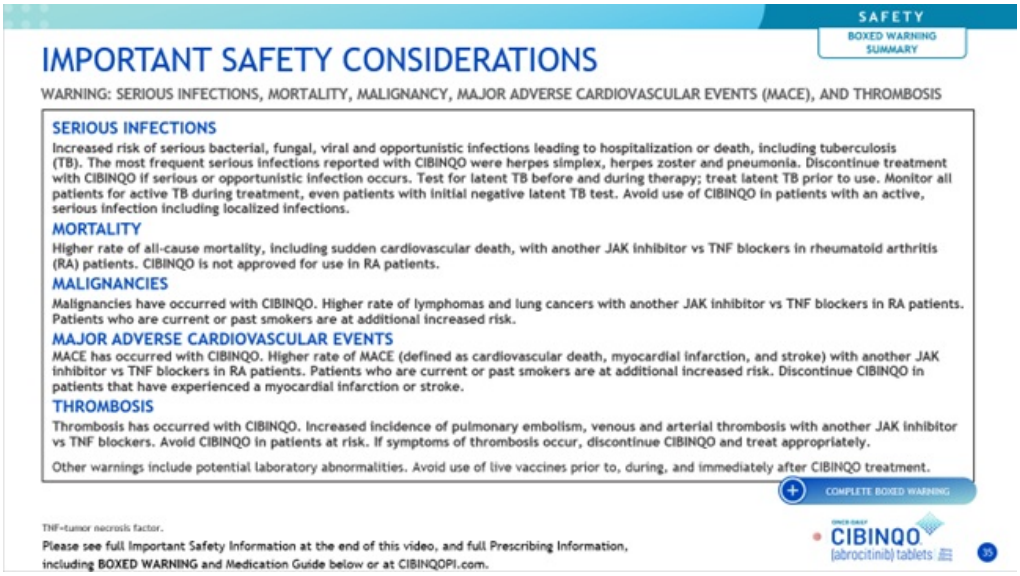
For the same Peak Pruritus-NRS4 endpoint in the JADE TEEN study, the proportion of pediatric patients who achieved Peak Pruritus-NRS4 at week 2 was higher with CIBINQO 100 mg which we saw in 13% and 200 mg which we saw in 25% compared to placebo which

we saw in 8%.[1]

FRAME 35:

We will now review the important safety information for CIBINQO, including pooled safety data from the clinical trial program.

FRAME 36:

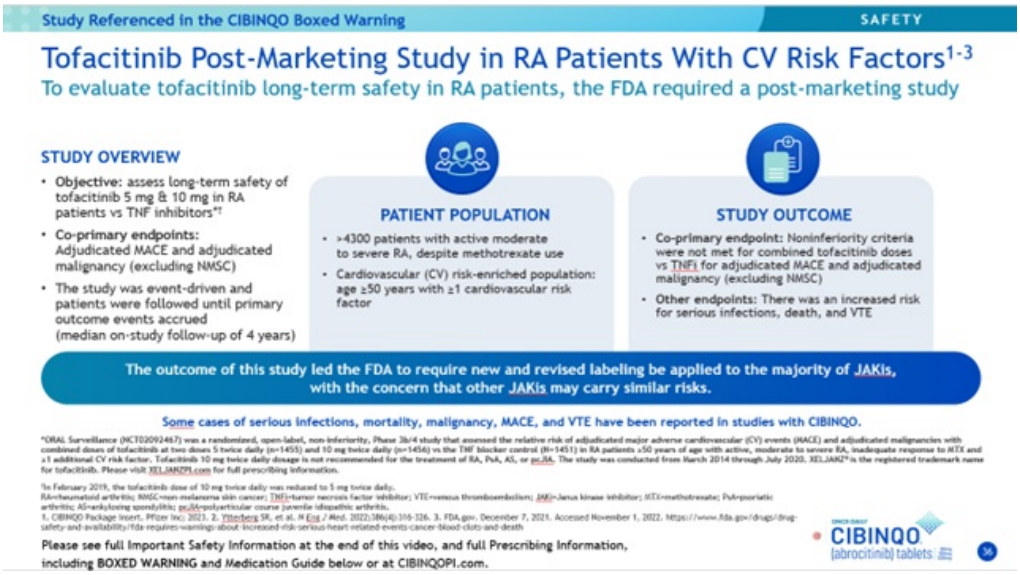


As mentioned earlier, CIBINQO has a Boxed Warning for serious infections, mortality, malignancies, MACE, and thrombosis.

Other warnings include potential lab abnormalities.

We'll now discuss additional details about these warnings and the adverse reactions observed in the JADE clinical trial program.

FRAME 37:



It may be helpful to understand additional background related to the study that is referenced in the CIBINQO Boxed Warning.

To evaluate tofacitinib long-term safety in rheumatoid arthritis (RA) patients, the FDA required a post-marketing study.[2] As a reminder, CIBINQO is not approved for the treatment of RA.[1,3]

Study Overview: The study, called ORAL Surveillance, is a long-term safety study that evaluated tofacitinib 5 mg and 10 mg against a TNF inhibitor.[3,4]

The co-primary endpoints were adjudicated MACE and adjudicated malignancies (excluding non-melanoma skin cancers). Other endpoints included mortality, serious infections, and thromboembolic events.

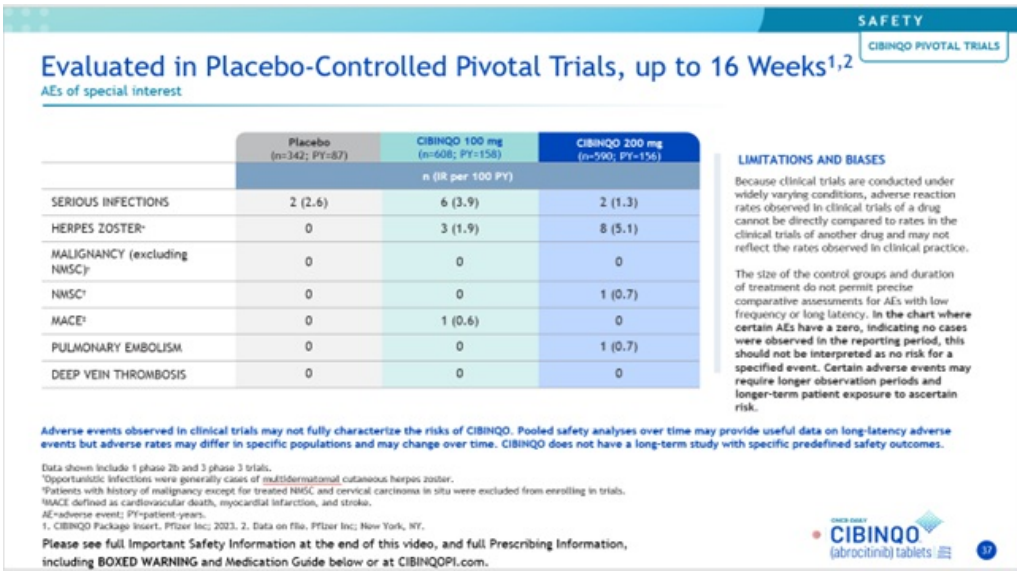
The study was event-driven and patients were followed until a sufficient number of primary outcome events accrued. The median on-study follow-up time was 4.0 years.

Patient Population: Over 4300 patients were included in this trial with active moderate-to-severe rheumatoid arthritis despite methotrexate who were 50 years of age or older and had at least one cardiovascular risk factor.[3,4]

Study Outcomes[3,4]:

- The study found that the risks of the co-primary endpoints (adjudicated MACE and adjudicated malignancy, excluding non-melanoma skin cancers) were found to be higher with the combined doses of tofacitinib than with a TNF inhibitor. For these endpoints, the noninferiority criteria were not met for the comparison of the combined JAKi doses to the TNF inhibitor
- Analysis of other endpoints found an increased risk for serious infections, adjudicated venous thromboembolic events, and death from any cause with tofacitinib than with a TNF inhibitor
- The findings from ORAL Surveillance led the FDA to require new and revised labeling be applied to the majority of JAK inhibitors, with the concern that other JAKis in the class may carry similar risks[2]
- Some cases of serious infections, mortality, malignancy, major adverse cardiovascular events, and thrombosis have been reported in studies with CIBINQO.1 So, let's transition back to the safety profile for CIBINQO

FRAME 38:



We will first look at a pooled analysis of specific adverse reactions from the 16-week placebo-controlled trials.

Serious Infections:

- Serious infections were reported in 2 subjects (2.6 per 100 patient-years) treated with placebo, 6 subjects (3.9 per 100 patient-years) treated with CIBINQO 100 mg, and 2 subjects (1.3 per 100 patient-years) treated with CIBINQO 200 mg

Herpes Zoster:

- Opportunistic infections were generally cases of multidermatomal cutaneous herpes zoster. Herpes zoster was reported in 0 subjects treated with placebo, 3 subjects (1.9 per 100 patient-years) treated with CIBINQO 100 mg, and 8 subjects (5.1 per 100 patient-years) treated with CIBINQO 200 mg

Malignancy:

- No malignancy was reported in subjects treated with placebo or CIBINQO 100 mg and in 1 patient (0.65 per 100 patient-years) treated with CIBINQO 200 mg
- Including all malignancies, which included non-melanoma skin cancer (NMSC). Patients with history of malignancy except for treated non-melanoma skin cancer and cervical carcinoma in situ were excluded from enrolling in trials

Major Adverse Cardiovascular Events[1]:

- MACE was reported in 1 subject (0.6 per 100 patient-years) treated with CIBINQO 100 mg

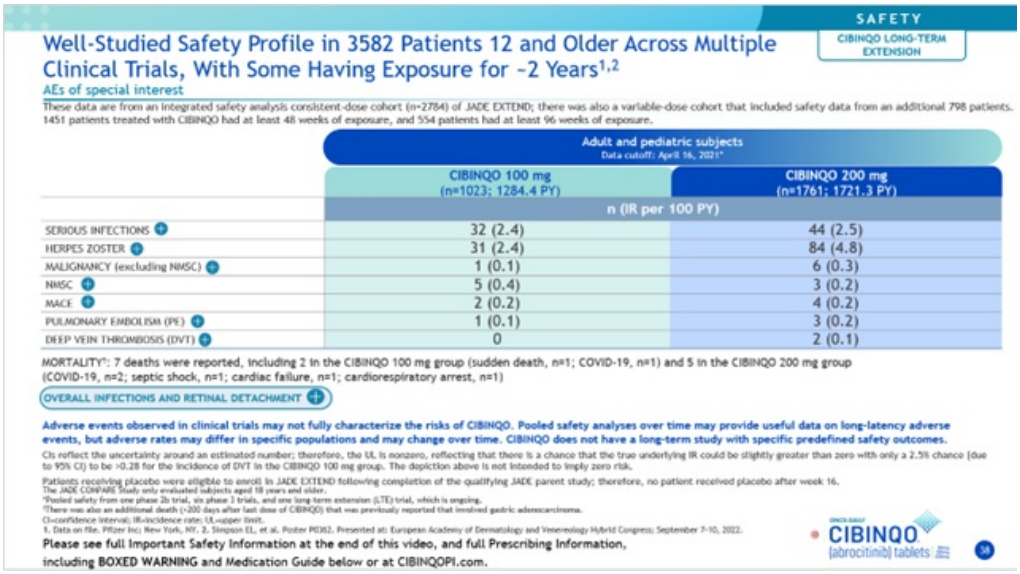
Pulmonary Embolism:

- Pulmonary embolism was reported in 1 subject (0.7 per 100 patient-years) treated with CIBINQO 200 mg

Deep Vein Thrombosis:

- And there were no reports of deep vein thrombosis
- Instances where you see zeros are not meant to be translated as zero risk; rather, it depicts what actually occurred in the placebo-controlled trials up to 16 weeks

FRAME 39:



Now, let's look at the pooled safety analysis including the long-term extension data.

This is a pooled analysis that can help provide useful data on long-latency adverse events.

So it is important to note that CIBINQO does not have a long-term study with specific pre-defined safety outcomes.

So Let's look at the data.

Serious Infections:

- Serious infections were reported in 32 subjects (2.4 per 100 patient-years) treated with CIBINQO 100 mg and 44 subjects (2.5 per 100 patient-years) treated with CIBINQO 200 mg. The most reported serious infections were herpes simplex, herpes zoster, and pneumonia

Herpes Zoster:

- Herpes zoster was reported in 31 subjects (2.4 per 100 patient-years) treated with CIBINQO 100 mg and 84 subjects (4.8 per 100 patient-years) treated with CIBINQO 200 mg
- Opportunistic infections were generally cases of nonserious multidermatomal herpes zoster. There was 1 event of adjudicated tuberculosis

Malignancy:

- Malignancy was reported in 1 subject (0.1 per 100 patient-years) treated with CIBINQO 100 mg and 6 subjects (0.3 per 100 patient-years) treated with CIBINQO 200 mg
- This includes all malignancy, including non-melanoma skin cancer (NMSC). Patients with a history of malignancy, except for treated NMSC and cervical carcinoma in situ, were excluded from enrolling in the trials
- There were 8 reported cases of NMSC: 5 subjects (0.4 per 100 patient-years) on 100 mg and 3 subjects (0.2 per 100 patient-years) on 200 mg

Major Adverse Cardiovascular Events:

- Major adverse cardiovascular event was reported in 2 subjects (0.2 per 100 patient-years) treated with CIBINQO 100 mg and 4 subjects (0.2 per 100 patient-years) treated with CIBINQO 200 mg.
- MACE was defined as cardiovascular death, myocardial infarction, and stroke

Pulmonary Embolism:

- Pulmonary embolism was reported in 1 subject (0.1 per 100 patient-years) treated with CIBINQO 100 mg and 3 subjects (0.2 per

100 patient-years) treated with CIBINQO 200 mg
- One pulmonary embolism event (not adjudicated) was included

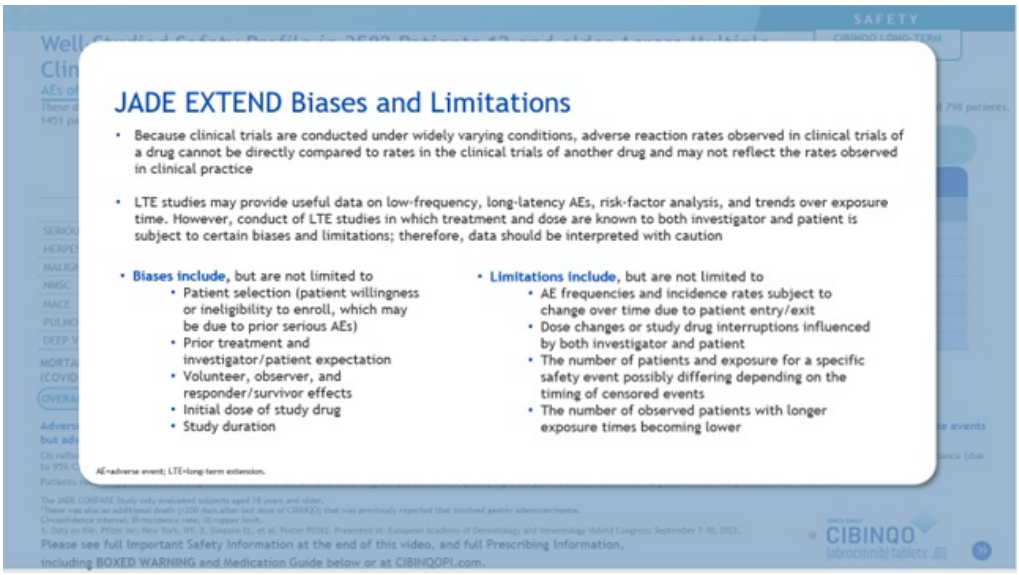
Deep Vein Thrombosis:

- Deep vein thromboses was reported in 2 subjects (0.1 per 100 patient-years) who were treated with CIBINQO 200 mg

Mortality:

- Seven deaths were reported: 1 subject with sudden death and 1 subject with COVID-19 infection treated with CIBINQO 100 mg, and 2 subjects with COVID-19 infection and 1 subject each with septic shock, cardiac failure, and cardiorespiratory arrest treated with CIBINQO 200 mg
- Instances where you see zeros are not meant to be translated as zero risk. For example, in the CIBINQO 100 mg group, no cases of DVT were reported in the clinical trials, but the incidence rate is estimated to be between 0.00 and 0.28

FRAME 40:

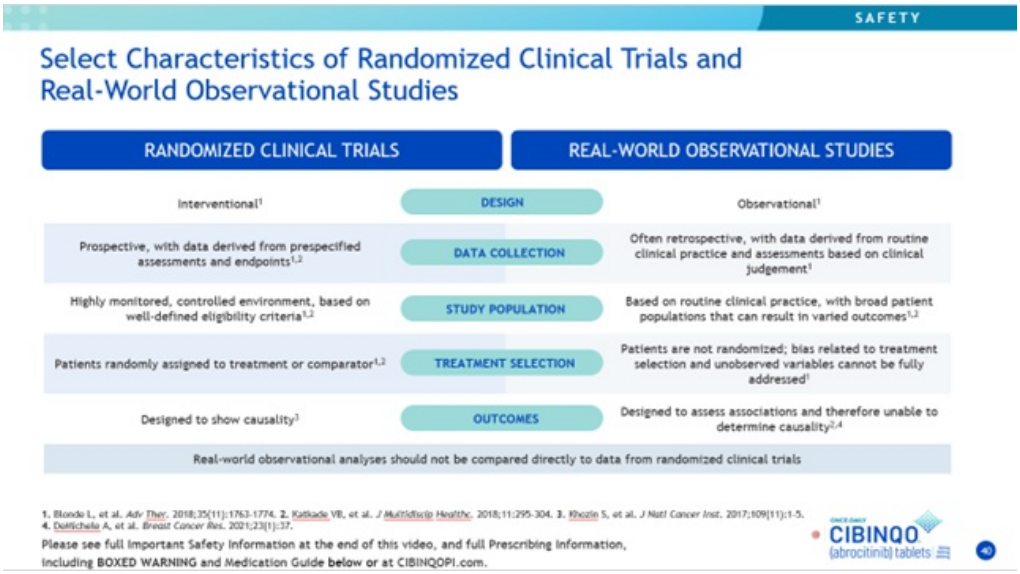


The adverse reaction rates observed in clinical trials of a drug cannot be compared to rates in clinical trials of a different drug. Also, the rates may not be reflective of the rates that are actually observed in clinical practice.

Additionally, although data from LTE studies may be useful, it should be interpreted with caution as the treatment and dose are known to the investigator and patient and may be subject to biases.

There are specific biases and limitations listed here for your reference as well. We will pause for a few moments to ensure you have had enough time to review these.

FRAME 41:



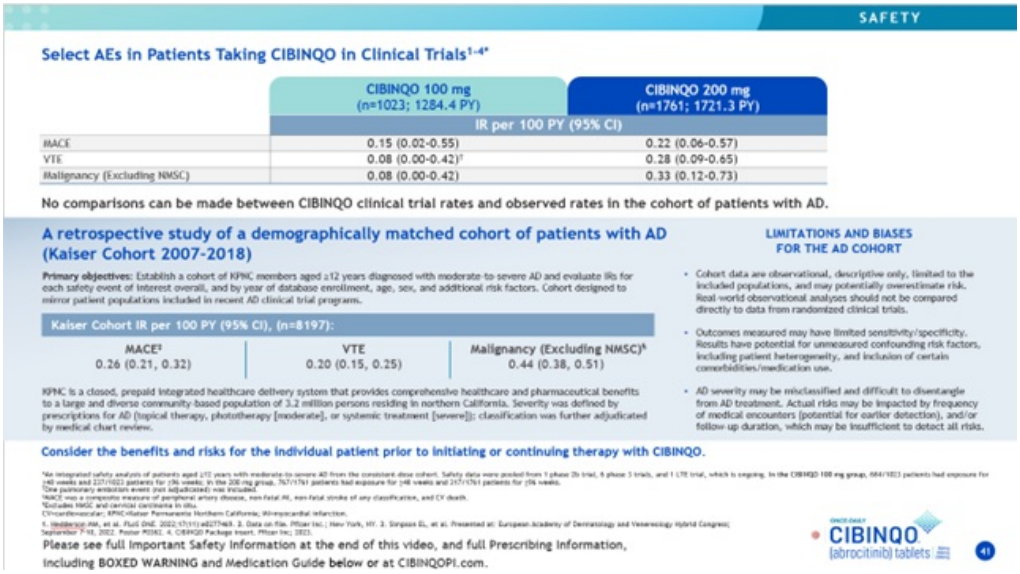
The pooled safety data we just looked at came from clinical trials.1 On the following slide, though, we are going to take a look at observational data from a retrospective study of a demographic-matched cohort of patients with AD. So it is important that we understand the differences between these 2 types of studies before looking at the data.

Randomized clinical trials are interventional, prospective studies with data derived from pre-specified assessments and endpoints. These studies are highly monitored and controlled, with the study population being based on well-defined eligibility criteria. In randomized clinical trials, patients are randomly assigned to treatment or comparator arms. And the outcomes are designed to show causality.

In contrast, real-world observational studies are often retrospective, with data derived from routine clinical practice and assessments based on clinical judgement. The study population is typically broad, which can result in varied outcomes. Patients in real-world observational studies are not randomized, so certain biases related to treatment selection and unobserved variables cannot be entirely addressed. The outcomes in this type of study are designed to assess associations and therefore cannot determine causality.

Given the differences between these two different types of studies, it is important to keep in mind that real-world observational analyses should not be compared directly to data from randomized clinical trials.

FRAME 42:



This slide shows the incidence rates per 100 patient-years that we reviewed for CIBINQO's long-term, dose-controlled pooled data for MACE; VTE; and malignancy, excluding non-melanoma skin cancers. As a reminder, 1 case per 100 patient-years is the same as saying 1 case was observed among 100 patients during 1 year of exposure.

In the chart below, for each of these AEs, you see a Kaiser cohort consisting of 8197 patients aged ≥12 years of age with moderate-to-severe AD, designed to mirror patient populations included in recent atopic dermatitis clinical trial programs.[1,2]

These data may help provide HCPs with a frame of reference for incidence rates of these AEs in a demographically matched cohort of patients with moderate-to-severe atopic dermatitis. As a reminder, no comparisons can be made between CIBINQO clinical trial rates and observed rates in the cohort of patients with AD.

Before we take a closer look at the data, let's discuss some additional limitations associated with interpreting the results:

- Cohort data are observational and may overstate risk. Data from these studies should not be directly compared to data from randomized clinical trials due to differing characteristics such as those discussed on the previous slide
- Additionally, the outcomes may not fully capture all details and unmeasured risk factors like patient differences and specific health conditions. It is also important to be mindful that it may be challenging to distinguish AD severity from AD treatment effects, which could result in misclassification. Lastly, the actual risks may be influenced by how often patients have medical visits as well as the duration of follow-up

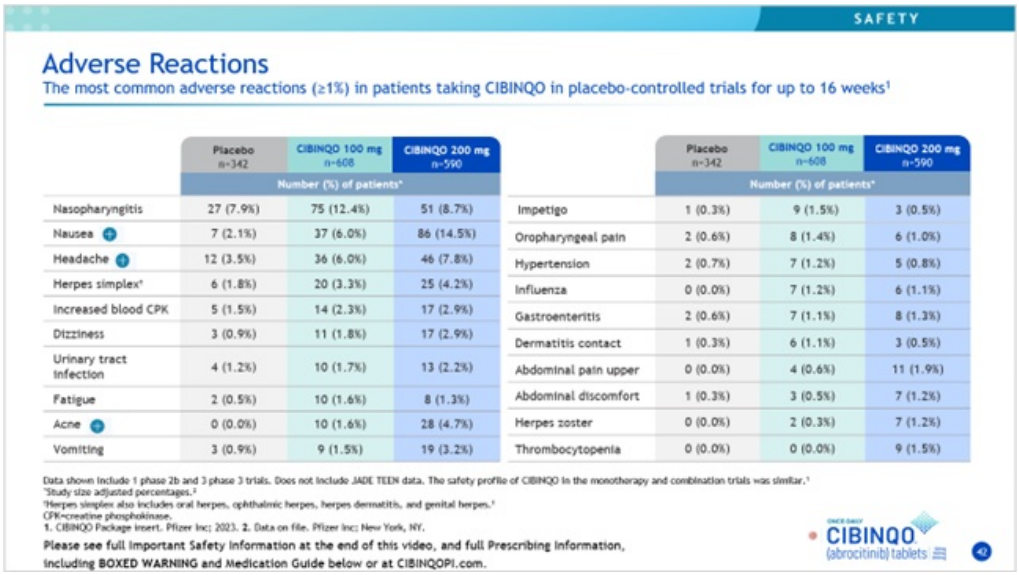
CIBINQO Incidence Rates[3]:

- The incidence rate per 100 patient years; PY (95% CI) for MACE with CIBINQO in the clinical trial program was 0.15 (0.02-0.55) with CIBINQO 100 mg and 0.22 (0.06-0.57) with CIBINQO 200 mg
- The incidence rate of VTE was 0.08 (0.00-0.42) with CIBINQO 100 mg, which included one pulmonary embolism event (not adjudicated). The incidence rate of VTE with CIBINQO 200 mg was 0.28 (0.09-0.65)
- And finally, the rate of malignancy, excluding NMSC, was 0.08 (0.00-0.42) in the CIBINQO 100 mg group and 0.33 (0.12-0.73) in the CIBINQO 200 mg group

Cohort Incidence Rates[1,2]:

- The incidence rate per 100 PY (95% CI) for MACE in the Kaiser cohort was 0.26 (0.21-0.32)
- The incidence rate of VTE was 0.20 (0.15-0.25) in the Kaiser cohort
- The Kaiser cohort excluded both non-melanoma skin cancers and cervical carcinoma in situ in their reported incidence rates, which were 0.44 per 100 PY (95% CI, 0.38-0.51)

FRAME 43:


SAFETY

Adverse Reactions

The most common adverse reactions (≥1%) in patients taking CIBINQO in placebo-controlled trials for up to 16 weeks[1]

	Placebo n=342	CIBINQO 100 mg n=608	CIBINQO 200 mg n=590
	Number (%) of patients*		
Nasopharyngitis	27 (7.9%)	75 (12.4%)	51 (8.7%)
Nausea	7 (2.1%)	37 (6.0%)	86 (14.5%)
Headache	12 (3.5%)	36 (6.0%)	46 (7.8%)
Herpes simplex†	6 (1.8%)	20 (3.3%)	25 (4.2%)
Increased blood CPK	5 (1.5%)	14 (2.3%)	17 (2.9%)
Dizziness	3 (0.9%)	11 (1.8%)	17 (2.9%)
Urinary tract infection	4 (1.2%)	10 (1.7%)	13 (2.2%)
Fatigue	2 (0.5%)	10 (1.6%)	8 (1.3%)
Acne	0 (0.0%)	10 (1.6%)	28 (4.7%)
Vomiting	3 (0.9%)	9 (1.5%)	19 (3.2%)

	Placebo n=342	CIBINQO 100 mg n=608	CIBINQO 200 mg n=590
	Number (%) of patients*		
Impetigo	1 (0.3%)	9 (1.5%)	3 (0.5%)
Oropharyngeal pain	2 (0.6%)	8 (1.4%)	6 (1.0%)
Hypertension	2 (0.7%)	7 (1.2%)	5 (0.8%)
Influenza	0 (0.0%)	7 (1.2%)	6 (1.1%)
Gastroenteritis	2 (0.6%)	7 (1.1%)	8 (1.3%)
Dermatitis contact	1 (0.3%)	6 (1.1%)	3 (0.5%)
Abdominal pain upper	0 (0.0%)	4 (0.6%)	11 (1.9%)
Abdominal discomfort	1 (0.3%)	3 (0.5%)	7 (1.2%)
Herpes zoster	0 (0.0%)	2 (0.3%)	7 (1.2%)
Thrombocytopenia	0 (0.0%)	0 (0.0%)	9 (1.5%)

Data shown include 1 phase 2b and 3 phase 3 trials. Does not include JADE TEEN data. The safety profile of CIBINQO in the monotherapy and combination trials was similar.[1]
*Study size adjusted percentages.[1]
†Herpes simplex also includes oral herpes, ophthalmic herpes, herpes dermatitis, and genital herpes.[1]
CPK=creatine phosphokinase.
1. CIBINQO Package Insert. Pfizer Inc; 2023. 2. Data on file. Pfizer Inc; New York, NY.

Please see full Important Safety Information at the end of this video, and full Prescribing Information, including BOXED WARNING and Medication Guide below or at CIBINQOPI.com.

CIBINQO (abrocitinib) tablets

On this slide, we will take a look at the most common adverse reactions we just mentioned in the important safety information.

CIBINQO was studied in 1198 adults and adolescents with moderate-to-severe AD from 4 randomized, placebo-controlled clinical trials (2 monotherapy, 1 combination therapy with topical corticosteroid, and 1 dose-ranging) for up to 16 weeks.

Nasopharyngitis occurred in 7.9% of patients in the placebo group, 12.4% of patients in the CIBINQO 100 mg group, and 8.7% of patients in the 200 mg group.

Nausea occurred in 2.1% of patients in the placebo group, 6.0% of patients in the CIBINQO 100 mg group, and 14.5% of patients in the 200 mg group.

Headache occurred in 3.5% of patients in the placebo group, 6.0% of patients in the CIBINQO 100 mg group, and 7.8% of patients in the 200 mg group.

Herpes simplex occurred in 1.8% of patients in the placebo group, 3.3% of patients in the CIBINQO 100 mg group, and 4.2% of patients in the 200 mg group.

Increased blood CPK occurred in 1.5% of patients in the placebo group, 2.3% of patients in the CIBINQO 100 mg group, and 2.9% of patients in the 200 mg group.

Dizziness occurred in 0.9% of patients in the placebo group, 1.8% of patients in the CIBINQO 100 mg group, and 2.9% of patients in the 200 mg group.

Urinary tract infection occurred in 1.2% of patients in the placebo group, 1.7% of patients in the CIBINQO 100 mg group, and 2.2% of patients in the 200 mg group.

Fatigue occurred in 0.5% of patients in the placebo group, 1.6% of patients in the CIBINQO 100 mg group, and 1.3% of patients in the 200 mg group.

FRAME 44:

Discontinuation rates due to adverse events for JADE MONO-1, JADE MONO-2, and JADE COMPARE, respectively, are as follows:

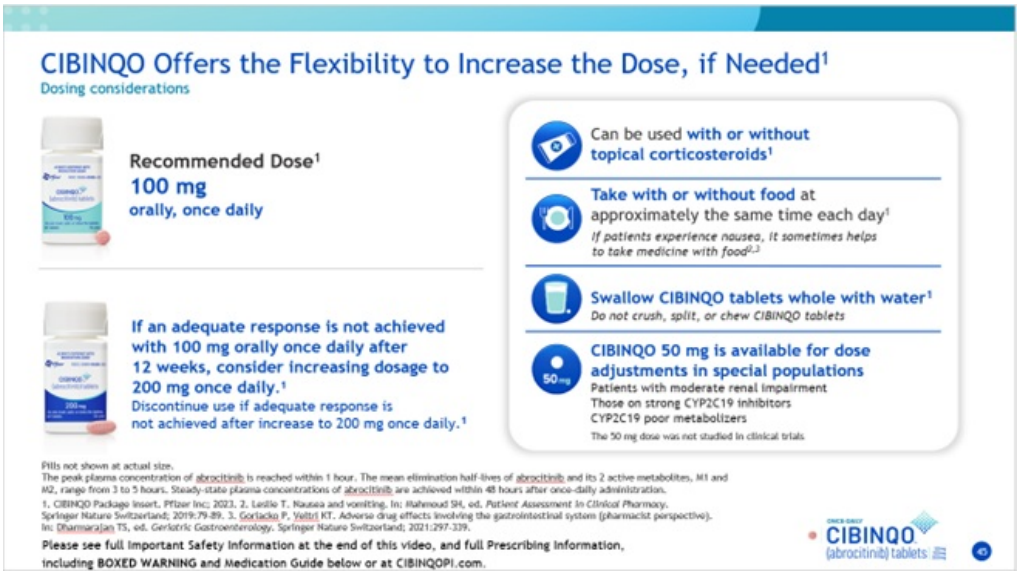
- For placebo: 9.1%, 12.8%, 3.8%
- CIBINQO 100 mg: 5.8%, 3.8%, 2.5%
- And CIBINQO 200 mg: 5.8%, 3.2%, 4.4%

The most frequent adverse event leading to discontinuation was atopic dermatitis, occurring more frequently in the placebo treatment group (5.5%) than in patients taking either dose of CIBINQO (1.2%). Other frequent adverse events leading to discontinuation, occurring more frequently in the CIBINQO group, included nausea which was 0.3% and headache (0.2%).

FRAME 45:

In this section, we are going to talk about getting patients started on CIBINQO.

FRAME 46:



Having discussed an overview of the efficacy and safety of CIBINQO in the clinical trials, we'll now talk about how CIBINQO offers the flexibility to increase the dosage if needed.[1]

- The recommended dosage of CIBINQO is 100 mg orally, once daily
- After 12 weeks, if a patient's response to 100 mg is inadequate you can consider increasing to 200 mg
- If inadequate response is seen after dosage increase, then discontinue use

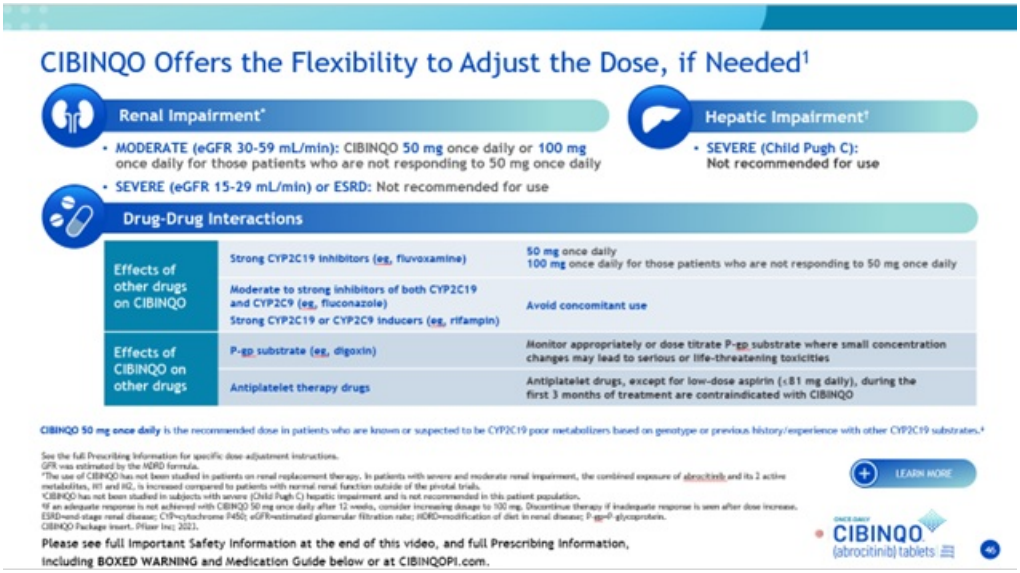
CIBINQO can be used with or without topical corticosteroids.[1]

It should be taken with or without food at approximately the same time each day.[1]

- If a patient experience nausea, it sometimes helps to take medicine with food[2,3]
- Swallow CIBINQO tablets whole with water. Do not crush, split, or chew CIBINQO[1]

There is a 50 mg dose available for dose adjustments, which we will talk about on the following slide.[1]

FRAME 47:



The recommended dosage of CIBINQO is 100 mg orally once daily, and if an adequate response is not achieved with this dosage, consider increasing to 200 mg orally once daily. However, these are some dose adjustment considerations. As a reminder, CIBINQO 50 mg is available for dose adjustments in special populations; however, the 50 mg dose was not studied in clinical trials.

Renal Impairment:

- Patients with mild renal impairment can take the recommended dose of CIBINQO 100 mg once daily
- Patients with moderate (eGFR 30 to 59 mL/min) renal impairment can take CIBINQO 50 mg once daily
  - In subjects with mild and moderate renal impairment, if an adequate response is not achieved after 12 weeks, the dose of CIBINQO can be doubled
- Patients with severe renal impairment (eGFR of 15 to 29 mL/min) or end-stage renal disease (eGFR of less than 15 mL/min) **should not take CIBINQO**
- CIBINQO has not been studied in patients with end-stage renal disease, including those on renal replacement therapy. In phase 3 clinical trials, CIBINQO was not evaluated in patients with AD with baseline creatinine clearance values less than 40 mL/min
- In a phase 1 study, the combined exposure of abrocitinib and its 2 metabolites, M1 and M2, increased in patients with moderate and severe renal impairment compared to placebo with normal renal function

Hepatic Impairment:

- Dose adjustment is not required in patients with mild (Child Pugh A) or moderate (Child Pugh B) hepatic impairment, based on similar active moiety AUCinf values, compared to patients with normal hepatic function. In clinical studies, CIBINQO was not evaluated in patients with severe (Child Pugh C) hepatic impairment or in patients screened positive for active hepatitis B or hepatitis C infection. Avoid use of CIBINQO in patients with severe (Child Pugh C) hepatic impairment

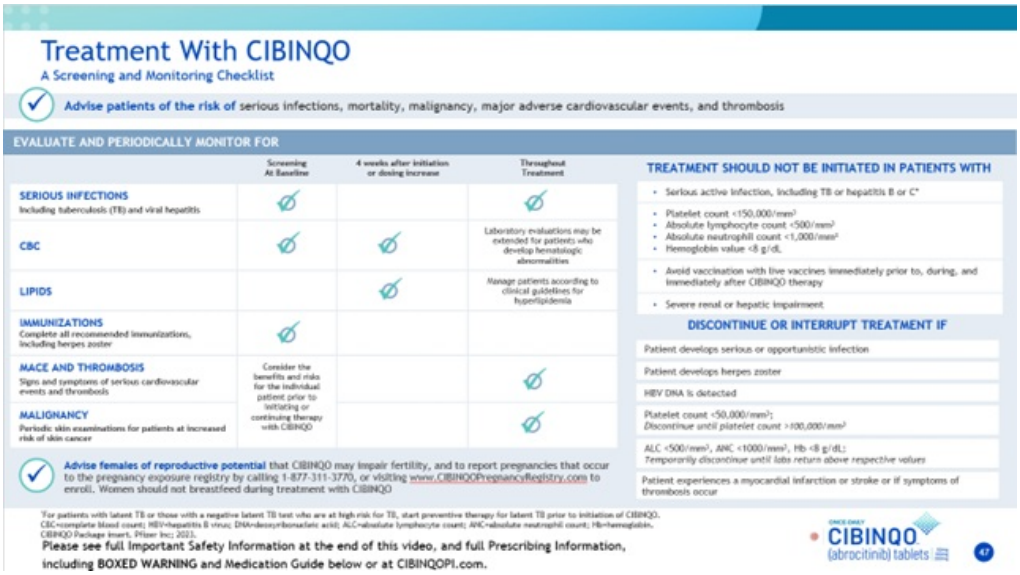
Drug Interactions:

- **Effects of other drugs on exposure to CIBINQO and/or its metabolites:** CIBINQO is metabolized predominantly by cytochrome P450 (CYP) enzymes CYP2C9 and CYP2C19; therefore, concomitant use of CIBINQO should be avoided with drugs that are moderate to strong inhibitors of both CYP2C9 and CYP2C19, and strong CYP2C9 or CYP2C19 inducers. The starting dose should be reduced to 50 mg when CIBINQO is coadministered with strong CYP2C19 inhibitors
  - Dose reduction is also recommended in patients who are known or suspected to be CYP2C19 poor metabolizers
- **Clinically significant interactions of CIBINQO affecting other drugs:** With P-gp substrates where small concentration changes may lead to serious or life-threatening toxicities, appropriate monitoring is recommended. Additionally, antiplatelet drugs, except for low-dose aspirin (so less than or equal to 81 mg daily), are contraindicated with CIBINQO during the first 3 months of treatment

due to potentially increased bleeding risk

Additional details on recommended dose adjustments can be found in the full CIBINQO Prescribing Information. The 50 mg dose was not studied in clinical trials.

FRAME 48:



Perform the following tests and evaluations prior to CIBINQO initiation:

- Screening for serious infection
  - Tuberculosis (TB) infection evaluation and viral hepatitis screening in accordance with clinical guidelines
    - CIBINQO initiation is not recommended in patients with serious active infection, including TB or hepatitis B or C infections
    - For patients with latent TB or those with a negative latent TB test who are at high risk for TB, start preventive therapy for latent TB prior to initiation of CIBINQO
- A complete blood count (CBC)
  - CIBINQO initiation is not recommended in patients with a platelet count less than 150,000/mm^3, an absolute lymphocyte count less than 500/mm^3, an absolute neutrophil count less than 1000/mm^3, or a hemoglobin value less than 8 g/dL
- Immunizations
  - Prior to CIBINQO initiation, complete all recommended immunizations, including herpes zoster vaccinations, in agreement with current immunization guidelines
  - Avoid vaccination with live vaccines immediately, prior to, during, and immediately after CIBINQO therapy
- Treatment with CIBINQO should not be initiated in patients with severe renal or hepatic impairment

Also, prior to treatment, advise patients of risk of serious infections, mortality, malignancy, major cardiovascular events, and thrombosis.

Advise female patients of reproductive potential of the following

- Advise females of reproductive potential that oral administration of CIBINQO may impair fertility, based on the findings in rats. Impaired fertility in female rats was reversible 1 month after cessation of abrocitinib oral administration
- Advise women not to breastfeed during treatment with CIBINQO
- There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to CIBINQO during pregnancy. Advise patients to report their pregnancy by calling 1-877-311-3770, or visiting www.CIBINQOPregnancyRegistry.com to enroll

During treatment with CIBINQO, monitor for the following:

- *Serious infections*: Signs and symptoms of infection, including yearly TB screening (in highly endemic areas) and viral hepatitis monitoring for reactivation, in accordance with clinical guidelines

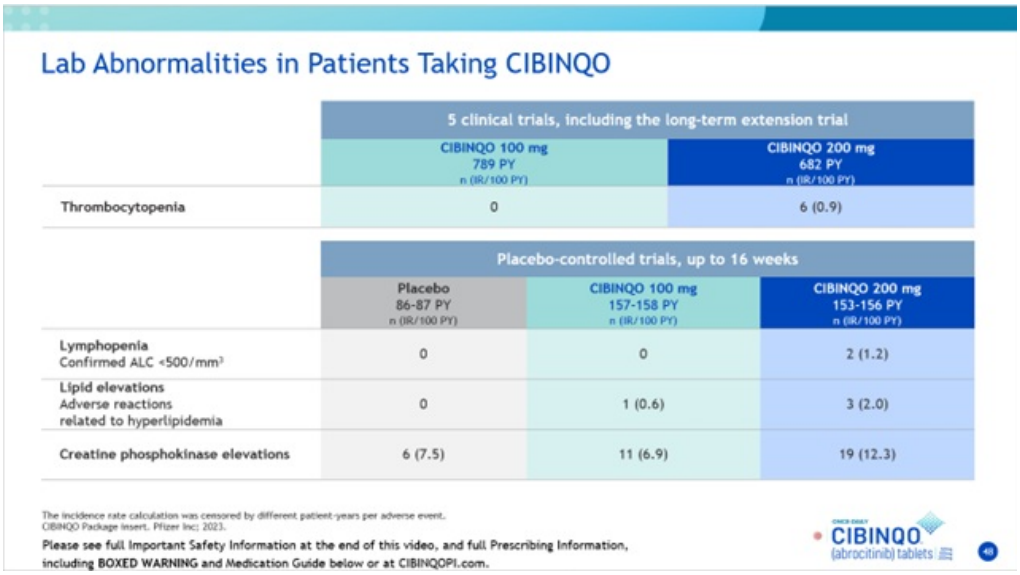
- *MACE and thrombosis*: Signs and symptoms of serious cardiovascular events and thrombosis
- *Complete blood count*: CBC 4 weeks after treatment initiation and 4 weeks after dosing increase
- *Lipid parameters*: Lipid parameters 4 weeks following CIBINQO initiation
- *Malignancy:* Periodic skin examinations for patients at increased risk of skin cancer

CIBINQO treatment should be discontinued or interrupted if:

- Patients develop serious or opportunistic infection and infection should be controlled. The risks and benefits of treatment with CIBINQO should be carefully considered prior to reinitiating therapy with CIBINQO
- Patient develops herpes zoster (consider interrupting until episode resolves)
- HBV DNA is detected during therapy with CIBINQO; consult a liver specialist
- Patient has experienced a myocardial infarction or stroke
- Symptoms of thrombosis occur
- Platelet count <50,000/mm^3 (discontinue until platelet count >100,000/mm^3)
- ALC <500/mm^3, ANC <1000/mm^3, Hb <8 g/dL (temporarily discontinue until ALC, ANC, Hb return above respective values)

Laboratory evaluations may be extended for patients on chronic CIBINQO therapy who develop hematologic abnormalities.

FRAME 49:



Lab abnormalities reported in patients taking CIBINQO include
Thrombocytopenia:

- Treatment with CIBINQO was associated with an increased incidence of thrombocytopenia
- Maximum effects on platelets were observed within 4 weeks, after which the platelet count returned toward baseline despite continued therapy
- In all 5 clinical trials, including the long-term extension trial, 6 subjects (0.9 per 100 patient-years) treated with CIBINQO 200 mg had adverse reactions of thrombocytopenia; no subjects treated with CIBINQO 100 mg had an adverse reaction of thrombocytopenia
  In 16-week placebo controlled trials

Lymphopenia:

- Treatment with CIBINQO was associated with an increased incidence of lymphopenia
- Confirmed ALC <500/mm^3 occurred in 2 subjects (1.2 per 100 patient-years) treated with CIBINQO 200 mg and in 0 subjects treated with CIBINQO 100 mg or placebo. Both cases occurred in the first 4 weeks of exposure

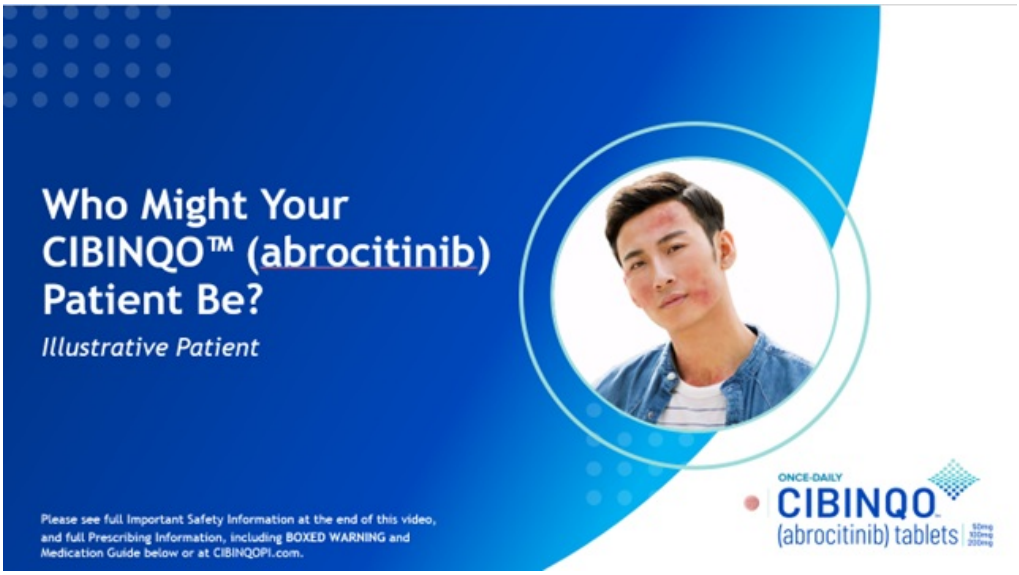
Lipid Elevations:

- There were dose-dependent percentage increases in LDL-C, total cholesterol, and HDL-C relative to placebo at week 4, which remained elevated through the final visit in the treatment period
- Adverse reactions related to hyperlipidemia occurred in 1 subject (or 0.6 per 100 patient-years) exposed to CIBINQO 100 mg, and in 3 subjects (2.0 per 100 patient-years) exposed to CIBINQO 200 mg

Creatine Phosphokinase Elevations:

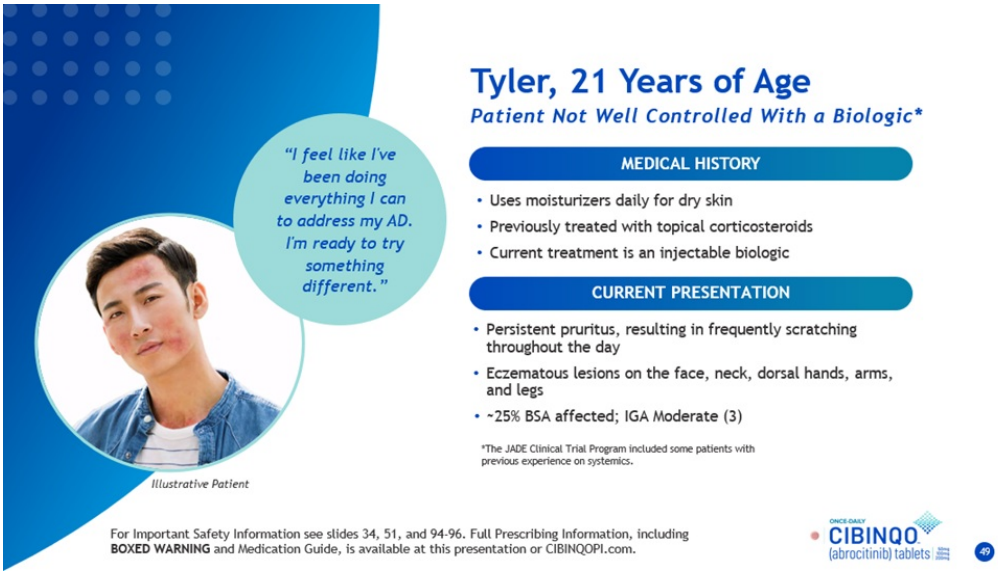
- Events of blood CPK increases were reported in 6 subjects (or 7.5 per 100 patient-years) treated with placebo, 11 subjects (or 6.9 per 100 patient-years) treated with 100 mg of CIBINQO and 19 subjects (or 12.3 per 100 patient-years) treated with 200 mg of CIBINQO
- Most elevations were transient

FRAME 50:



Let's take a closer look at Tyler now that we have gone through the CIBINQO data.

FRAME 51:



We discussed on earlier slides that Tyler, a 21-year-old male patient, had been diagnosed with moderate-to-severe atopic dermatitis that is not well controlled on an injectable biologic.

Because he was presenting with persistent pruritus as well as visible lesions that made him concerned, it was appropriate to consider a different treatment option.

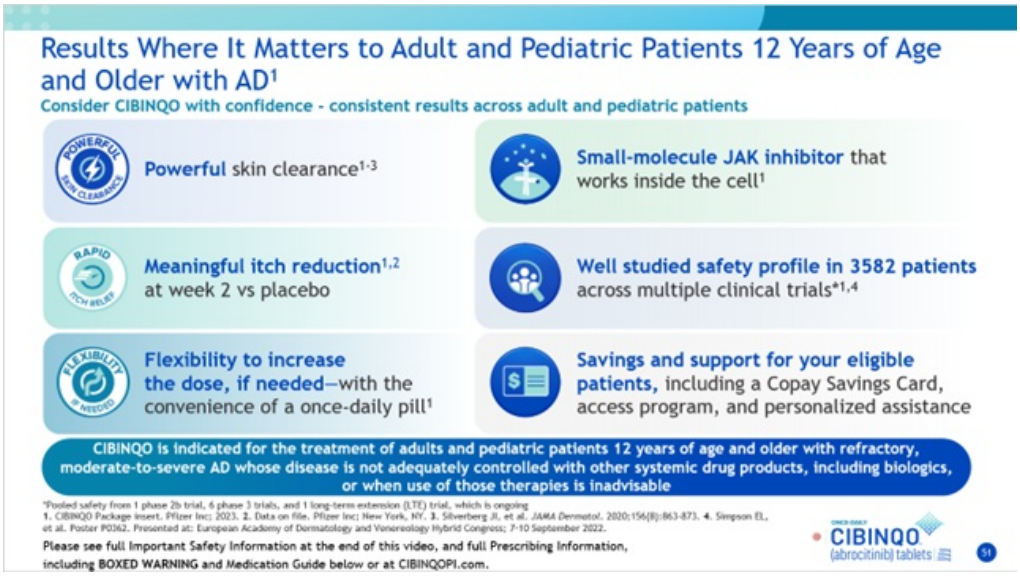
Let's discuss how we would start a patient on CIBINQO. First, as we have done with Tyler, you would determine if the patient is an appropriate candidate for CIBINQO. This decision should involve a discussion about the safety profile of CIBINQO and level-setting the patient's treatment expectations.

This discussion is also your opportunity to educate your patient about the screening and monitoring that they can expect when starting and while taking CIBINQO.

After ordering baseline labs, screening for serious infections, reviewing the patient's medical history (including malignancies and cardiovascular risk factors, and ensuring administration of all recommended vaccines) you would determine the appropriate starting dose (100 mg or 50 mg, if he meets the criteria for dose adjustments).[1]

Continue to monitor Tyler throughout treatment, including for serious infections, cardiovascular events, thromboses, and malignancy.[1]

FRAME 52:



Let's summarize what we have discussed throughout this presentation, CIBINQO is indicated for the treatment of adults and pediatric patients 12 years of age and older with refractory, moderate-to-severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies is inadvisable.[1]

- For example, our patient Tyler, a 21-year-old with moderate-to-severe atopic dermatitis who was being treated with topical corticosteroids and a biologic, was still experiencing uncontrolled symptoms.

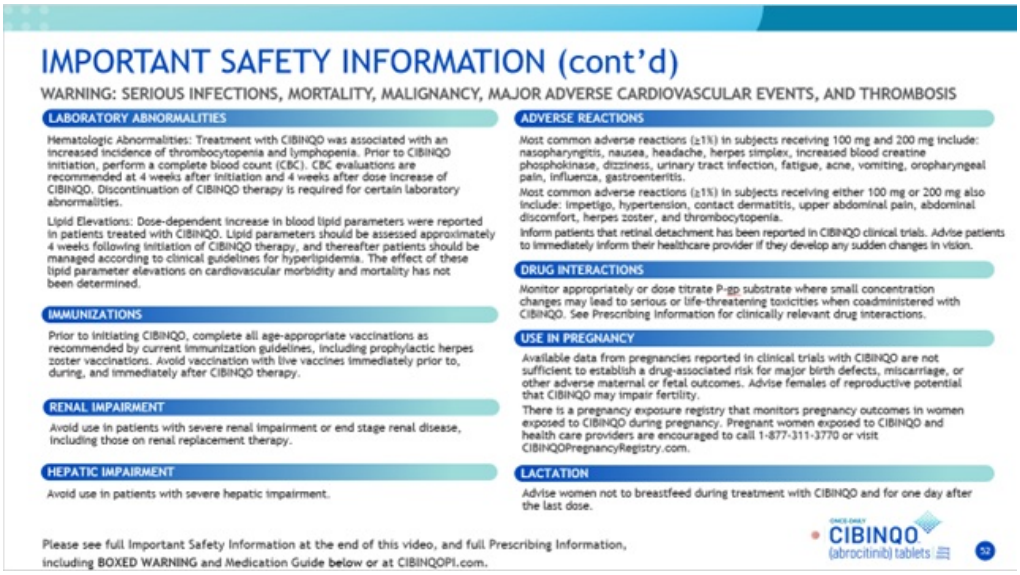
Because Tyler's treatment regimen was insufficient, we decided to consider a new pathway of managing his atopic dermatitis and started him on CIBINQO, a small-molecule JAK inhibitor that works inside the cell.[1]

It provides the flexibility to increase the dose after 12 weeks if the disease remains uncontrolled on CIBINQO 100 mg.[1]

CIBINQO has

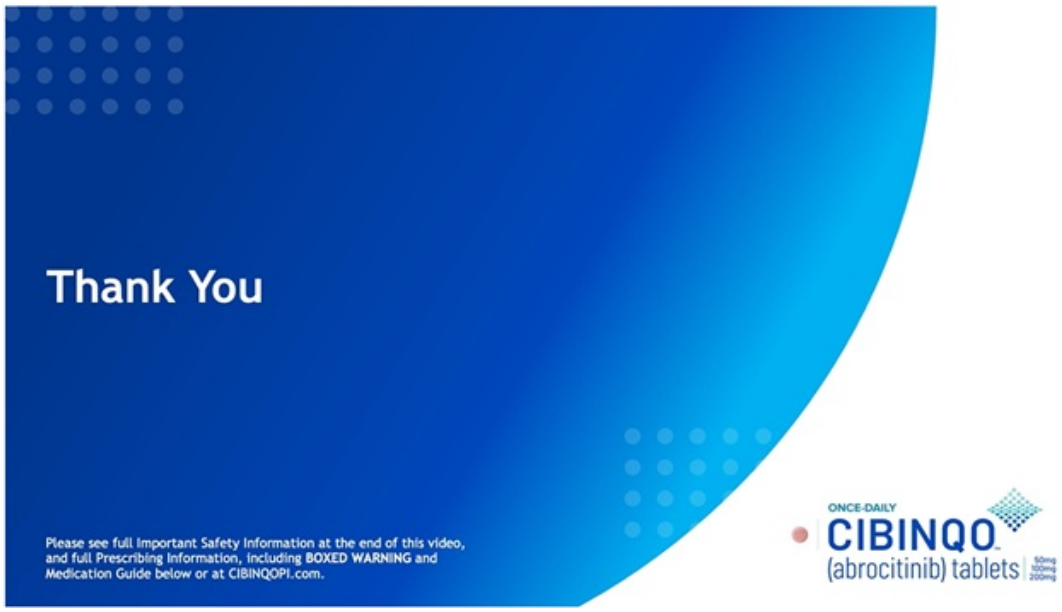
- Powerful skin clearance at week 12 vs placebo[1-3]
- Meaningful itch reduction at week 2 vs placebo[1,2]
- A safety profile that has been evaluated in 3582 patients across multiple clinical trials[1,4]

FRAME 53:



Lastly, let's look at some additional important safety information.

FRAME 54:



Thank you for taking the time to listen to today's presentation.

FRAME 55:

Please see full Important Safety Information at the end of this video, and full Prescribing Information, including **BOXED WARNING** and Medication Guide below or at CIBINQOPI.com.