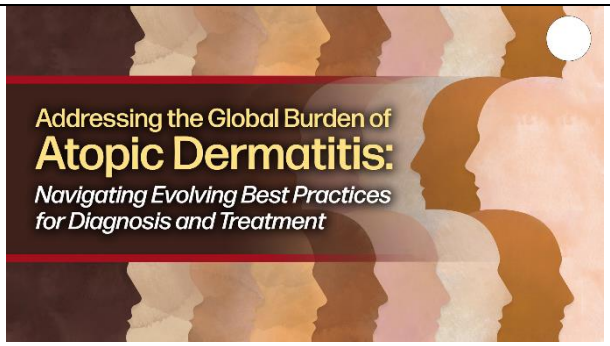
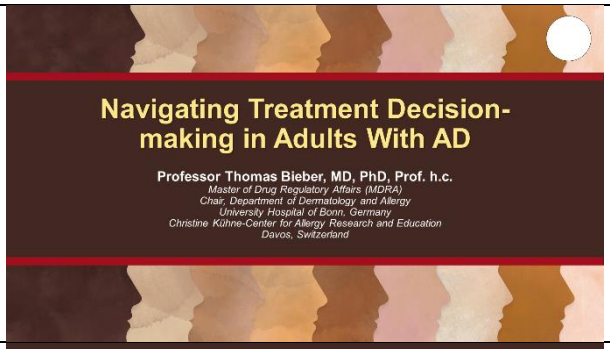
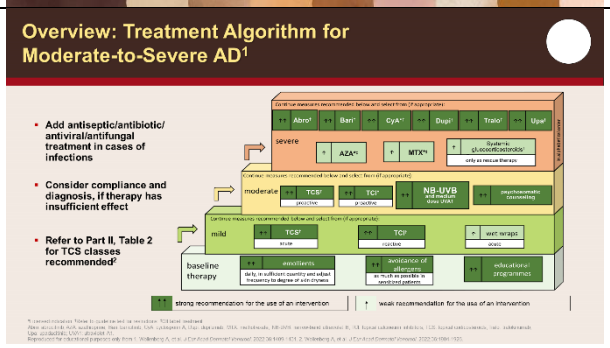
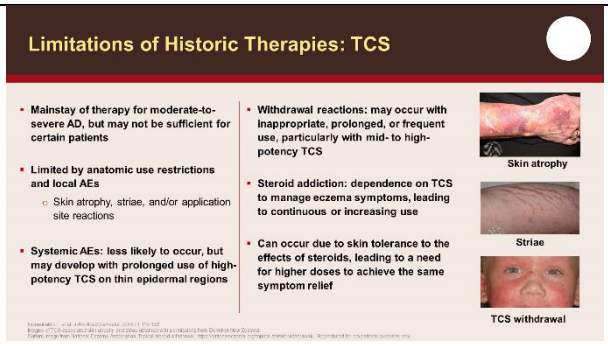
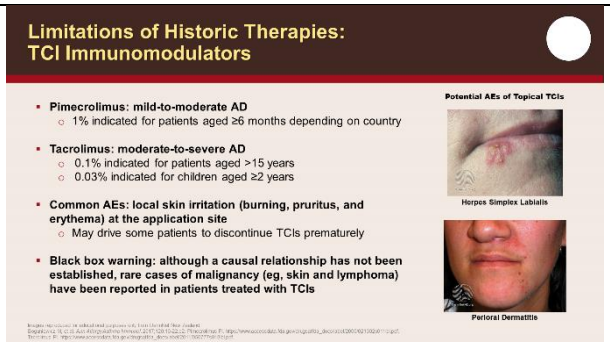
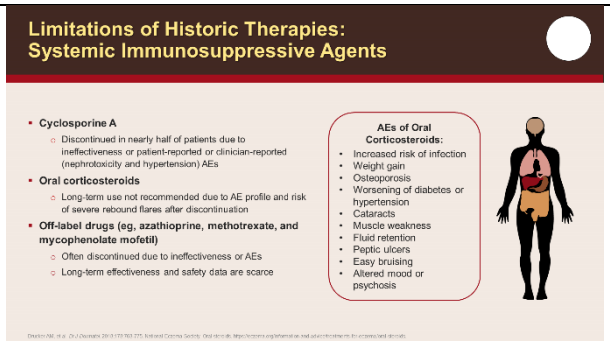
1		Hello, my name is Thomas Bieber. I'm a dermatologist and allergist at the University of Bonn in Germany, and I welcome you to this series of presentations, Addressing the Global Burden of Atopic Dermatitis.
2		And today, I would like to address the treatment decision-making in adult patients with this disorder.
3		I think that, for most of you, I don't need to present the clinical pictures of the phenotype of this disorder, but I just would like to remind you the key points, that is, that this is the most important and most common inflammatory skin disorder globally. It affects 1 in 4 adults, particularly in adult-onset disease. It affects many more children, but this will not be the topic of this presentation. And we know that this huge heterogeneity in the clinical phenotype is somehow mirroring what happens in the immune system and in the skin self. So, the complex pathogenesis involves genetics, immunology, and environmental factors, and probably also epigenetic regulation, that are all contributing to that highly itching and particularly complex disorder. The disorder itself has a number

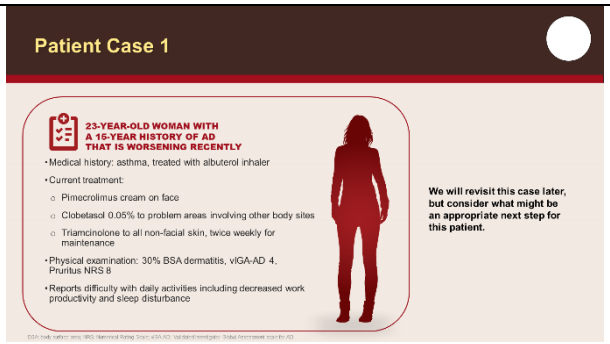
		of consequences in terms of impacts on the quality of life of these patients, and particularly also in the families and the relatives or caregivers. And I would like to suggest that you also visit Activity 1 to learn a little bit more about the pathophysiology of this disorder. That will guide you a little bit to the pharmacological interpretive options for this particular disorder.
4		And that's exactly what we would like to discuss in the following minutes, that is, the current management and treatment options and recommendations that are currently, at least according to the guidelines, available.
5		So this picture just shows you one of the figures of the most recent guidelines. Looking at the stepped-tier plan for adults, in that case, patients with atopic dermatitis. And as you can see here, this is what you see in all or almost all the guidelines worldwide, starting with the kind of baseline or basic therapy, which includes, on one hand, the use of emollients and other preparations aimed to address the barrier dysfunction. Of course, the avoidance of allergens, because we know that in a subpopulation of patients, allergies may play a significant role in the induction of exacerbations. And also, the educational programs should not be forgotten because these

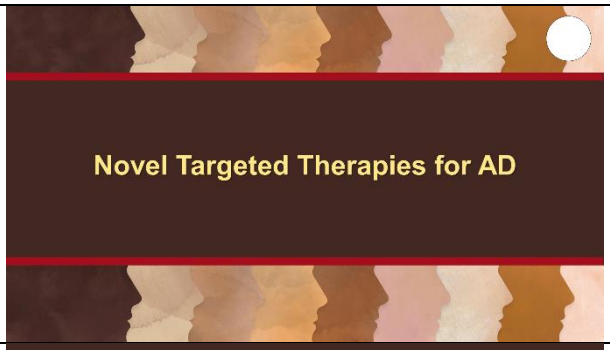
		are extremely important, particularly because these patients are always keen to learn more about the disorder. And the issue of compliance is really something that is relevant in the management of these patients. And then as in almost all the diseases that we know, we have to approach these patients depending on the severity. So, the treatment algorithms are different depending on whether you are looking at the mild patients, moderate patients, or more severe patients, as shown on this slide. For the mild patients, you can afford to treat the acute flares with topical steroids in a more reactive way. While for the more mild to moderate forms, I would say the use of topical steroids and topical calcineurin inhibitors in a proactive way is very useful, in order to better control the disease on the long run and to avoid frequent exacerbations. And this has been nicely shown in a number of studies about a decade ago in the context of the line extension of Protopic, for example. As an add-on therapy, and I would really specify that this is not an alternative, this is not something which is in between the topical treatment and the systemic treatment. It's just an add-on, the UVB treatment that is, I think, extremely helpful for a number of patients,

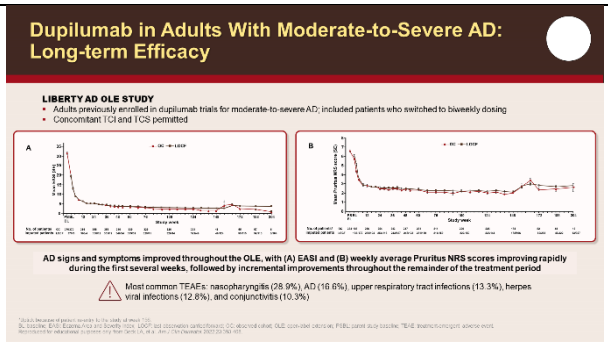
		particularly those that report that the disorder is improving, typically during the summer time. Psychosomatic counseling is also of importance because it, again, very much contributes to an increased compliance of these patients. And for the more severe patients you have to rely on kind of systemic treatment and currently we have, and we will go to that more in details afterwards, I would say the old-fashioned treatments, like the immunosuppressive treatments, like cyclosporine and methotrexate, azathioprine, and the systemic steroids. While on the other hand, you have the more modern treatment with the biologics (dupilumab, tralokinumab), and the JAK kinase inhibitors (baricitinib, upadacitinib, and abrocitinib).
6		Coming back to the limitations of the historic therapies, particularly the TCS as you see here, you probably have seen a number of these patients who have used topical steroids for many, many weeks and months, leading sometimes to this kind of steroid addiction situation as you see on the lower right part of the slide, in this kid that has used TCS for a longer period of time and then experienced this withdrawal with acute

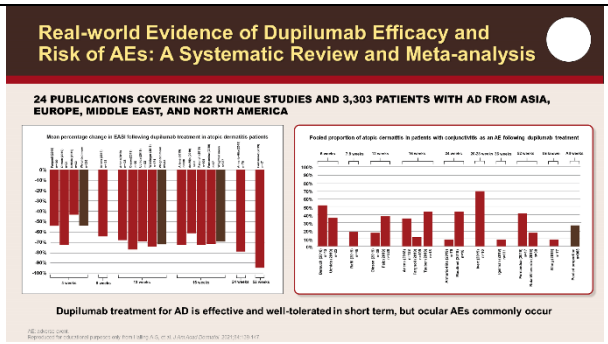
		exacerbation of the disorder.
7		On the other hand, we also have the TCIs. I wouldn't say that these are really immunosuppressive drugs, but immunomodulators topically, but we have two drugs available — pimecrolimus and tacrolimus. Pimecrolimus clearly is not so efficient as tacrolimus. And it's certainly the first choice for the treatment of patients with more mild-to-moderate forms, particularly in the pediatric populations. While the tacrolimus treatment is very effective in moderate and sometimes severe patients that are suffering from this disorder. But for both compounds, you know, and the patients will report this, this typical local irritation is a kind of tingling and burning sensation, particularly during the first few days after the first application. So, you have to explain to the patients this kind of side effect and that the side effect will fade, most probably, once the inflammation has been improved, the barrier function has been restored somehow, and the drug will be much less aggressive, I would say, in terms of side effects. You all are aware about the black box warnings issued in 2005 in the context of these two products. Meanwhile, we know that there is no scientific evidence for this

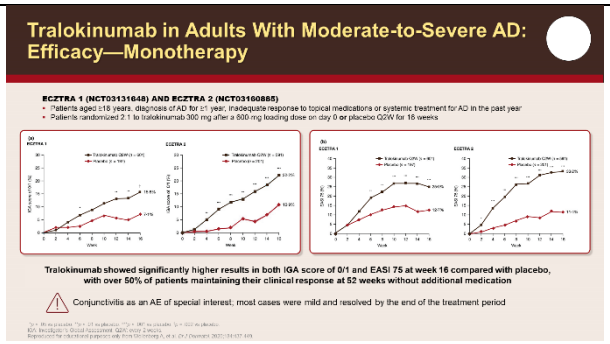
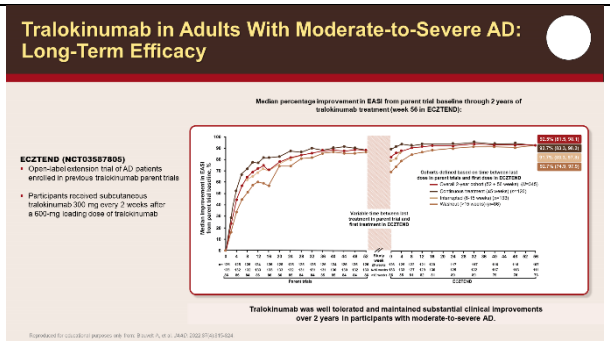
		black box warning, and that both drugs are really safe in the management of these disorders.
8		So, with regard to the systemic immunosuppressive agents, like cyclosporine A, topic and oral steroids, and off-label drugs azathioprine and methotrexate particularly, we all know and are aware about the use of this drug. In Europe, cyclosporine A is the only one which is approved by the European Medicines Agency, while azathioprine, methotrexate, and mycophenolate are not approved, and I assume will never be approved for this indication. And you know that the use of oral steroids, according to the last guidelines, is very much restricted to very particular situations. When you have a patient with a very severe flare, maybe you can afford to use oral steroids, but certainly not for mid-term or long-term use as we still unfortunately, we still see in some patients that are referred to us. And the problems related to the oral steroids are nicely shown here on the right side of the slide. You know all about these steroids' side effects and I think, nowadays, we have enough new drugs available as an alternative to this kind of treatment.

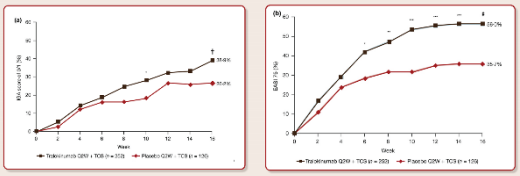
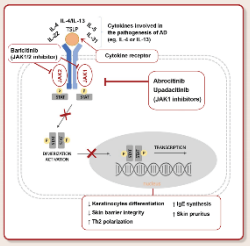
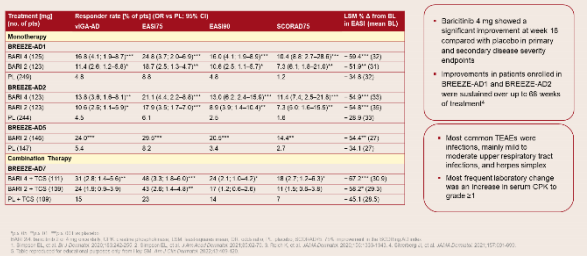
9		So, this is a typical patient, I would say, that I would like to briefly present here and we will come back to that patient afterwards. This is a 23-year-old woman that has a 15-year history of atopic dermatitis that worsened recently. Very important in the history is the fact that she's a typical atopic patient, particularly suffering from asthma as another atopic comorbidity, and she is treated with an albuterol inhaler. The current management of the disorder was tried with pimecrolimus on the face, clobetasol on the problem areas, and triamcinolone to nonfacial skin twice weekly for maintenance. What is interesting is the body surface area which is 30%, which is quite a lot and, as you can see here, the vIGA, which is 4, which is in fact implying that this patient is classified as a severe form. Not surprisingly, having a pruritus NRS of 8. And of course, not unexpected, this young lady reports about issues with the daily activities, particularly the impact on the working productivity and the sleep disturbance. So, this is a kind of archetypical patient that we will come back in a moment to.

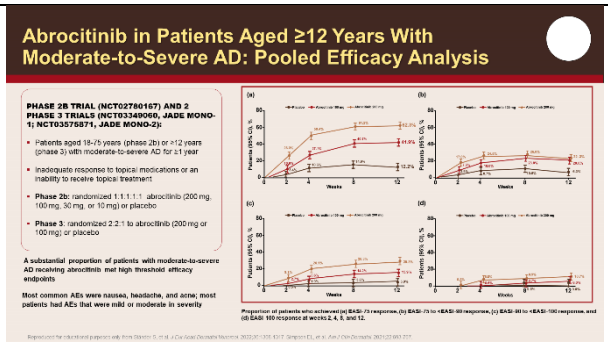
10		So now let's speak about the new therapies.
11	**Biologic and JAK1 Inhibitor Therapies for Moderate-to-Severe AD** **Therapy / Class / Mechanism of Action / Indication(s)** **FDA-approved** Dupilumab subcutaneous injection[1] — Biologic (mAb) — IL-4Rα antagonist — • Treatment of adult and pediatric patients aged ≥6 months with moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable • Can be used with or without TCS Tralokinumab[2] — Biologic (mAb) — IL-13 antagonist — • Treatment of moderate-to-severe AD in adult patients whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable • Can be used with or without TCS Abrocitinib[3] — Oral small molecule — JAK1 inhibitor — • Adults and pediatric patients aged ≥12 years with refractory, moderate-to-severe AD whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies is inadvisable Upadacitinib[4] — Oral small molecule — JAK1 inhibitor — • Adults and pediatric patients aged ≥12 years with refractory, moderate to severe AD whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies are inadvisable **EMA-approved** Baricitinib[5] — Oral small molecule — JAK1/2 inhibitor — • Treatment of moderate to severe AD in adult patients who are candidates for systemic therapy	We roughly have in the States these four products, while in Europe we have a fifth one. So, in the US situation we have the two main biologics available, dupilumab and tralokinumab. And in the States, you also have upadacitinib and abrocitinib as the typical JAK kinase inhibitors. In Europe, we also have baricitinib, which is a JAK1 and 2 inhibitor that is available for the treatment of moderate-to-severe patients.
12	**Biologic Therapy for Moderate-to-Severe AD: Dupilumab and Tralokinumab** Dupilumab FDA-approved indication: • Adult and pediatric patients aged ≥6 months with moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable Normal IL-4 signaling Normal IL-4 signaling No IL-13 signaling Signaling or Decoy? Tralokinumab FDA-approved indication: • Adult patients with moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable	Now, with regard to the mode of action, as you know, the biologic therapy for moderate-to-severe topic dermatitis currently is feasible by two main products. Dupilumab, which has primarily been approved for atopic dermatitis, but meanwhile had a line extension for other indications like asthma, chronic rhinosinusitis, and eosinophilic esophagitis, and most recently also for prurigo nodularis. So the drug itself is now approved for a whole range of patients suffering from this disorder down to patients that are aged 6 months and older. On the other hand,

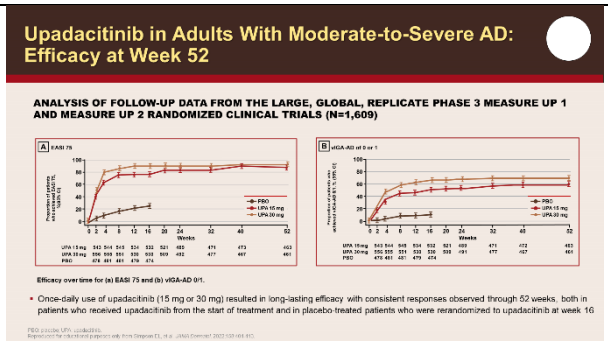
		we have tralokinumab, which is also FDA-approved for adult patients, but the approval for adolescence is currently ongoing. And the same indication as for dupilumab — moderate-to-severe patients that are not adequately controlled with the topical prescription therapy or for those patients where the therapy is not advisable. So, let's have a look at some data of these different products.
13		First with dupilumab, and you are probably aware about the number of studies which have been done. It's really incredible the phase 3 program that Regeneron and Sanofi have started in the context of the clinical development of that particular drug. And this slide just shows you the long-term efficacy of dupilumab in patients that have been exposed, as shown here, for up to 4 years to dupilumab. And you see clearly there is, in fact, nothing that looks like a kind of escape mechanism. So, the patients that are responsive for this drug, they stay responsive for a longer period of time. And I think this is really good news for these patients that have this chronic disorder and that need a long-term management. And the slide shows you, on one hand, improved easy scoring, on the left side, and on the right side you have this really nice response in

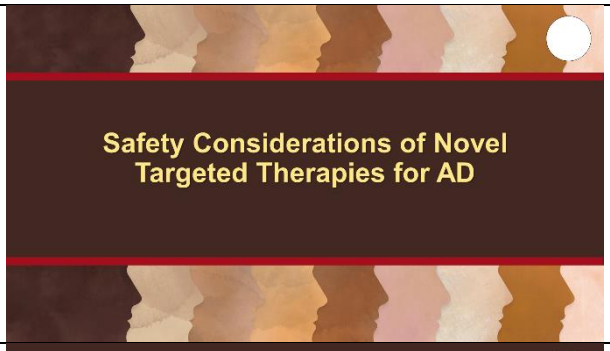
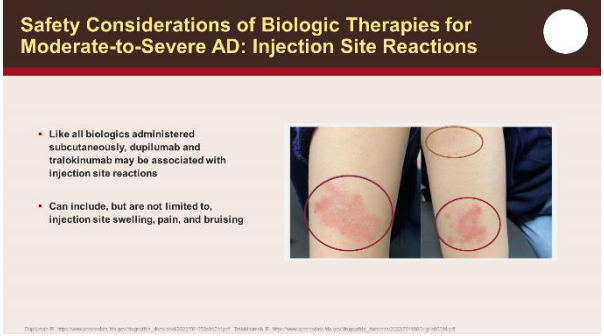
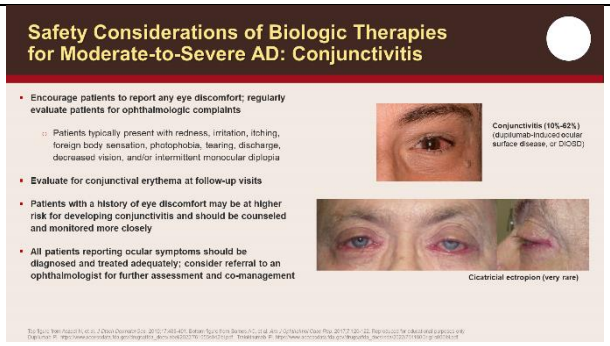
		terms of improvement of the pruritus, starting from a very substantial scale of 7 points typically, going down to 2 points, and very stable response here.
14		And these are the data from the phase 3 trial when you now are trying to look at what happens really under real-world conditions. And we are very lucky because we have, really, a high number of publications reporting the experience with dupilumab in many, many different centers worldwide. We have now more than 3,300 patients from different countries, which have been included in these real-world studies. And the bottom line and result of this is that the data that have been generated in the context of the phase 3 trials have been really nicely reproduced in the context of the real world. On the other hand, as you know, I think the single issue that may be related with the use of dupilumab are — or is — the conjunctivitis. And not unexpected, you will see that in the real-world evidence reports across the literature, you will also see that signal of this eye problem that has been reported, and you can see here on the right side. Typically, there is a kind of correlation between the duration of the treatment and the proportion of patients reporting that kind of side effect.

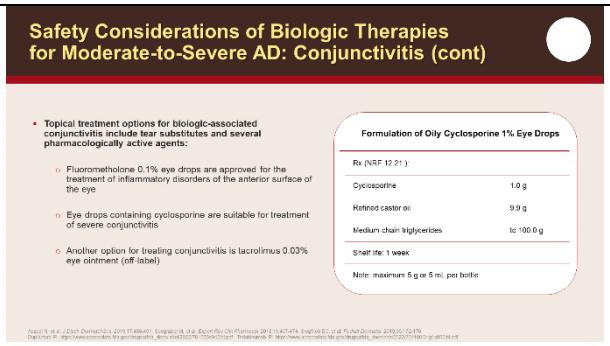
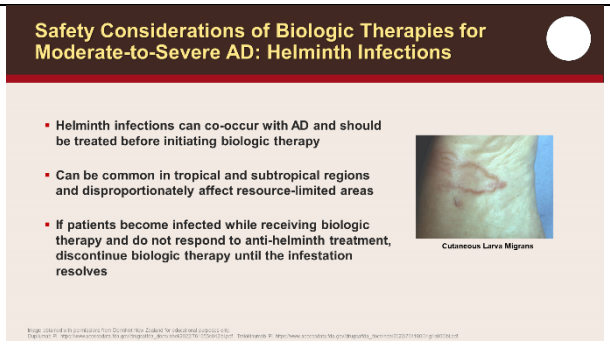
15		Now, tralokinumab is the second product that is currently available for the treatment of atopic dermatitis of the moderate-to-severe form. And these are the results that are summarizing the two endpoints: IGA 0/1 on the left side and EASI-75 on the right side. And if you would take IGA 0/1 as, I would say, the most stringent endpoint currently available, that approximately corresponds to an EASI improvement of 90% and more. You see here that you have an average response of 20%, 22% of patients that have reached that IGA score 0/1. But as you can also see on these curves, they do not plateau at week 16.
16		And in a further slide you will see that, in fact, when you are looking at the response of these patients up to week 52, there is a further increase in the response of these patients. So, in other words, when you are putting patients on tralokinumab you have to explain to them that the maximum response will not be reached until I would say week 20, week 24. So, they need to be patient and you need to explain to these patients that it takes a little bit longer than dupilumab in order to reach the maximal efficacy.

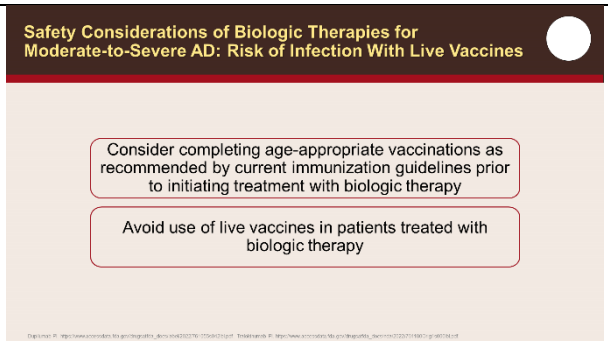
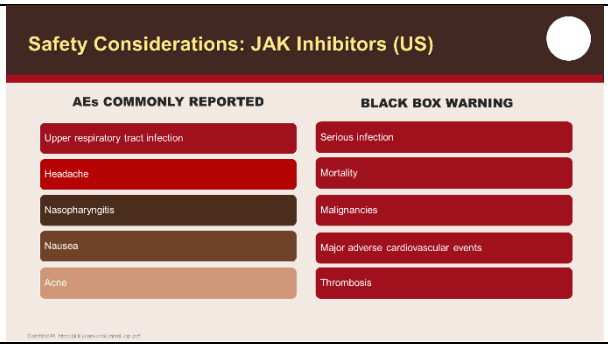
17	**Tralokinumab in Adults With Moderate-to-Severe AD: Efficacy—Combination With TCS** **EGZTRA 3 (NCT03363854)** • Aged ≥18 years, diagnosis of AD for ≥1 year, inadequate response to topical medications or systemic treatment for AD in the past year • Tralokinumab 600-mg loading dose followed by tralokinumab 300 mg Q2W or placebo and TCS for 16 weeks  • At week 16, significantly more patients receiving tralokinumab achieved the IGA 0/1 and EASI 75 compared with placebo • Overall frequency and severity of AEs were comparable between tralokinumab and placebo; majority nonserious and mild or moderate in severity	This efficacy can be improved, typically with the combined use with topical steroids. And this is, by the way, the same situation for dupilumab where, in the so-called CHRONOS study, they have shown that that the combo of dupilumab and TCS indeed provides a plus, I would say, in terms of response, of something like 10% to 15%.
18	**Oral JAK1 Inhibitors for Moderate to Severe AD** **ABROCITINIB** • Selective JAK1 inhibitor • Approved in the US, EU, and Japan for treatment of adult and pediatric patients aged ≥12 years with refractory, moderate-to-severe AD **UPADACITINIB** • Selective JAK1 inhibitor • Approved in the US, EU, and Japan for treatment of adult and pediatric patients aged ≥12 years with refractory, moderate-to-severe AD **BARICITINIB** • JAK1/2 inhibitor • Approved in many countries, including the EU and Japan, for the treatment of adult patients with moderate-to-severe AD who are candidates for systemic therapy  	So now let's switch to the next class of molecules — the oral JAK kinase inhibitors. The oral JAK kinase inhibitors are of three different drugs: Abrocitinib, which is a selective JAK1 inhibitor; upadacitinib, which is also a selective JAK1 inhibitor; and baricitinib, which is the JAK1 and 2 inhibitor. All these products are approved in the different countries except baricitinib, which is not approved currently in the States for this indication.
19	**Baricitinib in Adults With Moderate-to-Severe AD: Efficacy at Week 16[1-5]**  • Baricitinib 4 mg showed a significant improvement at week 16 compared with placebo in primary and secondary disease severity endpoints • Improvements in patients enrolled in BREEZE-AD1 and BREEZE-AD2 were sustained over up to 68 weeks of treatment[4] • Most common TEAEs were infections, mainly mild to moderate upper respiratory tract infections, and herpes simplex • Most frequent laboratory change was an increase in serum CPK to grade ≥1	So, let's start with baricitinib, which was the first drug, or the first class approved for the treatment of moderate-to-severe atopic dermatitis, in Europe at least. And as you can see here, again, based on the vIGA for the studies looking at two different doses, 4 mg and 2 mg. You see here that an average 20% of the patients have reached that particular endpoint, a little bit more of course for EASI-75. This clearly shows you that that

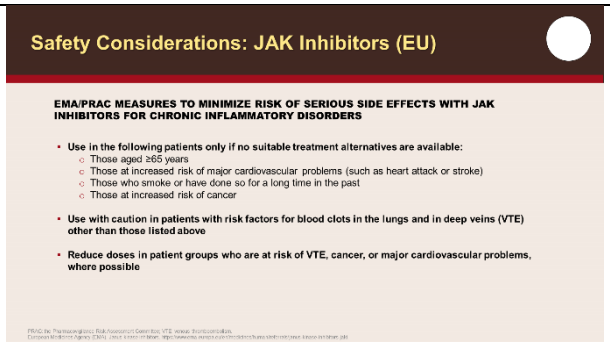
		drug, at least compared to the others (and if you are doing a kind of network meta-analysis this will be more obvious), baricitinib seems to be less efficacious compared to, I would say, the competitors like abrocitinib and upadacitinib. But again, as I mentioned, the combination therapy with TCS allows you to have a plus of at least 10% to 15% in terms of efficacy. As for most of the JAK kinase inhibitors, you will see a number of potential side effects; we will come to that later. But for baricitinib, particularly the safety profile was, at least in my experience, clinically really acceptable compared to what I have seen with other drugs.
20		Now, abrocitinib is the JAK1 selective inhibitor which is a really interesting molecule. It is currently approved also for adolescents, which is not yet the case for upadacitinib. And as you can see here again on this slide, when you look at the number of patients who have reached EASI-75 response, which is the upper left panel of the slide, you see here 60% of these patients have reached that endpoint. That's really remarkable. That's really something that could be classified as a really excellent response. And this is also translated in terms of EASI-90 — that is

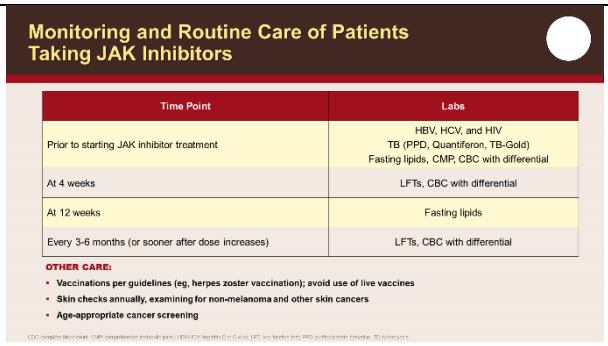
		in the panel C just below that, with something that's 30% of the patients. That's really a remarkable response.
21		Similarly, upadacitinib seems to have the same kind of efficacy, maybe a little bit better in some clinical trials, particularly for the highest dose, which is 30 mg here. But as you can see here, and in contrast to the biologics, you have quite a rapid mode of action here. You've reached a plateau in terms of efficacy already after 8 to 12 weeks, which is really in sharp contrast to what we know from dupilumab and particularly tralokinumab. And this is true, of course, again for EASI-75 on the left side and IGA 0/1 on the right side. One important point, which is not mentioned on this slide, is the dramatic difference between dupilumab, tralokinumab on one hand and the JAK kinase inhibitors with regards to their efficacy in terms of controlling the pruritus. So, the kinetics, in terms of response for the pruritus as a symptom, is really very, it's really amazing to see how fast the JAK kinase inhibitors are inducing a substantial relief of the pruritus and pain sensation of most of these patients. This is, in my opinion, one of the most important differences between these small molecules on one hand,

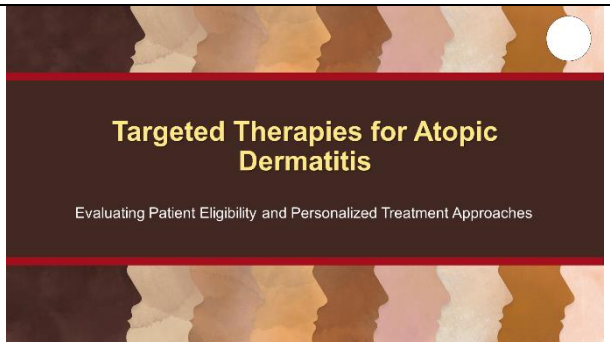
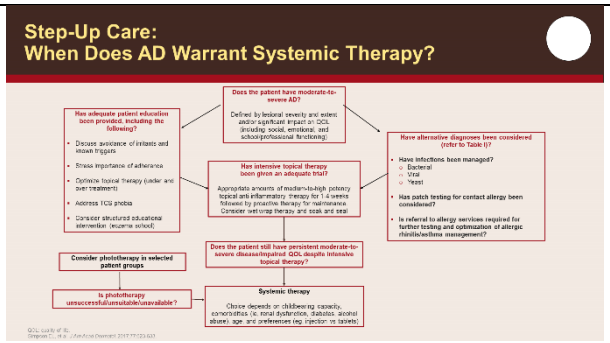
		and the biologics on the other hand.
22		So, let's look about the safety considerations that I already have mentioned a little bit before.
23		So of course, for the biologics, we are all aware about the side effects, particularly related to the injection site. And this is something that you can see in almost all the products that are injected; whether these are biologics or something else, this doesn't make any difference.
24		The difference is made by the side effect that I mentioned already, which is the conjunctivitis. So, the conjunctivitis is reported in 10% to 11% in the first phase 3 trial with dupilumab and the highest rate was reported in one particular real-world evidence report, where this high frequency has been quite uniquely reported in that publication. So, I think it's important also to mention that typically in, at least in our experience clinically, if a patient already had conjunctivitis, which is quite frequent in atopic dermatitis, before you start with dupilumab, there is a substantial risk that this symptom will be even exacerbating during the treatment with

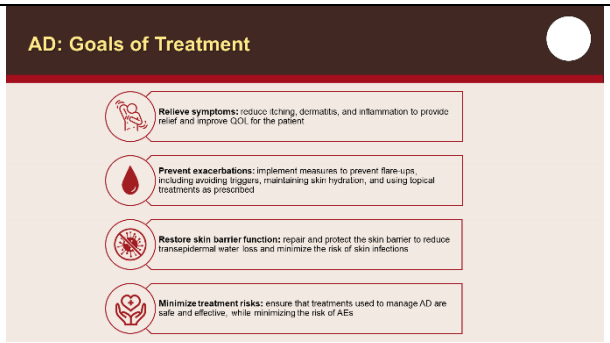
		dupilumab. It must not be, but there is a risk for exacerbation of that particular symptom. Very rarely, you will see cicatricial ectropion as shown on the right side of the slide — a very rare complication of the use of dupilumab in these patients.
25		So, this is something that we know from the daily practice. However, at least in my routine and experience empirically, I have only a limited number of patients that require stopping the treatment because of that side effect. In most of the cases it remains mild-to-moderate, and most importantly it can be treated by either topical or eye drops containing steroids, or by eye drops containing cyclosporine A, and the formulation is shown on the right side of the slide. And there are also some options for treating this with an eye ointment which contains tacrolimus, but this is an off-label use, of course.
26		As you know, dupilumab also blocks IL-13, which makes sense to control the inflammation in the skin, as I mentioned, but also blocks IL-4. And IL-4 is well known also to be important for the fight against parasites. So, if you see patients that have a helminth infection that occurs during the treatment with AD, you

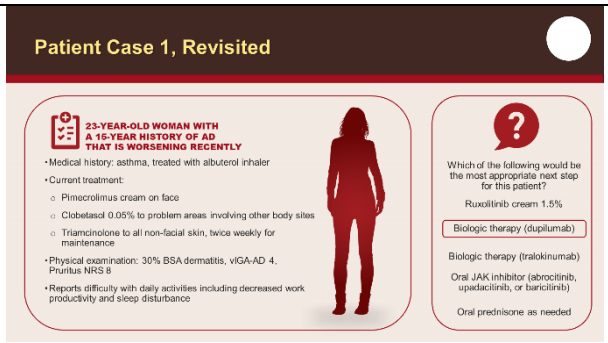
		should think about this and also maybe transiently stop the treatment, focus on the treatment of the helminth infection, and then you can restart the treatment. I know from colleagues in South America, that not seldomly when they are starting the treatment with dupilumab they are even giving some systemic anthelmintic treatment in order to avoid any kind of complication related to the initiation of the treatment with dupilumab.
27		So, with regard to further considerations of the biological treatment, something that is frequently asked by the patients, particularly in the context of the COVID infection and vaccination strategies, I think it is wise before you start the treatment to recommend the vaccinations to be done. Because you never really know what the potential interference could be, and particularly avoid the use of live vaccinations during the treatment with biological therapy. But this is also the case, by the way, for the JAK kinase inhibitors.
28		Now, in terms of safety profile for the JAK kinase inhibitors, we know, and this is the situation for the US, that there is a black box warning that has been issued by the FDA based on the safety profile. And this black box issue mentions

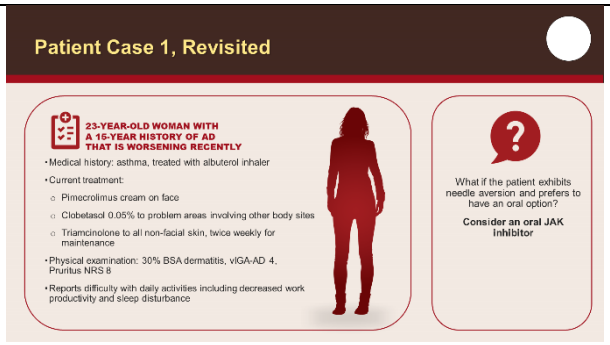
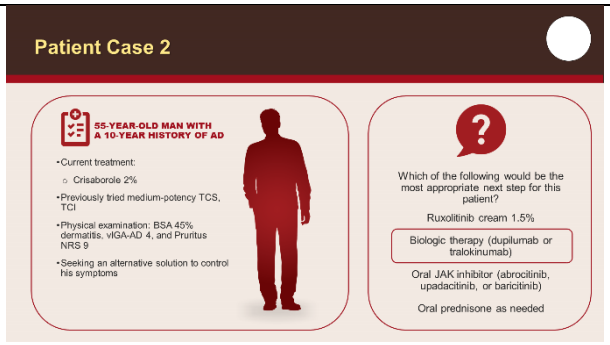
		the serious, the potentially serious infections. Mortality was extremely rare in the clinical development program. Malignancies have been rarely reported. Major adverse cardiovascular events and thromboses are potentially a risk, but it's all about the selection of the right patients to be treated with this particular kind of drug.
29		The safety profile has also been an issue of discussion within the European Medicines Agency and the competent PRAC, which is the committee which is working on the pharmacological and the risk assessment. And just work that has been completed a couple of weeks ago, this committee has decided to include some recommendations for the prescription of JAK kinase inhibitors in patients with inflammatory disorders, not only atopic dermatitis, but it also considers rheumatoid arthritis, IBDs, and others. And the restrictions or recommendations are quite simple to be considered: Those patients who are aged 65 and more; those who at increased risk for major cardiovascular problems, particularly at the heart — heart attack or stroke in the history; active smokers or patients who have a long history, a long time smoking in the past; and particularly those patients who have an

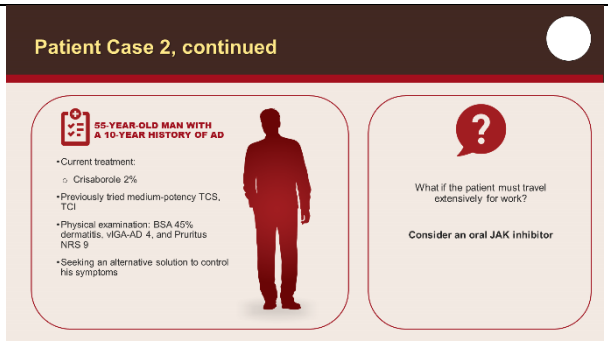
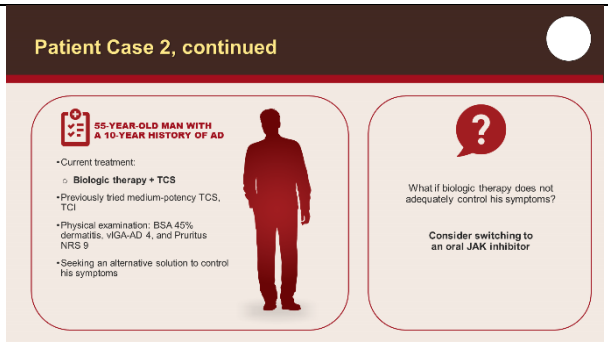
		increased risk or history of cancer are those patients at high risk. And you should reconsider the treatment of these patients, if you think about starting with JAK kinase inhibitors; the same also, by the way, for patients who have particular risk to develop thrombosis and preliminary embolism.
30		So, what kind of routine work should be done before treating patients with JAK kinase inhibitors? Prior to starting the treatment, you have a little bit of lab work. You have to look at virus infections like HIV, hepatitis. Of course, you have to exclude tuberculosis and you have to look at lipids and to do a CBC in order to be sure that these patients do not have any kind of underlying disorder. After 4 weeks, minimal work to be done with the CBC, and looking at the lipids again after 12 weeks, and then every 3 to 6 months a little lab work in order just to control that everything is OK. As I mentioned, the vaccinations per guidelines, very important, and to avoid the live vaccinations. Skin checks should be done for nonmelanoma skin cancer. And of course, for all patients, always advisable: the age-appropriate cancer screening.

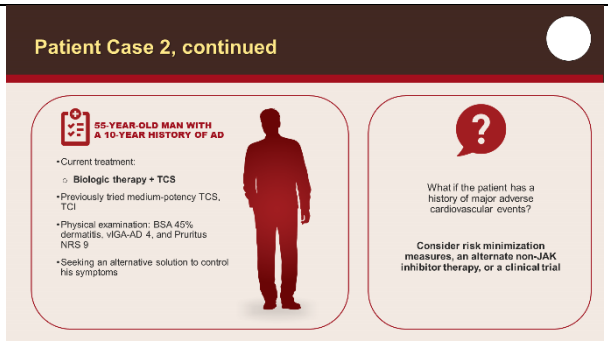
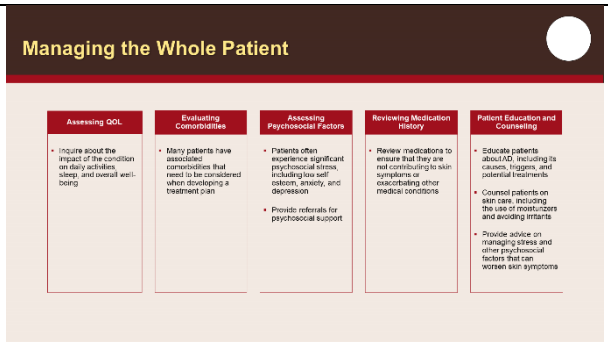
31		So now, with all these drugs available and the multiple options and the multiple kind of disease situations and the heterogeneous phenotype backgrounds of all these patients and not only the kids, but particularly in the adults, let's discuss a little bit the option of the target therapy and the so-called shared decision-making process that is involved here in a modern management of these patients.
32		So, the first question of course, is: Among all these patients that you are taking care of with this particular disorder, when do you advise or when do you discuss with the patient that he warrants a systemic therapy? And I would urge you to look at this paper by my colleague Eric Simpson, published in 2017, where we tried to collect all, let's say, the evidence, the pros and cons, and suggesting this kind of, let's say, decision tree that would guide you to the decision of deciding a systemic therapy for a particular patient. And again, I would like to highlight here that the phototherapy is not an alternative, in my opinion, for any kind of treatment. It can only be considered as an alternate, as an add-on option, either for topical or for systemic therapy.

33		So, what are the goals of the treatment when you see this kind of patient and you discuss with him clearly what you would like to reach together with him in the context of this treatment? First, of course, to relieve the symptoms, particularly itching. But you also would like to prevent exacerbation. Which is an issue which is, in many patients, really relevant and sometimes also related to some kind of provocations, but not only sometimes related to skin care which is not appropriately done, and many other things. And this brings me to the issue of the restoration of the skin barrier function, which is absolutely mandatory. So the baseline treatment, the basic therapy using emollients, is absolutely mandatory in the management of this disorder. And last, but not least, you always have to minimize the treatment risk, and here I come back to the issue we just discussed before, when it comes to discuss with the patients the pros and cons of each kind of treatment, biologics and particularly JAK kinase inhibitors. And that's what we would like to do now in the next exercise, in the next couple of minutes.

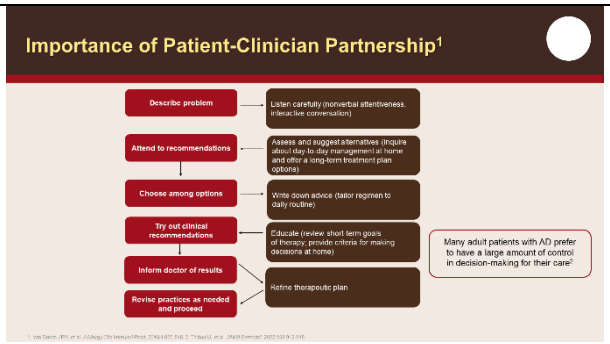
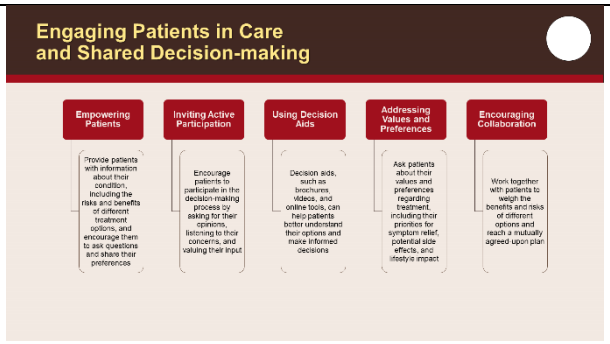
34		I come back to that lady that I have presented before. And as you remember, this lady has a more severe form of the disorder, with a quite substantial body surface area which is affected, 30%. But obviously, and most importantly, she has asthma, which is important in this history to be collected, because this will guide you first in the treatment option. So, if you ask the question, “Which of the following would be the most appropriate next step for the patient?” Either, just starting to treat with ruxolitinib topically, JAK kinase 1/2 inhibitor. By the way, only available at least in the US, not so far available in Europe, unfortunately. Or you provide, or you advise the patient to use a biologic like “dupi” or “tralo,” or an oral JAK kinase inhibitor, or potentially the use of oral prednisone. And here, obviously, I think the choice is quite easy. I would advise to prescribe or to initiate a treatment with dupilumab, not so much with tralokinumab, because this patient has asthma, and as you know, asthma is another indication for dupilumab. So, dupilumab would be my first choice, not tralokinumab. With dupilumab you would have, for this particular patient, I'd say, according to the motto, “buy one, get two indications treated,” and this would be the optimal

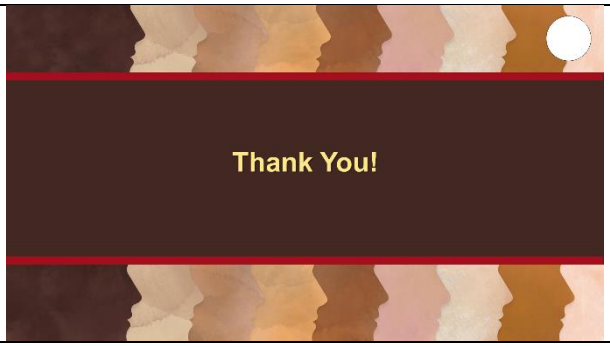
		situation for this particular patient.
35		However, if the patient exhibits needle aversions and prefers to have an oral option, what would be the option that you would choose? She's a young lady. She has severe atopic dermatitis, obviously not really controlled by the topical treatment. So, she is, in that case, a candidate for an oral JAK kinase inhibitor, clearly. And you have the choice between, in Europe, baricitinib, abrocitinib, and upadacitinib or just “abro” and “upa” in the States.
36		Another patient, 55 years old, a man with a 10-year history of atopic dermatitis. The current treatment crisaborole 2%, which I think is nonsense, to be honest, with regards to the severity of this patient. A body surface area of 45%, a vIGA of 4, so clearly a severe patient with a high pruritus score of NRS 9. So, it doesn't make sense at all to try crisaborole in that particular patient. So, which of the following would be the most appropriate next step for this patient? Trying another topical treatment with “ruxo.” Or switch to a biological therapy with “dupi” or “tralo.” Or an oral JAK kinase inhibitor like “abro,” “upa,” or baricitinib. Or again trying to control the disease, but only at the short term, with

		a shot of oral prednisolone. I think again in these patients you should first start with the biologic treatment. And in that case, I think you can have the choice between dupilumab and tralokinumab, because the patient is not suffering from asthma, so you can have the option of using tralokinumab, but you have to explain to the patient that this takes a little bit longer in order to fully control the disorder.
37		The problem is that biologics have to be kept in the fridge, and if you have a patient that due to his work is extensively traveling, you have a problem, because the patient will ask you, say, “I'm sorry I cannot use. I cannot bring with me all this stuff. You know the syringes and the biologic because this is too cumbersome to be put in my luggage and to keep it cool” and all these kind of things. So, what could be the other option? And clearly here this would be a candidate for an oral JAK kinase inhibitor, provided that he is not a patient at risk.
38		And the question of course is, here, if nothing works with the biologics? Or something else? So, you have to consider to switch from the biologic to the JAK kinase inhibitor. So, imagine you have a patient who was on the biologics or under an off-label

		treatment, and it is not fully controlled. You may be considering switching to an oral JAK kinase inhibitor.
39		But now comes the situation: He is 55 years old; he may have a risk for cardiovascular disorder because he potentially already had, let's say, a stroke or a heart attack; so he's certainly not the best candidate for JAK kinase inhibitor. But you have to consider this, you have to discuss this intensely with the patient and try to find something else. Maybe coming back to an off-label use. Maybe to an intense treatment with UVB plus topical treatment or even include him in a clinical trial. But again, with the clinical trial, you will potentially face the issue of the compliance if he is traveling very often; so this is really a very difficult case to manage.
40		So now comes the point, what I mentioned before already, that is you need to discuss all these issues with your patients. So shared decision-making now is, I think, in my experience, the most powerful way to find out what is the optimal treatment option for a given patient. You have to assess not only the severity, to be honest, you have to look at other dimensions. You have to look at the impact on the quality of life, for example. You have to ask about the

		comorbidity. Think about asthma. Recently, I had a patient who had asthma and EOE and chronic rhinosinusitis, and he came with atopic dermatitis, so he was the ideal candidate for dupilumab, because this drug is approved for all these different kinds of atopic comorbidities. Psychosocial factors — important to be considered in the management. The medication history, as I mentioned before, you know, you have to know what are these patients taking. Please also think about the drug–drug interaction issues, particularly when you are using small molecules like the JAK kinase inhibitors that may potentially interact with other drugs, particularly in older patients. And do not forget the patient education and counseling. This is so important to increase the compliance of these patients, that's absolutely mandatory, and I think we need to spend some time. I know that in daily practice, time is probably the thing that is lacking for most dermatologists. But in the context of the care of patients with atopic dermatitis, you need to spend some time to explain to the patients what it is about and what is the best therapeutic option for this patient.

41		So, this is a little bit, you know, the kind of process that you should go within your brain in order to find out what is the optimal treatment for a given patient that you are taking care of. You have to describe the problem, to look at the recommendations, to choose among the options that are available. Maybe to try out some clinical recommendations and to refine the therapeutic plan. That's something that is part of your daily practice. You have to look at all these points when it comes to finding the optimal treatment for a given patient.
42		And the shared decision-making with the patient is based on these five pillars: Empowering the patients. Inviting for active participation, and here again the compliance is extremely important. Using decision aids: There are currently a number of documentations and brochures, videos, and online tools that are available for this kind of decision aids. Addressing values and preferences, that's a very individual issue, whether the patients have particular kinds of concerns. And finally, encouraging the collaboration. You can only reach that final goal of having the optimal treatment option when, in fact, the patients are

		working with you, understands to weigh the benefit and risk of the different options that you have discussed with this patient. I was, I hope I was able to give you a little bit an insight on the current therapeutic options available for the treatment of moderate-to-severe atopic patients, adult patients by the way. The management of kids with atopic dermatitis has been addressed in another presentation.
43		Again, thank you very much for your attention.