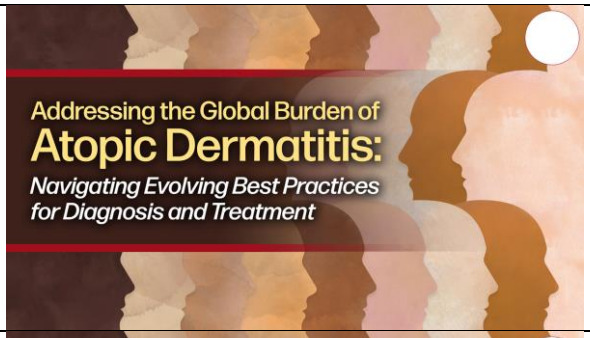
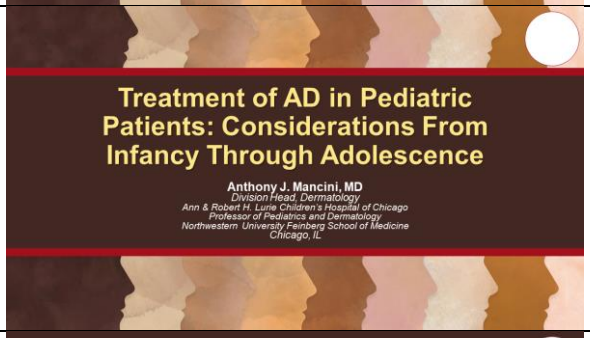
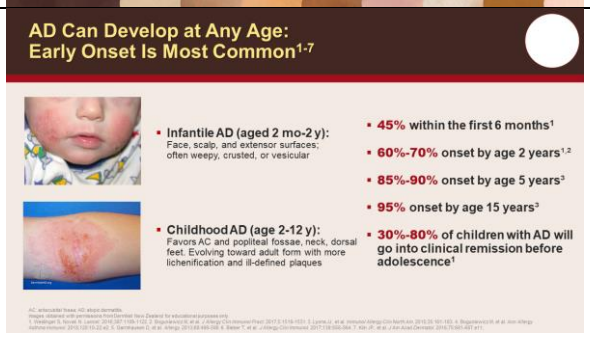
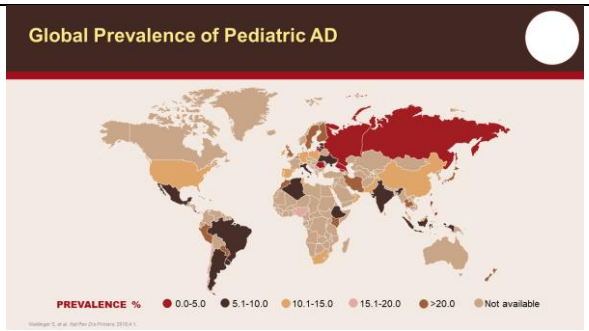
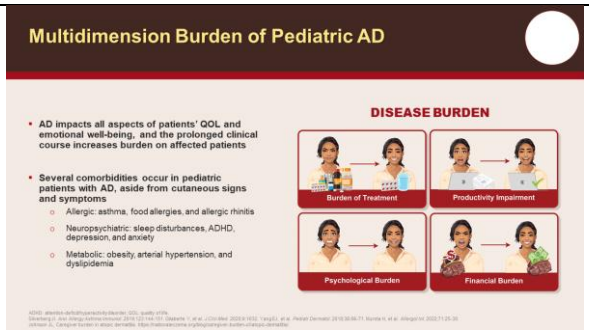
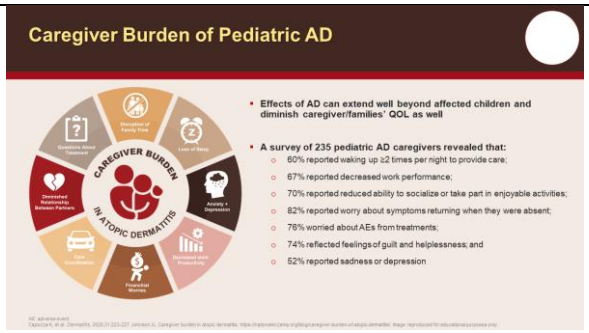
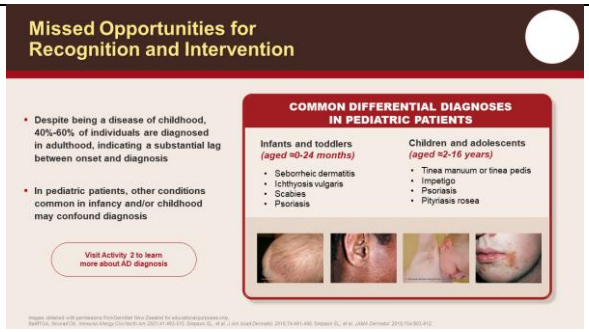
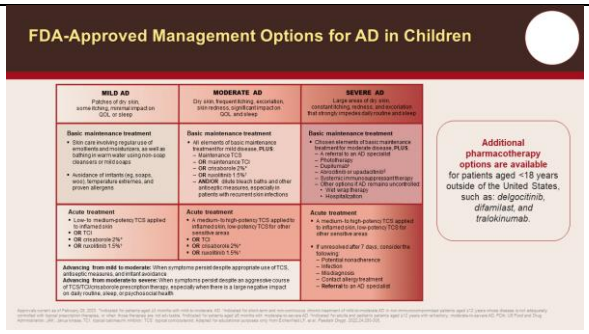
Addressing the Global Burden of Atopic Dermatitis: Navigating Evolving Best Practices for Diagnosis and Treatment

Treatment of AD in Pediatric Patients: Considerations From Infancy Through Adolescence

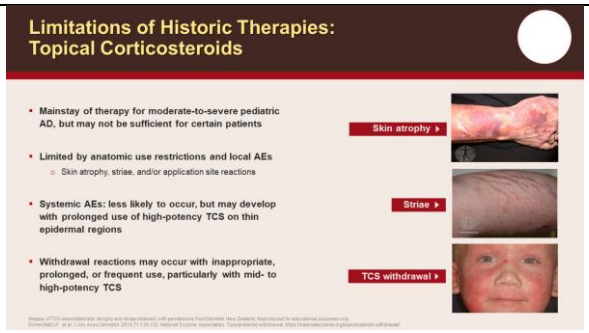
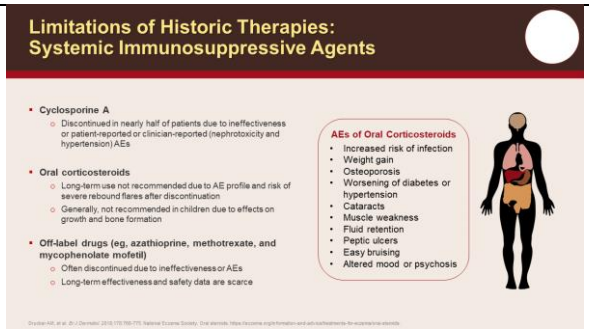
1		Hello and welcome to this program, Addressing the Global Burden of Atopic Dermatitis, Navigating Evolving Best Practices for Diagnosis and Treatment.
2		I'm Dr. Tony Mancini. I'm a pediatric dermatologist at Lurie Children's Hospital in Chicago and Northwestern University Feinberg School of Medicine. And in this module, we'll be discussing treatment of atopic dermatitis in pediatric patients, considerations from infancy through adolescence.
3		So, as everyone knows, atopic dermatitis can develop at any age, but really, early onset is most common. It's suggested that about 45% of patients have onset of the disease within the first 6 months of life, 60% to 70% by 2 years, 85% to 90% by 5 years, and 95% by 15 years of age. While about 30% to 80% of children, based on different studies, will go into clinical remission eventually before adolescence, most typically, we do have to acknowledge that there are adults that have atopic dermatitis, and it can persist throughout a lifetime. It can also show up at later ages. So, infantile atopic dermatitis classically involves the face, often the scalp, and then the extensor surfaces of the extremities. So it's more commonly going to be the outer surfaces rather than the classic and antecubital or popliteal involvement we typically think about with atopic dermatitis. Infants often have disease that may be a little more truly eczematous, weepy, crusted, often secondarily infected, and at times, even vesicular. As you get into toddlers and older children, it begins to favor more the antecubital and popliteal regions, so, that flexural involvement rather than the extensor involvement. You might also get more involvement of areas like the neck, the hands, the dorsal feet, and it really evolves more towards an adult type of picture with more lichenification as children become more able to scratch and rub effectively.

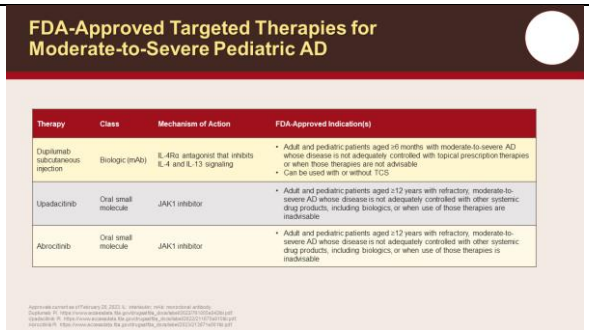
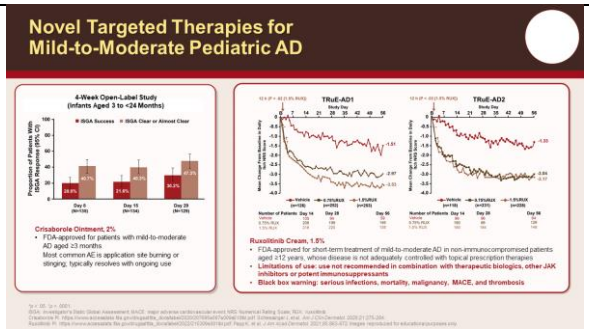
4		This slide looks at a 2018 review of the global prevalence of atopic dermatitis in kids, and you can see United States with a prevalence around 10% to 15%. That's similar to some areas in South Africa, in Europe, in the Far East. And then if you look at the dark red in the upper right, that's Russia, very low prevalence of atopic dermatitis. Whereas the dark brown, which represents greater than a 20% prevalence of pediatric disease, you can see in a few select areas in, I'm sorry, not the dark brown but more the chocolate brown, not quite the darkest brown, some areas in South America as well as throughout Europe, a couple of areas there in Africa. The very dark brown, which is a 5% to 10% prevalence, a little less than the United States, you see through a majority of Central and South America, again some areas in Africa, and the Middle East and Europe.
5		Well, atopic dermatitis really has a multidimensional burden. There's a significant burden on quality of life for both patients and their parents. It really can impact all aspects of a patient's well-being — emotional and physical. And the prolonged disease course, the fact that this can go on for years, with flares and remissions, can really put a burden on affected patients and their families. There are several comorbidities which occur in pediatric patients with atopic dermatitis, and these include other atopic conditions. So, reactive airways disease or asthma, food allergy, and allergic rhinoconjunctivitis. Neuropsychiatric disorders, we know that sleep disturbances are very common in young children with atopic dermatitis. There appears to be an increased prevalence of attention deficit disorder with hyperactivity, and it's well known that things like depression and anxiety occur with increasing prevalence. And some recent studies have even shown other comorbidities, including things like obesity, hypertension, and dyslipidemia. So, the cartoons on the right just summarize various disease burdens, the burdens of treatment. You can see multiple different medications there in the cartoon. Productivity impairment, especially for adults with the disease, but also in in this module — we're talking about pediatric atopic dermatitis — but the parents of those children, someone has to take care of them. Someone is up with them all night when they're scratching and not sleeping. Someone is getting the calls from the schools that there's an issue. Financial burden, visits to the doctor,

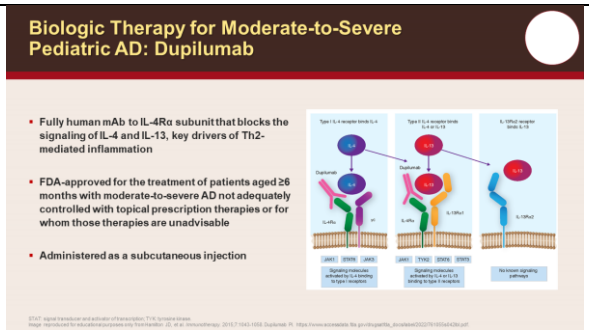
		laboratory testing visits to various specialists, and paying for all these medications, as well as lost time from work. And the psychological burden, which is really, really important.
6		So again, the effects of atopic dermatitis can extend well beyond the affected children and really have an impact on caregivers and the families and their quality of life. A survey of 235 pediatric atopic dermatitis caregivers showed several really important findings: 60% reporting frequent awakening at night; 67%, decreased work performance; 70%, reduced ability to socialize or take part in enjoyable activities because they're so busy with treatments or trying to catch up on sleep; 82%, worried about symptoms returning when the child was doing well. Three out of 4 worried about adverse events from treatments. Three out of 4 reporting feelings of guilt, feelings of helplessness. And over half reporting sadness or depression. So, if we go over the caregiver burden circle on the left, we can just see a summary of several of these features and others. Disruption of family time; starting at the top and then going towards the right, sleep disruption; anxiety, depression, and other psychiatric comorbidities; decreased work productivity; financial concerns; difficulties with just coordinating care, especially with your younger children, whether it's daycare or school; diminished or effects on the relationship between adult partners and families; questions or concerns about treatments and their potential adverse events.
7		So, despite being a disease of childhood, remember that 40% to 60% of individuals may be diagnosed during adulthood, even though they probably had onset earlier, and this indicates a substantial lag between onset and diagnosis. However, I will say we have to modify this by stating that we also now realize there are different types of natural histories in populations with atopic dermatitis, and there are forms that have their onset later in life. In pediatric patients, other conditions that are common in infancy or early childhood can also confound the diagnosis. So, the box on the right looks at just a little bit of a snapshot of some of the differentials. And usually this is a fairly straightforward diagnosis, but when you have patients that don't present quite classically or aren't responding as you expect to a treatment, you might want to consider other differentials. So, in infants and toddlers, things like

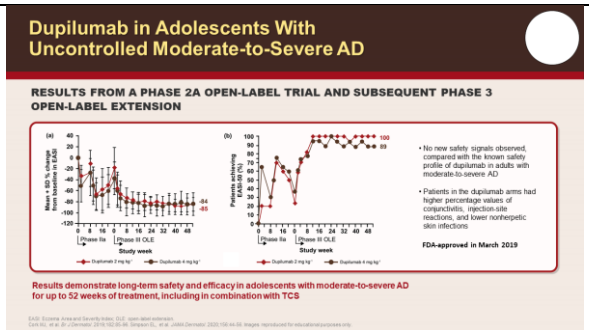
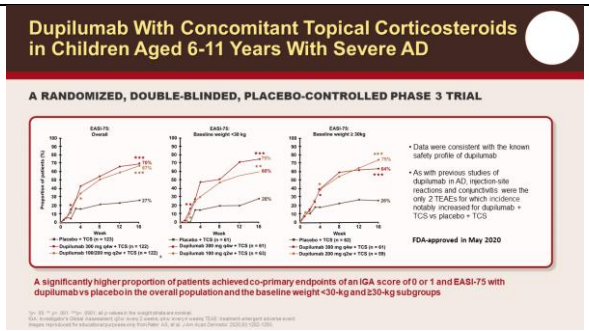
		seborrheic dermatitis; psoriasis; ichthyosis vulgaris, which often goes along with atopic dermatitis and not too commonly confused with it; and scabies infestation, when it's more severe, can be in the differential. And on the far right, children, older children, and adolescents — things like tinea and impetigo when it's more extensive, psoriasis or other papulosquamous disorders like pityriasis rosea. And the photos on the bottom, let's just look at these. The far left, seb-derm in an infant. So that's typical presentation of cradle cap, but that could be a presentation of atopic dermatitis as well. It can be different, difficult to differentiate sometimes. Fortunately, at that young age, those two really are treated fairly similarly. The next photo to the right is just demonstrating ichthyosis changes. You see that polygonal scaling, which often goes along with atopic dermatitis. The next photo to the right of the axilla in the young boy shows scabies nodules. Those would not be too likely to be confused with eczema, but when you have Norwegian or crusted scabies and more dermatic or secondary infection is present, it really could be confused. And the far-right panel shows impetigo, crusted impetigo, but that can often be confused with atopic dermatitis or, remember that often staph infection is a concomitant feature in many pediatric patients with the disease.
8		I'm going to spend a minute on this slide because it's really important. This is a slide that really summarizes, currently, the treatment landscape for pediatric atopic dermatitis, and it also has a treatment algorithm. So if we look at mild atopic dermatitis, the far-left column, basic maintenance treatment, which is really true for all levels of severity: Skin care; dry skin care. Most of us recommend daily short baths or showers with warm water; use of fragrance-free products and hypoallergenic products and trying to avoid irritants whenever possible; and regular emolliation. As you go into the lower left-hand corner of this box, acute treatment in the setting of mild disease. Here, we're talking typically about low-to-medium strength or potency corticosteroids topically; or TCIs, that's topical calcineurin inhibitors, or crisaborole, which is the first topical phosphodiesterase-4 inhibitor available; or now we also have, in patients 12 years of age and older, topical ruxolitinib, which is the first topical JAK inhibitor for treatment. So, several options for acute therapy, depending on your age. Let's look at the moderate atopic dermatitis column. So here, basic maintenance

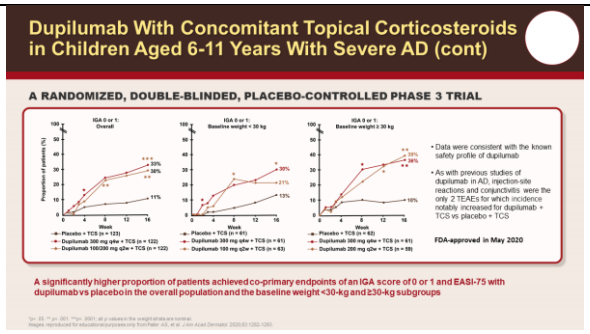
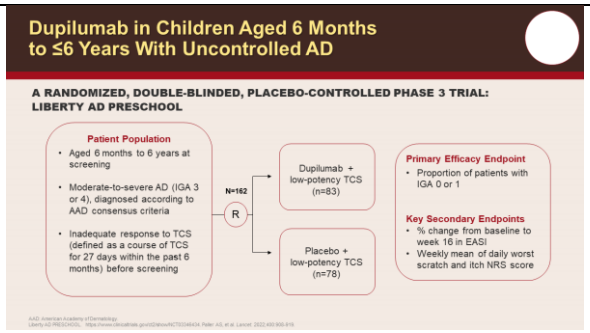
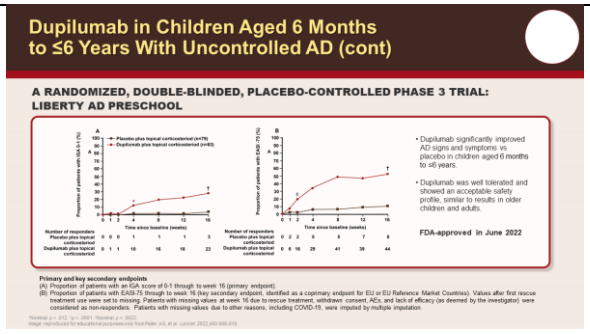
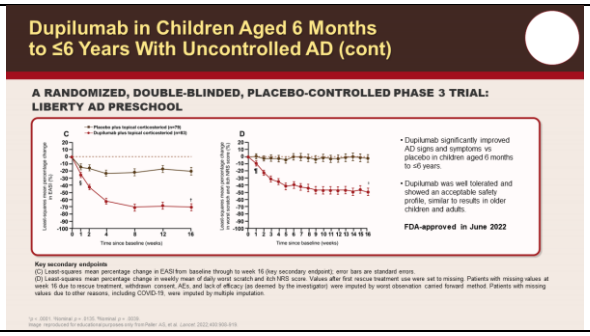
		treatment is the same, everything we talked about for mild, but now you might think about preventative therapy because these are the patients that are more likely to get recurrent flares, often in discrete locations that the parents and the families will know. So here, we might be talking about things like maintenance corticosteroids a few nights a week or use of calcineurin inhibitors as maintenance (crisaborole), ruxolitinib, the things we just talked about. And here you might think about adding things like bleach baths or a sodium hypochlorite cleanser, and that's because these are patients that are also more likely to have colonization and/or true infection caused by *Staphylococcus aureus*. During acute flares for this moderate group, you're going to be looking more at moderate or medium-to-high potency topical corticosteroids, although we may still use low-potency steroids for certain areas, like facial fold areas, like the axilla and the groin. But we also have options again with calcineurin inhibitors topically — crisaborole — or ruxolitinib creams. Let's look at severe atopic dermatitis, the column on the far right. So again, basic maintenance treatment is going to be very similar, but here's where we might really want to escalate treatment. So, this might include, if you're not one of them, a referral to an atopic dermatitis specialist; phototherapy, which we consider in patients 12 years of age and older predominantly, and that's predominantly we're talking about narrow band and UVB phototherapy. Dupilumab, an injectable biologic agent. Abrocitinib or upadacitinib, which are both now approved 12 years and older for moderate-to-severe resistant atopic dermatitis as an oral therapy. Systemic immunosuppressive therapy, the classic ones being used more so in the past, including methotrexate, cyclosporine, mycophenolate, mofetil, and azathioprine. And then other options if it remains poorly controlled: hospitalization for inpatient intensive therapy or wet wrap therapy, which can be performed both in the hospital or at home by the families. Acute treatment in this severe category again and medium-to-high potency topical corticosteroid, lower potency for other areas. And then the very far lower right-hand corner of the box, if not improving after 7 or even 7 to 14 days of treatment, consider nonadherence with therapies, secondary infection, maybe the diagnosis is wrong and that could be allergic contact dermatitis or any of a variety of the other differential diagnoses, or that it's time for referral to an atopic dermatitis specialist.

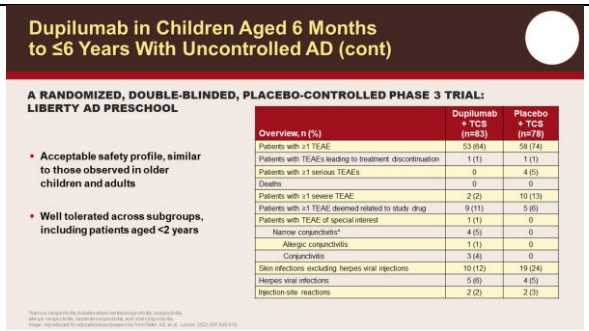
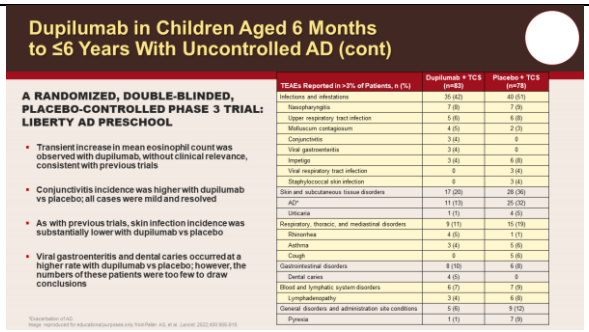
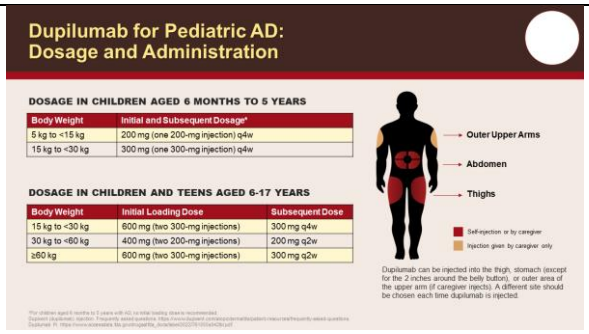
		Now there are additional pharmacologic treatments available for patients under 18 years of age outside of the United States, a few of those are listed here on the far right.
9		All right. What are the limitations of historic therapies? Well, topical corticosteroids, they're still a mainstay of therapy. We love topical corticosteroids, they are still very effective and very safe when used appropriately, even in young children. But in certain patients, we have to think about overuse, strengths that are too strong, effects that you see on the far right, skin atrophy at the top. And in that photograph, that's obviously combined with some senile purpura. But atrophy is something we really have to consider. Striae or stretch marks, as you can see in the middle photo. There are anatomic use restrictions that we have to think about. Obviously, we don't want to be using potent to ultrapotent steroids in areas like thin skin regions of the axilla, the groin, the face; even the medial thighs are more prone to striae. Systemic adverse events are far less likely to occur with topical corticosteroids. But they could occur, for instance, with widespread use of an agent that is too potent, especially in a younger patient which has a larger body surface area or a larger skin surface to body surface area ratio, and hence you have a higher chance for systemic absorption. Then there's this phenomenon of steroid withdrawal you see in the bottom bullet and in the bottom photo on the far right. So, corticosteroid withdrawal syndrome, which is a somewhat controversial topic, but really has been increasingly recognized as patients that require escalating potencies of their topical corticosteroids and when they don't use them regularly, they have massive rebound flares. It can really be problematic.
10		What about historic systemic immunosuppressive agents? So, there are several that have been used. Cyclosporine A really not used as much in the current era because of concerns about long-term adverse events. So, kidney toxicity, hypertension, and the risk of malignancy are big on the list there. Oral corticosteroids are rarely, rarely recommended. They might be used occasionally for a brief burst while you're getting other therapies going, just to get the patient under control more quickly. But long-term use is never recommended due to the adverse event profile. You can see that summarized in

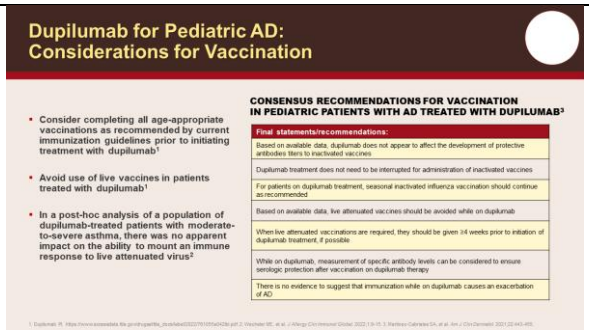
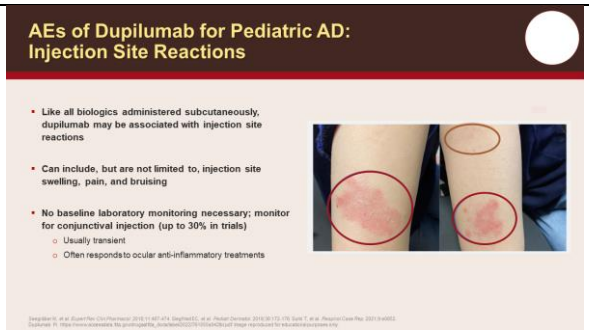
		the box on the right. These are all side effects I think that are familiar to all viewers with chronic oral corticosteroid therapy. We also really try to avoid these agents and young children because of effects on growth and bone formation. And then other off-label agents that I mentioned earlier, azathioprine, methotrexate, mycophenolate: They're often discontinued because of either ineffectiveness or concerns about adverse events in long-term safety. I will say of all the drugs on this slide, methotrexate is the one we use, at least I use personally, most often before we had newer agents and really could help and still can help patients with more moderate-to-severe disease if there are contraindications or concerns about newer systemic therapies.
11		Well, what are FDA-approved targeted therapies for moderate-to-severe pediatric atopic dermatitis? We have dupilumab by subcutaneous injection. This is a biologic agent. It's an antagonist of interleukin-4 receptor alpha and that modulates both IL-4 and IL-13 signaling, which are prominent inflammatory cytokines seen in atopic patients. It's FDA-approved for adult and pediatric patients 6 months of age and older with moderate-to-severe atopic dermatitis, whose disease has not otherwise been adequately controlled with topical prescription therapies. And it can be used with or without topical corticosteroids. More recently, we have two JAK1 inhibitors approved in the pediatric population 12 years of age and older — upadacitinib and abrocitinib. These are both oral small molecule therapies. They're JAK inhibitors and, again, indicated for refractory moderate-to-severe atopic dermatitis when disease is not adequately controlled with other systemic agents including biologics, or when those other agents are inadvisable.
12		So, let's look at some clinical data. So here I'm going to show you some novel targeted therapies for mild-to-moderate pediatric atopic dermatitis, and on this slide, these are both topical therapies. So, on the far left is crisaborole ointment, which has been around now for pediatric use for several years. This was a 4-week open-label study in infants aged 3 to 24 months of age. This is crisaborole 2% ointment and you can see, in red, investigator global assessment success that's defined as probably having a two-grade improvement and getting to clear or almost clear. And in the light brown, you see what the numbers were if you

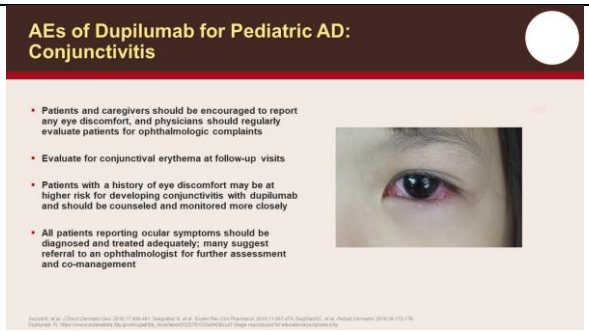
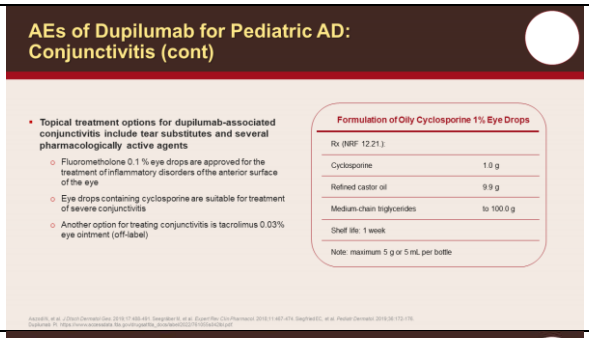
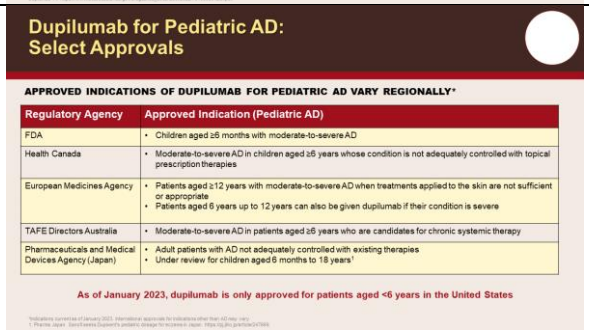
		just look at those that became clear or almost clear without having to jump two points on the scale and this is the proportion of patients who developed that endpoint response. So you can see significant responses. This led to approval down to 3 months of age. The most common adverse events with crisaborole ointment being application-site burning or stinging, which often gets better with continued use. The panel on the far right now is the pivotal trials data for ruxolitinib cream, approved 12 years of age and older for short-term treatment of mild-to-moderate atopic dermatitis in non-immunocompromised patients whose disease is not otherwise adequately controlled. So, this is the TRuE-AD1 and TRuE-AD2 studies, and we're looking here at the mean reduction in that numerical rating scale score for itch. OK, so vehicle is in red and then you have two different strengths of ruxolitinib, in dark brown and light brown. The light brown is the higher strength, and that's the one that was subsequently approved by the FDA. And you can see the marked separation between vehicle and the drug arms here as early as 7 days of treatment, and you can see that for both pivotal trials. Limitations of use for ruxolitinib cream: Not recommended in combination with therapeutic biologics, other JAK inhibitors, or potent immunosuppressants. And remember there is a black box warning on this class of drug and that's related primarily to the systemic agents and their initial approval in adults with other comorbidities who were being treated with these agents orally for things like rheumatoid arthritis.
13		Dupilumab: Biologic therapy that's approved for moderate-to-severe pediatric atopic dermatitis. So, this is a human monoclonal antibody to again the IL-4 alpha receptor subunit that blocks signaling of both interleukin-4 and interleukin-13. Remember these are key inflammatory cytokines that via the JAK-STAT pathway turn on production of inflammation. So, this is FDA-approved for treatment of patients 6 months of age and older with moderate-to-severe atopic dermatitis that's not otherwise adequately controlled. The cartoons on the left panel, you see here interleukin-4 binding to IL-4 alpha receptor and via JAK/STAT signaling turning on production of these inflammatory cytokines. And IL-13 here binding again to the IL-4 alpha receptor and dupilumab blocking that competitively, OK. And this is administered as a subcutaneous injection.

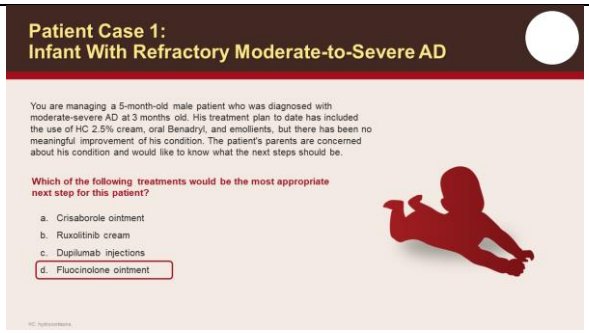
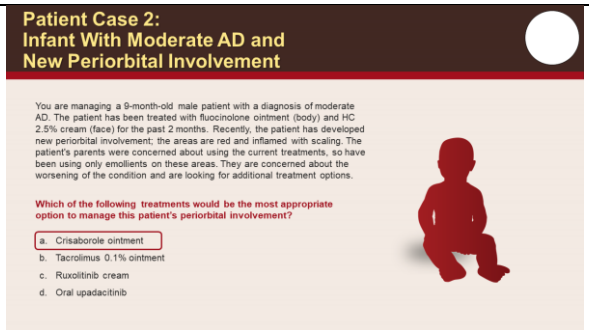
14		So, this is some trials data from adolescents. So, this is 12- to 18-year-olds with uncontrolled moderate-to-severe atopic dermatitis. This was an open-label trial and subsequently the phase 3 open-label extension in that population. You see dupilumab at low dose in red and a higher dose in brown, and here we're looking at the phase 2A data and the drop in that baseline EASI score — that's the eczema area and severity index score — so, the lower the EASI score, the better the patient's doing. So, you can see the initial drop and then during the phase 3 open-label extension really maintenance of effect outwards to 52 weeks. Over on the far right, we're looking at the EASI-50 scores. So, this means how many patients achieved 50% improvement in their EASI score. Again, during the phase 2A trial, you could see this increasing and then during the open-label extension a sharp increase and plateau with a sustained effect outwards to 52 weeks of treatment. There were no new safety signals observed compared to the known safety profile of dupilumab that was known from adult studies. There was a higher percentage of conjunctivitis in the dupilumab group as well as injection-site reactions, but there was a decrease in nonherpetic skin infections. So, bacterial skin infections we're actually seeing a decreased frequency in the dupilumab arms of these studies. This was approved in adolescents, then, in March of 2019.
15		What about children 6 to 11 years of age with severe atopic dermatitis? This was a randomized, double-blinded, placebo-controlled phase 3 trial. We're looking here on the far left at the EASI-75, so that's a 75% improvement in that EASI score overall. Placebo in dark brown on this slide, and dupilumab at two different dosing regimens in red and in the light brown, and you can see here the number of patients that achieved a 75% improvement in their EASI score, 67% to 70% in the dupilumab arms. And you see a large separation from vehicle as early as the 2-week time point. What about when you break that down by weight? Those under 30 kilograms and those over 30 kilograms, you can see really similar graphs, with the dupilumab arms statistically superior to vehicle. Now remember, in these studies they were allowed to use topical corticosteroids as well and, based on this data, dupilumab was approved in children as young as 6 years of age, in May of 2020.

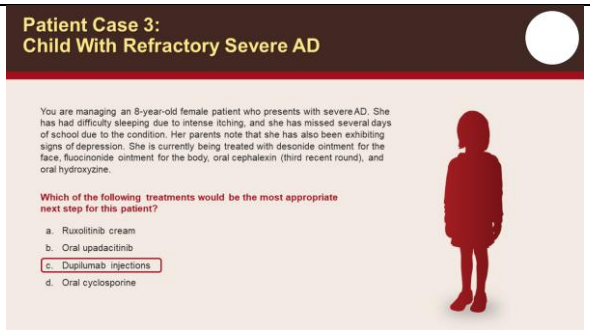
16		Here we're looking at similar graphs. Looking at the investigator global assessment of achieving clear or almost clear, that's 0 or 1 overall. The graph in the middle is under 30 kilograms and the right is over 30 kilograms. Very similar graphs, as you can see here. And again, different dosing of dupilumab, and they were allowed to use topical corticosteroids; the adverse event profile is very similar to other studies.
17		All right. How about children aged 6 months to 6 years? These patients had moderate-to-severe atopic dermatitis. We're talking here about a randomized, prospective, double-blinded, placebo-controlled phase 3 trial, and they were diagnosed according to the American Academy of Dermatology consensus criteria. They had had an inadequate response to topical corticosteroids, randomized to dupilumab with low-potency steroids, or just placebo with low-potency steroids. The primary endpoint being those that achieved clear or almost clear on the investigator's global assessment. And secondary endpoints included the percent change in the EASI score or the decrease in the numerical rating score for itch.
18		And here's the data. You can see here we're looking at patients that achieved an IGA score of 0 to 1 in the far-left graph, and on the far-right graph we're looking at those that achieved that 75% improvement in the EASI score. You can see dupilumab in red on both graphs and placebo in brown. And, again, appreciate the separation and the statistical superiority of dupilumab over placebo as early as 4 weeks for the IGA and as early as 2 weeks for achieving that EASI-75 score. This drug was approved then by the FDA for use down to 6 months of age last summer, in June of 2022.
19		And here we're looking at similar graphs, looking at the drop in the EASI score and the drop in the numerical rating score for itch. Again, you can see the separation between dupilumab and placebo in patients down to 6 months of age.

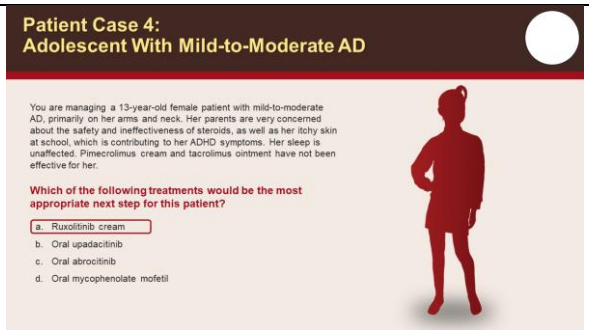
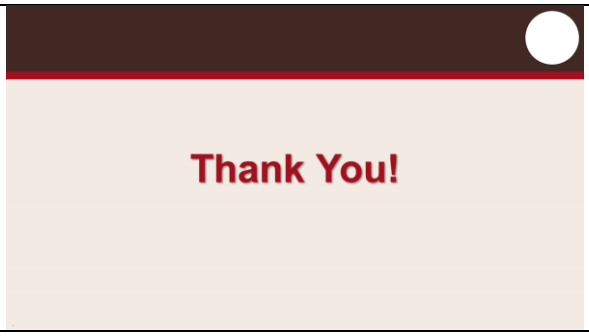
20		What about safety? This table on the right lists treatment-emergent adverse events and, remember that most of these were deemed to be not related to the drug by the study investigators. I want to highlight conjunctivitis, narrow conjunctivitis basically, includes all forms of conjunctivitis — allergic, bacterial, viral, and atopic — and it was higher in the dupilumab group, but still relatively low compared to the placebo group. But I also want to highlight this column of skin infections, excluding herpes virus infections, which is actually lower in the treated dupilumab group than in the placebo group.
21		Again, this chart now lists in detail the various different events reported during the clinical trial. Remember this is how clinical trials are performed and the study investigators, the PIs, really judged that the majority of these were not likely to be related to the study drug. You can see on here, impetigo, a bacterial infection, actually lower in the dupilumab with steroid group compared to the placebo with steroid group. Conjunctivitis, again higher in the dupilumab group, which is well known to be a risk of this agent. Viral gastroenteritis and dental caries both occurred at higher rates in the dupilumab group, but the numbers were so low that really conclusions could not be drawn. And the top bullet here on the left, you can just see that there was an increase, a transient increase, in the eosinophil count, but without any clinical relevance.
22		How about dosing? Well, it really depends on your age and your weight. So, children aged 6 months to 5 years depends on their weight, but you can see that they're all given dupilumab just once monthly. It's an every 4-week injection. Lower dose if you're under 15 kilos, higher dose if you're under 30 but over 15 kilos. And remember, there's no loading dose here, just the same dose every 4 weeks. In children and teenagers, so over 6 years of age, it depends on your weight and if you're between 15 and 30 kilos. You still only have to be injected once a month, which is great for these younger pediatric patients. Once you get over 30 kilograms, then it becomes a bimonthly injection at different doses based on your weight. Recommended dosing sites: Upper outer arms, abdomen, or the thighs. Remember, this is a subcutaneous injection.

23		What about considerations for vaccination? It's really recommended that all age-appropriate vaccines are completed prior to starting treatment with dupilumab, and that use of live virus vaccines should be avoided while on treatment. Those should be given at least 4 weeks before starting, and if a patient who's already on dupilumab really needs to have a live virus vaccine, that drug should be held. The time it's held is not really clear, with different recommendations according to different atopic dermatitis specialists. I've heard typically 4 to 8 weeks; some recommend longer, some shorter. In a post hoc analysis of a population of dupilumab-treated patients who had moderate-to-severe asthma, there was no apparent impact on the ability to mount an immune response to a live-attenuated virus. So, this box on the right gives consensus recommendations for vaccination. So, based on available data, dupilumab does not appear to affect the development of protective antibody titers in inactivated vaccines. Does not need to be interrupted to administer inactivated vaccines. The seasonal inactivated flu vaccine should continue to be recommended, even for patients on dupilumab. Live-attenuated vaccines, though, because of lack of available data, should be avoided while on dupilumab, and they should be given, if they're going to be given before treatment, at least 4 weeks before you initiate therapy. You can measure specific antibody levels if you receive vaccines while on dupilumab, or the patient does, and you want to check, and there's no evidence to suggest that immunization while on dupilumab will cause an exacerbation of the atopic dermatitis.
24		Injection-site reactions are something we have to always warn our families about. They may be seen, as you see in these pictures, here, they are transient, they are treated symptomatically, and they tend to be self-limiting. We should be monitoring our patients for conjunctival injection. When you look at different trials, conjunctivitis has been reported up to 30%, but really in clinical use I've seen it in less than 10% of patients, more around 5% of my patients.

25		What about the conjunctivitis? So, we have to encourage our families to report it to us regularly if they develop it. Evaluate for it when we see them at follow-up visits. I often comanage these patients pretty much always with my pediatric ophthalmology colleagues. And those that have a history of eye discomfort may be at risk, a higher risk for developing conjunctivitis; maybe they had some preexisting conjunctivitis to begin with that was clinically not visible. And they should be monitored appropriately.
26		There are a variety of topical treatments for dupilumab-associated conjunctivitis listed on this slide. The box on the right shows the formulation of the oily cyclosporine eye drops that contain both castor oil and medium-chain triglycerides in conjunction with cyclosporine. But again, I only have these patients managed in conjunction with my pediatric ophthalmology colleagues.
27		Select approvals for pediatric atopic dermatitis based on your geographic location. So, the FDA has approved dupilumab for atopic dermatitis down to 6 months in patients with moderate-to-severe disease. What about Canada? It's approved for moderate-to-severe disease in those 6 years of age and older. In Europe, 12 years of age and older, but they state that 6- to 12-year-olds can be given it if their condition is severe. In Australia, it's approved for moderate-to-severe disease in patients 6 years of age and older who are candidates for a chronic systemic therapy. And in Japan, it's really only approved in adults, but under review for children ages 6 months to 18 years. As of January of this year, dupilumab is only approved for patients under 6 years of age in the United States.
28		What about geographic variations? Well, in patients who are in Latin American countries, they have approved dupilumab for use in adolescents and adults. Some of those countries, including Brazil, have also approved it down to younger ages. Costs may be a barrier and we have to remember in terms of treatment considerations, helminthic parasitic infections can co-occur with atopic dermatitis and really should be treated before initiating dupilumab. If a patient who is on dupilumab develops a parasitic infestation and they don't respond to treatment, they should discontinue the dupilumab until the infestation resolves.

		And just as an example of a parasitic infestation, on this slide we included cutaneous larva migrans, which is a fairly common cutaneous parasitic infestation.
29		All right, we're going to end with some patients, with some cases now. I'm going to read some options for correct choices, give you a minute to make your selection, and then we'll discuss the appropriate answer. You're managing a 5-month-old male patient who was diagnosed with moderate-to-severe atopic dermatitis at 3 months of age. His treatment plan to date has included 2.5% hydrocortisone cream, oral Benadryl, and emollients. There's been no meaningful improvement in his condition. His parents are concerned about his condition, and they'd like to know what are the next steps? So which of the following choices here would be the most appropriate next step for this 5-month-old? Crisaborole ointment, ruxolitinib cream, dupilumab injections, or fluocinolone ointment? Take a minute to make your selection. All right. The best choice here, really, is fluocinolone ointment. So, what I was getting to with this case is that this child has only been treated with low-potency corticosteroids, he's got moderate-to-severe disease, so if we're going to do anything out of these four, the next step is going to be to increase the potency of that corticosteroid. Crisaborole, it's approved, it's approved under 3 months, but unlikely to really be effective for a patient with moderate-to-severe disease. Ruxolitinib cream is only approved under 12 years and dupilumab injection is not approved under 6 months, so not approved here yet.
30		You're managing a 9-month-old male patient with a diagnosis of moderate atopic dermatitis. The patient's been treated with fluocinolone ointment for the body, hydrocortisone 2.5% cream for the face for the past 2 months. Recently, he developed new periorbital involvement, and those areas are red and inflamed with scaling. The patients, excuse me, parents are concerned about using the current treatments, so they've been using really only emollients around the eyes. And they're concerned about the fact that his condition is getting worse, and they want to know what are additional treatment options. So, which of the following treatments here would be most appropriate as an option to manage his periorbital involvement? Would it be crisaborole ointment,

		tacrolimus 0.1% ointment, ruxolitinib cream, or oral upadacitinib? Go ahead and make your choice here. All right. Now of these choices, really the best option will be crisaborole ointment. We have an approval down to 3 months of age. It's steroid-free. It's very safe to use around the eyes. Tacrolimus would have been a great choice, but it's not approved down to this age. And in fact, the 0.1% ointment, which is the higher strength, is only approved at 16 years and older. Ruxolitinib cream has only been approved down to 12 years of age, and oral upadacitinib clearly would not be the option and it's approved for 12 years of age and older.
31		Alright, case 3, you're managing an 8-year-old female patient who presents with severe atopic dermatitis. She's had difficulty sleeping because of intense itching and she's missed several days of school because of her condition. Her parents note that she's also been exhibiting some signs of depression. She's currently being treated with desonide for the face, fluocinonide ointment for the body, and her third recent round of oral cephalexin for presumed secondary infection. She also takes oral hydroxyzine for itch and sleep at night. So, which of the following treatments would be the next step that's most appropriate for this patient? Ruxolitinib cream, oral upadacitinib, dupilumab injections, or oral cyclosporine? Go ahead and make your choice. And for this patient, really, I would choose dupilumab. Why is that? She's 8 years old. We have an approval at her age. She's had severe disease, lots of itching. She's missed school, and now she's depressed and she's on a Class 2 steroid for the body and extremities. Right? Fluocinonide, she's been treated for infection, been treated with an oral antihistamine for sleep. Ruxolitinib only approved 12 years of age and older and wouldn't be an appropriate choice for a severe disease anyway. Oral upadacitinib again only approved at 12 years of age and older. And oral cyclosporine, an older immune suppressant that few would select in this setting.

32		All right. And our last case is a 13-year-old female who has mild-to-moderate atopic dermatitis primarily on her arms and neck. Her parents are very concerned about the safety and ineffectiveness of topical steroids and her itchy skin at school, which her teachers feel is contributing to her attention deficit disorder symptoms. Her sleep is unaffected. She's used pimecrolimus cream and tacrolimus ointment as steroid-free options because her parents were concerned about steroids. But they have not been effective for her. So, which of the following treatments would be the most appropriate consideration next for this patient? Would it be ruxolitinib cream, oral upadacitinib, oral abrocitinib, or oral mycophenolate mofetil? Go ahead and make your selection. All right. And for this patient, really, ruxolitinib cream is going to be the most appropriate choice. It's approved for 12 years of age and older. She has mild-to-moderate disease. She has parents who are concerned about steroids, and she's failed topical calcineurin inhibitors. Oral upadacitinib and abrocitinib are both approved 12 years of age and older, but for mild-to-moderate disease is not the first choice I would make. And oral mycophenolate mofetil, again, an older immunosuppressant agent that had been used a lot in the past, but most would probably choose one of the newer agents over an immunosuppressive agent in this setting.
33		All right. Thank you so much for your attention. I hope you enjoyed this module.