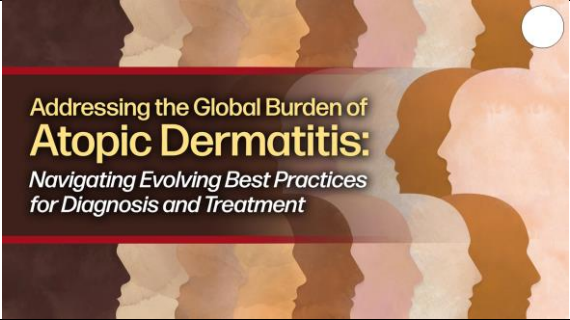
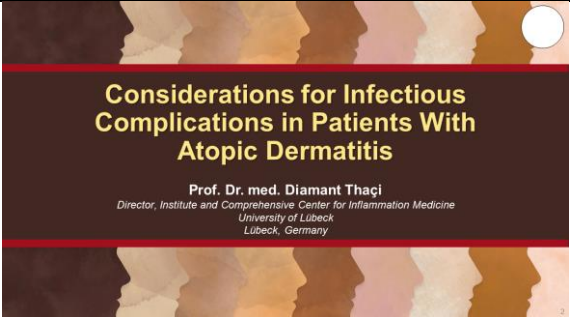

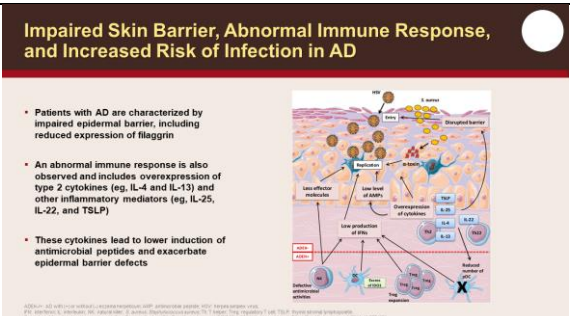


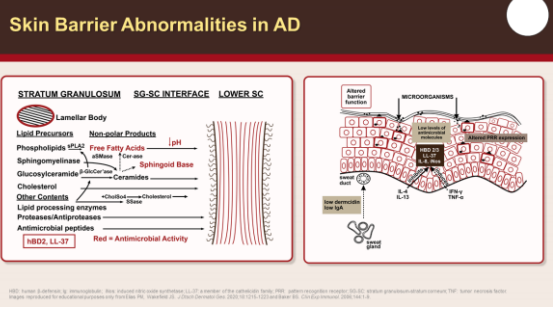
# Addressing the Global Burden of Atopic Dermatitis: Navigating Evolving Best Practices for Diagnosis and Treatment

## Considerations for Infectious Complications in Patients With Atopic Dermatitis

1		<p>Ladies and gentlemen, dear colleagues, it's my pleasure to be part of Addressing the Global Burden of Atopic Dermatitis, as an important tool for us as dermatologists to navigate evolving best practices for diagnosis and treatment.</p>
2		<p>I will consider today and focus more on infectious complications in patients with atopic dermatitis. My name is Diamant Thaçi, I'm a university professor at the Comprehensive Center for Inflammation Medicine at University of Lübeck, in Lübeck, Germany, and I'm very pleased to be here today with you.</p>
3		<p>Let me introduce atopic dermatitis as one of the most common skin diseases that we are facing every day in our daily practice, which affects not only children but also adolescents and also adults. In the past, we thought that mainly children are affected, with a high prevalence between 15% and 30%, and today we know that this is also a frequent disease in adults, where we assume that about 2% to 10% of adults may have atopic dermatitis. It's a complex disease — we agree all about this complexity. It is genetically driven. Immunological factors are playing a very important role. Environmental factors and stimuli are also very important; they are leading to the more immune dysregulation at one part, but at the other side we have also the skin barrier which is impaired. And, of course, the disease is accompanied with itch, which aggravates the signs and symptoms of atopic dermatitis. Finally, atopic dermatitis is also associated with different comorbidities, which may also increase the risk for cutaneous but also systemic infection.</p>
4		<p>Let me start with the first part of my talk, at the beginning of the introduction, showing you the pathophysiology of atopic dermatitis, which is very crucial, as a better understanding of the pathophysiology is leading to a better understanding of the risk for cutaneous and also systemic infection. You might see that in a patient with atopic dermatitis, we</p>

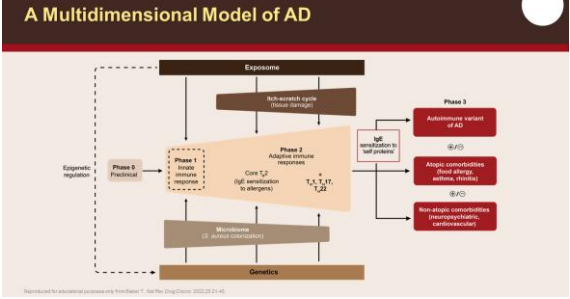
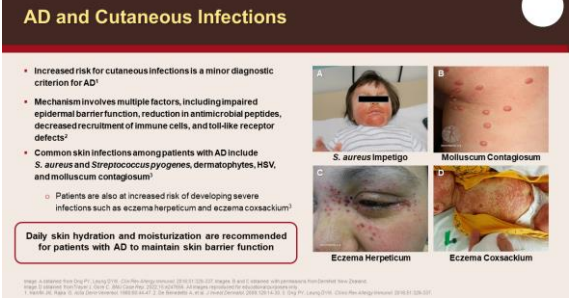
# Addressing the Global Burden of Atopic Dermatitis: Navigating Evolving Best Practices for Diagnosis and Treatment

## Considerations for Infectious Complications in Patients With Atopic Dermatitis

		<p>have type 2 inflammation, at least at the beginning. And this type 2 inflammation in general is leading to the lower production of antimicrobial peptides. A low production of antimicrobial peptides means that the keratinocytes are producing less of these antibiotics of the skin to protect us against different microorganisms, including staphylococci, including also viral infection, which may penetrate easily through the skin of the patient with atopic dermatitis, because as we mentioned at the beginning, it is a disease where we have also impairment of the skin barrier. And if the skin barrier is not working properly, then not only antigens, superantigens, environmental stimuli, whatever, can penetrate easily through the skin, but also viruses, like herpes simplex, or also bacteria, like <i>Staphylococcus aureus</i>. And these may interact with the immune system, aggravating the atopic dermatitis at one side, but at the other side also leading to diseases of the skin, cutaneous infection, or even to the systemic infection. And I think this is also particularly important once we are going to the next slide and looking, how is this happening?</p>
5	 <p>The slide, titled "Skin Barrier Abnormalities in AD", contains two diagrams. The left diagram shows the skin layers: STRATUM GRANULOSUM, SG-SC INTERFACE, and LOWER SC. It details the Lamellar Body and lists components: Lipid Precursors (Phospholipids, Sphingomyelinase, Glucosylceramide, Cholesterol), Non-polar Products (Free Fatty Acids, Ceramides), and pH. It also lists Other Constituents (Lipid processing enzymes, Proteases/Antiproteases, Antimicrobial peptides) and notes that HBD2, LL-37, and Red indicate Antimicrobial Activity. The right diagram shows Microorganisms (Staphylococcus aureus, Staphylococcus epidermidis, Malassezia, Candida) penetrating the skin barrier, with cytokines IL-4 and IL-13 shown to inhibit the barrier's function.</p>	<p>If you start with the skin barrier, we do agree that the skin barrier in atopic dermatitis is totally different. The abnormalities in the skin barrier, for example, filaggrin mutations, can lead to increased vulnerability of the skin to penetration by microorganisms. Furthermore, certain local factors such as differences in pH, free fatty acids, sphingoid bases, and decreased production of antimicrobial peptides contribute to the increased susceptibility of the skin in patients with atopic dermatitis to microbial penetration. And of course, that what we see here that IL-4 and -13 is inhibiting directly the production of antimicrobial peptides, among them, human beta-defensin 2 and 3, cathelicidin, and also the others. And we see also that the others, for example, type 1 inflammation like interferon-alpha may induce the production of antimicrobial peptide. Therefore, in diseases which are type 1 driven, we have a lot of interferon-gamma, and interferon-gamma protects the skin against the viral infection but also increases the production of antimicrobial peptides,</p>

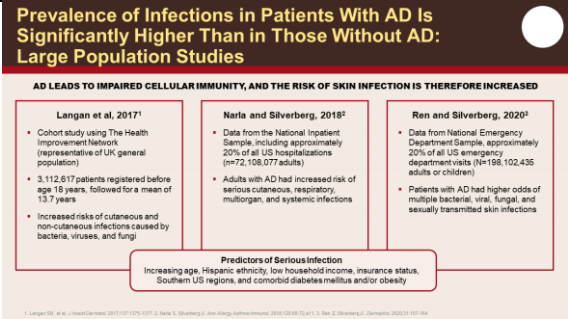
# Addressing the Global Burden of Atopic Dermatitis: Navigating Evolving Best Practices for Diagnosis and Treatment

## Considerations for Infectious Complications in Patients With Atopic Dermatitis

		<p>protecting the skin from infection. And — this is very crucial to understand — the skin barrier in patients with atopic dermatitis is impaired and can lead to more frequent infections.</p>
<p>6</p>	 <p><b>A Multidimensional Model of AD</b></p> <p>The diagram illustrates the progression of Atopic Dermatitis (AD) through three phases. It starts with the <b>Exposome</b> (top) leading to the <b>Immune cycle (skin barrier)</b>. <b>Phase 1</b> involves <b>Phase 1: Skin barrier defects</b> (Epigenetic regulation, Phase 0: Preclinical). <b>Phase 2</b> involves <b>Phase 2: Allergic immune responses</b> (Core 1, 2: IgE sensitization to allergens; Core 3, 4: T<sub>H</sub>1, T<sub>H</sub>17, T<sub>H</sub>22). This leads to <b>Phase 3: Autoimmune variant of AD</b> (B/V/D) and <b>Atopic comorbidities</b> (Food allergy, asthma, rhinitis) (B/V/D). <b>Non-atopic comorbidities</b> (Neuropsychiatric, cardiovascular) (B/V/D) are also shown. <b>Morbidity (e.g. asthma comorbidity)</b> and <b>Genetics</b> (bottom) are also indicated.</p>	<p>But generally, if you look at the model of atopic dermatitis, we do see that genetics are playing a very important role. But also, the environment is influencing, also, the occurrence of the disease and worsening of the disease. At the very early beginning, we might see that microbiome and especially <i>Staphylococcus aureus</i> colonization may drive also the disease, and not only simply being something that may cause infection, but something which can also influence the course of the disease. And we do see that in the late phases, or phase 3, we have comorbidities like autoimmune-variant comorbidities, like food allergy, asthma, rhinitis, morbidities like neuropsychiatric, cardiovascular. And all these comorbidities can also increase the risk for infection in patients with atopic dermatitis, especially patients with a moderate-to-severe form of atopic dermatitis.</p>
<p>7</p>	 <p><b>AD and Cutaneous Infections</b></p> <ul style="list-style-type: none"> <li>Increased risk for cutaneous infections is a minor diagnostic criterion for AD<sup>1</sup></li> <li>Mechanism involves multiple factors, including impaired epidermal barrier function, reduction in antimicrobial peptides, decreased recruitment of immune cells, and toll-like receptor defects<sup>2</sup></li> <li>Common skin infections among patients with AD include <i>S. aureus</i> and <i>Streptococcus pyogenes</i>, dermatophytes, HSV, and molluscum contagiosum<sup>3</sup> <ul style="list-style-type: none"> <li>Patients are also at increased risk of developing severe infections such as eczema herpeticum and eczema cocksackium<sup>4</sup></li> </ul> </li> </ul> <p>Daily skin hydration and moisturization are recommended for patients with AD to maintain skin barrier function</p> <p>Images: A: S. aureus impetigo; B: Molluscum Contagiosum; C: Eczema Herpeticum; D: Eczema Cocksackium</p>	<p>If you look carefully at our patients with atopic dermatitis in daily practice, we do see that patients with atopic dermatitis have increased risk for cutaneous infection. This is even part of the criteria, once we are discussing about the criteria, how to do the diagnosis of atopic dermatitis. There are different mechanisms, as I mentioned. The skin barrier is impaired in patients with atopic dermatitis. Especially in children, we might see a higher increase of risk for viral infection, like for example molluscum contagiosum. And if you see the skin in the patient with atopic dermatitis having molluscum contagiosum, it is not always the inflamed skin. So, it may occur also in the region where we do not really have inflamed skin. Furthermore, the patient with atopic dermatitis has also itch. Itch and scratching is spreading the infection easily from one place to another place. This is more evident in children, but can happen also in adolescents and also in adults, for example, with impetigo. Impetigo is very frequent in children, which is caused by staphylococci,</p>

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


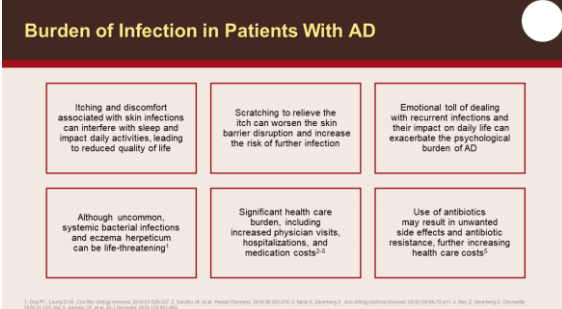
## Considerations for Infectious Complications in Patients With Atopic Dermatitis

		<p>sometimes also streptococci, sometimes also a mix of both of them, and we see that this is also aggravating the disease. And sometimes it's leading to the need for systemic treatment of children with drugs, which are important to fight the infection in these patients. It is also very important to understand that the patient with atopic dermatitis — children, adolescents, and also adults — may also develop life-threatening diseases like eczema herpeticum, which may occur after a very simple infection with herpes simplex virus. So, I think this is also important. Also, eczema coxsackium can occur in children. So this means that infection in patients with atopic dermatitis can be very mild but also may be life-threatening and very severe, requiring a need for a more intensive treatment. Therefore, it's always very important that we have daily skin hydration and moisturization, that the skin must not be dry because this will aggravate — increase — the risk of infection in patients with atopic dermatitis.</p>			
8	 <p><b>Prevalence of Infections in Patients With AD Is Significantly Higher Than in Those Without AD: Large Population Studies</b></p> <p><b>AD LEADS TO IMPAIRED CELLULAR IMMUNITY, AND THE RISK OF SKIN INFECTION IS THEREFORE INCREASED</b></p> <table border="1"> <tr> <td> <p><b>Langan et al., 2017<sup>1</sup></b></p> <ul style="list-style-type: none"> <li>Cohort study using The Health Improvement Network (representative of UK general population)</li> <li>3,112,617 patients registered before age 18 years, followed for a mean of 13.7 years</li> <li>Increased risks of cutaneous and non-cutaneous infections caused by bacteria, viruses, and fungi</li> </ul> </td> <td> <p><b>Naria and Silverberg, 2018<sup>2</sup></b></p> <ul style="list-style-type: none"> <li>Data from the National Inpatient Sample, including approximately 20% of all US hospitalizations (n=72,106,077 adults)</li> <li>Adults with AD had increased risk of serious cutaneous, respiratory, multiborgan, and systemic infections</li> </ul> </td> <td> <p><b>Ren and Silverberg, 2020<sup>3</sup></b></p> <ul style="list-style-type: none"> <li>Data from National Emergency Department Sample, approximately 20% of all US emergency department visits (N=198,102,435 adults or children)</li> <li>Patients with AD had higher odds of multiple bacterial, viral, fungal, and sexually transmitted skin infections</li> </ul> </td> </tr> </table> <p><b>Predictors of Serious Infection</b> Increasing age, Hispanic ethnicity, low household income, insurance status, Southern US regions, and comorbid diabetes mellitus and/or obesity</p>	<p><b>Langan et al., 2017<sup>1</sup></b></p> <ul style="list-style-type: none"> <li>Cohort study using The Health Improvement Network (representative of UK general population)</li> <li>3,112,617 patients registered before age 18 years, followed for a mean of 13.7 years</li> <li>Increased risks of cutaneous and non-cutaneous infections caused by bacteria, viruses, and fungi</li> </ul>	<p><b>Naria and Silverberg, 2018<sup>2</sup></b></p> <ul style="list-style-type: none"> <li>Data from the National Inpatient Sample, including approximately 20% of all US hospitalizations (n=72,106,077 adults)</li> <li>Adults with AD had increased risk of serious cutaneous, respiratory, multiborgan, and systemic infections</li> </ul>	<p><b>Ren and Silverberg, 2020<sup>3</sup></b></p> <ul style="list-style-type: none"> <li>Data from National Emergency Department Sample, approximately 20% of all US emergency department visits (N=198,102,435 adults or children)</li> <li>Patients with AD had higher odds of multiple bacterial, viral, fungal, and sexually transmitted skin infections</li> </ul>	<p>Looking at the prevalence of the atopic dermatitis infection, from the different databanks we can realize that the risk of infection is much higher in patients with atopic dermatitis. We have increased risk for noncutaneous infection caused by bacteria virus and also by fungi. A very large dataset from a national inpatient sample study demonstrated that patients with atopic dermatitis are at risk of developing severe cutaneous, respiratory, and systemic infections. Data from national emergency departments have also shown that both adults and children with atopic dermatitis have higher odds of bacterial, viral, fungal, and other skin infections. These findings show the importance of gaining a better understanding of the disease, as well as selecting appropriate and adequate treatment options for these patients. Predictors of serious infection include younger patients (children), but also patients with comorbidities such as diabetes or obesity, or patients with lower socioeconomic status, where we see that infections can occur more frequently.</p>
<p><b>Langan et al., 2017<sup>1</sup></b></p> <ul style="list-style-type: none"> <li>Cohort study using The Health Improvement Network (representative of UK general population)</li> <li>3,112,617 patients registered before age 18 years, followed for a mean of 13.7 years</li> <li>Increased risks of cutaneous and non-cutaneous infections caused by bacteria, viruses, and fungi</li> </ul>	<p><b>Naria and Silverberg, 2018<sup>2</sup></b></p> <ul style="list-style-type: none"> <li>Data from the National Inpatient Sample, including approximately 20% of all US hospitalizations (n=72,106,077 adults)</li> <li>Adults with AD had increased risk of serious cutaneous, respiratory, multiborgan, and systemic infections</li> </ul>	<p><b>Ren and Silverberg, 2020<sup>3</sup></b></p> <ul style="list-style-type: none"> <li>Data from National Emergency Department Sample, approximately 20% of all US emergency department visits (N=198,102,435 adults or children)</li> <li>Patients with AD had higher odds of multiple bacterial, viral, fungal, and sexually transmitted skin infections</li> </ul>			



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

## Considerations for Infectious Complications in Patients With Atopic Dermatitis

		<p>dysbiosis with more pronounced <i>Staphylococcus aureus</i> is leading to the nonhistaminergic itch pathway, which means that it is causing not only the aggravation of the disease, but also increase the itch in patients with atopic dermatitis.</p>
11		<p>Understanding this is also part of the pathophysiology of atopic dermatitis. We see at one side more acute inflammation, which is leading to the itch, which is at the beginning probably more superficial. But later on, we see the deep excoriations, which are with oozing and crusting with bacteria and especially staphylococci, can lead very fast to the colonization. We might see that around these scratches, around this excoriation, very fast we have also the occurrence of the inflammation bringing this together, that in patients with atopic dermatitis, we see that colonization but also infection and penetration of staphylococci is triggering at one side the disease, sometimes aggravating the disease, sometimes aggravating the itch, which is leading to the worsening of the clinical signs and symptoms of atopic dermatitis.</p>
12		<p>Finally, burden of disease, in general, of atopic dermatitis, especially because of itch and discomfort in patient with a skin infection, is the complaint of sleep loss. The patient cannot do their daily activities. The skin is not only itchy, not only burning, but it's also hurting. And also, due to the inflammation, is leading to more emotional stress. This is leading to significant health care burden, which includes also higher rates of hospitalization. At the other side, this also increases the costs of treating these patient. And in some cases, especially when we are talking about the eczema herpeticum, this can be also life-threatening. So sometimes we need also to act very fast. Especially in children where the risk can be also very, very high. At the other side, sometimes we use also antibiotics. Maybe also need, especially in a younger patient where we have a more severe infection, and this might cause also higher cost and may increase also antibiotic resistance.</p>

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

## Considerations for Infectious Complications in Patients With Atopic Dermatitis

<p>13</p>	<h3>AD and Systemic Infections</h3> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"> <p><b>COVID-19 Infection</b></p> <p>Large cohort study (N=436,709)<sup>1</sup></p> <ul style="list-style-type: none"> <li>Adults with AD have slightly higher risk of COVID-19 infection, but also have higher prevalence of baseline comorbidities known to be COVID-19 risk factors, compared with adults without AD</li> </ul> </div>	<p>I think we are talking mainly about the cutaneous manifestation, the cutaneous infection, but sometimes we forget that patients with atopic dermatitis in general, they have a higher risk also for other infections. OK, chicken pox. We know this from the skin, but influenza and pneumonia, especially patients with comorbidities like asthma, is very frequent. Ear infection is also more frequent in patients with atopic dermatitis, as well as other infections. Even COVID-19 infection is more frequent in patients with atopic dermatitis, and this correlates very well also with the disease severity; in patients with more severe disease, we see even higher risk of COVID-19 infection.</p>
<p>14</p>	<h3>Overview: Treatment Algorithm for Moderate-to-Severe AD<sup>1</sup></h3> <ul style="list-style-type: none"> <li>Add antibiotic/antibiotic/antifungal treatment in cases of infections</li> <li>Consider compliance and diagnosis, if therapy has insufficient effect</li> <li>Refer to Part II, Table 2 for TCS classes recommended<sup>2</sup></li> </ul> <p>Legend: ** strong recommendation for the use of an intervention; * weak recommendation for the use of an intervention</p>	<p>And today, we have a different treatment option. According to the guidelines, we do have a stepwise approach where we start with a baseline treatment; mild, moderate, and severe diseases are also disease activity adapted, treated. While it is very important to understand the baseline treatment, which accompanies also the systemic and topical treatment because it helps, while it is important to understand baseline treatments that involves systemic and topical approaches, understanding the significance of emollients is equally important. Emollients are very important because they reduce skin dryness, a factor that facilitates the more effective colonization of bacteria, viruses, and other microorganisms, leading to skin infections.</p>
<p>15</p>	<h3>Novel Biologic and Targeted Therapies for Moderate-to-Severe AD</h3> <ul style="list-style-type: none"> <li>Dupilumab binds to the IL-4/IL-13 effector subunit, blocking signaling of both IL-4 and IL-13, while tralokinumab specifically binds to IL-13</li> <li>Crucial JAK inhibitors work by selectively inhibiting JAK1 (abrocitinib, upadacitinib) or both JAK1 and JAK2 (baricitinib), which play a crucial role in the signaling pathways of various cytokines, including IL-4 and IL-13</li> </ul>	<p>When discussing systemic treatments, there are generally two main groups. The first group comprises biologics such as dupilumab and tralokinumab. Dupilumab inhibits IL-4 and IL-13, and tralokinumab only targets the IL-13 cytokine. Both drugs are highly specific and well-tolerated. The second group of drugs includes JAK inhibitors, specifically, JAK1 inhibitors such as abrocitinib, and upadacitinib. We also have baricitinib, which inhibits JAK1 and JAK2. These drugs interrupt the intracellular pathway that transmits signals to the nucleus and prevents the overproduction of proinflammatory cytokines. Basically, these treatment options, novel treatment options, have changed totally the understanding of</p>

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

## Considerations for Infectious Complications in Patients With Atopic Dermatitis

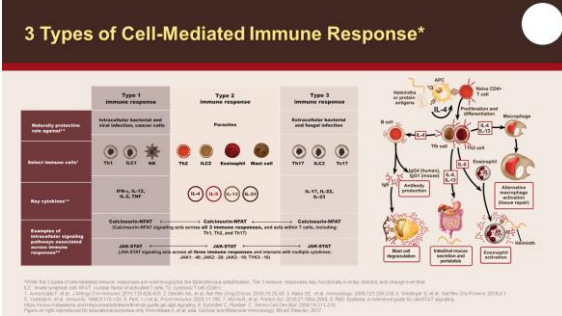
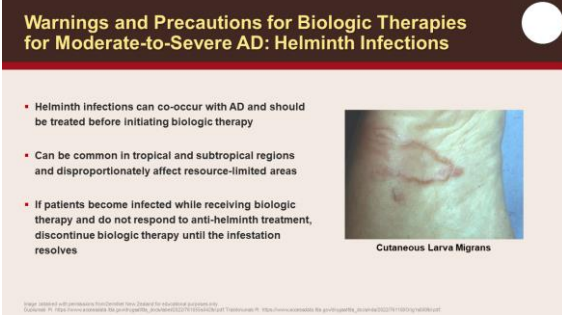
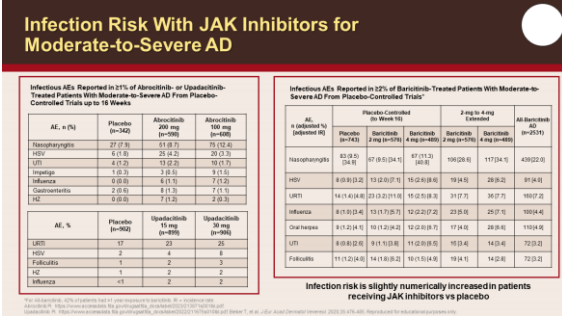
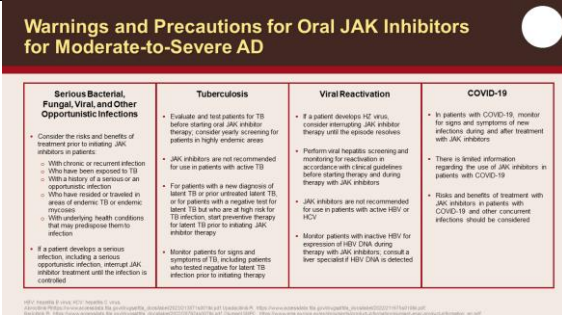
		<p>the disease and have offered us better opportunities to treat our patients compared to the previous treatment with immunosuppressives like corticosteroids, cyclosporine, azathioprine, and also the others.</p>																																																					
<p>16</p>	<div data-bbox="395 405 968 719"> <h3>Infectious AEs Associated With Novel Therapies for Moderate-to-Severe AD</h3> <table border="1"> <thead> <tr> <th colspan="2">BIOLOGICS<sup>1,2</sup></th> <th colspan="3">ORAL JAK INHIBITORS<sup>3,4</sup></th> </tr> </thead> <tbody> <tr> <td><b>Dupilumab</b></td> <td><b>Tralokinumab</b></td> <td><b>Abrocitinib</b></td> <td><b>Upadacitinib</b></td> <td><b>Baricitinib</b></td> </tr> <tr> <td> <ul style="list-style-type: none"> <li>Black Box Warning: None</li> <li>Incidence <math>\leq 1\%</math> conjunctivitis, hepatitis, oral herpes, hepatitis, and other HSV infection</li> </ul> </td> <td> <ul style="list-style-type: none"> <li>Black Box Warning: None</li> <li>Incidence <math>\geq 1\%</math> LRTIs and conjunctivitis</li> </ul> </td> <td> <ul style="list-style-type: none"> <li>Black Box Warning: Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to death, including TB</li> <li>Incidence <math>\geq 1\%</math> respiratory infections, HSV, UTI, influenza, and gastroenteritis</li> </ul> </td> <td> <ul style="list-style-type: none"> <li>Black Box Warning: Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to death, including TB</li> <li>Incidence <math>\geq 1\%</math> LRTIs, respiratory infections, HSV, UTI, influenza, and gastroenteritis</li> </ul> </td> <td> <ul style="list-style-type: none"> <li>Black Box Warning: Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to hospitalization or death, including TB</li> <li>Incidence <math>\geq 2\%</math> respiratory infections, HSV, UTI, influenza, oral herpes, LTI, and hepatitis</li> </ul> </td> </tr> </tbody> </table> <p><sup>1</sup>Initiation of Use: Not recommended for use in combination with other JAK inhibitors, biologics, immunomodulators, or with other immunosuppressants<sup>1</sup>.</p> <p><sup>2</sup>Combination with cyclosporine or other potent immunosuppressants has not been studied and is not recommended<sup>2</sup>.</p> </div>	BIOLOGICS <sup>1,2</sup>		ORAL JAK INHIBITORS <sup>3,4</sup>			<b>Dupilumab</b>	<b>Tralokinumab</b>	<b>Abrocitinib</b>	<b>Upadacitinib</b>	<b>Baricitinib</b>	<ul style="list-style-type: none"> <li>Black Box Warning: None</li> <li>Incidence <math>\leq 1\%</math> conjunctivitis, hepatitis, oral herpes, hepatitis, and other HSV infection</li> </ul>	<ul style="list-style-type: none"> <li>Black Box Warning: None</li> <li>Incidence <math>\geq 1\%</math> LRTIs and conjunctivitis</li> </ul>	<ul style="list-style-type: none"> <li>Black Box Warning: Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to death, including TB</li> <li>Incidence <math>\geq 1\%</math> respiratory infections, HSV, UTI, influenza, and gastroenteritis</li> </ul>	<ul style="list-style-type: none"> <li>Black Box Warning: Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to death, including TB</li> <li>Incidence <math>\geq 1\%</math> LRTIs, respiratory infections, HSV, UTI, influenza, and gastroenteritis</li> </ul>	<ul style="list-style-type: none"> <li>Black Box Warning: Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to hospitalization or death, including TB</li> <li>Incidence <math>\geq 2\%</math> respiratory infections, HSV, UTI, influenza, oral herpes, LTI, and hepatitis</li> </ul>	<p>If you look to the biologics, if you look at the black box warnings, there are no black box warnings. Biologics have a very low risk, generally, of infection. For example, upper or upper respiratory tract infection, it's a very, very low rate with tralokinumab and also dupilumab. And also other infections, like herpes infection, also the others are not in the prescription information [in a black box warning]. If you go to the oral JAK inhibitors, we see they have a black box warning, especially the risk of serious bacterial, fungal, and viral and opportunistic infection; all of them — abrocitinib, upadacitinib, and baricitinib. And of course we have to take care, to take into account that the reactivation of TB can be also an issue, and also the activation of the viral infection may be also an issue. Therefore, it's very important before we start any treatment with oral JAK inhibitor to exclude and decrease the risk for any infection or reactivation of already existing diseases.</p>																																						
BIOLOGICS <sup>1,2</sup>		ORAL JAK INHIBITORS <sup>3,4</sup>																																																					
<b>Dupilumab</b>	<b>Tralokinumab</b>	<b>Abrocitinib</b>	<b>Upadacitinib</b>	<b>Baricitinib</b>																																																			
<ul style="list-style-type: none"> <li>Black Box Warning: None</li> <li>Incidence <math>\leq 1\%</math> conjunctivitis, hepatitis, oral herpes, hepatitis, and other HSV infection</li> </ul>	<ul style="list-style-type: none"> <li>Black Box Warning: None</li> <li>Incidence <math>\geq 1\%</math> LRTIs and conjunctivitis</li> </ul>	<ul style="list-style-type: none"> <li>Black Box Warning: Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to death, including TB</li> <li>Incidence <math>\geq 1\%</math> respiratory infections, HSV, UTI, influenza, and gastroenteritis</li> </ul>	<ul style="list-style-type: none"> <li>Black Box Warning: Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to death, including TB</li> <li>Incidence <math>\geq 1\%</math> LRTIs, respiratory infections, HSV, UTI, influenza, and gastroenteritis</li> </ul>	<ul style="list-style-type: none"> <li>Black Box Warning: Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to hospitalization or death, including TB</li> <li>Incidence <math>\geq 2\%</math> respiratory infections, HSV, UTI, influenza, oral herpes, LTI, and hepatitis</li> </ul>																																																			
<p>17</p>	<div data-bbox="395 1196 968 1509"> <h3>Infection Risk With Biologic Therapies for Moderate-to-Severe AD</h3> <p>Infectious AEs Occurring in <math>\geq 1\%</math> of the Dupilumab Monotherapy Group or the Dupilumab + TCS Group in AD Trials Through Week 16</p> <table border="1"> <thead> <tr> <th rowspan="2">AE, n (%)</th> <th colspan="2">Dupilumab Monotherapy</th> <th colspan="2">Dupilumab + TCS</th> </tr> <tr> <th>Dupilumab 300 mg Q2W (n=52)</th> <th>Placebo (n=57)</th> <th>Dupilumab 300 mg Q2W + TCS (n=13)</th> <th>Placebo + TCS (n=21)</th> </tr> </thead> <tbody> <tr> <td>Conjunctivitis</td> <td>8 (15)</td> <td>12 (21)</td> <td>10 (78)</td> <td>18 (86)</td> </tr> <tr> <td>Herpes</td> <td>2 (4)</td> <td>1 (2)</td> <td>2 (15)</td> <td>2 (10)</td> </tr> <tr> <td>Oral herpes</td> <td>20 (4)</td> <td>8 (14)</td> <td>3 (23)</td> <td>5 (24)</td> </tr> <tr> <td>Keratitis</td> <td>1 (2)</td> <td>0</td> <td>4 (31)</td> <td>0</td> </tr> <tr> <td>Other HSV infection</td> <td>10 (2)</td> <td>0 (0)</td> <td>1 (8)</td> <td>1 (5)</td> </tr> </tbody> </table> <p>Infectious AEs Occurring in <math>\geq 1\%</math> of the Tralokinumab Monotherapy Group or the Tralokinumab + TCS Group in AD Trials Through Week 16</p> <table border="1"> <thead> <tr> <th rowspan="2">AE, n (%)</th> <th colspan="2">Tralokinumab Monotherapy</th> <th colspan="2">Tralokinumab + TCS</th> </tr> <tr> <th>Tralokinumab 300 mg Q2W (n=182)</th> <th>Placebo (n=38)</th> <th>Tralokinumab 300 mg Q2W + TCS (n=24)</th> <th>Placebo + TCS (n=12)</th> </tr> </thead> <tbody> <tr> <td>LRTIs</td> <td>28 (15)</td> <td>7 (18)</td> <td>7 (29)</td> <td>19 (16)</td> </tr> <tr> <td>Conjunctivitis</td> <td>8 (4)</td> <td>12 (32)</td> <td>33 (14)</td> <td>6 (5)</td> </tr> </tbody> </table> <p>In clinical trials, patients with AD receiving dupilumab or tralokinumab reported conjunctivitis more often than patients receiving placebo<sup>1,2</sup>.</p> <p>Most cases were mild or moderate in severity, transient, and had good response to topical treatment.</p> </div>	AE, n (%)	Dupilumab Monotherapy		Dupilumab + TCS		Dupilumab 300 mg Q2W (n=52)	Placebo (n=57)	Dupilumab 300 mg Q2W + TCS (n=13)	Placebo + TCS (n=21)	Conjunctivitis	8 (15)	12 (21)	10 (78)	18 (86)	Herpes	2 (4)	1 (2)	2 (15)	2 (10)	Oral herpes	20 (4)	8 (14)	3 (23)	5 (24)	Keratitis	1 (2)	0	4 (31)	0	Other HSV infection	10 (2)	0 (0)	1 (8)	1 (5)	AE, n (%)	Tralokinumab Monotherapy		Tralokinumab + TCS		Tralokinumab 300 mg Q2W (n=182)	Placebo (n=38)	Tralokinumab 300 mg Q2W + TCS (n=24)	Placebo + TCS (n=12)	LRTIs	28 (15)	7 (18)	7 (29)	19 (16)	Conjunctivitis	8 (4)	12 (32)	33 (14)	6 (5)	<p>Looking from the data from clinical trials of dupilumab and tralokinumab, we do realize that comparing to placebo there are similar rates of infection, for example, oral herpes and also upper respiratory tract infection. But we see for sure, in the signal, patients who are treated with IL-4 and/or -13 inhibitor, dupilumab or tralokinumab, they do show a higher rate on the conjunctivitis. The question is, is this the conjunctivitis which is viral or bacterial? Today, we think that is not a viral and not really bacterial, either. However, we have to take into account and also differential diagnoses of bacterial or any other infection should be excluded.</p>
AE, n (%)	Dupilumab Monotherapy		Dupilumab + TCS																																																				
	Dupilumab 300 mg Q2W (n=52)	Placebo (n=57)	Dupilumab 300 mg Q2W + TCS (n=13)	Placebo + TCS (n=21)																																																			
Conjunctivitis	8 (15)	12 (21)	10 (78)	18 (86)																																																			
Herpes	2 (4)	1 (2)	2 (15)	2 (10)																																																			
Oral herpes	20 (4)	8 (14)	3 (23)	5 (24)																																																			
Keratitis	1 (2)	0	4 (31)	0																																																			
Other HSV infection	10 (2)	0 (0)	1 (8)	1 (5)																																																			
AE, n (%)	Tralokinumab Monotherapy		Tralokinumab + TCS																																																				
	Tralokinumab 300 mg Q2W (n=182)	Placebo (n=38)	Tralokinumab 300 mg Q2W + TCS (n=24)	Placebo + TCS (n=12)																																																			
LRTIs	28 (15)	7 (18)	7 (29)	19 (16)																																																			
Conjunctivitis	8 (4)	12 (32)	33 (14)	6 (5)																																																			





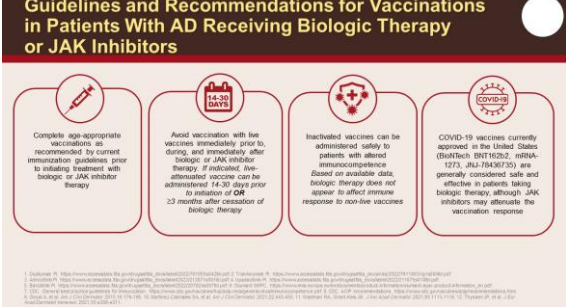
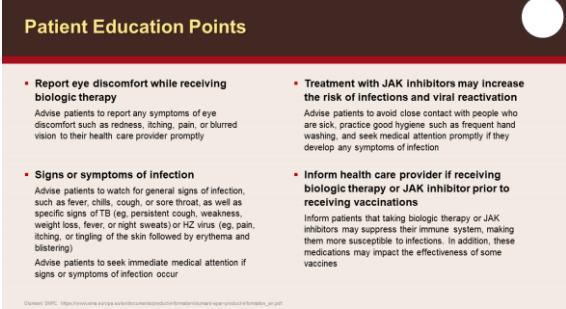
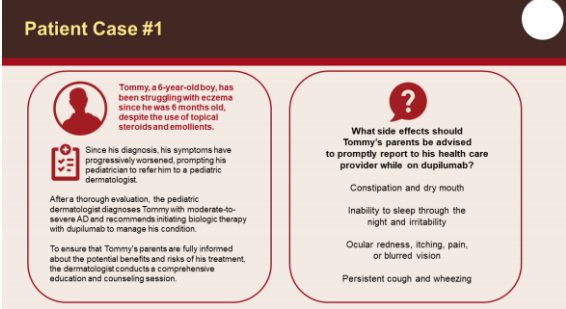
# Addressing the Global Burden of Atopic Dermatitis: Navigating Evolving Best Practices for Diagnosis and Treatment

## Considerations for Infectious Complications in Patients With Atopic Dermatitis

		<p>the cytokines, which is not the case with immunosuppressives.</p>																																																																																				
<p>21</p>	 <p><b>3 Types of Cell-Mediated Immune Response*</b></p> <p>The diagram illustrates three types of immune responses: Type 1 (Th1), Type 2 (Th2), and Type 3 (Th17). Type 1 involves interferon-gamma and TNF, leading to Th1 cells and IFN-γ. Type 2 involves IL-4, IL-5, and IL-13, leading to Th2 cells and IL-4, IL-5, IL-13. Type 3 involves IL-17, IL-22, and IL-23, leading to Th17 cells and IL-17, IL-22, IL-23. A central diagram shows the interaction of these cells and cytokines with various tissues and organs.</p>	<p>The second issue that we usually look at in type 2 immune response, we do know that type 2 inflammation is there to protect us, to protect us against parasites. This is that what we have learned in the books; the parasites are that, why the type 2 inflammation is there, that production of IL-4 and -13 is there to protect the intestinal mucus and secretion and also peristaltic. This is also leading to the B cells to produce more anti-IgE to have the mast cell degranulation to fight the parasites and the same eosinophilic activation has to lead that our body should eliminate the helminths.</p>																																																																																				
<p>22</p>	 <p><b>Warnings and Precautions for Biologic Therapies for Moderate-to-Severe AD: Helminth Infections</b></p> <ul style="list-style-type: none"> <li>Helminth infections can co-occur with AD and should be treated before initiating biologic therapy</li> <li>Can be common in tropical and subtropical regions and disproportionately affect resource-limited areas</li> <li>If patients become infected while receiving biologic therapy and do not respond to anti-helminth treatment, discontinue biologic therapy until the infestation resolves</li> </ul> <p><b>Cutaneous Larva Migrans</b></p>	<p>But this is also leading to something which is also important once we are treating with biologics, we have to exclude the helminth infection, they cannot co-occur. This is not happening in the north of Germany. This might happen in tropical and subtropical region. Also the reports are very scarce, but if the patient has any disease, for example cutaneous larva migrans, then treatment with biologic will not be probably the best treatment of choice.</p>																																																																																				
<p>23</p>	 <p><b>Infection Risk With JAK Inhibitors for Moderate-to-Severe AD</b></p> <p><b>Infectious AEs Reported in 21% of Abrocitinib- or Upadacitinib-Treated Patients With Moderate-to-Severe AD From Placebo-Controlled Trials up to 18 Weeks</b></p> <table border="1"> <thead> <tr> <th>AE, n (%)</th> <th>Placebo (n=342)</th> <th>Abrocitinib 200 mg (n=595)</th> <th>Abrocitinib 400 mg (n=595)</th> </tr> </thead> <tbody> <tr> <td>Herpesviruses</td> <td>27 (8.0)</td> <td>13 (2.2)</td> <td>13 (2.2)</td> </tr> <tr> <td>HSV</td> <td>4 (1.2)</td> <td>2 (0.3)</td> <td>2 (0.3)</td> </tr> <tr> <td>VZV</td> <td>4 (1.2)</td> <td>13 (2.2)</td> <td>10 (1.7)</td> </tr> <tr> <td>Herpes</td> <td>1 (0.3)</td> <td>1 (0.2)</td> <td>1 (0.2)</td> </tr> <tr> <td>Influenza</td> <td>6 (1.8)</td> <td>6 (1.0)</td> <td>7 (1.2)</td> </tr> <tr> <td>Cytomegalovirus</td> <td>2 (0.6)</td> <td>1 (0.2)</td> <td>1 (0.2)</td> </tr> <tr> <td>MRSA</td> <td>6 (1.8)</td> <td>7 (1.2)</td> <td>2 (0.3)</td> </tr> </tbody> </table> <p><b>Infectious AEs Reported in 22% of Baricitinib-Treated Patients With Moderate-to-Severe AD From Placebo-Controlled Trials*</b></p> <table border="1"> <thead> <tr> <th rowspan="2">AE, n (adjusted %)</th> <th colspan="2">Placebo-Controlled (n Weeks 18)</th> <th colspan="2">2 mg to 4 mg Extended (n Weeks 24)</th> <th rowspan="2">All Baricitinib AD (n=2371)</th> </tr> <tr> <th>Placebo (n=151)</th> <th>Baricitinib 4 mg (n=151)</th> <th>Baricitinib 2 mg (n=151)</th> <th>Baricitinib 4 mg (n=151)</th> </tr> </thead> <tbody> <tr> <td>Herpesviruses</td> <td>63 (4.2)</td> <td>67 (4.4)</td> <td>67 (4.4)</td> <td>100 (6.6)</td> <td>430 (22.0)</td> </tr> <tr> <td>HSV</td> <td>6 (0.4)</td> <td>15 (1.0)</td> <td>15 (1.0)</td> <td>19 (1.3)</td> <td>37 (2.0)</td> </tr> <tr> <td>VZV</td> <td>14 (9.3)</td> <td>23 (1.5)</td> <td>15 (1.0)</td> <td>31 (2.1)</td> <td>107 (5.8)</td> </tr> <tr> <td>Herpes</td> <td>6 (0.4)</td> <td>15 (1.0)</td> <td>15 (1.0)</td> <td>19 (1.3)</td> <td>37 (2.0)</td> </tr> <tr> <td>Influenza</td> <td>6 (0.4)</td> <td>15 (1.0)</td> <td>15 (1.0)</td> <td>23 (1.5)</td> <td>59 (3.2)</td> </tr> <tr> <td>Cytomegalovirus</td> <td>2 (0.1)</td> <td>1 (0.1)</td> <td>1 (0.1)</td> <td>1 (0.1)</td> <td>3 (0.2)</td> </tr> <tr> <td>MRSA</td> <td>6 (0.4)</td> <td>15 (1.0)</td> <td>15 (1.0)</td> <td>19 (1.3)</td> <td>37 (2.0)</td> </tr> </tbody> </table> <p><b>Infection risk is slightly numerically increased in patients receiving JAK inhibitors vs placebo</b></p>	AE, n (%)	Placebo (n=342)	Abrocitinib 200 mg (n=595)	Abrocitinib 400 mg (n=595)	Herpesviruses	27 (8.0)	13 (2.2)	13 (2.2)	HSV	4 (1.2)	2 (0.3)	2 (0.3)	VZV	4 (1.2)	13 (2.2)	10 (1.7)	Herpes	1 (0.3)	1 (0.2)	1 (0.2)	Influenza	6 (1.8)	6 (1.0)	7 (1.2)	Cytomegalovirus	2 (0.6)	1 (0.2)	1 (0.2)	MRSA	6 (1.8)	7 (1.2)	2 (0.3)	AE, n (adjusted %)	Placebo-Controlled (n Weeks 18)		2 mg to 4 mg Extended (n Weeks 24)		All Baricitinib AD (n=2371)	Placebo (n=151)	Baricitinib 4 mg (n=151)	Baricitinib 2 mg (n=151)	Baricitinib 4 mg (n=151)	Herpesviruses	63 (4.2)	67 (4.4)	67 (4.4)	100 (6.6)	430 (22.0)	HSV	6 (0.4)	15 (1.0)	15 (1.0)	19 (1.3)	37 (2.0)	VZV	14 (9.3)	23 (1.5)	15 (1.0)	31 (2.1)	107 (5.8)	Herpes	6 (0.4)	15 (1.0)	15 (1.0)	19 (1.3)	37 (2.0)	Influenza	6 (0.4)	15 (1.0)	15 (1.0)	23 (1.5)	59 (3.2)	Cytomegalovirus	2 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	3 (0.2)	MRSA	6 (0.4)	15 (1.0)	15 (1.0)	19 (1.3)	37 (2.0)	<p>And the second part of the treatment that we are usually also using in our patient are JAK inhibitors. We do see that infection rate is numerically higher in the JAK inhibitors, in abrocitinib and upadacitinib, but also in baricitinib we see a higher rate, especially on herpes zoster, more in the higher dosages and less in the lower dosages, and the risk generally of infection, viral but also bacterial, is slightly numerically increased in the patient who are receiving the JAK inhibitors.</p>
AE, n (%)	Placebo (n=342)	Abrocitinib 200 mg (n=595)	Abrocitinib 400 mg (n=595)																																																																																			
Herpesviruses	27 (8.0)	13 (2.2)	13 (2.2)																																																																																			
HSV	4 (1.2)	2 (0.3)	2 (0.3)																																																																																			
VZV	4 (1.2)	13 (2.2)	10 (1.7)																																																																																			
Herpes	1 (0.3)	1 (0.2)	1 (0.2)																																																																																			
Influenza	6 (1.8)	6 (1.0)	7 (1.2)																																																																																			
Cytomegalovirus	2 (0.6)	1 (0.2)	1 (0.2)																																																																																			
MRSA	6 (1.8)	7 (1.2)	2 (0.3)																																																																																			
AE, n (adjusted %)	Placebo-Controlled (n Weeks 18)		2 mg to 4 mg Extended (n Weeks 24)		All Baricitinib AD (n=2371)																																																																																	
	Placebo (n=151)	Baricitinib 4 mg (n=151)	Baricitinib 2 mg (n=151)	Baricitinib 4 mg (n=151)																																																																																		
Herpesviruses	63 (4.2)	67 (4.4)	67 (4.4)	100 (6.6)	430 (22.0)																																																																																	
HSV	6 (0.4)	15 (1.0)	15 (1.0)	19 (1.3)	37 (2.0)																																																																																	
VZV	14 (9.3)	23 (1.5)	15 (1.0)	31 (2.1)	107 (5.8)																																																																																	
Herpes	6 (0.4)	15 (1.0)	15 (1.0)	19 (1.3)	37 (2.0)																																																																																	
Influenza	6 (0.4)	15 (1.0)	15 (1.0)	23 (1.5)	59 (3.2)																																																																																	
Cytomegalovirus	2 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	3 (0.2)																																																																																	
MRSA	6 (0.4)	15 (1.0)	15 (1.0)	19 (1.3)	37 (2.0)																																																																																	
<p>24</p>	 <p><b>Warnings and Precautions for Oral JAK Inhibitors for Moderate-to-Severe AD</b></p> <table border="1"> <thead> <tr> <th>Category</th> <th>Key Points</th> </tr> </thead> <tbody> <tr> <td><b>Serious Bacterial, Fungal, Viral, and Other Opportunistic Infections</b></td> <td> <ul style="list-style-type: none"> <li>Evaluate and test patients for TB before starting oral JAK inhibitor therapy; consider yearly screening for patients in high endemic areas</li> <li>JAK inhibitors are not recommended for use in patients with active TB</li> <li>For patients with a new diagnosis of latent TB or prior untreated latent TB, or for patients with a negative test for latent TB but who are at high risk for TB infection, start preventive therapy for latent TB prior to initiating JAK inhibitor therapy</li> <li>Monitor patients for signs and symptoms of TB, including patients who tested negative for latent TB infection prior to initiating therapy</li> </ul> </td> </tr> <tr> <td><b>Tuberculosis</b></td> <td> <ul style="list-style-type: none"> <li>Evaluate and test patients for TB before starting oral JAK inhibitor therapy; consider yearly screening for patients in high endemic areas</li> <li>JAK inhibitors are not recommended for use in patients with active TB</li> <li>For patients with a new diagnosis of latent TB or prior untreated latent TB, or for patients with a negative test for latent TB but who are at high risk for TB infection, start preventive therapy for latent TB prior to initiating JAK inhibitor therapy</li> <li>Monitor patients for signs and symptoms of TB, including patients who tested negative for latent TB infection prior to initiating therapy</li> </ul> </td> </tr> <tr> <td><b>Viral Reactivation</b></td> <td> <ul style="list-style-type: none"> <li>If a patient develops HCV virus, consider interrupting JAK inhibitor therapy until the episode resolves</li> <li>Perform viral hepatitis screening and monitoring for reactivation in accordance with clinical guidelines during starting therapy and during therapy with JAK inhibitors</li> <li>JAK inhibitors are not recommended for use in patients with active HBV or HCV</li> <li>Monitor patients with inactive HBV for expression of HBV DNA during therapy with JAK inhibitors; consult a liver specialist if HBV DNA is detected</li> </ul> </td> </tr> <tr> <td><b>COVID-19</b></td> <td> <ul style="list-style-type: none"> <li>In patients with COVID-19, monitor for signs and symptoms of new infections during and after treatment with JAK inhibitors</li> <li>There is limited information regarding the use of JAK inhibitors in patients with COVID-19</li> <li>Risks and benefits of treatment with JAK inhibitors in patients with COVID-19 and other concurrent infections should be considered</li> </ul> </td> </tr> </tbody> </table>	Category	Key Points	<b>Serious Bacterial, Fungal, Viral, and Other Opportunistic Infections</b>	<ul style="list-style-type: none"> <li>Evaluate and test patients for TB before starting oral JAK inhibitor therapy; consider yearly screening for patients in high endemic areas</li> <li>JAK inhibitors are not recommended for use in patients with active TB</li> <li>For patients with a new diagnosis of latent TB or prior untreated latent TB, or for patients with a negative test for latent TB but who are at high risk for TB infection, start preventive therapy for latent TB prior to initiating JAK inhibitor therapy</li> <li>Monitor patients for signs and symptoms of TB, including patients who tested negative for latent TB infection prior to initiating therapy</li> </ul>	<b>Tuberculosis</b>	<ul style="list-style-type: none"> <li>Evaluate and test patients for TB before starting oral JAK inhibitor therapy; consider yearly screening for patients in high endemic areas</li> <li>JAK inhibitors are not recommended for use in patients with active TB</li> <li>For patients with a new diagnosis of latent TB or prior untreated latent TB, or for patients with a negative test for latent TB but who are at high risk for TB infection, start preventive therapy for latent TB prior to initiating JAK inhibitor therapy</li> <li>Monitor patients for signs and symptoms of TB, including patients who tested negative for latent TB infection prior to initiating therapy</li> </ul>	<b>Viral Reactivation</b>	<ul style="list-style-type: none"> <li>If a patient develops HCV virus, consider interrupting JAK inhibitor therapy until the episode resolves</li> <li>Perform viral hepatitis screening and monitoring for reactivation in accordance with clinical guidelines during starting therapy and during therapy with JAK inhibitors</li> <li>JAK inhibitors are not recommended for use in patients with active HBV or HCV</li> <li>Monitor patients with inactive HBV for expression of HBV DNA during therapy with JAK inhibitors; consult a liver specialist if HBV DNA is detected</li> </ul>	<b>COVID-19</b>	<ul style="list-style-type: none"> <li>In patients with COVID-19, monitor for signs and symptoms of new infections during and after treatment with JAK inhibitors</li> <li>There is limited information regarding the use of JAK inhibitors in patients with COVID-19</li> <li>Risks and benefits of treatment with JAK inhibitors in patients with COVID-19 and other concurrent infections should be considered</li> </ul>	<p>What we see the major risk that we are facing is the risk of TB reactivation, which is rare in North America but can occur even in Europe and also in endemic countries. The viral reactivation, especially hepatitis B and C, can be of particular importance; therefore, vaccination against the hepatitis B and C is very, very crucial. Recently, during the COVID-19 pandemic, it was shown that JAK inhibitors may have negative effects on some infections of COVID-19. And generally, serious bacterial, fungal, viral, and other opportunistic</p>																																																																										
Category	Key Points																																																																																					
<b>Serious Bacterial, Fungal, Viral, and Other Opportunistic Infections</b>	<ul style="list-style-type: none"> <li>Evaluate and test patients for TB before starting oral JAK inhibitor therapy; consider yearly screening for patients in high endemic areas</li> <li>JAK inhibitors are not recommended for use in patients with active TB</li> <li>For patients with a new diagnosis of latent TB or prior untreated latent TB, or for patients with a negative test for latent TB but who are at high risk for TB infection, start preventive therapy for latent TB prior to initiating JAK inhibitor therapy</li> <li>Monitor patients for signs and symptoms of TB, including patients who tested negative for latent TB infection prior to initiating therapy</li> </ul>																																																																																					
<b>Tuberculosis</b>	<ul style="list-style-type: none"> <li>Evaluate and test patients for TB before starting oral JAK inhibitor therapy; consider yearly screening for patients in high endemic areas</li> <li>JAK inhibitors are not recommended for use in patients with active TB</li> <li>For patients with a new diagnosis of latent TB or prior untreated latent TB, or for patients with a negative test for latent TB but who are at high risk for TB infection, start preventive therapy for latent TB prior to initiating JAK inhibitor therapy</li> <li>Monitor patients for signs and symptoms of TB, including patients who tested negative for latent TB infection prior to initiating therapy</li> </ul>																																																																																					
<b>Viral Reactivation</b>	<ul style="list-style-type: none"> <li>If a patient develops HCV virus, consider interrupting JAK inhibitor therapy until the episode resolves</li> <li>Perform viral hepatitis screening and monitoring for reactivation in accordance with clinical guidelines during starting therapy and during therapy with JAK inhibitors</li> <li>JAK inhibitors are not recommended for use in patients with active HBV or HCV</li> <li>Monitor patients with inactive HBV for expression of HBV DNA during therapy with JAK inhibitors; consult a liver specialist if HBV DNA is detected</li> </ul>																																																																																					
<b>COVID-19</b>	<ul style="list-style-type: none"> <li>In patients with COVID-19, monitor for signs and symptoms of new infections during and after treatment with JAK inhibitors</li> <li>There is limited information regarding the use of JAK inhibitors in patients with COVID-19</li> <li>Risks and benefits of treatment with JAK inhibitors in patients with COVID-19 and other concurrent infections should be considered</li> </ul>																																																																																					

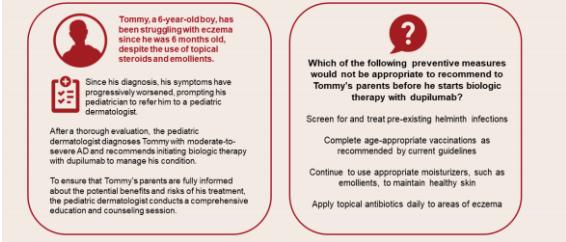
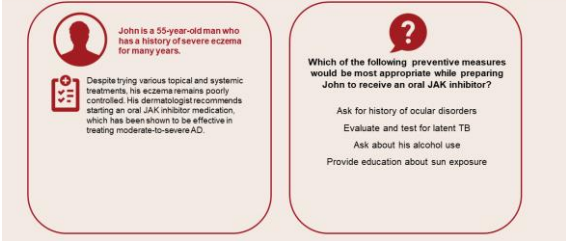
# Addressing the Global Burden of Atopic Dermatitis: Navigating Evolving Best Practices for Diagnosis and Treatment

## Considerations for Infectious Complications in Patients With Atopic Dermatitis

		infection have been shown to occur more frequently other patient who are treated with the JAK inhibitor, especially data from rheumatology are showing this kind of potential.
25	 <p><b>Guidelines and Recommendations for Vaccinations in Patients With AD Receiving Biologic Therapy or JAK Inhibitors</b></p> <ul style="list-style-type: none"> <li><b>Complete age-appropriate vaccinations as recommended by current immunization guidelines prior to initiating treatment with biologic or JAK inhibitor therapy.</b></li> <li><b>Avoid vaccination with live vaccines immediately prior to, during, and immediately after biologic or JAK inhibitor therapy. If indicated, live-attenuated vaccine can be administered 14-30 days prior to initiation of JAK inhibitor therapy or 2-3 months after cessation of biologic therapy.</b></li> <li><b>Inactivated vaccines can be administered safely to patients with altered immunocompetence. Based on available data, biologic therapy does not appear to affect immune response to non-live vaccines.</b></li> <li><b>COVID-19 vaccines currently approved in the United States (BioNTech, mRNA-1273, J&amp;J-704X(175)) are generally considered safe and effective in patients taking biologic therapy, although JAK inhibitors may attenuate the vaccination response.</b></li> </ul>	So finally, in the guidelines, which I think regarding how to treat a patient with atopic dermatitis with JAK inhibitors, I think it's important that we advise to do an appropriate, an age-appropriate vaccination, to avoid vaccination with live vaccine, for in this patient, inactivated vaccines can be used and the COVID-19 vaccines have shown that they are effective. But the question is, are they as effective as without the JAK? So it is necessary to interrupt the treatment with the JAK inhibitor before and slightly after the vaccination.
26	 <p><b>Patient Education Points</b></p> <ul style="list-style-type: none"> <li><b>Report eye discomfort while receiving biologic therapy</b> Advise patients to report any symptoms of eye discomfort such as redness, itching, pain, or blurred vision to their health care provider promptly.</li> <li><b>Signs or symptoms of infection</b> Advise patients to watch for general signs of infection, such as fever, chills, cough, or sore throat, as well as specific signs of TD (eg, persistent cough, weakness, weight loss, fever, or night sweats) or HZ virus (eg, pain, itching, or tingling of the skin followed by erythema and blistering). Advise patients to seek immediate medical attention if signs or symptoms of infection occur.</li> <li><b>Treatment with JAK inhibitors may increase the risk of infections and viral reactivation</b> Advise patients to avoid close contact with people who are sick, practice good hygiene such as frequent hand washing, and seek medical attention promptly if they develop any symptoms of infection.</li> <li><b>Inform health care provider if receiving biologic therapy or JAK inhibitor prior to receiving vaccinations</b> Inform patients that taking biologic therapy or JAK inhibitors may suppress their immune system, making them more susceptible to infections. In addition, these medications may impact the effectiveness of some vaccines.</li> </ul>	What I think is very important is that we educate the patient. That we tell them to report any eye discomfort. We should tell them that treatment with JAK inhibitor may increase the risk of infection, viral reactivation, but we'll do everything to avoid this. Signs and symptoms of infection should be also carefully observed by the patient and in case for example of eczema herpeticum, patients should know how to react and to inform us how can we help them much faster, much adequately, and much early in order to have the benefit of that?
27	 <p><b>Patient Case #1</b></p> <p>Tommy, a 6-year-old boy, has been struggling with eczema since he was 6 months old, despite the use of topical steroids and emollients.</p> <p>Since his diagnosis, his symptoms have progressively worsened, prompting his pediatrician to refer him to a pediatric dermatologist.</p> <p>After a thorough evaluation, the pediatric dermatologist diagnoses Tommy with moderate-to-severe AD and recommends initiating biologic therapy with dupilumab to manage his condition.</p> <p>To ensure that Tommy's parents are fully informed about the potential benefits and risks of his treatment, the dermatologist conducts a comprehensive education and counseling session.</p> <p><b>What side effects should Tommy's parents be advised to promptly report to his health care provider while on dupilumab?</b></p> <ul style="list-style-type: none"> <li>Constipation and dry mouth</li> <li>Inability to sleep through the night and irritability</li> <li>Ocular redness, itching, pain, or blurred vision</li> <li>Persistent cough and wheezing</li> </ul>	Let me, at the end, show you a case. Tommy, a 6-year-old boy, has been struggling with eczema since he was 6 months old. Despite the use of topical steroids and emollients since his diagnosis, his symptoms have progressively worsened, prompting his pediatrician to refer him to pediatric dermatology. After a thorough evaluation, the dermatologist diagnosed Tommy with moderate-to-severe atopic dermatitis and recommends initiating biologic therapy with dupilumab to manage his condition. To ensure that Tommy's parents are fully informed about the potential benefits and risk of his treatment, the dermatologist conducts a comprehensive education and counseling session. So, what side effects should Tommy's parents be advised to be promptly reported to his healthcare provider while on dupilumab: constipation and dry mouth; inability to sleep through the night and


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

## Considerations for Infectious Complications in Patients With Atopic Dermatitis

		<p>irritability; ocular redness, itching, pain, or blurred vision; or persistent cough? And we see. So, I hope that you have the right answer. I think all of them, they are very important to report, but this is the one particular one which is occurring more frequently under the patient who are treated with dupilumab as a known adverse event which can be reported and should be reported during that period of time. This is ocular redness, itching, pain, or blurred vision.</p>
28	<p><b>Patient Case #1 (cont)</b></p>  <p>Tommy, a 6-year-old boy, has been struggling with eczema since he was 6 months old, despite the use of topical steroids and emollients.</p> <p>Since his diagnosis, his symptoms have progressively worsened, prompting his pediatrician to refer him to a pediatric dermatologist.</p> <p>After a thorough evaluation, the pediatric dermatologist diagnoses Tommy with moderate-to-severe AD and recommends initiating biologic therapy with dupilumab to manage his condition.</p> <p>To ensure that Tommy's parents are fully informed about the potential benefits and risks of his treatment, the pediatric dermatologist conducts a comprehensive education and counseling session.</p> <p><b>Which of the following preventive measures would not be appropriate to recommend to Tommy's parents before he starts biologic therapy with dupilumab?</b></p> <ul style="list-style-type: none"> <li>Screen for and treat pre-existing helminth infections</li> <li>Complete age-appropriate vaccinations as recommended by current guidelines</li> <li>Continue to use appropriate moisturizers, such as emollients, to maintain healthy skin</li> <li>Apply topical antibiotics daily to areas of eczema</li> </ul>	<p>Let me continue with Tommy again. Which of the following preventive measures would not be appropriate to recommend to Tommy's parents before he starts biologic therapy with dupilumab? Would <b>not</b> be appropriate. Screen for and treat preexisting helminth infection; complete age-appropriate vaccination as recommended by current guidelines; continue to use appropriate moisturizers, such as emollients, to maintain healthy skin; or apply topical antibiotics daily to areas of eczema? Very curious to hear. Of course, not to use topical antibiotics daily. This is totally counterproductive, something which we should avoid in our daily practice.</p>
29	<p><b>Patient Case #2</b></p>  <p>John is a 55-year-old man who has a history of severe eczema for many years.</p> <p>Despite trying various topical and systemic treatments, his eczema remains poorly controlled. His dermatologist recommends starting an oral JAK inhibitor medication, which has been shown to be effective in treating moderate-to-severe AD.</p> <p><b>Which of the following preventive measures would be most appropriate while preparing John to receive an oral JAK inhibitor?</b></p> <ul style="list-style-type: none"> <li>Ask for history of ocular disorders</li> <li>Evaluate and test for latent TB</li> <li>Ask about his alcohol use</li> <li>Provide education about sun exposure</li> </ul>	<p>Another case. John, a 55-year-old man who has had a history of severe eczema for many years. Despite trying various topical and systemic treatments, his eczema remains poorly controlled. His dermatologist recommends starting an oral JAK inhibitor medication, which has been shown to be effective in treating moderate-to-severe atopic dermatitis. Which of the following preventive measures would be most appropriate whilst preparing John to receive an oral JAK inhibitor: ask for history of ocular disorders; evaluate the test for latent TB; ask about his alcohol use; or provide education about sun exposure? Everything is important, but I think that what is very important: evaluate and test for latent TB.</p>

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

## Considerations for Infectious Complications in Patients With Atopic Dermatitis

30	<p><b>Patient Case #2 (cont)</b></p> <div style="display: flex; justify-content: space-between;"> <div style="width: 45%; border: 1px solid #ccc; border-radius: 10px; padding: 10px;"> <p><b>John is a 55-year-old man who has a history of severe eczema for many years.</b></p> <p>Despite trying various topical and systemic treatments, his eczema remains poorly controlled. His dermatologist recommends starting an oral JAK inhibitor medication, which has been shown to be effective in treating moderate-to-severe AD.</p> </div> <div style="width: 45%; border: 1px solid #ccc; border-radius: 10px; padding: 10px;"> <p><b>Assume that John has inactive HBV. What would be the most appropriate next step for this patient?</b></p> <p>Follow clinical guidelines for monitoring potential reactivation before and during JAK inhibitor therapy.</p> <p>Discuss the possibility of using a biologic therapy instead of an oral JAK inhibitor because they are contraindicated in patients with HBV.</p> <p>Consult with a liver specialist and begin antiviral medication prior to starting JAK inhibitor therapy.</p> <p>Begin JAK inhibitor therapy while regularly checking his liver enzyme levels.</p> </div> </div>	
31	<p><b>Microbiome: Puppy Power</b></p> <p>Babies who share their homes with a dog are much less likely to grow up into adults with allergies than those who don't.</p> <p>Once anathema, it now seems that a "dirty" environment can enrich a baby's microbiome and lessen their likelihood of developing everything from obesity to asthma. Again, it seems that we can rely on man's best friend to help us out.</p> <p>— Sujata Gupta</p> 	<p>I think this is very important for all of us. We have to take care about our patient. We have to be very cautious how we are managing this. However, in the daily life, some of the dysbiosis might be also productive. Contact with microorganism very early we should not avoid, infection is not a contamination. Our microbiome should be interacted and sometimes we are learning that once that was in the past avoiding the microorganism, it was not the solution. The solution was always to try to find out how can we have a steady-state disease that the skin is always in the contact with the microorganism, that we have this heterogeneity of the microbiome, which will allow us not to have the colonization with <i>Staphylococcus</i>. So, I think this is something that we are learning again and again: Hygiene hypothesis is not optimal, but that what we have to care about in our patient is infection, either they're cutaneous or systemic.</p>
32	<p style="text-align: center; font-size: 2em; font-weight: bold; color: #800000;">Thank You!</p>	<p>With this, I would like to thank you very much for your attention.</p>