Genital Psoriasis: The Disease and Its Treatment

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Disclosure

I have been a speaker, consultant and/or researcher for:

• 3M
• Abbvie
• Allergan
• Altana
• Amgen
• Astellas
• Avène
• Barrier
• Basilea
• Berlex
• Biogen Idec
• Boehringer Ingelheim
• Celgene
• Centocor
• Cipher
• Eli Lilly
• EMD Serono

• Galderma
• Graceway
• Glaxo Smith Kline
• Global Trox
• H3 Pharmaceuticals
• Hyal
• Isotechnika
• Innovaderm
• Janssen
• J&J
• Lederle
• Leo Pharma
• Lever Ponds
• L’Oréal
• Merck Frosst
• NanoBio
• Novartis

• Ontario Government (DQTC)
• Ortho Biotech
• Pfizer
• Pierre Fabre
• PremPharm
• Procyon
• Roche
• Sanofi Aventis
• Schering Plough
• Stiefel
• TEVA
• Tribute
• UCB
• Valeant
• Westwood Squibb
• Wyeth
Objectives

- With regards to genital psoriasis, to review its
  - Prevalence
  - Clinical features
  - Risk factors, and
  - Burden of disease
- Discuss current treatments for genital psoriasis
- Review a placebo-controlled ixekizumab trial in genital psoriasis
Prevalence

Questionnaire-based surveys

- **29%-46%** Patients with psoriasis who are impacted by genital psoriasis at some point during the course of their disease\(^1-3\)

Physical exam

- **38%** Adults with current genital involvement\(^4\)
- **63%** Adults with a current and/or previous history of genital involvement\(^4\)
- **79%** Patients with inverse psoriasis who had genital involvement\(^3,5\)

Lack of Disease Awareness

- Genital psoriasis is common among patients with psoriasis,\(^1\) however, poor communication and low HCP awareness may lead to inappropriate diagnosis and self-treatment\(^2,3\)

HCP=healthcare provider

Clinical Presentation: Genital Psoriasis

- Both penile and vulvar psoriatic lesions generally appear as symmetrical, bright red thin plaques with a well-defined edge\(^1\text{-}^4\)
  - Patients may misidentify lesions as STDs\(^4\)
  - HCPs may misidentify lesions as dermatitis or tinea\(^4\)
- Lesions often lack scale due to moisture and maceration\(^1\text{-}^4\)

HCP=healthcare provider; STD=sexually transmitted disease


Skin is generally red, thin, and less scaly
Clinical Presentation: Genital Psoriasis (2 of 2)

- Painful fissures\(^1\) and erosions\(^2\) may be present

- Severe pruritus may lead to scratching, significant excoriations (abrasions), and lichenification (diffuse thickening of the epidermis)\(^3\)

\(^1\) Meeuwis KA et al. Acta Derm Venereol 2015;95:211-6
\(^3\) Weichert GE. Dermatol Ther 2004;17:129-33
Factors Associated With Development of Genital Psoriasis

**Disease Characteristics**

- $\leq 40$ years: Younger age of psoriasis onset
- BSA: More severe disease
- Scalp involvement
- Nail involvement
- Axillary involvement
- Inframammary involvement

**Patient Characteristics**

- Younger age
- Male gender

Patient Perspective on Genital Psoriasis Symptoms

Itch
Burning skin
Pain
Redness
Scaliness
Induration

Note: Self-reported mean intensity scores of itch, burning, and pain all differed significantly (4.2±2.9 vs. 3.5±2.9 vs. 2.8±2.7; p<.0001), as did the mean intensity scores of redness, scaliness, and induration (5.1±2.5 vs. 3.7±2.8 vs. 2.4±2.6; p<.0001)

Meeuwis KA et al. Dermatology 2012;224:271-6
Patient Quality of Life With Genital Psoriasis

- Genital psoriasis has a negative impact on patient quality of life

- Worse quality of life vs. patients without genital involvement, as measured by various quality of life scales

- Significantly greater feeling of stigmatization and lower self-esteem than involvement of visible areas such as face and hands, regardless of overall psoriasis severity

Impact of Genital Psoriasis on Sexual Health

- Genital psoriasis has a significant impact on sexual health\textsuperscript{1-3}
  - Women with psoriatic lesions in the genital region have especially high levels of sexual distress\textsuperscript{1}

- Compared with patients without genital involvement, significantly higher impact on\textsuperscript{2}:
  - Sexual function
  - Sexual frequency
  - Fear of sexual relations

- 34\% of patients reported worsening of genital psoriasis after intercourse\textsuperscript{2}

Paucity of Data on Treatment for Genital Psoriasis

- To date, there are limited published trials on genital psoriasis treatment
  - Open-label trials of topical treatments
  - A step-wise treatment algorithm of topical treatments
  - Scattered case reports

AAD Treatment Guideline
Recommendations for Genital Psoriasis

- Traditional topical therapies may be used in genital psoriasis, taking steps to reduce irritation or toxicity
  - Including corticosteroids, calcipotriol, calcitrol, or vitamin D analogs

- Systemic therapy recommended if genital psoriasis adversely affects quality of life

- Given the profound impact on quality of life, the presence of genital disease may redefine what would normally be considered mild psoriasis as being moderate or severe
  - Genital disease may therefore warrant systemic treatment

Proposed Treatment Paradigm for Genital Psoriasis

- A proposed treatment paradigm specifically for genital psoriasis has been published as part of a systematic review

**First-line Therapy**
- Weak topical corticosteroids
- Higher potency topical corticosteroids if needed for short periods of time

**Second-line Therapy**
- Addition of topical vitamin D analogs or mild tar-based preparations

**Systemic Therapy**
- May be beneficial for severe and extensive psoriasis in the genital area

Anthralin, tazarotene, ultraviolet light, and laser therapy should be avoided in the genital area

Meeuwis KA et al. Acta Derm Venereol 2011;91:5-11
Limitations of Topical Therapies for Genital Psoriasis

- Genital skin is highly sensitive and is therefore at increased risk of adverse reactions to topical treatments\(^1,^2\)

- Weaker potency corticosteroids are often insufficient for maintenance treatment\(^3\)

- Use of higher potency corticosteroids is limited due to the development of skin atrophy and striae\(^4\)

- Irritation is commonly reported with vitamin D analogs\(^2\)

- Topical calcineurin inhibitors (eg, pimecrolimus, tacrolimus) may improve genital psoriasis, but they have limitations
  - Can cause irritation or stinging\(^2\)
  - Have shown mixed results\(^5\)
  - Are not indicated for the treatment of psoriasis\(^1\)

References:
Open-label study in 12 male patients with genital psoriasis
- Tacrolimus 0.1% ointment b.i.d. on the affected areas of the penis and scrotum for 8 weeks
- 5 patients were clear after 8 wks
- Pruritus was reported by 2 patients (duration < 6 days) and a burning sensation was reported by 5 patients (duration < 5 days, except 1 patient, 37 days)

Alternatives to Topical Therapies for Genital Psoriasis

- Systemic therapy is generally reserved for second-line treatment or more severe cases\(^1,2\)
  - Presence of genital disease may mean a patient is classed as moderate or severe\(^2\) and could therefore qualify for (earlier) systemic treatment according to some current guidelines\(^1,2\)
  - It has been shown that patients with mild psoriasis but major QoL impairment benefit from the use of systemic agents\(^3\)

- Use of psoralen and ultraviolet A (PUVA) and ultraviolet B (UVB) should usually be avoided in the genital region
  - Potential carcinogenic adverse effects, particularly in males\(^4-6\)
  - Potential to burn thin genital skin\(^7\)

IxEKIZUMAB placeBO-CONTROLLED Study

Study code: I1F-MC-RHBQ
Clinicaltrials.gov identifier: NCT02718898

Objective
♦ To evaluate the effect of ixekizumab on the severity of genital psoriasis compared with placebo during 12 weeks of treatment
Screening

149 patients randomized 1:1

Blinded Treatment Period

IXE-treated patients received 160-mg starting dose

IXE Q2W (N=75)

PBO (N=74)

WEEK 0

IXE Q2W: 80 mg IXE every 2 weeks

PBO: Placebo

WEEK 12

a Given as 2 80 mg subcutaneous injections at Week 0. Patients assigned to placebo received 2 subcutaneous injections of placebo at Week 0

IXE=ixekizumab; R=randomization
Key Eligibility Criteria

Inclusion Criteria

- Male or female ≥18-years-old
- Chronic plaque psoriasis for ≥6 months
- Plaque psoriasis in a non-genital area
- sPGA of Genitalia ≥3
- Overall sPGA ≥3
- BSA ≥1%\(^a\)
- Failed to respond to/intolerant of ≥1 topical therapy\(^b\) for genital psoriasis

\(a\) Approximately 40% of patients enrolled were to have had BSA involvement of 1% to <10%, and the majority were to have had ≥10% BSA involvement

\(b\) Corticosteroids, calcineurin inhibitors, and/or vitamin D analogs

BSA=body surface area; sPGA=static Physician’s Global Assessment
Key Eligibility Criteria

- Recent suicide attempt (≤30 days), suicide risk, or QIDS-SR<sub>16</sub> Item 12 score of 3
- Significant uncontrolled cardiovascular, cerebrocardiovascular, or other unstable medical or psychiatric conditions
- Active or recent infection that would pose an unacceptable risk to the patient
- Received/currently receiving treatment for active candidiasis or tinea in the genital area
- Received treatment with IL-17 antagonists

IL-17=interleukin-17; QIDS-SR<sub>16</sub>=Quick Inventory of Depressive Symptomatology–Self Report (16 items)
**Primary Endpoint**

- Proportion of patients achieving sPGA of Genitalia (0,1)

sPGA of Genitalia
- Measurement of the patient’s psoriasis severity in the genital region at a given time point on a 6-point scale:

0: Clear
1: Minimal
2: Mild
3: Moderate
4: Severe
5: Very Severe

- labia majora, labia minora, and perineum
- penis, scrotum, and perineum

`sPGA = static Physician’s Global Assessment`
Major Secondary Endpoints

- Proportion of patients achieving overall sPGA (0,1)

- Proportion of patients achieving a ≥3-point improvement in genital itch numeric rating scale (gen-itch NRS)
  - Among patients with a baseline score of ≥3

- Proportion of patients whose frequency of sexual activity was never or rarely limited by genital psoriasis (SFQ Item 2 score 0 or 1)
  - Among patients with a baseline score ≥2

SFQ Item 2: In the past week, how often did your genital psoriasis limit the frequency of your sexual activity?

- Never: 0
- Rarely: 1
- Sometimes: 2
- Often: 3
- Always: 4

*gen-itch NRS=genital itch numeric rating scale; SFQ=Sexual Frequency Questionnaire; sPGA=static Physician’s Global Assessment*
### Baseline Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th></th>
<th>PBO (N=74) (%)</th>
<th>IXE Q2W (N=75) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>44.4 (12.6)</td>
<td>43.1 (13.0)</td>
</tr>
<tr>
<td><strong>Male, n (%)</strong></td>
<td>57 (77)</td>
<td>56 (75)</td>
</tr>
<tr>
<td><strong>Weight, kg</strong></td>
<td>95.1 (26.3)</td>
<td>91.9 (23.1)</td>
</tr>
<tr>
<td><strong>Time since psoriasis onset, years</strong></td>
<td>16.1 (12.5)</td>
<td>16.9 (12.8)</td>
</tr>
<tr>
<td><strong>Time since genital psoriasis onset, years</strong></td>
<td>8.3 (8.2)</td>
<td>9.3 (10.0)</td>
</tr>
<tr>
<td><strong>Percentage of BSA involved</strong></td>
<td>16.8 (15.7)</td>
<td>14.2 (12.6)</td>
</tr>
<tr>
<td><strong>BSA 1 to &lt;10%, n (%)</strong></td>
<td>28 (38)</td>
<td>31 (41)</td>
</tr>
<tr>
<td><strong>BSA ≥10%, n (%)</strong></td>
<td>46 (62)</td>
<td>44 (59)</td>
</tr>
<tr>
<td><strong>sPGA of Genitalia</strong></td>
<td>3.5 (0.5)</td>
<td>3.4 (0.6)</td>
</tr>
<tr>
<td><strong>sPGA of Genitalia=3, n (%)</strong></td>
<td>41 (55)</td>
<td>45 (61)</td>
</tr>
<tr>
<td><strong>sPGA of Genitalia=4, n (%)</strong></td>
<td>32 (43)</td>
<td>27 (36)</td>
</tr>
<tr>
<td><strong>sPGA of Genitalia=5, n (%)</strong></td>
<td>1 (1.4)</td>
<td>2 (2.7)</td>
</tr>
<tr>
<td><strong>sPGA</strong></td>
<td>3.5 (0.6)</td>
<td>3.5 (0.6)</td>
</tr>
</tbody>
</table>

Data are mean (standard deviation) unless otherwise stated.

BSA=body surface area; IXE Q2W=80 mg ixekizumab every 2 weeks; PBO=placebo; sPGA=static Physician’s Global Assessment.
sPGA of Genitalia (0,1) Response Rate
NRI, Blinded Treatment Period, ITT Population

♦ 7 out of 10 ixekizumab-treated patients achieved clear or almost clear genital skin at Week 12
♦ Percentage of patients achieving clear or almost clear genital skin was significantly greater for ixekizumab as early as Week 1

+ PBO (N=74) + IXE Q2W (N=75)

* p<.01 vs. PBO; † p<.001 vs. PBO
ITT=Intent-to-Treat; IXE Q2W=80 mg ixekizumab every 2 weeks; NRI=non-responder imputation; PBO=placebo; sPGA=static Physician’s Global Assessment
The sPGA of Genitalia (0,1) response with ixekizumab at Week 12 was consistent, regardless of the percent BSA involved at baseline.

![Bar chart showing response rates for BSA ≥10% and BSA 1 to <10% for PBO and IXE Q2W.

Legend:
- PBO (N=74)
- IXE Q2W (N=75)

- BSA ≥10%:
  - PBO: 13% (75 response)
  - IXE Q2W: 71% (71 response)

- BSA 1 to <10%:
  - PBO: 0% (0 response)
  - IXE Q2W: 75% (75 response)

†p<.001 vs. PBO

BSA=body surface area; ITT=Intent-to-Treat; IXE Q2W=80 mg ixekizumab every 2 weeks; NRI=non-responder imputation; PBO=placebo; sPGA=static Physician’s Global Assessment
Photos: Male Patient Treated With Ixekizumab

**Week 0**
- sPGA of Genitalia = severe (4)
- Randomized to IXE Q2W

**Week 2**
- sPGA of Genitalia = minimal (1)
- 2 weeks of IXE Q2W

**Week 12**
- sPGA of Genitalia = clear (0)
- 12 weeks of IXE Q2W

IXE Q2W=80 mg ixekizumab every 2 weeks; sPGA=static Physician’s Global Assessment
7 out of 10 ixekizumab-treated patients achieved clear or almost clear skin overall at Week 12.

Percentage of patients achieving clear or almost clear skin overall was significantly greater for ixekizumab as early as Week 1.

*p<.001 vs. PBO
ITT=Intent-to-Treat; IXE Q2W=80 mg ixekizumab every 2 weeks; NRI=non-responder imputation; PBO=placebo; sPGA=static Physician’s Global Assessment
6 out of 10 ixekizumab-treated patients had clinically meaningful improvements\(^a\) in genital itch at Week 12.

Percentage of patients achieving clinically meaningful improvement in genital itch was significantly greater for ixekizumab as early as Week 2.

\(^a\) p<.001 vs. PBO

\(\geq 3\) point improvement in gen-itch NRS

gen-itch NRS=genital itch numeric rating scale; ITT=Intent-to-Treat; IXE Q2W=80 mg ixekizumab every 2 weeks; NRI=non-responder imputation; PBO=placebo
Approximately 8 out of 10 ixekizumab-treated patients were no longer or rarely limited by the impact of genital psoriasis on frequency of sexual activity at Week 12.

Percentage of patients who were no longer or rarely limited by the impact of genital psoriasis on frequency of sexual activity was significantly greater for ixekizumab as early as Week 1.

‡ p<.05 vs. PBO; * p<.01 vs. PBO; † p<.001 vs. PBO

ITT=Intent-to-Treat; IXE Q2W=80 mg ixekizumab every 2 weeks; NRI=non-responder imputation; PBO=placebo; SFQ=Sexual Frequency Questionnaire
## Safety Overview

**Blinded Treatment Period, Safety Population**

<table>
<thead>
<tr>
<th>n (%)</th>
<th>PBO (N=74)</th>
<th>IXE Q2W (N=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall TEAEs</strong></td>
<td>33 (44.6)</td>
<td>42 (56.0)</td>
</tr>
<tr>
<td><strong>Mild</strong></td>
<td>15 (20.3)</td>
<td>23 (30.7)</td>
</tr>
<tr>
<td><strong>Moderate</strong></td>
<td>15 (20.3)</td>
<td>18 (24.0)</td>
</tr>
<tr>
<td><strong>Severe</strong></td>
<td>3 (4.1)</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td><strong>Serious adverse event</strong></td>
<td>1 (1.4)(^a)</td>
<td>0</td>
</tr>
<tr>
<td><strong>TEAE related to study treatment</strong></td>
<td>7 (9.5)</td>
<td>14 (18.7)</td>
</tr>
<tr>
<td><strong>Discontinuation due to AEs</strong></td>
<td>6 (4.1)(^b)</td>
<td>1 (1.3)(^c)</td>
</tr>
<tr>
<td><strong>Most common TEAEs(^d)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Upper respiratory tract infection</strong></td>
<td>5 (6.8)</td>
<td>11 (14.7)</td>
</tr>
<tr>
<td><strong>Injection-site reactions</strong></td>
<td>2 (2.7)</td>
<td>8 (10.7)</td>
</tr>
<tr>
<td><strong>Headache</strong></td>
<td>4 (5.4)</td>
<td>3 (4.0)</td>
</tr>
<tr>
<td><strong>Oropharyngeal pain</strong></td>
<td>2 (2.7)</td>
<td>3 (4.0)</td>
</tr>
<tr>
<td><strong>Pruritus</strong></td>
<td>2 (2.7)</td>
<td>3 (4.0)</td>
</tr>
</tbody>
</table>

\(^a\)Pancreatitis acute (n=1); \(^b\)Worsening psoriasis (n=4), worsening psoriatic arthritis (n=1), liver function test increased (n=1); \(^c\)Eczema (n=1); \(^d\) Experienced by ≥4% of patients in the IXE Q2W arm

AE=adverse event; IXE Q2W=80 mg ixekizumab every 2 weeks; PBO=placebo; TEAE=treatment-emergent adverse event
Conclusions

- Genital psoriasis is common, but often underappreciated by HCPs and inappropriately self-treated\(^1,2,3,4\)
- Itch, pain and sexual impairment are common\(^1,3,5\)
- The quality of life is significantly worse in patients with genital psoriasis compared to those without it\(^6,7\)
- In genital skin, there are more adverse effects with topicals\(^4,8\)
- Systemic therapy should be considered for severe, or extensive genital psoriasis, or for patients with a negative impact on QoL\(^2,4\)
- Ixekizumab:
  - Is an efficacious treatment for moderate-to-severe genital psoriasis regardless of the baseline BSA
  - Rapidly clears genital skin
  - Improves genital itch
  - Minimizes how often genital psoriasis limits the frequency of sexual activity
