Hidradenitis Suppurativa
Therapeutic Update

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Faculty Disclosure*:

Amgen
Actelion
AbbVie
Galderma
Janssen
Genentech
Pfizer
Merck
Novartis
Celgene
Lilly
Regeneron

*Dr. Kerdel has been involved in clinical studies, has participated in advisory boards and is a speaker for the above companies.
Hidradenitis Suppurativa (HS)

1% prevalence
Commonly presents early second decade
Declines after age 50
1/3 have family history
Linked to chromosome 1p21.1-1q25.3 (γ-Secretase complex)(NCSTN,PES-NEN,PSEN1 genes)
Obesity and smoking - risk factors
May present in pts with Crohn’s, PG & arthritis
Elevated inflammatory markers in pts with severe disease
Hidradenitis Suppurativa (HS) Diagnosis and Associated Symptoms

- Apocrine gland folliculitis
- Pain
- Draining fistulae
- Fever, chills, lethargy
- Comedones
- Scarring and tissue damage
- Compromised integrity of skin may lead to bacterial colonization
HS comorbidities

- Follicular occlusion tetrad
- Metabolic syndrome
- Inflammatory bowel disease
- Spondyloarthritis
- Depression
- Pyoderma gangrenosum
Hidradenitis Suppurativa: Staging

• Hurley staging

  Stage I – Lesion formation, single or multiple without sinuses or scarring

  Stage II - Recurrent lesions with sinuses and scarring, widely separated

  Stage III – Diffuse involvement of entire area
Hidradenitis Suppurativa – Clinical Scores

- Sartorius sore – (+/- modified) counting individual lesions and distances between them, extra points for Hurley stage III
- Physician global assessment – clear to very severe depending on number and type of lesions
- Hidradenitis suppurativa severity index – lesions, pain, dressing changes and affected area
- Hidradenitis Suppurativa Clinical Response – 50% reduction in nodules with no change in abscesses or fistulas
HS: Underlying Mechanism and Treatment Strategies

• Mechanism
  – Follicular gland occlusion followed by an inflammatory response vs. apocrine gland primary target followed by follicular duct pathology

• Treatments
  – Hygiene, weight and friction reduction
  – Cessation of smoking, topical antibiotics and cleansers
  – Systemic antibiotics (minocycline, clindamycin/rifampicin)
  – Topical and systemic corticosteroids
  – Cyclosporine, anti-androgens, retinoids
  – Local radiation
  – Photodynamic therapy, Hyperbaric oxygen
  – Surgery
  – Laser
  – Biologic therapy (anti-TNF)
HS: Rationale for Using Anti-TNFα Agents

• Indirect Evidence
  – Anti-TNFα drugs are efficacious in the treatment of other diseases associated with an inflammatory process (psoriasis, rheumatoid arthritis, ulcerative colitis, pyoderma gangrenosum, and acne conglobata)

• Direct Evidence
  – Anti-TNFα drugs are effective in treating HS
    • Adalimumab  Blanco R et al, Arch Dermatol  2009;145:580-584
Infliximab for Hidradenitis Suppurativa

Sullivan TP. Welsh E. Kerdel FA. Burdick A. Kirsner RS.

Br J Dermatol 2003;149:1046
HS: Significant Improvement Observed After Treatment with Infliximab

Before treatment with infliximab

After treatment with infliximab
Infliximab therapy for patients with moderate to severe hidradenitis suppurativa: a randomized, double blind, placebo-controlled crossover trial

Grant A, Gonzalez T, Montgomery M O, Cardenas V, Kerdel F A
Study Design

**Double-blind Phase (8 wks)**
- Week 0
- Week 2
- Week 6
- Week 8
- Week 10
- Week 14

**Open-label Phase (22 wks)**
- Week 22

**Observational Phase (22 wks)**
- Week 30

**Placebo**
- Week 0
- Week 2
- Week 6
- Week 8
- Week 10
- Week 14
- Crossover to infliximab 5 mg/kg

**Infliximab 5 mg/kg**
- Week 6
- Week 30
- Week 52

**Double-blind Phase (8 wks)**

**Open-label Phase (22 wks)**

**Observational Phase (22 wks)**
# HS Severity Index Score (HSSI)

<table>
<thead>
<tr>
<th>Score/Category</th>
<th>Number of Sites</th>
<th>Body Surface Area (%) SAGE*</th>
<th>Number of Lesions (Erythematous, Painful)</th>
<th>Drainage (Number of Dressing Changes/ Working/ Leisure Hours)**</th>
<th>Pain (VAS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0-1</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1-2</td>
<td>1</td>
<td>2-4</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>2-3</td>
<td>2-3</td>
<td>1</td>
<td>2-4</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>4-5</td>
<td>4-5</td>
<td>&gt;1</td>
<td>5-7</td>
</tr>
<tr>
<td>4</td>
<td>&gt;4</td>
<td>&gt;5</td>
<td>&gt;5</td>
<td></td>
<td>8-10</td>
</tr>
</tbody>
</table>

Sites
- left armpit, right armpit, left chest, right chest, left groin, right groin, perianal area, sacral area, perineal area

**Composite Scoring (0-19)**

<table>
<thead>
<tr>
<th>Mild (0-7)</th>
<th>Moderate (8-12)</th>
<th>Severe (&gt;13)</th>
</tr>
</thead>
</table>

Sample Score: 3 sites, 2% Body Surface Area, 4 Lesions, 1 Dressing Change and VAS 10

3 + 2 + 3 + 2 + 4 = 14 (Severe)

*www.sagediagram.com

**Interferes with daily activities
Inclusion Criteria

- HSSI ≥8
- HS >1 year with multiple ER/Doctor visits
- Failed topical/systemic therapy
- Failed surgery
- Age >18 years
- Adequate birth control
- Negative history for TB, PPD and CXR
## Demographics and Baseline Disease Severity

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Infliximab</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yrs)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>23</td>
<td>15</td>
<td>0.994</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>33.2 (11.42)</td>
<td>34.0 (13.44)</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>17-61</td>
<td>16-58</td>
<td></td>
</tr>
<tr>
<td><strong>Gender, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9 (31.0)</td>
<td>3 (20.0)</td>
<td>0.099</td>
</tr>
<tr>
<td>Female</td>
<td>14 (60.9)</td>
<td>12 (80.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Race, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black/African American</td>
<td>7 (30.4)</td>
<td>3 (20.0)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>6 (26.1)</td>
<td>8 (53.3)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>8 (34.8)</td>
<td>3 (20.0)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2 (8.7)</td>
<td>1 (6.7)</td>
<td>0.265</td>
</tr>
<tr>
<td><strong>HSSI, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>18 (78.3)</td>
<td>14 (93.3)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>5 (21.7)</td>
<td>1 (6.7)</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>14.8 (2.43)</td>
<td>16.0 (2.07)</td>
<td>0.123</td>
</tr>
<tr>
<td><strong>DLQI, Mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16.5 (7.07)</td>
<td></td>
<td>17.2 (8.06)</td>
<td>0.848</td>
</tr>
<tr>
<td><strong>VAS, Mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>46.8 (29.53)</td>
<td></td>
<td>53.3 (25.96)</td>
<td>0.716</td>
</tr>
</tbody>
</table>
Primary Endpoint: Proportion of Patients With $\geq 50\%$ Reduction From Baseline in HSSI at Week 8

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=18)</th>
<th>Infliximab 5 mg/kg (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion (%)</td>
<td>5.6</td>
<td>26.7</td>
</tr>
</tbody>
</table>

$p=0.092$
Decrease from Baseline in HSSI at Week 8

- Placebo (n=18)
- Infliximab 5 mg/kg (n=15)

Percent of Patients

- <25%: 88.9%
- 25-49%: 13.3%
- ≥50%: 5.6%

p<0.001 vs. placebo
Mean Improvement From Baseline to Week 8 in Patient-Reported Pain VAS

![Graph showing Mean Improvement in Pain VAS]

- Placebo: n=18, Mean Improvement = 0.6
- Infliximab 5 mg/kg: n=15, Mean Improvement = 39.8

p < 0.001
Improvement from Baseline in DLQI Component Scores

Mean Improvement from Baseline

<table>
<thead>
<tr>
<th>Component</th>
<th>Placebo (n=18)</th>
<th>Infliximab 5 mg/kg (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms &amp; Feelings</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Daily Activities</td>
<td>0.4</td>
<td>2.1</td>
</tr>
<tr>
<td>Leisure</td>
<td>0.6</td>
<td>2.2</td>
</tr>
<tr>
<td>Work &amp; School</td>
<td>0.2</td>
<td>1.1</td>
</tr>
<tr>
<td>Personal Relationships</td>
<td>-0.3</td>
<td>1.5</td>
</tr>
<tr>
<td>Treatment</td>
<td>0.4</td>
<td>0.9</td>
</tr>
<tr>
<td>Total DLQI</td>
<td>10.0</td>
<td>1.6</td>
</tr>
</tbody>
</table>

p-values:
- Symptoms & Feelings: p=0.004
- Daily Activities: p=0.031
- Leisure: p=0.016
- Work & School: p=0.037
- Personal Relationships: p=0.035
- Treatment: p=0.202
- Total DLQI: p=0.003
PGA at Week 8

- Placebo (n=18)
- Infliximab 5 mg/kg (n=15)

Percent of Patients

- Worse (0%)
- Unchanged (0-24%)
- Slight (25-49%)
- Fair (50-74%)
- Good (75-99%)
- Excellent (100%)

p=0.009 vs. placebo
Mean ESR and CRP at Baseline and Week 8

- **Baseline**
  - Placebo (n=18)
  - Infliximab 5 mg/kg (n=15)

- **Week 8**
  - Placebo (n=18)
  - Infliximab 5 mg/kg (n=15)

**Mean CRP**
- Baseline: Placebo 3.6, Infliximab 4.0
- Week 8: Placebo 2.0, Infliximab 1.0

**Mean ESR**
- Baseline: Placebo 25.3, Infliximab 31.2
- Week 8: Placebo 23.0, Infliximab 11.3
Mean Improvement in HSSI Scores in Double-Blind and Open Label Phases

![Bar chart showing mean improvement in HSSI scores in double-blind and open label phases.]

- **Double-blind phase**
  - PBO, Wk 0-8 (n=18): 0.6
  - IFX, Wk 0-8 (n=15): 6.0

- **Open label phase**
  - PBO, Wk 0-8 (n=8): 0.3
  - IFX, Wk 8-16 (n=8): 2.6
Mean PGA Scores in Double-Blind and Open Label Phases

<table>
<thead>
<tr>
<th></th>
<th>PBO, Wk 0-8 (n=18)</th>
<th>IFX, Wk 0-8 (n=15)</th>
<th>PBO, Wk 0-8 (n=8)</th>
<th>PBO→ IFX, Wk 8-16 (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double-blind phase</td>
<td>4.7</td>
<td>1.8</td>
<td>4.8</td>
<td>2.0</td>
</tr>
<tr>
<td>Open label phase</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **p<0.001**
- **p=0.003**
Improvement after 8 Weeks of Treatment with Infliximab

Before Treatment

After Treatment
Right Axilla

Before

After
Before

Gluteal area

After
Etanercept in Hidradenitis Suppurativa

- Open label Phase II
- 10 patients
- 12 weeks therapy: 50 mg SC once weekly
- Endpoints:
  - Disease Activity Score
  - Sartorius score
  - VAS (cm)

Changes in visual analogue scale (VAS)

- Etanercept 50 mg SC once weekly

- *p=0.019 vs baseline
- **p=0.024 vs baseline
- $p=0.042$ vs baseline
A Prospective Clinical Trial of Open-Label Etanercept for the Treatment of Hidradenitis Suppurativa


Etanercept 50mg/week proved ineffective in patients with Hurley’s stage I and II H.S. (15 pts)
Treatment of Hidradenitis Suppurativa with Etanercept Injection
Adams D R et al Arch Dermatol 2010;146:501-504

- Double blind placebo-controlled trial
- 20 patients
- Etanercept 50mg BIW
- 12 weeks double blinded, 12 weeks open label
- No significant efficacy
Adalimumab in Hidradenitis Suppurativa

Open-Label Study

Dose: same as Crohn’s 160-80-40qow

## Hidradenitis Suppurativa Severity Index (HSSI) Preliminary Data

<table>
<thead>
<tr>
<th>Patients</th>
<th>HSSI Screening</th>
<th>HSSI Week 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>3</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>4</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>6</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>7</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>8</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>9</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td><strong>16.22</strong></td>
<td><strong>14.33</strong></td>
</tr>
</tbody>
</table>
Fig. 1

HSSI score

Week 0  2  4  8  12

Pat 1
Pat 2
Pat 3
Pat 4
Pat 5
Pat 6
Pat 7
Pat 8
Pat 9
Pat 10
Fig. 2

VAS score (mm)

Week 0  2  4  8  12
Fig. 3
Efficacy and Safety of Adalimumab in Treatment of Moderate to Severe Hidradenitis Suppurativa: Results from the Placebo-Controlled Portion of a Phase II, Randomized, Double-Blind Study

AB Kimball¹, Y Gu², M Okun², G Jemec³

¹Harvard Medical School, Boston, MA; ²Abbott Laboratories, Abbott Park, IL; ³Roskilde Hospital, Roskilde, Denmark;

Presented at the 69th Annual Meeting of the American Academy of Dermatology, February 4-8, 2011, New Orleans, LA
# Study Design

<table>
<thead>
<tr>
<th>Screening Period</th>
<th>Double-blind Placebo Controlled Period (Period 1)</th>
<th>Open-label Period&lt;sup&gt;a&lt;/sup&gt; (Period 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 28 days</td>
<td>16 weeks</td>
<td>36 weeks</td>
</tr>
<tr>
<td></td>
<td>Adalimumab 40 mg ew (n=51)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Adalimumab 40 mg eow</td>
</tr>
<tr>
<td></td>
<td>Adalimumab 40 mg eow (n=52)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Adalimumab 40 mg eow</td>
</tr>
<tr>
<td></td>
<td>Placebo (n=51)</td>
<td>Adalimumab 40 mg eow&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

- White lines denote period included in current analysis.
- <sup>a</sup>Dose escalation for PGA≥3 at Weeks 28 or 31.
- <sup>b</sup>From Week 4, after 160 mg dose at Week 0, 80 mg at Week 2.
- <sup>c</sup>From Week 1, after 80 mg dose at Week 0.
- <sup>d</sup>From Week 17, after 80 mg dose at Week 16.
# HS-PGA Scale

<table>
<thead>
<tr>
<th>PGA Rating</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear</td>
<td>0 abscesses, 0 draining fistulas, 0 inflammatory nodules, and 0 non-inflammatory nodules</td>
</tr>
<tr>
<td>Minimal</td>
<td>0 abscesses, 0 draining fistulas, and 0 inflammatory nodules</td>
</tr>
<tr>
<td>Mild</td>
<td>0 abscesses, 0 draining fistulas, and &lt;5 inflammatory nodules or 1 abscess or draining fistula and 0 inflammatory nodules</td>
</tr>
<tr>
<td>Moderate</td>
<td>0 abscesses, 0 draining fistulas, and ≥5 inflammatory nodules or 1 abscess or draining fistula and ≥1 inflammatory nodule or 2-5 abscesses or draining fistulas and &lt;10 inflammatory nodules</td>
</tr>
<tr>
<td>Severe</td>
<td>2-5 abscesses or draining fistulas and ≥10 inflammatory nodules</td>
</tr>
<tr>
<td>Very Severe</td>
<td>&gt;5 abscesses or draining fistulas</td>
</tr>
</tbody>
</table>

HS-PGA, Hidradenitis suppurativa physician’s global assessment
## Baseline Demographics and Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=51)</th>
<th>ADA eow (n=52)</th>
<th>ADA weekly (n=51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs), Mean (SD)</td>
<td>37.8 (12.10)</td>
<td>36.1 (12.50)</td>
<td>35.1 (10.69)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>36 (70.6)</td>
<td>38 (73.1)</td>
<td>36 (70.6)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>37 (72.5)</td>
<td>36 (69.2)</td>
<td>37 (72.5)</td>
</tr>
<tr>
<td>Weight (kg), Mean (SD)</td>
<td>96.5 (24.80)</td>
<td>99.8 (26.75)</td>
<td>95.4 (22.94)</td>
</tr>
<tr>
<td>HS-PGA moderate, n (%)</td>
<td>33 (64.7)</td>
<td>35 (67.3)</td>
<td>35 (68.6)</td>
</tr>
<tr>
<td>HS-PGA severe/very severe, n (%)</td>
<td>17 (33.3)</td>
<td>16 (30.8)</td>
<td>16 (31.4)</td>
</tr>
<tr>
<td>Patients receiving p.o. doxycycline or minocycline, n (%)</td>
<td>4 (7.8)</td>
<td>6 (11.5)</td>
<td>8 (15.7)</td>
</tr>
<tr>
<td>VAS skin pain, Mean (SD)</td>
<td>57.8 (28.51)</td>
<td>53.0 (26.35)</td>
<td>52.0 (24.51)</td>
</tr>
</tbody>
</table>
Proportion of Patients Achieving Clinical Response at Weeks 2, 4, 8, 12, and 16 During Period 1

Proportion of patients achieving clinical success (%)\(^a\)

- **Placebo (n=51)**
- **ADA eow (n=52)**
- **ADA ew (n=51)**

- **Week 2**: 2.0, 2.0, 2.0
- **Week 4**: 5.8, 9.6, 11.8
- **Week 8**: 7.8, 7.8, 5.8
- **Week 12**: 5.9, 7.7, 21.6\(^*\)
- **Week 16**: 9.6, 17.6\(^*\)

\(^a\) Proportion of patients achieving an HS-PGA score of clear, minimal, or mild, with at least a two grade improvement relative to Baseline.

\(^*\) P < 0.05, placebo vs. ADA ew.

ITT, NRI. One of the 16 responders was Hurley Stage III; this patient was in the ADA ew group.
Proportion of Patients Achieving an HS-PGA of Clear, Minimal, or Mild at Week 16

Proportion of Patients (%)

- **placebo** (n=51)
- **ADA eow** (n=52)
- **ADA ew** (n=51)

Proportion of Patients (%)

- 23.5
- 21.2
- 49.0*

*P < 0.01, placebo vs. ADA ew, ITT, NRI
HS Lesions Following ADA eow Treatment for 16 Weeks
Mean Change in hs-CRP from Baseline to Week 16

Mean Change in hs-CRP from Baseline to Week 16 (mg/L)

- Placebo (n=35)
- ADA ew (n=40)
- ADA ew (n=32)

*P<.05 ADA ew vs. placebo.
Phase 3 Adalimumab: PIONEER I, II, and OLE

Study centers in US, Canada, Australia, and Europe

Screening

Period A
Double-blind Placebo-controlled

Period B
Double-blind Placebo-controlled

OLE

Entry Criteria
• Completed prior study OR
• In prior study, met pre-specified escape criteria

Randomization

Statistics & Re-randomization

Statistical Analysis

Week: 0 12 16 36

At least 60 weeks

Study centers in US, Canada, Australia, and Europe
Main Inclusion and Exclusion Criteria

Inclusion Criteria

• Adults with a diagnosis of HS for at least 1 year prior to Baseline

• HS lesions in at least two distinct anatomic areas, one of which must be at least Hurley Stage II or Hurley Stage III

• Stable HS for at least 2 months prior to Screening and also at the Baseline visit

• Inadequate response to at least a 3-month trial of an oral antibiotic for treatment of HS (or intolerance to, or have a contraindication to, oral antibiotics for treatment of their HS)

• Total abscess and inflammatory nodule (AN) count of greater than or equal to 3 and draining fistula count of less than 20 at the Baseline visit

Exclusion Criteria

• Prior treatment with adalimumab or other anti-TNF therapy, or participation in an adalimumab trial

• Subject received oral concomitant analgesics (including opioids) for HS-related pain within 14 days prior to the Baseline visit

• Subject received prescription topical therapies for the treatment of HS within 14 days prior to the Baseline visit

• Subject received systemic non-biologic therapies for HS less than 28 days prior to Baseline visit

• **PIONEER I only:** Subject received any oral antibiotic treatment for HS within 28 days prior to the Baseline visit
Efficacy Endpoints\textsuperscript{1,2}

- **Primary endpoint**
  - Proportion of patients achieving Hidradenitis Suppurativa Clinical Response (HiSCR) at Week 12.
  - HiSCR defined as $\geq 50\%$ reduction from baseline in AN (total abscess and inflammatory nodule) count and no increase in abscess or in draining fistula counts.

- **Three ranked secondary endpoints**
  - Proportion of patients achieving AN count of 0, 1 or 2 among patients with HS severity of Hurley Stage II at Week 12.
  - Proportion of patients achieving at least 30\% reduction and at least 1 unit reduction from baseline in Patients’ Global Assessment of Skin Pain numerical rating scale (NRS) based on 24-hour recall of worst pain at Week 12, among patients with baseline NRS$\geq 3$.
  - Change from baseline in Modified Sartorius Score.

Hidradenitis Suppurativa Clinical Response (HiSCR)

HiSCR requires:

- At least a 50% reduction in the total abscess and inflammatory nodule count (AN count) relative to baseline, AND
- No increase in abscess count, and
- No increase in draining fistula count.
HiSCR at Week 12; Primary Efficacy Endpoint

- **All Primary Efficacy Endpoint**
- **Hurley Stage II**
- **Hurley Stage III**

<table>
<thead>
<tr>
<th>Group</th>
<th>HiSCR at Week 12</th>
<th>PBO (% w/N)</th>
<th>ADA Weekly (% w/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIONEER I¹</td>
<td>26.0/40/154</td>
<td>41.8*</td>
<td>45/163</td>
</tr>
<tr>
<td>PIONEER II²</td>
<td>27.6/64/155</td>
<td>58.9†</td>
<td>96/163</td>
</tr>
<tr>
<td>PIONEER I¹</td>
<td>29.8/25/84</td>
<td>44.6‡</td>
<td>37/83</td>
</tr>
<tr>
<td>PIONEER II²</td>
<td>36.8/32/87</td>
<td>62.4†</td>
<td>53/85</td>
</tr>
<tr>
<td>PIONEER I¹</td>
<td>21.4/15/70</td>
<td>38.6‡</td>
<td>27/70</td>
</tr>
<tr>
<td>PIONEER II²</td>
<td>17.1/13/76</td>
<td>55.1†</td>
<td>43/78</td>
</tr>
</tbody>
</table>

*Note: PBO = Placebo, ADA Weekly = ADA Weekly Treatment
Ranked Secondary Endpoints Results at Week 12\textsuperscript{1,2}

- **AN Count 0, 1 or 2\textsuperscript{†}**
  - Pioneer I\textsuperscript{1}: 28.6%
  - Pioneer II\textsuperscript{2}: 32.2%

- **Improved Skin pain\textsuperscript{‡}**
  - Pioneer I\textsuperscript{1}: 24.8%
  - Pioneer II\textsuperscript{2}: 27.9%

- **Improvement in Modified Sartorius Score\textsuperscript{§}**
  - Pioneer I\textsuperscript{1}: 28.9\textsuperscript{*}
  - Pioneer II\textsuperscript{2}: 24.4%
Reduction in DLQI from Baseline at Week 12

**PIioneer I**
- Improvement, mean: -2.9

**PIioneer II**
- Improvement, mean: -2.3

-5.4* -5.1*
Experience with ustekinumab for the treatment of moderate to severe Hidradenitis suppurativa

- Three pts
- Significant improvement (pt #1)
- No adverse events
• 5 Patients
• Anakinra 100 mg SC daily
• At 8 weeks modified Sartorious score decreased by 34.8 points
• Physician/Pts VAS decreased by 45.8 & 35.6 points (8 wks)
• DLQI decreased by 8.4 points (8 wks)
• C reactive protein decreased by 16.7 points
Canakinumab for severe Hidradenitis Suppurativa
Preliminary Experience in 2 cases

- Canakinumab an IgGk anti IL-1β monoclonal antibody
- Two patients, Hurley stage III
- Positive response in both patients
- No reported adverse events
MABp1 targeting interleukin-1alpha for moderate to severe hidradenitis suppurativa not eligible for adalimumab: a randomized study.

Kanni T et al  J Invest Dermatol, accepted for publication.

- Double blind, placebo controlled study
- 20 patients, Hurley II/III
- Primary end point at 12 weeks
- Pts ineligible for adalimumab
- Concomitant antibiotic allowed
- HiSCR(50% decrease inflammatory lesions ) in 60% compared to 10% in placebo
- Decrease in IL-8 and ultrasound improvements in treated pts
Apremilast in the treatment of moderate to severe hidradenitis suppurativa: A case series of 9 patients

- 9 patients
- 3 patients failed
- 6 patients showed promising response
  
  Sartorius from 73.17 +/- 67.76 to 56.17 +/- 44.89
  
  VAS from 7.17 +/- 0.98 to 2.00 +/- 2.10
Phase two open label single center study to evaluate the efficacy of apremilast for the treatment of moderate hidradenitis suppurativa.

Study Design

- 20 patients
- Open label
- Hurley I and II (III excluded)
- Primary endpoint (HiSCR 30) week 16
- Length of study 28 weeks
- Clinical scores: HiSCR, modified Sartorius, PGA, DLQI,
Statistical Analysis

• Primary endpoint: proportion of patients with HiSCR (30% reduction in abscesses and nodules) at week 16
  – 50% reduction was an exploratory endpoint
  – Both 30% and 50% reductions were analyzed at weeks 16 and 24
  – LOCF was used for missing data

• Responder analysis
  – Non-responders/failures were any patient who discontinued due to an adverse event or lack of efficacy

• LOCF was implemented in an ITT analysis for all continuous variables (Sartorius, PGA, VAS pain, DLQI)

• An “As Treated” analysis, which included all available observations for all treated patients (no missing data imputed), was also performed

DLQI: Dermatology Life Quality Index; HiSCR: Hidradenitis Suppurativa Clinical Response; ITT: intention-to-treat; LOCF: Last observation carried forward; PGA: Physician global assessment; VAS: Visual Analogue Scale.
Patient Disposition

Screened (n=22)

- Screen failures (n=2)

At least one dose of medication (n=20)

- Completed (n=11)
- Discontinued (n=9)
  - Adverse events (n=4)
  - Lack of efficacy (n=1)
  - Other* (n=4)

ITT analysis with LOCF† (n=20)

*Other includes conflicting schedule (n=2), lost to follow up (n=1), and relocation (n=1)
†For continuous variables.
HiSCR: 30% Reduction in Abscesses and Nodules

Week 16:
- n=20
- 65 patients

Week 24:
- n=20
- 65 patients
HiSCR: 50% Reduction in Abscesses and Nodules

Week 16: 55 patients ($n=20$)

Week 24: 60 patients ($n=20$)
Responders Analysis Based on Treatment Failures*

*Responders were patients considered non-failures. Treatment failures/non-responders were patients who discontinued due to an adverse event or lack of efficacy by weeks 16 and 24.
Modified Sartorius Score: Change from Baseline

* $P<0.001$ versus baseline; † $P=0.0352$ for week 24 versus week 28.

Analysis based on LOCF.

n=20 for baseline to week 24; n=11 for week 28 (completers).

Analysis of change from baseline to week 28 (4 weeks untreated) not relevant.
PGA Score: Change from Baseline

*P<0.05 versus baseline; †P=0.0078 for week 24 versus week 28.
Analysis based on LOCF.
n=20 for baseline to week 24; n=11 for week 28 (completers).
Analysis of change from baseline to week 28 (4 weeks untreated) not relevant.
VAS Pain Score: Change from Baseline

*P<0.05 versus baseline. P=NS for week 24 versus week 28.
Analysis based on LOCF.
n=20 for baseline to week 24; n=11 for week 28 (completers).
Analysis of change from baseline to week 28 (4 weeks untreated) not relevant.
DLQI Score: Change from Baseline

*P<0.01 versus baseline; †P=0.0273 week 24 versus week 28.
Analysis based on LOCF.

n=20 for baseline to week 24; n=11 for week 28 (completers).
Analysis of change from baseline to week 28 (4 weeks untreated) not relevant.
Proportion of Patients with PGA and VAS Pain Reductions

- PGA: 1-point reduction
- VAS pain: 2-point reduction

- Week 16:
  - PGA: 45 patients
  - VAS pain: 60 patients

- Week 24:
  - PGA: 50 patients
  - VAS pain: 50 patients

Sample size: n=20 for each group.
Conclusion

• The data available thus far suggests that Infliximab is effective in the treatment of Hidradenitis Suppurativa

• Adalimumab is also effective, now the only FDA approved biologic for HS

• Etanercept does not appear to be effective but higher doses ? necessary

• These studies support the rationale for the use of anti-TNFα agents in HS

• Ustekinumab ?

• IL-1R, IL-1α, IL-1β, IL-17(Bimekizumab, UCB),IL-23 inhibition

• PDE4 inhibition (Apremilast) showing promise