New Agents and Therapeutic Classes Are Needed for the Treatment of Moderate to Severe UC

David T. Rubin, MD, FACG, AGAF, FACP, FASGE
Joseph B. Kirsner Professor of Medicine
Section Chief, Gastroenterology, Hepatology and Nutrition
Inflammatory Bowel Disease Center
University of Chicago Medicine
Chicago, IL
Our current medical therapy for IBD is effective in some patients.

There is a large unmet need for patients with IBD.

We are learning how to better use the medications we have and optimize therapy.
  – Combination therapy
  – Therapeutic drug monitoring
  – Prognostication

There still remains a large number of patients with IBD who face surgery.

Continued and future research focusing on disease treatment is needed.

IBD = inflammatory bowel disease.
Clinical Remission in UC: ACT (Infliximab), ULTRA-2 (Adalimumab), and PURSUIT (Golimumab)

Patients failing 5-ASA/steroids/IS


5-ASA = 5-aminosalicylic acid; UC = ulcerative colitis.
## Infliximab Discontinuation Due to Treatment Failure

<table>
<thead>
<tr>
<th>% Infliximab Discontinuation Due to Treatment Failure</th>
<th>Leeds 2012 n=210</th>
<th>Netherland 2011 n=152</th>
<th>Leuven 2009 n=614</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonresponse</td>
<td>9</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>Loss of response</td>
<td>19</td>
<td>25</td>
<td>19</td>
</tr>
<tr>
<td>Adverse events</td>
<td>16</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Total discontinuation</td>
<td>44</td>
<td>30</td>
<td>41</td>
</tr>
</tbody>
</table>

P127 Anti-TNFs Patterns of Use in Clinical Practice in Inflammatory Bowel Disease (VERNE Study)

Background

• One of the aims of this study was to learn about the patterns of the use of anti-TNF therapies in Spain when used in biologic-naïve patients for the treatment of IBD.

Methods

• A retrospective, noninterventional study, conducted in 24 hospitals in Spain. 310 adult patients who started first treatment with anti-TNFs between June 2011 and June 2013 (194 with CD and 116 with UC) were consecutively recruited. Patient characteristics (including comorbidities and extraintestinal manifestations) and anti-TNF management were collected. Kaplan–Meier analyses were used to evaluate time to treatment intensification and time to discontinuation.

Bastida G, et al. Presented at: 14th Congress of ECCO; March 6-9, 2019; Copenhagen, Denmark. Abstract #P127.
Results

- Median time from diagnosis to first anti-TNF use was 45.5 months.
- Median follow-up time after administration of anti-TNFs was 59.8 months.
- Comparable fractions of patients used infliximab and adalimumab in CD (43.8% vs 56.2%). In UC, infliximab was preferred to adalimumab (87.1% vs 12.9%).
- Treatment intensification was needed for 31.9% of patients (28.9% in CD and 37.1% in UC), most commonly dose escalation and interval shortening.
- Median time to intensification was 9.2 months (CD: 14.3 months; UC: 5.3 months).
- Median time to intensification was longer for adalimumab than for infliximab (10.6 vs 8.2 months).
Results (continued)

- Treatment discontinuation occurred in 50.6% of patients (CD: 47.4%; UC: 56.0%).
- The most common cause for discontinuation was loss of response, reported in 29.9% of patients (CD: 30.4%; UC: 29.2%).
- Adverse events accounted for 20.4% of discontinuations (CD: 21.7%; UC: 18.5%).
- Median time to discontinuation was 20.9 months (CD: 24.7%; UC: 17.4%)

Conclusion

- About one-third of bio-naïve patients who started anti-TNF treatment required intensification, and 1 in every 2 discontinued therapy, with loss of response as the most common cause for discontinuation.
Results

- Three hundred ten patients with IBD.

- Most frequent comorbidities were chronic obstructive pulmonary disease (COPD) (3.7%), connective tissue disease (3.0%), diabetes mellitus (2.3%), mild chronic hepatopathy (2.0%), myocardial infarction (1.7%), solid tumors (1.7%), congestive heart failure (1.3%), and cerebrovascular disease (1.3%).

- Logistic regression models showed that COPD was an independent factor associated with lack of response and myocardial infarction of loss of response to anti-TNF therapy.
Results (continued)

• The concomitant use of corticosteroids was an additional independent factor associated with lack of response and loss of response.

• In contrast, CD was a negative independent predictor of lack of response and loss of response.

Conclusion

• In this population of IBD patients who received first anti-TNF treatment, the most frequent comorbidities were COPD, connective tissue disease, diabetes, and hepatopathies. Those associated with lack and loss of response were COPD and myocardial infarction, respectively. Results suggest that patients characteristics should be considered when selecting the optimal biological treatment.
Targeting the Immunological Pathway – Differentiating Available Agents Within Various Therapeutic Classes

William J. Sandborn, MD
Professor of Medicine
Adjunct Professor of Surgery
Chief, Division of Gastroenterology
Vice Chair for Clinical Operations, Department of Medicine
Director, UCSD IBD Center
University of California, San Diego & UC San Diego Health System
La Jolla, CA
### Table 2. Outcome Measures at Week 6 in the Trial of Induction Therapy.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Placebo (N = 149)</th>
<th>Vedolizumab (N = 225)</th>
<th>Percentage-Point Difference (95% CI)*</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical response†</td>
<td>38 (25.5)</td>
<td>106 (47.1)</td>
<td>21.7 (11.6–31.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinical remission‡</td>
<td>8 (5.4)</td>
<td>38 (16.9)</td>
<td>11.5 (4.7–18.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Mucosal healing¶</td>
<td>37 (24.8)</td>
<td>92 (40.9)</td>
<td>16.1 (6.4–25.9)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* Percentage-point differences were adjusted for two stratification factors: concomitant use or nonuse of glucocorticoids, and concomitant use or nonuse of immunosuppressive agents or prior use or nonuse of TNF antagonists.
† A clinical response was defined as a reduction in the Mayo Clinic score of at least 3 points and a decrease of at least 30% from the baseline score, with a decrease of at least 1 point on the rectal bleeding subscale or an absolute rectal bleeding score of 0 or 1.
‡ Clinical remission was defined as a Mayo Clinic score of 2 or lower and no subscore higher than 1.
¶ Mucosal healing was defined as a Mayo Clinic scale endoscopic subscore of 0 or 1.
OP34 VARSITY: A Double-blind, Double-dummy, Randomized, Controlled Trial of Vedolizumab versus Adalimumab in Patients With Active Ulcerative Colitis

Background

• A head-to-head study of the efficacy and safety of vedolizumab and adalimumab for treatment over 52 weeks in adults with moderately to severely active UC.

Methods

• A phase 3b, double-blind, double-dummy, multicenter, active-controlled trial enrolling patients with moderately to severely active UC who had failed other conventional therapies. Prior TNF antagonist exposure was capped at 25% of the patient population. Patients were randomized 1:1 to either: (1) active VDZ intravenous (IV) infusions (300 mg)/placebo subcutaneous (SC) injections; or (2) placebo IV infusions/active ADA SC injections (160/80/40 mg). Dose escalation was not permitted. The primary endpoint was clinical remission at week 52.

ADA = adalimumab; VDZ = vedolizumab.
Schreiber S, et al. Presented at: 14th Congress of ECCO; March 6-9, 2019; Copenhagen, Denmark. Abstract #OP34.
OP34 VARSITY: A Double-blind, Double-dummy, Randomized, Controlled Trial of Vedolizumab versus Adalimumab in Patients With Active Ulcerative Colitis

Results

• Patients (N=769) were randomized to VDZ (n=383) or ADA (n=386).
• At Week 52:
  – Overall clinical remission rates were 31.3% for VDZ and 22.5% for ADA.
  – Mucosal healing (Mayo endoscopic subscore ≤1) was achieved in 39.7% of patients treated with VDZ and in 27.7% of patients treated with ADA.
  – Corticosteroid-free remission rates showed a numerical but nonsignificant difference in favor of ADA.
• 62.7% (VDZ) and 69.2% (ADA) of patients experienced an adverse event (AE).
• Serious AEs occurred in 11.0% (VDZ) and 13.7% (ADA) of treated patients.

Schreiber S, et al. Presented at: 14th Congress of ECCO; March 6-9, 2019; Copenhagen, Denmark. Abstract #OP34.
Conclusion

• This is the first study to directly compare 2 biological agents in IBD. VDZ was superior to ADA in achieving clinical remission and endoscopic mucosal healing at Week 52, whereas VDZ and ADA were both generally safe and well-tolerated in patients with moderately to severely active UC.

Schreiber S, et al. Presented at: 14th Congress of ECCO; March 6-9, 2019; Copenhagen, Denmark. Abstract #OP34.
Background

• We performed a systematic literature review and indirect treatment comparison of randomized controlled trials (RCTs) of biologics and tofacitinib (TOFA) for UC.

Methods

• Medline, Embase, and Cochrane Library databases were searched from 1997 to July 2018 to identify RCTs of vedolizumab (VDZ), adalimumab (ADA), infliximab (IFX), golimumab (GOL), and TOFA. Efficacy outcomes were sustained response and remission at 1 year. Safety outcomes were overall adverse events (AEs), serious AEs (SAEs), overall infections, serious infections, and AEs leading to discontinuation, as reported at 1 year.
Results:

- Odds ratios and number-needed-to-treat for sustained remission with vedolizumab and other treatments for ulcerative colitis.

Jairath V, et al. Presented at: 14th Congress of ECCO; March 6-9, 2019; Copenhagen, Denmark. Abstract #P325.
Results:
• Odds ratios and number-needed-to-harm for safety outcomes with vedolizumab and other treatments for ulcerative colitis.
Conclusion

• Indirect treatment comparisons from this network meta-analysis suggested that VDZ may achieve higher rates of both sustained response and sustained remission than comparator therapies in the overall study populations and was associated with lowest risk of AEs. These findings support the favorable benefit–risk profile of VDZ in UC, especially in bio-naïve patients. Head-to-head trials are required to confirm the findings.
Efficacy of JAKs in UC: Tofacitinib (Phase 3)

**Primary endpoint:**
Remission at Week 8

**Key secondary endpoint:**
Mucosal healing at Week 8

**Remission:**
Total Mayo score ≤ 2; no subscore > 1; rectal bleeding subscore of 0

**Mucosal healing:**
ES of 0 or 1

**OCTAVE 1:**
Induction

- **Placebo**
- **Tofacitinib 10 mg BID**

**OCTAVE 2:**
Induction

- **Placebo**
- **Tofacitinib 10 mg BID**

Moderately to severely active UC (Mayo score ≥ 6, rectal bleeding subscore ≥ 1; centrally read ES ≥ 2. Prior failure of intolerance to ≥ 1 of: corticosteroids, azathioprine, 6-mercaptopurine, or TNF inhibitors (TNFi). Washout TNFi 8 weeks; IMM 2 weeks. Concomitant CS: max dose 25 mg/kg; stable during study.

CS = corticosteroid; ES = endoscopic subscore.
Background

- Tofacitinib is an oral, small-molecule Janus kinase inhibitor approved in several countries for the treatment of ulcerative colitis (UC). We report updated tofacitinib safety analyses from the UC program, with exposure up to 5.4 years.

Methods

- Patients who received placebo or tofacitinib 5 or 10 mg twice daily (BID) were analyzed as 2 cohorts: Maintenance (P3 maintenance, n=592) and Overall (patients receiving tofacitinib 5 or 10 mg BID in P2, P3, or the OLE study, n=1157; 2050.5 patient-years’ exposure; data at November 2017). Proportions and incidence rates (IR; unique patients with events per 100 patient-years) were evaluated for adverse events (AEs) of special interest.

In total, 1157 patients received ≥1 dose of tofacitinib 5 or 10 mg BID. Demographics and disease characteristics were generally similar among treatment groups across cohorts.

For the Overall cohort, most patients (n=956; 83%) received an average tofacitinib dose of 10 mg BID.

IR for AEs of special interest were death 0.2; serious infection 1.9; herpes zoster 3.8; opportunistic infection 1.2; malignancy (excluding non-melanoma skin cancer [NMSC]) 0.6; NMSC 0.8; MACE 0.3; and gastrointestinal perforation 0.1.
Conclusion

• The safety profile of tofacitinib in patients with UC was manageable and similar to the tofacitinib rheumatoid arthritis program and that of other UC therapies, including biologics. The IR for AEs of special interest did not increase with longer exposure relative to previously reported analyses from the OCTAVE program. A dose-dependent risk of herpes zoster was observed.

Interpreting the Latest Clinical Data on Efficacy and Safety for Investigational Anti-Integrin, Anti-IL-23, JAK-1 Inhibition, and S1P Receptor Modulators

Peter D. Higgins, MD, PhD, MSc
Professor of Internal Medicine
University of Michigan
Ann Arbor, MI
P224 Responder Definitions for the Ulcerative Colitis Patient-reported Outcomes Signs and Symptoms (UC-PRO/SS) Tool Using Patients With Ulcerative Colitis Treated With Etrolizumab

Background

• The UC-PRO/SS is the first PRO to undergo a rigorous development process outlined by health authorities, with input from patients and clinical experts. Responder definitions for the UC-PRO/SS may allow for it to be a valuable tool for use in clinical trials and practice. We propose responder definitions for the UC-PRO/SS using patients treated with etrolizumab from the phase 3 open-label induction cohorts of HICKORY (NCT02100696) and LAUREL (NCT02165215).
Methods

- Analysis included patients with moderate to severe ulcerative colitis who were treated with etrolizumab 105 mg every 4 weeks during a 10- or 14-week induction period. The UC-PRO/SS consists of 2 separately scored scales: a 3-item functional symptoms domain and a 6-item bowel signs and symptoms domain. The domain score is equal to the sum of the items (0-12 for functional and 0-27 for bowel; no combined total score). Item scores were calculated as an average of 4-7 days during a 9-day window before follow-up. Minimum clinically meaningful differences were calculated using distributional- and anchor-based methods. Responder definitions were triangulated from the anchor-based thresholds based on a reduction of ≥16 points in the Inflammatory Bowel Disease Questionnaire and >3 points in the full Mayo Clinic Score at Week 10 or 14.
### The UC-PRO/SS

<table>
<thead>
<tr>
<th>Bowel (0-27)</th>
<th>Item 1: # of BMs</th>
<th>0-7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Item 2: Liquid BM</td>
<td>0 (never) - 4 (always)</td>
</tr>
<tr>
<td></td>
<td>Item 3: Blood in BM</td>
<td>0 (no) - 4 (always)</td>
</tr>
<tr>
<td></td>
<td>Item 4: Mucus in BM</td>
<td>0 (no) - 4 (always)</td>
</tr>
<tr>
<td></td>
<td>Item 5: Stool/blood/liquid leakage</td>
<td>0 (no) - 4 (always)</td>
</tr>
<tr>
<td></td>
<td>Item 7: BM right away</td>
<td>0 (no) - 4 (very severe)</td>
</tr>
<tr>
<td>Functional (0-12)</td>
<td>Item 6: Pass gas</td>
<td>0 (no) - 4 (very often)</td>
</tr>
<tr>
<td></td>
<td>Item 8: Pain in belly</td>
<td>0 (no) - 4 (very severe)</td>
</tr>
<tr>
<td></td>
<td>Item 9: Bloating in belly</td>
<td>0 (no) - 4 (very severe)</td>
</tr>
</tbody>
</table>

BM = bowel movement; UC-PRO/SS = ulcerative colitis patient-reported outcomes signs and symptoms.

Higgins P, et al. Presented at: 14th Congress of ECCO; March 6-9, 2019; Copenhagen, Denmark. Abstract #P224.
P224 Responder Definitions for the Ulcerative Colitis Patient-reported Outcomes Signs and Symptoms (UC-PRO/SS) Tool Using Patients With Ulcerative Colitis Treated With Etrolizumab

Results for Functional Domain – responder definition: a reduction ≥1.5 points in the functional domain

IBDQ = inflammatory Bowel Disease Quality of Life Index; MCS = Mayo Clinic score.

Higgins P, et al. Presented at: 14th Congress of ECCO; March 6-9, 2019; Copenhagen, Denmark. Abstract #P224.
P224 Responder Definitions for the Ulcerative Colitis Patient-reported Outcomes Signs And Symptoms (UC-PRO/SS) Tool Using Patients With Ulcerative Colitis Treated With Etrolizumab

Results for Bowel Domain - responder definition: a reduction ≥ 5 points in the functional domain

<table>
<thead>
<tr>
<th></th>
<th>Non-Responder (n = 79)</th>
<th>Responder (n = 68)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MCS Anchor</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>-4.5</td>
<td>-9.2</td>
</tr>
<tr>
<td>SD</td>
<td>4.09</td>
<td>1.99</td>
</tr>
<tr>
<td>Mean</td>
<td>-4.5</td>
<td>-9.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Non-Responder (n = 20)</th>
<th>Responder (n = 107)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IBDQ Anchor</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>-2.9</td>
<td>-7.3</td>
</tr>
<tr>
<td>SD</td>
<td>4.08</td>
<td>3.98</td>
</tr>
<tr>
<td>Mean</td>
<td>-1.5</td>
<td>-7.8</td>
</tr>
</tbody>
</table>

Higgins P, et al. Presented at: 14th Congress of ECCO; March 6-9, 2019; Copenhagen, Denmark. Abstract #P224.
### P224 Responder Definitions for the Ulcerative Colitis Patient-reported Outcomes Signs and Symptoms (UC-PRO/SS) Tool Using Patients With Ulcerative Colitis Treated With Etrolizumab

Baseline, Week 10/14, and change from baseline in UC-PRO/SS scores by domain.

<table>
<thead>
<tr>
<th></th>
<th>Functional</th>
<th>Bowel</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>218</td>
<td>218</td>
</tr>
<tr>
<td>Mean</td>
<td>4.93</td>
<td>12.97</td>
</tr>
<tr>
<td>Median</td>
<td>5.00</td>
<td>13.15</td>
</tr>
<tr>
<td>Range</td>
<td>0, 10.28</td>
<td>3.14, 23.43</td>
</tr>
<tr>
<td><strong>Week 10/14</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>152</td>
<td>152</td>
</tr>
<tr>
<td>Mean</td>
<td>2.90</td>
<td>6.22</td>
</tr>
<tr>
<td>Median</td>
<td>2.50</td>
<td>4.93</td>
</tr>
<tr>
<td>Range</td>
<td>0, 8.7</td>
<td>0.8, 20.7</td>
</tr>
<tr>
<td><strong>Change from baseline at week 10/14</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>152</td>
<td>152</td>
</tr>
<tr>
<td>Mean</td>
<td>-2.02</td>
<td>-6.81</td>
</tr>
<tr>
<td>Median</td>
<td>-1.86</td>
<td>-6.13</td>
</tr>
<tr>
<td>Range</td>
<td>-10.28, 3.28</td>
<td>-17.7, 9.16</td>
</tr>
</tbody>
</table>

Higgins P, et al. Presented at: 14th Congress of ECCO; March 6-9, 2019; Copenhagen, Denmark. Abstract #P224.
Conclusion

• Preliminary definitions for response to treatment using the UC-PRO/SS are a reduction of ≥1.5 points in the functional domain or ≥5 points in the bowel domain. These cutoffs will be confirmed in the ongoing, phase 3, UC placebo-controlled studies.

Higgins P, et al. Presented at: 14th Congress of ECCO; March 6-9, 2019; Copenhagen, Denmark. Abstract #P224.
OP11 Etrolizumab Open-Label Extension in TNF-IR

- Etrolizumab is an anti-β7 integrin
- Induction in αTNF-IR patients with moderate to severe UC
- SF remission: mean score of \( \leq 1 \) with \( \geq 1 \)-point reduction from baseline
- RB remission: mean score of 0 with \( \geq 0.5 \)-point reduction from baseline
- FCP reduced by 57% at week 14

RB = rectal bleeding; SF = stool frequency; TNF-IR = inadequate response to tumor necrosis factor; FCP = fecal calprotectin.
DOP54 Efficacy and Safety of Ustekinumab Through Week 16 in Patients With Moderate-to-Severe Ulcerative Colitis Randomized to Ustekinumab: Results From the UNIFI Induction Trial

Background
• To evaluate the efficacy and safety of ustekinumab (UST) through Week 16 induction among patients with moderate to severe UC randomized to UST in the UNIFI phase 3 clinical trial. Week 8 induction data have been previously reported.

Methods
• Rates of overall clinical response and clinical remission among blinded patients randomized to IV UST induction were used to evaluate efficacy through Week 16. The number of patients who achieved each endpoint included patients who achieved the endpoint at Week 8 after initial IV UST induction and patients who achieved the same endpoint at Week 16 following a blinded dose of UST 90 mg SC at Week 8 if they were not in clinical response at Week 8.

Danese S, et al. Presented at: 14th Congress of ECCO; March 6-9, 2019; Copenhagen, Denmark. Abstract #DOP54.
Results

• Among patients randomized to UST at Week 0:
  – 77.6% achieved clinical response within 16 weeks: 56.5% at Week 8 after IV induction and an additional 21.1% at Week 16 after receiving UST SC at Week 8.

• Among the Week 8 nonresponders to UST IV induction who received UST SC at Week 8:
  – 57.9% achieved clinical response at Week 16.

• Among patients randomized to UST at Week 0:
  – 18.8% achieved clinical remission within 16 weeks: 15.6% at Week 8 after IV induction and an additional 3.2% at Week 16 after receiving an additional UST dose at Week 8.

Danese S, et al. Presented at: 14th Congress of ECCO; March 6-9, 2019; Copenhagen, Denmark. Abstract #DOP54.
Results (continued)

• Among the Week 8 nonresponders to UST IV induction who received UST SC at Week 8:
  – 9.4% achieved clinical remission at Week 16

• The proportions of patients who achieved clinical response within 16 weeks was lower for patients with a history of biological failure compared with nonbiological failure patients: 70.6% vs 84.9%.

• Similarly, the proportions of patients who achieved clinical remission during induction within 16 weeks were lower for biological failure patients compared with nonbiological failure patients: 13.3% vs 24.7%.

Danese S, et al. Presented at: 14th Congress of ECCO; March 6-9, 2019; Copenhagen, Denmark. Abstract #DOP54.
Conclusion

- UST is a safe and effective induction therapy in patients with moderate to severe UC. Similar to results from the Crohn’s disease program, these data support a clinical rationale for continuing treatment with UST through at least 1 SC dose 8 weeks after IV induction in patients with moderate to severe UC.
Background

• To evaluate the safety and efficacy of SC ustekinumab (UST) as maintenance therapy in UC patients who were in clinical response to a single IV induction dose of UST.

Methods

• A Ph3, double-blind, randomized withdrawal study in patients with moderate–severe active UC who failed conventional or biologic therapy (including anti-TNF and/or vedolizumab) and were in clinical response 8 weeks after receiving a single UST IV induction dose. The primary study population included 523 patients randomized 1:1:1 to placebo (PBO) SC, UST 90 mg SC q8w or q12w at Week 0. Primary endpoint was clinical remission at Week 44 (52 weeks after IV induction).
Ustekinumab is an anti-IL-12/23 monoclonal antibody

Responders randomized to 44 week maintenance

Endoscopic Healing
- UST 90 q8w: 43.6%
- UST 90 q12w: 28.6%
- PBO: 24.0%

Clinical Remission
- UST 90 q8w: 43.8%
- UST 90 q12w: 38.4%
- PBO: 24.0%

IL = interleukin; PBO = placebo.
Sandborn WJ, et al. presented at: 14th Congress of ECCO; March 6-9, 2019; Copenhagen, Denmark. Abstract #OP37.
OP09 Histological Remission and Mucosal Healing in a Randomized, Placebo-controlled, Phase 2 Study of Etrasimod in Patients With Moderately to Severely Active Ulcerative Colitis

Background

- Etrasimod (APD334), an oral, selective sphingosine-1-phosphate receptor modulator, was evaluated in the phase 2 OASIS study in patients with moderately to severely active ulcerative colitis. Here, we describe histological remission and mucosal healing results at Week 12.

Methods

- Patients were randomized to receive once-daily etrasimod 1 mg (n=52) or 2 mg (n=50), with no dose titration, or placebo (n=54). At baseline and Week 12, endoscopic severity was assessed by sigmoidoscopy with central readings, using the Mayo endoscopic subscore.
Results

• Of 156 patients randomized, 90% completed the study. Etrasimod 2 mg compared with placebo at 12 weeks, resulted in:
  – Significantly more patients who achieved endoscopic improvement (43.2% vs 16.3%; \( P=0.003 \))
  – Histological improvement (31.7% vs 10.2%; \( P=0.006 \))
  – Histological remission (19.5% vs 6.1%; \( P=0.027 \))

• Mucosal healing was seen in 19.5% and 4.1% of patients treated with etrasimod 2 mg and placebo (\( P=0.010 \)).
Conclusion

• Etrasimod 2 mg induced significantly higher rates of endoscopic improvement, histological improvement and remission, and mucosal healing in patients with moderately to severely active UC when compared with placebo. Mucosal healing may prove to be an achievable and objective measure of drug efficacy in UC induction studies.
OP14 Improved Endoscopic Outcomes and Mucosal Healing of Upadacitinib as an Induction Therapy in Adults With Moderately to Severely Active Ulcerative Colitis: Data From the U-ACHIEVE Study

Background

• This analysis evaluates the endoscopic improvement, endoscopic remission, histological improvement, histological remission, and mucosal healing rates at Week 8 of the U-ACHIEVE study.

Methods

• Adult patients with Adapted Mayo Score of 5–9 points and centrally read endoscopy subscore of 2–3 were randomized to receive extended-release upadacitinib 7.5, 15, 30, 45 mg once daily (QD) or placebo for 8 weeks. Patient randomization was stratified by previous biologic use, baseline corticosteroid use, and baseline adapted Mayo score (≤7/>7).

• N = 250 total

OP14 Improved Endoscopic Outcomes and Mucosal Healing of Upadacitinib as an Induction Therapy in Adults With Moderately to Severely Active Ulcerative Colitis: Data From the U-ACHIEVE Study

- Upadacitinib (JAKi) for 8 weeks, dose ranging
- Endoscopic and histologic results

### 8-Week Upadactinib Induction

<table>
<thead>
<tr>
<th></th>
<th>Upa 45</th>
<th>Upa 30</th>
<th>Upa 15</th>
<th>Upa 7.5</th>
<th>PBO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Histologic Remission</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Geboes score &lt;2</td>
<td>2.6%</td>
<td>13.6%</td>
<td>24.4%</td>
<td>35.6%</td>
<td>45.1%</td>
</tr>
<tr>
<td><strong>Endoscopic Healing</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mayo score 0-1</td>
<td>2.2%</td>
<td>14.9%</td>
<td>26.9%</td>
<td>30.6%</td>
<td>35.7%</td>
</tr>
</tbody>
</table>

Conclusion

• In this dose-ranging, 8-week induction study, upadacitinib 30 and 45 mg QD consistently demonstrated significant improvement in endoscopic outcomes, histological outcomes, and mucosal healing compared with placebo in patients with moderately-to-severely active ulcerative colitis.