CARE PERSPECTIVES
ECCO/CDDW 2017

Commentary and content provided by the CARE Gastroenterology Faculty

ECCO 2017 - EUROPEAN CROHN’S AND COLITIS ORGANISATION - BARCELONA, SPAIN - FEBRUARY 15-18, 2017
CDDW 2017 - CANADIAN DIGESTIVE DISEASES WEEK - BANFF, ALBERTA - MARCH 3-6, 2017
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HIGHLIGHTS FROM ECCO/CDDW 2017

CARE (Community. Academic. Research. Education.) believes in: optimization of current therapy, innovation with new treatments, accessibility, and competition; considered in ways that deliver better healthcare solutions to Canadians.

In keeping with these beliefs, this issue of CARE Perspectives explores abstracts and research presented at both the 12th annual ECCO (European Crohn’s and Colitis Organisation) congress held in Barcelona, Spain (February 15-18, 2017) and the CDDW (Canadian Digestive Diseases Week) meeting in Banff, Alberta (March 3-6, 2017).

This report includes content on inflammatory bowel disease and irritable bowel syndrome, as well as updates on what the CARE Gastroenterology Faculty has been working on. Content is contextualized and framed from a Canadian perspective.

We hope you find this valuable and stay tuned for more gastroenterology updates in 2017!

John Marshall, MD, FRCP(C)
McMaster University

The content that follows is written in the language in which it was presented and is adapted from the abstracts from the ECCO/CDDW conferences. Perspectives are provided by the CARE Gastroenterology Faculty. Canadian authors have been identified with a 🇨🇦.
Conclusion: Cessation of rectal bleeding was achieved by significantly more patients with mesalazine enema than with placebo enema. In addition, the time taken to cease rectal bleeding was significantly shorter in patients receiving combination oral and enema mesalazine than oral mesalazine alone, demonstrating improved efficacy of combination treatment in reducing the symptoms of UC.

**CARE FACULTY PERSPECTIVE:** The PINCE trial considered the impact of mono oral mesalazine (PENTASA®) therapy versus combination (oral and enema) mesalazine therapy in patients with mild-to-moderate UC. Results found that combination therapy was more effective in relieving rectal bleeding symptoms rapidly. A supplemental analysis from this trial looked specifically at the QoL of patients taking combination vs. monotherapy and found a measurable benefit (using the Euro-Quality of Life Scoring System) in terms of mobility, usual activity and anxiety/depression in patients receiving combination therapy (oral PENTASA® & enema) with active UC. (ECCO 2017. P261; C.S.J. Probert et al.)

A SUPPLEMENTAL ANALYSIS FOUND A MEASURABLE BENEFIT IN TERMS OF MOBILITY, USUAL ACTIVITY AND ANXIETY/DEPRESSION IN PATIENTS RECEIVING COMBINATION THERAPY (ORAL PENTASA® & ENEMA) WITH ACTIVE UC.

### 5-ASA THERAPY

**ECCO 2017. P151. Shorter time to cessation of rectal bleeding with combined oral and topical mesalazine (PENTASA®) for ulcerative colitis: Results from the PINCE trial**

P. Marteau1, S. Lindgren2, P. Broberg3, C.S.J. Probert4

1Lariboisière Hospital, Paris, France; 2University Hospital MAS, Malmö, Sweden; 3Ferring Pharmaceuticals, Saint Prex, Switzerland; 4University of Bristol, Bristol, United Kingdom

**Results:** Rectal bleeding ceased in 40/52 patients (76.9%) in the mesalazine enema group, and in 16/30 patients (53.3%) in the placebo enema group (eight patients in the active group and 13 in the placebo group did not have rectal bleeding at baseline). The mesalazine enema group had a significantly shorter time to cessation of rectal bleeding than the placebo enema group (p = 0.0025). Mean duration of rectal bleeding was 21.0 days with mesalazine enema and 24.4 days with placebo enema (Table 1). In 35.0% and 25.0% of patients, rectal bleeding ceased within 7 days of study start in the mesalazine and placebo enema groups, respectively; rectal bleeding ceased later than day 28 in 32.5% and 37.5%, respectively. In 50% of mesalazine enema patients, there was cessation of rectal bleeding at -28 days (from Kaplan–Meier analysis), whereas this was achieved after >56 days in the placebo enema group. The time to the cessation of rectal bleeding in patients with frank blood at baseline was also shorter with mesalazine enema and in these patients, there was cessation of rectal bleeding in 50% of the mesalazine enema group at ~21 days, whereas it took >56 days in the placebo enema group.

**Table 1. Time to cessation of rectal bleeding (days), ITT population**

<table>
<thead>
<tr>
<th>ENEMA</th>
<th>BASELINE SCORE</th>
<th>N</th>
<th>MEAN</th>
<th>RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesalazine</td>
<td>Traces of blood</td>
<td>11</td>
<td>18.4</td>
<td>0–51</td>
</tr>
<tr>
<td></td>
<td>Frank blood</td>
<td>25</td>
<td>20.5</td>
<td>0–53</td>
</tr>
<tr>
<td></td>
<td>Mainly blood</td>
<td>4</td>
<td>31.5</td>
<td>1–46</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>40</td>
<td>21.0</td>
<td>0–53</td>
</tr>
<tr>
<td>Placebo</td>
<td>Traces of blood</td>
<td>7</td>
<td>21.3</td>
<td>1–51</td>
</tr>
<tr>
<td></td>
<td>Frank blood</td>
<td>7</td>
<td>18.9</td>
<td>3–49</td>
</tr>
<tr>
<td></td>
<td>Mainly blood</td>
<td>2</td>
<td>54.5</td>
<td>46–63</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>16</td>
<td>24.4</td>
<td>1–63</td>
</tr>
</tbody>
</table>
A novel high-dose mesalazine tablet is as effective as conventional low-dose mesalazine tablets in inducing remission in patients with mildly to moderately active ulcerative colitis (UC): A double-blind, double-dummy, multicentre, randomised trial

A. Dignaß*1, R. Schnabel2, J. Romatowski3, V. Pavlenko4, A. Dorofeyev5, J. Derova6, L. Jonaitis7, T. Nacak8, R. Greinwald8

1Agaplesion Markus Krankenhaus, Dept. of Medicine I, Frankfurt a.M., Germany, 2Pannónia Magánorvosi Centrum Kft, Budapest, Hungary, 3Gastromed sc, Białystok, Poland, 4Stavropol State Medical University, Stavropol, Russian Federation, 5Regional Bowel Diseases Centre of Donetsk State Medical University, Donetsk, Ukraine, 6Latvian Maritime Medical Centre, Riga, Latvia, 7Lithuanian University of Health Sciences, Dept. of Gastroenterology, Kaunas, Lithuania, 8Dr. Falk Pharma GmbH, Clinical Research, Freiburg, Germany

Results: In total, 306 patients were randomised and considered for the safety (SAF) and full analysis set (FAS), 278 patients for the per protocol (PP) population for final analysis (217 PP patients for a pre-planned interim analysis I). The primary endpoint results for clinical remission are summarised in Table 2. High endoscopic remission rates were obtained for both treatment regimens: 68.9% in the M1000 group and 68.4% in the M2x500 group (FAS). Both treatment regimens were safe and no serious adverse event was observed. Importantly, the majority of patients preferred the intake of one high-dose mesalazine tablet (47.7%) over 2 low-dose mesalazine tablets (10.5%).

Table 2. Clinical Remission

<table>
<thead>
<tr>
<th>NUMBER (%) OF PATIENTS IN CLINICAL REMISSION AT WEEK 8</th>
<th>DIFFERENCE BETWEEN PROPORTIONS* [95%CL]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1000 mg mesalazine (TID)</td>
<td>2x500 mg mesalazine (TID)</td>
</tr>
<tr>
<td>PP Interim</td>
<td>48/103 (46.6%)</td>
</tr>
<tr>
<td>PP Final</td>
<td>64/134 (47.8%)</td>
</tr>
<tr>
<td>FAS Final</td>
<td>68/151 (45.0%)</td>
</tr>
</tbody>
</table>

*Primary analysis, stop of patient recruitment for efficacy after interim analysis I
Sensitivity analysis including 61 overrunning patients
Level of significance: 0.0043
1000 mg mesalazine TID vs. 2x500 mg mesalazine TID, non-inferiority margin: -15%

Conclusion: A novel high-dose 1,000 mg mesalazine tablet was non-inferior to the registered Salofalk® 500 mg mesalazine tablet for induction of clinical remission in mildly to moderately active UC. The high endoscopic remission rates obtained in this clinical trial confirm that oral mesalazine is a powerful and safe first-line treatment modality in patients with mild to moderate UC.

CARE FACULTY PERSPECTIVE: Patient adherence to oral medication can often be a problem. Instead of taking two low-dose tablets, a high-dose mesalazine tablet was developed as a once-daily oral medication to reduce the pill burden for UC patients.

This study aimed to compare the efficacy, safety, and tolerability between the 1000 mg mesalazine tablet versus the 500 mg mesalazine tablet (Salofalk®) for patients with mild-to-moderate UC.

Results found that the higher dose was non-inferior to the Salofalk® tablet, and confirms that oral mesalazine is a safe and effective first-line treatment.
BIOLOGIC THERAPY

CURRENTLY AVAILABLE THERAPIES

Research has demonstrated that currently approved biologics are effective therapeutic options for induction and maintenance of remission in moderate to severe ulcerative colitis (UC) and Crohn’s disease (CD). Table 3 shows the various agents that are approved for UC and CD and can be considered for use in clinical practice in Canada.

Table 3. Health Canada Approved Biologic Therapies for IBD

<table>
<thead>
<tr>
<th>CROHN’S DISEASE</th>
<th>ULCERATIVE COLITIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-Tnf agents</td>
<td>Anti-Tnf agents</td>
</tr>
<tr>
<td>adalimumab (Humira®)</td>
<td>adalimumab (Humira®)</td>
</tr>
<tr>
<td>infliximab (Remicade®)</td>
<td>infliximab (Remicade®)</td>
</tr>
<tr>
<td>infliximab biosimilar (Inflectra®)</td>
<td>infliximab biosimilar (Inflectra®)</td>
</tr>
<tr>
<td>Anti-integrin agent</td>
<td>Anti-integrin agent</td>
</tr>
<tr>
<td>vedolizumab (Entyvio®)</td>
<td>vedolizumab (Entyvio®)</td>
</tr>
<tr>
<td>Anti-interleukin agent</td>
<td></td>
</tr>
<tr>
<td>ustekinumab (Stelara®)</td>
<td></td>
</tr>
</tbody>
</table>

Results:

Figure 1. Proportion of patients with remission (CDAI <150 or HBI <5) by BL disease duration

P values are from Cochran-Armitage exact test across disease duration groups.

Conclusion: In 9 CD clinical studies, ADA-treated pts with shorter disease duration achieved a better clinical benefit than pts with longer disease duration. Overall safety of ADA was consistent between disease duration groups.
ECCO 2017. DOP018. Effect of adalimumab on extraintestinal manifestations among patients with ulcerative colitis in a clinical practice setting; results from INSPIRADA

1 Oxford University Hospitals, Oxford, United Kingdom
2 Robarts Research Institute, London, Canada
3 University Hospital of Nancy, Les Nancy, France
4 University of Calgary, Calgary, Canada
5 Istituto Clinico Humanitas, Milan, Italy
6 AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany
7 AbbVie Inc., North Chicago, United States

Results: Data from 461 patients were analysed. At BL, 88 patients (19.1%) had an extraintestinal manifestations (EIMs). The most commonly reported EIM was arthritis (84 of 88 patients). Pyoderma gangrenosum, erythema nodosum, and uveitis each were reported in <1% of patients at BL and at Weeks 2, 8, and 26. The overall percentage of patients with any EIM decreased significantly (p<0.001) from BL over time: 13.2%, 11.7%, and 10.8% had any EIMs at Weeks 2, 8, and 26, respectively. Similar decreasing percentages were seen for patients with arthritis: 13.0%, 11.7%, and 10.8% at Weeks 2, 8, and 26, respectively.

Among those with any EIM at BL, resolution of EIMs increased over time: 39.8%, 52.3%, and 63.6% at Weeks 2, 8, and 26, respectively; durable resolution was 23.9% and 44.3% at Weeks 2 and 8, respectively.

Among those with arthritis at BL, resolution rates were 36.9%, 50.0%, and 61.9% at Weeks 2, 8, and 26, respectively; durable resolution was 20.2%, 41.7%, and 61.9%, respectively.

Conclusion: ADA therapy reduced EIMs among patients with moderate to severe UC in usual clinical practice, with EIM resolution in 60% by Week 26.

CDDW 2017. AI23. Increasing Time on Treatment is Predictive of Improved Long-Term Retention for Stable Remicade® (infliximab) Inflammatory Bowel Disease Patients in Canada

J. Marshall1, M. Marrache1, E. Ewara1
1 Janssen Inc, Toronto, ON, Canada; 2 McMaster University and Farncombe Family Digestive Health Research Institute, Hamilton, ON, Canada

Results: 4,360 patients had ≥2 years of claims history and had been on IFX for ≥1 year. Within-group comparisons showed that the probability of being retained on IFX in subsequent 12 month periods increased with cumulative time on IFX. Patients on IFX for 2-5 years showed significantly higher retention in the subsequent 12 months compared to patients on IFX for only 1 year (P<0.05). Similar trends were observed across when stratified by gender and insurance type, as well as in patients in Ontario, aged 19-64 years, and those who were biologic-naïve. Annual retention up to and including 5 years was significantly better for patients who were publicly insured, and lived in Ontario and Eastern Canada when compared to patients who were privately insured, and lived in British Columbia, respectively.

Conclusion: Real world patients treated with IFX have excellent long-term treatment retention. Previous duration of IFX treatment appears to predict better future retention, becoming statistically significant after 2 years. The results were robust and consistent amongst various subgroups of stable Canadian IBD patients.
ECCO 2017. DOP061. Phase III randomised, double-blind, controlled trial to compare biosimilar infliximab (CT-P13) with innovator infliximab in patients with active Crohn’s disease: early efficacy and safety results

Kim Y.H.1, Ye B.D.1, Pesegovà M.1, Alexeeova O.1, Osipenko M.1, Lahat A.1, Dorofeyev A.1, Salamon A.1, Fishman S.1, Levchenko O.1, Cheon J.H.2, Scriban M.L.2, Mateescu R.-B.1, Lee K.M.1, Eun C.S.3, Lee S.J.3, Lee S.Y.3

1Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea 2University of Utah College of Medicine, Salt Lake City, USA 3Seoul National University College of Medicine, Seoul, South Korea

Results: Of 220 patients randomised in 58 study centres across 16 countries, 214 patients completed study up to Week 6. At Week 6, CDAI-70 response rate of CT-P13 was quite similar to that of INX (CT-P13, 71.4%; INX, 75.2%; p-value = 0.5613). Similar and consistent trends were observed in proportion of patients achieving CDAI-100 response (CT-P13, 61.9%; INX, 64.4%; p-value=0.7744) and clinical remission rate of 42.9% and 44.6% (p-value = 0.8329) in CT-P13 and INX treatment group, respectively. The number of patients with at least one treatment-emergent adverse event (TEAE) showed a similar proportion in the 2 treatment groups (CT-P13, 30.6% [34/111]; INX, 35.8% [39/109]). The proportion of number of patients with at least one treatment-emergent serious adverse event (TESAE) was also comparable between treatment groups (CT-P13, 1.8% [2/111]; INX, 1.8% [2/109]). TEAEs of special interest including infusion-related reactions and infections related to study drug were reported in similar between the 2 treatment groups (CT-P13, 5.4% [6/111]; INX, 5.5% [6/109] as infusion-related reactions, CT-P13, 2.7% [3/111]; INX, 1.8% [2/109] as infections).

Conclusion: The efficacy of CT-P13 was similar to INX in terms of CDAI-70, CDAI-100 and clinical remission up to Week 6 in patients with CD. In addition, CT-P13 was well tolerated with a similar safety profile to that of INX up to Week 6. These results are consistent with randomised controlled studies of INX and other published studies and further reinforced now within the randomised controlled settings.

Other Related Abstracts of Interest

- **ECCO 2017. DOP062.** Biosimilar infliximab (CT-P13) is not inferior to originator infliximab: explorative IBD subgroup-analyses in Crohn's disease and ulcerative colitis from the NOR-SWITCH trial. Jørgensen K.K. et al.

- **ECCO 2017. P540.** Efficacy and safety of infliximab’s biosimilar (REMSIMA) for IBD. J. Yoon Suk et al.

**CARE Faculty Perspective:** We are pleased to see an update on the NOR-SWITCH trial, as well as other biosimilars in development (REMSIMA™). The NOR-SWITCH trial, while underpowered, showed minimal difference between the biosimilar (INFLектRA™) and the innovator biologic (REMICADE™). The South Korean study demonstrated excellent short-term response for REMISIMA™ & good safety in moderate-to-severe CD and UC. More prospective studies with longer follow-up are needed to confirm the efficacy and safety of these biosimilars, and they should not be considered interchangeable with their innovators.

**CARE Faculty Perspective:** CT-P13/Inflectra™ (infliximab biosimilar) was approved in Europe, the United States, and Canada in 2016. This double-blind, randomized, parallel-group, phase III trial was conducted in South Korea and focused on patients suffering from moderate-to-severe CD with the primary aim of comparing the efficacy of CT-P13 and infliximab. It appears that overall, the efficacy of the two agents is similar. Some payers may soon direct treatment naïve patients to a biosimilar rather than the innovator biologic. As new clinical data appears, physicians continue to assess their confidence in these new therapeutic alternatives.
**BIOSIMILARS INITIATIVES**

Biosimilars are a relevant topic to the Canadian landscape, given the recent introduction of Inflectra™ and several other biosimilars expected to be available shortly. The CARE Faculty has been looking at the impact of biosimilars since 2015, given the significance of this topic across both chronic & acute specialties.

**Needs Assessments (2015-2016)**

Needs assessments focused on biosimilars have been conducted across multiple specialties, starting in oncology, then gastroenterology, followed by hematology, and rheumatology. The aim was to understand current perceptions of biosimilars and address gaps in knowledge and their use in Canada across numerous disciplines. Results were collected and shared back with Canadian specialists.

**CARE Multidisciplinary Summit (October 2016)**

CARE organized a summit to bring together a multidisciplinary group of CARE Faculty members from across Canada. This was the first time such a diverse group of specialists were brought together to discuss biosimilars. They discussed the various needs assessment data/results, identified gaps that exist in clinical data, and the potential impact biosimilars could have within their respective fields (opportunities and challenges). There was an agreement among participating faculty to host a larger meeting involving multiple stakeholders.

**CARE Congress (January 2017)**

On January 13th, 2017, a pan-Canadian group of more than 100 stakeholders gathered in Toronto to consider how biosimilars may be incorporated in the Canadian landscape. Among these thought leaders were Health Canada representatives, private and public payers, specialists, pharmacists, nurses, advocacy groups, and legal representatives.

From this meeting, it became evident that:

- Education needs to be provided to all stakeholders (nurses, pharmacists, specialists, legal, payers, advocacy groups, etc.)
- Larger-scale Canadian studies need to investigate biosimilars further
- Studies with endpoints relevant to Canadian patients and clinicians are needed
- Registries need to be developed to monitor/track who is getting which drug and when
- There is need for advocacy groups to host a working group to help shape policies

For more information on biosimilars and specifically to review the meeting highlights and conference proceedings from CARE Congress on biosimilars, please visit: www.CAREeducation.ca

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**ECCO 2017. 583. Real-world use and effectiveness of golimumab for ulcerative colitis in Canada**

B. Bressler1, M. Williamson2, F. Camacho3, B. Sattin2, A. H. Steinhart4

1University of British Columbia, Vancouver, Canada, 2Janssen Inc, Toronto, Canada, 3Damos Inc, Toronto, Canada, 4University of Toronto, Toronto, Canada

**Results:**

**Figure 3. Kaplan-Meier survival curve showing rate of persistence in golimumab responders**

**Summary of the Number of Censored and Uncensored Values**

<table>
<thead>
<tr>
<th>Treatment duration (days)</th>
<th>Total</th>
<th>Failed</th>
<th>Censored</th>
<th>Percent Censored</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>136</td>
<td>41</td>
<td>95</td>
<td>69.85</td>
</tr>
</tbody>
</table>

**Conclusion:** In this large national cohort, 63% of responders to GLM persisted on therapy after 1 year, and few underwent dose optimisation. The median time to GLM discontinuation was 530 days. This dataset represents the largest real-life analysis of GLM patients to date. This real-life cohort is consistent with others showing a substantiated rate of persistence compared with that seen in randomised controlled trials (RCTs).
Anti-Integrin Agents

CDDW 2017. A133. Effectiveness and Safety of Vedolizumab Induction Therapy in Patients with Ulcerative Colitis: Real-world Experience in a Tertiary IBD Centre

P. Zezos1, B. Kabakchiev1, A.Y. Weizman1, G.C. Nguyen3, N. Narula1, K. Croitoru1, H. Steinhart1, M.S. Silverberg1

1Mount Sinai Hospital, Toronto, ON, Canada; 2Lunenfeld Tannenbaum Research Institute, Toronto, ON, Canada

Results:

Table 4. Treatment Outcomes at Week 0, 6, and 14

<table>
<thead>
<tr>
<th>TREATMENT OUTCOMES</th>
<th>WEEK 0 (N=68)</th>
<th>WEEK 6 (N=68)</th>
<th>WEEK 14 (N=53)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical remission</td>
<td>n/a</td>
<td>57%</td>
<td>36%</td>
</tr>
<tr>
<td>Steroid-free clinical remission</td>
<td>n/a</td>
<td>31%</td>
<td>32%</td>
</tr>
<tr>
<td>On steroids</td>
<td>49%</td>
<td>37%</td>
<td>24%</td>
</tr>
<tr>
<td>Median clinical Mayo Score</td>
<td>7</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Median CRP (mg/L)</td>
<td>7.6</td>
<td>5</td>
<td>2.6</td>
</tr>
<tr>
<td>Adverse events (side effects)</td>
<td>16 (11 pts – 5 headache/migraines, 2 transient rash, 2 folliculitis, 1 gastroenteritis, 1 pruritus)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vedolizumab discontinuation Surgery (colectomy)</td>
<td>12% (9 primary response)</td>
<td>7% (n=5)</td>
<td></td>
</tr>
</tbody>
</table>

Week 6=post 3rd infusion, week 14=post 4th infusion

Conclusion: VDZ is an effective, safe and well tolerated treatment option in refractory UC patients. Clinical remission and steroid-free clinical remission can be achieved in 1/3 of the patients after the induction phase. This real-life series in a tertiary care centre demonstrates similar efficacy results as the other real-world clinical studies. Assessment of VDZ response after the 3rd infusion could be critical to determine treatment benefits and decide further management.

CARE FACULTY PERSPECTIVE: This Canadian study provided real-world efficacy and safety of vedolizumab and examined predictors at remission. Vedolizumab appears to be an effective agent for patients with refractory UC; response should be assessed after the third infusion to determine benefit.

Anti-Interleukin Agents

ECCO 2017. P573. Assessment of serum C-reactive protein, faecal lactoferrin, and faecal calprotectin in patients with Crohn’s disease: results from the UNITI-1 and UNITI-2 Ustekinumab induction studies

C. Gasink4, Y. Lang, D. Jacobstein1, J. Johanns1, P. Rutgeerts5, W. de Villiers1, J.-F. Colombel6

4Janssen R & D, LLC, Spring House, Pennsylvania, United States; 5University Hospital Gasthuisberg, Department of Haematology, Leuven, Netherlands; 6Universiteit Stellenbosch University, Stellenbosch, South Africa; 1Mount Sinai, Icahn School of Medicine, New York, New York, United States

Results: In UNITI-1 & 2, each of these 3 markers of inflammation was elevated in 60%-87% of patients at baseline; UNITI-1 (CRP 78.3%, fCal 63.4%, and fLac 86.9 %) and UNITI-2 (76.8%, fCal 62.9%, and fLac 83.6%). The median CRP at baseline was greater in UNITI-1 compared with UNITI-2 (9.88mg/L vs 8.05mg/L). In both studies, significantly greater reductions from baseline in CRP concentration at weeks 3, 6, and 8 were observed in both the UST-6mg/kg and 130mg groups vs PBO (p < 0.001 for all). By week 8 in both studies, whereas both UST groups had greater reductions than PBO, the UST-6mg/kg group had greater median reductions in CRP than the UNITI-1 group (9.88mg/L vs 8.05mg/L). In both studies, the ~6 mg/kg and 130 mg UST groups compared with the PBO group, and greater proportions of pts also achieved normalised levels in these markers with both doses in both UNITI-1 & 2.

Conclusion: UST was efficacious in reducing both serum based markers of inflammation (CRP), as well as faecal based markers (fLac and fCal). Reduction in or normalisation of CD inflammatory biomarkers with induction treatment shows that UST, besides decreasing clinical activity of CD, improves biological activity both in pts who have already failed anti-TNF, as well as after conventional therapy failure.

CARE FACULTY PERSPECTIVE: Ustekinumab was approved in December, 2016 as an induction therapy (based on UNITI-1 and UNITI-2 trials) and maintenance therapy (based on IMUNITI trial) for both anti-TNF naïve and exposed patients with CD.

Ustekinumab is effective at reducing clinical activity of CD. It is also effective in reducing serum based markers of inflammation and faecal based markers.
AGENTS IN DEVELOPMENT

ECCO 2017. P468. Etrolizumab treatment improves histological activity as assessed by the Robarts histopathology index

1University of Western Ontario, London, Canada 2University of Leuven, Leuven, Belgium 3Université de Lorraine, Vandoeuvre-lès-Nancy, France 4University of Chicago Medicine, Chicago, United States 5Genentech, South San Francisco, United States

Results: Analysis included 89 (of 119 efficacy-evaluable) patients with BL histological data and BL RHI ≥1. Mean week 10 RHI reduction was greater for etrolizumab- compared with PBO-treated patients regardless of previous aTNF experience, and a greater proportion of patients receiving etrolizumab achieved histological improvement compared with PBO. Of patients with an endoscopic subscore (ES) ≥1 at week 10, 89% experienced histological improvement. Mean (SD) RHI change was −14.2 (5.5) in patients with an ES ≥1 at week 10 versus −2.5 (9.5) in patients with an ES >1.

Figure 4. Histologic Improvement

Conclusion: RHI-measured histological activity improved after 10 weeks of etrolizumab treatment. Consistent with the clinical remission rates observed in EUCALYPTUS, the magnitude of histological improvement was greater in the aTNF-naive vs aTNF-IR subgroup. RHI reductions are associated with improved ES at week 10.

CARE FACULTY PERSPECTIVE: Etrolizumab is an anti-β7 monoclonal antibody targeting α4β7 and αEβ7 integrins, being investigated for moderate-to-severe UC patients. This trial assessed the effect etrolizumab has on histological inflammation in mucosal biopsies using the Robarts histopathology index (RHI). Histological improvement was better with etrolizumab versus placebo in both anti-TNF naïve and experienced populations, however it was better among the former.

ECCO 2017. OP025. A randomized, double-blind placebo-controlled phase 2a induction study of MEDI2070 (anti-p19 antibody) in patients with active Crohn’s disease who have failed anti-TNF antibody therapy

B.E. Sands1, J. Chen1, M. Perney1, P. Newbold2, R. Faggioni2, R. van der Merwe2, K. Patra1, P. Kleikotka1, E. Pulkstenis1, J. Drappa1, R.A. Gasser, Jr.1
1Icahn School of Medicine at Mount Sinai, Dr. Henry D. Janowitz Division of Gastroenterology, New York, NY, United States, 2MedImmune, Clinical Development, Gaithersburg, MD, United States, 3Amgen, Clinical Development, Thousand Oaks, CA, United States

Results: 121 subjects (61 placebo, 60 MEDI2070) were randomized, with 1 subject per arm not dosed. 57 placebo and 55 MEDI2070 subjects completed W8. Baseline characteristics were similar, with mean (SD) baseline CDAI 319 (58), 71.4% with CRP ≥5, and 75.9% with FCP ≥250. 31.1% had 1 prior anti-TNF agent; 68.9% had ≥2. 38.7% had primary anti-TNF failure. With MEDI2070, 49.2% had clinical effect at W8 vs. 26.7% with placebo (P=0.010). At W8, clinical remission was noted in 27.1% with MEDI2070 vs. 15.0% with placebo (P=0.010 and clinical response in 45.8% and 25.0%, respectively (P=0.017). A composite outcome of clinical effect AND ≥50% reduction from baseline FCP or CRP was achieved in 42.4% with MEDI2070 vs. 10.0% with placebo (p<0.001). No increased rate of adverse events with active treatment was observed over 12 weeks as compared to placebo.

Conclusion: MEDI2070, a specific anti-IL-23 antibody, demonstrates clinical effect in patients with active CD who have failed anti-TNF therapy, and has a favourable safety profile over 12 weeks.

CARE FACULTY PERSPECTIVE: Previous research has suggested benefit in targeting IL-12 and IL-23 in patients with CD who have failed anti-TNF treatment. This study looked at the specific anti-IL-23 antibody, MEDI2070, in patients 18-65 years old with active CD and inflammation, who had all received one or more anti-TNF agent and experienced either primary non-response, loss of response, or intolerance. Results from this phase 2a trial suggest that MEDI2070 has clinical efficacy and safety after 12 weeks. We await Phase 3 trial data.
**ECCO 2017. DOP071.** Tofacitinib plasma concentration monitoring is not needed for optimisation of induction therapy in moderate-to-severe ulcerative colitis: results of pooled exposure-response analyses of Phase 3 induction studies

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Results: The PK analysis included concentrations from 866 patients on tofacitinib, and the ER analysis included 217 placebo patients with no exposure. Estimated PK parameters for a typical study subject were oral clearance (CL/F) = 25 L/hr and oral volume of distribution (V/F) = 105 L. Inter-patient variability (coefficient of variation) in CL/F was 19.9%. C avg was a significantly better predictor of efficacy than C trough for both efficacy endpoints. Predicted difference from placebo in remission for patients in the lowest to highest quartiles of C avg at the 10 mg BID dose was 13.7%, 14.7%, 14.4%, and 17.6%, respectively, and 15.1% for all patients at this dose.

Conclusion: The highly similar remission rate observed across the 4 quartiles in plasma exposure at the 10 mg BID dose indicates that monitoring of tofacitinib plasma concentrations is not necessary for treatment optimisation during induction therapy with tofacitinib.

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**Spotlight on Patient Support in IBD**

**Patient Support Programs (PSPs)**

Inflammatory bowel disease is a chronic, life-long condition. Patients and their families benefit from patient support programs (PSPs) to relieve symptoms, reduce stress, and improve their overall quality of life. They have been developed to provide a customized and responsive support system tailored to each patient’s needs, while also providing access, management tools, education, and even drug funding. Patients, specialists, and their nursing teams have come to rely on them.

In Canada, there are currently three biologic therapy patient support programs for patients with IBD: 1) BioAdvance, 2) AbbvieCare, and 3) YourVantage. These PSPs help with the process (e.g., organizing the infusion closer to patients’ homes, injection support, and accessing the drug promptly) as well with monitoring the drug (e.g., ensuring that antibody screening and biomarker testing are available and these costs are covered).

The COMPANION study presented at ECCO 2017 looked at the impact adalimumab’s PSP on clinical outcomes in IBD. (Abstract P699; Marshall et al.) Results found that patients using tailored services in the form of ‘care coach calls’ are more likely to achieve HBI remission within 6-18 months.

**Technology in IBD**

Smartphone apps are now offering patients a way to be more involved in their IBD management by enabling patients to monitor and track their symptoms, what they eat and drink, bowel movements, appointments, etc. News presented at CDDW 2017 analysed 15 IBD management smart phone apps and ranked them in order of quality by a validated scoring system. (Abstract A148; E.Y. Liu et al.) Physicians can use this information to recommend the best apps for their patients to keep them involved.

At a specialist level, IBD management apps have also been developed by innovator companies. The evaluation and increased use of these management apps is also of interest.

The use and adoption of technology that could help improve patient outcomes is of interest to the CARE Faculty. We look forward to future studies that plan to look at the correlation between clinically validated scoring systems and information collected by high quality IBD management apps identified in this study. More updates to follow.
IRRITABLE BOWEL SYNDROME (IBS)

CDDW 2017. A269. Irritable Bowel Syndrome Patient Experience in Canada

G. P. Attara 1, J. Gray 1, G. Aumais 2

1Gastrointestinal Society, Vancouver, BC, Canada; 2Université de Montréal, Montreal, QC, Canada

Results: Respondents from every province and territory totalled 2,961. 90% were between 30-69 years of age, 86% female, 97% were adults with IBS. 53% had IBS for more than 10 years. 35% had IBS-D, 18% IBS-C, 41% IBS-M, and 6% unsure. In IBS-C patients, abdominal pain was identified as a distinct predominant symptom. Those with IBS-D experienced many symptoms, with abdominal pain, bloating, urgency, and diarrhea identified as highly concerning. 24% experienced severe abdominal pain in the last 3 months, with severe pain being constant in a high proportion. 62% of patients indicated they experienced pain continuing after bowel movement. The top factors driving patients to see their physician were pain/discomfort and impact of IBS on their personal/professional/daily life. Approximately 93% and 49% of patients consulted with a family doctor and gastroenterologist, respectively, for their IBS. 60% had a colonoscopy. 12% have been hospitalized for IBS. 76% indicated that their symptoms interfere with everyday life and 46% missed work or school due to IBS. Most IBS patients use ≥2 medications on a regular basis to control their symptoms yet only 21% are confident their symptoms are under control. Compounding the issue, 16% are unable to afford any of their prescribed medications, and 26% can only afford some of them.

Conclusion: Canadian IBS patients suffer from multiple symptoms, with the pain experienced by patients being the prime motivating factor to seek care. 79% have symptoms not under control. The conventional standard of care for IBS requires many different treatments to manage the multiple symptoms, with the majority of IBS patients requiring 2 or more treatments on a regular basis. IBS patients experience a wide range of symptoms and comorbidities. It can be a struggle for them to find treatments that are effective and affordable.

CARE FACULTY PERSPECTIVE: IBS is a chronic functional gastrointestinal disorder that affects 13-20% of Canadians. There are a number of symptoms associated with IBS, and research has shown that abdominal pain and bloating are some of the most bothersome symptoms. Lifestyle interventions, such as increased dietary fiber, water intake, and exercise, for the treatment of IBS are universally recommended. However, lifestyle modifications are often not enough.

This study found that one of the main reasons patient seek treatment is due to pain. Linaclotide is approved for both IBS-C and CIC, and has shown to consistently provide abdominal pain relief. In the field of IBS-D, eluxadoline was approved by Health Canada on January 27th, 2017 and is expected to come to market in the spring and rifaximin is currently under review by Health Canada. Both appear to be promising.

ABDOMINAL PAIN AND BLOATING ARE SOME OF THE MOST BOTHERSOME SYMPTOMS. LINACLOTIDE IS APPROVED FOR BOTH IBS-C AND CIC, AND HAS SHOWN TO CONSISTENTLY PROVIDE ABDOMINAL PAIN RELIEF.
The Management of Chronic Constipation

Published in the
Canadian Journal of Hepatology & Gastroenterology 2017

Treatment Algorithm for Chronic Idiopathic Constipation and Constipation-Predominant Irritable Bowel Syndrome Derived from a Canadian National Survey and Needs Assessment on Choices of Therapeutic Agents

Drs. Louis Liu, Yvonne Tse, David Armstrong, John Marshall, Alain Bitton, Brian Bressler, Christopher Andrews

Members of the CARE Gastroenterology Faculty have been researching the proper approach to management of chronic constipation for several years. In 2013, they developed a treatment algorithm based on the available options at that time. By 2015, the faculty thought this algorithm was outdated and developed a needs assessment to investigate the management of CIC and IBS-C. The results from this survey provided practical insights into the management of chronic constipation in Canada, and led to the development of an updated Canadian-centric management algorithm. This needs assessment formed the basis of an abstract that was presented at ACG 2015 in Hawaii, led by Dr. Louis Liu. In 2016, the algorithm was updated again to stay current and a clinical paper was submitted.

This clinical paper was published on February 8th, 2017 in the Canadian Journal of Hepatology & Gastroenterology. This publication provides insight from the original needs assessment questionnaire, as well as an in-depth overview of how to manage chronic constipation in the Canadian landscape based on the developed algorithm.

Please visit www.CAREeducation.ca or https://doi.org/10.1155/2017/8612189 for the full publication.

CDDW 2017. A16. Success of Enhanced Primary Care Pathways in Managing Routine GI Referrals

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Results: From January 2015-June 2016, 667 cases were triaged to an EPCP thus the referral was sent back for management in the medical home. Over this time period, 54 EPCP patients (7.9%) had an emergency room visit in the Calgary zone. Of the 667 EPCP patients, the re-referral rate to GI was 9.6% (64 cases). The reasons for re-entry back into the system are shown in Table 5. All 64 patients went on to have an endoscopic procedure (EGD=47, colonoscopy=17). Forty-one of the 64 endoscopies (64%) were reported as normal. Significant findings included esophagitis (n=7), non-dysplastic Barrett’s esophagus (n=3) and moderate left-sided ulcerative colitis (n=1). No malignancies were detected.

Table 5. Reasons for Referral to GI After EPCP Pathway Enacted (n=64)

<table>
<thead>
<tr>
<th>REASON</th>
<th>NUMBER OF PATIENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worsening abdominal pain</td>
<td>39 (60.1%)</td>
</tr>
<tr>
<td>Symptoms despite completion of EPCP path</td>
<td>11 (17.1%)</td>
</tr>
<tr>
<td>New development of red flag features</td>
<td>8 (12.5%)</td>
</tr>
<tr>
<td>Abnormal diagnostic imaging</td>
<td>4 (6.2%)</td>
</tr>
<tr>
<td>Barrett’s screening</td>
<td>2 (3.1%)</td>
</tr>
</tbody>
</table>

Conclusion: The majority of non-urgent GI referrals were successfully managed in a primary care setting using EPCPs thus providing an alternative to traditional queue-based GI consultations. This process has served as a template for other specialty groups in Calgary looking to address similar care gaps. Future plans include physician/patient satisfaction surveys and focus groups to determine if any additional supports are needed to aid the medical homes in caring for these patients.
CARE AT DDW 2017

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