Conference Report on Gastroenterology
Commentary and content provided by the CARE Gastroenterology Faculty
Conference Report on Gastroenterology

HIGHLIGHTS FROM DDW 2016

Members of the CARE Gastroenterology Faculty recently attended the DDW 2016 conference held in San Diego, California (May 21-24). At this conference, the annual CARE at DDW education meeting was held. This meeting brought together a pan-Canadian Faculty of KOLs to showcase news and developments in gastroenterology. Presentations featured cutting edge content with discussion on relevant cases and treatment strategies. CARE at DDW was attended by Canadian gastroenterology professionals. Attendees included academic and community specialists, and residents.

The CARE Perspectives Conference Report from DDW 2016 provides a summary of the most compelling stories and news presented at this event, and is augmented with additional perspectives from the CARE Gastroenterology Faculty. The content that follows is written in the language in which it was presented.

CARE GASTROENTEROLOGY FACULTY WHO HAVE CONTRIBUTED TO THIS REPORT:

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FOR AN UPDATE FROM
CARE GASTROENTEROLOGY FACULTY CHAIR
DR. JOHN MARSHALL
What follows is an overview of the presentation made by Dr. Alexandra Ilnyckyj at the recent CARE at DDW education meeting, and is augmented with abstract content from DDW 2016 and additional perspectives from the CARE Gastroenterology Faculty.

IRRITABLE BOWEL SYNDROME (IBS)

DDW 2016. ABSTRACT 258. FODMAPs Alter the Metabolome and Symptoms in Irritable Bowel Syndrome Patients
Stephen Vanner1, Keith McIntosh1, David E. Reed1, Teresa Schneider1, Frances Dang1, Ammar H. Keshteli1, Guada de Palma2, Karen Madson2, Premysl Bercik3
1 Medicine, Queen’s University, Kingston, Ontario, Canada; 2 St. Joseph’s Health Centre, London, Ontario, Canada; 3 Hotel Dieu Hospital, Kingston, Ontario, Canada; 4 University of Alberta, Edmonton, Alberta, Canada; 5 Farncombe Family Digestive Health Research Institute, Hamilton, Ontario, Canada

Results: Thirty-seven patients (19 low FODMAP; 18 high FODMAP) completed the 3 week diet. The IBS-SSS was reduced in the low FODMAP group (P<0.001) but not the high FODMAP group. Metabolic profiling of urine showed both patient groups were similar at baseline but differed significantly after the 3 week diet (P<0.01). Three metabolites (histamine, p-hydroxybenzoic acid, azelaic acid) were primarily responsible for discrimination between the two groups. Histamine was reduced 6 fold in the low FODMAP group (p<0.05) but not the high FODMAP group (NS increase from baseline). LB Ts showed a minor reduction in H₂ gas production with the low FODMAP diet that was not significant unless corrected for baseline differences (P <0.05). Partial 16s rRNA gene profiling did not reveal differences in α and β diversity of the fecal microbiota before and after the diets but when comparing diets after 3 weeks we observed increased bacterial richness (P = 0.047) in the low FODMAP group (IBS-C excluded). The low FODMAP diet decreased the relative abundance of Propionibacteriaceae (Actinobacteria) and several butyrate producing bacteria.

Conclusions: A low FODMAP diet reduced IBS symptoms and was associated with significant changes in the metabolome. Alterations in histamine levels suggest FODMAPs are linked to immune activation and could worsen symptoms, given the evidence that histamine sensitizes nerves that mediate pain. Microbiota changes resulting from the low FODMAP diet could improve symptoms by decreasing FODMAP fermentation products (e.g. gas and SCFA) although long term use may create a niche for bacteria that are potentially detrimental to patient’s health.

CARE FACULTY PERSPECTIVE: Clinical studies have documented that a low FODMAP diet can decrease symptoms in patients with IBS-D, yet the mechanism of this benefit remains poorly understood. This abstract provides further validation that a low FODMAP diet can decrease IBS symptoms. Moreover, it provides insights into two possible mechanisms by which a low FODMAP diet can benefit patients. In this Canadian study, Vanner et al demonstrate changes in urinary histamine levels and altered fecal microbiota supporting possible alterations of immune and bacterial physiology. This work provides important insights to propel further research into the mechanism of the low FODMAP effect.

Eric D. Shah1, Ali Rezaie2, Mark Pimentel3,4
1 Cedars-Sinai Medical Center, Los Angeles, California, United States; 4 University of Michigan Health System, Ann Arbor, Michigan, United States

Results: Three randomized double blind Phase II and III registered trials of eluxadoline were included representing 2,209 patients on therapy and 968 on placebo. The NNT was 12.7 (RR=1.5, 95% CI 1.3 to 1.8) based on the FDA responder endpoint. The pooled rate of study withdrawal due to adverse events was 8.0% on therapy and 4.4% on placebo, resulting in a statistically significant number needed to harm (NNH=28.3, RR=1.9, 95% CI 1.4 to 2.6). The excess incidence of constipation was 4.6%, resulting in a NNH of 21.6 (RR=2.9, 95% CI 1.9 to 4.4). Regarding serious adverse events, the rate of pancreatitis on eluxadoline was 0.7% in phase II evaluation and 0.4% in pooled analysis (with no pancreatitis on placebo), though notably phase III trials excluded patients with specific additional risk factors of pancreatitis.

Conclusions: Eluxadoline is efficacious in treating IBS-D, though constipation is not uncommon and may hamper the observed benefit of eluxadoline based on its mechanism of action. There was a slightly increased rate of pancreatitis on eluxadoline. In the chronic treatment of a non-lethal illness such as IBS, this finding warrants further population-level evaluation as well as appropriate patient selection and monitoring.

CARE FACULTY PERSPECTIVE: Finding an appropriate and effective treatment strategy for patients with IBS-D is especially important in order to improve patients’ overall quality of life (QoL). Treatment should address symptoms and their severity, as well as psychosocial factors.

"ELUXADOLINE OFFERS A CONVENIENT METHOD OF DELIVERY THAT SIGNIFICANTLY IMPROVES SYMPTOMS, ALLOWING FOR PATIENTS TO REGAIN CONTROL OVER THEIR BOWELS AND IMPROVE THEIR QoL OVERALL."

Eluxadoline offers a convenient method of delivery (twice daily oral medication) that significantly improves symptoms, allowing for patients to regain control over their bowels and improve their quality of life overall. More research is needed to determine which patient populations would benefit most from this treatment regimen.
### GASTROPARESIS

**DDW 2016. M01589.** Placebo-Controlled, Double-Blind Study to Evaluate the Effects of Relamorelin on Satiation, Gastric Volume, Gastric Accommodation, and Distal Gastric Function in Healthy Volunteers

Alfred D. Nelson, Michael Camilleri, Andres Acosta, Irene Busciglio, Sara Linker Nord, Amy Boldingh, Deborah Rhoten, Michael Ryks, Duane Burton

Results: The participant demographics in the two treatment groups were similar. Relamorelin, 30µg, significantly increased the number of contractions in the distal antrum during 0-60 minutes post-meal when compared to placebo (p=0.022); this was also observed in the first two 15-minute periods (p=0.008 and 0.015 for # of contractions and M<sub>0-60</sub>). There was a borderline increase in M<sub>0-60</sub> (p=0.055) and numerically increased M<sub>4-30</sub> and MI<sub>0-60</sub>. The amplitude of contractions was not significantly increased. Relamorelin did not significantly alter fasting or postprandial gastric volumes, gastric accommodation, or satiation volumes and symptoms (aggregate and nausea, fullness, bloating, pain).

**Effects of Relamorelin and Placebo on Distal Antral Pressure Activity**

<table>
<thead>
<tr>
<th>Score</th>
<th>Baseline</th>
<th>4 weeks</th>
<th>12 weeks</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>69.2</td>
<td>41.5</td>
<td>&lt;0.001</td>
<td>37.3</td>
</tr>
<tr>
<td>Days of abdominal pain</td>
<td>81.6</td>
<td>58.3</td>
<td>&lt;0.001</td>
<td>49.2</td>
</tr>
<tr>
<td>Bloating</td>
<td>71.8</td>
<td>43.8</td>
<td>&lt;0.001</td>
<td>37.2</td>
</tr>
<tr>
<td>Satisfaction with bowel habit</td>
<td>84.4</td>
<td>49.9</td>
<td>&lt;0.001</td>
<td>39.2</td>
</tr>
<tr>
<td>IBS interfering with life</td>
<td>81.5</td>
<td>57.4</td>
<td>&lt;0.001</td>
<td>49.2</td>
</tr>
<tr>
<td>Total IBS-SSS</td>
<td>386.1</td>
<td>247.8</td>
<td>&lt;0.001</td>
<td>214.0</td>
</tr>
</tbody>
</table>

Conclusions: Linaclotide was effective in IBS-C patients in a real-world setting, with significant reductions in IBS-SSS scores and straining, and a significant increase in mean number of stools per week. Responder rates at 4 and 12 weeks were 45% and 36% respectively. 40% of patients reported AEs, with diarrhoea the commonest, occurring in 26% of patients. Previous literature has reported a lower frequency of AEs, which infrequently led to withdrawal of linaclotide. However, in our study the occurrence of AEs led to discontinuation in 21% of patients.

**CARE FACULTY PERSPECTIVE:** 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.

"IN ADDITION TO THE PROVEN EFFICACY OF LINACLOTIDE IN TERMS OF RELIEVING IBS-C, IT HAS SHOWN TO SIGNIFICANTLY REDUCE ABDOMINAL PAIN AND BLOATING IN THIS PATIENT POPULATION."

In addition to the proven efficacy of linaclotide in terms of relieving IBS-C, it has shown to significantly reduce abdominal pain and bloating in this patient population. This, in turn, has shown to have a substantial impact on quality of life for patients suffering from IBS. This study confirmed these findings, showing that in a real-life setting patients experience less abdominal pain and bloating, improved satisfaction with bowel habit, and an improvement in IBS interfering in their life. Overall, this appears to be a very effective agent that should be used in this patient population.
ACHLASIA

TREATMENT-RELATED ADVERSE EVENTS

**DDW 2016. ABSTRACT TU2049.** Long Term Outcomes of PerOral Endoscopic Myotomy (POEM) in Achalasia Patients With a Minimum Follow-Up of 2 Years: A Multicenter Study


CARE FACULTY PERSPECTIVE:

*Gastroenterology, Johns Hopkins Hospital, Baltimore, Maryland, United States; 1 Digestive Diseases Center, Showa University, Koto-Tosu Hospital, Tokyo, Japan; 2 King’s College Hospital WFS Foundation Trust, London, United Kingdom; 3 Svanston Hospital, Evanston, Illinois, United States; 4 Gastroenterological and Endocrine Surgery, University of Strasbourg, Strasbourg, France; 5 Digestive Diseases and Endoscopy, Deenanath Mangeshkar Hospital and Research Center, Pune, India; 6 Surat Institute of Digestive Sciences, Surat, India; 7 Gastroenterology and Endoscopy Unit, Digestive Disease Department, Edouard Herriot Hospital, Lyon, France; 8 Humanitas University School of Medicine, Milan, Italy; 9 Humanitas Research Hospital, Milan, Italy

Results: Clinical success rates after peroral endoscopic myotomy

![Clinical Success](image)

Conclusions: POEM is safe and provides high initial clinical success and excellent long-term outcomes. Less than 10% of patients who had clinical response at 6 months had recurrent symptoms at 2 years. History of prior pneumatic dilatation is associated with clinical failure. Post-POEM symptomatic reflux occurs in quarter of patients and esophagitis is found in 15% of asymptomatic patients.

**CARE FACULTY PERSPECTIVE:** Peroral endoscopic myotomy for the treatment of achalasia is gaining momentum as a minimally invasive procedure with excellent short term clinical response. The established standard of care, namely pneumatic dilatation and Heller myotomy, demonstrate durable outcomes. Thus, the data regarding the durability of POEM is needed. This abstract reports a minimum 2 year follow up of 179 patients treated in ten different centers and documents 90% of patients meeting criteria for responder (Eckardt score ≤2 out of 4) in 4 studies. Comparability domain was quite acceptable (good), while exposure domain was poor in all studies (score=I out of 3). Potential biased effect size and publication bias were also detected in the included case-control studies. Analysis of the 7 interventional studies with domperidone in gastroparesis including 706 patients revealed no cardiac adverse event.

Conclusions: Domperidone statistically increases the odds of serious ventricular arrhythmia and sudden cardiac death with domperidone use

Mohammad Bashashadi, Irene Sarosiek, Sharareh Moraveji, Alak Divedi, Tariq Siddiqui, Richard W. McCalmont

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Results: From the 7 case-control studies, 5 studies were from Europe; one was from Taiwan and one from Canada. The meta-analysis indicated that domperidone is a risk for sudden cardiac death and/or serious ventricular arrhythmia (pooled unadjusted OR: 1.88 [95%CI: 1.48-3.39] and pooled adjusted OR 1.60 [95% CI: 1.46-1.74]). On the other hand, NOS indicated only a fair quality for all of these 7 studies. Detailed evaluation indicated poor or fair quality on the selection domain (score=2 out of 4) in 4 studies. Comparability domain was quite acceptable (good), while exposure domain was poor in all studies (score=I out of 3). Potential biased effect size and publication bias were also detected in the included case-control studies. Analysis of the 7 interventional studies with domperidone in gastroparesis including 706 patients revealed no cardiac adverse event.

Conclusions: Domperidone statistically increases the odds of cardiotoxicity, but the quality of the conducted case-control studies does not permit any final conclusion. No association between domperidone and serious cardiac events is noted by the findings of interventional studies in gastroparesis and accompanying nausea and vomiting. We believe that patients should not be denied access to domperidone, but physicians should closely monitor and follow the investigational new drug (IND) protocol when domperidone is prescribed.

**CARE FACULTY PERSPECTIVE:** In 2004, the FDA suspended the use of domperidone due to reports of sudden cardiac death. In Canada, there has been no restriction on use of the drug. The Health Canada website acknowledges the reports of sudden cardiac death but mandates no pre-screening or monitoring. For colleagues practicing in the US, use of domperidone requires application for use of an investigational new drug. The paucity of agents to treat gastroparesis has mobilized researchers to present data demonstrating drug safety. In this systematic review, 7 interventional studies in patients with gastroparesis demonstrated no increase in cardiac events.

Hopefully in time, a more comprehensive and detailed analysis of the data will appear in published form to allow the FDA to review its current position. In the meantime, Canadian physicians and patients have no barriers to face in accessing this drug.

**VISIT THE CARE YOUTUBE CHANNEL FOR AN UPDATE FROM CARE GASTROENTEROLOGY FACULTY MEMBER DR. ALEXANDRA ILYNCKYJ**
ULCERATIVE COLITIS

What follows is an overview of the presentation made by Dr. Brian Bressler at the recent CARE at DDW education meeting, and is augmented with abstract content from DDW 2016 and additional perspectives from the CARE Gastroenterology Faculty.

ANTI-TNF AGENTS

**DDW 2016. MO1902. Real World Use and Effectiveness of Golimumab for Ulcerative Colitis in Canada**

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**Results:** Persistence of Golimumab in Ulcerative Colitis

![Graph showing survival probability over time](image)

Conclusions: In this large national cohort, 63% of responders to GLM persisted on therapy after 1 year and few underwent dose optimization. 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 to that seen in RCTs.

**CARE FACULTY PERSPECTIVE:** Golimumab is a monoclonal antibody approved in Canada for the treatment of ulcerative colitis. The benefit of golimumab has been established in clinical trials, however its applicability in the real-world has not been well studied. This trial examined golimumab in a large ‘real-life cohort’ of Canadian UC patients who were both anti-TNF naïve and exposed, as well as looked at the rate of persistence and assessed factors that predict discontinuation during GLM maintenance treatment. Data in this study was collected from the patient support program (PSP), BioAdvance. This PSP provides patients with customized care to help guide them through the treatment process, and records patient information (i.e. Demographics, prescription data) in the database. For more information on patient support, see page 11.

This study tells us that over half (63%) of patients persisted on therapy after one year of being on golimumab therapy, with the median time to treatment discontinuation being 530 days. The results of this study provide practical insight into how golimumab is being tolerated in the ‘real-world’.

**DDW 2016. ABSTRACT 516. Accelerated Dosing of Infliximab Prevents Colectomy Within 90 Days in Only Half of Patients With Severe Ulcerative Colitis**

Shail M. Govani1, 2 Akbar K. Walla3, 4, Ryan W. Siddham1, Peter Higgins1, Karin Hardiman5

1Internal Medicine, University of Michigan, Ann Arbor, Michigan, United States; 2VA Hospital, Ann Arbor, Michigan, United States; 3VA Center for Clinical Management Research, Ann Arbor, Michigan, United States; 4Surgery, University of Michigan, Ann Arbor, Michigan, United States

**Results:** During the study period, there were 57 patients with severe UC treated with IFX. Of these 17 received accelerated dosing, starting in 2013. The population was 61.4% female with an average age of 33.4 (+/- 12.2). The average disease duration was 5.4 years (+/- 7.0). The 90-day colectomy rate for typical dosing was 12.5% compared to 47.1% among those receiving accelerated dosing (p=0.01). The average admission albumin and C-reactive protein (CRP) did not differ between the 2 groups. The average CRP on day of first IFX infusion was higher for accelerated dosing patients than typical dosing (5.8 mg/dL +/- 3.7 mg/dL vs 3.7 mg/dL +/- 3.0 respectively, p=0.06) but the average decline in CRP between admission and 1st infusion was greater for accelerated dosing than typical dosing (2.0 mg/dL +/- 4.4 for accelerated dosing vs. 5.1 mg/dL +/- 6.1, p=0.09). Twelve of the 13 patients who had a colectomy within 90 days underwent the procedure at our institution. For those patients who underwent colectomy, the 30-day post-operative readmission rate was higher among those given accelerated dosing (57.1% vs 20%, p=0.29) but the post-operative complications were similar.

**Conclusions:** At our institution, accelerated dosing of IFX spared about 50% of patients from colectomy, far below the success rate reported in the initial study. Patients given accelerated dosing of IFX who underwent colectomy had an increased rate of 30-day re-admissions. Larger studies are needed to understand the risks and benefits of administering accelerated dosing IFX.

**CARE FACULTY PERSPECTIVE:** Research has shown that infliximab is effective in reducing colectomy for patients with steroid-refractory severe UC. In a previous study, infliximab was able to save 93.3% of patients from colectomy (Yamada, 2014). This study by Govani et al. aimed to validate these findings and discovered that accelerated dosing of IFX saves approximately 50% of patients from colectomy. More research is required to better understand the best way to dose optimize IFX in severe hospitalized steroid refractory UC.
**DDW 106. SA1888. Efficacy and Predictors of Outcomes of Vedolizumab for Ulcerative Colitis in Clinical Practice**

Farhad Peerani1, Neeraj Narula1, Parambir S. Dula1, Khadija Chaudrey1, Diana Whitehead1, David Hudesman1, Eugenia Shmidt2, Diwana J. Lukin2, Arun Swaminath2, Aghsa Nguyen2, Joseph Meserve2, Sunanda V. Kane3, William Sandborn4, Bruce E. Sands5, Jean-Frederic Colombel6, Corey A. Siegel6, Edward V. Loftus3, Siddharth Singh1, Dana J. Lukin6, Arun Swaminath7, Nghia Nguyen1, Joseph Meserve1, Sunanda V. Kane3, William Sandborn4, Bruce E. Sands5, Jean-Frederic Colombel6, Corey A. Siegel6, Edward V. Loftus3, Siddharth Singh1, Dana J. Lukin6, Arun Swaminath7, Nghia Nguyen1, Joseph Meserve1, Sunanda V. Kane3, William Sandborn4, Bruce E. Sands5, Jean-Frederic Colombel6, Corey A. Siegel6, Edward V. Loftus3, Siddharth Singh1, Dana J. Lukin6, Arun Swaminath7, Nghia Nguyen1, Joseph Meserve1, Sunanda V. Kane3, William Sandborn4, Bruce E. Sands5, Jean-Frederic Colombel6, Corey A. Siegel6, Edward V. Loftus3, Siddharth Singh1, Dana J. Lukin6, Arun Swaminath7, Nghia Nguyen1

**Results:** We included 125 patients (mean ± SD age 38.7 ± 15 years, 53% male) with a mean (± SD) follow-up of 9 (± 4) months. A concomitant steroid or immunomodulator was used in 65% and 40% of patients, respectively. RES, REM, and CSFR were achieved in 57% (n=71/125), 20% (n=25/125), and 57% (n=47/82), respectively, after induction. Prior exposure to anti-TNF therapy was observed in 62% (n=89/125) of patients, and on multivariate analysis prior anti-TNF use was associated with a reduced likelihood for achieving REM (Hazard Ratio [HR] 0.34, 95% Confidence Interval [CI] 0.16-0.76, p=0.008) after induction. During maintenance therapy, RES, REM, and CSFR were achieved in 60% (n=75/125), 39% (n=49/125), and 63% (n=50/79), respectively. MH was achieved in 45% (n=34/76), and 15% (n=19/125) required colectomy. On multi-variate analysis, prior anti-TNF use was associated with a reduced likelihood for achieving overall RES (HR 0.53, 95% CI 0.32-0.87, p=0.013) or overall REM (HR 0.37, 95% CI 0.20-0.71, p=0.002). Patients with a longer disease duration (> 5 years) were more likely to achieve MH (HR 2.15, 95% CI 1.04-4.43, p=0.038). Kaplan-Meier curves demonstrated that any prior anti-TNF use or use of 2 or more anti-TNF agents prior to VDZ was associated with reduced treatment efficacy.

**Conclusions:** In this multi-center consortium, CSFR and MH were achieved in over 40% of UC patients. Prior anti-TNF use significantly impacted clinical response, remission, corticosteroid free response or remission, and need for colectomy. Further studies are needed to determine if using VDZ prior to anti-TNF therapy or after the first anti-TNF failure improves outcomes.


Frank I. Scott1, Yash Shah3, Karen Lasch4, Michelle Lu5, James Lewis1,2

1 Division of Gastroenterology, University of Pennsylvania, Philadelphia, Pennsylvania, United States; 2Center for Clinical Epidemiology and Biostatistics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, United States; 3University of Pennsylvania, Philadelphia, Pennsylvania, United States; 4Takeda Pharmaceuticals, U.S.A., Inc., Deerfield, Illinois, United States

**Results:** Incremental Effectiveness of Early VDZ with Longer Time Horizons

**Conclusions:** This model suggests that incorporating VDZ early in the treatment paradigm results in the greatest potential benefit for individuals with moderate to severe UC who require steroid-sparing therapy.

**CARE FACULTY PERSPECTIVE:** Vedolizumab was approved in 2015 for the treatment of UC. It works by targeting the gut, which directly reaches the inflammation causing symptoms of UC (and Crohn’s Disease). It is the first and only ‘gut selective’ biologic therapy approved for patients who have had an inadequate response to immunomodulators, TNF agents, or corticosteroids.

With vedolizumab now available in Canada, clinicians have been wondering how to optimize the efficacy of this agent. The results from this study suggest that incorporating vedolizumab early on for patients with moderate to severe UC, maximizes the efficacy of this agent in this patient population.

**“VEDOLIZUMAB IS THE FIRST AND ONLY ‘GUT SELECTIVE’ BIOLOGIC THERAPY APPROVED FOR PATIENTS WHO HAVE HAD AN INADEQUATE RESPONSE TO IMMUNOMODULATORS, TNF AGENTS, OR CORTICOSTEROIDS.”**
JANUS KINASE (JAK) INHIBITORS

DDW 2016. ABSTRACT 767. Efficacy and Safety of Oral Tofacitinib As Induction Therapy in Patients With Moderate to Severe Ulcerative Colitis: Results From Two Phase 3 Randomized Controlled Trials


1 Division of Gastroenterology, University of California, San Diego, California, United States; 2 Pfizer Inc, Groton, Connecticut, United States; 3 Pfizer Inc, Collegville, Pennsylvania, United States; 4 Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, New York, United States; 5 Department of Gastroenterology, Academic Medical Centre, Amsterdam, Netherlands; 6 Department of Gastroenterology, University Hospitals Leuven, Leuven, Belgium; 7 Klinik für Innere Medizin I, Universitätsklinikum Schleswig-Holstein, Kiel, Germany; 8 IBD Center, Department of Gastroenterology, Humanitas Research Hospital, Milan, Italy; 9 Hospital Clinique de Barcelona, IDIBAPS, CIBERehd, Barcelona, Spain; 10 McMaster University, Hamilton, Ontario, Canada; 11 Roberts Clinical Trials Inc, Roberts Research Institute, Western University, London, Ontario, Canada

Results: At baseline, 53–58% of patients had prior TNFi exposure across treatment groups in both studies. At Week 8, significantly more patients receiving tofacitinib 10 mg BID achieved remission, mucosal healing, and clinical response in both studies vs placebo. Efficacy was similar for TNFi-treated vs TNFi-naive patients. Improvements in partial Mayo score were rapid and significantly greater with tofacitinib vs placebo at Weeks 2, 4 and 8. Adverse event (AE) rates were similar across groups; rates of serious AEs were not higher with tofacitinib vs placebo. One patient died (tofacitinib 10 mg BID; dissecting aortic aneurysm). Increases in serum lipid (total cholesterol, low-density and high-density lipoprotein) and creatine kinase levels were seen with tofacitinib treatment.

Conclusions: Tofacitinib demonstrated significantly greater efficacy vs placebo based on remission and mucosal healing endpoints. Efficacy was similar in TNFi-treated vs TNFi-naive patients. Improvements in Week 2 partial Mayo score (first post-baseline assessment) support early onset of treatment effect. Safety data from this 8-week induction study showed no new or unexpected observations from results in the tofacitinib studies in other populations.

CARE FACULTY PERSPECTIVE: Tofacitinib is an oral agent that is effective and safe for the management of moderate to severe UC, and would be a valuable addition to our current medical options. These large studies demonstrate both safety and efficacy for Tofacitinib for moderate to severe UC. It is our expectation that this new medical option will be available in Canada, providing an important new therapy for patients.

THERAPY-REFRACTORY ULCERATIVE COLITIS

DDW 2016. ABSTRACT 992. Therapy Refractory Ulcerative Colitis Patients May Benefit From Appendectomy: Early Result From the Passion Study

Saloomeh Sahami1, Chistinehne Bukens1, Desmond C. Winter1, Sean Martin1, Pieter Tanis1, Mark Löwenberg2, Gis van den Brink3, Cynel Ponsioen4, Glenn A. Doherty5, Garrett Cullen1, Hugh Mulcahy1, Geert R. D’Haens1, Willem Berendel1

1 Surgery, AMC, Amsterdam, Netherlands; 2 St. Vincent’s University Hospital, Dublin, Ireland; 3 Gastroenterology, AMC, Amsterdam, Netherlands; 4 Gastroenterology, St. Vincent’s University Hospital, Dublin, Ireland

Results: In total, 30 pts (57% female) with a median age of 40 (IQR, 33 – 47) underwent appendectomy with a mean preoperative total Mayo score of 9 (SD 2). The mean baseline IBDO was 125 (SD 34). After 3 months, clinical response was seen in 16 (53%) pts of whom 7 (30%) were in remission (7 pts refused endoscopy at this time point).

THERAPY-REFRACTORY ULCERATIVE COLITIS CONTINUED...

Improvement in IBDO was seen in 14 (47%) pts with a mean of 120 (SD 29) that increased to 168 (SD 29). After 12 months, 11 pts failed (7 colectomy, 4 trial medication) and 5 did not yet reach the endpoint. In the remaining 14 pts, 9 (36%) had lasting clinical response of whom (23%) were in remission (3 pts refused endoscopy).

Conclusion: Appendectomy was effective in at least 30% of therapy refractory UC pts. These early results suggest that UC pts may benefit from appendectomy and that this effect is maintained for a longer period of time. However, follow up of at least 2 years is warranted to exclude a possible placebo effect.

THERAPY RELATED ADVERSE EVENTS

DDW 2016. SA1900. Flat Low Grade Dysplasia in Inflammatory Bowel Disease

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Results: Forty-seven IBD pts with a confirmed diagnosis of fLGD were identified. Twenty-five were male. The median (IQR) disease duration at index colonoscopy was 16.6 (8-26) years with a median time from previous colonoscopy of 1 (1-3) year. Thirty-one pts had dysplasia on more than one occasion. Twelve (26%) progressed to advanced neoplasia (10 high grade dysplasia (HGD), 2 cancers). The mean time from diagnosis of LGD to progression was 1.2 years. Twenty-seven pts (57%) ultimately had surgery. The median (IQR) time from diagnosis of LGD to colectomy was 1 (0.4-2.3) year. Six had surgery for surveillance-detected HGD or cancer and the diagnosis was confirmed at colectomy in all six. The remaining 21 underwent colectomy for LGD (persistent LGD in 13, isolated LGD in 8). One had cancer, 5 HGD, 11 LGD and 4 no dysplasia. Of the 8 who underwent colectomy for isolated LGD, one had HGD, 3 no dysplasia and 4 LGD. Twenty subjects continued surveillance. Twelve had no further evidence of dysplasia on surveillance and none progressed to either HGD or cancer at the time of follow up. The median (IQR) follow up in this group was 5.4 (4.1-8.2) years and the median (IQR) number of surveillance colonoscopies in this group was 4 (4-6.8).

Conclusions: These data highlight the heterogeneity of dysplasia in the setting of IBD. 26% of the pts progressed to advanced neoplasia a mean of 1.2 years after diagnosis of LGD, but only half of these were detected on surveillance with the remaining cases incidentally diagnosed at colectomy. Clinicians must remain cautious when adopting a surveillance strategy for dysplasia in IBD.
What follows is an overview of the presentation made by Dr. Alain Bitton at the recent CARE at DDW education meeting, and is augmented with abstract content from DDW 2016 and additional perspectives from the CARE Gastroenterology Faculty.

**MONITORING DISEASE ACTIVITY**

**DDW 2016. SU1800.** Fecal Immunochemical Testing and Fecal Calprotectin Predict Mucosal Healing in Inflammatory Bowel Disease: A Prospect Study

Christopher Ma, Rowan Lumb, Rae Fothaught, Thuc Nhi T. Dang, Sanam Verma, Vivian Huang, Karen Kroeker, Karen Wong, Levinus A. Dieleman, Brendan P. Halloran, Richard N. Fedorak

1 University of Alberta, Edmonton, Alberta, Canada

Results: Eighty patients (40 CD, 40 UC) were enrolled. Disease extent was predominantly ileal in CD (50%) and pancolonic in UC (60%). Twenty-three patients (28.8%) were on biologic therapy and 50 patients (62.5%) had endoscopic MH. FCP <150ug/g had a sensitivity of 0.97 for detection of MH and an area under the curve (AUC) of 0.75 [95% CI: 0.63–0.86]. In comparison, FIT <50ng/mL was less sensitive (0.70) but more specific for MH (AUC 0.79 [95% CI: 0.69–0.90]). When used in additive combination (FCP+FIT), performance characteristics were modestly improve. Combined FCP+FIT score <375 had a sensitivity of 0.80 and specificity of 0.69 for MH. FIT testing was more sensitive for predicting MH in UC compared to CD.

Conclusions: FCP and FIT are highly sensitive non-invasive methods for predicting MH in IBD patients. They may be used to rule out active disease as an alternative to endoscopic evaluation, especially in UC.

**CARE FACULTY PERSPECTIVE:** Endoscopic assessments are costly and invasive. Fecal immunochemical testing & fecal calprotectin can offer patients alternative methods for predicting MH that are less costly, less-invasive, and are equally effective.

**THIOPURINES**

**DDW 2016. ABSTRACT 853.** The TOPPIC Trial: A Randomized, Double-Blind Parallel Group Trial of Mercaptopurine vs Placebo to Prevent Recurrence of Crohn’s Disease Following Surgical Resection in 240 Patients

Ian Arnott, Craig Mowat, Holly Ennis, Catriona Keerie, Steff Lewis, Nicholas Kennedy, Aidan Cahill, Allan J. Morris, Malcolm Dunlop, Stuart Bloom, James D. Lindsay, Sreedhar Subramaniam, Jack Satsangi

1 Edinburgh Clinical Trials Unit, University of Edinburgh, Edinburgh, UK, United Kingdom; 2 Gastroenterology, NHS Lothian, Edinburgh, United Kingdom; 3 Gastroenterology, NHS Tayside, Dundee, United Kingdom; 4 Gastroenterology, NHS Greater Glasgow and Clyde, Glasgow, United Kingdom; 5 Gastroenterology, Royal Liverpool University Hospital, Liverpool, United Kingdom; 6 Gastroenterology, Barts Health NHS Trust, London, United Kingdom; 7 Gastroenterology, University College Hospital NHS Trust, London, United Kingdom

Results: Kaplan-Meier survival analysis of time to primary endpoint in mercaptopurine and placebo groups

Conclusions: TOPPIC is the largest, double-blind trial of thiopurines to prevent post-operative recurrence in CD. MP modestly reduces the frequency of clinical post-operative recurrence of CD. This was significant amongst smokers, but not in non-smokers. Adverse events did not differ between groups.
5-ASA THERAPY

DDW 2016. MO1318. Direct Comparison of In Vivo Drug Release Profiles of Three Locally-Acting Drug Products of Mesalamine in the Gastrointestinal Tract and Correlation With Systemic Exposure and Fecal Concentrations in Healthy Humans

Ann F. Fionatto, Alex Yu, Jason Baker, Kristen Colling, Bo Werl, Ying Wang, Ruejuan Lu, Siwei Li, Barry Bleise, Mark Johnston, Mark Koenigsknecht, William L. Hasler, Duxin Sun

Results: Fecal 5-ASA and Ac-5-ASA Levels After Ingestion of 3 Oral Mesalamine Preparations

Conclusions: Three locally-acting mesalamine formulations designed to delay and sustain release to maximize drug exposure to the intestine were studied. Using novel GI aspiration catheters, we showed highly variable release of 5-ASA and its metabolite at all sites from the stomach to the small bowel. Comparable fecal levels of the metabolite were noted, suggesting similar release and dissolution in the colon. These innovative in vivo methods may help in development and validation of bioequivalence standards for locally-acting modified-release products specifically designed to release active pharmaceutical ingredients to target inflammatory bowel disease in different regions of the small bowel and colon.

CARE FACULTY PERSPECTIVE: 5-ASA therapies are used for patients with mild-to-moderate ulcerative colitis and Crohn’s disease. This study compared three different mesalamine preparations, LIALDA, PENTASA, and APRISO.

- LIALDA* (mesalamine) are delayed release tablets. Patients should be given two to four 1.2 g tablets once daily with food for induction therapy, and two 1.2 g tablets once daily with food for maintenance therapy.
- PENTASA* (mesalamine) extended-release tablets should be taken four times daily (2 g daily dose), with an increased dose to 1g four times daily if needed (4g daily dose).
- APRISO* (mesalamine) are delayed—and extended—release delivery tablets taken once-daily (1.5g/day) in the morning, for maintenance of remission for patients with UC.

While these agents are similar, there are differences in accessibility, convenience, and overall offering. Several 5-ASA therapies offer a patient service program that helps patients who have limited financial resources, and provides patients and caregivers with access and support.

OPTIMIZING ANTI-TNF THERAPY

DDW 2016. MO1899. Evaluation and Long-Term Benefit of Deep Remission in Crohn’s Disease Patients Treated With Infliximab

Guillaume Pineton de chambrun, Louise Libier, Michael Collins, Maria Nachury, Corinne Gouer-Rousseau, Philippe Zerbib, Antoine Cortot, Jean-Frederic Colombel, Pierre Desreumaux, Pierre Blanc

Results: In our center, 153 CD patients received IFX between 2007 and 2010 with a median time between diagnosis and IFX introduction of 62 months (Q1-Q3: 18-152). The mean follow-up duration after IFX introduction was 42±22 months. Sixty-seven patients (44%) had a clinical evaluation 3 to 6 months after IFX start and a follow-up colonoscopy within a mean delay of 25±17 months. In these patients, the rate of deep remission was 30% (20/67). Demographic and clinical characteristics before IFX introduction were similar between CD patients with or without deep remission. More patients with deep remission received azathioprine concomitantly with IFX compared to patients without deep remission (65% vs. 28%, p=0.004). Looking for long-term CD outcomes, patients with deep remission had fewer hospitalizations (10% vs. 36%, Log-rank p=0.041) and fewer therapeutic modifications (20% vs. 51%, Log-rank p=0.028) compared to patients without deep remission. During follow-up, no patient with deep remission underwent CD related intestinal resection (0% vs. 17%, Log-rank p=0.049), stopped IFX for loss of response (0% vs. 21%, Log-rank p=0.041) or switched to another anti-TNFα (0% vs. 17%, Log-rank p=0.07).

Conclusions: In our cohort, deep remission was achieved in a third of CD patients treated with IFX as maintenance therapy and was associated with less hospitalization, surgery, treatment modification and discontinuation of IFX during follow-up. Results of this study suggested that deep remission should be considered as an important therapeutic goal for CD patients treated with IFX.

"THESE INNOVATIVE IN VIVO METHODS MAY HELP IN DEVELOPMENT AND VALIDATION OF BIOEQUIVALENCE STANDARDS FOR LOCALLY-ACTING MODIFIED-RELEASE PRODUCTS SPECIFICALLY DESIGNED TO RELEASE ACTIVE PHARMACEUTICAL INGREDIENTS TO TARGET INFLAMMATORY BOWEL DISEASE."
DDW 2016. ABSTRACT 692: Drug-Level Based Dosing Versus Symptom-Based Dose Adaptation in Patients With Crohn’s Disease: A Prospective, Randomized Multicenter Study (TAILORIX)

Geert R. D’Haens1, Severine Vermeire1, Guy Lambrechts1, Filip J. Baert2, Peter Bossuyt2, Maria Nachury3, Anthony Buusson4, Yoram Boubnik5, Jerome Filipi6, Christien Janneke Van Der Woude1, Philippe Van Hoeckegem1, Jacques Moreau7, Edouard Louis8, Denis Franchimond9, Martine De vos10, Faiza Mana11, Laurent Peyrin-Biroulet12, Mèdia Brix13, Matthieu Allez14, Philip Caenepeel15, Alexandre Aubourg16, Bas Oldenburg17, Marie Pierik18, Sylvie Chevreul19, Ann Gils20, David Labane21
1Academic Medical Center, Amsterdam, Netherlands; 2Erasmus Medical Centre, Rotterdam, Netherlands; 3Hospital St Lucas, Brugge, Belgium; 4Hospital Rangueil, Toulouse, France; 5Hospital Saint-Tilman, Liege, Belgium; 6Hospital Enarme, Bruxelles, Belgium; 7University Hospital, Gent, Belgium; 8University Hospital, Brussels, Belgium; 9Hospital Brabois, Nancy, France; 10Hospital Robert Debre, Reims, France; 11Hospital Saint-Louis, Paris, France; 12University Hospital, Leuven, Belgium; 13Hospital St Jans, Genk, Belgium; 14Hospital Trousseau, Tours, France; 15University Medical Center, Utrecht, Netherlands; 16University Medical Center, Maastricht, Netherlands; 17Biostatistics Department, Hospital Saint-Louis, Paris, France; 18Hospital Haut-Leveau, Bordeaux, France; 19Hospital Damiata, Oostende, Belgium; 20Hospital Heilig Hart, Roeselare, Belgium; 21Hospital Imelda, Bonheiden, Belgium; 22Hospital Claude Huriez, Lille, France; 23Hospital Estang, Clermont-Ferrand, France; 24Hospital Beaujon, Clichy, France; 25Hospital Archet, Nice, France

Results: 167 patients were screened at 27 sites and 122 were randomized (71 F, median age 29.8 years). All three arms had comparable patient characteristics. The primary endpoint based on local endoscopy reads was attained in 21/45 (47%) in group 1, 14/37 (38%) in group 2 and 16/40 (40%) in group 3 (p=NS); proportion of patients without ulcerations at week 54 were 36%, 43% and 48%; p=NS) and with endoscopic remission (CDEIS<3) 49%, 51% and 45% (p=NS); dose intensification was done in 51%, 65% and 40% of the patients.

Conclusions: In this prospective randomized exploratory trial in patients with active CD, proactive trough-level based dose intensification was not superior to dose intensification based on symptoms alone. Results with centrally read endoscopy are being awaited as well as detailed pharmacokinetic, immunogenicity and biomarker analysis.

CARE FACULTY PERSPECTIVE: Recent research has suggested that therapeutic drug monitoring (TDM) could offer a rationale to dose optimization which could decrease cost and antibody formulation.

"RESULTS INDICATE THAT DOSE INTENSIFICATION BASED ON PROACTIVE TROUGH-LEVEL WAS NO BETTER THAN DOSING BASED ON SYMPTOMS ALONE."

This study looked prospectively at TDM to determine whether it would lead to higher remission rates compared with symptom-based dose adjustments. Results indicate that dose intensification based on proactive trough-level was no better than dosing based on symptoms alone. More research/data is awaited to provide further insight.

DDW 2016. MO1784: Long-Term Efficacy and Safety of Adalimumab in Paediatric Patients With Crohn’s Disease

William Faubion1, Maria Dubinsky2, Frank Ruemmele1, Johannha Eisch3, Joel R. Rosh4, Jeffrey S. Hyams2, Samantha Eichner5, Yao Li6, Nathaniel Reilly6, Anne M. Robinson7, Andreas Lazzer8
1Mayo Clinic, Rochester, Minnesota, United States; 2Icahn School of Medicine at Mount Sinai, New York, New York, United States; 3Hospital Becker-Enfants Malade, Universite Sorbonne Paris-Cite, Paris, France; 4Erasmus MC-Sophia Children’s Hospital, Rotterdam, Netherlands; 5Gayeb Children’s Hospital/Atlantic Health, Monroeville, New Jersey, United States; 6Connecticut Children's Medical Center, Hartford, Connecticut, United States; 7AbbVie Inc., North Chicago, Illinois, United States; 8AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany

Results: As of 31 January 2015, cumulative exposure to ADA was 498 patient-years in the 192 patients enrolled in IMAgINE 1, and 27% (N=52) of patients had at least 5 years of exposure during IMAgINE 1 and 2. Of 100 patients enrolled in IMAgINE 2, two-thirds of patients entered IMAgINE 2 in clinical remission and 95% entered with response. Remission/response rates remained high through wk 240 of IMAgINE 2 (Table). Similar remission rates were achieved by IFX-naïve and -experienced patients. Mean PCDAI decreased from 40 at IMAgINE 1 baseline (BL) to 10 at IMAgINE 2 BL, and remained low (7) through wk 288 of IMAgINE 2. There were no new safety signals with prolonged ADA use, no malignancy and no death occurred, and rates of serious AEs and infections were lower or consistent with the lead-in study.

Table. PCDAI clinical remission and response rates in IMAgINE 2

| Week | 0 | 6 | 18 | 28 | 36 | 48 | 60 | 72 | 90 | 108 | 120 | 132 | 144 | 156 | 168 | 180 | 240 |
|------|---|---|----|----|----|----|----|----|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| PCDAI | 53.9 | 46.7 | 69.8 | 56.0 | 70.1 | 65.0 | 70.3 | 64.5 | 70.9 | 65.5 | 71.0 | 66.1 | 71.6 | 66.6 | 71.7 | 66.8 | 71.9 |
| PCDAI | 53.9 | 46.7 | 69.8 | 56.0 | 70.1 | 65.0 | 70.3 | 64.5 | 70.9 | 65.5 | 71.0 | 66.1 | 71.6 | 66.6 | 71.7 | 66.8 | 71.9 |
| PCDAI | 53.9 | 46.7 | 69.8 | 56.0 | 70.1 | 65.0 | 70.3 | 64.5 | 70.9 | 65.5 | 71.0 | 66.1 | 71.6 | 66.6 | 71.7 | 66.8 | 71.9 |
| PCDAI | 53.9 | 46.7 | 69.8 | 56.0 | 70.1 | 65.0 | 70.3 | 64.5 | 70.9 | 65.5 | 71.0 | 66.1 | 71.6 | 66.6 | 71.7 | 66.8 | 71.9 |

Note: Data are reported through week 240 which was the latest time point completed by all ongoing patients in IMAgINE 2.

PCDAI clinical response, PCDAI ≤ 15 points from IMAgINE 1 baseline

Conclusions. In the IMAgINE 2 extension trial, prolonged ADA treatment beyond 5 years in children with CD demonstrated high remission and response rates and a safety profile that was consistent with IMAgINE 1 and previous reports.

CARE FACULTY PERSPECTIVE: Pediatric CD is a chronic disease affecting up to 200,000 children worldwide, and can pose a significant psycho-social burden in younger patients. This can in turn, affect the quality of life of both the patient and their caregivers. The Phase 3 IMAgINE-1 trial showed significant improvements in select measures of health-related quality of life at 12 weeks, and further analysis showed that pediatric patients continued to experience QoL improvements at 52 weeks. The IMAgINE 2 study reported from week 52 to 4 years, and concluded that treatment with adalimumab helped pediatric patients reach high remission and response rates. Adalimumab has the ability to help treat patients who are suffering from CD at such a young age, and improve lives of both patients and caregivers by reducing the psycho-social burden.
NOVEL THERAPIES

**DDW 2016. ABSTRACT 439.** The PROSIT-BIO Cohort of the IG-IBD: A Prospective Observational Study of Patients With Inflammatory Bowel Disease Treated With Infliximab Biosimilars

Gianata Fiorina, Natalia Manetić, Angela Vanoš, Fabrizio Bosca, Giulia Rizutto, Alessandra Aimuzza, Alessandra Massari, Silvia Ghione, Laura Cantoro, Greta Lorenzo, Walter Fries, Maria Laura Annunziata, Francesco Costar, Maria M. Terpen, Maria Beatrice Principi, Claudio C. Cortezz0, Lia Bioncone, Armando Amapolo, Pietro Ochelutin, Silvia Mazzioli, Sandra Aridzzone, Maria Di Giolamapi, Patrizia Avioli, Giannicole Meuccii, Luigi Caserta, Simon Sabeni, Carlo Petruzelli, Anna Ronchetti, Fabiana Castiglioni, Silvia Danesi, Anna Massella, Donana Fanara, Ambrogio Orlando, Vito Airena, IBD Unit, Universitati, Rozzano, Milan, Italy; 2Gastroenterology, University of Padua, Padua, Italy; 3Clinical and Experimental Medicine, University of Messina, Messina, Italy; 4Gastroenterology, IRCCS S. Donato Milanese, San Donato, Milan, Italy; 5Gastroenterology, AOUP, Pisa, Italy; 6Gastroenterology, AO Legnami, Legnami, Italy; 7Gastroenterology, University Bari, Bari, Italy; 8Gastroenterology, AO di Enrico Foradamez, Vanese, Rome, Italy; 9Gastroenterology, Tor Vergata University, Rome, Italy; 10Gastroenterology, Valduce Hospital, Como, Italy; 11Gastroenterology, ADU Maggiorie Hospital, Novara, Italy; 2 DEA - Gastroenterology, ADU Careggi, Florence, Italy; 12Gastroenterology, S. Pellegrino Hospital, Tri, Italy; 13Gastroenterology, Fatebenefratelli Ospital, Milan, Italy; 14Gastroenterology, University of Modena, Modena, Italy; 15Pediatric, Maggiorie Hospital, Bologna, Italy; 16Gastroenterology, S. Giuseppe Hospital, Milan, Italy; 17Gastroenterology, S. Martino Hospital, Genoa, Italy; 18Gastroenterology, Savini Hospital, Rho, Italy; 19Gastroenterology, Poliambulanza Foundation, Brescia, Italy; 20Internal Medicine, AO Hospital, Lecco, Italy; 21Gastroenterology Sección, DiBiMis University of Palermo, Palermo, Italy; 22Gastroenterology, Sacro Cuore Hospital, Negrar Verona, Italy; 23Gastroenterology, Federico II University, Naples, Italy; 24On behalf of Italian Group for the Study of IBD, IO-IBD, Italy; 25Gastroenterology, IRCCS-CSS Hospital, S. Giovanni R, Italy; 26Internal Medicine, Villa Sofia Cervello Hospital, Palermo, Italy; 27Internal Medicine and Gastroenterology, Columbus-Catholic University, Rome, Italy; 28Gastroenterology and IBD Unit, University Hospital Sacco, Milan, Italy; 29Gastroenterology and Nutrition, Meyer Children’s Hospital, Florence, Italy; 30Gastroenterology, S. Camillo-Forlanini Hospital, Rome, Italy.

**Results:** Summary of data of efficacy of CT-P13

Conclusions: No clear signal of difference in safety was reported, however, a 5-fold increase of loss of response after the switch (12.2% vs 2.3%, p=0.001), and a trend towards more frequent primary failure and loss of response in UC compared to CD patients (11.3% vs 5.8%, 7.7% vs 2.6%, respectively; P=0.06) was recorded. These findings should be evaluated with caution due to the short follow-up.

**CARE FACULTY PERSPECTIVE.** It is no argument that biologics have revolutionized the treatment of chronic inflammatory conditions. In the last few years, biosimilars have been developed. They are monoclonal antibodies that are similar but not identical to the reference biologic drug. Biosimilars have not yet been approved in Canada in the field of gastroenterology, but we should expect it shortly.

This study tells us that patients who are already stable on a biologic, should likely not switch to a biosimilar given the 12% loss of response that can occur. Additionally, the overall patient population with UC experienced a high rate of primary failure (11%) and loss of response (8%). Biosimilars should be used with caution in these patient populations.

**DDW 2016. ABSTRACT 708.** A Phase 3 Randomized, Multicenter, Double-Blind, Placebo-Controlled Study of Ustekinumab Maintenance Therapy in Moderate-Severe Crohn’s Disease Patients: Results From IM-UNITI


**Results:** Maintenance of Clinical Response and Remission in IM-UNITI at Week 44

<table>
<thead>
<tr>
<th></th>
<th>Placebo† N=131†</th>
<th>90 mg ustekinumab every 12 weeks N=128†</th>
<th>90 mg ustekinumab every 8 weeks N=130†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Remission</strong></td>
<td>35.9%</td>
<td>44.8%</td>
<td>55.1%</td>
</tr>
<tr>
<td><strong>Clinical Response</strong></td>
<td>44.3%</td>
<td>58.1%</td>
<td>59.4%</td>
</tr>
<tr>
<td><strong>Corticosteroid-Free Clinical Remission</strong></td>
<td>29.8%</td>
<td>42.6%</td>
<td>46.9%</td>
</tr>
<tr>
<td><strong>Sustained Clinical Remission</strong></td>
<td>26.0%</td>
<td>40.3%</td>
<td>46.1%</td>
</tr>
<tr>
<td><strong>Clinical Remission in patients with loss of clinical remission at start of maintenance therapy</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Who are TNF antagonist refractory/intolerant</strong></td>
<td>26.2%</td>
<td>38.6%</td>
<td>41.1%</td>
</tr>
<tr>
<td><strong>Who failed conventional therapy</strong></td>
<td>44.2%</td>
<td>56.3%</td>
<td>62.5%</td>
</tr>
<tr>
<td><strong>Who are TNF antagonist naive</strong></td>
<td>49.0%</td>
<td>56.6%</td>
<td>65.4%</td>
</tr>
</tbody>
</table>

Clinical remission is defined as CDAI score < 150. Clinical response is defined as reduction in CDAI of at least 100 points or being in clinical remission. The PBO group consisted of patients who were in response to a single dose of UST IV induction and were randomized to receive PBO at week 0 of maintenance. Patients who achieved 100 point clinical response to UST at start of maintenance therapy 1. Defined as clinical remission at Week 36, 40 and 44. Ap < 0.01, bp < 0.05, cp < 0.005, dp = NS nominally significant.

Conclusions: UST 90 mg q8w and q12w maintained clinical response and remission among patients with moderate-to-severe CD induced into clinical response with IV UST, with a favorable safety profile through week 44. The q8w regimen more consistently demonstrated efficacy than the q12w regimen across the range of endpoints.

**CARE FACULTY PERSPECTIVE:** Ustekinumab has demonstrated efficacy in patients with Crohn’s Disease who have failed conventional therapy and failed anti-TNF therapy (UNITI I&II). This study assessed ustekinumab in the maintenance setting. The safety and efficacy of three different groups were evaluated: 1) placebo, 2) ustekinumab (90mg/8 weeks) and 3) ustekinumab (90mg/12 weeks). These results were highly anticipated, and showed significant rates of clinical response and remission at 44 weeks in patients treated with ustekinumab at 8 weeks and 12 weeks over placebo. These data are very promising, and we await further insights into ustekinumab’s impact on endoscopic healing, and immunogenicity. In the near future, we expect ustekinumab to be approved by Health Canada as a maintenance therapy for patients with CD.
**DDW 2016. MO1879: Response and Remission Rates With Up to 3 Years of Vedolizumab Treatment in Patients With Crohn’s Disease**

Severine Vermeire1, Brian G. Feagan2, Reema Mody3, Alessandra Previtali4, Brihad Abhyankar4

1University Hospital Gasthuisberg, Leuven, Belgium; 2Robarts Clinical Trials, Robarts Research Institute, University of Western Ontario, London, Ontario, Canada; 3Takeda Development Center Americas, Inc, Deerfield, Illinois, United States; 4Takeda Development Centre Europe Ltd, London, United Kingdom

**Results:** GEMINI LTS enrolled 1349 patients with Crohn’s disease; 145 had week 6 response and completed 52 weeks of vedolizumab treatment in GEMINI 2; at the time of this interim data cut, 70 of 145 had completed an additional 100 weeks of vedolizumab in GEMINI LTS (152 weeks cumulative) and 10 had discontinued because of lack of efficacy. After 152 weeks of treatment, 39% and 46% of patients from the Q8W/Q4W and Q4W/Q4W populations, respectively, were in remission (Harvey-Bradshaw Index score ≤4) with a mean change from baseline C-reactive protein concentration of -12.8 and -7.7 mg/L, respectively. When analyzed by prior tumor necrosis factor α antagonist treatment history, 62% and 45% of patients with prior failure (from the Q8W/Q4W and Q4W/Q4W populations, respectively) and 23% and 48% of patients, respectively, who were tumor necrosis factor α antagonist naive were in remission. Among all patients, health-related quality of life improvements were reported. Of all enrolled patients with Crohn’s disease, 329 (25%) reported anal fistula history; at interim analysis, 82 (6%) had experienced anal fistula as an adverse event.

**Conclusions:** Patients with moderately to severely active Crohn’s disease receiving vedolizumab during GEMINI 2 and GEMINI LTS (up to 3 years total) experienced long-term clinical benefits.

**CARE FACULTY PERSPECTIVE:** On May 19, 2016, Health Canada approved vedolizumab for the treatment of adults with moderate to severely active CD. This is positive to see, as vedolizumab can offer a new option for patients who don’t respond to or have failed on other treatments. This study confirms that patients can expect long-term clinical benefits when taking vedolizumab.

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**DDW 2016. ABSTRACT 855. Efficacy and Safety of Tofacitinib for Oral Induction Therapy in Patients With Moderate to Severe Crohn’s Disease: Results of a Phase 2B Randomized Placebo-Controlled Trial**


1Academic Medical Centre, University of Amsterdam, Amsterdam, Netherlands; 2University of Calgary, Calgary, Alberta, Canada; 3University of Michigan, Ann Arbor, Michigan, United States; 4Robarts Research Institute, London, Ontario, Canada; 5Pfizer Inc, Collegeville, Pennsylvania, United States

**Results:** 180 patients were randomized, of which 128 had received tofacitinib in the induction study. The proportions of patients with clinical response-100 or remission at Week 26 were 39.5% for tofacitinib 5 mg BID, 31.8% for placebo, and numerically higher with 10 mg BID (55.8%). At Week 26, the change from maintenance baseline was significant (p<0.0001) for CRP and FCP with 10 mg BID and significant for FCP (p<0.05) with 5 mg BID, compared with placebo. There were 2 cases of non-serious herpes zoster with 10 mg BID, 1 intestinal perforation with 5 mg BID and no deaths or malignancies. The proportions of adverse events (AEs) were similar across all groups. The most common AEs were in the gastrointestinal disorders and infections System Organ Classes, with higher observed rates of the latter with both tofacitinib doses than placebo.

**Conclusions:** After 26 weeks of maintenance therapy, clinical response-100 or remission was observed in a higher proportion of patients receiving tofacitinib than placebo, though the difference was not statistically significant. Biomarkers supported a treatment effect with tofacitinib 10 mg BID. Tofacitinib appeared to be well-tolerated.

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**THE IMPORTANCE OF PATIENT SUPPORT IN IBD**

- Travel coordination
- Infusion clinics
- Local pharmacy services and home delivery for injection medications
- Patient materials
- Patient associated links
- Disease specific education
- Secure reimbursement and appeals
- Co-pay assistance
- Bridging medication to public reimbursement group
- 1:1 contact with patient and physician
- Management of renewals (insurance, prescriptions, medical orders)
- Co-pay
- Delivery of drug
- Schedule appointments
- 24/7 helpline
- Injection support kits and training
- Patient co-ordination
- Reimbursement to public

Inflammatory bowel disease is a chronic, life-long condition. With the number of developments in the field of IBD, it is important that patients as well as their families are not only provided with the best treatment options but also the most valuable/accessible treatment regimen/plan. This will help relieve symptoms, and improve their overall quality of life. Some treatments are now including patient support programs to provide patients with access, management tools, education, and even funding, to achieve the care they need.

Patient support programs have been developed to provide a customized and responsive support system tailored to each patients needs. These programs are committed to helping patients get access to treatment as quickly as possible. Additionally, they provide ongoing communications to update healthcare teams, education and helpful tools to manage symptoms.
What follows is an overview of the presentation made by Dr. David Wong at the recent CARE at DDW education meeting, and is augmented with additional abstracts from DDW 2016 and perspectives from the CARE Gastroenterology Faculty.

HEPATITIS C

The integration of effective, curable, antiviral therapies into HCV clinical practice is expected to eventually lead to the disappearance of liver failure and transplant, and the stabilization or decrease in the rates of liver cancer. While many patients have already received these agents, there are still considerations that need to be addressed to optimize survival and patient outcomes. Firstly, with the majority of the therapies being all oral regimens, patient adherence is a concern as it may impact (increase) the incidence of treatment failure. Another consideration that needs to be addressed is delivery of care, and the need to move from hepatologists being the only providers of HCV care to having increased involvement from our gastroenterology, infectious disease, and primary care counterparts. This will be imperative in order to accommodate the sheer number of patients that are in need of therapy. Lastly, the high cost of therapy is another major concern and needs to decrease in order to improve access for all patients.

Beyond 2020, increased screening and using treatment as prevention are anticipated to be the focus of HCV research and care.

DDW 2016. 754. Clinical Benefits of Successful Treatment in HCV Infected Patients With Decompensated Cirrhosis Treated With Sofosbuvir/Velpatasvir (Sof/VEL)

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Results: Of the 267 patients randomized and treated, the majority were male (70%), white (90%), IL28B non-CC (76%) and treatment experienced (55%). The median CPT score was 8 (range 5-10) and median MELD score of 10 (range 6-24). The overall SVR12 rates by treatment regimen were 83% (SOF/VEL 12 weeks), 94% (SOF/VEL + RBV 12 weeks) and 86% (SOF/VEL 24 weeks). Of the 234 subjects who achieved SVR12, 47% had an improvement in CPT score (range: 1−5 points) while 43% had no change from baseline to post-treatment Week 12. Decreases in CPT score were primarily due to improvements in albumin (68%) and bilirubin (36%). Among patients who had a MELD score ≥15 at baseline and achieved SVR12, 84% had an improvement in MELD (range 1-11 points) while 62% improved to MELD <15. In patients with baseline MELD score <15, 52% had an improvement (range 1-7 points). Improvements in MELD score were largely due to decreases in total bilirubin. An exploratory analysis of baseline predictors of changes in MELD scores in patients who achieved SVR12 is shown in Table 1. Patients without clinical manifestations of portal hypertension (no vs. severe ascites, 56% vs. 17%), shunting (grade 0 vs grade 1-2 hepatic encephalopathy, 71% vs. 46%), and lower BMI (<30 vs. ≥30, 60% vs 49%) had a greater proportion with MELD score improvement. Clinical and laboratory changes at post-treatment week 24 will be presented.

Conclusions: Treatment with SOF/VEL regimens had high efficacy rates in patients with decompensated cirrhosis. Patients who achieved SVR12 had a higher probability of clinical improvement if they had a higher MELD score, lower (<30) BMI or the absence of ascites and encephalopathy at the time of enrollment.
HEPATITIS B

Recent advances in Hepatitis B research have currently made it one of the most exciting topics within the field of hepatology. One of the most important of these advances is that we now have the ability to grow HBV in a test tube, allowing researchers to more effectively develop new therapies. There are now several potential cures currently in early phase trials. We have a lot to look forward to over the next few years as we see this data mature.

DDW 2016, TU1667, RNA-Seq Analysis of Innate Immune Response in Hepatitis B

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Results: (1) In IFNα-treated PBMCs, 159 genes were up-regulated, among which previously reported 60 ISGs were included and 100 genes were detected by DNA microarray analysis. (2) Serial gene expression profiling of PBMCs from hepatitis B patient clearly demonstrated up-regulation of ISGs during IFN therapy. Importantly, PBMCs at the peak of disease flare (day 2 sample) showed up-regulation of several ISGs compared with those harvested after clinical recovery (day 72 sample). Since the former time point was before the start of IFN administration and the latter one was 30 days after the cessation of the therapy, this result suggested the endogenous type I IFN response at the active phase of hepatitis B. (3) In contrast to IFNα-treated HepG2-hNTCP cells where 22 out of top 40 up-regulated genes were ISGs, only one ISG was included among top 40 up-regulated genes in HBV-infected HepG2-hNTCP cells, indicating that only marginal type I interferon response was induced by HBV-infected cells.

Conclusions: RNA-seq was useful for the transcriptome analysis of innate immune response in hepatitis B. Our results suggested that HBV infection induces type I interferon response in blood immune cells but only marginally in HBV-infected hepatocytes. The identification of cell types that recognize HBV and the elucidation of their recognition mechanism are warranted in the future study.
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