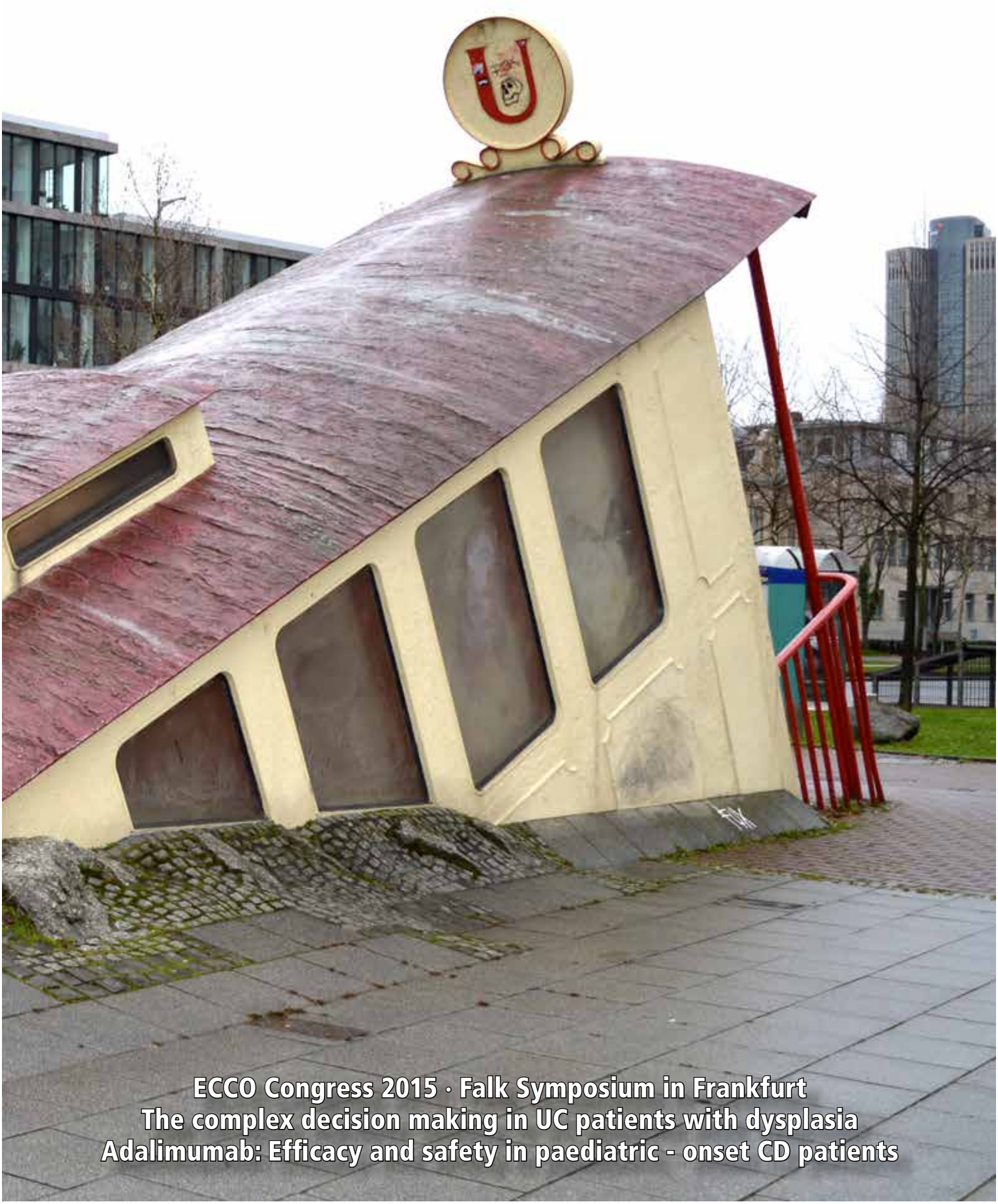
iBD CONGRESS NEWS #1/15

FRANCE

The magazine that covers major international congresses and symposia focusing on inflammatory bowel disease (IBD)



ECCO Congress 2015 · Falk Symposium in Frankfurt
The complex decision making in UC patients with dysplasia
Adalimumab: Efficacy and safety in paediatric - onset CD patients

Sender: Mediahuset i Göteborg AB, Marieholmsgatan 10C, SE-415 02 Göteborg, Sweden

IBD CONGRESS NEWS

IBD Congress News is a publication with three issues per year.
The magazine is distributed free of charge to all specialists in the field of Gastroenterology, GI Surgery and Endoscopy in 14 European countries including Austria, Belgium, Denmark, Finland, France, Germany, Ireland, Italy, Norway, Spain, Sweden, Switzerland, the Netherlands, and the UK.
The content of the magazine is in English and will include reports from the largest congresses and symposia held in Europe and the US, including UEGW, ECCO Congress, DDW and many more. It will also cover the major Industry Symposia held in Europe and include features and interviews with Gastroenterologists from Europe and America.

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Advertising:
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As a result of placing an advertisement within this magazine you will reach every specialist in the field of Gastroenterology in these countries.
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Production:
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Marieholmsgatan 10C
SE-415 02 Göteborg, Sweden
www.mediahuset.se

Layout:
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Printing:
ÅkessonBerg, Emmaboda, Sweden
ISSN: 2001 – 399X

Cover photo:
Bus stop in Frankfurt. Photo: Fotolia

Content:

EDITORIAL
TOM ØRESLAND

WHAT IS IT ABOUT – DOCTORS AND RESEARCH?

Do doctors need to engage in research and if the answer is yes why should they do so?

From my point of view the answer is a very loud yes. We are working in a profession that is extremely knowledge based. Everything we do and decide upon is based on some kind of knowledge of the human body and mind. To understand the body of truths or facts one has to understand how our knowledge base is created. Most of our activities in medicine are in fact empirical, some derived from ancient times. A doctor is faced with a problem and then starts thinking on how to solve it. After some trial and error a solution comes up that seems to work in most cases and this is communicated to colleagues and most often passed on to the next generations. This is empirical knowledge and we know that often when we challenge this with well-designed studies comparing alternatives our preset minds have to reset. This in turn is a process that is not as easy achieved as one imagines. Simple well documented new facts such as the waste of using antibiotics on patients with uncomplicated diverticulitis are very hard to implement. In my mind those colleagues with a research background are much more likely to understand and implement new methods in daily care. They are also much better prepared to discard the useless methods we often adhere to in spite these methods have been shown not to stand the tests of evidence based medicine.

To have research experience will give us much better understanding of the relative importance of new often overrated research. Gastroenterologists are overwhelmed with seemingly well conducted blinded randomized controlled trials showing the superiority of new therapies. Being able to read those papers and think behind the stage so to say, to really understand what has been done and perhaps not readily accept all conclusions, is what makes doctors better. The long time perspective is not always easy to see. It's not that next years "mab" will revolutionize treatment and half of that we think is right today will prove to be wrong in the next decades. The problem being of course that we do not know which half. To have education in research makes us better prepared to relate to these things. Doctors who update themselves only on the doctors pages on the internet will at the best be popular with their patients, but they will never achieve excellence in medicine.

To read IBD Congress News is just to get the overview and the incitement to dig deeper into the facts. Hope you enjoy this issue and the easy to digest reading from the pen of Per Lundblad and others.

TOM ØRESLAND

ECCO CONGRESS 2015

The 10th ECCO Congress took place in the Spanish city Barcelona in February 19-21. Eighty two speakers and Chairs participated in 12 Scientific Sessions, and 13 Satellite Symposia were held. It is the largest annual Congress on IBD in the world.

At the Opening Ceremony, all delegates were welcomed to the city which is the capital of the Spanish region Catalonia by Dr Eugeni Domènech, the President for the Spanish IBD organisation GETECCU.

ECCO's President Prof Severine Vermeire then proudly told the participants that the Congress had once again set an all time high in attendance: 5 420 delegates from 80 countries came to Barcelona. A record number 856 of accepted abstracts were presented.

– This means that we do something you appreciate, was her conclusion.

She also said that ECCO now have 35 member countries, since Moldavia and Cyprus has joined the Organisation.

– We also have two new working groups – in histopathology and dieticians, Prof Vermeire stated.

Lifestyle factors that play a role in IBD

In the first Scientific Session, Prof Gerhard Rogler talked about the impact of lifestyle changes on disease course.

– It is very difficult to do lifestyle research – causes will impact outcome many years later, he started by saying.

It has been assessed that lifestyle and environmental factors in industrialised countries impacts 70 % of the incidence and course of IBD. The genetic susceptibility stands for 30 %, Prof Rogler continued.

He presented a summary of lifestyle factors discussed to play a role in IBD. One of these was breastfeeding.

– Meta-analyses report conflicting data on the protecting effect. If there *is* one, it may be related to the duration of breastfeeding.

Smoking is a risk factor for Crohn's disease (CD), and has a negative effect on disease course.

– It is a well established fact. But we could *not* establish this as a risk factor for surgery in the Swiss cohort!

When it comes to diet, a high intake of polyunsaturated fatty acids, saturated fats, omega-6 fatty acids and meat increases the risk of CD.

– High perceived stress and ineffective coping strategies have been linked to disease exacerbation in IBD. Sleep disturbance can lead to an increased risk of disease flares.

Quality of life is improved, and stress is reduced, in patients with CD who engage in regular low-intensity exercise, Prof Rogler also pointed out.

Pathophysiological pathways need to be identified

Another environmental factor is antibiotics. Several studies indicate that antibiotics use increases the risk for IBD.

Prof Rogler also mentioned titanium oxide. This is used in coffee whiteners, pastry, tooth paste, chewing gums and ibuprofen among other commonly used products.

– It activates the immune system via IL-1B release.

Another aspect of lifestyle is that we spend a lot of time in airplanes. High altitude journeys and flights are associated with an increased risk of flares in IBD patients.

– We think this is due to hypoxia (a con-

dition in which the body or a region of the body is deprived of adequate oxygen supply).

He summarised his lecture by underlining that many studies on environment are biased by confounders. Pathophysiological pathways need to be identified.

– "Non-classical life style factors", such as hypoxia or heat wave exposure – which data also indicate increases the risk for a flare – may play a role.

Effects may be mediated via the intestinal microbiota, or directly via innate immune mechanisms in epithelial cells, Prof Rogler also said.

He finished his lecture by underlining that further studies are most urgently needed.

The CCIB - the Barcelona International Convention Centre - is an integral part of Diagonal Mar, the newest section of Barcelona's seafront.

Environmental factors are associated with epigenetic changes

Prof Jack Satsangi talked about epigenetics and IBD. He began by explaining that the high hope of a cure – solving the riddle of IBD – via genetics not has been fulfilled so far.

Epigenetics is the study of control of gene expression through modification of DNA or chromatin proteins. So why should one study epigenetics and IBD?

– There are many reasons: Explaining the "hidden heritability" (which means there are more SNP:s truly associated with the complex trait of interest which have not been discovered yet) and proportion of variance unexplained and exploring gene-environmental interactions are two of these reasons. And also the implications for therapeutic intervention and biomarker discovery, Prof Satsangi said.

Many of the environmental factors implicated in IBD – notably smoking, nutrition and gut flora – are associated with epigenetic changes in vitro, ex vivo or in models. But *causality* of these epigenetic changes in disease is still yet to be proven.

Emerging data implicate epigenetic alterations in the pathogenesis of CD and several other immune-mediated diseases.

– These alterations may underlie key gene-environmental interactions, and contribute to the unexplained paradox of hidden heritability of diseases.

As in other common diseases, the potential for clinical translation emerges as a key focus, Prof Satsangi summarised.

Costs are higher for CD than for UC

At a Session on optimal use of resources, Dr Keith Bodger talked about the true cost of IBD care. He pointed out that in IBD it is the top 10 % of patients that account for over 50 % of all costs.

– But knowledge of the true costs of IBD care remains incomplete. Estimates of average costs vary widely, Dr Bodger continued.

CD is more costly than ulcerative colitis (UC). The COIN study from the Netherlands had found that 23 % of patients with CD were treated with anti-TNF, compared to 4 % of patients with UC.

In the pre-biologics era, inpatient costs dominated. Now there is a shift towards biologics becoming the dominant cost driver.

– The relative cost-effectiveness of rival strategies that exists in clinics is poorly understood. The impact of practice variation requires further study, Dr Bodger said.

Keith Bodger

Cost is predominantly outpatient driven in Australia

A study assessing the natural history and health care cost in a population based IBD cohort in Australia was presented by Dr Olga Niewiadomski. The aims of the study were to assess early disease progression, and the health care costs in the first year of diagnosis.

– This is the first study of its kind in Australia, Dr Niewiadomski explained.

Incidence cases of IBD were identified from 2007-2008 and 2010-2013. Details about disease state after diagnosis were prospectively assessed by 6 monthly reviews of case notes. Severity was assessed by need for hospitalization, surgery and biological use.

– We found that aggressive disease is less common than previously reported. There is a high immunomodulator and biologic prescribtion in the first year, and the risk of surgery and hospitalisation is highest in the first year, she said.

For annual healthcare costs, the study – just as Dr Bodger – found that these were greater for CD than UC.

– In both groups, cost is predominantly outpatient driven. Expenditure from inpatient services is lower than previously reported.

Dr Niewiadomski also stated that surgery costs remains high in CD in the first year – and that the use of 5-ASA is expensive in IBD.

Surgery and hospitalisation rates did not differ between East and West

The use of biological therapy and immunomodulators is increasing, but influence ➤

from this on long-term disease outcome is still unknown. Only a few population-based inception cohorts exist from the era of biological therapy and early aggressive treatment with immunomodulators.

The ECCO-EpiCom study is a European inception cohort study investigating occurrence, treatment strategies and disease course of IBD in Eastern and Western Europe. EpiCom aims to assess a possible West-East gradient in 3-years outcomes – and to investigate the impact of treatment choices on disease course.

Data from the 3-year follow-up cohort was presented by Dr Johan Burisch.

– We found earlier and more aggressive treatment with biologicals than in previous population-based cohorts. We also saw a limited use of biologicals in Eastern Europe, he said.

However, surgery and hospitalisation rates did *not* differ between regions – the rates were comparable to the pre-biological era.

– A long-term follow-up of the EpiCom cohort is in progress, Dr Burisch told the audience.

Surgical alternatives to biological therapy

Surgeon Omar Faiz pointed out that historically, surgery has been required for 80 % of patients with CD in the last 20 years.

– *When* should we intervene in IBD – and with *what*, he asked.

By using data from the TREAT registry – with nearly 20 000 patient-years of follow-up – a study on the safety of infliximab, Mr Faiz could point out that the safety of infliximab is similar to that of conventional immunomodulators.

He compared the costs of biological agents and surgery, and showed that the cost for one year treatment with infliximab was more than double as high as an ileocaecal resection.

The ideal treatment should be safe, have a high benefit, be effective in the long term and affordable, Mr Fariz continued.

– Surgery for CD is an effective treatment! A huge escalation of Quality of life-data shows this.

He presented a – in his view – *true* top down approach: One that *begins* with surgery!

– A study on early versus late surgery for ileocaecal CD found that if you operate early, the patient will have a longer remission – but not the same progression of disease. A comparison of various treatment strategies for prevention of postoperative recurrence found that infliximab came out best.

Approximately one in four patients with UC requires surgery. Indications include failed medical therapy, emergency or dysplasia/cancer.

– We know that patients are keen to avoid proctocolectomy with a stoma. But surgery achieves cure for UC.

This is however not true in CD – patients will relapse eventually.

– But the same goes for biologics! We can *help* patients with disabling disease – help them to have productive and fruitful lives, Mr Fariz summarised.

Johan Burisch

Omar Fariz

"APPROXIMATELY ONE IN FOUR PATIENTS WITH UC REQUIRES SURGERY"

Nurse's relationship with patients

One Session had the topic of delivering quality to the patients. The first Speaker was Marian O'Connor, Consultant IBD Nurse.

– We all know that IBD is an unpredictable, complex and chronic condition with symptoms which are unpleasant, embarrassing and painful. Annually the global incidence is rising, she said.

Nurse O'Connor also stressed that the majority of patients will remain capable of leading a reasonably normal life. But the individual with IBD will often require intensive, and on-going, input from health professionals.

– They rely on *us* to deliver robust care!

She continued by talking about the development of IBD nursing in UK and Europe.

– The relationship I have with the patient is different than the gastroenterologist's or the surgeon's relation. As an IBD nurse, it is my role to listen to the *patient talking about living* with the disease.

In order for patients to be involved in their care, they need to be educated. N-ECCO Statement 3D underlines the advanced IBD nurse role in providing education to patients and their relatives on individual needs, preferences and coping capability.

– The aim is to enable and empower the patient to live with IBD, Nurse O'Connor explained.

She reminded the audience of the administrative burden that biologics carry.

– The advanced IBD nurse involved in the management and delivery of biologic therapy is in a position to ensure that appropriate screening and identification of any contraindications to therapy are identified and recorded.

The IBD nurse provides an important role in care

Nurse led clinics are ideal for new diagnosis, rapid access clinics (i.e. flare clinics), drug counselling and transitional care (paediatrics to adult care).

– In the words of a patient, IBD-nurses are necessary to maintain the *balance* between doctor and the patient. Nurses are

the patient's advocate at IBD multidisciplinary meetings, the links with family doctor or General practitioner. They also ensure referral and coordination of care to other specialists – such as rheumatology, dietetics and counselling.

Nurse O'Connor summarised by underlining that the IBD nurse provides a pivotal and important role in the care of the IBD patient – which benefits the patient, the multidisciplinary team and the healthcare provider.

– The UK IBD National Audit demonstrated that IBD nurses, as part of a multidisciplinary team, can assist to reduce hospital admissions, increase the proportion of people with IBD to self-manage – and are pivotal in offering greater patient choice of care.

She ended her talk with a quote from UK Dept. of Health from 2004:

"Good chronic disease management can make a real difference, helping to prevent crisis and deterioration, and enabling people living with chronic conditions to attain the best quality of life".

Better information improves outcomes

Dr Valerie Pittet presented a national IBD cohort study performed in the centre of Europe (The Swiss IBD cohort study) in order to explore patient's information needs, sources of information and satisfaction.

– Questionnaires were sent to 1506 patients. 728 (48 %) responded, she said.

The study found that information remains insufficient for patients with IBD.

– Types and sources of information should be adapted – at least to gender, age and type of disease.

Dr Pittet said that a lack of information in specific domains could cause stress or anxiety and hinder detection of symptoms, or clinical outcomes.

– Better information should be considered as a potentially important component in improving outcomes – e.g. patients' adherence to treatment and quality of life, was her conclusion.

Positive development of endpoints not found in Germany

Prof Andreas Stallmach presented a study on patient-relevant outcomes in IBD – have changes occurred in Germany over the last 12 years?

The finding was that a positive development for the patient-relevant endpoints

– hospitalisation, rates of surgical procedures and premature mortality rates – was *not* observed between the year 2000 and 2013 in patients that suffer from IBD in Germany.

– The percentage of patients with immunosuppressive therapies seems to be significantly lower than expected – if rates of controlled studies were extrapolated, or suggestions from guidelines were consequently implemented, Prof Stallmach said.

The Session then finished with a panel debate on the topics it had covered.

The science behind biosimilars

The arrival of biosimilars to infliximab was a hot topic at the ECCO Congress 2015.

In a Session entitled *Anti-TNF: originators & biosimilars,* Prof Gonzalo Calvo talked about the science behind biosimilars. He described the process behind the development programme.

– The ultimate goal of the biosimilar clinical comparability exercise is to exclude any relevant differences between the biosimilar and the reference medicinal product. Therefore, studies should be sensitive enough with regard to design, conduct, endpoints and/or population to detect such differences, Prof Calvo summarised.

Biosimilars are not expected to re-demonstrate the benefit-risk across the whole clinical spectrum of patients – not just similarity to the reference medicinal product RMP), he continued.

– The biosimilarity exercise is based on a proper physicochemical, functional and

Marian O'Connor

pharmacokinetic and pharmacodynamic characterisation and comparability to the RMP – plus, where necessary, clinical data in the most sensitive clinical model.

Efficacy trials of biosimilars do *not* aim at demonstrating efficacy per se – since this already has been done with the reference product.

– The purpose of the efficacy trials is to confirm *comparable* clinical performance of the biosimilar and the reference product, Prof Calvo underlined.

When biosimilar comparability has been demonstrated in one indication, extrapolation of clinical data to other indications of the reference product could be acceptable, but needs to be scientifically justified.

– Rheumatoid arthritis is in fact the most sensitive model, he stated.

Different rules on substitution in EU countries

Switching (from RMP to a biosimilar) is an issue surrounded by conflict. Prof Calvo described the changes made over time when manufacturing the RMP, and that every time such changes are made the authorities want data on safety and efficacy.

– For infliximab, such changes have been made more than 30 times. Does this have consequences for switchability? I don't think so, he said.

In EU there are different rules about substitution. In France, at the start of treatment, doctors must state on the prescription "substitutable, start of treatment". Pharmacists are allowed to substitute only if the biological medicines belong to the same group and the patient is starting the treatment – and the prescriber has not excluded the substitution.

At ongoing treatment in France, doctors must state on the prescription "no-substitutable, ongoing treatment" and pharmacists are not allowed to substitute if the patient already has started the treatment with a specific medicine.

– In Spain, biologics can not be substituted at all.

Prof Calvo ended with what he underlined was *his* conclusions:

– Biosimilars can confidently be prescribed in Europe. Extrapolation is a theoretical concern, rather than a real issue.

On switchability he stated that it is possible – and perhaps desirable.

– But I would be *against* substitution not authorised and supervised by the treating physician – and agreed upon by the patient!

New drugs for IBD

In a Session on new therapies and targets Prof Brian Feagan talked about positioning the new molecules in practice.

He started this by underlining the need for new drugs. By presenting long-term data on anti-TNF and their efficacy, he could point out there is a need for alternatives.

– Optimisation of treatment has been discussed a lot at this Congress. But even with that, we *still* need more options.

Prof Feagan continued by talking about vedolizumab and described the mechanism of this drug.

– It is the first viable "out of class" monoclonal for the treatment of IBD, he said.

The problem of PML with natalizumab is unlikely to re-emerge. The systemic immunity is preserved with vedolizumab.

And there are more new drugs on the horizon. Prof Feagan presented promising data on etrolizumab from a Phase II study.

– It is now moving to Phase III. I suspect this will be a drug we will see in the clinic in the future, he said.

Promising new agents

Ustekinumab is blocking the IL12 and IL23 pathway, which has turned out to be highly effective. It has been shown to be effective for CD in a Phase II b study – and there are signals of efficacy in previous anti-TNF failures.

– If the efficacy in CD is confirmed, and there are no safety signals, this will be a very interesting drug for CD. I think it also will be good for UC.

Targeting cytokine signalling of Janus Kinease (JAK) with tofacitinib has shown very impressive data in rheumatology, and Prof Feagan said that it is now in Phase III trials for IBD.

A very new agent is Mongersen, an oral, topically active Smad7 antisense oligonucleotide. It has a modified release through pH-dependent coating to deliver Mongersen into the terminal ileum and right colon – and hence avoid systemic adsorption.

– Data presented at the UEG Week makes this an agent that has generated a lot of interest, and it is now moving to Phase III.

The precise role of these new agents in comparison to standard treatments will require experience in the clinic, safety registry data and potentially results from large scale, comparative trials, Prof Feagan summarised.

Ozanimod

Prof William Sandborn presented data from a randomised, double-blind, placebo-controlled induction trial of an oral S1P receptor modulator ozanimod in moderate to severe UC.

– It was conducted at 57 sites in 13 countries. The induction period completion rate was 95 %, Prof Sandborn said.

The primary efficacy endpoint was the proportion of patients in clinical remission at week 8, defined as a Mayo score of 2 or less with no subscore higher than 1 point.

Ozanimod induced clinical remission at week 8 in 16,4 % of patients on high dose (HD) and 13, 8 % for patients on low dose (LD) and 6,2 % for patients on placebo (PBO).

Brian Feagan

William Sandborn

The proportion of patients with clinical response was 58.2% for HD, 53.8% for LD, and 36.9% for PBO. The proportion of patients with mucosal improvement was 34.3% for HD, 27.7% for LD, and 12.3% for PBO.

The improvement in Mayo score from baseline was 3.3 points for HD, 2.6 points for LD, and 1.9 for PBO.

– A dose response relationship was observed for all primary and key secondary efficacy endpoints. Ozanimod was well tolerated with a favourable benefit-risk profile, Prof Sandborn concluded.

New surgical technique in IBD

It is the multidisciplinary team that takes the decision for surgery, and the team also

"VERIFY PAIN SOURCES AND EXCLUDE DISEASE COMPLICATIONS"

has to come up with a good plan, said Prof Willem Bemelman.

– This includes perioperative optimalisation of the patient, and enhanced recovery after surgery. Above all, the surgery should be minimally invasive. We now also know how to minimalise complications.

He described the surgical evolution from the 18th century up to 2015, a timeline that ends in laparoscopy and incisionless surgery. Prof Bemelman presented data from two studies that had compared single port access versus multiport laparoscopy for ileocolic resection for CD. The first study (2011) found for case matched a similar outcome – the second (2012) found that, when case matched, single port access had a shorter stay and shorter period of pain.

TAMIS stands for transanal minimal invasive surgery, which Prof Bemelman called "bottom up" – i.e. through the anus.

– For rectal dissection this procedure has several potential advantages: It's an easier and safer dissection, no extraction is required and it gives less pain, accelerated recovery, no adhesions, no incisional hernia and has no cosmetic issues.

TAMIS procedures in IBD include intersphincteric proctectomy and proctocolectomy, redo pouch surgery, salvage leaking pouch and sleeve advancement of rectovaginal fistula.

Prof Bemelman showed a film on TAMIS and laparoscopic proctocolectomy with ileostomy.

– We leave as much fat as possible, in order not to create a hole in the tissue.

He concluded by stating that TAMIS is a very promising new technique.

Algorithm for abdominal pain treatment

Managing the manageable: Chronic pain and fatigue was the title for a Session on the last day of Congress. During this, Prof Andreas Sturm talked about abdominal pain.

– Verify pain sources and exclude disease complications such as adhesions, cancer, abscess among others, he advised.

Before one start therapy for pain in IBD patients, Prof Sturm stressed the importance of taking patient's history.

– Ask when the pain comes? Has it changed over time? There are unbelievable many reasons for pain.

Then one must determine if a chronic pain therapy is needed – or if pain relief on demand is sufficient. Be sure the patient has sufficient pain medication at home.

He also talked about opioid side-effects.

– But many of those – like constipation – are not so relevant for the IBD patient.

For a low pain level, Prof Sturm recommended Mebeverine and Tramadol. For medium pain level he recommended Metamizole and Tramadol.

– For medium to intense pain I suggest Buprenoorphine, Oxycodon or Fentanyl.

Most patients with chronic pain are also depressed, so Prof Sturm said one should consider tricyclic antidepressants.

Don't forget to discuss alternative therapies, such as mind-body therapies, acupuncture, yoga and biofeedback among others. Suggest psychosomatic therapy and don't hesitate to consult a pain therapist, he summarised.

Algorithm for the management of fatigue

Prof Janneke van der Woude talked about fatigue.

– IBD-related fatigue is a distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness, she defined.

The fatigue is not proportional to recent activity and interferes with normal individual daily activities.

– In my opinion this is underdiagnosed, and affects the patient's quality of life. It also affects work productivity and causes costs for the society.

Therefore fatigue, that rarely is an isolated symptom, should be screened and managed. Perform initial screening by asking the patient where on a scale from 0 to 10 they are when it comes to fatigue.

Then it is important to assess concurrent symptoms – inflammation, anaemia, sleep disturbance medication side-effects were among those she mentioned.

– Non-pharmacological interventions include physical activity, psychosocial interventions to manage stress and cognitive interventions, Prof van der Woude said.

Pharmacologic interventions could be anti-TNF:s or thiamine. She reported that in oncology dexamphetamine has showed promising results.

– Patients and families should be informed that fatigue can persist. IBD-related fatigue should be included in health outcome studies – and acknowledgement of fatigue should start at diagnosis, Prof van der Woude ended her talk.

Successful chefs

Then the ECCO Congress 2015 was over, and President Prof Severine Vermeire thanked all Speakers and the Scientific Committee for all the efforts they had made to "cook up the Meeting" as the final ECCO film jokingly referred to.

– And of course I want to thank all of you who came to Barcelona to attend. Please come back to the next Congress – which is going to be held in Amsterdam March 16 – 19 in 2016!

Per Lundblad

WHAT'S THE CHALLENGE FOR 9 OUT OF 10 UC PATIENTS?

At a Satellite Symposium at the ECCO Congress, the importance of adherence to therapy and monitoring the disease was discussed. The Symposium was sponsored by Tillotts Pharma.

After Dr Eugeni Domènech, who was the Chair, had greeted the delegates welcome, he introduced Dr Andrew Robinson who presented a lecture entitled *Communicating with the patient – Hit the target and save time.*

5-fold increased risk for relapse for non-adherent patients

In his presentation, Dr Robinson acknowledged that non-adherence to treatment has a significant clinical impact but is also complex and multifactorial.

– As an example, the risk of relapse in patients non-adherent to 5-ASA is 5-fold increased, he said.

Dr Robinson highlighted that a number of studies have identified simplifying dosing regimens that may improve treatment adherence in chronic diseases.

He also reminded the audience that the main attributes for patients for treatment choice in ulcerative colitis (UC) were efficacy and safety parameters – and that regimen parameters were among the less important criteria cited.

– Moreover, most recent meta-analyses suggest that there is no statistical difference in either preventing relapse or improving treatment adherence in favour of once daily regimens, Dr Robinson pointed out.

Address patients' beliefs

Treatment adherence was linked to other patient related factors, which needs to be addressed.

These factors include patient fears about the long-term effects of the drugs (safety and loss of efficacy over time), becoming dependent of the therapy, or lack of information on the therapy.

Dr Robinson concluded that the single most important intervention is the one that addresses patient *beliefs,* which could generate high treatment adherence, thus improved disease control and further reinforcing patient belief in the therapy.

Eugeni Domenech, Gerhard Rogler and Andrew Robinson.

Ultrasound a good tool for monitoring

Professor Gerhard Rogler talked about monitoring UC patients for better disease control.

– Monitoring is an essential component of UC patient care that is conducted at diagnosis and within every step of the fluctuating disease activity - to assess disease activity and treatment efficacy during acute flares, chronic activity and remission, he explained.

Prof Rogler highlighted that while endoscopy is the standard method for evaluating disease activity in UC, ultrasound (when placed in experienced hands) may substitute for endoscopy in many cases and situations for the monitoring of UC patients.

Monitoring can increase patient's quality of life

He also indicated that faecal markers such as calprotectin and lactoferrin are superior to CRP.

– They can be used for monitoring treatment efficacy and for predicting flares/relapses and calprotectin levels correlates well with endoscopy.

A Robinson, G Rogler

Finally Prof Rogler reminded the audience that monitoring may guide treatment decisions such as optimization of 5-ASA therapy and therefore can "pay off" for better disease control and better quality of life for UC patients.

Caroline Charles

UCANDME™

In conjunction with the ECCO Congress, the pharmaceutical company Tillotts Pharma arranged a Breakfast Meeting about an exciting new digital program to help physicians to improve adherence of their patients.

In a Tillotts survey on ulcerative colitis (UC) presented at the Congress, the result was that 93 percent of people with UC have low to medium adherence to medication, putting them at five times greater risk of relapse.

The survey was conducted in order to understand the needs, concerns and attitudes of people with UC. 507 people with UC and 27 healthcare professionals from eight European countries were interviewed.

Based on the findings of the survey, Tillotts partnered with a scientific committee of leading medical experts to develop the UCandME™ toolbox to further support the Gastroenterology community in improving patient adherence and education.

Good communication is appropriate

The Meeting began with Mattias Norrman, Chief Operations Officer at Tillotts.

– Why patient adherence programs? Because poor adherence to medications is a major problem, he said.

Patient adherence programs need to be more individualised. Next-generation adherence programs recognise that a single solution may not fit with every patient's needs or motivations.

Dr Stuart Bloom talked about the need for improvement in patient education in UC management.

– Compliance with the treatment of UC is a key factor to prevent the aggravation of the disease. In IBD, non compliance is mainly due to a low perceived severity of the disease, or the fear of side-effects, Dr Bloom said.

The implications of non-adherence are significant, and its cost to global healthcare systems is huge. The effect on human health is equally severe. Dr Bloom described barriers for adherence, and underlined the need of good communication between patients and doctors and nurses.

Main sources of information

– There is a five-fold increased risk of relapse in patients non-adherent to medication. And this leads to more hospitalisations and more colectomies, said Prof Laurent Peyrin-Biroulet.

Laurent Peyrin-Biroulet, Stuart Bloom and Susanna Jäghult.

In the short term – the first months – adherence is OK. But it is getting lower with time.

– We normally discuss with the patient what happens when they take the drug – but not what happens when they don't take it, he continued.

The main sources of information on UC are gastroenterologists and IBD Nurses (73 %) or Internet (67 %).

Partnership with the patient

The UCandME™ program is created by medical experts to help health care professionals to provide patients with the information they need. Prof Peyrin-Biroulet described how it works:

– It is a program in two steps. The first step is to define your patient's needs and concerns via the UCandME™ questionnaire.

This is an online patient-centred questionnaire with 10 quick questions that can be completed by the patient in the waiting room, at home or during consultation.

– The second step is to create your pack of patient-specific information – UCandME™ education.

This is a full range of online tools and resources that helps the physician or nurse to educate the patient and provide the information he or she needs.

– By defining patients' needs and tailoring specific information, UCandME™ represents a new approach in the management of UC, Prof Peyrin-Biroulet concluded.

Afterwards in a panel discussion, IBD Nurse Susanna Jäghult pointed out that the patient is managed by a team.

– We have to invite the *patient* to that team. I – as an IBD Nurse – have a lot of knowledge about the disease. The patient has a lot of knowledge about living with the *disease*. That's where a partnership comes into the picture!

Per Lundblad

MANAGING ULCERATIVE COLITIS: A PATIENT-FOCUSED APPROACH

The degree of burden of ulcerative colitis (UC) may be perceived differently by patients versus their physician. An appropriate treatment, with attributes that address a patient's individual needs, was discussed at a Satellite Symposium sponsored by Abbvie.

Prof Edouard Louis was the Chair, and in his opening statement he underlined that the disease burden in UC is high.

– The patients' main fear is still surgery, but also for cancer.

The disease burden is often underestimated – and some times misinterpreted – by healthcare professionals. Prof Louis showed data from a North American study including 451 patients and 300 gastroenterologists.

– It found a striking difference between patients and physicians in symptoms validation.

Taking patients' preference into account is part of patients' empowerment and may improve outcome, he continued.

– But this is not going to be easy. It requires a structured collaboration between patients and healthcare professionals.

Engage patients in the decision-making process

Prof Laurent Peyrin-Biroulet talked about balancing patient and physician aspirations.

– Typical physician goals in the long-term perspective include inducing remission and maintaining steroid-free remission, he said.

Typical patient goals with short term perspective are to minimise symptoms and get fast relief, sustained symptom relief and to avoid steroids and colectomy.

Prof Peyrin-Biroulet presented data from an as-observed analysis from 2014 on discontinuation of corticosteroids up to 4 years on adalimumab.

– They show that after 4 years, 60 % of patients are still off steroids.

Shared decision-making is a process that aims to reach healthcare decisions based on mutual agreement.

Edouard Louis, Laurent Peyrin-Biroulet and Alessandro Armuzzi.

– A meta-analysis of 127 studies in a variety of medical conditions showed that healthcare professionals' communication significantly and positively correlated with patient adherence. When the communication was poor, patients had 19 % higher risk of non-adherence.

In his conclusion, Prof Peyrin-Biroulet said that anti-TNF:s can help achieve both physician and patient treatment goals.

By balancing healthcare professionals' and patients' aspirations we can more effectively engage patients in the decision-making process.

– We can provide optimal therapeutic strategies that improve patients' clinical and quality of life outcomes.

Real-life data

Translating clinical trials into real-world experience was the title of Dr Alessandro Armuzzi's talk. He began this by underlining that patients enrolled in randomised controlled trials do not represent the IBD patient population.

– A retrospective study of patients with IBD at a US referral centre showed that 31 % of patients were not eligible for participation in a clinical trial of biologic therapy.

Dr Armuzzi continued by presenting examples of tailored management of UC patients from his own practice.

– The benefits of real-life data gives us information collected on drug effectiveness in a practical, real-life setting, a diverse study population and it is useful to understand and move outcomes from clinical trials into clinical practice, he said.

In this setting, adalimumab demonstrated sustained effectiveness across measures that are relevant to patients and physicians, Dr Armuzzi concluded.

– The effectiveness of adalimumab has been shown in different UC patient types, including bio-naïve as well as tough-to-treat patient populations.

Patient's selection, disease categorisation and physician-patient goal-sharing are key aspects of best practice in UC care, he also said.

Per Lundblad

BIOSIMILARS IN IBD – EXPANDING TREATMENT CHOICES AND PATIENT ACCESS

Dr Eugeni Domènech, the Chair, greeted delegates at the ECCO Congress welcome to the first Hospira sponsored symposium in IBD. Inflectra is a biosimilar to infliximab, and it is launched in several European countries in 2015.

Dr Domènech introduced Prof João Goncalves as the first Speaker. He talked about extrapolation in IBD.

Robust scientific basis

– Biosimilars in EU is a science-based experience. It has a long history, and follow a large pathway of regulation, Prof Goncalves stated, and continued by describing this process in detail.

He pointed out that a large number of changes have been made to infliximab to date.

– We can rely on the progress – made in regulatory science for over 20 years – to come to a consistent, fair and science-based conclusion of biosimilarity, Prof Goncalves said.

Comparability has been used as the basis for complete extrapolation between all indications, as well as full interchangeability for each indication – irrespective of whether the mechanism of action is known, or whether any clinical studies at all have been conducted on the post-change product.

– Analytical and pharmacodynamic high similarity is the most robust scientific basis for comparing independently sourced biologics. Scientific principles demonstrate that Inflectra *is* infliximab, Prof Goncalves concluded.

Similar efficacy and safety

Prof Stefan Schreiber then talked about the two studies PLANETRA and PLANETAS, that has been performed on the biosimilar, and began with the latter.

– It was an equivalence trial in ankylosing spondylitis. In this, patients were randomised to infliximab or Inflectra. It was amazing how similar the two drugs were in clinical efficacy. They were also identical in safety. Prof Schreiber said.

Luis Correia, João Goncalves, Stefan Schreiber and Eugeni Domènech.

He added that the immunogenicity was also similar in the two groups.

PLANETRA was conducted in patients with rheumatoid arthritis – and the outcome was the same.

– The results overlap, side effects frequency was the same and no marked difference in immunogenicity was found. At this point we have seen that clinical equivalence has been confirmed in clinical trials.

Thus, the totality of evidence indicated similar efficacy and safety of the biosimilar and the reference product in all therapeutic indications of infliximab, he summarised.

Follow-up in Portugal

– We now move from the lab and clinical trials to clinical practice, Chair Dr Domènech continued and introduced Dr Luis Correia.

His lecture was on clinical experiences of Inflectra in IBD.

Dr Correia began his talk by presenting a clinical case of Crohn's disease.

– There were multiple severe ulcers, and steroids was started, then azathioprine – to no result. Then the patients received Inflectra, and much of the mucosa healed, he said.

In Portugal, where Dr Correia is working as a clinician, Inflectra has been available for some time. Therefore, he has had the opportunity to perform a short follow-up at four Portuguese hospitals.

– There were 34 patients in total. 79 % of them had Crohn's disease, 18 % ulcerative colitis and 3 % had indeterminate colitis.

Infusion-related reactions occurred in 9 % of the patients – 2 at induction and 1 during maintenance – but no serious adverse events.

The conclusion of this short follow-up on Inflectra was that it was efficacious in inducing and keeping response and remission in 89 % of patients with IBD, Dr Correia stated.

Per Lundblad

IBD TREATMENT AT THE CROSSROADS

Two challenging cases of IBD, with the treatment decisions made and the relevant criteria that drove the choice of therapy at each stage, was presented at a Satellite Symposium at the ECCO Congress. The Symposium was sponsored by Takeda.

Prof Michael Kamm, who was the Chair, stated in his welcoming address that monoclonal antibodies now play a central role in IBD management.

– There are many potential targets: Inflammatory *mediators* as TNF-alpha, and it is now possible to target the *recruitment* of inflammatory cells.

Vedolizumab (brand name Entyvio) is an antibody that attaches to activated lymphocyte α4β7, which binds to gut-associated addressin MAdCAM-1. It was approved by FDA and the European Union for moderate to severe ulcerative colitis (UC) and Crohn's disease (CD) in May 2014.

– Tonight two of the world's best IBD experts will present the management of one of their own patients, Prof Kamm said and introduced the first expert – Prof Jean-Frederic Colombel.

Michael Kamm, Jean-Frederic Colombel and Gert van Assche

Biologic-naïve patient with UC

Prof Colombel presented a case that was referred to him for second opinion. It was a man with UC, treated for a year but unable to taper steroids less than 10 mg. The patient also had a history of hypertension and hypercholesterolemia, and progressive symptoms of diarrhoea and rectal bleeding.

– Colonoscopy showed colon diffusely inflamed from the splenic flexure distally.

Prof Colombel presented data on vedolizumab in UC – results from week 6 and 52 in intention-to-treat population

– After 52 weeks 45 % were in clinical remission, 56 % had mucosal healing and 45 % were in steroid-free remission.

He also talked about the risks with anti-TNF:s – infections and lymphoma (if combo with immunomodulators). Vedolizumab has a more favourable safety profile.

– The patient in the case received vedolizumab plus azathioprine 2mg per kg per day. He was in clinical remission at week 12, with Mayo endoscopic score 1, Prof Colombel told the audience.

Patient with CD after anti-TNF therapy

Prof Gert van Assche continued with a case of CD in an 18 year old woman.

– The earlier we start a biologic, the more is the benefit for the patient, he said.

The pros and cons of combination therapy were discussed, and the patient was reluctant to start combination with azathioprine. She therefore started on adalimumab monotherapy.

– The patient responded well within 4 weeks, and was in clinical remission after eight weeks.

Two years later she developed dry skin and eczema and, in spite of treating her with steroid cream, the eczema worsened in the scalp and she had hair loss. The dose of adalimumab was increased, but no improvement was seen.

Prof van Assche presented data on Vedolizumab in CD (GEMINI II and III). They show that 27 % of anti-TNF failures – i.e. where his patient fits in – had clinical remission at week 10.

– The long term results with Vedolizumab are also encouraging, he continued.

Today Prof van Assche's patient is on a waiting list to receive vedolizumab.

It is good we have a choice

Despite early efficacy and clinical remission with anti-TNF:s, systemic side effects can be a problem in the longer term. There is a limited role for second-line anti-TNF, in failures with adequate drug levels.

– Switching to another class – e.g. vedolizumab – is a viable option for lack of response or intolerance to anti-TNF:s. Vedolizumab can also be considered as a first-line biologic in CD, Prof van Assche summarised.

In his wrap up Prof Kamm said he always had envied the rheumatologists.

– They have several biologic options when they want to treat the patient. I think it is very good that we now also got a *choice*!

Per Lundblad

PATIENTS BEYOND GUIDELINES

Although biologics has been a revolution and a success-story in treatment of patients with IBD, it is obvious that some patients will not benefit from them. There is a need for options for these patients, and this was discussed at Satellite Symposium, sponsored by Otsuka.

The Symposium concerned patients with refractory ulcerative colitis (UC), and had lectures on the ART trial and the long term outcomes in UC.

The Adacolumn apheresis system

Prof Wolfgang Kruis, who was the Chair, began by talking about the current picture of UC and the difficulty of treating patients beyond guidelines.

He pointed out that there indeed exists an option for patients that are refractory to standard treatment – by using leucocytapheresis. This involves extracorporeal removal of leucocytes through an adsorptive system of cellulose acetate beads.

It is well appreciated that leukocytes play an important role in the pathogenesis of UC, and it has been shown that activated leucocytes infiltrate the bowel mucosa and cause extensive tissue injury.

The *Adacolumn* apheresis system is a selective granulocyte/monocyte adsorptive medical device. In a study from 2005, performed by Prof Kruis, the conclusion was that in patients with steroid refractory UC, 5 apheresis with a depleting filter showed potential short-term efficacy and that tolerability and technical feasibility of the procedure are excellent.

Another trial from 2007 showed that selective leukocyte apheresis may be associated with an impact on health-related quality of life in patients with active UC.

Results from interim analysis

At the Symposium in Barcelona, results from 2nd interim analysis on efficacy and safety at week 24 and 28 from the ART trial were presented by Dr Ayesha Akbar, St. Mark's Hospital, Harrow.

– The objective of ART was to observe and document the efficacy and safety of 5 or more Adacolumn treatments in a specific subset of UC patients, Dr Akbar said.

The indication studied was steroid-dependent active UC and insufficient response or intolerance to immunosuppressants and or biological therapies.

Prof Wolfgang Kruis

– The first interim analysis was completed after data were collected from the 12-week follow-up period on 86 patients enrolled where over 50% of patients benefited from the treatment and remained enrolled for the follow-up period, where concomitant medications were recorded, she continued.

Up to 29,8 % of patients showed sustained remission or response through to 48 weeks under concomitant immunosuppressant medication – despite prior resistance, irresponsiveness or intolerance – while steroids could be reduced, Dr Akbar summarised.

– No new safety signals were seen up to week 48.

She ended her talk by underlining the need for randomised controlled studies.

Real world data

SiMAC is a system for monitoring aphaeresis in UC. It is a collaborative project between GETECCU (the national IBD Society in Spain) and three regional agencies in Spain for the evaluation of health care technologies to get data on efficacy and safety of apheresis in clinical practice – under real conditions.

Dr Rodolfo Sacco, Pisa University Hospital, Italy presented data from SiMAC at the Symposium.

– Granulocyte and monocyte adsorption apheresis (GCAP) is efficient in inducing clinical remission in steroid-dependent UC, even in those patients who did not respond to thiopurines or infliximab, Dr Sacco stated.

He continued by pointing out that GCAP is also efficient for steroid-refractory UC.

– However, clinical remission is less likely in patients with severe activity, suggesting that alternative treatment algorithms should be explored in this subset of patients, he concluded.

Per Lundblad

REMSIMA – THE FIRST BIOSIMILAR MONOCLONAL ANTIBODY

Biologics are the latest revolution in medical therapeutics. These drugs are complex to make, and are not cheap. Although clearly efficient, they are a significant burden for healthcare systems. This was pointed out at a Satellite Symposium sponsored by Celltrion Healthcare.

Chair Dr Antonio López-Sanmorán defined a biosimilar.

– It is a biological medicine developed to be similar to an existing biological medicine (RMP = reference medicinal product). When approved, its variability and any differences between it and its reference medicine will have been shown not to affect safety or effectiveness.

Antonio López-Sanmorán, Jørgen Jahnsen and Gonzalo Calvo.

The biosimilarity exercise

EMA permits biosimilars to be approved across the indications for which the RMP is also approved. Celltrion's first infliximab biosimilar – Remsima – was approved for use in EU, based on extrapolation of data obtained in several indications from the RMP, Dr López-Sanmorán summarised.

Prof Gonzalo Calvo then talked about the rationality of biosimilarity.

– Biosimilars are not expected to *re-demonstrate* the benefit-risk across the whole clinical spectrum – but just similarity to the RMP, he underlined.

The biosimilarity exercise is based on a proper physicochemical, functional and pharmacokinetic (PK) and pharmacodynamic (PD) characterization and comparability to the RMP.

– Extrapolation of indications is inherent to the concept of biosimilarity!

Remsima has compelling biosimilarity – analytical and functional similarity – across all mechanisms of actions of infliximab, Dr Calvo continued.

– Remsima has highly similar efficacy profiles in rheumatoid arthritis and ankylosing spondylitis. A pivotal study for these conditions showed a comparable safety profile and a highly similar immunogenicity profile.

Extrapolation to all other clinical indications is supported by extensive analytical and in vitro mode-of action assays, he concluded.

Norwegian study across all indications

Prof Jørgen Jahnsen then talked about experiences with Remsima in treatment of IBD.

– Remsima has been used in Norway since January 2014. It costs significantly less the reference product, and is first line treatment when starting biologic therapy in new IBD patients, he stated.

At Akershus University Hospital, where Prof Jahnsen works, they have at present 74 IBD patients – 44 with Crohn's disease (CD) and 30 with ulcerative colitis (UC) that are treated with Remsima.

– 17 CD-patients were previously operated on with bowel resections, and three patients have peri-anal fistulas.

Prof Jahnsen reported that they have seen a significant reduction in Harvey Bradshaw index after 14 weeks (three infusions) on Remsima. Also a significant reduction in calprotectin and CRP.

– In UC patients, we've seen a partial Mayo score significant reduction, and the same in simple activity index, calprotectin and CRP.

Therefore he summarised that the efficacy and safety of Remsima in the treatment of IBD appears to be similar to innovator infliximab.

Prof Jahnsen also mentioned the ongoing study NOR-SWITCH. This is funded by the Norwegian Government, and it aims to test interchangeability from the reference product to Remsima.

– It's a randomised, double-blind parallel group study with 500 patients across all indications. Disease worsening is the primary endpoint, and data are expected in 2016, said Prof Jahnsen.

Per Lundblad

ADALIMUMAB: EFFICACY AND SAFETY IN PAEDIATRIC – ONSET CD PATIENTS

Adalimumab, a humanized anti-tumour necrosis factor antibody, is an effective treatment in adult patients with refractory Crohn's disease (CD) (1).

The available literature on its efficacy in children remains limited. The published experiences of ADA in children come mainly from tertiary centers where ADA is effective in rescue therapy in nearly two thirds of patients with Infliximab (IFX) failure (2, 3).

The major result comes from the Imagine trial, a phase 3 induction and maintenance trial in pediatric CD that showed its clinical efficacy in, associated with an improvement of height velocity and a decrease of CRP (4).

We know that pediatric-onset CD patients have a more aggressive phenotype and frequently develop disease complications as growth retardation and delayed puberty (5,6).

The advent of anti-TNF agents has allowed significant progress in the treatment of pediatric CD refractory to standard medications. Infliximab (IFX) was the first biologic approved for the treatment of moderate to severe pediatric CD (7).

In addition to limited information on the efficacy of ADA in pediatric patients, there are continuing safety concerns about ADA.

The ADA clinical efficacy, its effect on growth status and on biomarkers, and its safety profile have never been evaluated at the population level in pediatric CD.

We performed a retrospective study on "the real-life" about the prescription, the efficacy and safety profile of ADA after IFX failure through our population-based paediatric-onset IBD cohort.

From 1st January 2001 to 31st December 2010, a total of 325 patients newly diagnosed as having CD and younger than 17 years of age were recorded from population-based Epimad Registry (8,9). A total of 147 patients received IFX treatment. Of them 27 (8%) required treatment with ADA because of IFX failure, including 14 girls (52%) with a median age at CD diagnosis of 11 years [Q1=9;Q3=12]. Demographic and phenotypic characteristics of the study population are shown in Table 1. Median disease duration at ADA initiation was 3 years [2;4]. At ADA initiation, a majority of children (60%) had ileocolonic disease (L3) and inflammatory behavior (B1) according to the Montreal classification (10).

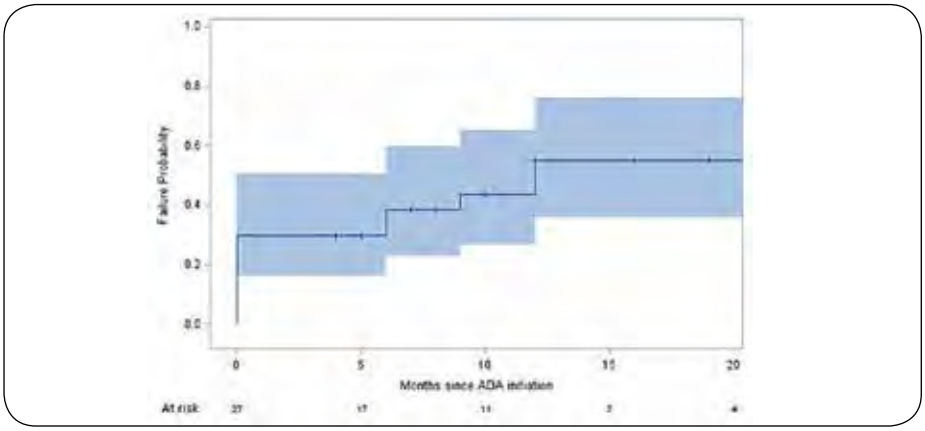

Figure 1: Cumulative probability of failure to ADA in population-based paediatric-onset CD patients treated by ADA after IFX failure. Kaplan-Meier estimates of cumulative probability of failure to ADA treatment were 38.4% (CI 95% 22.7-59.9) at 6 months and 54.9% (35.7-76.1) at 1 year.

Median age at initiation of ADA was 15 years [12;16]. Median BMI Z score was -0.80 [-0.15;0.4]; median Z score weight for height (W/H) -0.7 [-1.2;0.5], and median Z score height for age (H/A) -0.5 [-1.4;0.7]. When ADA was introduced, median C-reactive protein rate (CRP) was 24 mg/L [5;44] and median orosomucoid 1.7 g/L [1.5;2.6].

Indication for ADA treatment was loss of IFX response in 60% of patients, primary IFX failure in 14% and IFX intolerance in 26% defined as AE leading to IFX discontinuation. Median duration of IFX treatment was 13 months [8;19].

Efficacy of ADA treatment

Median follow-up of this cohort was 16 months [8;26] after ADA initiation and median duration of ADA treatment was 10 months [5;19]. ADA was effective, defined by clinical remission with physician global assessment score (PGA) =1 or decrease of at least 2 points of PGA score 6 months after ADA initiation, in 70% of children and maintained efficacy was observed in 52% of children at maximal follow-up. Primary failure was observed in 30% and loss of response or secondary failure in 19%. A total of 14 patients (52%) underwent an optimization during follow-up, including dose escalation in 6 patients, reduction of intervals between injections in 1 patient, and both in 7 patients. Response to optimization was observed in 10 patients (71%). According to Kaplan-Meier analysis, cumulative probability of failure to ADA treatment was 38.4% (22.7%-59.9%) at 6 months and 54.9% (35.7%-76.1%) at 1 year (Figure 1). According to the indication of ADA treatment, ADA was effective in 7 of 7 (100%) in children intolerant to IFX, and in 1 of 4 (25%) children in primary failure to IFX. At the date of maximal follow-up, 17 patients were receiving ADA. Intestinal

resections were performed in 5 patients after ADA initiation.

Effects of ADA treatment on nutritional growth status and growth

At maximal follow-up, median BMI Z-score was -0.2 [-1.5;0.3], median W/H Z-score was -0.5 [-1.3;0.3], and H/A Z score was -0.2 [-1.3;0.6]. No significant changes in growth and nutritional status occurred during the study period in both groups (efficacy and failure).

Effect of ADA treatment on inflammation

In patients with ADA efficacy (n=19), a significant decrease in both median CRP (15 mg/L [4.0;44.0] vs. 9.0 [3.0;19.0]; p=0.05) and orosomucoid (1.6 g/L [1.5; 2.6] vs. 1.1 g/L [0.8;1.9]; p=0.001) levels was observed from ADA initiation to maximal follow-up. No significant changes were observed among patients with primary failure to ADA (n=8).

Safety of ADA treatment

A total of 11 patients (40%) experienced a total of 19 adverse events (AEs). Main AEs were as follows: cutaneous (xerosis (dry skin); n=6, depigmentation; n=3, acne; n=2 and psoriasis: n=1); local reactions (pain, inflammatory reaction) at the injection site (n=3); and transient arthralgia and/or myalgia (n=4). None of them resulted in ADA discontinuation. There were no opportunistic infections or other infectious complications. AEs were observed in 4 of 7 children intolerant to IFX, 2 of 4 children with primary failure to IFX, and 5 of 16 children with secondary loss of response to IFX. No death or malignancy was observed.

In this retrospective study we report on the efficacy and safety profile of ADA therapy in 27 children with CD with IFX failure using a well-defined population-based registry. We showed that two-thirds of children had clinical benefit and that ADA efficacy has been found in 100% of children intolerant to IFX.

As observed in adults (11), it appears that switching from IFX to ADA is more efficacious in children who were IFX intolerant than in those with prior loss of IFX response.

Even our results are comparable to reports on the ADA efficacy in pediatric CD (2,3,12,13), the rate of response was higher than in randomized clinical trials (RCTs) in both children treated with IFX and those who were IFX naïve (4). Differences in defining clinical response and clinical remission likely explain such discrepancy between RCTs and "real-life" experience.

We found an important impact of ADA on biomarkers such as CRP as in previous result of role of anti TNF therapy on biological markers of inflammation.

In our cohort, induction and maintenance of ADA therapy are safe and well tolerated, no serious adverse events were observed and anyone adverse events resulted in ADA discontinuation. There were no deaths or malignancies in this study cohort. No opportunistic infections or others infectious complications were recorded. Adverse events were observed in 40% of patients. The most common side effect was a type of skin reaction to xerosis.

Table 1: Characteristics of the population

Variables	N (%)	Median (Q1-Q3)
Female	14 (52)	
Age at diagnosis (years)		11 (10-12)
Age at the entry (years)		15 (13-15)
Disease location at diagnosis		
Ileum (L1)	2 (7)	
Colonic (L2)	6 (22)	
Ileo-colonic (L3)	19 (70)	
Upper tract (L4)	10 (37)	
Perianal location (p)	9 (33)	
Disease behavior at diagnosis		
Inflammatory (B1)	25 (93)	
Stricturing (B2)	0 (0)	
Penetrating (B3)	2 (7)	
Extra-intestinal location	11 (40)	
Previous treatment		
Corticosteroids	24 (88)	
Enteral nutrition	16 (59)	
Azathioprine	26 (96)	
Methotrexate	20 (74)	
Concomitant medications		
Corticosteroids	5	
Azathioprine	1	
Methotrexate	1	
Growth status at ADA initiation		
BMI z-score		-0.8 (-1.7-0.4)
Weight/Height z-score		0.5 (-1.7-0.7)
Height/Age z-score		-0.3 (-1.7-0.8)
Biomarkers at ADA initiation		
CRP (mg/L)		24 (5-44)
Orosomucoid (g/L)		1.7 (1.5-2.6)

ADA: adalimumab; BMI: body mass index; CRP: C-reactive protein

No immediate hypersensitivity reaction or delayed requiring discontinuation of ADA was observed. This confirms the low immunogenicity of the ADA, a fully human recombinant antibody.

In conclusion, this first population-based study evaluating efficacy and safety of ADA in children suggests that ADA is a well-tolerated and effective rescue therapy for the induction and maintenance of remission of pediatric CD. These findings "in real-life" reinforce the data from the placebo-controlled clinical trials of ADA for the treatment of moderate to severe inflammatory CD in children, and are in agreement with other early reports of the safety and efficacy of ADA in clinical practice.

Corinne Gower-Rousseau

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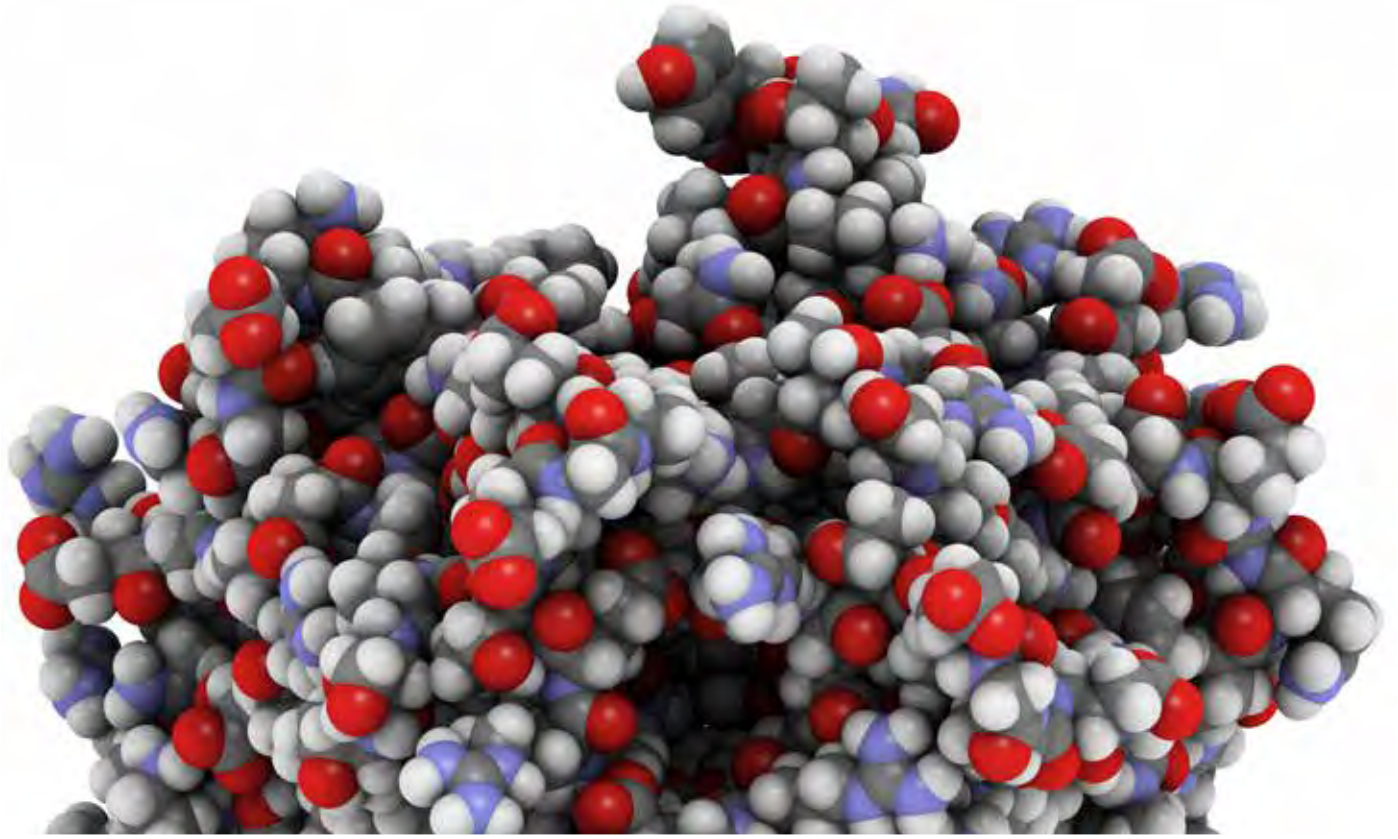


THE COMPLEX DECISION MAKING IN UC PATIENTS WITH DYSPLASIA

Colorectal cancer is a concrete threat for patients with ulcerative colitis (UC), since they have an increased risk of developing colorectal cancer (CRC) than the general population.

A major difference between the common type of CRC affecting the general population ("sporadic") and the UC-related neoplasia is that in the former case the tumor occurs on a precancerous lesion (adenoma), while in the second case the risk of neoplastic degeneration is present across the colonic mucosa.

It has also been recently highlighted as aneuploidy, a marker of genomic instability, is present, in patients with UC, even on morphologically normal mucosal cells

Unfortunately UC patients, with a diagnosis of CRC, present often with a more advanced grade of tumors (3 or 4) than in a sporadic cancer and are also more often mucinous. This reflects in a 2-fold increase in the mortality, compared to patients with sporadic cancer.

Endoscopic surveillance strategies have been developed and widespread, based on the abovementioned data. The aim is to avoid prophylactic resections in patients with very low risk to develop cancer and, on the other side, they can help in improving the outcomes of patients in two aspects: not only to reduce the risk of developing CRC by 60-80% (by sending patients at risk for it to surgery), but to also improve the outcomes in terms of survival, from a rate of 36% (people not followed-up) to 77% (by sending the patients with already a cancer to surgery at an earlier stage).

In order to achieve this, it is essential to identify the different groups of patients.

Many studies, from institutional case-series to population based studies reviewed with this aim the characteristics of UC patients having developed cancer, identifying some risk factors.

The chronic inflammatory environment characterizing UC plays an important role in the pathogenesis of cancer. The risk of cancer starts to increase after 8 to 10 years from the diagnosis: at 10 years of disease, the risk is about 1%, at 30 years from the beginning of UC, the risk of cancer increases up to 18.4%. So, the first risk factor is long standing colitis.

The other most important risk factor related to the development of cancer is the extension of UC: pancolitis increases of 15 fold the risk of CRC compared to the general population; for patients with only limited, left-side colitis the risk drops to 2.8 fold and in case of proctitis alone it is similar to healthy people.

The remaining independent risk factors for developing cancer include the young age at diagnosis, the simultaneous presence of primary sclerosing cholangitis and a family history of colorectal cancer.

Patients undergoing surveillance could at some point during their disease course read the word "dysplasia" on the pathologic report on their biopsies.

What kind of clinical relevance do we (and should we) give to the finding of dysplastic changes on biopsies performed during the follow-up of the disease remains source of great discussion among clinicians.

First, we have to confirm the diagnosis, since inflammatory changes may mimick dysplastic changes: no decision should therefore be taken before another independent pathologist have confirmed the presence/absence of dysplasia. Actually, to complicate things a bit more, it was also shown that the agreement among different expert pathologist on the presence of dysplasia and on its grade is not high. But that's what multidisciplinary teams are for: eventual disagreement should be solved by a general and "holistic" discussion about the situation in that environment.

If the response of the biopsies report is "high-grade dysplasia" (HGD) on flat mucosa the risk of a syncronous malignancy is between 42% to 67%. So this should not give rise to a big discussion, since the risk of cancer is too high.

Antonino Spinelli

There is still a big debate about what to suggest to patients found to have a low-grade dysplasia (LGD) in biopsies specimens taken during colonoscopy: from retrospective series we know that patients with LGD undergoing surgical resection have been found to already have a CRC in 19% of cases (in literature between 4% to 43%). Moreover between 30% to 50% of patients with LGD move to an HGD or CRC in a 5-year period of follow-up.

Particular attention must be paid to the presence of dysplasia on biopsies taken on DALM lesions. The same consideration has to be done in case of dysplasia on biopsy of area of mucosa with no alteration. Both situations are to be considered as predisposing factors for the onset of the CRC.

Very recent data are much different and

apparently more reassuring: a recent retrospective chart review on a total of 2130 patients who had surgery for UC, 329 had a preoperative diagnosis of dysplasia (either low and high). The authors found that the risk of undetected cancer was only 2% in the subgroup of patients with diagnosis of LGD at random surveillance biopsies. In case of biopsies taken on endoscopically visible lesions the risk was still quite low (3%). In case of HGD the risk of undetected cancer was still 3%. The authors explain these so different results with a better control of UC with new therapies and an improvement in the endoscopic surveillance especially with the advance in endoscopic techniques such as chromoendoscopy, narrow-band imaging, (auto)-fluorescence imaging, magnification colonoscopy with pit pattern analyses, and confocal endomicroscopy.

ECCO guidelines for timing and surveillance colonoscopy for CRC in UC suggest the beginning of surveillance at 8 years after the onset of symptoms, considering as risk factors the presence of a pancolitis, endoscopic or histological inflammation, pseudopolyps and a family history of CRC. According to a score patients are at high risk (colonoscopic surveillance scheduled every 1-2 years) or at low risk (every 3-4 years).

When surgery becomes indicated it is important to stress a technical point, which could, among other factors, play a role in the worse outcomes of UC-related CRC cases: differently from what is usually done in the case of proctocolectomy performed for UC refractory to medical therapy, in case of association with HGD, the operation must be conducted with oncological criteria (ligation of the main vessels at their origins for maximal lymph node harvesting) for the risk of a CRC in the histological specimen. Since in a certain number of patients dysplasia and cancer are not known preoperatively, we can speculate that in such cases a suboptimal operation, from the oncological point of view, may be performed.

> "ONE RISK FACTOR RELATED TO THE DEVELOPMENT OF CANCER IS THE EXTENSION OF UC"

The decision to proceed with surgery in case of LGD, in patients with UC, has to be taken in the course of multidisciplinary consultation with endoscopists, gastroenterologists and pathologists and has to be extensively discussed with the patient, even longer in the not rare case of an asymptomatic patient.

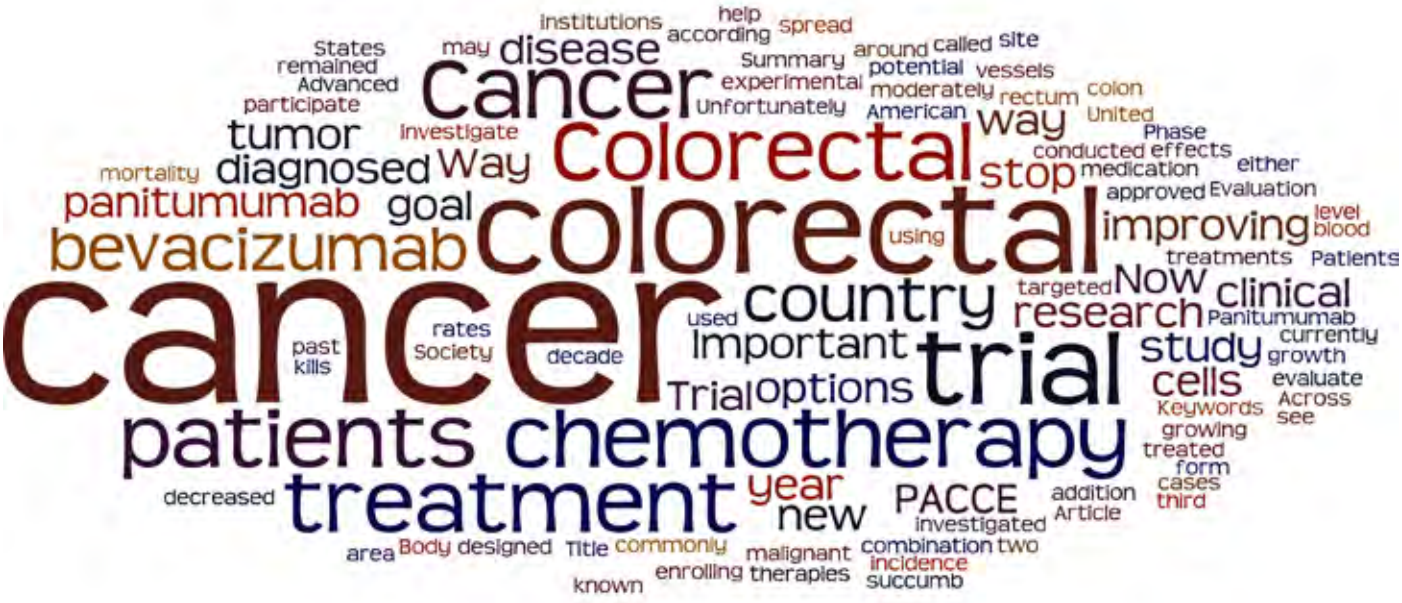
Less obviously, during the multidisciplinary discussions about the proposed route in case of LGD (follow-up versus surgery), we have to give more importance to patients: not every patient is a good candidate for follow-up! Our proposal must be appropriate to the clinical state of the patient who must also be fully aware of the type and frequency of follow-up that is necessary if a conservative approach is chosen.

What do we expect from the next years?

On our whishing list, to improve the outcomes we included:

1. a drug able to control the disease working also as chemoprevention agent
2. an endoscopy with even higher detection modalities, deeply integrating with pathology (beyond actual limits of endomicroscopy)
3. pathological unequivocal markers for early degeneration
4. timely and safe surgery (oncologic when needed) for patients identified by the enhanced endoscopy and pathology

Antonino Spinelli



CRITICAL EVALUATION OF CURRENT CONCEPTS

The full title of Falk Symposium 196 in Frankfurt, March 6 – 7, was Critical evaluation of current concepts and moving to new horizons in the management of IBD. It aimed to critically discuss established and emerging concepts in the diagnosis and treatment of IBD – reflecting the recent advances in the ethiopathogenesis of the disease.

Prof Axel Dignass was the Chair of the Scientific Committee, and he was very pleased to welcome 660 delegates from 51 countries to his home town Frankfurt in Germany.

– There have been many changes in the management of IBD, therefore we have created this programme, he said and thanked the Scientific organization.

Prof Dignass also presented several images of Frankfurt, and pointed out it is the city of the famous German author Goethe (1749 – 1832). He presented a quote from him: *"It is not enough to know, we have to utilize our knowledge."*

– And that fits very well with this Meeting, Prof Dignass said.

Dr Roland Greinwald, Head of Research & Development Dr Falk Pharma (left) and Prof Axel Dignass (right) awarded Konstantinos Papamichail the 1:st Poster Prize.

The gut is a ecosystem

The first Session concerned the "omics" era of research.

Dr Vicky de Preter defined "omic" methodologies.

– It is the study of related sets of biological molecules in a comprehensive manner.

She continued talking about metabolomics in IBD. The potentials for this include differentiating between healthy controls and patients – and studying metabolic differences between IBD subtypes.

– It enables us to link metabolites to biochemical pathways. But we need to validate and confirm this in large clinical trials. In IBD, metabolomics will be continued, she stated.

Prof Arthur Kaser pointed out that there are complex gene-gene-environment interactions in IBD.

– Modelling genetically-affected pathways may open a window to raise and test hypotheses on environmental triggers of disease.

He ended by talking about personalised treatment – i.e. matching treatment to patient with different targeted therapies for different subgroups.

Prof Philippe Seksik talked about the microbiome, and underlined that the gut consists of an *ecosystem*.

– We have to keep this in mind when we are looking at the microbiota. There are many micro organisms – bacteria, virus and fungi, among others.

The human gut microbiota is a real organ with key functions. It is implemented from birth up to two years of age.

– Omics is relevant in studying the microbiota, because it is so complex and difficult, he said.

We need to go from "who is there?" to "what are they doing?" he summarised.

Bowel ultrasound is coming in more countries

Imaging in IBD was next Session's topic. Prof Torsten Kucharzik started this by talking about the role of bowel ultrasonography (US) in IBD.

He underlined the advantage of bowel US for evaluation of stratification and histology.

– Another advantage is evaluation of vascularisation and motility. No other imaging technique can visualise motility as UC, he said and showed images on this.

US is now included in important guidelines – such as ECCO's and ESGAR's.

Prof Kucharzik also described contrast-enhanced US (CEUS) in IBD. He showed an example of differencing an abscess from inflammatory mass, and stated that CEUS should be used to evaluate this. He also urged the audience to be aware of radiation safety, and therefore avoid CT-scan.

– A conservative estimate is that CT causes one tumour per 5 000 investigations.

Transrectal US (TRUS) in perianal Crohn's disease (CD) is equivalent compared to MRI.

– Bowel US has been performed in IBD patients by gastroenterologists only in a

few countries so far. But now, in more and more countries, they are integrating bowel US in their management protocols, Prof Kucharzik continued.

It is an easy to use, accurate, cost-effective and pleasant method for diagnosis and monitoring of IBD, he concluded.

– CEUS may be useful in some situations in IBD – particularly for detection of abscesses, Prof Kucharzik summarised.

The MaRIA index

– Radiologists see things others can't, said Dr Hans Herfarth in his talk about magnetic resonance imaging (MRI).

He continued by presenting a meta-analysis of prospective studies comparing computed tomographic enterography (CT-E) and magnetic resonance enterography (MR-E) in patients with CD.

– Both are the same – there is no difference anymore, he said and demonstrated this with examples.

Dr Herfarth also talked about capsule endoscopy compared to MR-E.

– We performed a small study on this, and with the capsule we saw more – but this had no therapeutic impact.

He presented the Magnetic Resonance Index of Activity (MaRIA), which he thought is great for clinical trials, but not for clinical practice yet.

Diffusion-weighted imaging (DWI) depicts differences in motion of the water molecules in tissue.

– Potential advantages of DWI compared to "conventional" MRI are no need for oral or iv contrast, it enables quantification of inflammation and characterization of inflammation versus fibrosis.

In his summary, Dr Herfarth underlined that rectal contrast significantly increases the sensitivity for MR-E of the colon. He also said that magnetization transfer in MRI and DWI are promising complimentary tools for evaluation of inflammation and fibrosis.

Most patients would disappear

Prof Gerhard Rogler talked about integrating imaging into clinical practice.

– The topic of this Meeting is to take a critical look at current concepts, and I will do that now, he started by saying.

Prof Rogler continued by asking *when* we need monitoring for our IBD patients, and his own answer to this was: At fluctuating disease activity.

He quoted a Treat-to-Target algorithm for CD that stated "Six months intervals between colonoscopy procedures may be a reasonable compromise between selecting a time after which additional mucosal healing is unlikely to occur and a time interval between procedures that would be acceptable to patients".

– Well, I'm not sure on that. If I suggested this to my patients (i.e. colonoscopy every 6:th month), most of them would probably disappear...

Prof Rogler added that he did not believe this was the way to go. Instead US have many advantages he stated.

– I have it in my outpatient clinic.

So, when to use US in IBD? Prof Rogler said for CD it is useful for diagnosis, staging, monitoring of disease course and for complications such as fistulae or stricture.

– For ulcerative colitis (UC) it is useful for diagnosis and monitoring of the disease course. For UC it is also very useful when you have to decide the next step in treatment.

A mix of MRI, US and colonoscopy

Imaging for monitoring will be an essential component of future IBD care, Prof Rogler continued.

– However, in my opinion, imaging should be problem-driven – is there a question to answer, will the results of imaging change treatment – and should not be performed on a strict regular basis.

US may substitute for endoscopy in many cases and situations for the monitoring of IBD patients.

– I think that is the way to go, he said.

New endoscopy techniques will be available at specialised centers for specific management questions, and new MRI techniques will be available more broadly soon.

Hans Herfarth

– In the future, imaging and monitoring of disease activity will guide treatment decisions and optimize therapy. This will pay off – ensure better disease control and a better quality of life for our patients.

Prof Rogler ended his talk by presenting his treatment algorithm, in which a *mix* of MRI, US and colonoscopy is utilized for monitoring of treatment efficacy.

Early recurrence is often anastomotic failure

Surgeon André D'Hoore and Gastroenterologist Prof Gert van Assche had a tandem talk: *Penetrating CD: a balancing act between surgeons and physicians?*

– If you have a patient with abscesses, take the right decision – surgery! Not the wrong decision – further medical treatment, Dr D'Hoore started by saying.

He presented a case history supporting ➤

this, but Prof van Assche presented another CD-case.

– It was a clear cut for surgery, but the patient was referred to us for a second opinion. A multidisciplinary conference – including a surgeon – decided upon medical treatment. The patient is still fine – four years later. So obviously, surgery was not the right decision for *him*, Prof van Assche said.

He continued by presenting an algorithm of intra-abdominal abscess in patients with CD.

– Surgery is one option in the end. Anti-TNF:s is another.

Dr D'Hoore underlined that when surgeons say that a patient has very early recurrence, it is most often an anastomotic failure.

– But we *say* it is recurring disease.

He reminded the audience that surgery for CD in 2015 is minimally invasive, safe, effective and bowel sparing. He also presented a study that showed that percutaneous drainage (PD) results in less morbidity than immediate surgery – and that surgery after PD results in less morbidity than immediate surgery.

– The key to success is the *timing* of surgery. Wean them off steroids first, and treat with anti-TNF:s after, he told the audience.

Most patients will need surgery

Do all patients need surgery after an internal abscess has been drained?

– Not all, but probably a majority, Dr D'Hoore continued.

Prof van Assche pointed out that there is not much in the literature on intra-abdominal abscesses.

– If surgery is inevitable, we *should* go there – not drag patients through medical therapy, he said.

They ended with a summary that they both agreed upon:

Intra-abdominal abscesses in patients with CD usually herald a fistula or a stricture. After percutaneous or surgical drainage most patients will need early elective surgery.

– In selected cases a medical approach with biological therapies can be considered. Early detection of endoscopic recurrence and medical treatment after initial surgery is paramount, Prof van Assche summarised their views.

Flat dysplasia has a significant risk of progression

Another tandem talk between a surgeon and a physician was then held. The topic was IBD with dysplasia-associated mass or lesion / intraepithelial neoplasia (DALM/IEN) and long term disease: Limited resection or proctocolectomy?

Surgeon Alastair Windsor and Gastroenterologist Prof Andreas Sturm together talked about this.

– Dysplastic lesions arising in the colon of IBD patients are a heterogeneous group. The risk for adenocarcinoma is based on the location and appearance of the change, said Prof Sturm.

Flat dysplasia has a significant risk of progression, particularly for high grade dysplasia.

– If typical adenomatous appearance, proximal to colitic zone – perform polypectomy and treat as sporadic adenoma, Prof Sturm said.

If appearance is typical adenomatous, in colitic zone – polypectomy and biopsy from adjacent mucosa, he continued.

– If the histology is typical, consider the polypectomy as sufficient. Lesion should satisfy these criteria: Discrete lesion, complete excision with clear margins, no surrounding flat dysplasia and patient and colon easy to survey.

In case of atypical appearance or adjacent flat dysplasia – regard as DALM and consider colectomy, Prof Sturm summarised.

DALM equals colectomy

Mr Windsor began with a word of caution.

– When you are on the cutting edge, things can go wrong very quickly. *Any* dysplasia is a *bad* dysplasia!

He stated that DALM equals colectomy.

– A very surgical view is to resect the risk.

Mr Windsor presented a study from 2014 in which it was found that the risk of cancer in patients with high grade dysplasia or DALM is substantial.

– Despite low risk for cancer in patients with flat low grade dysplasia, the threshold for surgery should be low given the high prevalence of postoperative histological findings.

Only in selected cases colonoscopic surveillance after discussion of associated risks may be acceptable – provided high patient compliance can be assured.

– Surgery should be considered in all other cases, because it is the only modality that can eliminate the risk of cancer.

Andreas Sturm

Jean-Frederic Colombel

In his summary Mr Windsor said that if a lesion is arising from flat mucosa – *worry!*

– We aim to save lives – not colons, he stated.

IBD patients with cancer

Prof Jean-Frederic Colombel talked about previous cancer and/or lymphoma and refractory IBD.

– This is one of the most critical clinical problems in IBD, he said.

Managing IBD patients with past or current malignancy is an increasingly common problem. But few studies are done in patients with IBD.

Prof Colombel underlined the need for caution using thiopurines if cancer therapy will produce bone marrow suppression.

Laurent Beaugerie

– But fear of using anti-TNF:s in patients with current cancer may not be well-founded, he pointed out.

Decisions about treatment need to be made on a case-by-case basis with an oncologist, taking patient awareness and preferences into consideration.

He ended his talk with recommendations for using immunosuppressants in IBD:

– If there is a past history of cancer, consider the history of the previous cancer (organ, stage, histological type and prognosis). Also consider the time from completion of cancer treatment. Take into account the current severity of IBD and the expected impact of immunosuppressant on the previous cancer.

Rule out active cancer elsewhere and try a step-up approach.

– For a patient with current cancer there is a waiting period for 2 years before immunosuppressants. Treat with 5-ASA, steroids, nutritional therapy and surgery. There is a longer waiting period of 5 years for aggressive cancers such as melanomas, aggressive breast cancer, sarcoma and myelomas.

Sun protection and skin surveillance essential

Prof Laurent Beaugerie then gave a lecture on the safety of thiopurines.

– Investigate patients who develop liver test abnormalities, portal hypertension or fever and/or lymphadenopathy, he said.

Prof Beaugerie talked about myeloid disorders – acute myeloid leukaemia and myelodysplastic syndromes. How do thiopurines promote these disorders? This question caused him to talk about mismatch repair (MMR) cells (a genetic repair pathway).

– Cells with microsatellite instability that are MMR defective escape from the cytotoxicity of thiopurines.

He also talked about urinary tract cancer in patients with IBD. These are prevalent in over 65 year-old patients.

– Consider to limit the use of thiopurines in men over the age of 65.

In young males, consider to limit combo-therapy to 2 years and avoid thiopurines in those Epstein-Barr virus negative.

– Educate patients at diagnosis for long-term sun protection and skin surveillance, and be aware of the long-term risk of myeloid disorders, were Prof Beaugerie's take-home messages.

Calcineurin inhibitors normally give an immediate response

Advices on best practice for thiopurines in IBD were presented by Prof Eduard F. Stange.

– Respect proper indications. Evidence for thiopurines are based for steroid dependence – not for induction, he pointed out.

Clearly, thiopurines are working when they enhance the effect of infliximab where they prevent antibody formation, Prof Stange continued.

– Wait for delayed response, 3 – 6 months, but stop it if you fail to wean steroids.

For best practice, there is an absolute requirement for leukocyte counts and liver enzymes.

– You have to keep checking these data.

Switch to 6-MP (mercaptopurine) from azathiopurine and give full dose at night time.

– Then the patient will sleep through the nauseating phase. Drug levels are helpful in non-response, but not mandatory for responders.

Prof Stange also talked about methotrexate in CD. It can be used for steroid-dependent CD with or without anti-TNF, but he pointed out that the evidence level for combo with infliximab is not high.

Calcineurin inhibitors in IBD are evidence based for steroid refractory UC. They are indicated for induction of remission. They normally give an immediate response – in days, he said.

– The biggest disadvantage is that there is no interest from the industry. In Germany it is not labelled at all – but I use it in my clinic.

On tacrolimus Prof Stange said an open label trial showed that it was as effective as infliximab in steroid-refractory UC.

Magnitude of costs drive change

The future of academic gastroenterology: Is the past a prologue to the future?

This was the title for a Special Lecture, given by Dr Daniel K. Podolsky.

– As a leader for a medical centre, I have to ensure the best care for our patients. I also have to face the expectations of our GI-specialists, Dr Podolsky said.

He said that there are two things that are certain, and one of them is that the world is changing.

– I will come back to the other certainty at the end of my talk.

After presenting facts on US health care (spending a total of more than 825 million dollars in 2012), he asked a question.

– Why will rising costs drive change *now* when it hasn't in the past?

His answer was that the sheer *magnitude* of costs makes it inescapable, and that patients and providers will be acutely aware and make decisions based on price.

Healthcare is now provider centered, price driven and has hidden price and quality info. In the future it will be individual price centered, value driven and have transparent price and quality.

– Darwinian forces are closing in on academic medical centers (AMC). When payers are going to pay for their care, they are going to ask for price and quality. Payers are forming narrow networks, that are excluding AMCs. Risk is put onto providers – you will receive this amount of money for this care, but if you spend more, it will be your problem, Dr Podolsky said.

Same as on the threshold of modern medicine

So what will AMCs response be?

According to Dr Podolsky they will supersize, have a systemic approach to care delivery and seek out new competences such as integration, coordination, efficiency and population health.

– The vulnerabilities of growth are that not all missions are scaleable – and growth beyond optimal size can lead to diffuseness and loss of synergies.

GI divisions have to escape the trap of being defined by technology. They have to ➤

seize ownership of the *new* value proposition: Disease management, ensuring patients achieve the best outcomes with most effective use of resources.

– When ultimate progress in diagnostic technology and self-correcting automated therapy has taken place, the ultimate value of the gastroenterologist will be the intangible value of the humanist caring for the patient – i.e. the *same* as it was at the threshold of modern scientific medicine, Prof Podolsky stated.

Which led him to his second "certainty", which he said also was his conclusion.

– There will be ups and downs on the road ahead. We have to be resilient to that!

Autologous HSCT

Prof Matthieu Allez talked about cell-based therapies in IBD.

– I will concentrate on three therapies – hematopoietic stem cell transplantation (HSCT), mesenchymal stem cells and ex vivo expansion of regulatory T cells, he said.

Prof Allez described the study design of the ASTIC trial (Autologous Stem Cell Transplantation International CD Trial).

This was stopped because one of the patients died.

– Autologous HSCT is successful in inducing drug-free remission in CD with severe and highly refractory disease. Considering the risk of the procedure, it should be proposed only in patients with active CD refractory to immunosuppressants and biologics, and after consideration of all therapeutic options – including surgery, he stated.

On mesenchymal stem cells, preliminary results support further evaluation.

– Positive experiences are reported in graft-versus-host disease, and in CD for luminal and fistulizing disease.

Tr1 cells produce TGFβ, IL10 and IFNγ, but no IL2 and no IL4. A single injection of ex vivo expanded CD4 Tr1 cells (autologous ovalbumin-specific Tregs) showed some efficacy and a good tolerability in a phase I/II study, Prof Allez ended his talk.

Strategy should be endoscopy-driven

70 % of patients with CD need intestinal resection, and 70 % of patients who have had operations need further surgery.

– Within one year of surgery, endoscopic recurrence occurs at the anastomosis in 90 % of patients, said Prof Pierre Michetti.

His lecture was on postsurgical prophylaxis in CD, and he stated that there has to be a strategy for this. Can we identify the patients at higher risk for relapse?

"ON MESENCHYMAL STEM CELLS, PRELIMINARY RESULTS SUPPORT FURTHER EVALUATION"

By using data from the Swiss cohort, Prof Michetti pointed out that surgery for CD is associated with strictures and penetrating disease phenotype. Recurrence is the role, but he also said that in the cohort they could not find any data that indicate that recurrence has to do with the age of the patient.

– Which agents should we use? A Cochrane review shows benefit for azathioprine over 5-ASA in preventing recurrence. Anti-TNF:s show a big difference compared to placebo.

Prof Michetti also described the Post Operative Crohn's Endoscopic Recurrence (POCER) study.

– The results show that active care is useful. It also found that the difference between adalimumab given to patients from start, versus patients who had adalimumab step-up, was not significantly different.

So the strategy for these patients after ileal resection should, according to Prof Michetti, be endoscopy-driven.

– Rutgeerts score is useful. Patients with a low score have very few recurrences, but those with a high score have many.

He summarised his talk by saying that several studies also suggest it is very useful to follow up with calprotectin measurements.

– And the antibiotic imidazole for three months works in some patients, but not all.

Treat-to-target in IBD

Current therapeutic strategies for IBD do not modify long-term sequelae. Therapies are based on symptoms, not prognosis.

– Similar to other chronic diseases, treating to prognostic markers can improve long-term outcomes, Prof Stephen B. Hanauer said.

He was talking on the treat-to-target concept. This was originally developed in cardiovascular (CV) disease, which is common and associated with considerable morbidity and mortality.

– Trial designs in CV progressed from "treatment versus placebo" to "standard treatment versus intensive treatment".

Symptom-control strategies evolved into preventive treatment strategies, Prof Hanauer explained.

Today this concept is also used in hypertension, type 2 diabetes and rheumatoid arthritis.

– They are all chronic progressive diseases, and failure to treat early can lead to serious complications and disability.

Upon treat-to-target in IBD, Prof Hanauer said that while remission should be a clear target based on available evidence, low disease activity may be an acceptable alternative therapeutic goal – particularly in established disease.

– Until the desired treatment target is reached, drug therapy should be adjusted at least every 3 months. Measures of disease activity must be obtained and documented regularly. The patient has to be informed about the treatment target – and the strategy to reach this target.

He concluded his talk by stating that prospective studies are needed to confirm prognostic criteria, relevance of individual targets, impact on long-term outcomes and socioeconomic values of targeted approach.

Per Lundblad

CONGRESSES 2015–2016

Digestive Disease Week
May 16 - 19 2015
Washinton DC USA
www.ddw.org

Gastro Update Europe
June 12 - 13 2015
Budapest, Hungary
www.gastro-update-europe.eu/

International Congress of Mucosal Immunology
July 14 - 18 2015
Berlin, Germany
http://www.socmucimm.org/meetings-events/icm15/

Mastering Clinical Challenges and Emerging Therapies in IBD
July 18 2015
Chicago, USA
http://www.imedex.com/challenges-therapies-ibd-conference/

European Society of Coloproctology
September 23 - 25 2015
Dublin, Ireland
www.escp.eu.com/

Falk Symposium 198
IBD: East Meets West
September 11 - 12 2015
Shenzhen, China
www.drfalkpharma.com/uploads/tx_tocfpshoperw/FS198_Shenzhen_2015_Announcement_01.pdf

Gastro 2015 AGW/WGO International Congress
September 28 - October 2 2015
Brisbane, Queensland Australia
www.gastro2015.com/

Japan Digestive Disease Week
October 8 - 11 2015
Tokyo, Japan
www.jddw.jp/jddw2015/en/index.html

XXI Russian Gastroenterological Week
October 12 - 14 2015
Moscow, Russian Federation
www.gastro.ru/

Falk Symposium 200. Therapeutic Strategies in Diseases of the Digestive Tract - 2015 and Beyond
October 16 - 17 2015
Freiburg, Germany
www.drfalkpharma.com/uploads/tx_tocfpshoperw/FS200_Freiburg_2015_Announcement_01.pdf

UEG Week
October 24 - 28 2015
Barcelona, Spain
www.ueg.eu/week/

Advances in IBD
December 10 - 12 2015
Orlando, Florida
www.advancesinibd.com/

Canadian Digestive Diseases Week (CDDW 2016)
February 26 - 29 2016
Montreal, Canada
www.cag-acg.org/

ECCO Congress
March 16 – 19 2016
Amsterdam, The Netherlands
https://www.ecco-ibd.eu/ecco16