CONGRESS
iBD NEWS #1/16

IRELAND

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

The big questions in IBD · ECCO Congress 2016
Validation of the IBD disability index

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

B
Ekonomibrev

SVERIGE
PORTO BETALT
PORT PAYÉ

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.

Editor in Chief:
Tom Øresland
Faculty of medicine, University of Oslo
Akershus University Hospital
Oslo, Norway
tom.oresland@ahus.no

Senior writer:
Per Lundblad
per@mediahuset.se

Advertising:
Advertising space within IBD News is sold locally in each country.
As a result of placing an advertisement within this magazine you will reach every specialist in the field of Gastroenterology in these countries.
For questions concerning advertising:
Olle Lundblad
olle@mediahuset.se
Kristoffer Lundblad
kristoffer@mediahuset.se

Production:
Mediahuset i Göteborg AB
Marieholmsgatan 10C
SE-415 02 Göteborg, Sweden
www.mediahuset.se

Layout:
Eva-Lotta Emilsdotter
lotta@mediahuset.se

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

Cover photo:
Fotolia

Content:

EDITORIAL
TOM ØRESLAND

THE ECCO SUCCESS

Just returned from the ECCO congress, I now realize that the number one arena for IBD surgery updates must be the S-ECCO masterclass course. A full and long day packed with very good talks, often as pro – con debates, and even a very good tandem talk on early surgery or continued extensive medication, given by Andre D'Hoore and Severine Vermeire. The communicating skills of the speakers were excellent and the topics covered the main controversies in IBD surgery - notably more than two thirds were on Crohn's disease related problems. It is very evident that our scientific bases for the different treatment options are rather weak. Most obvious in the treatment of perianal Crohn's and fistula - a miserable condition with an abundance of options, the one not superior to the other it seems. Timing of surgery is another problem that was debated, and it now seems gastroenterologists and surgeons work together much better than we did a decade ago. This was also shown that among the 250 course participants - one third were actually gastroenterologists (the number of participants was limited and some could unfortunately not get in).

The whole ECCO Congress seems a success with an abundance of posters and small parallel sessions. In the main hall was a traditional ECCO program with the first day devoted to the very small bits that we think maybe causative for disease, the talks that are so difficult to follow. Luckily our senior writer Per Lundblad will update you on this in an understandable way further into this issue. The following days were mainly focused on treatment. The industry is providing us with more and more pharmaceutical options and the possibilities for personalized treatment are increasing. However there are pitfalls in that it is becoming more and more complex and that doctors may focus so much on the options that they eventually loose focus on the patient's Quality of life, trying several suboptimal regimens after each other over a long time. This is where MDT conferences and surgeons can help.

Enjoy reading this IBD Congress News issue and please give feedback on how we can improve. The IBD Congress News aims to be an easy to understand comprehensive overview of the research and treatment fronts in IBD.

TOM ØRESLAND

THE BIG QUESTIONS IN IBD

In late November 2015, 850 delegates from 49 countries came to attend the IBD 12 Congress, supported by Ferring Pharmaceuticals. They were all greeted by Prof Michael Kamm, who was the Chair. – Welcome to Lisbon, one of the oldest capitals in the world, he said.

The title for the Congress was *The Big Questions in IBD*. Prof Kamm explained that this was chosen to raise awareness that many unknowns still exists in optimising management, but that bringing together experts in the field we can start to collaborate to develop practical answers.

The logo was a fingerprint.

– This was chosen by the Scientific Committee. The fingerprint concept focuses on the idea of individualisation of IBD management – as unique as a fingerprint.

Prof Kamm also pointed out that they had an exciting programme.

– State of the Art lectures will showcase the latest evidence and thinking. Debates – a very practical way to shed light on different views – allow different perspectives to be presented to provide a broader understanding of the evidence. Case studies help to make the latest data relevant to the real world, and simplify uptake of the evidence into practice.

He ended his opening speech by thanking Ferring for their long-standing and generous commitment to independent medical education.

Risk factors differ

Dr Siew Ng was the first speaker in Lisbon. She stated that IBD is a modern disease of modern times that is rooted in industrialisation of society, and continued with a prediction of the global burden of IBD in 2025.

– There will be more than 5 million affected worldwide, 0,5 % of the population in the highest prevalence regions, Dr Ng said.

There is a steep rise in the rate of incidence in newly industrialised countries.

– Even if the prevalence plateaus at 0,1 %, China will have over 1,5 million cases of IBD by 2025!

She described the hygiene hypothesis: Modern living conditions cause defective maturation of regulatory T-cells and regulatory APC (= anaphase-promoting complex, plays a key role in the cell cycle) leading to development of immune mediated diseases.

She continued with early GI infections and risk of IBD.

– There is a proven potential, especially for *Campylobacter*, for altering intestinal barrier and promoting inflammatory responses.

Dr Ng said that risk factors differ at different stages of industrialisation – hygiene factors for developing countries and immunological factors for developed countries. Antibiotics in childhood is a divergent risk factor. Breast feeding is consistently protective.

Environmental determinates of IBD differently influence populations living in different world regions, which may explain the difference in incidence.

– I think the answer lies in the gut microbiota, and how it interacts with the genes.

Changes in gut microbiota, mediated via environmental factors, may contribute to the recent IBD "epidemic", Dr Ng ended her talk.

The beginning of a new era

The first debate was on manipulating the microbiota with food and antibiotics – is

this effective in decreasing IBD inflammation? Prof Peter Gibson thought so.

He described the current status of therapeutic manipulation of the microbiome.

– *Why* is dietary therapy important? There are many reasons: Patients want it because it provides a degree of self-control – and they are already doing it. One third of patients on gluten-free diets claim this decreases flares. And there is already unequivocal evidence in IBD – exclusive enteral nutrition works well!

He presented data from a randomised study presented at the UEGW 2015 on the effect of moderate versus low FODMAP diet on abdominal symptoms. (FODMAP stands for Fermentable, Oligosaccharides, Disaccharides, Monosaccharides And Polysols).

– There was a significant effect for low FODMAPs. They work very nicely for symptoms, but does not influence inflammation.

We are at the beginning of a new era for therapeutic manipulation of the microbiome, according to Prof Gibson.

– There are a lot of potential targets. The microbiome is a *major* functioning organ, and it's abnormal in IBD – is this the cause or the effect? Manipulating it represents a major therapeutic opportunity!

In his summary, Prof Gibson said TMM has strong theoretical basis for benefit for gut inflammation.

Essential investigative tools are emerging – we now have enough knowledge to look at the microbiome as a function of an organ.

– There are already evidence of benefit for therapeutic manipulation of the microbiome, using blunt instruments such as antibiotics and enteral nutrition – and relatively impotent instruments such as probiotics and proof-of-concept studies.

Different enterotypes and geographical differences

Prof Peter Lakatos did not agree.

– When it comes to diet and antibiotics, studies are inconsistent and subject to methodological limitations, he underlined and asked the audience how precisely they recalled last Thursday's dinner.

With this he underlined that diet is difficult to study. There are methodological limitations, mainly associative studies on disease susceptibility and no formal intervention studies.

– What do our UC patients eat? Most of them eat as the normal population.

Many factors influence the core human microbiome.

– What is the "normal" we wish to achieve?

Prof Lakatos also stressed there are different enterotypes (=a classification of living organism based on its bacteriological ecosystem in the gut microbiome), and that geographical differences still is an important point. Inter-individual variants also have to be taken into account.

In his summary he also pointed out that in studies on antibiotics, most were negative with the exception of postoperative short term use.

Unique management issues in Asian patients

A case that concerned a Chinese IBD patient in Australia was presented by Dr Bei Ye. It was a 54 year old male, who was a migrant from Shanghai in China to Australia in 1989 (then aged 28). He had largely adopted a western diet, and was diagnosed with Crohn's disease (CD) in 1997.

Dr Ye then presented a background on the incidence of IBD in Asia-Pacific region.

– It is increasing, probably related to increased urbanisation and changing environment.

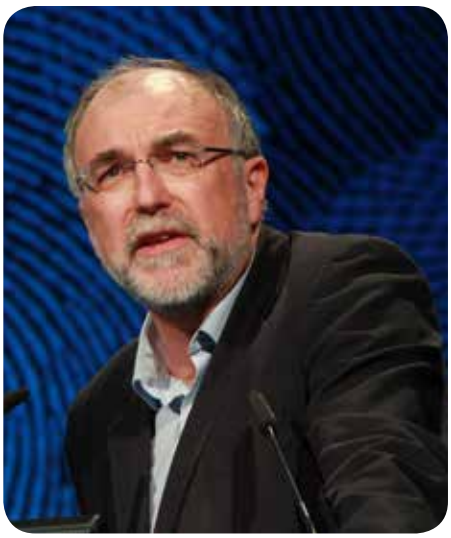
A study from 2015 showed that adult immigrants from low to high IBD incidence countries do *not* have an increased risk of IBD related to immigration.

– In contrast, immigration at a younger age – or the children of adult immigrants – begin to adopt the higher risk of their new country, she continued.

Findings from two studies from 2013 show that gut microbiota are influenced by ethnicity, geography and presence of disease.

The patient in the case had spontaneous bowel perforation 10 years after diagnosis. An ileal resection and ileostomy was performed. He commenced mercatopurine post-operatively and responded well.

– However, thiopurine induced leucopoenia is much more common in Asians. Thiopurine methyltransferase (TMPT) mutations are less frequent, and in Asians only accounts for 3,8 % of thiopurine induced leucopenia. So I believe that thiopurines in Asians should be initiated with caution, Dr Ye said.



Peter Gibson

Michael Kamm

The patient was found to have a hepatitis B infection. The ileostomy was reversed, and he started on a combination of thiopurine and allopurinol therapy.

– This patient responded well. But there are unique management issues in Asian patients – such as potential thiopurine adverse effects, Dr Ye summarised.

Therapeutic strategies should be different for the elderly

A session devoted to the older patient started with a debate.

Prof Jean-Frédéric Colombel had a talk in which he stated that the treatment of IBD in the elderly should be different to younger patients. He began this by quoting the famous French author Victor Hugo.

– Forty years is the old age of the youth. Sixty years is the youth of the old age...

Why should the treatment be different? According to Prof Colombel, the phenotype and natural history of the disease is different.

– And the risks and efficacy of IBD therapies are different – and the therapeutic strategies are different, he said.

Prof Colombel presented data from 2014 that showed that IBD location is different according to age of onset. So is the progression of CD.

– This affects our choice of therapy.

He underlined that IBD patients over 65 in average have 9 different drugs prescribed. They also have a higher risk when they receive surgery. Azathioprine also carries a significantly higher risk when prescribed to those over 65.

– Based on this, I state that therapeutic strategies should be different. In ulcerative colitis (UC) in the elderly, I personally prefer methotrexate and thiopurines. At any point surgery should be considered!

Jean-Frédéric Colombel

For CD, Prof Colombel suggested – and he admitted this is not based on data – that one should start with 5-ASA. If this is not enough, continue with budesonide MMX, then with methotrexate and, if not this is successful either, vedolizumab. The last resort is anti-TNF.

– And do not forget to always consider surgery.

Individualised medicine goes for the elderly too

Prof Severine Vermeire took the opposite view.

– The treatment of IBD in the elderly should *not* be different to younger patients!

She motivated this by stating that everybody deserves deep remission. This means clinical and biological remision with mucosal healing and no steroids.

> "MANY ELDERLY REMAINS ON A LONG DURATION OF STEROIDS. THEY ARE EXCLUDED FROM TRIALS"

She quoted Prof Colombel's claim that elderly-onset patients have a more benign disease course.

– But not all "elderly IBD patients" have been diagnosed after 60.

Prof Vermeire presented data from 11 724 incident cases of IBD, and pointed out that only 5 % of CD cases, and 11 % of UC cases, were diagnosed when the patient was over 60 years of age.

– They have had this disease for many years. I think individualised medicine is what this Meeting is all about – and that goes for the elderly too! They deserve the best drugs.

She said there is some evidence for a lower rate of short term clinical response for anti-TNF in the elderly – but the long term outcome in responding patients are equally good.

– Patient selection is *crucial*! The rate of adverse events is overall higher in elderly patients, regardless of the drug given. So it is important to check for comorbidities, polypharmacy and possible interactions, she finished.

Severine Vermeire

In the discussion afterwards they both agreed that timely surgery should not be avoided – only emergency surgery should.

– The age limit for a pouch has vanished. It used to be below 60, but today our surgeons perform pouches in 75-year olds. If the anal sphincter is still functioning, there's no reason not to, said Prof Vermeire.

Prof Colombel pointed out that we need trials in elderly patients.

– Today they are *excluded* from trials, so we really don't know anything. That is one reason why so many elderly remains on a long duration of steroids.

IBD and cancer

Treatment of IBD in patients with past or current cancer, was the topic for Prof Laurent Beaugerie's lecture.

– Data from treatment of rheumatoid arthritis (RA) tells us that anti-TNF is neutral in terms of cancer – but they bring a twofold risk for melanoma, Prof Beaugerie initially stated.

For patients with IBD and current cancer there are few data. However, there is a general agreement that immunosuppressants should be stopped until the cancer is controlled, he continued.

There is an increased risk of IBD flare under, or after, hormone therapy for cancer. A potential exacerbation of IBD colitis is associated with the use of docetaxel for breast cancer, ipilimumab for melanoma, and sunitinib and sorafinib for renal cell carcinoma.

On initiation of immunosuppressants for IBD in patients with *prior* cancer, Prof Beaugerie underlined that compared to ➤

sex- and age-matched individuals of *general* population, patients with prior cancer are more prone to develop a new cancer.

– Or to have already developed a growing latent cancer!

So when initiating or resuming immunosuppressive therapy in a patient with successfully treated cancer, one should be sure of the absence of second growing latent cancer.

Is there excess risk of new cancer attributable to this therapy? According to Prof Beaugerie, studies in chronic inflammatory diseases are underpowered – but there is no alarming signal existing.

Given the sites of immune blockade, there is no rationale for impact of vedolizumab on carcinogenesis of extra-digestive cancers – but prudence is needed regarding digestive cancers.

– Choose the immunosuppressive drugs according to their potential carcinogenic effect towards cancer, including the previous one. And always cooperate with oncologists, was his final message.

Steroids are rapid symptomatic relievers

Do we still need steroids for treatment of IBD patients? This was the focus for a new debate.

Prof Axel Dignass, was the first speaker.

– I admit that I still use steroids, and I will continue to use them. But I hate their side-effects, he said.

Steroids are probably still one of the most effective drugs we have in our IBD therapeutic armamentarium – inducing clinical remission and even mucosal healing. Steroids use and response are important predictors for outcome of disease, and can therefore serve as a prognostic marker in IBD. They have serious side-effects that can be reduced or avoided by appropriate use.

– But steroids are not indicated for maintenance therapy, Prof Dignass underlined.

They are good for short term induction to relieve symptoms – if one uses the correct dose and formulation.

– Use steroids as bridging therapy and try to achieve steroid-free remission with 5-ASA, immunosuppressants or biologics. Stop early if there is no response – for i.v. steroids after 4 - 7 days and for oral after 2 - 4 weeks, were Prof Dignass' key messages.

Dr Allesandro Armuzzi admitted that steroids are rapid symptomatic relievers, but stressed that they have no efficacy for remission maintenance.

– We should know that steroid-associated resistance or dependency are frequent!

Dr Armuzzi presented a long, detailed list of cosmetic, ocular, muscoskeletal, metabolic and psychological side effects of corticosteroids. He also pointed out that they carry an increased risk of opportunistic infections and increased risk for growth retardation in children.

– There are many potential serious adverse events with steroids, but they have little impact on mucosal lesions, he stated.

Look behind the mucosa wall

Imaging in IBD is for diagnosing intestinal inflammation, ruling out other differential-diagnosis and distinguishing between UC and CD. Also to determine disease extent, detect extra-intestinal manifestations and exclude complications, said Prof Andreas Sturm.

His lecture was titled *Cross-sectional imaging is the future of disease monitoring.*

– Imaging is also essential for monitoring therapy response and evaluating reasons for loss of response – and for determining the optimal point for therapy change. And we have very good scores for this, he continued.

The cross-sectional imaging tools are ultrasound (US), MRI and CT.

Prof Sturm showed images from contrast-enhanced US, and pointed out that in these one can see the inflammation.

– That is not possible with endoscopy!

The applications of cross-sectional imaging techniques in IBD are manifold.

– In cases of *suspected* CD, it is recommended in order to detect, stage and classify disease behaviour. In *established* CD, it assists to select treatment, to assess response and to quantify tissue damage.

Dr Sturm also said that in perianal fistulising CD, it complements the examination under anaesthesia.

– In suspected UC with a discontinuous endoscopic appearance of colonic inflammation, cross-sectional imaging should be considered to exclude small bowel inflammation indicating the differential diagnosis with CD.

In his summary, he pointed out that cross-sectional imaging is the only non-invasive technique to look behind the mucosa wall and gain a picture of the entire abdomen.

Andreas Sturm

Functional imaging

But Prof Ralf Kiesslich did not think that this imaging technique is the future of disease monitoring.

– Not at all, if you think about cancer progression, he said.

Prof Kiesslich presented data on the colon cancer incidence in Northern California 1998 - 2010. These showed that the incidence is 60 % higher in IBD patients – with no decreased incidence over time.

– The surveillance strategy is high-definition endoscopy!

He continued by quoting an article in Gastroenterology on surveillance and management of dysplasia in IBD: When performing surveillance with standard or high definition endoscopy, chromoendoscopy is recommended rather than white light endoscopy.

– Narrow band imaging (NBI) does not improve the detection of neoplasia in patients with UC, compared to high definition endoscopy, according to a randomised crossover trial. In addition, NBI proves unsatisfactory for differentiating neoplastic from non-neoplastic mucosa.

Prof Kiesslich also presented a study on methylene blue capsules with MMX technology, which are applied during bowel preparation. The first study proved successful.

– Two new huge studies – in screening and surveillance – are ongoing. Drug-based chromoendoscopy could be a reality soon, and standardise chromoendoscopy, he envisioned.

Finally Prof Kiesslich described endomicroscopy – a technique he called functional imaging.

– It allows to define local barrier dysfunction in IBD patients, and endomicroscopy can predict fares in IBD.

In his summary, he said that endoscopy has a pivotal role for detection of lesions and cancer.

Consider consequence of relapse

De-escalating therapy in IBD - when and how? was the title of Dr Filip Baert's talk.

– Why de-escalate? Because of safety concerns such as infections, malignancies, disabling side effects and costs – and that it is often the patient's choice, he explained.

When we consider de-escalating or stopping, in CD we also have to consider the disease behaviour and bowel extent at risk, and in UC the risk of colectomy and cancer.

– Always ask yourself: Do I have a back-up treatment?

For anti-TNFs decreasing dosage or increasing interval can be considered in patients in clinical remission who have elevated trough levels. For azathioprine-6MP, dose reduction is not recommended, unless 6-TGN/MCV levels are supra-therapeutic – or if the patient has persistent significant leucopenia. Steroids should always be tapered and stopped.

"TWO PROSPECTIVE TRIALS – SPARE AND CURE – OM DE-ESCALATION ARE NOW ONGOING"

A study from 2012 on infliximab withdrawal in patients in steady remission, receiving prolonged combination therapy with an immunosuppressant in CD, showed a relapse rate of 43,9 % a 1 year, and a 52,2 % relapse at 2 years.

– Anti-TNF is the safest of the two drugs, so therefore it is stopping the immunosuppressant that is of highest interest, Dr Baert underlined.

Before de-escalating, consider incidence, severity and consequence of IBD relapse – and the efficacy and safety of retreatment, was his first take-home message.

– Use objective markers, such as biomarkers, endoscopy and serum concentrations, was his second.

Two prospective trials – SPARE and CURE – on de-escalation are now ongoing, he ended his talk.

Clinical scenarios where measuring drug levels and antibodies are useful

Prof Severine Vermeire talked about drug levels. Are these the future of personalised therapy?

She began by asking the audience if they are checking infliximab trough levels (= the lowest level of drug in serum, just before the next infusion) in their patients with IBD.

It turned out that 56,1 % of the delegates did. The most common reason for not doing it (40,5 %) was that they do not have access to the technique. The remaining 3,4 % had chosen the answering alternative that they were not convinced trough levels matter.

– The whole story about drug levels started 15 years ago when an article from Filipe – the previous speaker – was printed in NEJM: *The influence of immunogenicity on the long-term efficacy of infliximab in CD,* Prof Vermeire continued.

There are interindividual differences with respect to efficacy of anti-TNFs. 10 - 20 % of patients are primary non-responders, 30 % are secondary non-responders and 10 % have infusion reactions or delayed hypersensitivity.

Therapeutic drug monitoring (TDM) is measuring of drug concentration in blood to help individual dose adjustment.

Filip Baert

Simon Travis

– That is what we are doing now. But in the future more factors (demographic etc.) will be included.

There are several clinical scenarios where measuring drug levels and antibodies are useful: In loss of response, primary non-response, maintenance of response and remission, following drug holiday and restart – and when patients want to stop immunomodulators.

De-escalate in supra-therapeutic levels

Prof Vermeire described the TAXIT trial, in which the surprising finding was that only 44 % of patients were on the expected drug levels.

– Those with sub-therapeutic levels we tried to optimise, and it did help. But once you have optimised, there's no need to constantly measure drug levels. 1 - 2 measures per year is enough.

In her conclusions, Prof Vermeire said that in the absence of prospective studies, systematic therapeutic drug monitoring is not recommended if the patient is in remission.

– However, do not wait until loss of response occurs! Measure early after induction, and optimise early. And remember that TDM should work in both directions – *de-escalate* in supra-therapeutic levels, and use TDM assistance in stopping immunomodulators.

From symptoms to no inflammation

Is the treatment paradigm of mild to moderate UC changing? Prof Michael Kamm stated it has in his lecture.

– In the last ten years, we had changes in treatment target, monitoring, big changes in drugs and how to use them – and also new treatments, he initially established.

Treatment targets have gone from treating symptoms to mucosal healing and no inflammation. In order to illustrate why this development has taken place, he presented data from Norway 2007 that showed that mucosal healing was associated with an outcome of avoiding colectomy.

– And at the DDW in 2015, it was shown that mucosal healing was a predictor of clinical outcomes – and that even mucosal *improvement* predicts better outcomes!

Prof Kamm reminded the audience that inflammation is associated with an increased cancer risk. A study from 2014 on mesalazine intensification in quiescent UC effect on calprotectin was shown to be effective for continued remission with faecal calprotectin less than 50ug/g.

– I love calprotectin as a marker – it's so easy and cheap to use.

Treatments have changed - not the paradigm

There has been some big changes to 5-ASA use: Higher 5-ASA content per dose, which means less tablets – and better compliance. Once per day dosing means taking tablets less often – and gives better compliance, he said.

– We also have newer formulations, with better release and more use of 5-ASA in acute UC, which means less steroids. Then on the other end we have a new drug – vedolizumab – that is a good option.

At the end of his talk he mentioned curcumin – a potent anti-inflammatory and cancer preventive molecule produced by some plants – as an attractive option to our standard therapies.

A study on faecal microbiota transplant (FMT) that Prof Kamm presented had a quarter of the patients in the active arm reaching remission. He ended his talk by presenting an invention of a new technique for delivery of stool: Stool containing capsules – that has been nick-named "crapsules".

– So indeed the paradigm is changing!

– Treatments have changed – but not the *paradigm*, was Prof Simon Travis opinion.

He based this statement on the goals for therapy: To achieve remission, maintain remission and to avoid complications.

– These goals are still the same. 60 years ago we looked for histology and endoscop-

ic remission. So what has really changed?

Prof Travis said he agreed that the *goal-posts* have changed.

– We are now trying to reach the target of no signs of inflammation. The third component of the old paradigm was to avoid complications. So keep sailing – straight as an arrow!

"Don't waste time"

Prof Kamm then continued to talk about acute severe UC, that most commonly occurs in the first year of disease. According to him, it is the most critical stage we face of UC.

– The reason for this is mortality. In two national studies on colectomy for UC, the acute patients had a mortality of 4 %. That's one in twenty-five!

According to ECCO guidelines, the patient should be treated with i.v. steroids first – but the guidelines also underlines that 40 % are steroid refractory.

– So if the patient that arrives has been on steroids – *don't waste time,* use something stronger and more effective!

One such drug is cyclosporine. A low dose (2mg/kg/day) is safe and effective.

– It is a great drug – but you have to know how to use it. It won't compensate for incompetence.

Physician - surgeon communication is mandatory

The other option in fulminant colitis is infliximab. Prof Kamm presented the first study – from Sweden 2005 – that showed a significant difference over placebo, already after one dose.

If the patient has the first severe episode, and is not on a thiopurine, one can choose *either* cyclosporine or infliximab. If it is the first episode, not on a thiopurine but have failed cyclosporine – use infliximab. If the patient *is* on thiopurine – choose infliximab.

– But remember infliximab is lost into the bowel lumen during acute inflammation, so the concentration of the drug in the stool is higher in non-responders than responders, he continued.

What about the effect of prior drug treatment on surgical outcome?

– Numeral series have demonstrated that prior cyclosporine does not impair surgical outcome. The data on infliximab is conflicting, Prof Kamm said.

He emphasized that drug therapy should be used without putting the patient at risk.

His take-home messages were several:

– In acute severe colitis act quickly and consistently. Don't persist with steroids, if the patient has failed or is failing.

He stressed the importance of physician - surgeon communication, and advocated a constant review – with a consultation twice daily.

– The best drug is the one you can use properly. Be strong, be brave – but don't be foolish!

Choices for therapy are increasing

The last Session in Lisbon was entitled *How can I choose the right drug?* Prof Axel Dignass talked about the place for vedolizumab, and began by describing the mechanism of the drug.

– It is selective inhibition of leucocyte adhesion, he explained.

Integrins on the surface of leucocytes interact with adressins on the epithelium. Vedolizumab specifically binds to the α4β7 integrin, blocking its interaction with mucosal addressin cell adhesion molecule-1 (MAdCAM-1), which is mainly expressed on gut endothelial cells.

Vedolizumab is slow acting. In a tough-to-treat CD patient population significant difference came first at week 10.

– The key message here is to allow the drug to take time.

Another drug, ertrolizumab, also use this mechanism and is at present in trials in IBD.

– In a few years I expect that we will have more drugs with this mode of action, Prof Dignass continued.

He presented data from a phase II study on ertrolizumab. They showed 21 % of UC patients to achieve remission in week 10 - and 44 % in anti-TNF naive patients.

There are also many conventional drugs, and Prof Dignass listed them. He reminded the audience of surgery being one option – especially for strictures, neoplasia, refractory disease and therapy-associated side effects.

– Therapy of IBD becomes more complex with more choices. We have to consider specific patient profiles and the mechanisms of different drugs in order to ensure an evidence-based and individualised IBD treatment. But this is feasible, was his conclusion.

Per Lundblad

VALIDATION OF THE INFLAMMATORY BOWEL DISEASE DISABILITY INDEX

Similarly to rheumatoid arthritis or multiple sclerosis (1,2), current therapeutic strategies in inflammatory bowel disease (IBD) are evolving, with the objective of avoiding disability.

Indeed, IBD is known to affect physical, psychological, familial and social dimensions of life (3,4).Disability indexes have been developed and validated in other chronic progressive diseases, such as the Health Assessment Questionnaire (HAQ) for rheumatoid arthritis (RA) and the expanded disability status scale (EDSS) for multiple sclerosis (MS). These instruments have been used in disease-modification trials (5,6) which assess the long-term effectiveness of different treatment algorithms. Given that UC and CD are chronic disabling diseases an international collaboration was initiated, which led to the development according to the WHO classification of the first IBD Disability index (IBD-DI), namely the International Classification of Functioning, Disability and Health (ICF) (7). Accordingly, the aim of Epimad's team was to validate the IBD-DI in an independent cohort of patients with IBD; to develop a valid scoring system for the IBD-DI to be used in clinical trials and cohort studies and to evaluate using this instrument the disability status of a well-defined population-based cohort of French IBD patients.

From February 2012 to March 2014, the IBD-DI questionnaire was administered to a random sample of adult patients with an established diagnosis of IBD who were participants in a population-based registry in France (8,9). The IBD-DI consists of 28 items that evaluate the 4 domains of Body Functions, Activity Participation, Body Structures and Environmental Factors. Validation included item reduction and data structure, construct validity, internal consistency, inter and intra-observer reliability evaluations.

> "IBD IS KNOWN TO AFFECT PHYSICAL, PSYCHOLOGICAL, FAMILIAL AND SOCIAL DIMENSIONS OF LIFE"

A total of 474 patients were contacted to reach a final number of 200 included patients (response rate 42%) without any significant differences between respondents and non-respondents concerning age, gender, IBD type, disease duration, disease location and behaviour at diagnosis. Socio-demographic and clinical details of the 200 IBD included patients are shown in Table 1. One hundred-fifty patients had CD (75%) and 50 UC (25%). Eighty-eight (44%) patients were males. The study population had amedian age of 26 years (IQR: 22-31) years at study entry. Median disease duration was 12 years (IQR: 3-17). In CD, 92 patients (61%) had inactive disease, 54 (36%) moderate disease and 4 had severe disease according to the Harvey Bradshaw Index. In UC, 13 patients (26%) had inactive disease and 37 (74%) mild or moderate disease according to the Montreal classification. None of the UC patients had severe disease at inclusion (Table 1). Concomitant medications at the time of interview were: 5-aminosalicylic acid (n=42; 21%), systemic steroids (n=5; 2.5%), immunosuppressants (azathioprine or methotrexate; n=46 (23%)), and anti-TNF therapy (n=82; 42%). In CD, 71 patients (47%) had at least one intestinal resection and in UC 8 patients (16%) had colectomy, including 4 patients with subtotal colectomy and ileorectal anastomosis and 4 with coloprotectomy with ileoanal anastomosis. Four patients (2%) had a current stoma. At the time of interview, 61 patients (32%) were active smokers.

The intraclass correlation coefficient for inter-observer reliability was 0.9 and Cronbach's alpha of internal consistency was 0.86. IBD-DI scores varied from 0 to 100 with a mean of 35.3 [Q1=19.6 ; Q3=51.8]. ➤

Table 1

Variables	IBD patients (n=200)	CD patients (n=150)	UC patients (n=50)
Median age years (IQR)	26·4 (22·0-31·0)	26·8 (22·0-31·0)	25·3 (21·0-27·0)
Males (%)	88 (44·0%)	70 (46·7%)	18 (36·0%)
Median follow-up years (IQR)	12.4 (3·0-16·8)	12.8 (8·0-17·2)	11.2 (7·0-14·9)
Active smoker (%)	61 (31·6%)	45 (31%)	16 (33·3%)
Ileocolonic location (L3; %)*		127 (84·7%)	
Complicated behavior (B2 or B3; %)**		88 (59%)	
Extensive colitis E3 (%)*			29 (58%)
Anoperineal lesions (%)		13 (8·7%)	

* According to Montreal classification (Satsangi et al, Gut 1996) ** B2 (structuring behaviour) and B3 (penetrating behaviour) have been pooled and considered as "complicated" behavior.

IBD-DI scores were highly correlated with IBDQ (-0.82. p<0.001) and SF36 (-0.61; p<0.05) scores. Female gender (mean of IBD-DI: 39.7; p<0.001), clinical disease activity (43.5; p<0.0001) and disease duration (39.8 for shorter duration <8 years; 38.1 for longer duration ≥17 years ; p=0.02) were associated with higher IBD-DI scores.

The strengths of our study are the methods used to validate the IBD-DI and the first description of the disability status in a population based cohort of patients with IBD. We used a thorough methodology including all steps (item reduction and data structure, reliability, and construct validity) of quantitative validation. We performed this validation in an independent cohort from the cohort used to develop the IBD-DI (7). Indeed, the recruitment of patients in our study from general population provided the full spectrum of disability necessary to validate the IBD-DI. Moreover the distribution of the IBD-DI in a population-based IBD cohort best reflects the real world setting.

The figure 1 shows the validated IBD-DI questionnaire which can be used.

In conclusion, a validated version of the IBD-DI is now available which can be utilized as an outcome measure in clinical trials and prospective epidemiological studies. Indeed, the resulting IBD-DI, containing 14 items, showed highly satisfactory internal consistency, inter-observer reliability, construct validity, and a moderate intra-observer reliability. Nevertheless, further research is needed to confirm the structural validity, to assess the responsiveness of IBD-DI, and to accumulate evidence of validation for IBD-DI.

Corinne Rousseau

References

1. Thompson PW, Pegley FS. A comparison of disability measured by the Stanford Health Assessment Questionnaire disability scales (HAQ) in male and female rheumatoid outpatients. Br J Rheumatol 1991;30:298–300.
2. Noseworthy JH, Vandervoort MK, Wong CJ, Ebers GC. Interrater variability with the Expanded Disability Status Scale (EDSS) and Functional Systems (FS) in a multiple sclerosis clinical trial. The Canadian Cooperation MS Study Group. Neurology 1990;40:971–5.
3. Peyrin-Biroulet L, Cieza A, Sandborn WJ, et al. Disability in inflammatory bowel diseases: developing ICF Core Sets for patients with inflammatory bowel diseases based on the International Classification of Functioning, Disability, and Health. Inflamm Bowel Dis 2010;16:15–22.
4. Casellas F, Lopez-Vivancos J, Vergara M, Malagelada J. Impact of inflammatory bowel disease on health-related quality of life. Digest Dis 1999;17/208-18.
5. Butzkueven H, Kappos L, Pellegrini F, et al. Efficacy and safety of natalizumab in multiple sclerosis: interim observational programme results. J Neurol Neurosurg Psychiatry 2014;85:1190–7.
6. Dasgupta B, Combe B, Louw I, et al. Patient and physician expectations of add-on treatment with golimumab for rheumatoid arthritis: relationships between expectations and clinical and quality of life outcomes. Arthritis Care Res (Hoboken). 2014;66:1799–807.
7. Peyrin-Biroulet L, Cieza A, Sandborn WJ, et al. Development of the first disability index for inflammatory bowel disease based on the international classification of functioning, disability and health. Gut 2012;61:241–7.
8. Gower-Rousseau C, Salomez JL, Dupas JL, et al. Incidence of inflammatory bowel disease in northern France (1988-1990). Gut 1994;35:1433–8.
9. Gower-Rousseau C, Vasseur F, Fumery M, et al. Epidemiology of inflammatory bowel diseases: new insights from a French population-based registry (EPIMAD). Dig Liver Dis 2013;45:89–94.

IBD DISABILITY INDEX

Pt ID: _____ Date: _____

PLEASE READ ALOUD THIS INSTRUCTIONS TO THE PATIENT The first question is about the overall health of the patient, including both physical and mental health.					
ANSWERS :0 = Very good ; 1=Good ; 2=Moderate ; 3=Bad ; 4=Very Bad	0	1	2	3	4
Overall Health					
1. In general, how would you rate your health today?					

PLEASE READ ALOUD THESE INSTRUCTIONS TO THE PATIENT Now I would like to review different functions of your body and activities of daily life. When answering these questions, I would like you to think about the last week, taking both good and bad days into account. When I ask about difficulty/problem, I would like you to consider how much difficulty/problem you have had on an average, in the past week, while doing the activity in the way that you usually do it. By difficulty I mean that you require increased effort, that you have discomfort or pain, or that the activity is slower or that there are other changes in the way you do the activity. Please answer this question taking into account any assistance you have available. (Read and show scale to respondent).					
ANSWERS :0 = None ; 1=Mild ; 2=Moderate ; 3=Severe ; 4=Very Extreme	0	1	2	3	4
Sleep and Energy					
2. Overall in the last week, how much of a problem did you have with sleeping, such as failing asleep, waking up frequently during the night or waking up too early in the morning?					
3. Overall in the last week, how much of a problem did you have due to not feeling rested and refreshed during the day (e.g. feeling tired, not having energy)?					
Affect					
4. Overall in the last week, how much of a problem did you have with feeling sad, low or depressed?					
5. Overall in the last week, how much of a problem did you have with worry or anxiety?					
Body Image					
6. Overall in the last week, how much of a problem did you have with the way your body or body parts looked?					
Pain					
7. Overall in the last week, how much of stomach or abdomen aches or pains did you have?					

ANSWERS :0 = None ; 1=Mild ; 2=Moderate ; 3=Severe ; 4=Extreme or cannot do	0	1	2	3	4
Regulating defecation					
8. Overall in the last week, how much difficulty did you have coordinating and managing defecation including choosing and getting to an appropriate place of defecation and cleaning oneself after defecation?					
9. Overall in the last week, how much difficulty did you have looking after your health, including maintaining a balanced diet?					
Interpersonal Activities					
10. Overall in the last week, how much difficulty did you have with personal relationship?					
11. Overall in the last week, how much difficulty did you have with participation in the community					
Work and Education (please answer to question 12a OR 12b)					
12a. Overall in the last week, how much difficulty did you have with work or household activities ?					
12b. Overall in the last week, how much difficulty did you have with school or studying activities ?					

ANSWERS : 0=0 ; 1=1-7; 2=8-18; 3=19-29; 4=>29	0	1	2	3	4
13. Number of liquid or very soft stools in the last week :					

ANSWERS : 0=No ; 4= Yes or uncertain	0	N/A	N/A	N/A	4
14. Is arthritis or arthralgia present?					

Total score = S*100/nx4 n=number of questions which have been answered S= sum of the n questions score S is possible if (14-n)/14<20%	Total score _____ ranging from 0 (no disability) to 100 (highest disability level)

N/A: not applicable

Figure 1

ECCO CONGRESS 2016

In 2006 the first European Crohn's and Colitis Organisation's (ECCO) Congress was held in Amsterdam. 350 delegates came to the Netherlands capital to participate. The number of participants has since increased for every year.

Ten years later ECCO Congress returned to Amsterdam – and this time this largest Meeting in the world devoted entirely to IBD attracted a record-breaking 6037 attendees.

They were all greeted welcome by Dutch Gastroenterologists Prof Janneke van der Woude and Dr Bas Oldenburg – and ECCO's President Severine Vermeire.

– The theme of this Congress is *"IBD innovations driving clinical decisions"*, Prof Vermeire stated.

Asymptomatic at follow-up

The first two Speakers were Dr Azucena Salas and Dr Elena Ricart Gomez, who gave a tandem talk about haematopoietic stem cell transplantation (HSCT). They began with a clinical case of a young woman with Crohn's disease (CD).

– The patient was referred from another centre 3 years after diagnosis, had more than 20 bowel movements per day with blood, abdominal pain and faecal incontinence. She was unable to eat and was fed by an enteral tube. The physical examination showed severe malnutrition, and a body mass index of 16, Dr Ricart Gomez told the audience.

Then the patient received haematopoietic stem cell transplantation in June 2013. At follow-up she was asymptomatic, had a normal food intake and had increased her weight to body mass index of 24.

– She went back to a normal life, and has had no active treatment for her CD since – at present not for 3 years.

3 000 patients worldwide have now been transplanted for immune-mediated diseases. Dr Ricart Gomez presented data on HSCT for patients with refractory CD from USA. 24 of them had been followed for 5 years. Of these, 9 were free of disease at year 5. 15 patients had to have the transplant a second time, and 8 of them were free from the disease and therapy.

Immune resetting

The ASTIC study included 45 patients with active CD not amenable to surgery, and refractory to 3 or more immunosuppressive or biological agents and corticosteroids. 23 were randomised to early haematopoietic stem cell transplantation, and 22 to standard CD therapy and *delayed* HSCT. The primary outcome was sustained disease remission at 1 year.

– The results showed no statistical difference between the two arms, but the secondary outcomes – a decrease in endoscopic findings and a better Quality of Life outcome – were more often seen in the early HSCT group, said Dr Salas.

Tariq Ahmad

She explained that conventional biological therapy is about immune modulation, and that HSCT is an "immune resetting".

– Autologous hematopoietic cell transplant provides a therapeutic alternative to CD patients with severe and refractory disease. Safety can be significantly improved by implementation of extraordinary supportive measures before, during and after transplant, she said.

HSCT induces "remodelling" of the peripheral immune compartment with a decrease in memory T-cells and an expansion of B-cells in peripheral blood and the intestinal mucosa.

– Further study of immune responses in patients that respond to HSCT, compared to those that do not benefit, will allow us to identify safer, more targeted therapies that can result in sustained drug-free remission, was their conclusion.

Azucena Salas and Elena Ricart Gomez

Pharmacogenetics

– We face three problems when we treat ➤

our patients. The first is their variation in response, said Dr Tariq Ahmad.

The second problem is choosing the therapy – caused by the increase of new drugs being launched into our clinics, he continued.

– The third problem is the increasing costs of IBD care. This comes from an increasing global incidence, increasing prevalence and an increased uptake of biologics.

Pharmacogenetics (the study of variations in DNA sequence as related to drug response) could help us with some of these problems – with respect to drug efficacy, dosing and side effects. But Dr Ahmad said that the progress so far has been very slow.

– There are currently limited pharmacogenetics applications in IBD care – in spite of the fact that genetic technologies no longer limit gene discovery or rapid application in the clinic.

Defining the drug response phenotype remains a big challenge for IBD pharmacogenetics research.

– But pharmacogenetics predictive panels will reach the clinic soon. There is a need for physician education, and systems to integrate genotypes to support clinical decisions, was his conclusion.

The time for precision medicine is now

The future of genetics in clinical medicine was the title of a lecture given by Prof Rinse Weersma.

– I am a clinician, and I know there is more to IBD than genetics. I also know expectations for genetics changing clinical medicine were too high – and that the progress is slow, he initially stated.

Can we identify IBD patients based on genetics? According to Prof Weersma, the answer is probably no. Can we *classify* IBD based on genetics?

– Yes, to some extent. Genetics correlate with disease *location*, he continued.

Prof Weersma envisioned that we will be able to classify patients using molecular markers. The molecular profiling will result in prognostic markers – markers predictive of drug sensitivity and resistance, and also markers predictive of adverse events. He called this *precision medicine*.

– This is what we want – the right drug to the right patient at the right time! We don't have it for IBD today, but in cancer treatment our colleagues are way ahead of us.

The time is right for precision medicine. We have electronic healthcare records and cheap sequencing technology.

– Genomics will be a part of clinical medicine in the future. And drug developers should take genetics into consideration, Prof Weersma summarised.

Azathiopurine does not enhance efficacy of adalimumab

The DIAMOND study is a prospective, multi-centre, open-labelled clinical trial on comparison of adalimumab monotherapy and a combination with azathioprine for patients with CD. It was presented in Amsterdam by Dr Takayuki Matsumoto.

A combination of infliximab and azathioprine has been shown to be more efficacious than infliximab monotherapy for CD. However, the efficacy of simultaneous azathioprine use for CD under adalimumab remains obscure, Dr Matsumoto said.

– So we aimed to compare the efficacy of adalimumab monotherapy and that of a combination of the two drugs in patients with CD.

63 patients completed the monotherapy, and 62 patients completed the combination therapy. The result was that the two therapies were equally efficacious for intermediate term maintenance of clinical remission.

– The combination therapy resulted in better endoscopic improvement at week 26 and 52, which were the secondary endpoints. However, side effects of the study medication occurred more in the combination group, compared to the monotherapy group.

Dr Matsumoto's conclusion was that simultaneous use of azathioprine did *not* enhance the clinical efficacy of adalimumab for patients with CD in a year.

Inflammation data to stratify cancer risk patients

There is an increased risk for colorectal cancer in patients with UC. Dr Chang Ho Ryan Choi underlined that the majority of these patients do not develop colorectal cancer, so there is a need for identifying high-risk patients.

He presented results from the UK:s largest and longest-running colonoscopic surveillance programme.

– We found that both severity and chronicity of microscopic inflammation are the most important risk factors for colorectal neoplasia. Therefore we must use inflammation data to stratify patients, Dr Choi said.

In the conclusion he also stated that risk stratification should be based on at least 5 – ideally 10 – year's worth of data.

– Macroscopic features of chronicity – tubular, featureless and shortened colon – can be helpful in identifying high-risk patients, Dr Chang established.

Takayuki Matsumoto

Cytomegalovirus colitis

One of the Sessions at the ECCO Congress was on viruses and IBD. Prof Britta Siegmund began this by asking if we should treat cytomegalovirus (CMV) in patients with ulcerative colitis (UC).

Cytomegalovirus is a DNA-virus, of which humans are the only reservoir. After primary infection there is often a persistence of the virus. Sites of latency are largely undefined, but probably include peripheral blood mononuclear cells and bone marrow progenitor cells. It is a common virus that can infect almost anyone, and since it rarely causes symptoms, most people are unaware of having it.

– Probably most of you in this room have cytomegalovirus, Prof Siegmund said.

So what is the problem? She explained there are three categories of CMV. One of these causes CMV colitis, an inflammation of the colon. This is really hard to treat.

Serious CMV infections can occur in people with weakened immune systems, which include patients on chemotherapy for cancer and on immune-suppressing medicines.

– CMV is frequently reactivated in patients with UC, treated with steroids or 6-mercaptopurine, but often disappears without antiviral therapy. CMV during immunomodulator or biological therapy is common, but nearly always self-limited even if therapy is continued.

Britta Siegmund

"SKIN/GENITAL HERPETIC FLARES ARE MORE FREQUENT IN AZATHIOPRINE COMPARED TO 5-ASA"

ECCO statement on opportunistic infections 4A states that "Screening for CMV is not necessary before starting immunomodulator therapy. In patients with acute steroid-resistant colitis CMV should be excluded, preferably by tissue PCR or immunochemistry, before increasing immunomodulator therapy".

A study from 2015 presented by Prof Siegmund concluded that patients with IBD and high density of CMV inclusions in intestinal biopsy benefit from antiviral therapy.

– Ganciclovir for 2 - 3 weeks is the therapy of choice for CMV infections. After 3 - 5 days, a switch to oral valganciclovir for the rest of the 2 to 3-week course may be considered if available – depending of the clinical course and local specialist advice, Prof Siegmund ended her lecture.

Risk factors for viral infections

Dr Jonas Halfvarson talked about other viral complications in clinical practice. He started by pointing out that genetic variants associated with IBD includes both innate and adaptive immunity.

– But there is no evidence of a systemic immune defect in IBD patients that has been associated with increased risk of viral infections or complications.

Corticosteroids, thiopurines, methotrexate, calcineurin inhibitors and biologics are associated with an increased risk of viral, bacterial, parasitic and fungal infections. Thiopurines are more commonly associated with viral infections.

– Despite different mechanisms of action, it seems like any of these drugs can lead to any type of infection, Dr Halfvarson continued.

Risk factors for viral infections in IBD patients include age, malnutrition and comorbidity.

– Viral infections are rare in the elderly, with the exceptions of influenza, reactivation of herpes zoster and viral gastroenteritis. Malnutrition and comorbidity is being linked to infections overall and not specifically viral infections.

Varicella zoster, Epstein-Barr and human papilloma virus

He continued by walking through the different viral infections in IBD patients on immunomodulators.

Herpes simplex virus – corticosteroids might be associated with more frequent skin/genital herpetic flares. Skin/genital herpetic flares are more frequent in azathioprine compared to 5-ASA. There is no clear association between anti-TNF and risk of herpes simplex infection, but reactivation with severe systemic infections has been reported.

–Forvaricellazostervirus(VZV),chickenpox is more often severe or life threatening in immunocompromised individuals. In a review of VZV in IBD, 5 out of 20 cases had a fatal outcome. Similarly, shingles are more severe with increased risk of post-herpetic neuralgia in immunocompromised patients, Dr Halfvarson said.

Hence immunosuppressants should not be initiated during active VZV, instead antiviral treatment (valaciclovir or famciclovir) should be started promptly.

In severe primary Epstein-Barr virus during immunomodulators, consider antiviral therapy. Discontinue, if possible, or reduce the dose of immunomodulators.

– In Epstein-Barr-virus driven lymphoproliferative disease during immunomodulators, refer the patient to appropriate specialists, and discontinue immunomodulators.

Human papilloma virus – it is unclear if immunosuppressants can modify its course.

– Treatment is surgery, chemo- or radiotherapy. There are no known antiviral agents for treatment of human papilloma virus. If there are extensive cutaneous warts or condylomata, consider discontinuation of immunomodulators.

Influenza, hepatitis C and HIV

For influenza virus, immunosuppression is considered to enhance the risk of severe or complicated infection. The epidemiological data are limited, but the incidence seems to be similar irrespectively of immunosuppressive therapy or not.

– In order to prevent influenza-related complications, treat promptly with antiviral therapy according to national guidelines, was Dr Halfvarson's advice.

Hepatitis C infection: Corticosteroids – steroid boluses are associated with increased viremia, fibrosis progression and reduced survival in liver transplanted patients, and should therefore be avoided. Thiopurines do not seem to influence the course or risk for end-stage liver disease – except for cases of co-infection with hepatitis B or HIV.

– For anti-TNF, a systematic review identified worsening of hepatitis C (HCV) in 1 of 157 infected patients. Etanercept seems to improve virological response to combined interferon-a2b/ribavirin therapy. Immunomodulator therapy can be used regardless of HCV, but used with caution when HCV treatment is considered due to potential drug interaction and exacerbation of IBD.

In HIV, case reports and small series indicate that anti-TNF therapy seems safe and can be used without worsening of the HIV infection.

In his summary Dr Halfvarson underlined that there are limited epidemiological data, and that viral complications are rare in patients with IBD.

– Patients on immunomodulators or combination therapy seem to be at highest risk. Specific viral infections like Epstein-Barr virus, varicella zoster, influenza virus and hepatitis B require prompt action!

Beyond mucosal healing

Mucosal healing in IBD – is it the Holy Grail? This question was the headline for a lecture given by Prof Geert D'Haens.

– Mucosal healing is something really difficult. What you see inside the gut does not reveal the extent of penetration in tissue. *Healing* means more than just in the mucosa, Prof D'Haens said.

He presented a study on endoscopic remission with mesalazine and relapse rate in UC patients. 23 % of those who had achieved endoscopic healing had a relapse in 1 year, to be compared to 80 % of those that had achieved clinical remission only.

– So the normalisation of the mucosa is really of value.

A meta-analysis on 13 studies, including 2073 patients showed that if mucosal healing was achieved at first endoscopy, the chance was 4,5 times higher for the patient to remain in remission.

A similar meta-analysis on a total of 673 patients with CD, showed similar outcomes. Both meta-analyses also showed that there was no difference in mucosal healing achieved on biologics, compared to non-biologics.

"WE CAN ACHIEVE MUCOSAL HEALING IN SEVERAL OF OUR UC AND CD PATIENTS"

– We can achieve mucosal healing in several of our UC and CD patients! But we have also to maintain it, Prof D'Haens stated.

He ended his talk by saying that we also should go beyond mucosal healing - i.e. strive to achieve histologic remission. An algorithm of "the ideal world" included early diagnosis, imaging and early precision treatment.

– And don't forget that some patients are candidates for early surgery!

Ustekinumab

IL-12 and IL-23 are key cytokines in the pathogenic immune cascade of CD. Ustekinumab is a fully human IgG1k monoclonal antibody that inhibits IL-12 and IL-23 mediated signalling, cellular activation and downstream cytokine production.

– It is approved for moderate to severe psoriasis and psoriatic arthritis, said Prof Paul Rutgeerts.

He presented UNIT-1, a phase III study to evaluate efficacy and safety of ustekinumab induction in patients with moderate to severe CD who have failed one or more anti-TNFs.

– Intravenous ustekinumab was found to significantly induce clinical response and remission, Prof Rutgeerts told the audience.

Clinical efficacy was confirmed by improvements in Health-Related Quality of Life and reductions in objective markers of inflammation.

Jonas Halfvarson

– Both i.v. ustekinumab induction regimens were well tolerated. There were no anaphylaxis or serious infusion reactions reported.

Prof Rutgeerts conclusion was that coupled with previously reported study results, induction efficacy with ustekinumab has been demonstrated across the moderately to severely active CD patient population – including anti-TNF naive and failure patients.

CD in children

IBD across the age spectrum – is it the same disease?

The question was asked by Prof Holm Uhlig in his talk on very early onset IBD. He pointed out that 15 - 25 % of IBD patients have paediatric onset and 10 - 15 % are more than 60 years old at onset.

– Contrary to common belief, studies have shown that there is less risk for surgery in those that are under 6 years of age at onset, he said.

Prof Alexandar Stojmirovic pointed out that development of new medical therapies for paediatric CD typically requires extrapolation of efficacy from adults, and is contingent on similar pathogenesis in both groups.

– Children with CD have more extensive disease at presentation, but genome wide association studies have not identified pathways that distinguish these two populations, he continued.

He presented a study that evaluated similarities between adults and children by computing disease profiles from intestinal biopsy gene expression datasets, comparing inflamed and non-inflamed samples within ileum and colon.

– We did see that intestinal CD profiles of children and adults are qualitatively similar within the same general anatomical location. There is a common inflammatory signature for both adults and children in the entire intestine.

He added that they also saw some apparent differences. Apart from genuine differences, these can be attributed to differences between platforms, treatment status (treatment naive versus TNF-refractory) and heterogeneity of sample sources.

– These findings suggest a common molecular profile and disease process in both populations, and lend support to the extrapolation of efficacy from adults to children in the development of new medical therapies for CD, Prof Stojmirovic concluded.

Limit invasive procedures

Should clinical trials be different in children?

Prof Dan Turner told the audience that there are only one 10th of available children, compared to adults, for studies.

– The investigation drug is often approved for adults and available off label. A care giver must make all choices for the best interest of his or her child, and can not consent to make the child altruistic, he underlined.

Children accept less pain and inconvenience than adults and in average they have a more severe and extensive disease – including growth and bone problems – that makes a placebo more problematic.

Prof Turner underlined that there are no examples of drugs that work in adults, but not in children. However, young children require higher dose per kg of biologics.

– In the era of mucosal healing evaluation, placebo is not so important anymore, he continued.

His recommendations were that we should in children focus on phase II studies with approximately 100 children, especially those younger than 10 years – but without placebo.

– If the pharmacokinetics and pharmacodynamics are similar to adult data – waive the need for phase III trials! Ensure effective treatment – i.e. no active screening period. Placebo may be used in those with complete and sustained clinical and biological remission with early escape.

Prof Turner also encouraged to limit invasive procedures and to focus on large scale post marketing surveillance cohorts with long term follow-up.

– Paediatric trials should be addressed differently!

He ended by stating that the views expressed in his presentation have been formally endorsed by European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPHGAN) and ECCO, and gained support of more than 90 % of European and Canadian paediatric IBD experts.

First study to standardize criteria for IBD-U

IBD-Unclassified (IBD-U) is a term referring to patients with disease limited to the colon, but with features that make the clinician uncertain whether the diagnosis is actually Crohn's colitis, rather than UC, said Dr Liron Birimberg-Schwartz.

She presented a study on development and validation of diagnostic criteria for IBD-U.

– Indeterminate colitis is now reserved for *histological* uncertainty.

The aim of the study was to derive and validate diagnostic criteria of IBD-U in children, based on prior work in the revised Porto criteria – using both judgmental approach and mathematical modelling on the largest IBD-U cohort ever constructed in paediatric IBD.

It was a multicenter retrospective longitudinal study including 749 children with isolated colonic involvement from 24 centers in 14 countries affiliated with the Porto IBD-working group of ESPGHAN.

Liron Birimberg-Schwartz

Dan Turner

– Our study is the first to standardize the diagnostic criteria of IBD-U, which hitherto has been universally subjective. It is the first step towards facilitating studies in IBD-U in order to further advance our understanding of this distinct entity, she summarised.

Dr Birimberg-Schwartz also explained that they are in the process of developing an open access simple website and application that can aid in quick calculation of the algorithm.

A therapeutic option with a potential

Dr Ailsa Hart talked about the microbiota. She said that in CD, reduction of a major member of Firmicutes, *Faecalibacterium prausnitzii,* is associated with higher risk of post-operative recurrence of ileal CD. Experimental replacement of *F. prausnitzii* has been shown to have anti-inflammatory effects.

Ailsa Hart

Sudarshan Paramsothy

– There are challenges in manipulating the microbiota in clinical practice – clinical, sampling and technical challenges. But also in communication between clinicians and other groups involved, Dr Hart underlined.

Antibiotics have a place in perianal CD, post-operative CD, paediatric CD and pouchitis. Probiotics have a place in pouchitis and in mild to moderate UC, but prebiotics have shown no benefit.

She continued by describing faecal microbial transplantation (FMT). This means administration of faecal material containing gut microbiota from a healthy person to a patient with disease or condition related to dysbiosis or an alteration in their gut microbiota.

– FMT is a therapeutic option in IBD with a potential.

The history behind FMT goes longer back than one might expect: In 4th century China (!) dysentery was treated with human "faecal suspension". In 1958 it was the first therapy in humans for pseudomembranous colitis.

– A meta-analysis of FMT in UC including 9 cohort studies, 8 case studies and 1 randomised controlled trial showed that overall 45 % achieved clinical remission. In cohort studies, 36 % achieved remission – and in sub-group analysis young patients achieved clinical remission, Dr Hart pointed out.

Effective therapy to induce clinical remission in UC

In Dr Hart's summary she stated that there is an exciting future for modalities targeting microbiota – with encapsulated formulations and defined microbial consortia in the immediate future.

– It also has far reaching potential in other, non-gastrointestinal diseases.

Results about the efficacy and optimal treatment modality of FMT in UC are conflicting, said Dr Sudarshan Paramsothy.

He presented the FOCUS trial on multi-donor intense FMT for resistant UC. It is a randomised, double blind, placebo-controlled study involving 3 medical centres with a central reading of all endoscopic images by a clinical panel blinded to patient's treatment.

Dr Paramsothy reported that the conclusion from FOCUS is that FMT therapy is effective in inducing clinical remission and endoscopic improvement or remission in patients with active UC, many of whom were resistant to standard drug therapy.

Steps to prepare for surgery

There are six steps in preparing for IBD Surgery, said Dr Richard Fedorak. The first of these steps is pre-operative counselling and psychological support.

– For the patient, psychological intervention and being well informed means improved outcome. This also means that the patient understand that surgery is *not* a failure – surgery is *treatment*. Also that fear of ostomy or scar, school and parenthood-related problems can *delay* surgery – leading to suboptimal timing and worsening of the disease, Dr Fedorak continued.

For the physician it is important to have communication and interpersonal competence and an ability to perceive, use, understand and manage patient's beliefs and emotions. Also to ensure a collaborative decision-making with the surgeon.

Next step is pre-operative diagnostic imaging.

– We need to know what we are dealing with.

The patient has to repeat MRE or CT to define intraabdominell abscesses and unexpected small bowel involvement.

– Repeat endoscopy to define extent and degree of colonic disease. Identify and drain any abscess, rather than antibiotic coverage alone. In this step the physician has to determine type of access – open or laparoscopic – and type of surgery – resection or strictureplasty.

The third step is pre-op nutritional therapy. BMI below 18 or a weight loss of more than 10 % in the last six months, and albumin below 30 g/L are high risk criteria.

– In high risk groups pre-op nutrition reduces complications from 25 % to near 0 %!

A multidisciplinary approach is required

The fourth step is to prevent venous thromboembolism.

– In IBD there is a three-fold risk for this. In IBD plus surgery there is a four-fold risk of death if venous thromboembolism occurs, Dr Fedorak stressed.

The physician has to consider the risk for venous thromboembolism in the decision. The sum of disease-induced hypercoagulable sites, steroid use, malnutrition, anaemia, thrombocytis and other factors have to be taken into account.

Then step five, which is pre-operative medical therapy. Should biologics be continued – and if so, does this bring a higher risk of post-operative complications?

– Yes, but likely marginal. Consider the "don't stop therapy rule" and the "8 – 12 week rule" – i.e. aim for the timing of surgery to be 8 - 12 weeks after last administration of the biologic.

Continuing immunosuppressives does not affect outcome, but reduce steroids to less than 20 mg per day in order to reduce post-operative complications.

Then he arrived at the last step: Surgery.

For the physician it is important to have a post-operative plan to prevent recurrence – and for the patient to *know* this plan, Dr Fedorak emphasised.

– All these steps requires a multidisciplinary approach, including a gastroenterologist, a colorectal surgeon, nutritionist, psychologist, ostomy nurse and – last but not least – the patient's friends and family, was Dr Fedorak's final message.

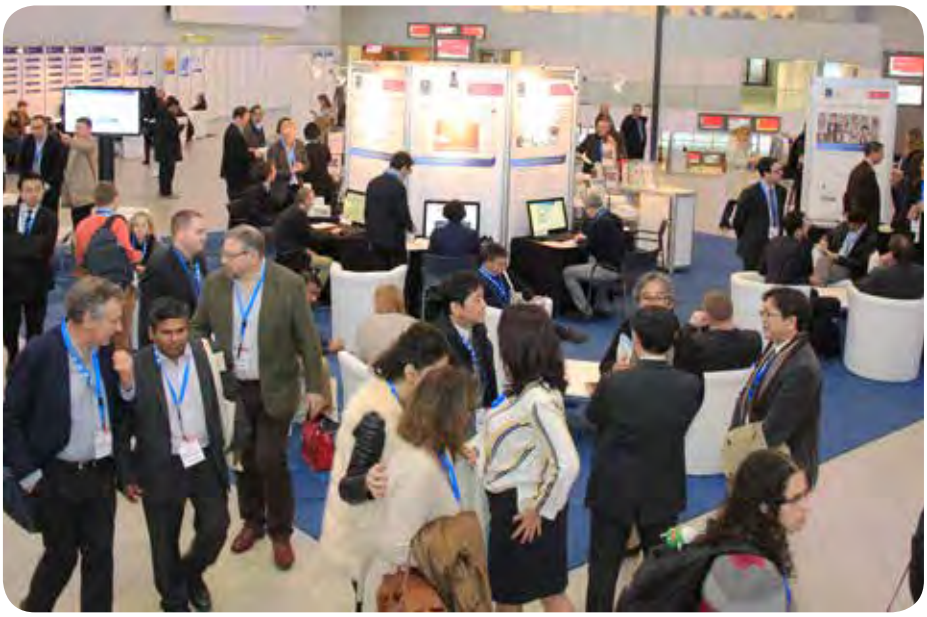
Anti-TNF associated with a higher risk

Up to 70 % of patients with ileocolonic CD have surgery during their disease progression. The post-operative morbidity widely varies – from 8 to 40 %. Retrospective studies have identified potential risk factors for post-operative complications before introduction of anti-TNF therapy – preoperative steroids, poor preoperative nutritional status and perforating CD. The influence of anti-TNF therapy itself remains controversial.

– These factors have never been validated in a large prospective study, said Dr Antoine Brouquet.

He presented an outcome analysis in a prospective nationwide cohort of 592 patients.

– We found that new other risk factors of postoperative morbidity can be proposed: Recurrent CD, preoperative Hb below 10 g/dl, operative time over 180 minutes – *and* preoperative anti-TNF therapy.



Therefore it was his conclusion that in patients treated with anti-TNF presenting with another risk factor, preoperative preparation and/or teporary ileocolostomy should be discussed.

"THERE IS A THREE-FOLD RISK OF DEATH IN VENOUS THROMBOEMBOLISM"

– The fact that anti-TNF is associated with an increased risk should be taken into account when deciding for treatment strategy when the two options anti-TNF and surgery are available, was the last of Dr Brouquet's conclusions.

Demands on knowledge are becoming higher

This also concludes our report from ECCO Congress 2016. On the last day, *IBD Congress News* spoke to a Gastroenterologist that had attended it, and asked for his views.

– I think it was a very good Congress, with many relevant topics covered by excellent Speakers, was his answer.

Many new therapies with new drugs are emerging, which means that gastroenterologists in the near future will have many different choices, the Gastroenterologist continued.

Richard Fedorak

– In turn, this means one has to specialize – and I have done that. I have stopped treating liver diseases and now only work with IBD patients.

This evolution of therapies also means that the demands on knowledge are higher.

– You have to learn *more* – and therefore it is so important that you attend the ECCO Congress, the Gastroenterologist finished by stating.

The 12th Congress of ECCO will take place in Barcelona, Spain, February 15 – 18. Mark the date in your calendar!

Per Lundblad

THE IMPORTANCE OF CONTROLLING INFLAMMATION IN IBD

To date, IBD management goals have focused on gastrointestinal symptom resolution and mucosal healing. However, IBD is often a systemic disorder. Common pathogenic pathways can lead to inflammatory manifestations beyond the gut. Therefore there is a need to reduce the overall inflammatory burden associated with IBD. This was discussed at a Satellite Symposium at ECCO Congress, sponsored by Abbvie.

Tissue-specific factors dominate

Prof Geert D'Haens was the Chair, and he introduced Prof Yehuda Chowers as the first Speaker. He began by describing the inflammatory process and the interaction between cells.

– Multiple cell types are involved in IBD pathogenesis. Effector cell function depends on local environment and immune conditions – T-cell effector function is plastic and can be shifted by changing conditions, Prof Chowers said.

He continued with protein-protein interactions between IBD and extra-intestinal manifestations. Perianal disease is a frequent complication that affects up to 40 % of IBD patients. The pathogenesis is not known.

– Common genes, inflammatory pathways and environmental factors may be involved in extra-intestinal manifestations, related immune-mediated diseases and perianal disease manifestations. However, tissue-specific factors may dominate the final pathophysiology and clinical manifestations, Prof Chowers concluded.

Geert D'Haens, Remo Panaccione and Yehuda Chowers.

PSC is the most serious

Extra-intestinal manifestations, which are systemic, identify patients with more severe forms of IBD, said Prof Remo Panaccione.

– Sometimes, these manifestations can be more debilitating than the intestinal disease. Early recognition of these manifestations should help guide therapy that will reduce overall morbidity in affected patients.

The most common extra-intestinal manifestations are muscoskeltal, such as arthritis – reported in 9 - 53 % of IBD patients. The second most common are dermatologic and oral – reported in 2 - 34 % of IBD patients.

– Ocular extra-intestinal manifestations are also common. The occur in 0,3 - 5 %. One of the most serious is primary sclerosing cholangitis (PSC), which has a strong association with IBD. 75 % of PSC patients have co-existing ulcerative colitis (UC) and another 5 - 10 % have Crohn's disease. However, only 5 % of UC patients and 2 % of CD patients develop PSC, Prof Panaccione said.

A multidisciplinary team is required

He continued with the epidemiology for perianal CD.

– 25 - 80 % of patients with CD will develop perianal disease. The disease may be continuous with active disease or remote from area of activity.

9 - 17 % of patients undergo proctocolectomy for perianal disease, and the presence of perianal fistula has been associated with a poor prognosis.

– For fistulizing CD, the goals of treatment are to drain sepsis, reduce frequency of abscess formation, preserve the sphincter, reduce drainage symptoms and to improve quality of life. These goals are best achieved trough multidisciplinary teams, Prof Panaccione stated.

This team includes an experienced radiologist, a thoughtful gastroenterologist and an appropriately aggressive surgeon who "takes sepsis draining personally and diverts when necessary", according to Prof Panaccione.

Anti-TNF successfully treats many of the common extra-intestinal manifestations.

– When thinking of overall management of IBD we need to consider the entire picture – not *only* the intestine. When choosing therapy it is important to consider treatment that will resolve intestinal symptoms, improve extra-intestinal manifestations and change the natural history of the disease, Prof Panaccione summarised.

Per Lundblad

HOW TO IMPROVE YOUR SUCCESS IN TREATING MILD AND MODERATE IBD

Success factors in the treatment of mild to moderate ulcerative colitis and Crohn's disease was discussed at a Satellite Symposia at the ECCO Congress. The Symposium was sponsored by Tillotts Pharma, and Prof Geert D'Haens was the Chair.

Prof D'Haens greeted everyone welcome.

– What we are going to focus on here today are the patients that you see the most, he underlined.

Extent of disease affects administration of drug

Dr Ailsa Hart talked about patients with ulcerative colitis (UC).

– Mild disease is defined as 4 or less stools per day, no systemic illness and normal erythrocyte sedimentation rate. Moderate disease has more than 4 stools per day and minimal signs of systemic toxicity. Severe disease is characterized by 6 or more bloody stools per day, high pulse, fever etc, she said.

A majority – 85 % – of patients with UC have mild to moderate disease.

Another way to score the disease is using the Mayo score, and Dr Hart presented it. She also showed endoscopic images.

– Remember to consider the *extent* of the disease, since this affects how we administer the medication.

There are three ways to optimise the use of 5-ASA: Maximise *dose*, increase the duration of the treatment and to combine oral and rectal 5-ASA.

– Enemas may not provide good 5-ASA delivery to the rectum, so consider enema plus suppository, she pointed out.

Use all tools available

Adherence is also an important factor, and Dr Hart presented data that shows that 70 % of non-compliance is intentional. In order to optimise adherence, one has to educate and motivate the patient.

– Educate about the disease and benefits of maintaining remission – and integrate the regimen in patient's life. Make it convenient for them – reduce complexity of treatment. Also treat depression, she continued.

Edouard Louis, Silvio Danese and Axel Dignass.

In Dr Hart's summary she stressed that one has to seek ways to avoid delay in diagnosis.

– Ensure the patient has the right drug in the right dose and right mode of delivery at the right time – at *every* time! This means you'll have to assess and monitor continuously.

Respect patient preference and motivate your patients.

– Develop models of care that fit your service. And remember, symptoms such as fatigue, pain and faecal urgency – to name a few – are not due to inflammation, but still need addressing. Use *all* tools available – diet, loperamide, anti-depressants and psychological therapy. Patient's that fall out of the system can have a very hard time ahead, Dr Hart ended her lecture.

Important role for the IBD nurse

Uncomplicated Crohn's disease (CD) is defined as the absence of bowel damage, fistulizing and/or stricturing CD, perianal fistulas and the need for surgery at diagnosis, said Dr Peter Hendryckx.

So how does one identify patients with risk for complicated disease?

– Age and disease location matter. Ileal location is associated with a complicated disease course, compared to colonic, Dr Hendryckx said.

For patients with mild disease there is a role for 5-ASA as first-line induction treatment. A meta-analysis he presented showed a benefit for budesonide over conventional steroids for adverse events.

– But budesonide is *not* to be used for maintenance treatment.

Strategies to improve adherence includes educational, behavioural and cognitive interventions and motivational strategies.

– Here we have an important role for the IBD nurse. And remember to educate the patient – and their relatives – on the risk association of smoking.

Treat according to risk stratification in order to prevent damage and minimise harm. And empower your patients – identify ideas, concern and expectations, were Dr Hendryckx take-home messages.

Per Lundblad

TAILORING MILD-TO-MODERATE IBD MANAGEMENT

Patient-reported outcomes (PROs) are becoming an increasingly important part of clinical research and patient centric approach. How they can be integrated with established clinical measures of disease activity was discussed at a Satellite Symposium at the ECCO Congress. The Symposium was sponsored by Ferring Pharmaceuticals.

Prof Silvio Danese, who was the Chair, began by talking about patient-reported outcomes in IBD.

– PROs represent what is most important to patients about a condition or its treatment, he explained.

Guidelines are based on medical evidence determined by validated composite scores, and do not currently include PROs.

– But biologics for other diseases – such as rheumatoid artrithis – have been investigated in the context of PROs, he said.

Geert D'Haens, Ailsa Hart and Peter Hendryckx.

The optimal treatment is the safest treatment

Prof Edouard Louis then talked about combining PROs and guidelines in clinical practice in Crohn's disease (CD). He began by presenting two cases.

– The first patient was afraid of steroids and was asking for the safest treatment. He was not significantly affected by the symptoms, and prioritised safety, Prof Louis told the audience.

He presented data on mesalazine that showed that mesalazine 4g/day in CD provides statistically significant improvement in remission rates, therapeutic benefit and decreases in treatment failure.

The second patient had developed intestinal obstruction and underwent a surgical resection of last 15 cm of ileum. The post-operative period was uneventful.

– Guidelines recommend thiopurines for preventing recurrence, but also states that high-dose mesalazine is an option. The patient was anxious about the risk of relapse, and did not want to stay off treatment. She was also afraid of immunosuppression.

Both patients were treated successfully with mesalazine.

– The optimal IBD treatment in IBD is the safest treatment that will lead to steroid-free deep remission, within one year of the diagnosis. This treatment has to be selected with the patient, taking into account the patient's preference, Prof Louis summarised.

IBD basic medications are safe during pregnancy

Prof Axel Dignass then talked about ulcerative colitis (UC). He presented a case of a pregnant woman who before conception was treated with mesalazine 2mg per day for maintenance of her UC.

The patient was anxious about how her IBD could affect the health of her baby, and concerned about the saftey of medication on any future unborn children.

– Risk of abortion and fetal abnormalities is not significantly associated with basic IBD medications, such as sulfasalazine, 5-ASA-derivatives, steroids and budesonide, Prof Dignass said.

So she was continued on mesalazine 2g/day and recommended regular monitoring including iron status and folate. In week 22 of pregnancy, she had a flare.

– We optimised 5-ASA: Increased oral mesalazine to 4g/day, and added mesalazine enema 1g/day for 2 weeks. The patient went into remission after 10 days, had a normal course of pregnancy and delivery of a healthy boy.

Prof Dignass underlined that combined treatment with oral and rectal mesalazine induces a more rapid improvement than oral therapy alone in extensive active UC.

– Conception should not occur at time of active disease in order to reduce the risk of disease activity during pregnancy – and to improve outcomes. Active IBD during pregnancy should be treated appropriately and effectively, was his summary.

In his conclusion, Chair Prof Danese stated that PROs for IBD must be developed and introduced into the guidelines.

– The use of data from multiple sources can ensure that guidelines fit better with clinical practice and patient's needs, he said.

Per Lundblad

WHEN BIOLOGICS ARE NOT THE ANSWER

In accession to the ECCO Congress in Amsterdam, an Expert Forum on the use of granulocyte and monocyte (GM) apheresis with Adacolumn was held. It was sponsored by Otsuka Pharmaceutical.

Prof Wolfgang Kruis, who was the Chair, initially pointed out that treatment effect of biologicals is less than 50 %.

– This means there is a need for *options*. Surgery is not healing, since it includes co-morbidities. Sometimes a colectomy is needed and should be performed, but tonight we are discussing an alternative, he said.

Wolfgang Kruis, Per Karlén, Giorgia Bodini and Gilles Bommelaer.

No treatment achieve more than 50 % remission

– The treatments we have for UC are not enough, said Prof Gilles Bommelaer.

Intolerance to 5-ASA occurs in up to 15 % of patients. Thiopurines are also far from perfect – in a meta-analysis on 286 patients, endoscopic remission was maintained in 64 of 115 patients on azathioprine, compared to 41 of 117 patients on placebo. There are also adverse effects with azathioprine, he underlined.

Prof Bommelaer continued by presenting data on maintenance treatment in UC with infliximab. 224 patients were followed up to 154 weeks. 30,6 % discontinued infliximab for adverse events, 10,5 % for lack of efficacy. 21, 3 % experienced serious adverse events.

– *No* single treatment – or combined treatment – achieve more than 50 % remission in active UC, except corticosteroids. No maintenance treatment offers long-term remission – we need safer, more efficacious and less expensive treatments. So what about a "no-drug" treatment?

Safe and efficacious therapy

He presented the results from the Adacolumn in Refractory disease Trial (ART). These were also presented on a poster at the ECCO Congress.

ART is an open-label, single-arm, multicentre, post-marketing study. The objective was to observe and document the efficacy and safety of 5 or more Adacolumn treatments in a specific subset of UC patients – with steroid-dependent active UC and insufficient response or intolerance to immunosuppressants and/or biological therapies.

Primary endpoint was remission rate at week 12, defined based on clinical activity index (CAI).

– Irrespective of the 12 week results, patients remained enrolled for a 48-week follow-up period and a 96 week retrospective survey of colectomy rates.

43,3 % of patients reached a reduction in CAI score by 3 or more at week 12.

– Adacolumn therapy is safe and efficacious in this subgroup of refractory UC patients. Colectomy rates at 96 weeks appear in line with anti-TNFs, despite only induction therapy, Prof Bommelaer reported.

Works in anti-TNF failure patients

The strengths of Adacolumn treatment in his opinion are that it represents a "no drug" treatment, with an "on demand" therapy at any stage of the illness.

– It works even in anti-TNF failure patients, the safety is good and the patient-reported outcomes are good.

The weaknesses are the weak level of evidence, and that GM apheresis is absent in major guidelines.

– Granulocyte and monocyte apheresis *has* a place in the armament against UC – and need to be further defined by prospective studies, was his conclusion.

Dr Giorgia Bodini then talked about a study on the role of GM apheresis in modulating cellular immunity. She was followed by Dr Per Karlén who presented a study on long-term follow-up with GM apheresis re-treatment in patients with chronically active IBD.

– No serious side-effects were seen. IBD patients with chronic disease – despite conventional therapy – who respond to an initial GM apheresis course, seem to benefit from GM apheresis maintenance treatment, were Dr Karlén's conclusions.

Per Lundblad

IN IT FOR THE LONG HAUL

Managing the complexity of Crohn's disease (CD) – the patient and their physician are in this together. They need to develop strategies and have tools available that help manage this chronic, relapsing disease and its range of complications in the long term. This was discussed in Satellite Symposium at the ECCO congress, sponsored by Takeda.

Blocking accumulation of lymphocytes

Prof Michael Kamm was the Chair, and he introduced Prof Remo Panaccione as the first Speaker.

– Often patients with CD, newly diagnosed, want to know *why* they have got the disease, he said.

But the etiology of CD is unknown. There are many proposed pathogenic mechanisms – genetic, environmental and host immune response. As there is no one cause, it is likely that CD is an outcome of interactions of these factors.

Prof Panaccione described the α4β7 integrin – MAdCAM-1 addressin interaction. This process relies on the key interaction between the two on the surfaces of the appropriate cell, and is one of the interactions that contributes to chronic inflammation in ulcerative colitis (UC) and CD.

– It leads to accumulation of excess infiltrating lymphocytes in the gastrointestinal tissue.

The mechanism of vedolizumab blocks this accumulation.

He also described the typical physician goals, which have a long-term perspective, and compared them with typical patient goals – which have a short-term perspective.

– We need to establish appropriate management goals *together* with the patient, Prof Panaccione underlined.

Very good safety signals

Anti-TNF therapy is an independent predictor of serious infections, Prof Panaccione continued.

– A prospective cohort study on 3079 patients over 10 years showed that patients more than 65 years old are at particularly high risk for infection.

He presented data on vedolizumab and serious infections.

– There are very good safety signals over 5 years.

Remo Panaccione

Stefan Schreiber

In his summary he pointed out that the benefit-risk profile supports that vedolizumab can be used as first-line biologic.

– Remember to think about the complexity of the disease – such as extraintestinal manifestations and perianal disease. The ENTERPRISE study showed that the reported probabilities of fistula closure with vedolizumab were 29 % at 6 months and 33 % at 12 months.

Prof Panaccione ended his talk by stressing the need to respect the patient's fear and concerns.

– Balance long-term benefit with long-term risk!

Real-life data

The real-world experience of treatment with vedolizumab in patients with CD was the topic of Prof Stefan Schreiber's talk. In this he referred to multiple "real-practice cohorts", with more than 800 patients with CD.

– Most included patients had failed one or more treatment with anti-TNF, he said.

Prof Schreiber stated that a broad confirmation of efficacy and safety is seen in registration and other real-world trials.

– It is remarkable how similar the numbers are from many real-life cohorts from all over the world.

Data show improvement of disease activity, decrease of steroid use and reduction of inflammation markers. Vedolizumab is effective in both UC and CD, and in CD the efficacy is higher in patients with colonic inflammation.

– Safety data from real-world trials is consistent with that reported in clinical trials.

Prof Schreiber also said that up to 30 % of patients with CD are receiving vedolizumab as first biologic.

– The limitation is of course that real-life data from cohorts at present are small, he ended his lecture.

Per Lundblad

CONGRESSES 2016

Digestive Disease Week
May 21-26
San Diego USA
www.ddw-2016.org

British Society of Gastroenterology Annual Meeting 2016
June 20-23
Liverpool UK
http://www.bsg.org.uk/events/bsg-annual-meeting-2016.html

Mastering Clinical Challenges and emerging therapies in IBD
July 23
Chicago USA
www.imedex.com/challenges-therapies-ibd-conference/index.asp

Putting the Puzzle Together: Inflammation and Gastrointestinal Disease
Falk Gastroenterology Symposium
September 16-17
Regensburg Germany
www.falk-foundation-symposia.org/symposia-and workshops/2016/?L=1

11th Scientific and Annual Meeting of European Society of Coloproctology
September 28-30
Milan Italy (New location!)
www.escp.eu.com

Oxford Masterclass 2016
September 17-21
Oxford UK
www.expmedndm.ox.ac.uk/masterclass

Australian Gastroenterology Week
October 10-12
Adelaide South Australia
www.agw2016.org.au/

UEG Week
October 15-19
Vienna Austria
www.ueg.eu/week

10th European Mucosal Immunology Group meeting
October 19-21
Copenhagen Denmark
www.emig2016.org/

New Treatment Targets in Gut and Liver Diseases Falk Symposium 205
October 21-22
Lucerne Switzerland
www.falk-foundationsymposia.org/symposia-and-workshops/2016/?L=1

Asian Pacific Digestive Week 2016
November 2-5
Kobe Japan
www.apdw2016.org/

Japan Digestive Disease Week 2016
November 3-6
Kobe Japan
www.jddw.jp/jddw2016/en/index.html

IBD Nordic Conference
November 10-11
Stockholm
www.ibdnordic

Advances in IBD 2016
December 8-10
Orlando USA
www.advancesinibd.com/