ECCO CONGRESS 2018

Once again the ECCO Congress set a record in number of delegates attending - 6 614 registrants from 86 countries had come to participate in the Meeting. It took place in Vienna, Austria, February 14-17. The motto for 2018 was "*Science changing patients life*". They were all greeted welcome at the Opening Ceremony by Prof Julian Panes, President of ECCO.

The first session had the title Exploring IBD over time, and Dr Joanna Torres, Portugal was the first speaker.

– An exponential increase in the number of IBD patients living in the Western world is expected – due to compounding prevalence. The number of patients with IBD in newly industrialised countries will likely approximate that in the Western world– owing to rising incidence and prevalence and rapidly growing populations, she started by stating.

The disease starts many years before it is detected

Why is prediction so important? According to Dr Torres, understanding the critical early events that take place before disease is diagnosed can ultimately lead to development of strategies directed at the primary and secondary *prevention* of IBD.

– The concept of a preclinical phase in immune mediated diseases has been extensively explored in rheumatoid arthritis or type 1 diabetes, she underlined.

So how can we gain insight into preclinical IBD? There are two ways: Studies in at-risk populations (families) and studies in the general population via serum repositories.

– But there are several limitations in prior studies in the general population – there is a limited number of patients, one sample per patient, and it is not possible to infer which pathways may be have been altered before diagnosis.

We do know that early life events and childhood exposures may be important in determining the risk of IBD.

– There is increasing incidence of IBD in young children, and in the second generation of immigrants coming from low- to high incidence areas. Caesarean section, exposure to antibiotics in childhood and pregnancy etc. increases risk in later life, Dr Torres said. Therefore understanding the preclinical stages of IBD might enable accurate identification of at-risk individuals for disease development and specific phenotypes.

– Available evidence suggests that the disease processes start many years before disease is clinically detectable, and that IBD may be predicted *before* diagnosis with good accuracy. The "preclinical" period of IBD may constitute a window of opportunity for modulating – or even intercepting – disease risk.

Hopefully, future studies prospectively collecting serum, genetic microbial and environmental biomarkers etc. could improve and define high risk groups for disease prediction and disease prevention trials, Dr Torres ended her lecture.

Barrier dysfunction a primary defect of CD

Dr Jonas Halfvarson, Sweden, presented a study on barrier dysfunction in Crohn's

disease (CD). It aimed to assess if intestinal barrier dysfunction is a primary defect or a consequence of inflammation – and to evaluate the influence of genetics and environmental exposure on paracellular and bacterial uptake in twins discordant for CD.

– Twins were identified from a previously described population based cohort of twins with IBD. Discordant twin pairs of the same sex with CD, without past extensive resection, were invited, he explained.

None-related individuals with normal ileum undergoing colonoscopy for polyp surveillance served as external controls.

– An increased paracellular permeability was observed in healthy co-twins in twin pairs discordant for CD – strongly suggesting that barrier dysfunction is a primary defect of CD, Dr Halfvarson reported.

The dysregulated barrier might be explained by the influence of genetics, as the authors observed a significant increase in paracellular permeability in healthy monozygotic co-twins, compared to dizygotic twins.

– Passage of *E.coli* seems to be a consequence of inflammation, rather than representing a primary defect, Dr Halfvarson concluded.

Biologics change serum immune profiles

In the last decade, anti-alpha4beta7 and anti-IL12/IL23p40 antibodies became available as an alternative to anti-TNF agents for patients with IBD. Many patients need to switch between different types of biological treatment during their disease course. Biological-naive patients had better outcomes compared to exposed patients.

– It is unclear if this is due to alterations in immune pathways triggered by biological exposure or more progressive disease, said PhD Magali de Bruyn, Belgium.

She presented a study with two aims: To study the influence of previous biological exposure on serum immune profiles in patients who need to switch to another biologic.

– Our second aim was to study if serum immune profiles differ in exposed versus naive patients. And if the answer is yes, is this due to previous biological exposure – or a more progressive disease?

Ms de Bruyn reported that the investigators had found that exposure to different types of biological treatments is associated with specific changes in serum immune profiles. These differ between exposed and naive patients due to both disease progression and biological exposure.

– Further studies should now prospectively characterise differences in serum immune profiles on a large scale to see if these can aid clinicians in personalised therapeutic decision making, was her conclusion.

> "THERE IS A DIFFERENCE IN PATHOLOGY, BUT WE HAVE DIFFICULTIES IN DIAGNOSING IT"

Early disease has different pathology

Evolution of disease pathways in early CD – early versus late disease was the title of a lecture given by Prof Gerhard Rogler, Switzerland.

– What is early disease, he started by asking.

The definition of IBD of short duration is that the disease duration has been less than 18 months, and there has been no previous use of disease modifying agents.

– That is a clinically useful definition, but it does not tell us anything about biology, Prof Rogler commented.

Do we diagnose IBD in time? Data shows there is a significant diagnostic delay.

– This is a problem that causes damage to these patients. They have a much higher risk of stricture and surgery – not being diagnosed early is a clinical problem for patients, he continued.

Is early disease different? Prof Rogler presented data that show that it is.

– There is a difference in pathology, but we have difficulties in diagnosing it.

There are conflicting data on early thiopurines for IBD. In cohort studies it has been shown that these reduce rates of surgery, but there is no convincing benefit for thiopurines in large population-based studies.

Pros and cons with early intervention

Evidence from the REACT trial from 2015, shows that the benefits of early combined immunosuppression for clinical remission were modest and non-significant compared with those on conventional management. However, it was noted a reduction in major adverse outcomes – such as surgery, hospital admission or serious disease-related complications.

– In ulcerative colitis (UC), prospective cohorts are needed to evaluate the impact of recent strategies of early use of disease-modifying therapies and treat-to-target approach with immunomodulators and biologics, Prof Rogler said.

He ended his lecture with data from a

Joanna Torres

Jonas Halfvarson

European population-based inception cohort on the natural disease course of CD during the first 5 years.

– Despite patients being treated early and frequently with immunomodulators and biological therapy in Western Europe, 5-year outcomes – including surgery and phenotype progression – in this cohort were comparable across East and Western Europe. Differences in treatment strategies between Western and Eastern Europe did not affect the disease course. But treatment with immunomodulators reduced the risk of surgery and hospitalisation, Prof Rogler said.

So there are both pros and cons with early intervention in CD.

– We should be cautious and use our brain. Treat early, but base your treatment decisions on an individualised risk/benefit analysis – and monitor efficacy regularly, was his take-home message.

Phase II study on apremilast in UC

Apremilast is an oral small molecule inhibitor of PDE4, an intracellular enzyme that promotes production of proinflammatory mediators and decreases production of anti-inflammatory mediators. Apremilast works intracellularly to modulate these mediators in UC and other inflammatory diseases. It is approved for the treatment of active psoriatic arthritis, and moderate to severe plaque psoriasis. Apremilast is being evaluated in UC and Bechet's disease.

Silvio Danese

Laurent Peyrin-Biroulet

Prof Silvio Danese, Italy, presented a Phase II study on apremilast for active UC. Patients were randomised 1:1:1 to receive aprimilast 30 mg, 40 mg or placebo. Data presented at ECCO were from 12 weeks. A blinded active treatment and extension phase is ongoing.

– Patients treated with apremilast achieved clinically meaningful improvements in disease activity as compared to placebo, Prof Danese said.

Patients in the 30 mg arm achieved improvements in clinical remission, endoscopy, biomarkers of hsCRP and faecal calprotectin – and mucosal healing by endoscopy and histology. Patients in the 40 mg arm achieved improvement in clinical response and hsCRP and faecal calprotectin.

– No new safety signals were detected with apremilast treatment in this study population, Prof Danese summarised the findings.

New drugs

Small molecules are back, Prof Laurent Peyrin-Biroulet stated in a lecture.

– Historically, management of IBD has been based on small molecule drugs – corticosteroids, thiopurines, methotrexate and aminosalicylates, he said.

In the last 20 years, the approval of monoclonal antibodies has been a revolution – but biologics have limitations.

– They have modest efficacy, with up to 30 % non-responders and 10 - 20 % loss of response per year, Prof Peyrin-Biroulet pointed out.

Also there is the risk of immunogenicity, costs and the fact that they require parenteral administration (intravenous or subcutanous).

JAK-inhibitors are small molecules. Prof Peyrin-Biroulet presented three of them: Tofacitinib, filgotinib and upadacitinib.

– Then we have a new mechanism in IBD – sphingosine-1-phosphate (S1P) receptor modulators. Therapeutic S1P1 modulators act as super agonists inducing sustained receptor internalisation, making T-cells unresponsive to he S1P gradient and trapping them in the lymph node.

Ozanimod and etrasimod are S1P receptor modulators being developed. The TOUCHSTONE study on ozanimod in UC shows similar outcomes to biologics.

In his conclusions, Prof Peyrin-Biroulet said that conventional small molecule drugs have played an important role for decades.

– Intrinsic characteristics of small molecule drugs could tackle problems of current IBD treatment paradigm – such as oral administration, no immunogenicity and being efficacious in case of biological failure.

Surgery can improve sexual function

Dr Eugeni Doménech, Spain, had a talk on sexual dysfunction in IBD. There are many potential factors that may impact sexuality in IBD – symptoms such a abdominal pain, body image and drug-related collateral effects.

When it comes to relationship status, the rates of partnership among IBD patients appear to be similar to the general population.

– There is no specific tool to measure sexual function in IBD. The gold standard scores to access sexual function is the International index of erectile dysfunction in men, and the Female sexual function index for women, Dr Doménech said.

Corticosteroids are the only drug that has been involved in sexual dysfunction – by alteration of body image (acne, weight gain etc.) and by disturbing in intimacy (oral and vaginal candidasis, diabetes, mood changes etc.) Methotrexate has been associated with impotence in rheumatoid arthritis.

– Treating these disorders psychiatrically has been shown to reduce these dysfunctions, Dr Doménec stated.

He then turned his attention to sexual dysfunctions after surgery.

– Pelvic surgery may damage pelvic nerves or induce structural pelvic changes leading to sexual dysfunction. But most studies include small sample sizes, focus on ileostomy and IPAA, and only measure post-operative dysfunction. Data suggests that these surgeries do not impact on sexual function – they even *improve* sexual function because of their impact on illness perception. IPAA seems superior to ileostomy because of lower impact on body image.

Sharing information is therefore important. Dr Doménech pointed out that 50 % of patients would like to know the impact of IBD on sexuality and intimacy at diagnosis – and believe their gastroenterologist is the suitable person for this.

– But there is a reluctance to discuss these topics when there is a patient - physician mismatch.

In his conclusions Dr Doménech said that women with IBD are at special risk for sexual dysfunction. Psychological problems are the main driver, depression being the greatest risk factor.

– Chronic illness perception, body image dissatisfaction and active disease seem to be the final causes of psychological disturbances. Screening for psychiatric symptoms, treatment for depression or anxiety and inducing IBD remission seem to be the easiest and more efficient way to restore quality of life – including sexual life, he ended his talk.

IBD disability index

Prevention of disability in IBD was the topic for a lecture given by Prof Jean-Frédéric Colombel, USA. He started by defining disability.

– I think there are misunderstandings on this. Disability refers to the problem that you have in different areas of health domains (objective), whereas quality of life refers to how you *feel* about these limitations and restrictions (subjective). For example: Difficulties in walking (disability), in contrast to how you feel about this (quality of life).

IBD is associated with significant disability, Prof Colombel noted.

– Lower socioeconomic status is associated with more disability in IBD.

He described the IBD disability index, and the validation of this objective tool and encouraged everyone to use it.

– It only takes 10 minutes to fill in!

The problem with IBD trials is that they last for maximum 12 months. Future disease modification trials should consider the inclusion of early IBD and the use of Lemann-index as validated endpoints.

– Patient empowerment and shared decision-making are keys to maximise personalised therapy and compliance – and minimise disability. The role of the environment and the caregivers in patient's well-being should be addressed, Prof Colombel summarised.

"WE CAN'T EDUCATE PATIENTS WITH PHONE-OVER-THE-SHOULDER-MEDICINE"

What the patients want

– We can do so much better for IBD care, Prof Cory Siegel, USA, stated.

He was talking on patients perspectives on treatment goals.

Anti-TNF was approved for IBD 20 years ago, but Prof Siegel presented data from 16,260 patients with CD that showed that only 3 % were on a biologic – 42 % were on corticosteroids.

– And these data are from last year! We are not taking advantage of the progress.

The overall use of biologics at any time point – i.e. "ever use" – was 19 % for CD patients and 6 % for UC, he added.

– Why is this so? I don't think it's about costs. I think it is that even though we want to educate our patients, we can't do that with "phone over the shoulder medicine" – there are too many steps to go through.

Prof Siegel underlined that we need to help patients understand the implications of their disease. But we don't want people to be too scared of their disease.

– But perhaps they need to be more scared than they are – enough to respect the significant, irreversible and destructive nature of bowel inflammation.

Patient-centered care means understanding what is most important to patients with IBD. According to Prof Siegel, to the *patient* mucosal healing is not so important.

– To be able to do the things they used to do – to live normally – is what *they* want. And that is the "hook" I use when I talk with them about their treatment.

He recommended to just ask the patient what their number one concern or goal is related to their IBD. This could be related to a symptom, worry for the future, or how IBD might impact an upcoming life event.

– Patients want what *we* want – remission, no ostomy, prevent cancer – but we need to help them understand that their goals can be achieved with optimisation of

Eugeni Doménech

Cory Siegel

medical treatment. Our patients' outcomes will be better if we can provide them personalised, proactive and patient-centered care, Prof Siegel concluded.

New rapid assays for TDM

Prof Ann Gils, Belgium, talked about therapeutic drug monitoring (TDM) to guide clinical decision-making. She continued by describing several different TDM assays and the general algorithm for loss of response on drug and anti-drug antibody (ADA) measurement.

– If the patient has low drug trough concentration, and no ADA – intensify dosing. If there are low drug trough concentration and ADA – switch within class. And finally, if there are sufficiently high drug concentration, with or without ADA, switch out of class, Prof Gils said.

One of the barriers of TDM in clinical practice is the time lag from test to result. Therefore Prof Gils talked about new, rapid assays. One is called *Fiber optic surface plasmon resonance (FO-SPR) and another Lateral flow* (LF) technology. She described these in more detail.

– With these point of care assays, the required time to perform is reduced, and they require a minimum of laboratory equipment. A Nurse can operate it, and they do not require transport to a central laboratory. They do not require multiple samples in order to be cost-efficient, and have several application opportunities, were Prof Gils' take-home messages.

E-health has a bright horizon in IBD

Dr Pascal Juillerat, Switzerland, talked about web-based registries, which are clearly linked to e-health.

– Our patients are ready for this, he stated.

Dr Juillerat presented several different smart-phone apps for patients, and talked about the reasons for an interest in registries.

– Only 6 % of patients, mostly with severe disease, participate in clinical trials. It can take years until these data are translated into useable information for them. Registries provide more "real practice" data.

He added that "patient-powered" patient registries and research networks exist since as early as 1995.

In his conclusion he underlined that e-health has a bright horizon in IBD, thanks to an ideal (i.e. mostly young) patient population.

– The amount of data collected trough different web-based registries is rising in complexity and heterogeneity. So there is a need for uniformisation of real world data.

It seems that the human/physician investment is going to be huge.

– The solution is probably a combined approach: Patients initiate registration and enter data, while physicians verify details through the same web portal, Dr Juillerat finished.

Optimise the patient before surgery

A lecture on how to get the patient ready for surgery was jointly held by Surgeon Paulo Kotze, Brazil, and Gastroenterologist Peter Irving, UK. Dr Irving talked about the importance to control sepsis and nutrition.

– An association between poor surgical outcomes and poor nutrition has been identified for nearly 100 years, he stressed.

Even so, up to 85 % of CD patients have poor nutrition.

There are many advantages of enteral nutrition: It avoids the need for central venous catheter, it is cheap and, contrary to what many believe, tolerable in most patients – with dietetic support.

– Limited data suggests it improves post-operative BMI, albumin and CRP. Also that it reduces post-operative anastomotic leaks, intra-abdominal abscess, wound infection and diverting stoma, Dr Irving continued.

Optimise patients by stop smoking, correct anaemia and hypoalbuminaemia and think about drugs. Discuss surgical plans with both the team and the patient, ensure thromboprophylaxis and consider post-operative plans, Dr Irving said.

Conflicting data on vedolizumab

Dr Kotze then talked about steroids. These are associated with a higher risk for post-operative complications.

– But azathioprine is not associated with a poor outcome, this is established in an ECCO statement, he underlined.

The first prospective study analysing postoperative complications and previous anti-TNF infliximab with serum levels in CD (2014) showed such an association. So Dr Kotze presented an algorithm for clinical practice.

Ann Gils

Pascal Juillerat

– In elective abdominal surgery, operate as far as possible from the last dose of biologic. Then create an anastomosis. In emergency surgery – if the patient are not on steroids, have a good nutrition and good local conditions – you can consider an anastomosis. If previous steroids, a malnourished patient with bad local conditions – create a stoma.

What if the patient has been on vedolizumab? There was an alarm report from Mayo clinic on postoperative outcomes for patients.

– But recent studies from Leuven (2017) were unable to confirm this. And a poster presented here at ECCO this year, on 45 IBD patients with 30 having detectable levels of vedolizumab, found no difference in high versus undetectable levels in postoperative morbidity, infectious complications and re-admissions, Dr Kotze continued.

He also described staging surgery for UC.

– The more you stage the operation, the less leaks you will have from IPAA, he pointed out.


Antonino Spinelli


Gionata Fiorino

Dr Irving then summarised their final messages.

– Complications in IBD surgery are multifactorial – bad medical techniques is as dangerous as bad surgical technique. Optimise patients – in CD there is normally time to do this.

Avoid steroids at all cost – and consider the risk/benefit with other drugs.

– And stomas are safe, in both CD and UC a staged procedure is often the safest.

"MINIMALLY INVASIVE SURGERY IN IBD IS GOLDEN STANDARD"

The importance of patient counselling

Surgeon Antonino Spinelli, Italy, and Dr Gionata Fiorino, Italy, also had a tandem talk. They talked about enhanced recovery pathways.

– The path to surgery for IBD patients has greatly evolved, said Dr Fiorino.

He went back to the nineties. Then there were no structural recommendations on drugs, and imaging techniques were not so evolved.

– Patients feared surgery, said Dr Spinelli.

Dr Fiorino continued with the multidisciplinary team (MDT), and quoted an article on MDT in presence of the patient in Colorectal diseases from 2017:

"The symptoms and the feeling of the patient are an essential part of the decision-taking process".

Dr Fiorino also described a study on pre-operative imaging with MR enterography for optimal surgical planning.

– In 68 of 75 patients (90,7 %) both the approach and the strategy were correctly predicted by MR enterography.

But sometimes patients expect too much from surgery, so he gave some advice on patient counselling.

– First – adjust expectations. Inform extensively patient and caregivers on expected course, logistics (plan discharge in advance), address practical issues as dehydration prevention if stoma. Remember that stoma preoperative counselling decreases postoperative anxiety.

Minimal invasive surgery a game changer

Dr Spinelli then talked about minimal invasive surgery and enhanced recovery pathways. He called it a "(R)Evolution in surgery".

– Minimally invasive surgery in IBD is golden standard, he pointed out.

Single port surgery is an evolution of laparoscopic surgery.

– It is not only about smaller scars, it is about minimising the surgical trauma, Dr Spinelli underlined.

He presented a study on enhanced recovery pathway combined with laparoscopic surgery after ileocecal resection for CD. It was a case-matched analysis, in which 20 patients were matched with 70 patients who underwent conventional care.

– The analysis found a significantly faster return of bowel function and shorter hospital stay for the enhanced recovery group compared to conventional care pathway.

In their conclusions they established that the perioperative path for IBD patients has improved dramatically over recent years. Minimally invasive surgery was a game changer for both the patient and the surgeon.

– Pre-, peri- and postoperative course benefits from multidisciplinary collaboration. The aim is to reduce the hit of surgery – not only technically!

A dedicated training programme for Ta-TME is needed

Ta-IPAA stands for transanal minimally invasive proctectomy with ileal pouch anal anastomosis. Dr Gianluca Pellino, Italy,

presented a study that aimed to assess the short term outcomes of Ta-IPAA by using data from the Ta-TME registry.

– Trans-anal total mesorectal excision is a bottom-to-up approach to proctetomy, originally proposed for rectal cancer. The procedure is particularly useful in male, obese patients with a narrow pelvis, Dr Pellino explained.

He told the audience that the investigators had found that transanal minimally-invasive proctectomy with IPAA is feasible and safe in patients with UC.

– It is associated with relatively low rates of re-operation and anastomotic leakage. And our data indicate that there might be a possible reduction in pouch failure, Dr Pellino said.

He pointed out at the end that a dedicated training program has to be established for Ta-IPAA – in order to ensure the quality of performing this procedure.

Recurrence is common in CD

Prof Pierre Michetti, Switzerland, talked about preventive strategy after resection surgery in CD.

– A large majority of patients with CD – 70 % – will experience resection surgery. And over 75 % of these patients are considered at high risk of recurrence with current criteria, he underlined.

Prof Michetti presented a meta-analysis of controlled trials on postoperative CD recurrence with anti-TNF therapy. This showed that post-operative prophylaxis with thiopurines and anti-TNF antibodies can reduce and delay recurrence.

– An endoscopic recurrence preceeds clinical recurrence, so endoscopy-driven strategy is currently the best approach. A follow-up strategy with calprotectin is being developed.

In the future, microbiota analysis looking for a reduction in *Faecalibacterium prausnitzii* may help to identify those with risk of recurrence.

– Novel stratification approaches and new interventions such as microbiota manipulations, should be further studied, Prof Michetti summarised.

The incidence of low-grade dysplasia

IBD patients have an increased risk for colorectal cancer (CRC). Previous low-grade dysplasia leads to a higher risk for CRC.

This was pointed out by PhD Michiel de Jong, The Netherlands, who presented a study on long-term risk of high-grade dysplasia and CRC in IBD.

– The aims were to determine long-term cumulative advanced neoplasia incidence following colonic low-grade dysplasia in IBD patients. Also to identify risk factors for advanced neoplasia development following colonic low-grade dysplasia in IBD patients, he said.

It was a nationwide retrospective cohort study, in which all IBD patients with colonic low-grade dysplasia between 1991 and 2005 were included. They were systematically followed up until January 2016.

– We found that the cumulative incidence of advanced neoplasia following colonic low-grade dysplasia in IBD is 21,9 % after 15 years. The risk factors of patients with low-grade dysplasia to develop advanced neoplasia are: Older age (55 years or more) when low-grade dysplasia appear, male gender and a duration of IBD more than 8 years at low-grade dysplasia diagnosis, Ms de Jong concluded.

Age and use of immunomodulators the main risk factors

Dr Thomas Greuter, Switzerland, presented a study that aimed to comprehensively analyse patients in the Swiss cohort in a cross-sectional and longitudinal manner to determine frequency and incidence rates of cancer – and to evaluate risk and protective factors.

– For longitudinal analysis, only IBD patients without cancer at the time of enrolment, and with at least one follow-up visit, were included, he said.

122 of 3119 patients (3,9 %) were identified with malignancy – gastrointestinal cancers were the most prevalent.

– Development of cancer was observed in 2,6 % of these patients over 5 years of follow-up in this large nation-wide cohort, Dr Greuter reported.

The conclusion was that IBD patients have an increased risk for Non-Hodgkin lymphoma and bilary cancer, while no such increased risk was observed for cancer overall in particular.

– Age and recent use of immunomodulators are the main risk factors for development of malignancies – while treatment with 5-ASA and biologics are protective, Dr Greuter summarised the findings.

Prof Julian Panes' two years term as President for ECCO had come to an end at the Conference.

– I want to thank the Governing Board, and all ECCO Committee Members, he said at the end of the Meeting.

– But I leave you in excellent hands. The new President is Prof Silvio Danese, Italy, and during this Meeting Prof Laurent Peyrin-Biroulet, France, has been chosen as President-elect.

Prof Panes also thanked the ECCO Office for their outstanding work all year round.

– And I want to thank everyone of you that has contributed to make this Meeting a success. I hope to see you all in Copenhagen for the next ECCO Congress in March 2019.

And with these words, ECCO 2018 was over.

Per Lundblad