At the Opening Session, all were greeted welcome by Prof Michael Manns, President for UEG, and the Chair of the Scientific Committee, Prof Magnus Simrén.

At this session Prof Harry Sokol, France, and Prof Arthur Kaser, UK, had a tandem talk entitled Host microbial crosstalk in IBD.

The host-microbe crosstalk is disrupted in IBD

They began by talking about different hypotheses for the increased prevalence of immune-related diseases. One of these hypotheses concerns the shrinking gut microbiome.

– The most clear evidence that the microbiota is involved in IBD, comes from animal models. Experimental colitis and ileitis do not develop in animals reared germ-free, said Prof Kaser.

Prof Sokol pointed out that even though the microbiota consists mostly of bacteria, there are also other life forms such as fungi and viruses.

– We think they also play a role, he said. Genes and microbiota modulate cytokine secretion, but this does not explain distinct phenotypes.

– We now have better insight into the immune system – microbes interactions that are required for mucosal homeostasis. The host-microbe crosstalk is disrupted in IBD, Prof Sokol continued.

But it is unclear how, there is no proven causative specific microbe, and if this is a cause or a consequence of inflammation.

– However it is clear there is a dysbiosis in the microbiota composition in IBD – there are structural microbial alterations, reduced diversity and less stable microbiota. Prof Sokol stated.

Encouraging results from early FMT studies in UC

Then they talked about faecal mucosa transplantation (FMT). There have been three randomised, controlled trials on FMT in IBD – all in ulcerative colitis (UC). Two of these were positive, but had a small number of participants.

– The effect size was similar to early phase conventional molecules, Prof Sokol said.

Is there a “golden donor”? In one of the trials, all patients in remission had the same donor (there were six donors in total).

In their conclusions they stated that inflammation causes dysbiosis and it is unknown whether dysbiosis also is a primary event. There are encouraging results of early FMT studies in UC, but the FMT effect size is not superior to conventional therapies.

– There are no FMT data in Crohn’s disease (CD), Prof Kaser underlined.

They thought that we might get defined, precise bacteriotherapy in the future.

– For IBD, we will probably have to combine interventions for the microbiota with interventions on the immune system, Prof Sokol, said.

Filgotinib demonstrate clinical efficacy

One session was on clinical trials in IBD.

Prof Severine Vermeire, Belgium, presented a post-hoc analysis from the Phase II FITZROY study on filgotinib, a selective JAK1 inhibitor. The primary endpoint was CDAI remission at week 10, the patients had moderate to severe CD.

– A total of 174 patients were randomised. 111 in the active arm, and 37 in the placebo arm completed the study, Prof Vermeire said.
The analysis found that filgotinib is the first JAK inhibitor to demonstrate clinical efficacy in patients with moderate to severe CD, consistently across all endpoints.

- This post-hoc analysis suggests that filgotinib is inducing numerically higher clinical remission rates than placebo—indeed, independently of disease duration and disease location.

A Phase III program in CD and UC is currently ongoing.

**Upadacitinib as induction treatment in CD**

Another oral, JAK1-selective inhibitor is upadacitinib, currently in Phase III studies in rheumatoid arthritis and under investigation for the treatment of CD, UC, psoriatic arthritis and atopic dermatitis.

The Phase II study CELEST’s objective was to assess the safety and efficacy of upadacitinib in subjects with moderately to severely active CD, who had an inadequate response or intolerance to immunosuppressants or TNF-antagonists. The findings from CELEST were presented by Prof William Sandborn, USA.

- Steroids were aggressively removed during induction, this was one of the first trials to do this. Almost all patients had failed biologics, so this was one of the most refractory patient groups to enter a trial.

They were randomised to 5 different doses and one placebo arm.

- Upadacitinib demonstrated efficacy and safety as an induction treatment in subjects with long-standing and refractory CD, was the first conclusion from Prof Sandborn.

Statistical significance was met for co-primary endpoints—endoscopic and clinical remission. A significant dose-response relationship compared to placebo for secondary endpoints was seen.

- Steroid-free remission was demonstrated during the 16-week induction, with early and significant improvements in hsCRP and faecal calprotectin. Safety and tolerability was consistent with observations in the Phase II studies in rheumatoid arthritis, Prof Sandborn summarised.

**Risankizumab in CD**

Prof Brian Feagan, Canada, presented two trials. The first was on open-label maintenance therapy with subcutaneous risankizumab in patients with moderate to severe CD.

The IL-23 pathway has been implicated in the pathogenesis of CD, and risankizumab is a humanised molecular antibody that targets the p19 subunit specific to IL-23.

- The objective was assessment of the efficacy and safety of open-label 180 mg risankizumab at week 52, he said.

The study found that this regimen was effective as maintenance therapy after one year. Subjects randomised to the 600 mg arm during period 1 had higher rates of week 52 endoscopic endpoints than subjects randomised to placebo or 200 mg risankizumab.

- Overall, risankizumab was well tolerated with no new safety signals detected during subcutaneous maintenance treatment. The specific blockade of IL-23 via inhibition of p19 warrants further investigation in CD, Prof Feagan summarised the findings.

**Ozanimod demonstrate early clinical improvement**

STEPSTONE is an open-label, Phase II trial on ozanimod, an oral, once-daily immunomodulator that selectively targets sphingosine 1 phosphate receptors 1 and 5. Ozanimod has demonstrated clinical efficacy in UC, and is being evaluated in CD. The STEPSTONE trial was on CD-patients, with a Crohn’s disease activity index (CDAI) of 220 - 450.

- Oral ozanimod demonstrated meaningful clinical improvements as early as week 4, and endoscopic improvements at week 12, as demonstrated by CDAI clinical response and remission, and reduction of 25% and 50% in Simple Endoscopic Score for Crohn’s Disease (SES-CD).

All endoscopic assessments were read in a blinded manner by an imaging core lab.

- Adverse event and serious adverse event rates appeared to be related to underlying CD. The overall safety profile in CD was similar to that observed in UC. No new safety signals were identified, Prof Feagan concluded.

**Endoscopic scores for CD**

Another session was on how to define therapeutic response in CD. Prof Alessandro Armuzzi, Italy, started this session by talking...
about clinical features and biomarkers.

– A study on CRP levels in CD-responders and non-responders found that early normalisation of CRP levels was associated with better sustained response. Also that loss of response was associated with significantly higher CRP levels over time, he said.

So how to define therapeutic response?

– For clinically meaningful response there should be a clear improvement in symptoms at different timepoints: Clinical judgement from week 2, and disease activity indices for longitudinal comparison. A drop or normalisation of CRP (if elevated at baseline) from week 4, and a drop or normalisation of faecal calprotectin (if elevated at baseline) from week 12, Prof Armuzzi summarised.

There are several endoscopic scores for assessment of severity in CD. So which one to use? This was the topic for Prof Oliver Pech’s, Germany, talk.

According to him, the endoscopic scores for CD are the Crohn’s disease index of severity (CDEIS) and the SES-CD.

– Change of both scores can be used to predict clinical response to therapy. Both scores have a substantial intra- and inter-observer agreement, he said.

Prof Pech added that SES-CD seems to be more responsive.

– In-vivo molecular imaging is a promising new method to predict therapeutic response to anti-TNF treatment, he ended his talk.

Are we ready for PROMs?

Patient reported outcomes measures (PROMs) are short, standardised, validated, self-completed questionnaires that measure patients perception of their own health condition or its treatment. There is no interpretation of the patient’s response by a clinician or anyone else.

– Why consider the patient’s perspective, asked Dr Johan Burisch, Denmark.

IBD affects many dimensions of life, and clinical outcomes are not always related to how patient feels, was his answer.

– Physicians commonly underestimate the severity of the illness, and overestimate treatment outcomes. And patients welcome being involved – a fact that gives significant health benefits in itself.

It also helps patients empowerment, and improves adherence. Dr Burisch described different adherence scores for PROMs, including those using e-health reporting.

– E-health is real-time capturing of PROMs, and enables monitoring of symptoms, self-management, e-learning and communication, he stated.

But PROMS need a purpose. A study from 2016 had found that response rate was low, below 50 %.

– Before we start handing out questionnaires, we must ensure that patients understand them, and why they are needed.

So, overall, are we ready for PROMS? Dr Burisch thought we are not quite there yet.

– Several PROMs are available, but their added value to normal practice is unknown. Must FDA guidelines be followed in development of new PROMs? And which PROMs should we use, and when and how should we measure them?

With these questions he ended his lecture.

Vedolizumab and extra-intestinal manifestations

One session concerned long time management with biologics. Dr Tim Raine, UK, who also was one of the Chairs, gave a State-of-the-art introduction.

– It is a paradox that when we start treatment of our patients, the drugs we use we choose from the results from registration trials – that are conducted in the short term, he pointed out.

Loss of response is a problem in the long term. Dr Raine showed results that demonstrate that immunomodulators reduce immunogenicity of infliximab and adalimumab.

– What about vedolizumab? A study
from 2017 showed that – in those patients that initially responded to vedolizumab – that loss of response had not increased after 152 weeks.

It also seems likely that ustekinumab have long term efficacy in those that initially responded to the drug, he said.

Dr Sara Tadbiri, France, then presented a post-hoc analysis of the OBSERV-IBD cohort of GETAID.

– The potential efficacy of vedolizumab on extraintestinal manifestations (EIM) of IBD is controversial. The drug has gut specificity, but on the other hand there is an active homing axis between the gut and inflamed joint in patients with ankylosing spondylitis, she said.

It was a prospective, multicentre observational cohort study. The cohort consisted of 173 patients with CD and 121 patients with UC.

– In the OBSERV-IBD cohort, vedolizumab was associated for achieving complete remission of EIMs in patients with IBD, Dr Tabiri continued.

Inflammatory arthralgia and/or arthritis may occur upon vedolizumab therapy – particularly in patients with CD and prior diagnosis of ankylosing spondylitis.

– Paradoxical cutaneous manifestation may occur on vedolizumab therapy, suggesting that paradoxical inflammation is not restricted to the anti-TNF drug class, was Dr Tadbiri’s final conclusion.

Ustekinumab an interesting therapeutic option in CD

Another GETAID study was reported by Dr Pauline Wils, France.

– The aim was to evaluate the long-term efficacy and safety of subcutaneous ustekinumab, and to identify predictive factors of ustekinumab failure-free survival in our multicenter cohort of anti-TNF refractory CD patients, Dr Wils explained.

It was a retrospective observational study, carried out in 20 centres affiliated with GETAID.

– We can report the first real-life experience of long-term outcome of ustekinumab in CD patients refractory to anti-TNF, with a median follow-up of more than 2 years. 55 % of patients maintained ustekinumab during the follow-up, without loss of response, intolerance or surgery, with a good safety profile, she told the audience.

No predictive factor of ustekinumab failure-free survival was identified.

– These results suggest that ustekinumab should be considered as an interesting and safe therapeutic option in highly refractory CD patients, Dr Wils summarised.

Combo therapy with adalimumab and immunomodulator

Dr Hiroki Tanaka, Japan, presented a subanalysis of the ADJUST study. The aim was to investigate the usefulness of combination therapy with adalimumab and immunomodulators based on the long-term retention rate of those who participated in ADJUST.

970 patients were included in the analysis.

– We found that this combination therapy significantly increased the retention of adalimumab – especially in infliximab-treated patients with higher CRP levels, and those who received concomitant treatment with prednisolone. However, combination therapy of adalimumab and immunomodulators did not appear to be effective for most of the patients who participated in this study, Dr Tanaka said.

Spacing of infliximab may be an option

Many IBD patients are currently in long term clinical remission with infliximab. To date, there are no clear guidelines on infliximab withdrawal. Previous studies have investigated the withdrawal of infliximab showing a clinical relapse in 50 % of cases at one year of remission, and in 30 % of the cases for patients in deep remission.

– Spacing of infliximab (i.e. allow for longer periods between administration) may be an option for IBD patients with
long standing treatment. It is already tested in patients with rheumatoid arthritis with interesting results, and empirically used in IBD patients in cohorts in France, said Dr Gaspard Dufour, France.

He presented a French retrospective multicenter study, that showed that more than 70% of patients remained in clinical remission after IFX spacing over 9 weeks. – A majority of the patients who had a clinical relapse after spacing, presented a clinical response after IFX intensification. Only one case of infliximab infusion reaction occurred after infliximab spacing, Dr Dufour continued.

CD patients with a long duration of infliximab treatment before spacing are less at risk for clinical relapse. – A larger multicenter retrospective study – The SPACE registry from the GETAID – is ongoing to confirm these preliminary results, he said.

Imaging can be useful for predicting response
In a session on multidisciplinary management of complicated luminal CD, Prof Stuart Taylor talked about imaging.

– Imaging is highly efficacious in detecting and staging complex CD, he established.

Choice of imaging modality depends on local availability, but MR, CT and ultrasound (US) all have supportive evidence base – but Prof Taylor encouraged to think of radiation exposure.

– We should not use CT as first line, due to radiation. But there is a caveat here: This is based on old studies, but new technology has changed that. I think that when they have upgraded your machines at your clinic, CT might be back again.

He also underlined that only repeated use of CT can cause radiation damage – not one.

– In pregnancy, US is safe – regardless of which trimester the patient is in.

Prof Taylor also pointed out that imaging might be useful for predicting response.

– If the intestine resume its motility within 12 weeks – which can be determined by imaging – the prognosis is good. We should use imaging to stratify patient management in complex CD, was his take-home message.

Immediate surgery or percutaneous drainage?
Then Prof Severine Vermeire and Prof André d’Hoore, both from Belgium, had a tandem talk on management of ileal abscess.


– Traditionally with emergency laparotomy and abscess drainage with or without bowel resection, said Prof d’Hoore.

Prof Vermeire presented a metaanalysis on abscess recurrence rate with percuta-
The pooled proportion of PD patients requiring surgery was 70.7%.

Or put in another way – surgery could be avoided in 30%. I think we can avoid surgery in some patients by using PD, she said.

I think that is the way to go. Surgery after PD is also associated with better outcome, Prof d’Hoore agreed.

In their conclusions they acknowledged the fact that a significant proportion of CD patients presents with ileal abscesses as first presentation. PD has replaced immediate surgical intervention.

Following drainage, sufficient time is needed for sepsis control, and decision for elective surgery or medical therapy needs to be made during multidisciplinary discussions between gastroenterologist and surgeon, they said.

Finally, anti-TNF treatment may be a valuable option – but close follow-up is needed, was their last message.

“THE POOLED PROPORTION OF PD PATIENTS REQUIRING SURGERY WAS 70.7%”

In order to mark the 25 years anniversary for UEG Week, a special session was held on the last day of the Congress – on major advances in gastroenterology and hepatology over the last 25 years.

Prof Michael Manns, President of ECCO, began by stating that what we have achieved in these years is all down to research.

Then selected speakers from different subspecialties talked about the main findings from their viewpoint. The first speaker was Prof Julian Panes, President of ECCO. He talked about IBD and biologics.

The first biologic was infliximab, and Prof Panes said it was “love at first sight”.

– This new drug was shown to achieve mucosal healing, he said and showed endoscopic pictures from 1995.

In clinical practice, achieving mucosal healing is associated with reduced risk of relapse, number of hospitalisations, surgery requirements and – probably – reduced dysplasia.

In clinical trials, assessment of mucosal lesions improves patient selection, reduces placebo response and are objective evidence of efficacy, Prof Panes continued.

But inflammation is a complex, redundant heterogeneous process – hence therapeutic response is also heterogeneous.

– After some time we saw that it was no longer like in the beginning – loss of response over the first year was 30 - 50%.

There were multiple causes for this – immunogenicity, target abundance, pharmacodynamics and target engagement.

He continued his talk with the development of small molecules, such as JAK-inhibitors.

IBD and biologics revolutionised our practice! They made lives of patients better, and we learned a lot – on pharmacokinetics and pharmacodynamics, targets etc. – together. It was the biggest revolution since corticosteroids, Prof Panes ended his talk.

And with this, IBD Congress News also ends its coverage from UEG Week. Next year the Congress will be given in Vienna, October 20 - 24. Mark the date!

Per Lundblad