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From the New and Complex Concepts to the Real Patient: Science and Clinic in IBD

Symposium 206
Madrid (Spain), March 31 – April 1, 2017

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Symposium 206
From the New and Complex Concepts to the Real Patient:
Science and Clinic in IBD
Scientific Organizers:

S. Danese
Rozzano
(Italy)

A. Dignass
Frankfurt
(Germany)

J.P. Gisbert
Madrid
(Spain)

F. Gomollón
Zaragoza
(Spain)

Publisher
FALK FOUNDATION e.V.
Leinenweberstr. 5
79108 Freiburg
Germany

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Christine Vetter
Specialist medical journalist, Cologne, Germany

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Advancements in the understanding of inflammatory bowel disease and new options for diagnosis and treatment are currently leading to a fundamental change in disease management. Although established treatments remain important, an increasing number of patients with a complicated disease progression course are requiring personalized therapy involving innovative treatments and treatment escalation at an early stage.

New treatment strategies, new therapeutic aims, and new medications are likely to shape the future of inflammatory bowel disease (IBD) management. These advances are based on an improved understanding of the disease in terms of the genetic background as well as in terms of epigenetic phenomena and environmental factors affecting pathogenesis. Furthermore, it is increasingly clear that the microbiome also has a considerable effect on the disease. The relationship between the various factors is very complex, which will likely be reflected in future treatment algorithms.

While established drugs will remain an important pillar of treatment, anti-TNF strategies, integrin antagonists, and IL-12/IL-23 blockers provide new treatment options that specifically target the pathogenesis of the disease for patients who experience severe disease courses. The pharmaceutical pipelines are full of development candidates that may dramatically change the treatment of chronic inflammatory conditions, thus also altering the treatment of IBD.

We are already seeing changes in treatment strategies and treatment goals right now. Due to the advances in diagnostic approaches and treatment options, it is now easier than ever to assess the nature of the disease in individual cases and predict the disease course. Because we can now provide customized treatment to suit the individual situation at an early juncture, we are increasingly able to make the best possible use of the “window of opportunity”. This can help us to influence the course of the disease and optimize the long-term outcome by using an appropriate treatment plan.

This goes hand-in-hand with the “treat to target” strategy which has already been proven to be successful in the field of rheumatology. This means no longer treating with a focus on the patient’s clinical symptoms, and instead treating with a focus on objective findings. The specific goal here is confirmation of mucosal healing with endoscopy. Furthermore, histologically confirmed remission is also being discussed as a possible treatment goal. This approach may ultimately change the long-term disease course and reduce or prevent complications such as the formation of fistulae and/or development of strictures and stenosis, finally reducing the need for surgical interventions and other associated treatments, which are often very burdensome for the patient.

Prof. Dr. A. Dignass
on behalf of the scientific organizing committee
Treating disease progression with proven strategies and innovations

Today, treatment for ulcerative colitis and Crohn’s disease is not limited to improving symptoms. Instead the goal is to intervene as early as possible in order to modulate the course of the disease and prevent its progression, including in particular the development of structural damage as a result of chronic inflammation. Mucosal healing as confirmed by endoscopy is a clear treatment objective and can be achieved in many patients using tried-and-tested therapeutic agents such as mesalazine or budesonide. In addition to such therapies, the treatment spectrum is currently expanding to include new active pharmaceutical ingredients and treatment approaches aimed at modulating the disease process in a targeted and individualized way.

Epigenetic modifications play a key role

According to A. Dignass, Frankfurt (Germany), there are other factors alongside genetics that trigger disease pathogenesis and chronic inflammatory processes. First and foremost among these are epigenetic modifications that modulate gene activity. As S. Schreiber, Kiel (Germany), explained, these modifications are a key factor in susceptibility as well as in the manifestation and progression of the disease.

Epigenetic signatures clearly exist and may be relevant for the respective phenotypes. However, this is not a static system and, as S. Schreiber noted, presumably involves “crosstalk” with additional factors, in particular with the microbiome. There even seems to be a direct link between epigenetic factors and the pattern of the microbiome, and a feedback loop between these two factors, which plays a decisive role in determining disease susceptibility, must be presumed.

Reduced diversity of the microbiome

According to F. Guarner, Barcelona (Spain), a reduction in the diversity of the microbiome is indicated by findings which show that disruptions to the normal microbial ecosystem in the intestine are generally found in patients with IBD. “This is also true during phases of remission,” the physician emphasized. These patients furthermore exhibit a reduction in bacterial species that are associated with potentially anti-inflammatory activity.

For a long time, gastroenterologists were certain that a better understanding of the genetic background of ulcerative colitis and Crohn’s disease was key to advancements in treating inflammatory bowel disease (IBD). It has since become clear that the genetics are far more complex than was long believed, and that these diseases are in no way monogenetic disorders.
While such changes are particularly noticeable in patients with Crohn’s disease, they appear less marked in patients with ulcerative colitis. F. Guarner explained that dysbiosis is particularly pronounced in patients with Crohn’s disease who experience a severe progression and numerous relapses as well as in patients with pancolitis.

**Making use of proven treatment strategies**

Thus far the findings on the microbiome have had little therapeutic relevance for IBD. Baseline therapy for ulcerative colitis continues to involve the administration of mesalazine. According to B. Siegmund, Berlin (Germany), this therapy is particularly appropriate for mild to moderate ulcerative colitis, both oral and rectal forms of administration should be used in combination to increase efficacy. Mesalazine also has a firmly established place in the treatment of pancolitis.

“In addition, there is a group of patients with Crohn’s disease who can be effectively treated with mesalazine,” B. Siegmund emphasized. If necessary, the drug can also be combined with budesonide.

**Innovations are expanding the therapeutic arsenal**

In cases where patients are refractory to proven treatment measures, physicians are increasingly turning to alternative therapies. The possibilities range from established biologics to innovative treatment options.

G. Rogler, Zurich (Switzerland), described a paradigm shift away from biologics and towards small molecules, which are expected to become increasingly important for the treatment of IBD in the future. Thus far, TNF inhibitors in particular have become established alongside other proven drugs. This drug class includes infliximab and its biosimilars as well as adalimumab, golimumab and certolizumab. G. Rogler named anti-integrins such as vedolizumab and etrolizumab as well as anti-interleukin 12 and anti-interleukin 23 antibodies such as ustekinumab and risankizumab as examples of further innovations.

According to the physician, however, the use of biologics is limited by their efficacy and the range of side effects, and intensive work is being done to develop further treatment alternatives. Hopes rest on the development of small molecules that specifically intervene in the disease process. As examples, G. Rogler pointed to Janus kinase (JAK) inhibitors as well as SIP receptor agonists and antisense oligonucleotides. These new drugs may lead to significant advances in the treatment of ulcerative colitis and Crohn’s disease, perhaps as monotherapies or more likely in combination with proven treatment options.

**New therapeutic concepts and treatment goals**

Advancements in IBD are not limited to innovative active ingredients, they also involve new developments in treatment goals. “In this respect, we have become far more ambitious,” said L. Peyrin-Biroulet, Vandoeuvre-lès-Nancy (France). Gastroenterologists are currently learning from other disciplines, e.g. from the treatment of rheumatoid arthritis in rheumatology and from the treatment of multiple sclerosis in neurology.

In addressing these conditions, which are also triggered by chronic inflammation, the focus is increasingly on making the most of the “window of opportunity”, in other words using effective anti-inflammatory treatment strategies to intervene in the disease process early on. “Disease management at the earliest possible stage is key,” explained L. Peyrin-Biroulet. For IBD, the goal is to quickly achieve the deepest remission possible in order to prevent further progression of the disease and the development of irreversible structural changes.
Crohn’s disease and ulcerative colitis remain a great medical challenge for the time being

Even though there have been advances in terms of our understanding of Crohn’s disease and ulcerative colitis, both diagnosis and treatment remain a medical challenge. This is not likely to change soon, as was clearly shown at the Madrid symposium. However, the advances that have already been made give us grounds to hope that in future, more patients can be spared burdensome interventions such as colectomy.

Highly complex: the genetic background of IBD

The identification of the NOD2 gene as a susceptibility gene for IBD was a breakthrough in the research into the genetic background of ulcerative colitis and Crohn’s disease. According to I. Cleynen, Leuven (Belgium), more than 240 IBD susceptibility genes are now known, which shows just how complex the conditions can be. In the genome-wide association studies (GWAS), associations with other immunologically triggered conditions, and with genes known to be involved in the control of intestinal barrier function and in permeability, have also been found.

Researchers’ attention is now increasingly focused on differentiating between “high-risk” and “low-risk” genes. The results could certainly be clinically relevant if corresponding patient profiles can be established that provide useful indications regarding individual prognosis, or if response or non-response to certain treatment regimens can be predicted based on genetic findings. It is also possible that genetic analysis could indicate potential side effects of certain forms of treatment. “This lays the foundation for customized treatment,” said I. Cleynen.

Differentiating between special phenotypes

The concept of achieving better treatment control by classifying different manifestations is by no means a new one according to C.L. Noble, Edinburgh (Great Britain). As early as the last century, attempts were made to classify specific phenotypes in Crohn’s disease and ulcerative colitis. The classification was based largely on the location of the inflammation and the age of the patient at disease onset.

This continued into the 21st century with the Vienna and Montreal classifications; however, it became increasingly clear that IBD was influenced by both genetic and environmental factors such as stress, smoking, and nutrition, as well as by the microbiome. “All of these factors may work together to determine the phenotype,” C.L. Noble explains. There is a mountain of data that needs to be compiled and rationally interpreted in order to better classify the disease phenotypes, and also to identify sub-phenotypes.
Changing diagnostic concepts

There is no one diagnostic test that can be used to diagnose IBD. Rather, the diagnosis is determined by the clinical picture, the detection and location of the inflammatory processes, and the endoscopic and histological findings, reports G.J. Mantzaris, Athens (Greece). Some important parameters here include the intestinal symptoms that occur, such as pain, chronic diarrhea, and rectal bleeding, and perhaps also other manifest symptoms such as fever, weight loss, and fatigue, or even extra-intestinal manifestations of IBD. Differential diagnoses that may need to be considered include enteral infection, irritable bowel syndrome, and celiac disease.

However, a change is currently underway, as we move away from more clinically-based diagnostics and towards a more precise, personalized kind of diagnostics that also takes molecular parameters into account. This makes it easier to determine the disease status, including any damage that has already manifested. It also makes it easier to predict future developments, which in turn has an impact on the treatment concepts. “We can use diagnostic parameters to predict, within certain limits, which patients can be sufficiently treated with the standard therapy and which patients require more aggressive treatment strategies,” explains G.J. Mantzaris. For instance, using the monitoring of the C-reactive protein (CRP), it is also possible to determine at an early stage whether or not a patient will respond to anti-inflammatory treatment with a TNF antibody, for example. And there is more: “If there is a pronounced drop in CRP after initiation of treatment, this indicates a very good clinical response, meaning that there is a good chance that mucosal healing will occur,” says G.J. Mantzaris.

In his view, the concept of “personalized diagnostics” should be viewed in a holistic manner. The psychological burden on the patient that is caused by the disease as well as the patient’s fears and needs must all be taken into account. Only such a comprehensive approach can do justice to the multifactorial pathogenesis and overall high level of complexity of IBD, allowing the development of a truly customized treatment concept.

Making the most out of the “window of opportunity”

Diagnostics and treatment should be implemented at an early juncture in order to make use of the “window of opportunity”. The aim here is to use a timely anti-inflammatory treatment strategy to achieve disease control at an early stage, thus helping to prevent the development of strictures, fistulae, and abscesses, and potentially sparing patients from surgical interventions.

This is why D.T. Rubin, Chicago (USA) insists that it is essential to develop personalized treatment concepts. He emphatically rejects the idea of “one size fits all” when it comes to IBD. Rather, it is all about finding “the right treatment for the right patient”. Part of this is good monitoring and, where necessary, adjustment of the treatment with the aim of achieving deeper remission in order to prevent the disease from worsening again and resulting in another acute flare-up.

According to M. Allez, Paris (France), in the case of Crohn’s disease, even stem cell transplantation cannot be ruled out. In patients with a very severe disease course who do not respond to any of the other treatment options, autologous hematopoietic stem cell transplantation should be considered. Other procedures such as mesenchymal stem cell transplantation are currently being developed.
Keeping disease complications in mind

According to M. Esteve, Barcelona (Spain), special attention must be paid to the development of disease complications when diagnosing and treating IBD. This includes the formation of strictures, which require at least one surgical procedure within 10 years in 80% of affected patients with Crohn’s disease. However, surgery does not usually cure the patients. About 70% of those affected develop another such lesion within one year, and this requires another surgical procedure within four years in 40% of cases. According to A. Spinelli, Rozzano (Italy), systematic anti-inflammatory treatment is always indicated alongside surgical treatment.

The hope that anti-TNF treatment strategies can prevent the development of strictures and stenoses has proven false according to A. Spinelli. Retrospective studies even suggest that strictures and obstructions can develop as a complication of infliximab treatment. This highlights the importance of surgical interventions. As an alternative, the possibilities of an endoscopic balloon dilatation and, if necessary, a stent implantation should be explored.

Suitable biomarkers still need to be found

Biomarkers are playing an increasingly important role in IBD diagnosis, particularly with regard to early detection of the disease, as B.E. Sands, New York (USA) points out. Various parameters are being tested, but as yet there is no ideal biomarker for IBD. Such a biomarker test would need to be non-invasive and simple to use, and it would need to deliver a valid result quickly, reliably, and economically. The test would also need to be standardized, and it would need to be specific to each disease and provide an accurate, reproducible result.

Potential biomarkers for IBD that are currently being investigated include, in particular, antimicrobial antibodies, acute phase markers such as CRP, the erythrocyte sedimentation rate, and fecal markers such as calprotectin and lactoferrin.

Imaging is extremely valuable

Until we have the ideal biomarkers, imaging remains an extremely important diagnostic method for IBD diagnosis. According to G. Fiorino, Rozzano (Italy), this applies to both computed tomography and magnetic resonance imaging as well as to ultrasound imaging for diagnostics in the small intestine. These procedures are used for primary diagnostics, including to determine disease activity, but they are also used to control and monitor treatment management, and to investigate specific disease situations and complications such as strictures and stenosis. While imaging has very high diagnostic value, it must always be viewed in context together with the endoscopy, emphasizes G. Fiorino.

Endoscopic procedures for IBD diagnostics in particular have undergone significant advances in the last few years. As an example, B. Sicilia, Burgos (Spain) cites chromoendoscopy, which is much better at detecting dysplasia than conventional endoscopy. “With this procedure, we detect about 94% of neoplastic lesions,” says the physician.
Cancer and IBD – What do we need to bear in mind?

Furthermore, we always need to keep in mind the possibility of development of a carcinoma, as the risk of this is significantly increased in IBD patients. If a carcinoma manifests in an IBD patient, according to L. Beaugerie, Paris (France), this would also affect the IBD treatment as follows: Immunosuppressants should be stopped until the tumor is under control.

As part of treatment, the additive myelotoxicity of the chemotherapy and of treatment with methotrexate and/or thiopurines as well as the risk of more severe IBD symptoms as a result of hormone therapy of the tumor must all be taken into account. For example, with docetaxel, sunitinib, sorafenib, and modern cancer immunotherapies, exacerbations of the IBD can be expected.

The risk of infection must be taken seriously

According to E. Domènech, Badalona (Spain), the drug-related infection risk in patients with Crohn’s disease and ulcerative colitis is a problem that must be taken seriously. A distinction must be made between a general infection risk, and the risk of severe infections and opportunistic infections.

There is no elevated risk of infection in the case of treatment with aminosalicylates such as mesalazine. Antibiotics are also no problem in this respect, apart from the risk of infection with clostridium difficile. However, the situation is quite different when patients are treated with systemically active steroids and/or immunomodulators such as thiopurines, methotrexate, or calcineurin inhibitors. Furthermore, in the case of treatment with anti-TNF antibodies, the elevated risk of infection must be taken into account.

Exploiting the therapeutic spectrum

The standard therapeutic agents continue to have a very high level of importance in treatment. According to P.D.R. Higgins, Ann Arbor (USA), in addition to mesalazine, these include immunomodulators such as azathioprine, whose side effects can be minimized using a combination of allopurinol and low-dose azathioprine, and methotrexate. With methotrexate, side effects such as nausea, vomiting and fatigue can be expected initially, but these usually subside in the further course. The affected patient should also be advised to take the drug in the evening.

Although not officially approved for this indication, according to E.F. Stange, Tübingen (Germany), treatment with calcineurin inhibitors such as cyclosporine A or tacrolimus can be considered for patients with steroid-refractory ulcerative colitis.

SPECIAL LECTURE
Inflammatory bowel disease: opportunities for prevention

The incidence and prevalence of inflammatory bowel disease is currently increasing worldwide. According to J.-F. Colombel, New York (USA), this automatically raises the question: To what extent can preventive concepts have an effect on IBD? “This is all the more true because it is mostly young people who are affected, and a cure is not possible, meaning that lifelong treatment is required. This brings with it a burden on the individual as well as socio-economic costs.”

A distinction should be made between primary, secondary, and tertiary prevention. In healthy persons, primary prevention may be achieved by reducing risk factors. This is especially important in families with a history of frequent manifestations of ulcerative colitis or Crohn’s disease.

In contrast, secondary prevention is about early detection of the disease using screening measures and early intervention – ideally in the preclinical stage. The idea behind this is to begin treatment as early as possible in order to have a positive influence on the subsequent course of the disease. “In this area, we should definitely learn lessons from other chronic diseases,” explains J.-F. Colombel.

However, realistically, the best opportunities for prevention appear to be in tertiary prevention, wherein we strive to prevent disease complications through better diagnostics and better treatment of patients.
New treatment options on the horizon

According to G. Van Assche, Leuven (Belgium), biologics have been a treatment option for IBD for 18 years now. The drugs have become well-established and, as F. Gomollón, Zaragoza (Spain) – among others – points out, TNF antibody biosimilars are also available. According to W.J. Sandborn, La Jolla (USA), vedolizumab, as the first integrin inhibitor, and ustekinumab as the first IL-12/IL-23 antibody have already expanded the therapeutic spectrum for IBD.

There is a wide array of other development candidates for the treatment of IBD in the pharmaceutical pipeline. S. Danese, Rozzano (Italy) names etrolizumab, another integrin inhibitor (but with a different molecular target) as an example. Small molecules such as Janus kinase inhibitors could also bring about new therapeutic innovations. According to G. Rogler, Zurich (Switzerland), tofacitinib is the first representative of this class of drug. Other promising drugs he mentions include the S1P receptor agonist ozanimod and the substances laquinimod and mongersen. However, it can be assumed that the small molecules will not be used in future as monotherapies for IBD, but will rather be used primarily in combination with other established therapeutics.

The advantages of small molecules are that they have oral availability, they undergo a defined metabolic process, they have only a short serum half life, they do not have an antigenic effect, and they can be produced using conventional chemical synthesis. This means that the manufacturing costs are lower than for biologics.

More ambitious treatment goals – “being able to live normally again”

Quite apart from the potential of new drugs, therapeutic strategies are also undergoing major change, as L. Peyrin-Biroulet, Vandoeuvre-lès-Nancy (France) explains: “We have grown far more ambitious in terms of the IBD treatment goals.” Efforts to intervene earlier in the disease process in particular are providing hope that we might be able to positively influence it. “The aim here is to help patients have a better quality of life, and ultimately lead a completely normal life again.” However, the prerequisite for this is a deep remission, which requires a correspondingly early intervention. “We need to move away from a reactive treatment strategy and towards a proactive one,” insists D.W. Hommes, Los Angeles (USA).

Therefore, according to L. Peyrin-Biroulet, the “treat to target” principle must be followed. This principle has proven to be successful in other conditions such as rheumatoid arthritis. The extent to which this approach can delay the development of complications is currently being tested in a GETAID study.
According to F. Magro, Porto (Portugal), what needs to be kept in mind here is that Crohn’s disease and ulcerative colitis are heterogeneous conditions. This means that the same treatment algorithm cannot be applied to all affected patients. Therefore, it is also essential to optimize strategies for preventing a recurrence of the disease in patients who have undergone a surgical intervention.

According to P. Irving, London (Great Britain), much remains to be done in this area as well. The patients should definitely continue to receive drug treatment even after the surgery. There are no “easy” patients.

In the case of IBD, we should be careful not to jump to the conclusion that the patient presenting to us is a patient who will be “easy to treat”. According to A. Sturm, Berlin (Germany), there are no such patients. This also applies to ulcerative colitis. For this condition, we have not yet established parameters that can be used to reliably predict the further course, so the supposedly “simple” disease could develop into a more severe manifestation of the condition. “Inflammation is the most important driver of progression here,” says A. Sturm. Therefore, according to him, systematic anti-inflammatory treatment is crucial: “An uncontrolled disease leads to structural changes, and ultimately to irreversible damage.” He named mesalazine the method of choice for treating mild-to-moderate ulcerative colitis. “Using this drug, about one in two patients can achieve good disease control, even in the long-term,” explains the gastroenterologist.

If the desired effect is not achieved, further efforts should initially be focused on optimizing the treatment. According to A. Sturm, the first step to be taken here is to check patient compliance. It is also important to check whether the best possible preparation is being used (granules, Eudragit-coated preparation). Furthermore, it is important to ensure that the site of the disease has been sufficiently taken into account, and that full advantage is taken of all of the available options – oral treatment, rectal treatment using foam, enemas, or suppositories, and combinations of these. In this context, he pointed out that once daily dosing with mesalazine preparations was found to be more effective in studies than three times daily dosing. A combination treatment with various formulations of mesalazine (rectal and oral) and also other drugs, such as budesonide or an immunomodulator, may be considered.
Treatment optimization before treatment escalation

According to J.O. Lindsay, London (Great Britain), this applies in a similar manner to Crohn’s disease, in which treatment optimization should be attempted before any treatment escalation. It should never be assumed that the data collected in studies can be automatically applied to everyday clinical practice without further analysis. Far from it – a personalized treatment concept needs to be worked out for each individual case.

This should be done in close interaction of the treating physician, the patient, and a specialist IBD nurse if possible. According to T. Øresland, Lorenskog (Norway), the surgical treatment options must also be taken into account in all cases, and this should be done particularly early in severe cases.

Future strategies

According to W.J. Sandborn, La Jolla (USA), in future we can expect increasingly personalized treatment of IBD patients. The pharmacokinetic properties of the prescribed drugs must be taken into account here, and the possibilities of combination therapy need to be explored. Furthermore, concrete treatment, end points and treatment goals must be defined, and treatment should be carried out in accordance with the “treat to target” principle.

This also raises the question of how long to treat, and when a particular treatment concept can, or indeed should be stopped. According to E. Louis, Liège (Belgium), this requires caution. Any attempt at treatment discontinuation necessitates a careful balance of benefit and risk, a good monitoring strategy, and close involvement of the patient in the decision-making process.
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Crossing New Borders in IBD: Thoughts and Demands – From Mechanisms to Treatment

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Scientific Organization
F. Magro, Porto (Portugal)
A. Dignass, Frankfurt (Germany)
As is the tradition at the Falk Foundation symposia, successful scientists were honored for their outstanding research at the 206th symposium in Madrid.

First prize was awarded to Marin J. de Jong from Maastricht (The Netherlands) and her colleagues for their work on the role of telemedicine in the care of patients with inflammatory bowel disease: "Telemedicine enables a safe shift from examination room based care to personalized care for inflammatory bowel disease: A pragmatic randomized multicenter trial with myIBDcoach".

The second prize was awarded to Laith Alrubaiy from Swansea (Great Britain) and team for their study of the quality of care of patients with IBD in the UK: "Inflammatory bowel disease in the UK: Is care improving?"

The third prize was awarded to Manuel Barreiro-de Acosta, Santiago de Compostela (Spain) and colleagues for their poster on the psychosocial burden on IBD patients: "Psychosocial impact of inflammatory bowel disease and its practice management as perceived by patients and physicians in Spain. The ENMENTE Project".
“Treating inflammatory bowel disease is becoming ever complex”

There have been significant advances in the diagnosis and treatment of inflammatory bowel disease in recent years. Prof. Dr. A. Dignass, Frankfurt (Germany), one of the scientific organizers of the 206th Symposium, explains what these advances are and what consequences they will have for treating physicians and patients.

Editor: Professor Dignass, what are the most important current trends in the diagnosis and treatment of inflammatory bowel disease?

Prof. Dignass: Recently, considerable progress has been made in terms of our understanding of inflammatory bowel disease. We now understand the molecular background better, and we have recognized that genetics is not the central cause of the disease, but rather that epigenetic phenomena and the microbiome are also decisive factors in pathogenesis. Due to this increase in knowledge, we are increasingly able to understand the nature of the diseases, and our increasing knowledge has already led to the development of new treatment approaches. This trend is set to continue in the future. The consequence of this will be that the diagnosis and treatment of Crohn’s disease and ulcerative colitis will become much more complex in the future.

How is treatment becoming more complex?

Previously, we only had a few drugs at our disposal, such as mesalazine or steroids. This has changed dramatically. In addition to those drugs (which are still very important), there is now also a wide array of biologics that have already been approved. Furthermore, there are more than 50 different active substance candidates in development that are currently being tested in phase 2 and phase 3 trials. It can therefore be assumed that in the near future, there will be an array of new treatment options for Crohn’s disease and ulcerative colitis. This means we will likely be able to create a personalized treatment regimen – tailoring treatment to the specific phenotype of the disease and patient type (age, comorbidities). We will also be able to use biomarkers to predict whether a drug has a good chance of working in an individual case, and to what extent side effects can be expected, as is already possible to a limited extent in the field of oncology. This will likely have direct consequences in terms of the treatment approaches that are selected in individual cases.

Will this result in fundamental changes to treatment?

I postulate that in the near future, monotherapy (which is currently still frequently being used and tested in studies), will hardly be used at all in the treatment of inflammatory bowel disease, since we only achieve remission rates of about 30–60% with the drugs used for this. Therefore I think that combination therapy will become the standard because the success rates will be higher. I would also postulate that in future, we will initiate treatment earlier and escalate treatment sooner where required in order to take advantage of the “window of opportunity”. The aim here is to intervene in the disease process early on in order to avoid the development of structural damage. In this way, we hope to prevent complications such as stenosis, strictures, and fistulae.

When is the ideal time to initiate treatment and what is the goal?

Because of the improved diagnostic possibilities, the degree of severity of the inflammation in the respective intestinal regions and the pattern of involvement can now be determined earlier than a few years ago. Therefore, treatment is no longer controlled based on clinical symptoms, but rather based on objective findings such as changes detectable in endoscopy, and endoscopic remission. As in the field of rheumatology, the principle of “treat to target” applies here. This means that the goal is no longer just to ensure that patients are free from symptoms, but rather to achieve objective remission of the inflammation – i.e. mucosal healing. However, the definition of the treatment goal is currently rapidly changing. Some experts claim that
histological healing should be the goal; however there is a lack of prospective data showing long-term benefit to support this.

**How is treatment controlled?**

We now know more about the drugs that we are using, and we know how quickly treatment success is typically achieved. For example, if intravenous administration of steroids is unable to achieve a marked improvement within five days, more than 90% of patients will not respond to steroid treatment in the further course. Treatment should then be switched to a different treatment regimen. Furthermore, if an anti-TNF treatment regimen is unable to achieve treatment success within six weeks, systematic treatment escalation is indicated. The same principle applies to other drugs such as mesalazine, azathioprine or vedolizumab.

**Is a complete cure of the patient a realistic goal for the future?**

The term “cure” would mean that with treatment, we not only prevent structural changes, but also reverse them to the extent that the patients no longer require treatment. In my opinion, this is currently not a realistic aim. At the moment, we assume that patients will need lifelong treatment, even if in some cases, treatment interruptions can be incorporated – i.e. treatment in special treatment cycles. However, with regard to this, it should be mentioned that the treatment goals are currently changing due to advances in the diagnosis and treatment of the disease.

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**What are the most important consequences of the new strategies and developments for treating physicians?**

Due to the higher level of complexity, which is becoming increasingly clear, close cooperation between general practitioners, gastroenterologists in private practice, and specialist treatment centers will be required. As before, in future, many patients will be treated for the most part by their general practitioner or gastroenterologist in private practice. However, treatment management in patients with a complicated disease course will largely be performed by specialized centers. Generally speaking, I would predict that treating physicians will require more training in inflammatory bowel disease – not least because of the dramatic expansion of treatment options that is expected to occur.

**How can we ensure that physicians receive the appropriate further training?**

That remains to be seen. In this field, continuing medical education is largely sponsored by the pharmaceutical industry, and increasing restrictions are making this more and more difficult. I believe that the Falk Foundation Symposia are a good example of how further training can be provided with support from the pharmaceutical manufacturer, while remaining unbiased. The symposia have been taking place on both a national and international level for decades, and they are organized by renowned scientists, without any companies influencing the speakers that are selected. Internationally renowned experts report on the latest findings regarding the diagnosis and treatment of inflammatory bowel disease. The symposia are held in high esteem within the scientific community – something that is reflected in the fact that the speakers that we (as scientific organizers of symposia) invite rarely decline to speak, even though they are not paid for their lectures.

**Professor Dignass, thank you very much for talking to us.**
XXV International Bile Acid Meeting: Bile Acids in Health and Disease 2018

July 6 – 7, 2018
Dublin, Ireland

Scientific Organization
U. Beuers, Amsterdam (The Netherlands)
D. Häussinger, Düsseldorf (Germany)
V. Keitel, Düsseldorf (Germany)
M. Trauner, Vienna (Austria)

Local Organizer
S. Keely, Dublin (Ireland)
Speakers, moderators and scientific organizers

Prof. Dr. Matthieu Allez
Service de Gastroentérologie
Hôpital Saint-Louis
1, avenue C. Vellefaux
75010 Paris, France
matthieu.allez@aphp.fr

Prof. Dr. Laurent Beaugerie
Service de Gastroentérologie
Hôpital Saint-Antoine
184, rue du Faubourg St. Antoine
75571 Paris, France
laurent.beaugerie@sat.aphp.fr

Prof. Dr. Isabelle Cleynen
Department of Human Genetics
KU Leuven
Herestraat 49, bus 602
3000 Leuven, Belgium
isabelle.cleynen@med.kuleuven.be

Jean-Frederic Colombel, M.D.
Professor of Medicine
Gastroenterology & Hepatology
Mount Sinai School of Medicine
One Gustave Levy Place
New York, NY 10029, USA
jean-frederic.colombel@mssm.edu

Prof. Dr. Silvio Danese
IRCCS in Gastroenterology
Istituto Clinico Humanitas IRCCS
Via Manzoni, 56
20089 Rozzano, Italy
sdanese@hotmail.com

Prof. Dr. Axel Dignass
Medizinische Klinik I
AGAPLESION
Markus Krankenhaus
Wilhelm-Epstein-Str. 4
60431 Frankfurt, Germany
axel.dignass@fdk.info

Dr. Eugeni Domenech
Department of Gastroenterology
IBD Unit
Hospital Universitari Germans Trias i Pujol
Carretera del Canyet s/n
08916 Badalona, Spain
eugenidomenech@gmail.com

Prof. Dr. Iris Dotan
Department of Gastroenterology
Tel Aviv Medical Center
Ichilov Hospital
6, Weizman Street
64239 Tel Aviv, Israel
irisd@tasmc.health.gov.il

Dr. Maria Esteve
Hospital Universitari
Mútua Terrassa
Plaza Dr. Robert 5
08221 Terrassa/Barcelona, Spain
mestevecomas@telefonica.net

Dr. Gionata Fiorino
IRCCS in Gastroenterology
Istituto Clinico Humanitas IRCCS
Via Manzoni, 56
20089 Rozzano, Italy
gionataf@gmail.com

Prof. Dr. Javier P. Gisbert
Hospital de la Princesa
Diego de Leon, 62
28006 Madrid, Spain
javier.gisbert@gmail.com

Prof. Dr. Fernando Gomollón
Hospital Clinico Universitario “Lozano Blesa”
Avenida San Juan Bosco 15
50009 Zaragoza, Spain
fgomollon@gmail.com

Dr. Yago González Lama
Gastroenterology and Hepatology Department
Puerta de Hierro University Hospital
Manuel de Falla, 1
28222 Majadahonda, Madrid, Spain
ygonzalezlama@telefonica.net

Dr. Francisco Guarner
Servicio de Patología Digestiva
Hospital General Vall d’Hebron
Paseo Vall d’Hebron 119
08035 Barcelona, Spain
fguarner@telefonica.net

Peter D.R. Higgins, M.D.
Associate Professor of Medicine
Division of Gastroenterology
Department of Internal Medicine
University of Michigan
SPC 5682
1150 West Medical Center Drive
Ann Arbor MI 48109, USA
phiggins@med.umich.edu

Daniel W. Hommes, M.D., Ph.D.
Professor of Medicine
UCLA Med – VA Greater LA Healthcare System
11301 Wilshire Blvd.
Los Angeles CA 90073, USA
ibdcenter@mednet.ucla.edu

Dr. Peter Irving
Department of Gastroenterology
First Floor College House
North Wing, St Thomas’ Hospital
Westminster Bridge Road
London SE1 7EH, Great Britain
peter.irving@gstt.nhs.uk
Speakers, moderators and scientific organizers

Dr. James O. Lindsay  
Endoscopy Unit  
The Royal London Hospital  
Whitechapel  
London E1 1BB, Great Britain  
james.lindsay@bartshealth.nhs.uk

Dr. Antonio López San Román  
Servicio de Gastroenterología y Hepatología  
Hospital Universitario Ramon y Cajal  
Cra Colmenar 9.1  
28034 Madrid, Spain  
alopezs@meditex.es

Prof. Dr. Edouard Louis  
Gastro-entérologie  
C.H.U. de Liège  
Domain du Sart Tilman  
4000 Liège, Belgium  
edouard.louis@ulg.ac.be

Dr. Fernando Magro  
Servicio de Gastroenterología  
Hospital de S. Joao  
Av. Prof. Hernani Monteiro  
4200-319 Porto, Portugal  
fm@med.up.pt

Prof. Dr. Gerassimos J. Mantzaris  
Department of Gastroenterology  
Evangelismos Hospital  
45–47, Ypsilantou str., Kolonaki  
106 76 Athens, Greece  
gjmantzaris@gmail.com

Dr. Colin L. Noble  
Western General Hospital  
Crewe Road South  
Edinburgh, EH4 2XU, Great Britain  
noble@edinburghgastroenterology.com

Prof. Dr. Tom Øresland  
Akershus  
Universitetssykehus  
Sykehusveien 25  
1478 Lorenskog, Norway  
tom.oresland@medisin.uio.no

Prof. Dr. Laurent Peyrin-Biroulet  
Dept. of Hepato-Gastroenterology  
Hôpitaux de Brabois  
C.H.U. de Nancy  
Allée du Morvan  
54511 Vandoeuvre-lès-Nancy  
France  
peyrinbiroulet@gmail.com

Prof. Dr. Dr. Gerhard Rogler  
Klinik für Gastroenterologie & Hepatologie  
Universitätsspital Zurich  
Rämistr. 100  
8091 Zurich, Switzerland  
gerhard.roger@usz.ch

David T. Rubin, M.D.  
Professor of Medicine  
Section of Gastroenterology, Hepatology & Nutrition  
The University of Chicago Medicine  
5841 S. Maryland Ave.  
MC4076, Room M410  
Chicago, IL 60637, USA  
drubit@medicine.bsd.uchicago.edu

William J. Sandborn, M.D.  
Professor of Medicine  
Division of Gastroenterology  
University of California San Diego  
9500 Gilman Drive, MC 0956  
La Jolla, CA 92039, USA  
wsandborn@ucsd.edu

Bruce E. Sands, M.D.  
Professor of Medicine  
Department of Gastroenterology  
Mount Sinai School of Medicine  
One Gustave L. Levy Place  
New York, NY 10029, USA  
bruce.sands@msm.edu

Prof. Dr. Stefan Schreiber  
Innere Medizin I  
Universitätsklinikum Schleswig-Holstein, Campus Kiel  
Arnold-Heller-Str. 3 (Haus 6)  
24105 Kiel, Germany  
schreiber@mucosa.de

Prof. Dr. Britta Siegmund  
Gastroenterologie  
Charité - Universitätsmedizin  
Campus Benjamin Franklin (CBF)  
Hindenburgdamm 30  
12203 Berlin, Germany  
britta.siegmund@charite.de

Prof. Dr. Antonino Spinelli  
Colon and Rectal Surgery Unit  
Humanitas Research Hospital  
Humanitas University  
Via Manzoni, 56  
20089 Rozzano, Italy  
antonino.spinelli@humanitas.it

Prof. Dr. Eduard F. Stange  
Innere Medizin I  
Medizinische Universitätsklinik  
Otfried-Müller-Str. 10  
72076 Tübingen, Germany  
eduard.stange@rbk.de

Prof. Dr. Andreas Sturm  
Innere Medizin/Gastroenterologie  
DRK-Kliniken Westend  
Spandauer Damm 130  
14050 Berlin, Germany  
a.sturm@drk-kliniken-berlin.de

Prof. Dr. Gert van Assche  
Gastroentérologie  
University Hospital Leuven  
Herestraat 49  
3000 Leuven, Belgium  
gert.vanassche@uz.kuleuven.ac.be
Workshop
Liver-Gut-Microbiome Interactions
Hamburg, Germany
January 25 – 26, 2018

Symposium 210
Crossing New Borders in IBD: Thoughts and Demands – From Mechanisms to Treatment
Lisbon, Portugal
April 20 – 21, 2018

Symposium 211
XXV International Bile Acid Meeting: Bile Acids in Health and Disease 2018
Dublin, Ireland
July 6 – 7, 2018

Symposium 212
IBD and Liver: East Meets West
Kyoto, Japan
September 7 – 8, 2018

Symposium 213
Tailored Therapies for IBD: A Look into the Future
Milan, Italy
October 5 – 6, 2018
Scientific Dialogue in the Interest of Therapeutic Progress