

ECCO

News WINTER



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Crohn's and Colitis
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Members save up to 20%



Be a bee in our hive to experience
the ECCO Spirit

To reach our objectives, our members can access the following ECCO Initiatives:

- Reduced Congress fee
- JCC – Journal of Crohn's and Colitis (12 online issues/year)*
- e-CCO Learning Platform incl. e-Courses & e-Library
- Monthly eNewsletter
- Access to online members' area
- Quarterly ECCO News – The society's magazine
- Educational and networking activities
- Guidelines, ECCO Fellowships, Grants and Travel Awards
- Access to ECCO Scientific Platform – Who does What?

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www.ecco-ibd.eu



*For Regular Members (incl. Y-ECCO) only; online access only

ECCO NEWS

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European Crohn's and Colitis Organisation

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Dear ECCO Friends,

Here is another ECCO News for you to enjoy! Now that it is again the time of year when the hours of daylight are at their shortest in Europe, when many of us leave for work in the dark and return home in the dark, what is more pleasant than some relaxation and reading in front of the fire? I admit this is my preferred place in the evening....

What do we have to offer in this ECCO News?

First, we are getting closer to our next **ECCO Congress in Amsterdam** and I of course hope to see many of you there! Please register if you have not already done so and if you want to save some money. The **late registration deadline is March 1, 2016** and if you are not yet convinced, then have a look at the scientific and educational programmes and the speaker names. For now I can only say that the Organising Committee for Amsterdam was in very good shape when it drafted the programme (you will find out why and how during the congress!). We also have high hopes that some top-line results of phase 3 studies will once again be presented during the Congress. So if you want to remain fully up to date in IBD, ECCO'16 Amsterdam is the place to be!

Also in this issue are reports on some of the **ECCO Activities that took place at UEGW 2015 in Barcelona**. We further dedicate some time and space to the **patient guidelines in IBD**, which is an ongoing joint initiative between ECCO and EFCCA, the European IBD patient organisation. We are very proud that these guidelines will be the **first patient guidelines on IBD worldwide!** They will serve as guidance for patients and will fit perfectly with the philosophy of ECCO and EFCCA to improve patient care and access to health care in Europe. If you want to learn more about the content of these guidelines, please sign up for the **press conference** that will take place during ECCO'16 in Amsterdam.

All committees are working hard behind the scenes during the year and I cannot sufficiently thank all those who dedicate their free time to ECCO! Here I would particularly like to mention the contribution of the Education Committee in organising another **educational workshop** in India this autumn. This workshop attracted no fewer than 480 physicians, demonstrating that there is still much value in hosting these regional ECCO Meetings! It is now 8 years since the first ECCO Workshop took place in Zagreb, Croatia.

It is a true privilege to be steering such a smoothly sailing ship full of young and diverse people! It makes the life of the Captain easy.

Enjoy reading!

SÉVERINE VERMEIRE
ECCO President



Séverine Vermeire © ECCO

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European
Crohn's and Colitis
Organisation

Announcement
2017

Inflammatory Bowel Diseases



12th Congress of ECCO
February 15-18, 2017

- CCIB Barcelona, Spain
- EACCME applied
- Register at the 11th Congress of ECCO in Amsterdam

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www.ecco-ibd.eu



ECCO'16 – Come to Amsterdam for IBD!

The 11th Congress of ECCO in Amsterdam is coming closer and so is the late registration deadline. Benefit from the late registration and register until March 1, 2016 (after this date the onsite registration fees apply).

Educational programme at ECCO'16:

Educational activities at the 11th Congress of ECCO will be held from Wednesday, March 16, 2016 to Friday, March 18, 2016. The educational programme covers activities for ECCO's different interest groups, including young gastroenterologists, surgeons, paediatricians, histopathologists, dietitians, IBD nurses and allied health professionals and scientists. An overview of these activities can be found on the right. For the detailed final programmes please refer to www.ecco-ibd.eu/ecco16. Please note that some of these courses/workshops will run in parallel and that some will have a limited capacity – please register by March 1, 2016.

- Educational programme
- Scientific programme

Wednesday March 16, 2016		Thursday March 17, 2016		Friday March 18, 2016		Saturday, March 19, 2016
Morning	Afternoon	Morning	Afternoon	Morning	Afternoon	Morning
14 th IBD Intensive Advanced Course	9 th Y-ECCO Career Workshop	14 th IBD Intensive Advanced Course	Scientific Programme Poster exhibition			
3 rd Basic ECCO: EduCational Course for Industry		3 rd ECCO-ESGAR Ultrasound Workshop	Industry exhibition			
	2 nd Advanced ECCO: EduCational Course for Industry	5 th ClinCom Workshop	Digital Oral Presentation Sessions 1-5		Digital Oral Presentation Sessions 6-10	
7 th N-ECCO School		5 th S-ECCO IBD Masterclass		1 st D-ECCO Workshop	2 nd Y-ECCO Basic Science Workshop	
1 st School for Clinical Trialists	3 rd N-ECCO Research Forum	10 th N-ECCO Network Meeting			ECCO Interaction: Hearts & Minds	
	1 st ECCO Endoscopy Workshop	3 rd EpiCom Workshop	1 st H-ECCO IBD Masterclass			
	EU Project Forum	Molecular aetiology of IBD				
	Press conference	3 rd P-ECCO Educational Course				
ECCO Business Meetings						

Look out for our digital oral presentations!

The 30 best abstracts (up from 28 in 2015) will receive an oral presentation slot in the scientific programme of the 11th Congress of ECCO. The next best 80–100 abstracts will be digital oral presentations, with a 5-minute oral presentation on either Thursday, March 17, 2016 from 17:15 to 18:15 or on Friday, March 18, 2016 from 18:05 to 19:05.



DOPs at ECCO'15, Barcelona © ECCO

Due to the great success of the DOP sessions at the past two congresses, the presentations will be split over two days this year. This will give you the chance to attend more presentations. The remaining accepted abstracts will be displayed as hard copy posters throughout the Congress. Please do join our vivid Guided Poster Session on Friday, March 18, 2016 during the lunch break.

For further information, please refer to: www.ecco-ibd.eu/ecco16

What's in store for ECCO Members at the ECCO Congress?

ECCO Members attending the 11th Congress of ECCO will enjoy a number of highly valuable privileges:

Special registration privileges:

- Payment of reduced registration fees, with a saving of EUR 300.- to 400.-
- Access to the educational programme (only for Members)

Onsite privileges:

General Assembly of ECCO Members

Thursday, March 17, 2016, 18:30-19:30, Elicium 1 (RAI Amsterdam)

The Annual General Assembly of ECCO Members is ECCO's highest deliberative body and the embodiment of one of the association's most elementary member privileges: The right to vote and help form ECCO's future. Join the election of the next ECCO President-Elect!

ECCO Members' Lounge

ECCO Members have the possibility to enjoy the informal atmosphere of the Members' Lounge, where they can meet ECCO Officers and network with colleagues. The lounge is located in the exhibition hall of the RAI Amsterdam.



Members Lounge at ECCO'15, Barcelona © ECCO

ECCO Congress bags 2016

As in 2015, our ECCO Congress bags will be produced by Township Patterns®, a company supporting female entrepreneurship in township communities outside Cape Town, South Africa. Hence, the ECCO Congress bags will be more than just a stylish accessory – they will offer a means of improving the lives of the African women who produce them in their own sewing cooperatives.

Congress bag special:

Every congress bag will include a copy of JCC – Journal of Crohn's and Colitis Issue 2/2016. Please do not forget to pick up your congress bag!



Congress bags ECCO'16, Amsterdam © ECCO

ECCO Interaction: Hearts and Minds

"ECCO Interaction: Hearts and Minds" is THE event at ECCO to see and be seen, to network and engage. Anyone who has been to a previous ECCO Congress will know that it is a must. Everyone is welcome, but places are limited.

This event is open to all congress delegates. The price of an entrance ticket purchased in advance is EUR 50.- for ECCO Members and EUR 95.- for Non-Members. **Please be informed that a 3-course buffet dinner is included in the entrance fee.** Tickets can be purchased during the online congress registration at www.ecco-ibd.eu/ecco16. Access to the event is strictly limited to those with ECCO Interaction Tickets.

Date: Friday, March 18, 2016

Start time: 20:00

Venue: Beurs van Berlage, Damrak 243, 1012 ZJ Amsterdam



ECCO Interaction at ECCO'15, Barcelona © ECCO

EU Project Forum Featuring FP7/Horizon 2020 projects



At the ECCO'16 Congress in Amsterdam, ECCO is pleased to convene for the first time an open access EU Project Forum in which successfully ongoing FP7/Horizon 2020 projects and their results are presented.

The forum aims at facilitating exchange of knowledge, sharing of project experience and finding of potential new synergies among senior and junior researchers; among basic scientists and clinicians.

Wednesday, March 16, 2016

*Preliminary Programme overview (as of December 04, 2015) -
EU Project Forum Featuring FP7/Horizon 2020 projects*

15:00 - 15:05	Welcome and Introduction Filip Baert, Roeselare, Belgium
15:05 - 15:35	EU Funding
	Talk tba Speaker tba
15:35 - 16:05	Session 1: Sadel Raja Atreya, Erlangen, Germany Andreas Sturm, Berlin, Germany
15:35 - 15:45	Introduction: Nanofitins and the SADEL project Olivier Kitten, Nantes, France
15:45 - 15:55	Pharmacological profile of Nanofitins: Fit for oral Magali Zeisser-Labouèbe, Geneva, Switzerland
15:55 - 16:05	In vivo oral administration of Nanofitins in IBD models Christel Rousseaux, Lille, France
16:05 - 17:40	Session 2: Biomarkers for clinical decision making in IBD, an unmet clinical need
16:05 - 16:35	IBD Character Jack Satsangi, Edinburgh, United Kingdom Morten Vatn, Oslo, Norway Jonas Halfvarson, Örebro, Sweden
16:05 - 16:15	Introduction to IBD Character Rahul Kalla, Edinburgh, United Kingdom
16:15 - 16:25	Proximity Extension Assay technology identifies novel serum biomarkers Niklas Nordberg, Uppsala, Sweden
16:25 - 16:35	A novel diagnostic test for determining microbial dysbiosis Christina Casén, Oslo, Norway
16:35 - 17:10	Coffee break
17:10 - 17:40	IBD - BIOM Vito Annese, Florence, Italy Jack Satsangi, Edinburgh, United Kingdom
17:10 - 17:20	Introduction to IBD BIOM Gordan Lauc, Zagreb, Croatia
17:20 - 17:30	The role of DNA methylation Nicholas Ventham, Edinburgh, United Kingdom
17:30 - 17:40	The potential of glycomics as an IBD biomarker Gordan Lauc, Zagreb, Croatia Manfred Wuhrer, Leiden, The Netherlands
17:40 - 18:10	Session 3: BIOCYLE Britta Siegmund, Berlin, Germany
17:40 - 17:46	The Global project Edouard Louis, Liège, Belgium
17:46 - 17:52	The spare trial Erik Hertervig, Lund, Sweden
17:52 - 17:58	The health care provider/patients survey Jean-Frédéric Colombel, New-York, United States
17:58 - 18:04	The biomarkers Jack Satsangi, Edinburgh, United Kingdom
18:04 - 18:10	Discussion
18:10 - 18:15	Closing Remarks Filip Baert, Roeselare, Belgium

Responsible Committee: Governing Board
Target audience: Basic Scientists, Clinicians, Researchers
Registration: Online Registration
ECCO Membership 2016 required: n.a.
Registration fee: n.a. subject to prior registration

Please contact the ECCO Office in case of questions
at ecco16@ecco-ibd.eu

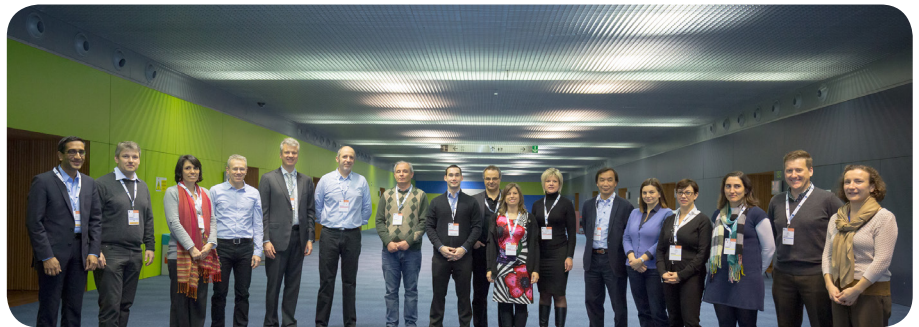
Targeting TNF at the site of inflammation: Progress report on the SADEL project and ECCO's engagement within the consortium

The European-funded SADEL project (Scaffolds for alternative delivery), which is part of the Seventh Framework Program (FP7), has made decisive steps to develop an orally administered Nanofitin-based anti-TNF therapy for the treatment of IBD patients

The SADEL consortium was founded in 2012 and consists of representatives from small- and medium-scale enterprises, academic institutions and universities, hospitals and a pharmaceutical company, who are bringing together their expertise to develop an orally administered Nanofitin-based anti-TNF drug for the treatment of IBD patients. ECCO is part of this collaborative effort and provides scientific and clinical advice in the development of the novel therapeutic compound. ECCO evaluates both the drug development programme leading towards the clinical trial and the contingency plans in respect of clinical implementation. With the support of the ECCO President and together with Andreas Sturm (Berlin), who is voluntarily involved as Senior Expert Officer, my colleague Johannes Meier (Berlin) began his work as ECCO EU Research Project Fellow in 2014 with the remit of providing clinical advice to all partners of the consortium throughout the development of the Nanofitin-based therapy. I succeeded Johannes in 2015 and would like to thank him for his previous work. I shall similarly endeavour to approach this project from a clinical viewpoint and ensure that the intended new therapeutic substance delivers the greatest clinical benefit for IBD patients. The design of a clinical phase 1 trial for the Nanofitin-based oral therapy will be one of the major components of ECCO's Activities within the consortium in the future.



In 2015, the SADEL consortium members first met during the ECCO Conference in Barcelona and then held subsequent meetings in Nantes and Lille to discuss the data obtained by the group. Mathieu Cinier (Afflogic) delivered an oral presentation during the ECCO Congress, where he reported on these data. The main aim of the SADEL consortium is to develop a first-in-class Nanofitin-based oral compound directed against TNF. The oral administration



SADEL Project Group © ECCO

should achieve high local drug concentrations and minimise systemic exposure and thereby unwanted side-effects and immunogenic reactions. It should, moreover, address the medical need of IBD patients for an orally administered therapy, which is often associated with high compliance. Nanofitins represent a new class of non-antibody affinity ligands that are characterised by their small size (optimal tissue penetration) and high affinity (low effective concentration needed). They are also extremely robust and exhibit strong resistance to pH and human intestinal fluids (long half-life in digestive track). Furthermore, their simple and effective manufacturing process should reduce therapeutic costs.

Mathieu presented the first in vivo data, relating to nine Nanofitin candidate compounds tested in an experimental Colitis model (TNBS-Colitis) via rectal and oral administration. It could be shown that some of the intrarectally administered compounds exhibited decrease in inflammatory lesions. These results were confirmed in another model (DSS-Colitis). Next, one of these compounds showed similar reduction in inflammatory lesions via intrarectal and oral administration, which was followed by oral dose response studies. These properties were then also demonstrated in a therapeutic setting, as oral administration was found, upon macroscopic and histological evaluation, to be able to reduce the inflammatory lesions significantly. Beside the preventive and therapeutic anti-inflammatory effect in vivo, the Nanofitin-based compound exhibited extreme stability, as its oral application was done without any formulation optimisation.

The further development of the Nanofitin-based compounds will be pursued by the SADEL consortium in its upcoming research activities, which, following regulatory consultations, should finally lead to a first-in-man study. ECCO is excited to be involved in this promising project and will help it to reach clinical implementation in a phase 1 trial. We will of course keep you updated regarding the progress of these activities.

RAJA ATREYA

ECCO EU Research Project Fellow

SADEL (Scaffolds for Alternative DELivery) is a project supported by the European Commission through the Seventh Framework Programme (FP7)



ECCO'16 Press conference on the ECCO-EFCCA Patient Guidelines

In December 2014 the European Crohn's and Colitis Organisation organised a meeting with IBD Patient Association Representatives and ECCO National Representatives (both nurses and physicians) with the aim to improve patient care and the quality of life for patients with Inflammatory Bowel Disease.

Patients, physicians and nurses were assembled in focus groups and reviewed topics of high relevance to patients. The overall outcome of this meeting was agreement that there is a pressing need for patient guidelines that will help patients to understand the latest clinical research and provide them with valuable information on their disease.

Following the meeting in December 2014, ECCO joined forces with the European Federation of Crohn's and Ulcerative Colitis Associations (EFCCA) in order to develop the ECCO-EFCCA Patient Guidelines. Two taskforces, one focussing on Crohn's Disease and the other one on Ulcerative Colitis, were formed. The taskforces consist of patients, physicians and nurses from different European countries. The working groups are responsible for selecting statements from the existing ECCO Clinical Guidelines which are most relevant to patients and for translating these statements into language that is readily understandable for patients. On November 23, 2015 the two taskforces met in Vienna to discuss the statements in-depth. The meeting has been very productive and a great success. The participants are eager to finalise the patient guidelines over the next months and are very much looking forward to the presentation during the ECCO'16 Press Conference.

The **ECCO-EFCCA Patient Guidelines** will be published on various channels (ECCO Website, EFCCA Website, IBD patient society websites, ECCO News, patient journals, etc.) in March 2016 and presented at a Press Conference on March 16, 2016 in Amsterdam.



Face to Face Patient Guidelines Meeting, November 2015, Vienna © ECCO

Global Press conference

Date: Wednesday, March 16, 2016

Time: 15:00-16:00

Venue: RAI Amsterdam

Media and patient representatives will be invited and the event will be open to all congress delegates. **Please make sure to register by March 1, 2016.**



United We Stand



European
Crohn's and Colitis
Organisation

ECCO Activities at UEGW

Committee Meetings

The committee meetings on the Sunday of the UEGW meeting offered a great opportunity to review and discuss all ongoing educational and scientific activities within ECCO. I can reliably inform you that the 11 committees and working groups have been very active throughout the year! Improving the quality of care worldwide should already be considered a great achievement of S-ECCO, EduCom and P-ECCO. The ECCO Educational Workshops are increasingly popular and ECCO receives many requests to hold these workshops

from both within and outside Europe.

GuiCom is publishing numerous papers (I can hardly keep up with the number published every year!) that will be used to guide decision making in daily practice. Y-ECCO is still very active in the field of basic research and its workshop during the ECCO Congress is always very well attended. EpiCom continues to analyse and publish their unique findings derived from a large prospective database. Histological healing is emerging as a new therapeutic target in Ulcerative Colitis, and the role of diet and nutrition in IBD



e-Learning Meeting, UEGW 2015 © ECCO

management is crucial. D-ECCO WG and H-ECCO WG, the 'newcomers' among the committees, are working on new initiatives and we can anticipate that the launch of further creative projects will be in accordance with the ECCO Spirit! ClinCom and SciCom continue to support European scientific projects and are contributing greatly to the improvement in the quality of clinical trials and research across Europe. How can we treat an IBD patient without a nurse? We all know that it is impossible! N-ECCO is working in close collaboration with all the committees to help countries that do not have universal provision of IBD nurses (such as France...). Nurses suitable for involvement in provision of IBD care will be identified and offered appropriate support, with the ultimate aim of improving quality of care. The N-ECCO School, the N-ECCO Network Meeting, the N-ECCO Research Forum and the School for Clinical Trialists, a joint initiative with ClinCom, demonstrate that N-ECCO has a key role in the past and current success of ECCO. Please view the podcast recordings with the committee chairs on the ECCO Website for more information on the activities of ECCO Committees.

ECCO Dinner

As always, the ECCO Dinner was a great success! Around 50 attendees shared beers and wine over a very good meal following what had been a long day due to all the committee meetings. It was nice to see the ECCO Office relaxing (it does not happen very often!) after their hard work in association with each committee meeting and, indeed, throughout the year. Without the ECCO Office, ECCO could not function as an organisation!

After the dinner, we went onto the roof deck of the hotel, which offered a very nice view of Barcelona. Some of the men were discussing soccer (I cannot tell you their names, but one is a surgeon in Brazil) and another a famous surgeon in Amsterdam while others were considering



ECCO Dinner, UEGW 2015 © ECCO

the quality of the wine (probably a French guy was involved in that conversation). The weather was good and it was rather warm outside despite it being the end of October (or perhaps the wine contributed in warming the atmosphere!). I left at midnight and hence cannot tell you how the party ended, but I am sure that the ECCO Spirit was present until the end of the night.

ECCO Booth



ECCO Booth, UEGW 2015 © ECCO

The ECCO Booth, situated in the UEG Association Village, was staffed all day long and all visitors received a warm welcome.

The ECCO Family Spirit was present during the entire UEGW meeting.

Even though ECCO is now very famous worldwide, further promoting ECCO during UEGW in a friendly manner is a mandatory measure for us. The ECCO Booth also provided a great opportunity to foster links between IBD physicians who are yet to join ECCO and existing ECCO Members. In summary, the ECCO Booth was the meeting point for all physicians with an interest in IBD!

Talking Heads

New initiatives are always welcome at ECCO! 'Talkings Heads' is a great example of what makes ECCO unique among professional societies. Briefly, one EduCom member invites several international experts to discuss the practical management of IBD patients. One could say that this is designed to move the management of IBD from theory to practice.

One hot topic addressed was the use of methotrexate in IBD following the disappointing results of the GETAID study in Ulcerative Colitis (the METEOR trial). The good safety profile of methotrexate makes this drug very attractive when used as combination therapy, especially given the relatively poor safety profile of thiopurines (which are associated with increased risk of lymphoma and non-melanoma skin cancers) and the experience with methotrexate in the treatment of rheumatoid arthritis.

Overall, all of the ECCO Activities during the UEGW meeting underscore **three key elements of ECCO's success: Innovation, creativeness and friendship.**

See you all in Amsterdam!

LAURENT PEYRIN-BIROULET

ECCO Secretary

Crohn's Disease: To cut or not to cut? A historical perspective

In the history of Crohn's Disease (CD) three different periods may be distinguished: The period of surgical therapy, the period of surgical and medical therapy and the period of biological therapy.

The period of surgical therapy

Although the earliest description of CD can likely be accredited to G.B. Morgagni in his treatise "The seats and causes of diseases" (1761), the landmark article that identified CD was written by B. Crohn, L. Ginzburg and G. Oppenheimer and published in 1932 in the Journal of the American Medical Association (JAMA). The paper followed the oral presentation entitled "Terminal ileitis", delivered by Crohn at the annual congress of the American

Medical Association (New Orleans, 1932). The presentation concerned 14 patients who showed segmental inflammation of the terminal ileum. As 13 of these 14 patients were treated successfully with surgery, the condition was considered to be a surgical disease.

The eponym "Crohn's Disease" arose by way of a fascinating set of circumstances. Among the authors of the above-mentioned article, Crohn was a gastroenterologist while Ginzburg and

Oppenheimer were pathologists. All worked at the Mount Sinai Hospital in New York City. An interesting question, therefore, is why the first report of a surgical disease did not include a surgeon among the authors. In fact, all the patients were operated on by A.A. Berg, senior surgeon at Mount Sinai. However, Berg refused to present the oral communication at the congress, instead preferring to investigate what the numerous antique dealers in New Orleans

had to offer. As at that time the journal policy was to order the authors alphabetically by last name, if Berg had presented the oral communication, today Crohn's Disease would probably be named Berg's Disease.

After the first published report on CD, many other cases of the disease were recognised across the United States and Europe, and CD was found to occur throughout the GI tract. However, the status of CD altered from a medical curiosity to a well-known disease only in 1956, when U.S. President Eisenhower required an emergent operation for bowel obstruction due to CD. At that time, and indeed throughout the period from 1932 to 1970, CD was regarded as almost exclusively a surgical disease, with ileal resection or ileo-colonic bypass representing the treatment of choice. In 1960 the British surgeon H.E. Lockhart-Mummery became the first to recognise CD of the colon and draw the distinction between Ulcerative Colitis and CD of the colon.

The period of surgical and medical therapy (1970–1997)

In the 1970s it became evident that there was a high incidence of postoperative recurrence after curative resection for CD (up to 75% at 1 year). The consequence was a dramatic change in treatment as surgeons became reluctant to operate on CD patients. Medical treatment (antibiotics, corticosteroids, budesonide, immunosuppressants, mesalazine) then became the first-line therapy, with surgery mainly reserved for complications (obstruction, perforation, abscesses, fistulas). The role of the surgeon thus shifted from central to marginal. In this period the prevention of postoperative recurrence was considered one of the most important issues in the management of CD. Endoscopy had proved to be the best method to detect postoperative recurrence. It was also demonstrated that the postoperative clinical course of CD could be predicted by the severity of endoscopic lesions during the first year after resection.

A number of drugs (antibiotics, mesalazine, corticosteroids, 6-mercaptopurine, azathioprine, methotrexate, tacrolimus) were studied by randomised clinical trials with the aim of preventing postoperative recurrence. However, available data, including meta-analyses, do not show a robust protective effect for any medical therapy.

The period of biological therapies (1997 to the present)

In 1997, S.R. Targan et al published in the NEJM the first clinical trial on the effectiveness of monoclonal antibody anti-TNF α (infliximab) for CD. This landmark article opened a completely new era in the treatment of IBD, and numerous other biological agents blocking various mechanisms of the inflammatory process are now available (adalimumab, certolizumab,

natalizumab, vedolizumab).

Using these agents, it was shown for the first time that mucosal lesions of CD may completely heal after treatment. Therefore the end points of the clinical trials completely changed. Historically patients were treated based on the reduction of clinical symptoms (CDAI). Today, we understand that symptoms correlate poorly with the underlying intestinal inflammation. Other more objective disease activity parameters (CRP, faecal calprotectin, reduction of intestinal lesions) have therefore been introduced. "Mucosal healing" is now the preferred primary endpoint in ongoing trials. The combination of symptom remission and endoscopic remission is called "deep remission". However, it must be taken into consideration that fibrostenotic lesions are irreversible and no treatment strategies are available.

Individualisation of therapy to optimise treatment is possible by stratifying patients according to whether the risk is low or high. Criteria for patients at low risk are: age >30 years; limited anatomical involvement; no peri-anal disease, stricturing or fistula; and no previous surgery. Criteria for patients at high risk are: age <30 years; extensive anatomical involvement; peri-anal disease; stricturing/fistula; and previous surgery.

The emergence of biological therapy for CD has led to a clinical debate about the "step-up" versus the "top-down" strategy. The former refers to the classic therapeutic approach, namely progressive intensification of treatment as disease severity increases. Treatment starts with corticosteroids/budesonide, moving to immunosuppressants (6-mercaptopurine, azathioprine, methotrexate) and eventually to biologics when the response is poor. By contrast, the top-down approach entails the early introduction of biologics, with an eventual switch down to immunosuppressants when the response is positive.

Although the existing guidelines recommend that selection of treatment strategy should be based on stratification of patient risk, most gastroenterologists in any case use anti-TNF α as first-line treatment and switch to other biologics when anti-TNF α fails. However, it should be taken into consideration that epidemiological studies have shown that over 50% of CD patients have mild disease over time and will never require aggressive therapies. Indiscriminate use of the top-down strategy would therefore represent an over-treatment for most CD patients. Toxicity and the high cost of biologics are also drawbacks to their indiscriminate use.

With the spread of biological therapies, surgery has in general become obsolete. However, it is common experience that medical therapy (including biologics) is poorly effective in patients with "stricturing" or "penetrating" CD and that 60%–70% of such patients still undergo surgery within 10 years of diagnosis. Results of recent trials with anti-TNF α have shown that mucosal healing in CD is associated with a higher clinical

response and reduced hospitalisation rates and need for surgery. On the other hand, recent data from population-based cohort studies have indicated that the rate of surgery within 5 years of diagnosis in the post anti-TNF α era is similar to that prior to the introduction of anti-TNF α .

Surgery therefore should not be dismissed as the end of the road after all medical options have failed, but should be considered a significant component of the entire management strategy for CD. Early surgery in the presence of obstruction, abscess/fistula or lesions limited to a short ileal segment continues to have a primary role. Very good results have also been reported when using minimally invasive laparoscopic surgery.

It appears that the advent of biologics has deeply changed clinical practice and the therapeutic algorithms in CD. The possibility of inducing mucosal healing holds out much hope of changing the natural history of CD, as has occurred in rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis. However, it has not yet been demonstrated that biological therapies can influence the long-term natural history of CD. Despite the great therapeutic advances in CD, no drug prevents or reverses established strictures.

To conclude, although the advent of biological therapies has deeply changed the conventional therapy of CD, the best management of these patients still results from close collaboration of the gastroenterologist and surgeon expert in IBD. We ultimately need cost utility analyses to help us in selecting the most appropriate medical or surgical therapies both for patients and for society.

RENZO CAPRILLI

ECCO Founder and First President



Renzo Caprilli © ECCO

ECCO Grant Study Synopses

Role of NADPH oxidase in the maintenance of intestinal homeostasis

Aim of the research project

Reactive oxygen species (ROS) are produced as a host defence response in several chronic disorders, including Inflammatory Bowel Diseases (IBD). ROS can be deleterious at high concentrations, but at low concentrations these messenger molecules serve complex and unique cell signalling functions. The role of ROS generated in the gut by phagocytes and their antimicrobial mechanism have been well studied; however, the input of epithelial ROS and the overall effect of modulating ROS levels on multifactorial gut inflammation are not well understood. The main sources of ROS in the intestine are the multimeric nicotinamide

adenine dinucleotide phosphate (NADPH) oxidase enzymes (Nox/Duox). Reduced ROS generation due to inactivation of Nox complex variants has been associated with Crohn's Disease or pancolitis, while overexpression of other NADPH oxidase isoforms has been detected in patients with Ulcerative Colitis. This project aims to study how tight NADPH oxidase regulation is required to balance antimicrobial versus pro-inflammatory ROS, thereby preserving a healthy gut homeostasis.

Methodology

To define the role of NADPH oxidases during the perturbation of homeostasis, an in vivo

multimodel approach and newly developed transgenic mouse lines will be employed.

GABRIELLA AVIELLO

ECCO Grant Awardee 2015



Gabriella AvIELLO © Gabriella AvIELLO

Metabolomic and microbiomic predictors of response to biologic therapy in moderate to severe Inflammatory Bowel Disease

Aim of the research project

Anti-TNF therapy constitutes an important part of the armamentarium when treating patients with moderate to severe Crohn's Disease and Severe Acute Colitis. Clinical response to anti-TNF therapy has been recorded at 70%–80%, with the increasing issue of loss of response recorded at rates of 23%–46% per year. There are currently no predictive biomarkers for determination of which patients will respond or lose response to anti-TNF therapy.

Metabonomics is used to identify chemicals which show the underlying profile of a biological system. It can already distinguish patients with IBD from those who are healthy.

The aim of this project is to establish a metabolic and microbiomic profile for predicting therapeutic response to anti-TNF medications in both Crohn's Disease (CD) and Ulcerative Colitis (UC). The two cohorts/arms of the project can be characterised as follows:

1) Patients newly commenced on anti-TNF therapy for CD. Aim: To determine the metabolic signature profile of stool, serum and urine samples and microbial dysbiosis in patients with CD at the time of anti-TNF initiation and

thereafter. Title: Crohn's Disease: Loss of response And Metabolomic Predictors (CLAMP).

2) Patients with Severe Acute Colitis commenced on salvage therapy. Aim: To determine the metabolic signature profile of stool, serum and urine and microbial dysbiosis in samples from patients with UC at the time of initiation of anti-TNF salvage therapy and thereafter. Title: Metabolomics of Severe Acute Colitis (MoSAiC).

Methodology

CLAMP: We aim to recruit 40 patients and ten healthy controls. This is a longitudinal study over 12 months. Patients will have been commenced on anti-TNF therapy with collection of three biofluids, serum, stool and urine, for analysis using nuclear magnetic resonance (NMR) and metagenomics.

MoSAiC: We will recruit ten patients and ten healthy controls. Patients will be followed up over 12 months, using the same methodology as in CLAMP. Patients will be inpatients and those with Severe Acute Colitis requiring salvage therapy.

Visits will take place every 3 months, with a total of five visits. Differences between pre and post anti-TNF therapy findings will be determined and ongoing clinical data will be obtained at each visit, including biochemical, faecal, endoscopic and radiological markers indicative of response. All biofluids will be analysed with NMR spectroscopy to determine predictors for non-response and loss of response over time.

NIK DING

ECCO Grant Awardee 2015



Nik Ding © Nik Ding

The role of galectin 3 in Acute Colitis

Aim of the research project

Galectin-3 (Gal-3) is an endogenous lectin with a broad spectrum of immunoregulatory effects: it plays an important disease-exacerbating role in inflammatory and malignant diseases. Pharmacological inhibitors of Gal-3 are already used to down-regulate inflammation and fibrosis. However, the precise role of Gal-3 in the pathogenesis of Ulcerative Colitis (UC) remains unknown.

The main aim of this project is to evaluate possible cellular and molecular targets of Gal-3 in the pathology of Acute Colitis. To this end, a model of dextran sulphate sodium (DSS)-induced Colitis that has a high degree of uniformity and reproducibility with respect to Colitis in humans will be used.

Methodology

A susceptibility to DSS-induced Colitis will be

tested in Gal-3-deficient mice. The effects of treatment with a selective inhibitor of Gal-3 (Davanat) will be analysed in wild-type C57BL/6 mice. The effect of genetic deletion or pharmacological inhibition of Gal-3 on the clinical, histological and immunological parameters of acute DSS-induced Colitis and on the phenotype and function of antigen-presenting cells (DCs and macrophages), neutrophils, eosinophils, mast cells, NK cells and

NKT cells that are found to play an important role in the pathogenesis of Acute Colitis will be analysed by flow cytometry, intracellular staining, immunohistochemistry, ELISA and real-time PCR. In order to determine the significance of Gal-3 in human UC, the expression of Gal-3 in colonic epithelium and the level of Gal-3 in sera of patients with UC will be determined by immunohistochemistry and ELISA and compared with findings in healthy "non-UC" controls.

The main significance of this project is in establishing Gal-3 as a new therapeutic target in Acute Colitis. If our results demonstrate that pharmacological inhibitors of Gal-3 significantly attenuate Acute Colitis in mice, inhibitors of Gal-3 could be further tested as potential therapy for Acute Colitis in humans.

VLADISLAV VOLAREVIC

ECCO Grant Awardee 2015



Vladislav Volarevic © Vladislav Volarevic

Clinical impact of hybrid imaging PET-MRE in fibrostenosing Crohn's Disease

Aim of the research project

The characterisation of stenotic lesions in patients with Crohn's Disease (CD) by means of magnetic resonance enterography (MRE) is challenging given the frequent overlap between fibrosis and inflammation. The two major features of inflammation on MRE, contrast enhancement and wall thickening, are influenced by fibrotic changes. Therefore, MRE evaluation of the responsiveness of stenosis to medical therapy is difficult. Positron emission tomography (PET) using fluorine-18-labelled fluoro-2-deoxy-D-glucose (FDG) is a functional imaging method that is sensitive to glucose metabolism. FDG accumulates in areas of active inflammation due to increased metabolic activity. PET can identify inflamed areas of the bowel and can be combined with MR. The additional value of PET over MRE for the assessment of stenotic lesions has not yet been evaluated; however, we hypothesise that it may provide valuable information in the work-up of obstructive

lesions and assist in the optimisation of medical treatment. The aim of this project is thus:

1. To determine the predictive value of combined PET and MRE with respect to achievement and maintenance of clinical responses to medical treatment in patients with stricturing CD;
2. To evaluate whether these findings can be predictive of the need for surgery on stenotic lesions.

Methodology

This pilot study will include, during a 2-year period, 25 patients with known CD and stenotic lesions detected at MRE and further evaluated by PET. We will determine the degree of activity on both MRE and PET at baseline and after 14 weeks of medical treatment by calculating the MaRIA score and maximum standardised uptake value respectively. Patients will be followed clinically every 8 weeks for at least 1 year. Clinical evaluation and serum and faecal

biomarkers will be determined at baseline and every 4 months until the end of the study. Patients will be classified as responders and non-responders according to the achievement and maintenance of clinical response. Changes on MRE and PET and alterations in biomarkers will be compared between the two groups.

JORDI RIMOLA

ECCO Grant Awardee 2015



Jordi Rimola © Jordi Rimola

Defining the role of long non-coding RNAs in the pathogenesis of early-onset Crohn's Disease

Aim of the research project

Crohn's Disease (CD) is caused by complex interactions among host genetics, the microbiome and environmental cues that lead to inappropriate chronic activation of the mucosal immune system. Our previous analyses focussed on protein coding mRNA expression associated with CD pathogenesis. We have defined novel ileal CD-specific host-microbe interactions in a large treatment-naïve paediatric cohort, identifying the ileum as the primary inductive site for CD. We have identified central upstream transcription factors that govern the transcribed landscape; however, expression of non-coding regulatory RNA elements that may play a central role in regulating this transcriptional landscape have not yet been characterised. The ever-increasing discoveries regarding non-coding RNA (ncRNA) diversity are revealing a fundamental and broader role for RNAs in shaping cellular functions and gene expression regulation in complex organisms and

are thus fostering interest in characterisation of their role in CD pathogenesis. In this project we will perform high-throughput bioinformatics analysis to characterise long ncRNAs associated with CD pathogenesis, prioritise them and validate prioritised long ncRNAs as a basis for future focussed mechanistic analyses and studies of potential associations with the microbiome in selected in vitro models.

Methodology

Differentially expressed long ncRNAs will be determined using mRNAseq using false discovery rate correction and analysed for fold change differences. Prioritisation will be done based on the "guilt-by-association" theory, looking at co-expression of ncRNAs with well-characterised protein coding mRNA, and on publicly available long ncRNA data sources. Validation will be done using quantitative PCR, northern blotting and RNA fluorescence in situ hybridisations.

Yael Haberman

ECCO Grant Awardee 2015



Yael Haberman © Yael Haberman

Study of the effect of the endocannabinoid-derived prostaglandin D2-glycerol ester (PGD2-G) in Colitis

Aim of the research project

Several bioactive lipids, such as the arachidonic acid-derived prostaglandins or the omega-3 fatty acid-derived resolvins and protectins, are known to play a role in the control of inflammatory reactions. In the context of IBD, we have shown that the endocannabinoid 2-arachidonoylglycerol is able to reduce colon inflammation in a mouse model of colon inflammation. Moreover, we recently demonstrated that a COX-2 metabolite of 2-arachidonoylglycerol, namely PGD2-G, has anti-inflammatory properties in vitro and in vivo. Based on the effect of 2-arachidonoylglycerol in Colitis and on the role of COX-2 in the GI tract, the aim of this project is to test the effect of PGD2-G on colon inflammation using IBD mice models. We will also explore PGD2-G's mechanism of

action by testing the effect of the prostaglandin PGD2 in the same models.

Methodology

We will begin by measuring the levels of the bioactive lipids of interest as well as the expression of the enzymes responsible for their metabolism. We will then administer PGD2-G in the DSS mouse model of IBD and determine its effect on the key parameters of colon inflammation, i.e. macroscopic and histological colon alterations, neutrophil infiltration and expression and production of pro-inflammatory cytokines. Because PGD2-G can be enzymatically or chemically transformed into PGD2, we will also assess these parameters in mice treated with PGD2. In addition, we will co-administer with PGD2-G antagonists of the

receptors potentially responsible for mediating the effects of PGD2-G in order to try to explore the mechanisms responsible for PGD2-G effects.

GIULIO MUCCIOLI

ECCO Grant Awardee 2015



Giulio Muccioli © Giulio Muccioli

Identification and characterisation of microbiota-specific T cell responses in Crohn's Disease

Aim of the research project

In Crohn's Disease (CD), T cell reactivity against harmless microbial antigens leads to chronic intestinal inflammation. After induction of remission, patients receive T cell-suppressing maintenance treatment, during the course of which 30% experience a relapse of inflammation. In order to define a target for immunosuppressive therapy and to predict the efficacy of maintenance treatment, better characterisation of inflammatory T cell responses is essential. A subgroup of CD patients has detectable immune responses to flagellin, a component of motile bacteria. In paediatric CD, anti-flagellin antibodies develop in half of all patients and are associated with severe disease. Flagellin-reactive T cells are detectable in

peripheral blood of a subgroup of CD patients, but low numbers have hampered further study. We have overcome this issue by developing a tool to highly enrich intestinal antigen-specific T cells from total CD4+ T cells in peripheral blood. In this study we will identify the phenotype and function of circulating flagellin-specific T cells in paediatric CD patients at different stages of disease.

Methodology

We will generate flagellin-specific T cell clones from biopsies of paediatric CD patients to determine HLA class II restriction and developmental programming of these cells. Using the obtained knowledge and tools, we aim to develop an immunosuppressant

sensitivity assay to identify differences in drug responses of flagellin-reactive T cells.

JANNEKE SAMSOM

ECCO Grant Awardee 2015



Janneke Samsom © Janneke Samsom

The risk of incident rosacea in patients with Ulcerative Colitis and Crohn's Disease

Aim of the research project

A protective effect, via an unknown mechanism, of cigarette smoke on Ulcerative Colitis (UC, triggering upon cessation) but not on Crohn's Disease (CD) has been shown, a reaction pattern that is inherent to very few diseases. This same unique reaction pattern to patients' smoking behaviour has been observed in patients with rosacea, an inflammatory facial skin disease. Because UC and rosacea are both inflammatory epithelial diseases presumably based on changes in the innate immune system, we aim to assess a possible association between UC and incident rosacea in a large epidemiological study. Although IBD is known to be associated with several skin diseases, an association between IBD and rosacea has not been quantified

previously. This study will advance the as yet incomplete understanding of the idiosyncratic pathogenesis of the individual subtypes of IBD.

Methodology

We performed a case-control analysis using data from the large UK-based Clinical Practice Research Datalink (CPRD). This database contains information on approximately 10 million patients who are enrolled with a general practitioner (GP) within the UK. The database contains information on patients' medical diagnoses, treatments, surgeries, hospitalisations, drug prescriptions, laboratory tests, etc. In a multivariate conditional logistic regression analysis, we calculated odds ratios with 95% confidence intervals for the relative risk of development of rosacea in

patients with UC or CD, stratified by different parameters of IBD disease duration and severity.

JULIA SPOENDLIN ALLEN

ECCO Grant Awardee 2015



Julia Spoendlin Allen © Bio Center Basel

DNA methylation profiles in IBD fibroblasts

Aim of the research project

Fibrosis is the result of chronic intestinal inflammation. More than one-third of patients with Crohn's Disease (CD) develop a fibrostenosing phenotype that can result in intestinal obstruction. The currently available anti-inflammatory therapies are not sufficient to avert or treat intestinal fibrosis. This means that an alternative approach is necessary to prevent or reduce an ongoing fibrotic process.

IBD fibroblasts respond to a pro-inflammatory environment and adapt a stably imprinted activated phenotype that, we hypothesise, is rooted in epigenetic modulation. These fibroblasts are then able to independently maintain inflammation and initiate the fibrotic process.

This project's aim is to unravel the epigenetic

regulation of IBD fibroblasts through a general study of the DNA methylation profile and, in addition, to focus on specific differentially expressed genes in IBD fibroblasts.

Methodology

To do so, we will gather and culture isolated mucosal fibroblasts from the intestine of CD and non-IBD patients. A genome-wide DNA methylation analysis (Illumina, 450k methylation array) will be performed on their DNA (hypothesis-free route). Also, the methylation status of genes that have previously been associated with CD will be directly assessed by MiSeq (method to assess methylation status of specific genes, hypothesis-driven route). Samples of multiple passages will be stored, and assessed with respect to the effect of the

passaging of cells during culturing. Further functional experiments will be planned on the basis of the results of these experiments.

ANJE TE VELDE

ECCO Grant Awardee 2015



Anje Te Velde © Peter Strelitski

Inflammatory bowel disease in the Faroe Islands

Aim of the research project

In 2010 and 2011, the ECCO EpiCom study found that the highest incidence of IBD worldwide was in the Faroe Islands: 83 per 100,000 person-years (European Standard Population, ESP). This high incidence was still present in 2012–2014. Population-based studies have examined the incidence of IBD in the periods 1964–1983 and 1981–1988.

The aim of this project is to explore the aetiology of IBD in the Faroe Islands by:

- 1) Investigating time trends in IBD incidence
- 2) Investigating the association between environmental exposures and IBD

The Faroe Islands is located in the North Atlantic Sea and includes 18 islands with a total population of 49,000. Our aim is to provide an extensive overview of all available data on IBD

incident cases and to study environmental factors at play within the high-risk Faroese population.

Methodology

IBD data are retrievable via the National Hospital of the Faroe Islands, covering 54 years of IBD registration. Data will be analysed according to diagnoses, sex, age groups and calendar periods, with age-standardised incidence rates for CD, UC, IBDU and all IBD. Furthermore, cumulative risk for selected birth cohorts will be provided alongside prevalence rates. Questionnaire responses and biological samples will constitute the data on environmental factors and will be derived from the Children's Health and the Environment in the Faroes (CHEF) project, which has collected extensive information on

the possible impact of chemical exposures on children's growth and development.

TURID HAMMER

ECCO Grant Awardee 2015



Turid Hammer © Turid Hammer

The use of benzimidazoles as co-medication for anti-TNF therapy in IBD

Aim of the research project

Clinical studies have shown that combination therapy using anti-TNF and thiopurines is more effective than monotherapy in the treatment of IBD. However, in many patients this combination is not feasible due to intolerance to thiopurines or severe adverse events. For this group, alternative co-medication would be a valuable option. We have previously shown that the clinical effectiveness of anti-TNF in IBD is correlated with the capacity to induce regulatory macrophages in an in vitro assay, the mixed lymphocyte reaction (MLR). Using this assay as a screening tool, we have tested a large panel (1,600) of FDA-approved compounds for their potential to boost the macrophage-inducing effects of anti-TNF. From this library, we have identified the anti-helminthic drug class of benzimidazoles as

good candidates for anti-TNF co-medication. In this project we aim to perform further validation and preclinical testing of benzimidazole and anti-TNF combination therapy.

Methodology

The in vitro assay will be used to confirm the data obtained in the compound screen and to determine the optimal dose of benzimidazoles as anti-TNF co-medication. The read-out will consist of the induction of regulatory CD14+CD206+ macrophages. The phenotype of these macrophages will be studied using flow cytometry and gene expression analysis and functionality will be determined in immunosuppression and wound healing assays. Finally, the potential of benzimidazoles to potentiate the effect of anti-TNF will be studied

in vivo in the T cell transfer model of Colitis.

MANON WILDENBERG

ECCO Grant Awardee 2015



Manon Wildenberg © Edoland Photographers

ECCO and the Eastern Europe perspective

Although IBD remains less prevalent in Eastern Europe than in the countries of Western Europe, the difference is smaller than in the past [1]. Put another way, the IBD burden is steadily increasing in Eastern Europe [2]. More limited access to specialist care, including IBD specialists, may mean that a more advanced stage of disease is present at diagnosis [1]. Furthermore, lower per capita expenditure on health care in Eastern European countries impacts on the reimbursement policy with regard to innovative drugs, resulting, for instance, in lower rates of use of biologicals [3]. Most Eastern European countries joined ECCO around a decade ago. While in some countries (e.g. Estonia, Slovakia, Slovenia) the number of individual members of ECCO can be considered average, reflecting the size of the population, the remaining countries have low membership numbers. In interpreting these figures, one must bear in mind both the generally lower numbers of medical workers in proportion to the population in Eastern Europe and the East-West discrepancy in salaries; the lower salaries in Eastern Europe may represent a hurdle to payment of a membership fee and also restrict participation in ECCO Congresses for some colleagues.

It is certainly the case that the Eastern European ECCO Members do their best to foster awareness of the growing burden of IBD in the medical environment and make the most of the educational offers of ECCO. During the past 2 years (2014 and 2015), four of the ten ECCO Educational Workshops were organised in this region of

Europe (in Bulgaria, Estonia, Czech Republic and Russia). ECCO urges Eastern European countries to apply to hold such workshops in order to continue to expand ECCO's support within these countries. The most promising trainees regularly participate in the ECCO Advanced IBD Course, held yearly just before the Congress.

It is worthwhile to recall the scientific opportunities that are provided by ECCO yet not fully recognised by all members in Eastern Europe. ClinCom's mission is to stimulate the development of high-quality investigator-initiated trials in IBD. Investigators planning studies are welcome to present their proposals for ClinCom assessment. During the first stage, applicants are called upon to provide a synopsis, including background, design, objectives, outcome parameters, major inclusion and exclusion criteria, statistics and co-variables, not exceeding four pages (a template is provided by the ECCO Office). Within 6 weeks of receipt, ClinCom will respond to the applicant with a preliminary review, either encouraging or declining the submission of a full protocol. Finally, the ECCO Grants and Fellowship Programme offers extra opportunities for applications from the Eastern European countries that are presented in detail at each call.

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EDYTA SYLWIA ZAGOROWICZ

ClinCom Member



Edyta Sylwia Zagorowicz © ECCO

A Focus Paper by the Epidemiology Committee of ECCO: New treatments and outcomes in IBD

The last 20 years have witnessed increased use of immunosuppressive (IM) therapy for the management of Inflammatory Bowel Disease (IBD), and in the past decade treatment with anti-tumour necrosis factor α (anti-TNF α) has been introduced. The overall effectiveness of these new approaches in modifying disease course and outcomes remains controversial. In addition, the cost of medical therapy for IBD is progressively increasing. Accurate evaluation of the changes in disease outcomes associated with different treatments may therefore assist

care providers when considering management options and discussing expectations of outcome with patients.

Against this background, members of the Epidemiological Committee (EpiCom) of the European Crohn's & Colitis Organisation (ECCO) conducted a review of the literature published on or before June 30, 2015 dealing with hospitalisation, surgery, infection, cancer and mortality rates in IBD patients. Preference was given to population-based studies, but when data from these sources were limited, large

cohort studies and randomised controlled trials were also considered.

Data on hospitalisation rates are strikingly heterogeneous; they are sometimes conflicting and are subject to a number of limitations. Population-based studies are scarce and the impact of introduction of IM therapy and biologics on hospitalisation rates has usually been evaluated indirectly. Moreover, there is generally no way to distinguish disease-related hospitalisations from those provoked by adverse drug reactions. In addition, temporal trends in

hospitalisation need to be adjusted for changes in the prevalence of IBD, but data on the latter are frequently incomplete.

Finally, the specific impact of biologics and/or IM therapy on IBD hospitalisation rates has never been assessed prospectively. A clear example of heterogeneity emerged in the ECCO EpiCom 2011 inception cohort: during the first year after diagnosis, hospitalisation rates for Crohn's Disease (CD) patients were significantly higher in Eastern Europe than in Western Europe/Australia, and significantly more CD patients received biologic therapy in the Western Europe/Australian centres.

Colectomy rates have clearly decreased since the introduction of these drugs, and a review of the epidemiological data tends to exclude the possibility that this reduction reflects changes in the nature or severity of Ulcerative Colitis or its increasingly early diagnosis. When analysing rates of surgery in general, it is important to consider that preventing intestinal resection may not be the ultimate goal of IBD treatment. Most clinical trial data indicate that the risk of serious infections is not increased in patients treated with anti-TNF α agents, but a different picture emerges from cohort studies. This discrepancy may reflect the select nature of the populations studied in RCTs, where the proportion of 'low-risk' patients is likely to be higher than that encountered in actual clinical

practice. Additional research is needed to determine whether the risk of infection is additionally increased when anti-TNF α therapy is given with IM. In this context it is of note that the risk of infectious complications seems to be higher in older patients treated with combination therapy.

There is a very strong body of evidence supporting the carcinogenic effects of thiopurines, particularly with regard to the risk of non-melanoma skin cancers and cancers of the lymphoproliferative system. The risk of cervical cancer may also be increased, although existing studies are difficult to compare. Nonetheless, the absolute risk of cancer in patients treated with thiopurines is still low, and has to be weighed against the therapeutic benefits of these drugs. As for biologic agents, on the basis of the available evidence, they do not appear to increase the risk of cancer in patients with IBD. However, the study with the longest follow-up published thus far covers a median of 3 years after the first infusion. Therefore, close monitoring for signs of possible drug-related cancer is advisable during biologic therapy.

The majority of studies reported in the literature have not revealed any increase in mortality with IM therapy or biologics/anti-TNF α agents. However, the studies themselves have a number of limitations, including short follow-ups, lack of adjustment for disease activity and

other confounders with a potential impact on outcome. For this reason, it is still too early to draw any definite conclusions regarding this risk. Biologic and non-biologic IM therapies both offer indisputable benefits for patients with IBD, and both have the potential to alter the prognosis. The positive and negative effects of these drugs on disease outcomes should be reflected by changing rates of mortality, hospitalisation, surgery, infections and cancer occurrence. However, data on these aspects are remarkably heterogeneous and difficult to summarise owing to the effects of confounding factors and organisational differences in the healthcare systems of different countries.

VITO ANNESE

EpiCom Member



Vito Annese © ECCO

UC Consensus Update

The process started in November 2014 with the call for participants in the UC Update 2015.

The two chairs, Marcus Harbord and Rami Eliakim, selected 26 participants, and at the beginning of February 2015, five working groups were defined:

- WG1: Definitions/classification/diagnosis (including endoscopy, imaging, SB endoscopy OMED-ECCO guidelines) / histopathology (synthesising histopathology guidelines)
Leader: Magro Fernando, Portugal
- WG2: Medical management of active disease
Leader: Carbonnel Franck, France
- WG3: Maintenance of remission / transitional care in UC (including Paediatric UC guideline)
Leader: Dignass Axel, Germany
- WG4: Pouchitis / cancer surveillance (including malignancy, imaging & endoscopy guidelines) / surgery (synthesising surgery guideline)
Leader: Gionchetti Paolo, Italy
- WG5: Extra-intestinal manifestations / anaemia / opportunistic infections / reproduction (synthesising the guidelines for each of these subjects)
Leader: Rieder Florian, USA

Literature research and draft of statements were completed for this project by April 24, 2015.

The first draft of the statements was submitted,



UC Consensus Meeting, Barcelona 2015 © ECCO

and the first online voting round took place in June. After the results of the first voting round became available, working groups had to concentrate on formally writing their draft sections, with each statement followed by the relevant section of text.

Submission of one WG masterfile for the second voting round by WG leaders was done by August 28, 2015, and the second online voting round was completed by October 12, 2015.

The Consensus Meeting took place on October 24, and all of the statements were discussed, despite the great majority having already reached the statutory agreement level of >80%. Many statements were changed and the feeling at the end of the Consensus Meeting was that the changes made had improved the statements significantly. The two ECCO UC Consensus Papers will be finalised over the next few months, ready for our ECCO'16 Amsterdam Congress, where Rami and Marcus will delight you by revealing the new UC Guidelines update.

Many Consensus Papers have now been published and another four (incl. Guidelines Updates) are to be published in 2015–2016. Over the past few years, several focussed Consensus Papers have been written (e.g. Histopathology, Endoscopy, Surgery, Anaemia, Pregnancy). The most recent Guidelines publication featured the topic of Malignancies in IBD and now comes the one on Extra-intestinal Manifestations. It is planned to update these more specialised papers approximately every 5 years. The big Consensus Papers (Crohn's Disease and Ulcerative Colitis) will be updated approximately every 3 years and will in future focus more on the modern, state of the art management of active disease and maintenance of remission. Encouragingly, these have become fast-moving fields with the appearance of several new drugs for treatment

of inflammation.

Therefore, subsequent to the Consensus Guidelines on Extra-intestinal Manifestations and the ECCO-ESCP Consensus Guidelines on Surgery in CD, there is no plan at present for a new Consensus Paper to appear in the future. Topical Reviews will be published. The first will be the Fibrosis Topical Review, to be published in the near future. At the UEGW in Barcelona, a panel was held to discuss the management of IBD in the elderly. The results of this discussion, as well as the Fibrosis project, will be presented at ECCO'16 in Amsterdam. After the completion and publication of the IBD in Elderly Topical Review in the first half of 2016, the next project will focus on the Role of Environmental Factors in IBD; this will be discussed in the Consensus Meeting during the ECCO'16 Congress in Amsterdam.

We hope that you will enjoy reading the upcoming ECCO Consensus Guidelines and Topical Reviews when they are published in Journal of Crohn's and Colitis next year.

PAOLO GIONCHETTI

GuiCom Member



Paolo Gionchetti © ECCO

41st ECCO Educational Workshop

The 41st ECCO Educational Workshop was held in collaboration with the Colitis & Crohn's Foundation, India during the 5th National IBD meeting on September 13, 2015 in Chandigarh, India.

The guest faculty from ECCO comprised James Lindsay (Consultant Gastroenterologist at Barts Health NHS Trust and Reader in Inflammatory Bowel Disease, Barts and The London School of Medicine) and Peter Irving (Consultant Gastroenterologist at Guy's and St. Thomas Hospital; Honorary Senior Lecturer, King's College London). The national faculty comprised Rakesh Kochhar, Ajit Sood, Ajay Kumar, Vinit Ahuja and Govind Makharia.

The workshop was very well attended, with a total of 480 participants from all parts of the country. Case-based discussions on topics relevant to the Indian context were held, covering management of infectious complications, management of

treatment-refractory moderate UC, new-onset and recurrent complicated ileocaecal Crohn's Disease and pouchitis. The workshop was very interactive, generating a lot of discussion involving the delegates. Bo Shen and Vijay Jaynik from the United States and Harminder Singh from Canada, who constituted the international faculty, also actively participated in the workshop.

The feedback from faculty and delegates was excellent, with requests for more frequent workshops of this nature to enable participants to update their knowledge of IBD.

AJIT SOOD

Local Workshop Coordinator



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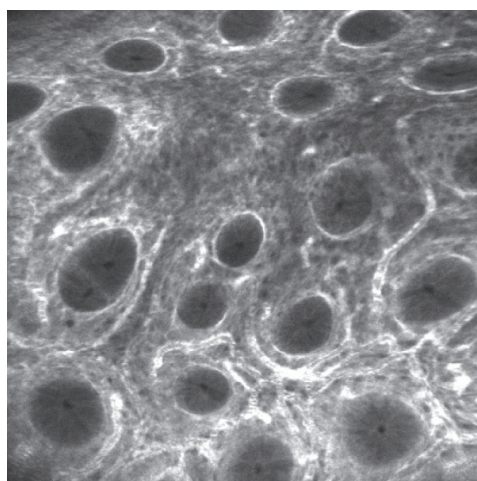


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Summary: Safety and long term outcome of ileocaecal resection for Crohn's Disease: A multicentre cohort analysis

JCC Article in preparation

A. de Buck van Overstraeten, E.J. Eshuis, S. Vermeire, G. Van Assche, M. Ferrante, G.R.A.M D'Haens, C. Ponsioen, A. Belmans, C.J. Buskens, A.M. Wolthuis, W.A. Bemelman, A. D'Hooe

Introduction

Despite improvements in medical therapy, most patients with Crohn's Disease (CD) still require surgical resection at some stage of their disease. The main drawbacks of surgical therapy are the supposed high recurrence rate and surgical morbidity. Recent data on the long-term outcome of ileocaecal resections are, however, scarce, while technical evolution, together with improved perioperative care, has increased surgical safety and short-term outcome [1, 2]. Laparoscopic surgery is probably the main achievement of the last decade in IBD surgery. Several series have documented a significantly improved outcome of patients operated on using a minimally invasive approach compared to open surgery [3–5].

Methods

All patients operated on for terminal ileocaecal CD at two referral centres were included. Patients operated on at the Academic Medical Center (AMC) in Amsterdam were included from 1998 until 2013, while patients operated on at the University Hospital Leuven (UZL) were included from 2001 until 2013. All patients who underwent a primary ileocaecal resection and had historically proven CD were included. Primary outcomes were the local CD recurrence rate, assessed either clinically or endoscopically (clinical recurrence rate), and the rate of surgical reintervention for disease recurrence (surgical recurrence rate). A secondary outcome was short-term morbidity.

Results

Between 1998 and 2013, 538 consecutive patients underwent a first ileocaecal resection for CD (215 male, 40%) at both institutions combined. Three hundred and eighty-three patients (71%) were operated on laparoscopically with a conversion rate of 12% (n=47). Thirty-one patients (5.8%) received either an end or a loop ileostomy. An additional seven patients (1.3%) underwent a stoma formation for anastomotic leakage. All but one patient had stoma reversal after a median period of 5 months (IQR 3.6–6.7). The overall complication rate, defined as in-hospital morbidity, was 22.7%. Anastomotic leakage occurred in 15 patients (2.8%), while a deep abscess was diagnosed in 13 (2.4%). ASA score of 3 or more [OR 4.34 (95% CI 1.12–16.77), $p=0.0334$], preoperative anti-TNF α therapy [OR 3.30 (95%

CI 1.09–9.99), $p=0.0353$] and specimen length [OR 1.06 (95% CI 1.03–1.09), $p=0.0002$] were all significant risk factors for anastomotic leakage. Median follow-up was 6 years (IQR 2–9). Clinical recurrence was diagnosed in 17.6%, 45.4% and 55% at 1, 5 and 10 years respectively. Only smoking [HR 1.67 (95% CI 1.14–2.43), $p=0.0077$] and microscopic positive section margins [HR 2.16 (95% CI 1.46–3.21), $p=0.0001$] remained as independent risk factors after multivariate regression analysis. Surgical recurrence was noted in 0.6%, 6.5% and 19.1% after 1, 5 and 10 years respectively. Only section margin positivity [HR 2.99 (95% CI 1.36–6.54), $p=0.0062$] remained as an independent risk factor after multivariate regression analysis.

Conclusion

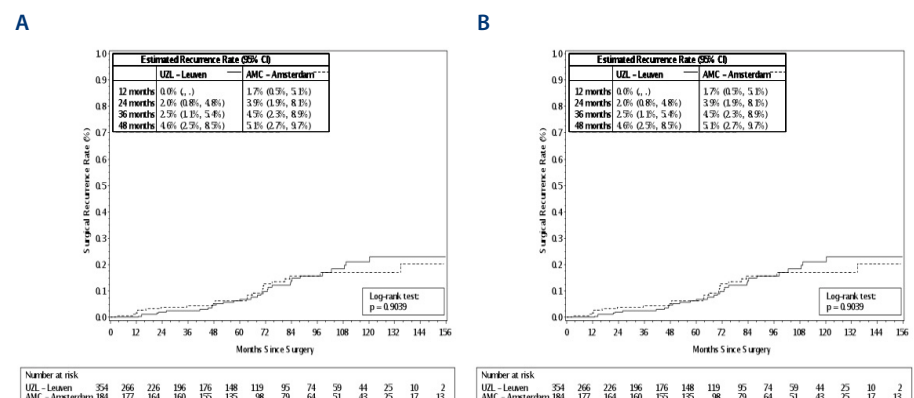
This multicentre study shows that ileocaecal resection in CD patients is a safe and effective operation that can be done laparoscopically in the majority of patients with low morbidity, low stoma rates, short hospital stay and a low long term surgical recurrence rate. Microscopically involved margins were independently and significantly associated with both clinical and surgical recurrence, which is contrary to what currently is believed. Smoking has a significant impact on clinical recurrence.

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ANTHONY DE BUCK

Department of Abdominal Surgery, UZ Leuven, Belgium



2nd S-ECCO International IBD Workshop Brazil - Report

The Surgeons of ECCO recently organised the 2nd S-ECCO International IBD Workshop, held on October 1–3, 2015 at the Bourbon Hotel in Foz do Iguaçu, Brazil.

ECCO was represented by six European speakers: Séverine Vermeire, Geert D'Haens, Gijs van den Brink and Peter Lakatos were the invited gastroenterologists, while Willem Bemelman and André D'Hoore represented the surgeons. During the 3 days of the workshop, a number of topics relating to medical and surgical aspects of IBD were discussed in sessions characterised by high-quality science, friendship and interaction.

A total of 170 attendees, comprising similar numbers of surgeons and gastroenterologists, were present from many Latin American countries, including Brazil, Argentina, Uruguay, Chile, Colombia and Mexico. A gigantic banner showing the famous Iguaçu Falls and the logo of the meeting provided a perfect backdrop to the scientific sessions. The lectures were equally divided into medical and surgical topics, and it was interesting to see gastroenterologists discussing surgical talks, including technical aspects of IBD management, while surgeons were equally engaged in medical topics, such as therapeutic drug monitoring. Among the debates held was a memorable discussion of the utility of azathioprine in Crohn's Disease. Geert D'Haens was responsible for the "rest in peace" title, while Séverine Vermeire



S-ECCO IBD Workshop, 2015 © GEDIIB

defended the position that physicians still need azathioprine. The winner was the audience, who were responsible for a lively discussion of this important topic. Several Brazilian and Latin American speakers also made important contributions to the meeting's high scientific level. An update on surgery for UC, highlighting new advances in transanal pouches, was brilliantly delivered by Willem Bemelman. André D'Hoore spoke on the important topic of how to prevent postoperative complications in CD and UC, presenting several challenging cases and considering extremely difficult situations in surgical practice.

This meeting definitely represented a landmark in Latin America, with endorsement from ECCO, organisation by GEDIIB (Brazilian Study Group for

IBD) and support from PANCCO (Pan-American Crohn's and Colitis Organisation). It was a brilliant example of the multidisciplinary approach to IBD, with surgeons and gastroenterologists in complete harmony, even on the football field, where a legendary match was played by teams comprising a mixture of faculty and attendees. One of the missions of S-ECCO is to spread knowledge on IBD not only in Europe but also globally. The next meeting has already been confirmed for 2017, and we hope that we can count on many of you to join us there with the goal of further improving the level of management of IBD in Latin America.

PAOLO KOTZE

S-ECCO Member

Neoplasia in IBD

As announced by Cord Langner in a previous edition of ECCO News, a working group dedicated to histopathology (H-ECCO) was launched at the 10th Congress of ECCO in Barcelona.

Like other ECCO Committees and Working Groups, H-ECCO aims to improve the standard of care for IBD patients across Europe in various ways. Among the different topics on which the H-ECCO Working Group will work actively is a better understanding of neoplastic lesions complicating IBD, i.e. dysplasia (or intra-epithelial neoplasia) and adenocarcinoma.

Dysplasia, defined as a "histologically unequivocal neoplastic epithelium without evidence of tissue invasion", is the most reliable marker of an increased cancer risk in patients with IBD. The histological classification of dysplasia is based on the Vienna classification of gastrointestinal epithelial neoplasia, which comprises four distinct categories: (i) negative for dysplasia (regenerating epithelium), (ii) indefinite for dysplasia ("questionable" dysplasia),

(iii) positive for low-grade dysplasia and (iv) positive for high-grade dysplasia. However, even for pathologists with expertise in gastrointestinal pathology, diagnosing dysplasia in IBD patients remains challenging owing to the poor inter-observer agreement for the categories "low-grade dysplasia" and "indefinite for dysplasia". Improving the reproducibility of diagnosing dysplasia is therefore a crucial point that will be covered by the 1st H-ECCO IBD Masterclass designed for both pathologists and clinicians during the next annual ECCO Congress, to be held in 2016 in Amsterdam.

One of the important missions of the H-ECCO Working Group is to develop basic and applied research. Moreover, our projects are guided by the promise of having a positive impact on patient care. Having several members of our working group highly experienced

in molecular pathology will permit the development of dedicated projects that allow a better understanding of the molecular events underlying the development of neoplastic lesions complicating IBD. We will focus particularly on IBD-related colorectal neoplasia displaying an MSI (microsatellite instability) phenotype. The MSI phenotype is associated with hereditary non-polyposis colorectal cancer (HNPCC) syndrome – recently renamed Lynch syndrome – and is due to germline mutations in the DNA mismatch repair (MMR) genes MLH1, MSH2, MSH6 or PMS2. MSI is also observed in approximately 10–15% of sporadic colorectal cancers, following epigenetic, bi-allelic silencing of MLH1 expression by de novo methylation of its promoter. We and others described the existence of MSI in about 10% of IBD-related colorectal neoplasia and showed that MSI-IBD-colorectal

neoplasia exhibits distinctive characteristics, both clinicopathological and molecular, when compared to other MSI colorectal tumours arising in different clinical contexts (sporadic and hereditary). Interestingly, cancers displaying an MSI phenotype are known to have an improved survival and a different response to chemotherapeutic agents compared with similar but non-MSI (or microsatellite stable) tumours in the same location. Recently, clinical benefit of anti-PD-1 immune checkpoint blockade was reported in metastatic MSI colorectal cancers. There is thus increasing clinical interest in identifying the MSI phenotype as a potential prognostic and predictive therapeutic biomarker in IBD patients with CRC. However, MSI IBD-related colorectal neoplasia is rare, and only a strong collaboration between several centres will allow a large cohort of patients to be studied. Our working group will also focus on neoplastic

lesions arising in the setting of combined IBD and primary sclerosing cholangitis (PSC). These patients are at increased risk of developing colorectal neoplastic lesions (dysplasia and carcinoma). Several types of dysplasia complicating IBD are described in the latest WHO classification: (i) intestinal type, (ii) serrated type and (iii) hypermucinous type. Dysplastic lesions among patients with both IBD and PSC are often difficult to classify and could constitute a distinct dysplasia from morphological and molecular points of view. Our group aims to develop a multicentre study to collect and investigate these rare lesions.

A review describing the molecular mechanisms underlying neoplastic lesions in IBD is also planned by our group in 2017.

H-ECCO offers an excellent opportunity for pathologists to belong to the ECCO Family, allowing interaction with clinicians and with

other ECCO Groups. This in turn will enhance improvements in our understanding of the neoplastic lesions arising in the setting of IBD by facilitating effective collaboration between specialties.

MAGALI SVRCEK

H-ECCO WG Member



Magali Svrcek © ECCO

A '500 word' update on translational nutrition research in IBD

There are very few diseases in which diet and nutrition are as important as in Inflammatory Bowel Disease(s) (IBD).

Diet in the aetiology of IBD:

As host susceptibility genes explain only a small fraction of the disease risk, various endeavours have been undertaken to unravel the role of gut microbiota and diet, and recently their interaction, in the pathogenesis of IBD. Large cohort studies are currently exploring the interplay between diet, genetics and microbiota, and its impact on IBD aetiology and risk of relapse. But these efforts are focussing mainly on the nutrient components of the diet, with very little research on non-nutrient constituents, which either occur naturally in food (e.g. phenolic acids) or have entered diet via the food industry and processing (food additives). *The exact role of diet in the onset of IBD remains elusive.*

Diet in the management of IBD:

Although there is compelling evidence on the effectiveness of exclusive enteral nutrition in the treatment of active Crohn's Disease (CD), clinical practices still vary around the world and its use is primarily limited to paediatric patients. While much of this variation may be attributed to the cost of enteral nutrition compared with other drug therapies and the way this is reimbursed across different healthcare systems, there are valid reasons to believe that a further causal factor is the lack of dedicated dietitians to support the treatment course and patients. There is also an unmet need for more research and evidence on the role of partial enteral nutrition as an adjunctive treatment to prolong disease remission. Finally, there is currently strong interest in the development of alternative, whole

food-based dietary therapies for IBD patients. *To date there is very little quality evidence to suggest a preference for one particular approach.*

Assessment and management of malnutrition:

Assessment of nutritional status is the cornerstone of nutritional support and dietetic counselling of patients with IBD. However, there are several caveats to consider and this is an area of research where evidence has not thus far been translated into routine clinical practice. IBD-specific alterations in body composition, with depletion of skeletal muscle and normal or increased fat mass, are now well documented. *Hence, a higher degree of adiposity and less lean mass should be expected for a given BMI compared with healthy people.* This is a finding which might be relevant in routine clinical practice, particularly as people with IBD experience a higher risk of adverse cardiovascular events, and obesity is becoming an especially common feature among IBD patients. It might be that the focus on the dietetic support of IBD patients should be extended from management of undernutrition to prevention and correction of obesity, a topic which has not been addressed in the various management guidelines published for people with IBD.

Micronutrient status and deficiencies:

Vitamins, minerals and trace elements are key nutrients for maintenance of whole body function and homeostasis and in disease dietary requirements may increase. A key aspect in the interpretation of body micronutrient status is

robust assessment. To date, measurement of micronutrient concentration in blood is the mainstream approach to assess body store adequacy in clinical practice, occasionally complemented by dietary assessment for selective micronutrients (e.g. calcium and iron). However, in the presence of a systemic inflammatory response, in conditions like IBD, the plasma concentrations of various micronutrients (e.g. zinc, selenium, copper, vitamin C, vitamin E, vitamin A) are substantially affected by non-nutrition-associated factors (e.g. changes in the concentration of nutrient carrier proteins); *hence these are unlikely to reflect frank body reserves and their clinical interpretation may be misleading and result in the initiation of inappropriate interventions.*

KOSTAS GERASIMIDIS

D-ECCO WG Member



Kostas Gerasimidis © ECCO

Evolving Concepts in Transitional Care

Tell us on how you would like to have them delivered in your consultation room...

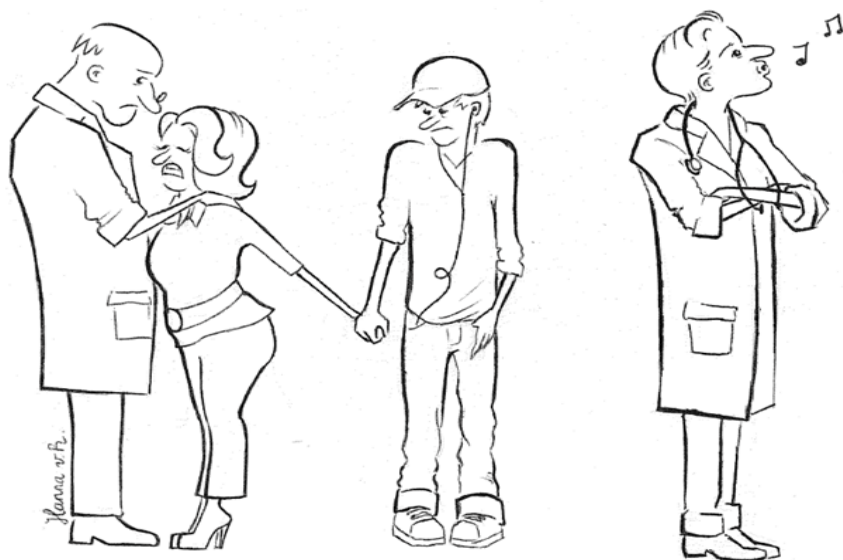


Figure 1. Hindrances to successful transition: Parents are unable to relinquish their grip, paediatricians are unable to let go, adult physicians are unwilling to take charge and the adolescent is indifferent to all of them. © Hanna v. H.

Clinical vignette:

An 18-year-old adolescent, who is accompanied by his mother, visits the adult gastroenterology department for the first time. His paediatrician last saw him 5 months previously, when his Crohn's Disease was in remission with a Paediatric Crohn's Disease Activity Index score of 5. Since the time he was diagnosed 2 years ago, he has had three disease flares. Each flare was successfully treated with exclusive enteral nutrition for 6 weeks with return to normal diet. According to the paediatrician's notes, the patient is on thiopurine maintenance.

At this appointment the boy says he is well and active. He claims to have no abdominal pain and normal bowel habits. This is when the mother pushes herself forward to join the conversation. She claims the opposite: Her son is lying on the couch all day and she is afraid that he will fail his final school exam.

Physical examination reveals a pale teenager who appears younger than his chronological age. Laboratory evaluation reveals anaemia and elevation of markers of inflammation, including an erythrocyte sedimentation rate of 65 mm/hour and a faecal calprotectin of 2500 µg/g. Additional testing reveals undetectable levels of thiopurine metabolites.

The boy admits he has stopped taking his medication. He experiences major symptomatic benefits since he started smoking marijuana.

Possible therapeutic options to treat the current active disease are discussed. The adult gastroenterologist recommends a biologic. The mother states that she wants the opinion of their former paediatric gastroenterologist.

Health professionals involved in the delivery of care to adolescents with IBD will recognise the uncomfortable situation described in the vignette. Transition from paediatric to adult-centered services is often poorly prepared and consequently unpleasant for all involved in the process (Figure 1). There is no uniform model for a successful transition, but the use of a protocol is critical. The Paediatricians of ECCO (P-ECCO) are currently preparing for an ECCO Topical Review on this subject, with a consensus meeting to be held next June in Vienna. Expert reviews such as this one are distinct from guideline papers and are reserved for areas with an as yet limited evidence base. Many papers have been published on transition of care in IBD, but none has transcended the level of single-centre experience.

By using a two-step approach, P-ECCO aims to take the topic "Transitional Care in IBD" to the next level. The Transition Survey (currently online: see the "link" below) marks a first step towards the writing of the expert review. This survey is meant to determine which ideas on transition are most important to health professionals. P-ECCO is particularly interested in the views of adult gastroenterologists and IBD nurses, who are responsible for the continuation of care for adolescents. The second step will be the selection of participants, whose most important role will be to synthesise current practice positions. The overall goal of this project is to define successful transition, to identify critical elements for the transition protocol, and to establish responsibilities for all players involved in the transition process. At the end of the

project we hope to create a "Transition Toolkit", a consensus-based checklist that will fit in the doctor's coat and can be used in daily practice.

To find the survey link please follow the steps below:

1. Go to the ECCO Website (www.ecco-ibd.eu)
2. Publications
3. Surveys
4. P-ECCO Transition Survey
5. Link to survey: Transition of care in IBD: a survey

RICHARD RUSSELL

P-ECCO Member



Richard Russell © ECCO

N-ECCO Activities and new initiatives - an update

**Dear N-ECCO Members,
Dear colleagues,**

In the autumn edition of ECCO News you will have been able to read in detail about the N-ECCO Activities available to you at the ECCO '16 Congress in Amsterdam.

The N-ECCO Committee is looking forward to welcoming and meeting as many of you as possible at the 10th N-ECCO Network Meeting on March 17, 2016. We have looked closely at the feedback and suggestions offered by delegates from the last meeting in Barcelona to help us develop a varied and interesting programme for experienced IBD nurses everywhere. In Amsterdam the sessions will be co-chaired by IBD specialist nurses from the Netherlands. This initiative allows non-committee members to take an active role in N-ECCO.

For nurses who are new to IBD, the 7th N-ECCO School will provide a one-day foundation course in Inflammatory Bowel Disease. The course content has been updated and will include a session on the psychosocial implications of living with IBD. Nurses wishing to attend the N-ECCO School are nominated by the National Representatives of their country. In 2016 the N-ECCO School is also open to dietitians wishing to increase their knowledge of basic IBD. EFCCA (European Federation of Crohn's and Ulcerative Colitis Associations) has kindly provided financial support to nurses attending the N-ECCO School in the past years and have confirmed that this support will also be available in 2016 for nurses and dietitians. We are looking forward to working with D-ECCO in Amsterdam!

The programmes for the 3rd N-ECCO Research Forum and the new 1st School for Clinical Trialists are also detailed in the autumn edition of ECCO News. There are also other educational opportunities available for nurses at ECCO'16, including the Y-ECCO Workshops, the EpiCom Workshop, the D-ECCO Workshop and the S-ECCO IBD Masterclass. (Please note that a separate registration fee applies for these courses.) The complete programmes for all the above-mentioned activities are available on the ECCO'16 Congress Website: www.ecco-ibd.eu/ecco16.

N-ECCO aims not only to provide educational opportunities for nurses involved in the care of patients with IBD but also to encourage networking with (international) colleagues. This year we have started to systematically interview our National Representatives using a questionnaire via e-mail. These interviews are



N-ECCO Members © ECCO

published on the N-ECCO page of the ECCO Website and they provide us with an awareness of the diversity (and similarities) of IBD nursing across Europe. A summary of the first interviews will be included in ECCO News next year.

The N-ECCO Committee highly appreciates the work of the National Reps. The National Reps form a link with N-ECCO and the IBD nurses in the individual countries, thus providing ECCO with candidates for the N-ECCO School and providing IBD nurses with educational possibilities available via ECCO such as the e-CCO Learning Platform.

N-ECCO looks forward to a close cooperation with the National Reps and ideas for initiatives or feedback are welcome! Furthermore, N-ECCO aims to promote the role of the IBD nurse and provide networking possibilities for all nurses involved in IBD care. The N-ECCO Travel Award offers an excellent opportunity for nurses to visit an established IBD centre of their choice to learn and observe good practice. For more information concerning the Travel Award, please contact the ECCO Office or a N-ECCO Committee member.

Another form of networking is to organise a Post N-ECCO event in your own country in your own language. This allows IBD nurses who are not in a position to attend an ECCO Congress or who do not have a sufficient command of the English language to receive education and hear about new developments to improve their service. This event has been a great success in the Netherlands and this year a Post N-ECCO event was held in Germany for the first time. Due to the success of this event a second Post N-ECCO is already being planned for next year. If you would like further information on how to organise a Post N-ECCO event please let us know.

The ECCO Congress provides the ideal environment for networking with colleagues

from other national and international centres. Networking during the rest of the year is of course also possible. Several opportunities are available to work with ECCO and meet interesting colleagues from around the globe. Nurses may apply to take part in ECCO Topical Reviews and Guideline projects. Currently four ECCO nurse members are involved in the development of ECCO-EFCCA Patient Guidelines. In the future there will be a chance for applicants to work with N-ECCO on further publications. We would like to encourage colleagues to join the N-ECCO Committee in the development of e-courses for the e-CCO Learning Platform. We would love to hear from you if you are interested!

This year we have had more applicants than ever before for the one open position on the N-ECCO Committee. All applicants were very good and we hope those who were not accepted this year will re-apply in the future.

Apart from becoming a committee member there are so many opportunities for anyone interested in working with ECCO.

Let's meet up and discuss this further in Amsterdam!

JANETTE GAARENSTROOM

N-ECCO Chair

ECCO EFCCA PATIENT GUIDELINES



Global press conference
Wednesday, March 16, 2016
15:00-16:00
RAI Amsterdam
Open access to everyone



United We Stand



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Dear Y-ECCO friends,

This will be my last members' address as Y-ECCO Chair. I shall be happy to hand over the position of chair to Tim Raine (UK) during the ECCO Congress 2016 in Amsterdam. Tim has now been on the Y-ECCO Committee for 3 years and has contributed substantially to the ECCO e-Learning platform. I am confident that he will do an excellent job and I wish him all the best! Nuha Yassin (UK) and Isabelle Cleynen (Belgium) will remain on the committee, while Sebastian Zeissig (Germany) steps down with me. This means that we have two open seats on our committee for next year, for which we have received eight excellent applications.

The election process has now been completed and the results will be announced during the General Assembly at the ECCO Congress in Amsterdam.

Y-ECCO represents a group of young people with tremendous energy and motivation and it is great to see this being translated into an increasing contribution of Y-ECCO Members in numerous ECCO Activities, which I shall briefly list below.

Workshops:

Every year Y-ECCO organises two workshops: one on career development and one basic science workshop. This time, the topic of the career development workshop will be "How to write and review a scientific paper".

The workshop will be led by Larry Egan, the editor in chief of the Journal of Crohn's and Colitis. We are convinced that this workshop will be a tremendous success, so make sure that you register on time!

The central themes of the basic science

workshop are "Mouse models in IBD" and "The role of the microbiota in IBD". During this workshop, selected Y-ECCO Members will be able to present their work and have a discussion with peers, guided by renowned senior experts. Selection for oral presentations will be performed on a competitive basis from amongst the basic science abstracts submitted to the ECCO'16 Amsterdam Congress. To be considered for presentation at the basic science workshop, please tick the respective checkbox when submitting your abstract.

Awards:

As in previous years, we will hand over five best abstract awards for the top five abstracts submitted for the ECCO Congress by Y-ECCO Members.

Guidelines and e-learning platform:

Y-ECCO is involved in the development of the ECCO Consensus Guidelines and e-Learning cases and in the recording of educational podcasts to be made available online and during the ECCO Congress. Next year, there will be a call by GuiCom to Y-ECCO to help in developing their topical reviews.

Co-chairship:

Every year, Y-ECCO Members can apply to become co-chair of scientific sessions at the ECCO Congress.

ECCO News:

We contribute to ECCO News by writing reviews and opinions on IBD-related papers that have recently appeared in high-ranked journals.

In the Y-ECCO Interview corner, Nuha Yassin publishes interviews with people who are of exceptional merit in ECCO and the IBD field.

Lastly, I would like to invite every Y-ECCO Member to send in original research proposals to ClinCom. They offer their expertise to review your research protocol and, if feasible, ECCO will endorse your study by using the large ECCO Network to facilitate participation in the study. If you are interested in any Y-ECCO-related activities or if you have ideas for new projects, please let us know by contacting ecco@ecco-ibd.eu. We are looking forward to hearing from you!

I would like to end with a word of thanks to my colleagues on the Y-ECCO Committee and to all Y-ECCO Members for their help, which has been greatly appreciated.

Warm regards,

PIETER HINDRYCKX

Y-ECCO Chair



Pieter Hindryckx © ECCO

Y-ECCO Literature review

Dear (Y-)ECCO Members,

We are happy to welcome you to the Y-ECCO Literature review section of ECCO News. In this section, Y-ECCO Members highlight and summarise recent landmark articles within the field of IBD. The articles can cover different topics, including clinical phase 3 trials, epidemiology, endoscopy, surgery, basic science, etc.

Y-ECCO Members who wish to participate in this initiative should contact Isabelle (isabelle.cleynen@med.kuleuven.be). The only thing you need to do is choose a recent relevant article and summarise the key findings and importance of the paper in one page. Your review will be published together with a personal picture and a short self-description.

ISABELLE CLEYNEN

Y-ECCO Literature review Admin



Isabelle Cleynen © ECCO

Systematic review of effects of withdrawal of immunomodulators or biologic agents from patients with inflammatory bowel disease

Torres J, Boyapati RK, Kennedy N, Louis E, Colombel JF, Satsangi J. *Gastroenterology*. 2015 Sep 14. pii:S0016-5085(15)01311-6. doi: 10.1053/j.gastro.2015.08.055.

Introduction

Treatment strategies in Inflammatory Bowel Disease (IBD) have changed considerably with the understanding that subclinical inflammation can lead to poor long-term outcomes [1]. Early use of immunomodulator and biologic therapy is becoming increasingly important in reducing the risk of the irreversible long-term complications of IBD [2]. However, the not insignificant cost and side effect profile of these medications means that strategies aiming at therapy withdrawal without leading to disease remission are important.

In this paper, Torres et al perform a comprehensive literature review of dose de-escalation strategies using a literature search of studies assessing withdrawal of therapy in patients with IBD. De-escalation was defined as cessation or reduction of the dose of immunomodulator/anti-TNF therapy. Studies were grouped into three categories: (1) those in patients de-escalating immunomodulator monotherapy, (2) those in patients on immunomodulator de-escalation from combination therapy and (3) those in patients de-escalating anti-TNF agents irrespective of immunomodulator use.

Key findings

In total, 69 studies were included in the final systematic review. Of these, 18 reported on de-escalation of immunomodulatory monotherapy, eight on immunomodulator withdrawal from combination therapy and 40 on de-escalation of anti-TNF agents. Overall, there were seven randomised controlled trials (RCT), 16 prospective cohort studies and 43 retrospective cohort studies.

1. De-escalation of immunomodulator monotherapy

In total, 11 studies reported on de-escalation in Crohn's Disease (CD) and eight in Ulcerative Colitis (UC). In CD, relapse rates at 12 months varied from 16% to 53%. Overall, relapse rates at 48 months were 31% in patients stopping immunomodulator monotherapy and 15% in those remaining on such therapy. In total, five studies had prolonged follow-up, with relapse rates at 5 years reaching up to 85% in patients stopping immunomodulator monotherapy compared to 61% in those remaining on treatment. Relapse rates in UC were quite similar to those reported in CD and increased over time (75%–87% at 5 years).

2. De-escalation of immunomodulator from combination therapy

The authors identified eight studies (six in CD and one in UC) reporting on de-escalation of immunomodulator from combination therapy. Of note, there was no statistically significant difference in relapse rates between patients remaining on anti-TNF alone and patients remaining on combination therapy. For example, in one RCT the relapse rate at 7 months was 35.9% in those stopping immunomodulator compared to 33.3% in those continuing combination therapy ($p>0.05$). Predictive factors for relapse included younger age at diagnosis and disease activity. Interestingly, the single study reporting immunomodulator withdrawal from combination therapy in UC demonstrated a statistically significant higher relapse rate in the discontinuation cohort (12% vs. 3%), although risk factors for relapse were not reported.

3. De-escalation of anti-TNF therapy

Overall, 40 studies assessed de-escalation of anti-TNF therapy. The majority of these studies reported on findings in CD. In most of the studies, anti-TNF was discontinued whilst patients were in clinical remission. It is interesting to note that across all adult studies, despite heterogeneous study designs/patient populations, relapse rates at 1 and 2 years were reasonably consistent. In most studies, where rates were available at 12 and 24 months, relapse rates ranged from 21.1% to 39% and from 37% to 55.7%, respectively. Interestingly, most studies also reported high cumulative relapse rates of between 49% and 88% by the end of follow-up. Median time to relapse was between 4.8 and 16.4 months across most studies. Predictive factors for relapse included the presence of poor prognostic indicators such as young age and the presence of non-symptomatic disease activity such as high CRP. In UC, reported relapse rates varied between 14% and 41.8% at 12 months and between 25% and 47.1% at 24 months. Interestingly, where mucosal healing was employed as part of the definition of remission, lower relapse rates were observed at 12 and 24 months (17%–25% and 25%–35%).

Conclusion

Overall, relapse rates are high in all patient groups and increase over time following de-escalation. However,

there appears to be no difference in relapse rates if immunomodulator is withdrawn from combination therapy in patients with CD. Importantly, 40%–50% of patients in whom anti-TNF therapy is withdrawn will relapse within 2 years. Most predictors of relapse reflect poor prognostic features, previous disease course or markers of sub-clinical disease activity. This would suggest that complete withdrawal of therapy currently is only possible in very select patient groups. However, long-term immunosuppressive therapy may not be sustainable and further studies are required to assess optimal drug withdrawal strategies in patients reaching deep and sustained remission.

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Barry Hall © Barry Hall

Loss of infliximab into feces is associated with lack of response to therapy in patients with severe Ulcerative Colitis

Brandse JF, van den Brink GR, Wildenberg ME, van der Kleij D, Rispens T, Jansen JM, Mathôt RA, Ponsioen CY, Löwenberg M, D'Haens GR. *Gastroenterology*. 2015 Aug;149(2):350–5.e2. doi:10.1053/j.gastro.2015.04.016. Epub 2015 Apr 25. PubMed PMID: 25917786.

Introduction

In recent years monoclonal antibodies against tumour necrosis factor (TNF) have become a mainstay in the treatment of patients with Inflammatory Bowel Disease (IBD). Infliximab (IFX) is one of the most prominent members of this drug class, with a proven track record in the management of severe cases of both Crohn's Disease and Ulcerative Colitis (UC). Nevertheless, a considerable proportion of patients fail to respond to anti-TNF administration either altogether (primary non-response) or by eventually losing their initial response (secondary loss of response) [1]. Secondary loss of response has been more extensively researched and has been reported to be related to the production of neutralising anti-drug antibodies as well as insufficient serum drug concentrations [2,3]. On the

other hand, the causes of primary non-response have not been elucidated. It has been suggested that the probability of response may correlate with the presence of the membrane-bound form of TNF in intestinal mucosa [4]. Another possible explanation is that an enhanced drug clearance process may lead to inadequate serum drug levels, thus rendering its anti-TNF effect mute. Monoclonal antibodies are typically cleared via proteolysis in the reticuloendothelial system [5]. However, it is known that severe UC results in massive losses of proteins and electrolytes through the inflamed epithelium [6]. Moreover, patients with severe colitis will often respond only to higher than standard doses of biological therapy [3]. By combining these observations, Brandse et al. hypothesised that IFX elimination through the faecal route as a result of

extensive mucosal ulceration may contribute to a poor therapeutic response to anti-TNF treatment in severe UC.

Methods

Thirty anti-TNF naïve patients with moderate to severely active UC (Mayo score 2/3), who were started on a dose of 5 mg/kg IFX, were included in this prospective study. At least four consecutive faecal samples were collected at specific time points during the first 2 weeks of treatment. Clinical disease activity was measured with the Simple Clinical Colitis Activity Index (SCCAI), while endoscopic assessment was performed with the aid of the Mayo score. Clinical response was assessed at weeks 0, 8 and 12 after initiation of IFX treatment. Clinical response was defined as a total score on the Simple Clinical Colitis

Activity Index of ≤ 4 points or a drop in the Simple Clinical Colitis Activity Index of $\geq 50\%$ from the baseline value. Endoscopic response was defined as improvement of the endoscopic Mayo score of at least 1 point from baseline to week 8. Patients who required additional or higher IFX doses or who underwent colectomy within the first 12 weeks were classified as non-responders. IFX levels were measured via ELISA in the fecal samples as well as in serum samples taken at week 2. Antibodies to IFX were also quantified via RIA at week 2. Furthermore, a comprehensive panel of relevant laboratory tests (including fecal calprotectin) was assessed at baseline and week 2.

Key findings

IFX was not detected in any of the faecal samples before treatment initiation. Conversely, IFX was detectable in the faeces of 25 of 30 patients (83%) and in 129 of 195 faecal samples in total (66%). The highest IFX levels in faeces were observed in the first days after the first infusion (22/30 patients). Eighteen of 30 (60%) patients had a clinical response by week 2, and 14 (47%) maintained that response by week 12. Two patients required treatment with higher IFX dosing. Endoscopy was performed in 21 patients, with 12 of them (57%) exhibiting endoscopic response. Patients who were clinical non-responders at week 2 (12 of 30) had significantly higher faecal IFX concentrations after the first day of treatment than patients with clinical response (median concentration, 5.01 mg/mL in non-responders vs 0.54 mg/mL in responders; $p=0.0047$). In endoscopic non-responders, there was a trend towards higher faecal IFX concentrations when compared to patients with endoscopic improvement (median, 4.66 mg/mL vs 1.16 mg/mL, respectively; $p=0.0588$). Patients without response by month 3 (16 of 30) also had higher faecal IFX concentrations at day 1 compared with responders, but this difference did not achieve statistical significance. More importantly, when multiple parameters were analysed, the only one that predicted endoscopic response to IFX administration was faecal IFX concentration at day 1. No difference was observed in the median serum IFX levels at week 2 between responders and non-responders.

No direct correlation between faecal and serum IFX levels was found. However, it was observed that patients with detectable faecal IFX levels had a significantly more severe colitis (as indicated by higher SCCAI scores and calprotectin levels at baseline) compared to patients with undetectable

IFX levels in faeces. Furthermore, in patients with low baseline serum albumin levels (lower than the median of the cohort), indicating more severe disease, higher faecal IFX levels at day 1 and lower serum IFX levels at week 2 were found.

Conclusion

This study is the first to describe that IFX can be lost in the faeces of patients with UC. It also reports that high faecal IFX levels in the first days after treatment initiation seem to be associated with primary non-response. The fact that peak faecal IFX concentrations were observed in the first 2 days after the initial IFX infusion, and that these concentrations were higher in patients with lower albumin, may suggest that these drug losses happen when the serum levels are highest and the mucosa exhibits more severe inflammation. Thus, a more damaged and "leaky" mucosa may lead to significant IFX intestinal loss. Faecal drug loss may play a role in the pathogenesis of primary non-response to anti-TNF therapy although other factors are involved, as the lack of correlation between faecal and serum IFX concentrations may imply. Recently, it was suggested that mucosal drug concentrations may be more important than serum ones, at least in severe UC. As a result, the excretion of IFX through faeces may represent an alternative elimination route affecting the mucosal rather than the blood drug compartment and influencing primarily the response in this subgroup of patients. On the other hand, the loss of IFX in faeces may be a reflection of increased disease activity rather than a cause of primary non-response. Therefore, it could be considered as a possible biomarker for disease activity, capable of identifying those patients at higher risk for non-response and at high risk for surgery. This would enable a prompt intensification of drug administration, with higher doses or shorter intervals, that could potentially prevent colectomy. In all, the authors report a novel route of IFX loss through the stools in patients with moderate to severe UC. High faecal IFX levels in the first days after the initial infusion are associated with an attenuated therapeutic response. Patients with more severe disease may benefit from intensive treatment regimens, in order to make up for this intestinal loss as well. These promising findings need to be expanded by additional studies so as to determine the pathogenesis of this phenomenon and its full effects.

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Spyros Siakavellas
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Identification of patients with variants in TPMT and dose reduction reduces hematologic events during thiopurine treatment of Inflammatory Bowel Disease

Coenen MJ, de Jong DJ, van Marrewijk CJ, Derijks LJ, Vermeulen SH, Wong DR, Klungel OH, Verbeek AL, Hooymans PM, Peters WH, Te Morsche RH, Newman WG, Scheffer H, Guchelaar HJ, Franke B; TOPIC Recruitment Team. *Gastroenterology.* 2015 Oct;149(4):907–917.e7. doi: 10.1053/j.gastro.2015.06.002

Introduction

Thiopurines are double-edged drugs: they are effective in inducing and maintaining remission in Inflammatory Bowel Disease (IBD), but they also carry significant risks. About one in four IBD patients discontinues thiopurines because of adverse reactions [1], most of which are haematological.

Both azathioprine (AZA) and 6-mercaptopurine (6-MP) are prodrugs, which require metabolism before they become active. This activation pathway is safeguarded by TPMT (thiopurine S-methyltransferase), an enzyme that converts thiopurine into inactive metabolites, thus controlling the amount of drug being converted to active

6-thioguanine (6-TG). Because the activity of this enzyme is regulated by genetic polymorphisms, some people can be deficient in TPMT, which leads to higher levels of 6-TG and risk of myelosuppression. Regarding these genetic variants, about one in 300 individuals carries a homozygous gene mutation that renders the enzyme inactive, and 11% are heterozygous for a variant associated with intermediate activity [2]. If these patients are treated with standard doses of thiopurines, low TPMT activity leads to excessive TGN production and risk of severe myelotoxicity.

Although current guidelines recommend haematological monitoring for patients treated with thiopurines, an approach using TPMT testing before

initiation of treatment would be more rational, in order to avoid severe adverse effects.

The TOPIC trial (Thiopurine response Optimisation by Pharmacogenetic testing in Inflammatory bowel disease Clinics) by Coenen et al. attempted to investigate whether pharmacogenetically guided dosing of thiopurines is useful in reducing the incidence of haematological adverse drug reactions (ADRs).

Study design

This was a prospective, unblinded study performed in 30 Dutch hospitals, which randomised IBD patients to either standard treatment (control group) or dose-adjusted therapy according to pretreatment

screening for three common variants of TPMT: TPMT*2, TPMT*3A and TPMT*3C (intervention group). The first group received standard daily doses of 2–2.5 mg/kg AZA or 1–1.5 mg/kg 6-MP. The second group received either 50% (heterozygotes) or 0%–10% of standard dose (homozygotes).

The primary outcome was the occurrence of haematological ADRs (white cell count $<3 \times 10^9/L$ or platelet count $<100 \times 10^9/L$). The follow-up period was 20 weeks from thiopurine initiation. Treatment efficacy was also measured at week 20 of treatment using disease activity scores. Hepatotoxicity, pancreatitis, anaemia and clinician-reported outcomes were also assessed.

Key findings

Altogether, 796 eligible patients were randomised, but only 783 were included in the final analysis (378 in the control group and 405 in the intervention group). There was no significant difference in the rate of ADRs between the groups (7.9% vs. 7.4%, relative risk 0.93), with 30 ADRs being observed in each group. This translates into a number needed to "genotype" of 200, which means that 200 patients should be genotyped in order to avoid one haematological ADRs. Also, no significant difference was observed between the groups regarding the median time to a haematological ADR (56 days, interquartile range 58 days vs. 42 days, interquartile range 69 days). On subgroup analysis of patients carrying a TPMT variant, there was, however, a significant reduction in haematological ADRs for the TPMT-guided therapy

group (22.9% vs. 2.6%, relative risk 0.11, $p=0.11$, number needed to treat = 5). In the study population, there was a significant discontinuation rate due to ADRs (37.8% in the control group, 42% in the intervention group), which was higher than in other studies [1]; however, the frequencies of haematological ADRs were similar to those reported in previous trials. Other ADRs commonly seen in thiopurine-treated patients, such as hepatotoxicity and pancreatitis, were reported with similar frequencies in the study groups, these results being consistent with previous work showing that these ADRs are not associated with TPMT activity [3]. Treatment efficacy as assessed by disease activity scores was similar in the two arms, proving that the dose reduction in variant carriers did not affect treatment outcomes.

Conclusions

Although the TOPIC trial did not show an overall reduction in haematological ADRs as a result of use of pretreatment TPMT screening, in patients carrying a genetic variant the TPMT-guided therapy was associated with significantly fewer haematological ADRs.

A personalised dose regimen based on pretreatment TPMT screening would greatly benefit IBD patients and should be considered for routine clinical practice.

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Vasile Balaban
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ECCO Country Member Profiles



Identity card

- Country: Ireland
- Name of group: Irish Society of Gastroenterology
- Number of active members: >200
- Number of meetings per year: 2 scientific meeting per year
- Name of president and secretary: Professor Padraic MacMathuna
- National Representatives: Dr Glen Doherty, Dr Jane McCarthy
- Joined ECCO in: 2007
- Incidence of IBD in the country: Estimated 20-25,000 patients



Identity card

- Country: Slovenia
- Name of group: No separate group for IBD. The disease is covered under the national organisation named Slovenian Association for Gastroenterology and Hepatology
- Number of active members: 70
- Number of meetings per year: 2
- Name of president and secretary: Bojan Tepeš (president), Samo Plut (secretary)
- National Representatives: Ivan Ferkolj, David Drobne
- Joined ECCO in: 2008
- Incidence of IBD in the country: UC 6,8/100 000, CD 5,7/100 000, total incidence including UBDU 13,7/100 000 (Baraga, Gastroenterolog 2014)



Identity card

- Country: Malta
- Name of group: Gastroenterologists within the Association of Physicians, Malta
- Number of active members: Number of gastroenterologists – 9
- National Representatives: Dr. Pierre Ellul
- Joined ECCO in: 2015
- Incidence of IBD in the country: 18 per 100,000

Questionnaire – Ireland



Irish Working Group © Glen Doherty

What has changed since your society became an ECCO Country Member?

The Irish Society of Gastroenterology (ISG) has maintained a very active IBD interest group with a dedicated IBD session at each of the two annual national scientific meetings. A highly successful ECCO Congress was held in Dublin in 2011, with over 3,500 registered participants. Since then, ECCO individual membership in Ireland has remained very healthy. In 2012, the ISG celebrated its 50th anniversary and the ECCO President, Simon Travis, and Past

President, Jean-Frederic Colombel, attended the meeting as guests and keynote IBD speakers.

Does your centre or country have a common IBD database or bio bank?

Over the last 5 years, the ISG has worked on development of a national IBD database. This common platform is now in use across several hospitals in the country and the roll out of the system to other hospitals continues.

What are your most prestigious/interesting past and ongoing projects?

Since 2011, the ISG has had a specific subgroup working to promote quality of care in IBD. In 2015 this group, in co-operation with the ISCC (Irish Society for Crohn's and Colitis, the national patient organisation) launched a joint report highlighting the burden of Inflammatory Bowel Disease in Ireland and focussing on the need for enhanced services for patients. This report was launched and presented to members of the Irish Parliament (see picture) and is the focus of an ongoing national advocacy campaign to improve awareness of IBD.

Which ECCO Projects/Activities is the group currently involved in?

The ISG supports research collaboration in IBD and is currently developing a national collaborative research network for IBD named INITiative (Investigator Network for IBD Therapy in Ireland – www.initiativeibd.ie). This network will work to attract more clinical trials and the first project will be participation in the ECCO sponsored I-CARE study. The current target is to achieve participation by over 25 investigators, with over 500 Irish patients enrolled.

**GLEN DOHERTY AND
JANE MCCARTHY**

ECCO National Representatives, Ireland

Questionnaire – Malta



What has changed since your society became an ECCO Country Member?

We have only recently joined.

What are the benefits to you of being an ECCO Country Member?

Membership will enable us to achieve better networking with other European countries.

Is your society making use of the ECCO Guidelines?

Yes.

Have you developed research projects with other countries through your ECCO Country Membership?

Yes: epidemiological and genetic studies.

What are your main areas of research interest?

Epidemiology and genetics

Does your centre or country have a common IBD database or bio bank?

Not yet, but we are working on creating an IBD registry. We do have a bio bank.

What are your most prestigious/interesting past and ongoing projects?

The most interesting ongoing project is the genetic study, which is being carried out in collaboration with another European country.

Which ECCO Projects/Activities is the group currently involved in?

EpiCom group

What are your aims for the future?

We aim to become more actively involved within ECCO.

How do you see ECCO helping you to fulfil these aims?

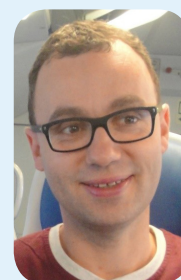
ECCO provides the ideal platform for promotion of collaboration among different professionals who share a common goal.

What do you use ECCO for? Network? Congress? How do you use the things/services that ECCO has to offer?

Networking, congresses

PIERRE ELLUL

ECCO National Representative, Malta



Pierre Ellul © Pierre Ellul

Questionnaire – Slovenia



Slovenian Working Group Ljubljana © David Drobne

What has changed since your society became an ECCO Country Member?

Since Slovenia joined ECCO we have realised that we are not alone in the battle against this disease, which has such a great impact on the lives of thousands of individuals and their families in Slovenia. ECCO's efforts in Western Europe to increase awareness of the burden of the disease have enabled us to make it possible for patients to obtain access to appropriate drugs at the most appropriate time, namely early in the course of the disease, when these drugs are most effective.

What are the benefits to you of being an ECCO Country Member?

To be part of the ECCO Family, to share experiences, positive and negative, and to learn from each other at meetings such as ECCO

Congresses and ECCO Workshops. It is amazing how one can discuss a difficult issue with a colleague by e-mail within a few minutes – this really helps in making correct treatment decisions.

Is your society making use of the ECCO Guidelines?

Definitely: ECCO Guidelines are central to our work.

Have you developed research projects with other countries through your ECCO Country Membership?

We have many regional educational meetings with neighbouring countries (Croatia, Serbia). This has proved very helpful as we share certain region-specific challenges.

What are your main areas of research interest?

Genetics, prediction of response to TNF inhibitors, therapeutic drug monitoring of thiopurines and TNF inhibitors, mesenchymal stem cells, epidemiology, CMV, fibrosis.

Does your centre or country have a common IBD database or bio bank?

We have collections of samples from different projects, but unfortunately not yet a common biobank.

What are your most prestigious/interesting past and ongoing projects?

Genetic polymorphism in the ATG16L1 gene in response to adalimumab, prediction of response to infliximab based on CD19+ cells in mucosa, paediatric epidemiological study.

Which ECCO Projects/Activities is the group currently involved in?

Study of follow-up of children exposed to TNF inhibitors in utero.

What are your aims for the future?

To develop a national registry of IBD patients and a national biobank of IBD patients. To ensure that IBD nurses are present in all IBD centres in Slovenia.

How do you see ECCO helping you to fulfil these aims?

By providing a common research platform.

What do you use ECCO for? Network? Congress? How do you use the things/services that ECCO has to offer?

We use ECCO for guidelines, congresses, IBD courses and provision of support for the patient organisation.

**IVAN Ferkolj and
David Drobne**

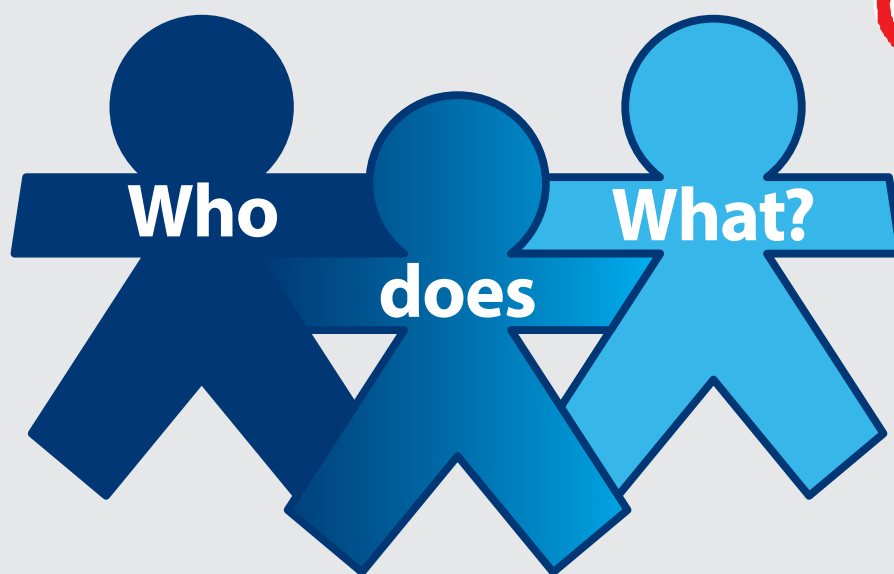
ECCO National Representatives, Slovenia



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Crohn's and Colitis
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