

Apheresis with Adacolumn® for treatment of Ulcerative colitis: is it cost-effective?

By guest editor – Dr. Daniel Ginard, Hospital Son Dureta, Palma de Mallorca, Spain.

The aim of this study was to assess the cost of moderate to severe Ulcerative Colitis (UC) management in two scenarios: traditional treatment vs alternative treatment, including granulocyte, monocyte adsorption apheresis (Adacolumn®) in steroid dependent patients. A year worth of immediate disease costs were calculated and cost effectiveness analysis was carried out.

To assess the disease cost we used a decision tree model from a prevalence approach, which includes the health status probabilities through the therapeutic management of the disease. The probabilities of the events modelled in the decision tree were derived from the literature and an expert consensus panel. We obtained percentages of the different health status over one year. We calculated the cost of immediate medical health resources (treatments and medical services costs) applied for each status.

Annual cost per patient was calculated as the average of the cost per patient for each health status. For the traditional treatment it was estimated at €6740.

In the alternative treatment scenario we included Adacolumn® in the treatment of steroid dependent patients. The inclusion of the new treatment in the therapeutic algorithm was not universal and we assumed that the Adacolumn® would be applied to 40% of steroid dependent patients (market share). The average annual cost per patient was €6959 for 3,8% of the patients, for whom Adacolumn® was included in the cost. Adding Adacolumn® in the therapeutic management of moderate to severe UC in steroid dependent patients increases the average annual cost per patient in €219. This increase is explained by the fact that Adacolumn® is used in a small subset of patients. ▶

Dear newsletter reader. I hope you had a relaxing summer holiday (despite the lack of sunshine in the Nordic region) and that you are prepared for the hectic autumn. This summer the Adacolumn apheresis treatment have had a lot of media attention, which has in turn drawn a lot of attention from the public.

In this edition we have two contributions from our Spanish doctors – one regarding their pharmacoeconomic study and the other one show the 5 treatments vs. 10 treatments study results. For the pharmacoeconomic aspects, the medical environment is unique in each European country, however, it might be an interesting comparison for the readers of this newsletter. These publications are available to order by using the order form on the last page of this newsletter, as well as by e-mailing us at: reprints@otsuka.se.





Life

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- ▶ The second aim was to perform a cost effectiveness analysis in the subset of steroid dependent UC patients by comparing Azathioprine and Adacolumn®. The analysis was done with a hypothetical cohort of 1000 patients treated in each arm. The proportion of patients achieving clinical remission with Adacolumn® would be 22,5% higher than in patients receiving traditional treatment, and surgery would be avoided in 4%. In steroid dependent patients the average annual cost per patient was €6059 for patients treated with Azathioprine and €11436 in the Adacolumn® group, and the cost per remission was €15738 and €18748, respectively.

In summary, adding Adacolumn® to the overall management of patients with moderate to severe UC flare ups entails a reasonable additional cost that could be afforded by Spanish Health System, and which is cost effective. ■

Digestive and Liver Disease 39 (2007) 617–625.

Clinical trials with Adacolumn®

Adacolumn is used for the treatment of different chronic inflammatory diseases. The main indication is ulcerative colitis (UC), where Adacolumn is used since about 10 years. Despite this large experience the question of the optimum dosing is still under discussion. The retrospective analysis of the first 100 patients treated in Scandinavia has revealed an average use of about 6 columns per patient. The standard recommendation is 5 treatments for moderate-to-severe UC. In order to learn about the best

treatment options for a patient we are currently performing a study – the CESA 5.10 study – with Adacolumn. The study is an open randomized controlled multicentre trial in patients with moderate to severe UC. Patients are treated with either 5 Adacolumn aphereses (one/week) or in a second group with 10 (2 weeks with 2 weekly treatments plus 6 weeks with 1 weekly treatment). The individual study duration per patients is 12 weeks. The study has been started few months ago.

More than 40 hospitals in France, UK, Germany, Italy, Spain and the Nordic countries participate in this trial. So far, more than 100 patients are enrolled.

Patient-recruitment will be continued until 31 October 2007. If you would like to know more about the study, please contact your sales rep or our Frankfurt Research Institute. ■

Dr. Marita Franz, Head of Medical Device Unit, Otsuka Frankfurt Research Institute

Recipients of Adacolumn® travel grant for UEGW

We would like to thank everyone who applied for our travel grant for the October UEGW meeting in Paris. Our scholarship committee, Prof. Löfberg and Dr. Ruuska have reviewed all the application and are delighted to present the recipients of the grant below. We are looking forward to our recipient's reports from UEGW, which will be published in our newsletter as well as on our homepage.



1. Karin Göransson R.N.

Department of Gastroenterology and Hepatology, Swedish Polypsis Registry, Karolinska University Hospital, Solna, Sweden

2. Kaisa Fritzell, R.N.

Department of Gastroenterology and Hepatology, Swedish Polypsis Registry, Karolinska University Hospital, Solna, Sweden

3. Aldis Pukitis, M.D.

Gastroenterology Center, Paul Stradin Clinical University Hospital, Riga, Latvia

4. Ladislav Hanik, M.D.

Dept. of Gastroenterology, Ängelholm Hospital, Sweden

5. Reetta Kiikeri, R.N.

Department of Medicine, Turku University Hospital, Finland

European events 2007 with Otsuka as exhibitor

DGVS-congress in Bochum

Sep. 12–15, Germany

Finnish Gastro autumn meeting

Sep. 13–14, Tampere, Finland

Danish Paediatric Gastro Meeting

Oct. 7–8, Hvidsgavl, Denmark

Swedish Paediatric Gastro Meeting

Oct. 11–12, Örebro, Sweden

UEGW

Oct. 27–31, Paris, France

Finnish Paediatric Gastro Meeting

Nov. 8–9, Kuopio, Finland

3rd Latvian Gastroenterology Congress

Nov. 10, Riga, Latvia

Nordic Paediatric Gastro Meeting (NAPGHAN)

Nov 23–24, Riga, Latvia

Kakkuro – correct solution

Thank you for sending us your Kakkuro solution for this summers newsletter challenge! Please find the correct solution below.

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		15	17	8	9	14	7	1	4	2	16
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8	6	2	33	9	7	5	4	8	8	2	6
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Review of Spanish 5 vs 10 study

By guest editor Dr. Elena Ricart, Gastroenterology Department Hospital Clinic Villarroel, Spain

Ulcerative colitis (UC) is a chronic relapsing inflammatory disorder. Corticosteroids are the mainstay of treatment to induce remission. However, long-term corticosteroid use is not recommended due to both toxicity and lack of efficacy. In addition, steroid dependency and resistance occur frequently in patients with UC. In these patients, immune modulators (azathioprine/6-mercaptopurine) and more recently, the chimerical monoclonal antibody against tumor necrosis factor, infliximab, have shown therapeutic efficacy, but a proportion of patients are intolerant or suffer adverse events related to these medications. Therefore, other therapies are needed to provide non-surgical and safe alternatives for patients who fail to respond to conventional treatment.

A growing body of evidence suggests that granulocyte/monocyte apheresis (GMA) with Adacolumn® can be an effective and safe therapeutic alternative for UC. Several controlled and uncontrolled studies have assessed the safety and efficacy of Adacolumn® in steroid-dependent UC, steroid-refractory UC, or as first-line therapy in naïve UC patients. However, the optimal treatment scheme is not well established. For this reason, our group decided to conduct a small pilot randomized controlled trial in five cent-

ers in Spain. The aim was to determine if there was a therapeutic gain by performing 10, as opposed to 5, apheresis sessions with Adacolumn® for induction of remission in patients with steroid-dependent active UC. Patients recruited in our study represented a UC population, which was particularly difficult to treat, because they had active disease despite steroids treatment for at least the last 2 weeks. 60% were under immune modulator treatment with azathioprine or methotrexate, and 20% had previously been treated with cyclosporine for steroid refractory UC. We established clinical remission at week 17 as the primary end of this study. Twenty patients with clinical and endoscopic evidence of moderately active UC, defined as a clinical activity index (CAI) ≥ 6 and ≤ 12 , and an endoscopic activity index (EAI) > 4 , were included in the study. At week 17, 3 out of 8 patients (37.5%) that were treated with 5 GMA with Adacolumn®, and 5 out of 11 patients (45.45%) that were treated with 10 GMA with Adacolumn® were in clinical remission. It should be noted that all patients who entered clinical remission, in both groups, were also in endoscopic remission at week 17. The steroid dose was reduced in both groups, but daily steroid

requirements were significantly lower in patients who received 10 GMA sessions. All but one of the patients who had clinical remission were free of steroids at week 17. Granulocyte/monocyte apheresis with Adacolumn® was very well tolerated and no major side effects were observed during the study. Seven of the 8 patients that were in remission at week 17 entered the yearlong follow-up. Six out of these 7 patients were in clinical remission and remained steroid free without any changes in UC therapy during this period. The overall 42% clinical and endoscopic remission rates obtained in the present study compare favorably with those of recent studies using infliximab. In conclusion, GMA with Adacolumn® seems to be an effective, safe, and well tolerated therapy which allows steroid withdrawal in steroid dependent moderately active UC patients and offers sustained response over time. Ten weekly GMA treatments did not provide an advantage in this patient population as compared to 5 treatments in terms of clinical or endoscopic remission but did show a significant steroid-sparing effect and might be considered in patients with refractory UC. ■

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Travel grant report from ESPGHAN

By Dr. Christian Jacobsen, Ph.D student, Paediatric Department, Hvidovre University Hospital, Denmark.

Report from the 40th annual ESPGHAN meeting in Barcelona 2007 – with special attention to Chronic Inflammatory Bowel Disease. The 40th annual ESPGHAN meeting in Barcelona of-

fered many new and interesting studies on paediatric gastroenterology especially inflammatory bowel disease (IBD). The studies covered topics such as the epidemiology, genetics, immunology and

treatment of paediatric IBD.

Epidemiology

To date there has been no consensus regarding phenotypical classification ►

► of paediatric IBD. A Scottish group suggested adoption of the Montreal classification from the adult gastroenterologists. Thereby making it easier to compare studies, but foremost as a reliable tool in studies on, for instance, disease course and treatment. A population-based study from Copenhagen, Denmark suggested that the previous reports on increasing incidence of paediatric IBD is starting to level out. A comparison between the study from Denmark and a population-based study from Lille, France showed some geographical difference in the number of ulcerative colitis patients with proctitis (4% vs. 14%) and extensive disease (77% vs. 60%). Data from a Scottish group was similar to the Danish, suggesting a European north-south difference in the phenotypical presentation. This could reflect differences in genetic and/or environmental factors. The German speaking society for paediatric gastroenterology (GPGE) presented data from the newly made German-Austrian paediatric IBD-registry (CEDATA). The registry contains 2289 IBD patients with a preponderance of Crohn's disease (CD) patients. Data was presented on diagnostic lag, heritability (first degree relatives) and treatment. Nearly half of the IBD patients were initially treated with steroids and 30% with azathioprine, but surprisingly only 4% of the CD patients in the registry were treated with enteral nutrition.

Genetics

Many genetic SNP studies were presented including studies on the recently discovered Interleukin-23 receptor (IL23R). A Scottish study found that the Arg381Gln variant in the IL23R gene was a susceptibility gene for IBD and CD, and that the GG genotype was associated with increased risk (OR 2.01) of IBD /CD. They found no genotype-phenotype associations in their cohort of 358 IBD patients. Genetic variants in the

nuclear pregnane X receptor (important component of the body's xenobiotics defence) have been implicated in adult IBD, a study on paediatric IBD patients could not demonstrate this association.

Recent studies have shown that the amount of defensins (the "antibiotic of the intestine") is reduced in CD patients. A study presented by an Italian group, investigated genetic variations in the beta-defensin gene and found several SNP's (single nucleotide polymorphism) that were more frequent in children with IBD than healthy controls. The functional consequence of these SNP's is unknown at present. An interesting study from France added to the evidence of the importance of a new subpopulation of T lymphocytes (TH-17 cells that are characterized by the production of IL-17) in the pathogenesis of IBD. They found that the intestinal mucosa (colonic and ileal) in CD and UC patients produced large amounts of IL-17 upon stimulation with bacterial motifs and/or CD3/CD28. Other

studies have shown that TH-17 cells and their production of IL-17 are important for the development of chronic inflammation upon stimulation with IL-23.

Treatment

An interesting study on apheresis treatment of IBD was presented on the third day. The study was done in collaboration between Finland, Sweden and Denmark and 38 children was included (23 UC, 11 CD and 4 IC). 82% of the steroid dependent or steroid refractory IBD patients experienced effect from the apheresis treatment. In the follow-up period 4/22 (18%) UC and 2/13 (15%) CD patients relapsed within 3 months, respectively.

The 40th Annual ESPGHAN meeting was very interesting and we are looking forward to the next meeting.

All abstracts from the 40th annual ESPGHAN meeting in Barcelona can be found at the following internet site: <http://www.jpagn.org>. ■



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- Evaluation of 5 vs 10 granulocyteapheresis sessions in steroid-dependent ulcerative colitis:** A pilot, prospective, multicenter, randomized study. Elena Ricart, Maria Esteve, Montserrat Andreu, Francesc Casellas, David Monfort, Miquel Sans, Natalia Oudovenko, Raúl Lafuente, Julián Panés, World J Gastroenterology 2007;13(15):2193–2197

- Treatment cost of ulcerative colitis Is apheresis with Adacolumn® cost-effective?** J. Panés, M. Guilera, D. Ginard, J. Hinojosa, P. González-Carro, V. González-Lara, V. Varea, E. Domènech, X. Badia, Digestive and Liver Disease 39 (2007) 617– 625.

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please visit www.otsukapharma.info -> **Medical professionals** -> **Literature database**.



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