Patient brochures available

Adacolumn® patient brochures in the following languages are available: English, Spanish, Italian, German, Swedish, Danish, Norwegian, Finnish. You can download pdf-files at www.otsukapharma.info -> Medical professionals -> Adacolumn® (Service center). From this site, you can also order printed patient brochures online.

Recipients of Adacolumn Travel Grants to UEGW 2008 in Vienna

1. **PhD-student Lars-Peter Jelsness-Jorgensen,** Gastroenterology Laboratory, Hospital Østfold Fredrikstad, Norway
2. **R.N. Lene Neergaard,** Herlev Hospital, Copenhagen, Denmark
3. **Dr. Friedemann Erchinger,** Haukeland University Hospital, Bergen, Norway
4. **Dr. Helen Rosenqvist,** Helsingborgs Hospital, Sweden
5. **R.N. Cecilia Lindberg,** Södersjukhuset, Sweden

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New Publications

- [ ] **The fundamental basis of inflammatory bowel disease. Strober W, Fuss I, Mannon P. The journal of Clinical Investigation 2007 Vol. 117 (3): 514–521:** Review on the fundamental nature of IBD pathogenesis with respect to immunology and gut microflora, including sections on mucosal immune defects, gut microbials and microflora, from both the clinical and basic experimental aspect. Brief mention of leukocytapheresis as a strategy to remove effector cells.
- [ ] **Intensive Granulocyte and Monocyte Adsorption Versus Intravenous Prednisolone in Patients with Severe Ulcerative Colitis: An Unblinded Randomised Multicentre Controlled Study. Hanai H, et al. Dig Liver Dis 2008 Jun;40(6):433–440 (in press):** Seventy patients with clinical activity index (CAI) 10–23 were randomly assigned to intensive GMA, at 2 sessions/week in the first 3 weeks and then 1 session/week for up to 11 sessions (n=35) or iv PSL, 40–60 mg/day for 5–10 days (n=35). At weeks 2, 6 and 12, the remission (CAI<4) rates (%) in the GMA group were 17.1, 54.4, 74.3, respectively. The corresponding values in the PSL group were 25.7, 51.4 and 48.6.
- [ ] **In Patients With Ulcerative Colitis, Adsorptive Depletion of Granulocytes and Monocytes Impacts Mucosal Level of Neutrophils and Clinically Is Most Effective in Steroid Naïve Patients. Tanaka T et al. Dig. Liver Dis. 2008 (in press):** Forty-five UC patients (26 steroid naïve and 19 steroid dependent) on GMA, steroid naive patients have better response (yet statistically not significant). Patients with deep colonic ulcers together with extensive loss of the mucosal tissue are not like to respond to GMA.
- [ ] **Current pharmacologic treatment paradigms for inflammatory bowel disease and the potential role of granulocyte/monocyte apheresis. Schwartz D and Ferguson JR. Current Medical Research and Opinion 2007. Vol. 23, No. 11, 2007, 2715–2728:** Overview
- [ ] **Regulatory T cells in patients with inflammatory bowel diseases treated with adacolumn granulocytapheresis. Cuadrado E, Alonso M, de Juan MD, Echaniz P, Arenas JI. World J Gastroenterol 2008 March 14 (10): 1521–1527:** 6 patients, 4 UC, 2 CD, Treg cell counts in peripheral blood before and after 5 sessions (1/week) increased in 5 responders (3 UC and 2 CD); cutaneous lesions healed after 13 sessions, relapsed, and remitted again after renewed ADA treatment.

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Adacolumn®

Adacolumn® News

No 1, May 2008

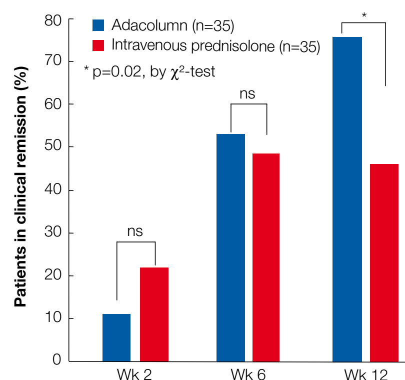
Steroid sparing with Adacolumn®

In press 2008: Adacolumn® provides a more sustainable effect than steroids.

Selective adsorption of granulocytes and monocytes has an excellent potential to spare corticosteroids in patients with active ulcerative colitis. In an article by Dr Hanai et al, the clinical efficacy was shown to be comparable or better with Adacolumn than with steroids.

Patients: The majority of patients suffered from severe ulcerative colitis with a clinical activity index (CAI) between 10 and 23. All patients were on salicylates, a majority on low dose prednisolone.

Remission from severe ulcerative colitis during 12 weeks



At week 2 clinical remission (CAI≤ 4) is more common with intravenous prednisolone. However, at week 6 the situation is reversed, and more patients have entered remission with Adacolumn. At week 12, the difference is statistically significant.

Treatment: Apheresis using Adacolumn were performed 2 sessions/ week in the first 3 weeks and then 1 session/week for up to 11 sessions. Intravenous prednisolone were given at a dose of 40–60 mg/day for 5–10 days, and then tapered with oral prednisolone in line with improvement.

Results clinical remission (CAI ≤ 4): Clinical efficacy is seen faster with intravenous prednisolone than with Adacolumn (not significant difference, $\chi 2$). At week 6 the situation is reversed, and more patients are in remission with Adacolumn. At week 12 significantly more patients treated with Adacolumn have enetered remission, compared to patients treated with prednisolone (74 % and 49 % respectively, p=0,02, $\chi 2$).

Results steroid sparing: At week 12, 77 % (27/35) patients using Adacolumn were steroid free, compared to 14 % (5/35) in the prednisolone group. ■

Hanai H, et al. Intensive Granulocyte and Monocyte Adsorption Versus Intravenous Prednisolone in Patients with Severe Ulcerative Colitis: An Unblinded Randomised Multicentre Controlled Study. Dig. Liver Dis. 2008 Jun;40(6):433–440 (in press).

Dear newsletter readers.
We are pleased to bring you the first Adacolumn newsletter of 2008. Days are getting longer and longer, beautiful flowers everywhere – summer is approaching. In this issue, we would like to start with reviewing Dr. Hanai's recently accepted publication on Adacolumn from the "steroid sparing" point of view. As a guest editor, Dr. T. Tanaka have contributed with an article based on the difference in clinical response in GMA between steroid naïve and steroid dependants (25/19). You will also find two travel grant reports from UEGW Paris. The travel grant recipients for the UEGW 2008 are announced here. For those of you who didn't apply this time, there will be another opportunity later on this year for a travel grant for ECCO 2009.

If you wish to be updated on the latest publications you are welcome to visit our homepage (http://www.adacolumn.net -> Information about Adacolumn® -> Medical professionals -> Literature database (Adacolumn) + 2.1 IBD. We are delighted to see that so many are using this function!

Mari Liljefors
Marketing Director
Otsuka Pharma Scandinavia AB

Otsuka

Adacolumn European events 2008

Swedish Gastrodays
May 7–9 Jönköping Sweden

Hematologists Congress
May 22–24 Bergamo Italy

Communication on Adacolumn
May 24 Bergamo Italy

Nordic Gastrodays
Jun. 4–6 Helsinki Finland

Meeting of the Spanish Society in Digestive Pathology
Jun. 5–8 Sitges Spain

Finnish Gastrodays – Autumn
Sep. 11–12 Oulu Finland

DGVS Congress
Oct. 1–4 Berlin Germany

GETECCU meeting
Oct. 3–4 Madrid Spain

Riksstämma
Nov. 26–28 Göteborg Sweden

BNG-Forum
Nov. 28–29 Hannover Germany

The Young IBD doctors meeting

– short activity report (Otsuka Pharmaceutical S.A.)

Supported exclusively by Otsuka Spain, the Young IBD doctors meeting was held in Mallorca from April 11–13. The meeting was attended by nearly 40 physicians from all over Spain, all of them members of the Young IBD physician group in GETECCU that designed this year's scientific program. JIMRO president Mr. Y. Yoshida and Dr. A. Saniabadi joined the meeting, underlining the support from Adacolumn manufacturer JIMRO's to this meeting, which was very much appreciated. ■

Irene Sáez-Torres – Director Medical Device Otsuka Pharmaceutical S.A.

ATICCA study

– the first patient enrolled

ATICCA (acronym for Adacolumn Therapy In Corticodependant Colitis Activity) is an international multicentre study enrolling 38 centres in Spain, 8 centres in Italy, 9 centres in Portugal and where some other European centres may adhere in the following weeks. So far, over 20 Spanish hospitals are already open for recruitment and 1 patient has been enrolled in the study. The sponsor of the study is GETECCU (Spanish Working Group on Crohn disease and Ulcerative Colitis), that extended the invitation to other European associations, and it is wholly financed by Otsuka Pharmaceutical S.A. ■

New website

Otsuka Italy's (www.otsuka.it) and Otsuka Spain's (www.otsuka.es) websites are up and running.

Clinical trail with Adacolumn® (GMA) in paediatric IBD

The treatment options in paediatric IBD are basically the same as for adult patients. This brings the same well known problems inherent to the relevant drug therapy. Especially the side effects from corticosteroids put a heavy burden on young patients. Several international IBD specialists have introduced Adacolumn GMA apheresis to a paediatric patient collective.

Two recent publications from Europe mirror the current level of experience in this therapeutic field:

- *T Ruuska et al (2007):* Leucocyte apheresis in the treatment of paediatric ulcerative colitis. Scand J Gastroentrol 42:1390–91.
- *Martin de Carpi J et al (2008):* Safety and efficacy of granulocyte and monocyte adsorption apheresis in paediatric inflammatory bowel disease: a prospective pilot study. J Pediatr Gastroenterol Nutr 46:1–7.

Otsuka decided to initiate a scientific data collection by conducting a larger clinical study with Adacolumn GMA in paediatric UC.

This prospective open clinical trial will start in late summer 2008. It will include about 50 children with UC in about 10 sites in Europe. Clinical data on disease activity, treatment safety and steroid sparing effects will be monitored along with Quality of Life. The study results are expected to be available in early 2011. ■

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

Adacolumn® Travel Grant report from 15th UEGW, Paris 2007

Dr. Ladislav Hanik, Dept. of Gastroenterology, Ängelholm Hospital, Sweden

Participating in a congress is rewarding. The first, and most remarkable, observation from this congress was that over the past five years there has not been a new, effective immunosuppressive medication free of adverse effects. This was not noted solely from this year's UEGW, but from DDW as well. The second observation is the use of faecal calprotectin (f-calprotectin) in the diagnosis of active inflammatory bowel disease (IBD) and the assessment of treatment efficacy. Various clinical activity indexes and a battery of expensive, not very specific tests are applied in the U.S. for the assessment of IBD, and it almost seems like the simple analysis of faecal calprotectin has been ignored.

Furthermore, the report from Ladislav Hanik covered TNF-alpha antagonists, the varying need for colonoscopic follow-ups in different patients groups, how some medications prevent dysplastic colorectal cancer in ulcerative colitis, as well as a study reporting the reduced risk of liver fibrosis with methotrexate.

The full report is available at www.otsukapharma.info -> Medical professionals -> Adacolumn Services -> Congress reports & events. ■

Steroid naïve and steroid dependent patients: A striking difference in response.

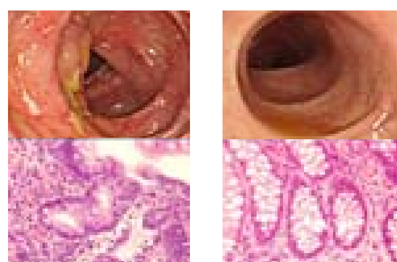
An article by Dr Tanaka et al, reports a striking difference in the clinical response to treatment with granulocyte and monocyte apheresis (GMA) between different subgroups of patients with ulcerative colitis.

With steroid dependence and deep colonic ulcers the rate of response is significantly lower. This could be due to the protective effects of corticosteroids on leucocytes and to the tendency for ulcerative colitis to worsen in the absence of an adequate dose of corticosteroids.

Patients: Patients with ulcerative colitis at the Hiroshima Chugoku Rosai Hospital. On entry, the main clinical activity index (CAI) was 12.6, ranging from 10 to 16. In the study 26 steroid naïve and 19 steroid dependent patients were included.

Treatment: Each patient was given up to an 11 GMA sessions over 12 weeks. No patient received additional medications within 4 weeks (steroid) to 8 weeks (other immunosuppressants) prior to entry or during the GMA course.

Results clinical remission: Colonoscopy and biopsy was done simultaneously on entry as well as within 2 weeks after the last GMA session. At this point, clinical remission rate (CAI $\leq$ 4) was 85 % (22/26) in the steroid naïve subgroup and 58 % (11/19) in the steroid dependent group. Steroid naïve patients showed a significantly better response (p-value=0.02). Colonoscopy revealed that most non-responders had deep colonic ulcers and extensive loss of the mucosal tissue. On average, remission was sustained for 7.8 months in all 33 responders.



Before GMA **After 12 weeks**

Restored mucosal vascular patterns and integrity after GMA in a steroid naïve patient.

Tomotaka Tanaka MD, PhD Internal Medicine, Chugoku Rosai Hospital, Japan

Results steroid sparing: All 22 steroid naïve patients who achieved remission avoided corticosteroid therapy. In steroid dependent patients, the dose of prednisolone was to be tapered in line with improvement of CAI. The mean daily dose of prednisolone in the 11 steroid dependent patients who achieved remission was 20 mg at entry and 5.8 mg (range 0–10) at week 12. ■

Tanaka T, et al. Treatment Of Patients With Ulcerative Colitis At The Hiroshima Chugoku Rosai Hospital. Dig Liver Dis 2008 (in press)

Adacolumn® Travel Grant report from 15th UEGW, Paris 2007

R.N. Karin Göransson, Gastroenterology open ward centre, clinic for gastroenterology and hepatology, Karolinska Hospital, Sweden

The ESGENA meeting offered a full program, mostly focusing on endoscopy. Rachel Lynch, a nurse from Leeds, spoke of an introductory booklet as a way to give a more structured education for endoscopy nurses. Something similar might be prepared in our endoscopy unit in Solna. Elina Mattila, from Tempere, Finland, described a model for follow-up phone calls after hospital discharge, in order to facilitate early discharge and increase the patient's self-confidence.

Furthermore, the report from Karin Göransson covered talks on electronic documentation using Endobase from Olympus, defining the competence needed for the specialised IBD nurse, the use of rotating staff between different hospitals' endoscopy units, and specialist nurse training to perform both upper and lower endoscopy examinations.

The full report is available at www.otsukapharma.info -> Medical professionals -> Adacolumn Services -> Congress reports & events. ■