Active Ulcerative Colitis Refractory to Steroids

Comparative Efficiency of Methotrexate and Azathioprine in Managing Crohn's Disease

S. Tan1, J. Hinojosa2, D. Malone3, M. Brown1. 1UCB, Slough, United Kingdom; 2Gastroenterology Unit, H. Sagunto, Valencia, Spain; 3University of Arizona, Tucson, AZ, United States

Introduction: The tumour necrosis factor alpha (TNFα) blockers infliximab, adalimumab and certolizumab pegol appear to be similar in efficacy and safety in managing Crohn’s disease (CD). Thus, the choice of therapy will probably be driven by other factors, eg economics, patient tolerance and convenience. Loss of response has been reported and can be managed with higher therapy exposure by increasing dosage, shortening dosing interval, or additional re-induction dosing or splitting the standard maintenance dose.

Aim: To compare the estimated induction and maintenance costs of infliximab, adalimumab and certolizumab pegol for a patient with CD weighing 65 kg.

Method: A simple cost analysis was conducted using recommended induction and maintenance dosing regimens for each agent over a 2-year time horizon. Ex-factory prices of CHF935.00 (€561) for infliximab 100 mg (Remicade®), CHF15,801.10 (€8872) for adalimumab 40 mg (Humira®) and CHF777.91 (€527) for certolizumab pegol (Cimzia®) were used in the estimations. It was assumed that the probability of responding to induction therapy was the same for each agent at 60%, but the probability of receiving adalimumab through Week 12 was 50% for a non-responder at Week 4 and the probability of needing higher therapy exposure by having re-induction with a single additional dose of 400 mg certolizumab pegol followed by standard dosing of 400 mg every 4 weeks, infliximab 10 mg/kg every 8 weeks or adalimumab 40 mg every other week was 40%. Cost for each infusion was assumed to be CHF120 (€72). A series of sensitivity analyses was performed for different dosing possibilities with each TNFα blocker for maintenance therapy.

Results: The estimated induction cost was approximately CHF11,600 (€6900), CHF9590 (€5300) and CHF5300 (€3200) per patient for infliximab, adalimumab and certolizumab pegol, respectively. For a responder, the 2-year expected maintenance cost was around CHF60,000 (€36,000), CHF58,000 (€35,000) and CHF44,000 (€26,000) for infliximab, adalimumab and certolizumab pegol, respectively. Including the induction cost, certolizumab pegol was estimated to potentially save more than CHF22,000 (€13,000) and CHF14,000 (€8,000) in the 2-year total therapy cost versus infliximab and adalimumab, respectively. A similar trend was observed in the sensitivity analyses; the scenario of splitting the standard maintenance dose of certolizumab pegol 400 mg every 4 weeks into 200 mg every other week offered greater cost savings.

Conclusion: This study suggests that, based on the recommended dosing regimens for each of the TNFα blockers for Crohn’s disease, certolizumab pegol appears to be associated with lower therapy costs than infliximab and adalimumab.

P135 Comparative Efficiency of Methotrexate and Azathioprine in Active Ulcerative Colitis Refractory to Steroids

I.V. Gubonina, A.M. Pershko. Military Medical Academy, Saint-Petersburg, Russian Federation

Aims: To evaluate clinical efficiency of methotrexate and azathioprine in active ulcerative colitis (UC) refractory to steroids.

Patients & Methods: 62 UC patients were included (30F:32M). Age was from 24 till 46 years, duration of UC 8.4±4.1 years (with duration of relapse from above 6 month). 26 patients were at treatment with methotrexate (25mg/week), 36 - at treatment with azathioprine (2-2.5 mg/day).

Results: Clinical and morphological remission at 16th week has been reached in 30.7% of cases in methotrexate group and 36.1% of cases in azathioprine group, significant decreasing of UC activity was in 40.1% and 38.9% according. In 23.2% (methotrexate) and 22.2% (azathioprine) of cases it was not clinical and morphological improvement. During therapy it was possible to stop steroid therapy for 11 (42.3%) patients received methotrexate, and for 10 (33.3%) patients for azathioprine.

It is important to note, that achievement of remissions was associated with the brief anamnesis (1-2 years), a male (r=0,628; p<0,001) and the beginning of disease in the age of more than 50 years (r=0,524; p<0,005) in azathioprine group. Predictors of good clinical efficiency of methotrexate were: the brief anamnesis (till one year), (r=0,631; p<0,001), presence of the system disorders (r=0,742; p<0,001) and concomitant psoriasis.

Conclusion: This study has not confirmed superiority of methotrexate or azathioprine in therapy of active ulcerative colitis refractory to steroids. Predictors of efficiency for both schemes of therapy were found.

P137 Improvement in Work Productivity with Adalimumab in Crohn's Disease Patients Who Failed Prior Infliximab: An Analysis of the Choice Trial

S. Lichtiger1, D.H. Present1, B. Persson2, E. Wu3, J.D. Kent4, K.G. Lomax4, J. Chao1, P. Mulani1, M. Sinai Medical Center, New York, NY, United States; 2Analysis Group, Boston, MA, United States; 3Abbott, Abbott Park, IL, United States; 4Abbott, Parsippany, NJ, United States

Aims: Adalimumab, a fully human monoclonal antibody targeting tumour necrosis factor, is approved for the treatment of adults with Crohn's disease. The Work Productivity and Activity Impairment (WPAI) questionnaire is a validated, self-administered tool assessing the impact of disease on productivity. We assessed the impact of adalimumab therapy in the CHOICE trial on WPAI scores in patients with Crohn's disease who previously failed therapy with infliximab.

Materials and Methods: CHOICE was a US-based, multicenter, open-label trial of 673 patients with moderately or severely active Crohn's disease who failed infliximab therapy. Planned study duration was at least 8 weeks. After a minimum period of 12 weeks since last infliximab exposure, patients received adalimumab induction therapy of 160/80 mg at Weeks 0/2, followed by 40 mg every other week maintenance dosing. At/after 8 weeks, patients could be switched to adalimumab 40 mg weekly for failure/non-response. The WPAI tool, as adapted for Crohn's disease, measures the percentage of overall impairment in work productivity (including absenteeism and presenteeism) and daily activity due to Crohn's disease (0%=no impairment; 100%=total loss of work productivity or activity). A 7% change in WPAI score is considered the minimal clinically important change. WPAI scores were recorded at baseline and at Weeks 4, 8, 12, and 24 of CHOICE. Paired t-tests assessed the changes from baseline in WPAI component scores.

Results: The mean age was 40.8 years, 59% were female, and 91% Caucasian. The mean baseline daily activity impairment (57.9%, N=662) and total work productivity impairment (49.4% among 394 employed patients) scores indicated severe impairment. The table below displays the average changes in WPAI components from baseline. For all outcomes, a large improvement in productivity, as illustrated by negative mean changes in WPAI components, was observed at Week 4 and maintained throughout the study period. Sensitivity analysis using a subset of employed patients with complete WPAI data at all scheduled visits (n=122) was performed and yielded similar results.

<table>
<thead>
<tr>
<th>WPAI Component</th>
<th>Baseline</th>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total work productivity</td>
<td>57.9%</td>
<td>-17.1%</td>
<td>-17.1%</td>
<td>-17.1%</td>
<td>-17.1%</td>
</tr>
<tr>
<td>Daily activity impairment</td>
<td>49.4%</td>
<td>-18.8%</td>
<td>-20.5%</td>
<td>-23.1%</td>
<td>-23.1%</td>
</tr>
<tr>
<td>Mean change from baseline in WPAI components with adalimumab therapy</td>
<td>333</td>
<td>317</td>
<td>256</td>
<td>136</td>
<td>136</td>
</tr>
</tbody>
</table>

Conclusion: Improvements in productivity as measured by the WPAI scale were achieved with adalimumab therapy by patients with moderately to severely active Crohn's disease who failed infliximab therapy.


P138 Maintenance of Remission in Patients with Ulcerative Colitis with Once- or Twice-Daily MMX™ Mesalazine: Results of an International Multicentre Randomised Trial

S. Schreiber1, K. Barrett2, K. Lees3, R. Joseph3, Christian-Albrechts Universität, Kiel, Germany; 2Shire Pharmaceuticals Inc., Basingstoke, United Kingdom; 3Shire Pharmaceuticals Inc., Wayne, PA, United States

Aim: MMX Multi Matrix System® (MMX) mesalazine (MEZAVANT™ XL [UK and Ireland] MEZAVANT™ [elsewhere] ULADAX™ [USA]) is a once-daily, high-strength (1.2g/tablet), prolonged-release formulation of 5-aminosalicylic acid (5-ASA). In this study, the safety and efficacy of MMX mesalazine when dosed once or twice daily, was evaluated in patients whose ulcerative colitis (UC) was in remission.

Methods: Patients enrolled into this randomised, multicentre, open-label,
Background: Serum Pepsinogen I (PG I) level reliably correlates with the number of chief cells in the gastric corpus mucosa. Gastric heterotopia of the small intestine in Crohn’s disease (CD) has been well described and PG I elevation noted on immunohistochemistry in the metaphasic pyloric and oxyntic glands in the ileum. Adiponectin levels are known to be elevated in patients with CD with mesenteric adipose tissue hypertrophy and not in patients with UC. ASCA has been associated with more proximal involvement rather than colonic CD. Diagnosis of small intestinal involvement in patients with CD has major implications on patient management. Aim: The aim of this study was to use serum PG I, serum adiponectin and Iga and Igg ASCA levels to develop a model that distinguishes patients with colonic CD from those with involving the small intestine.

Methods: Serum was prospectively collected and stored at -80°C from patients with histologically proven CD. PG I levels (Biohon, plc, Finland) and Adiponectin levels (B-bridge International, USA), Iga and IgG ASCA (Aeskulab, Germany) were determined in duplicate by ELISA. Patients were grouped into those with small intestinal involvement and those with colonic CD. Differences between groups were tested using Mann-Whitney U test of significance.

Results: Mean PG I levels in the small bowel CD group (n=18) was 97.9 ± 33.07 µg/l. Mean PG I levels in the colonic CD group (n=14) was 83.25 ± 29.74 µg/l (p=0.08). Mean Adiponectin levels in the small bowel CD group was 3.39 ± 1.87 ng/ml and in the colonic CD group was 2.65 ± 1.50 ng/ml (p=0.02). Area under the Receiver operating curve for Adiponectin was 0.74 and for Serum PG I was 0.68. A cut off value of more than 1.58 ng/ml for serum Adiponectin and more than 78 µg/l for serum PG I with either a positive Iga or IgG ASCA had a sensitivity of 88.9%, specificity of 85.7% and overall accuracy of 87.5% in detecting small bowel involvement in CD. Only 2 patients each with colonic and small intestinal CD were misclassified.

Conclusion: Adiponectin levels are significantly higher in CD patients with small bowel disease. This could be because patients with colonic CD alone are less likely to have mesenteric fat hypertrophy. Serum PG I levels showed a trend towards significance among patients with small intestinal CD. This could reflect both gastric heterotopia in the small intestine as well as inflammation due to CD in the stomach. Further studies are required to confirm these findings. A combination of Adiponectin, PG I levels and ASCA serology could help in non-invasive diagnosis of small bowel involvement in patients with CD.