Biosimilar infliximab CT-P13 treatment in patients with inflammatory bowel diseases. Results from single center retrospective study

HLAVATÝ T.

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Slovak Republic
Saints Cyril and Methodius (826-869, 815-885)

Greek: Κύριλλος καὶ Μεθόδιος; Byzantine Christian theologians – brothers

"Apostles to the Slavs".
Through their work they influenced the cultural development of all Slavs.
ECCO Governing Board

Voting block: 29% 😊
Infliximab biosimilar CT-P13

- Infliximab (IFX) treatment has shown significant success in patients with IBD. High costs limit however its affordability in many countries.

- Biosimilars are copies of biologic medicinal products.

- CT-P13 is the first EMEA, FDA approved IFX biosimilar
  - proven equivalent to IFX treatment in several rheumatoid disorders (PLANETAS, PLANETRA);
  - limited experience with use in IBD, heavy discussions at the beginning.
  - In Slovakia, CT-P13 first became available in February 2014.

References:
Controls of physicochemical and biological characteristics of CT-P13

Biological characteristics

- Antigen binding

Physicochemical characteristics

- N-terminal heterogeneity
- Amino acid modifications
- Hinge fragmentation
- Glycosylation
- Fucosylation, sialylation...
- Disulfide bond shuffling
- C-terminal heterogeneity

Effector functions
- Complement interaction
- Fc receptor interaction
CT-P13 registration studies AS,RA

• PLANETAS 2013: RCT, Phase I in pts with ankylosing spondylitis, Bioequivalence shown for AUC, Cmax, clinical response, immunogenicity, safety profile ¹

• PLANETRA 2013: large RCT, Phase III, 606 pts with rheumatoid arthritis resistant to MTX, CT-P13 vs IFX 3mg/kg. Biosimilar showed equal clinical efficacy and pharmacokinetic profile. CT-P13 was well tolerated, no difference in the frequency of AE, infusion reactions or ATI production ²

• EMEA 07/2013: extrapolation of data from trials to all indications, importance of post-marketing pharmacovigilance

2013: general attituted to biosimilars: sceptical

„In summary, we believe that there is an absence of good documentation on the use of biosimilar medicines for UC and CD. Unresolved questions about efficacy and safety are of great concern to the medical community.

It is our opinion that we specialist should lean towards a sceptical conservative approach. „

### 2013/4: Position papers of large medical societies

<table>
<thead>
<tr>
<th>Society</th>
<th>General perception</th>
<th>Switch</th>
<th>Extrapolation</th>
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</thead>
<tbody>
<tr>
<td>European Crohn´s and Colitis Organisation</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Negative</td>
</tr>
<tr>
<td>American College of Rheumatology</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Negative</td>
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<td>British Society for Rheumatology</td>
<td>Positive</td>
<td>Neutral</td>
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<tr>
<td>Polish National Consultants in Gastroenterology</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
<tr>
<td>Spanish Society of Rheumatology</td>
<td>Positive</td>
<td>Neutral</td>
<td>Neutral</td>
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<tr>
<td>Spanish Society of Gastroenterology</td>
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<tr>
<td>Mexican College of Rheumatology</td>
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<tr>
<td>Portugal Society of Rheumatology</td>
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<td>Positive</td>
<td>Neutral</td>
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<tr>
<td>Brazil Society of Rheumatology, Dermatology and Gastroenterology</td>
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<td>Neutral</td>
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</table>
## CT-P13 in IBD – publications 2014-16

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>N</th>
<th>Induction Response W8-14</th>
<th>Switch Sustained clinical response W48-54</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kang YS, 2014 South Korea</td>
<td>Retrospective, single center</td>
<td>17 IBD</td>
<td>CD: 2/3 (67%) UC: 5/5 (100%)</td>
<td>CD: 4/5 (80%) UC: 3/4 (75%)</td>
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<tr>
<td>Jung YS, 2015 South Korea</td>
<td>Retrospective multicenter</td>
<td>110 IBD</td>
<td>CD: 29/32 (91%) UC: 34/42 (81%)</td>
<td>CD: 25/27 (93%) UC: 6/9 (67%)</td>
</tr>
<tr>
<td>Park, J, 2015 South Korea</td>
<td>Retrospective multicenter</td>
<td>173 IBD</td>
<td>CD: 34/39 (87%) UC: 40/53 (76%)</td>
<td>CD: 25/31 (81%) UC: 11/11 (100%)</td>
</tr>
<tr>
<td>Jahnsen J, 2015 Norway</td>
<td>Prospective single center</td>
<td>78 IBD</td>
<td>CD: 33/43 (79%) UC: 18/32 (56%)</td>
<td>-</td>
</tr>
<tr>
<td>Gecse K, 2016 Hungary</td>
<td>Retrospective multicenter</td>
<td>210 IBD</td>
<td>CD: 79/103 (81%) UC: 45/58 (77%)</td>
<td>-</td>
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<tr>
<td>Hlavatý T, 2016 Slovakia</td>
<td>Retrospective single center</td>
<td>25 IBD</td>
<td>CD: 7/9 (78%) UC: 4/4 (100%)</td>
<td>CD: 5/7 (75%) UC: 1/1 (100%)</td>
</tr>
<tr>
<td>Smits LJT, 2016 The Netherlands</td>
<td>Prospective single center</td>
<td>83 IBD</td>
<td>-</td>
<td>CD: 78/81  (96 %)*</td>
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<tr>
<td>Farkas K, 2016 Hungary, Czech R</td>
<td>Prospective multicenter</td>
<td>63 UC</td>
<td>-</td>
<td>CD: 52/63 (82%) UC: -</td>
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<tr>
<td>Keil, R, 2016 Czech Republic</td>
<td>Prospective single center</td>
<td>52 IBD</td>
<td>CD: 30/30 (100 %) UC: 21/22 (95 %)</td>
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## ECCO 2016 Poster summaries

<table>
<thead>
<tr>
<th>Abstract No: Title</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>P311</strong>: No difference in immunogenicity of the original and biosimilar infliximab in patients with inflammatory bowel disease: short-term results K. Malickova</td>
<td>- Week 14 results demonstrate that IFX (n=60) and CT-P13 (n=71) have comparable immunogenicity (ATI, ANA, anti-dsDNA and anti-ENA) in IBD patients</td>
</tr>
<tr>
<td><strong>P327</strong>: Biosimilar infliximab in real-life CD anti-TNFalpha-naïve patients: a comparative observational cohort study (SIMRECRO study) L. Carvalho Lourenço</td>
<td>- Both rIFX (n=41) and CT-P13 (n=19) significantly decreased disease activity and CRP levels after 6 and 24 weeks</td>
</tr>
<tr>
<td><strong>P329</strong>: Infliximab biosimilar in the treatment of inflammatory bowel disease: a Japanese single-cohort observational study S. Hamanaka</td>
<td>- In this 24-week study (N=20), IFX biosimilar was considered to be efficacious and safe compared with rIFX in IBD patients</td>
</tr>
<tr>
<td><strong>P382</strong>: Comparison of efficacy and safety of biosimilar infliximab to originator infliximab in children with inflammatory bowel disease R. Muhammed</td>
<td>- Real-life clinical practice comparing rIFX (n=17) and CT-P13 (n=24) in IBD</td>
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<td></td>
<td>- Efficacy and safety of CT-P13 was comparable to rIFX</td>
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<tr>
<td><strong>P449</strong>: Efficacy and safety of switching between originator and biosimilar infliximab in patients with inflammatory bowel disease in practical clinic: results to 6 months L. Díaz Hernández</td>
<td>- In this observational, retrospective study (N=72), switching to the biosimilar IFX was effective in the maintenance of clinical remission at 6 months and no relevant AEs were observed</td>
</tr>
<tr>
<td><strong>P452</strong>: Safety and efficacy of infliximab biosimilar in Crohn’s disease patients in clinical practice: results after 6 months of treatment M. F. Guerra Veloz</td>
<td>- In this observational study (N=75), most CD patients who switched from Remicade to CT-P13 continued remission after 6 months. Mild AEs were noted in 5 patients</td>
</tr>
<tr>
<td><strong>P495</strong>: Biosimilar infliximab is effective and safe in inflammatory bowel disease patients naïve to anti-TNF therapy: a tertiary centre experience M. Bortlik</td>
<td>- In this observational study of anti-TNF-naïve IBD patients (N=104), the efficacy and safety of biosimilar IFX appeared to be comparable to that observed previously with originator IFX</td>
</tr>
<tr>
<td>Abstract No: Title</td>
<td>Summary</td>
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</tr>
<tr>
<td><strong>P513</strong>: Comparison of infliximab the originator and biosimilars in treatment of Crohn's disease: a Polish cohort study E. Zagorowicz</td>
<td>• In this observational study of adult CD patients (N=74) receiving the originator IFX (n=58) or the biosimilar (n=16), the response and remission rates were similar during the first 14 weeks of treatment</td>
</tr>
<tr>
<td><strong>P519</strong>: Efficacy and safety of biosimilar of infliximab (Inflectra) in adult patients with Crohn's disease during 1 year of treatment, followed by 6 months of observation: a one-centre retrospective study M. Kaniewska</td>
<td>• This retrospective, single centre study of Remicade (n=77), Inflectra (n=52) or Humira (n=47) in CD patients found Inflectra to be safe and efficacious in induction and 1 year therapy</td>
</tr>
<tr>
<td><strong>P530</strong>: Efficacy of biosimilar infliximab induction therapy in paediatric patients with Crohn’s disease: 1.5 years of experience J. Sieczkowska</td>
<td>• Paediatric patients (N=36) from 3 Polish hospitals had induction therapy with biosimilar IFX, which was demonstrated to be safe and effective</td>
</tr>
<tr>
<td><strong>P577</strong>: Croatian database from 5 centres: efficacy and safety of infliximab biosimilar in treatment of inflammatory bowel disease score patients N. Turk</td>
<td>• Study included 39 IBD patients: 31 (70%) reached clinical and laboratory remission, 10 (32%) reached MH and no serious AEs were reported</td>
</tr>
</tbody>
</table>
| **P600**: Safety and efficacy of infliximab biosimilar in ulcerative colitis disease patients in clinical practice: results after 6-months treatment M. F. Guerra Veloz | • Single cohort observational study (N=40) in naïve patients and those switching from Remicade to CT-P13 (n=31)  
• No serious AEs were reported; mild AEs in 2 patients and most UC patients who switched continued remission after 6 months |
| **P617**: Immunogenicity after switching from reference infliximab to biosimilar in children with Crohn’s disease J. Sieczkowska | • Paediatric CD patients (N=16) who had switched from rIFX to biosimilar IFX; no attributes of higher immunogenicity after switching from originator to biosimilar IFX were found |
| **P645**: Efficacy and safety of biosimilar of infliximab in rescue therapy in adult patients with severe ulcerative colitis M. Kaniewska | • Retrospective, single centre, Polish study in UC patients (N=67) receiving either Remicade (n=32) or Inflectra (n=35)  
• Rate of AEs was comparable as well as the efficacy of Inflectra in rescue therapy of UC and during 6 months of follow-up |
| **P655**: Biosimilar infliximab CT-P13 treatment in patients with inflammatory bowel diseases: a 1-year, single-centre retrospective study T. Hlavaty | • Retrospective cohort study (N=25;19 CD, 6 UC) of both CT-P13-induced (n=13) and switch (n=12) patients  
• Data indicates that CT-P13 is comparable to IFX in terms of effectiveness and safety |
Our experience

The aim of our study was to assess efficacy and safety of CT-P13 (Inflectra) in IBD patients over the first 12 months after the drug became available in Slovakia.
Methods

Study design: retrospective study, single center- IBD center, University Hospital Bratislava, Ruzinov

Patient population: all consecutive IBD patients treated with CT-P13 between 03-2014 and 04-2015 who received at least 3 CT-P13 infusions or if treatment had to be terminated earlier due to an adverse event. Included also patients who were switched to CT-P13 from maintenance IX

Assessment of induction treatment
• Clinical remission at w14 after the first infusion
• CD: HBI score < 5 and no active fistula , UC: pMayo score < 2

Assessment of maintenance treatment
• Sustained clinical response was assessed every 8 weeks, both in CT-P13-induced patients and those switching from IFX.
• CD: ΔHBI <3 , remained inactive fistulas, UC: ΔpMayo<2, no side effects.

Safety: adverse events of special interest included severe or opportunistic infections, acute or delayed hypersensitivity reactions and IBD-related hospital admissions or surgeries.
<table>
<thead>
<tr>
<th></th>
<th>All patients (n=25)</th>
<th>INDUCTION</th>
<th>SWITCH</th>
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</thead>
<tbody>
<tr>
<td><strong>Male/female</strong></td>
<td>18/7</td>
<td>6/3</td>
<td>9/1</td>
</tr>
<tr>
<td><strong>Median age (range), yrs</strong></td>
<td>39 (22–68)</td>
<td>33.9 (27.4–54.5)</td>
<td>40.3 (35.5–46.9)</td>
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<td></td>
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<td>35.8 (21.5–67.7)</td>
<td>48.7 (43.5–54)</td>
</tr>
<tr>
<td><strong>Median disease duration (range), yrs</strong></td>
<td>12.3 (0.5–27.8)</td>
<td>8.8 (0.4–27.7)</td>
<td>20.0 (6.6–27.8)</td>
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<td></td>
<td></td>
<td>11.8 (5.3–18.8)</td>
<td>12.3 (10.8–12.3)</td>
</tr>
<tr>
<td><strong>Location (%)</strong></td>
<td>-</td>
<td>L1: 1 (11%)</td>
<td>E1: 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L2: 1 (11%)</td>
<td>E2: 2 (50%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L3: 7 (78%)</td>
<td>E3: 2 (50%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L4: 0</td>
<td>E4: 2 (20%)</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>B1: 2 (22%)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B2: 3 (33%)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B3: 4 (45%)</td>
<td>-</td>
</tr>
<tr>
<td>IBD surgery (%)</td>
<td>8 (32%)</td>
<td>5 (56%)</td>
<td>0</td>
</tr>
<tr>
<td>Current smoking (%)</td>
<td>7 (28%)</td>
<td>3 (33%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Therapy at baseline</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroids (%)</td>
<td>7 (28%)</td>
<td>3 (33%)</td>
<td>4 (100%)</td>
</tr>
<tr>
<td>Azathioprine (%)</td>
<td>13 (52%)</td>
<td>6 (67%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>Previous anti-TNFα exposure</td>
<td>5 (56%)</td>
<td>0</td>
<td>0</td>
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<td>Adalimumab (%)</td>
<td>-</td>
<td>5 (56%)</td>
<td>0</td>
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<tr>
<td>Past episodic use of IFX</td>
<td>-</td>
<td>3 (33%)</td>
<td>1 (25%)</td>
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<tr>
<td>Median number of IFX infusions before switch (range)</td>
<td>22 (3–64)</td>
<td>37 (29–43)</td>
<td></td>
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</tbody>
</table>
Clinical response to CT-P13 induction therapy (HBI or pMayo), n= 13
Clinical response to CT-P13 induction therapy (HBI a pMayo), n= 13

- The box plot represents the maximum, upper quartile, median, lower quartile, and minimum values. The change in median values (triangles) are plotted with a thick black line.
- W0, baseline visit with the first infusion; W2, week 2; W6, week 6; and W14, week 14 after the first CT-P13 infusion.
- The p value was calculated using the Wilcoxon rank sum test comparing W0 to W14.
Disease-related quality of life of inflammatory bowel disease patients during CT-P13 induction treatment, determined using sIBDQ (n=13)

- W0, baseline visit with the first infusion; W2, week 2; W6, week 6; and W14, week 14 after the first CT-P13 infusion.
- The data are expressed as mean ± standard deviation.
- *p=0.002, **p=0.003 relative to W0, determined by paired t-test.
Maintainance of clinical response after induction therapy (n= 11)

- W2: 67% CD, 69% UC, 67% IBD
- W6: 100% CD, 77% UC, 78% IBD
- W14: 100% CD, 85% UC, 75% IBD
- W30: 100% CD, 80% UC, 75% IBD
- W52: 100% CD, 100% UC, 100% IBD

Legend:
- CD (n=9)
- UC (n=4)
- IBD (n=13)
Switch from the originator
n= 12 (10 CD, 2 UC)

<table>
<thead>
<tr>
<th></th>
<th>W24</th>
<th>W32</th>
<th>W48-52</th>
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<tbody>
<tr>
<td>CD</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>UC</td>
<td>100%</td>
<td>88%</td>
<td>75%</td>
</tr>
<tr>
<td>IBD</td>
<td>100%</td>
<td>86%</td>
<td>71%</td>
</tr>
</tbody>
</table>

Legend:
- CD (n=10)
- UC (n=2)
- IBD (n=12)
Disease-related quality of life of IBD patients during CT-P13 maintenance treatment after switching from IFX using sIBDQ (n=12)

The data are expressed as mean ± standard deviation.

CD, Crohn's disease; UC, ulcerative colitis; W0, baseline visit with the first infusion; W8, week 8; W16, week 16; etc. after the first CT-P13 infusion.
Adverse events

• A total of 128 infusions (median 5) administered

• No severe or opportunistic infections, no IBD-related hospital admissions or surgeries during the follow-up period

• The treatment with CT-P13 was discontinued in 4/25 patients (all CD) in 2 patients for acute infusion reaction in 1 patient for psoriasiform dermatitis in 1 patient for loss of response
Our experience summarized

• Clinical remission achieved after induction treatment 84% IBD patients (7/9 CD, 4/4 UC). 85% of patients who entered clinical remission following induction therapy had a sustained clinical response with maintenance therapy at week 30 (3/3 CD, 3/4 UC).

• In those who switched from originator IFX, clinical response was sustained in 100% at week 24 after switch, in 87.5% at w32 and in 75% at w48.

• No severe adverse events. Treatment was stopped for infusion reaction in 2, psoriasiform rash in 1 and LOR in 1 patient.

• Our experience suggests that, CT-P13 seems to be similar in safety profile as well as efficacy to that of original infliximab.
Changes in biosimilar knowledge among ECCO members: An updated survey

Methods: A 14-question anonymous survey was posted in the ECCO website. Members voluntarily participated in response to ECCO office invitations to participate in their surveys. Same questions in 2013 and 2015. Results were compared.

Danese S et al. JCC, 2016 (4) ePub, Manuscript Doi : 10.1093/ecco-jcc/jjw090
only 19.5% felt little or not confident in the use of biosimilars, as compared to 63% in 2013.

Danese S et al. JCC, 2016 (4) ePub, Manuscript Doi : 10.1093/ecco-jcc/jjw090
Use of IFX, Norway 12/2015, No of vials

Moum B, 2016, Falk Symposium
Total IFX prescription, Norway

Infliximab vials traded last 3 years in Norway

- 2013: 84,025
- 2014: 95,263 (+13%)
- 2015: 127,164 (+34%)

Moum B, 2016, Falk Symposium
Conclusion

- CT-P13 biosimilar infliximab is a first in class monoclonal biosimilar antibody
- Accumulating experience in IBD suggests it is identical in its efficacy and safety to its originator
- Switch from the originator safe with sustained clinical response similar to the originator
- These results have led to a large positive shift in the perception and adoption of biosimilars and their use in countries where they have been introduced.
THANK YOU FOR YOUR ATTENTION!