PrescQIPP Community Interest Company

Biosimilar infliximab – A summary for prescribers

Executive summary

The manufacture of biologic medicines is highly complex and no two batches of any given product are identical. This presents a huge regulatory challenge but it is one that has been successfully overseen by the European Medicines Agency (EMA) for several decades. Copies of existing biologics (biosimilars) have been approved for use for many years in the EU and their regulatory approval mimics that of the originator products in many ways.

A biosimilar of infliximab was recently launched in the UK in March 2015. Published data indicate a highly similar molecule with comparable efficacy and safety in clinical trials. Clinical data in inflammatory bowel disease (IBD) patients is lacking, but early small studies indicate similar levels of effectiveness.

Caution is being recommended initially by groups such as the British Society of Gastroenterology (BSG) so as to allow prescribers to become familiar with the biosimilar. However the biosimilar represents a highly cost effective alternative to the existing biologic and commissioners will be keen to see usage in their localities. Ideally a collaborative approach can be adopted that will allow providers, commissioners and patients all to benefit.

Introduction

A biosimilar medicine is a biological medicine that is developed to be similar to an existing biologic in terms of quality, safety and efficacy.[1] The biosimilar of infliximab will be the first of several biosimilar monoclonal antibodies to be launched within the EU over the next few years. This briefing paper aims to provide background to the manufacturing and regulatory processes in place for these biologic agents, as well as a summary of the currently available evidence, designed to inform the safe and appropriate uptake of biosimilar infliximab.

Biologic manufacture

Manufacturing biologic medicines, such as monoclonal antibodies (mAb), is a highly complex process. This complexity means that the characteristics of a particular brand, of any given biologic, cannot be exactly reproduced from one batch to another.[2]

In addition the methods used originally to manufacture a mAb, such as infliximab, will not be the same methods in use today and this also leads to variation in the composition in the originator product. These batch to batch variations and manufacturing process changes are overseen by the regulatory authorities in order to ensure the product is still sufficiently similar to the first batch to retain its license in the approved indications. For pre and post manufacturing changes this regulatory procedure is known as a "comparability exercise".[3] The regulators will require tests to be undertaken, ranging from structural analytics to clinical studies in humans, depending on the significance of the process change.

The EMA has been regulating the production of biologics, and now biosimilars, for many decades. From a scientific and regulatory point of view, the active substance of a biosimilar is just another version of the active substance of the originator.[4]

The same scientific principles underpinning the comparability exercise apply equally to:

(a) demonstrating similarity before and after a change in manufacturing process and

(b) the comparability exercise for the purpose of demonstrating biosimilarity.

The cornerstone of this process is the extensive comparison of the physicochemical and functional characteristics of the molecules using up-to-date analytical tools. This then allows for the abbreviated pre-clinical and clinical testing process required for regulatory approval of biosimilars.[5] Clinical studies are required primarily to target "residual uncertainty", i.e. the issues that analytics alone cannot resolve.[6] These are typically issues of safety and immunogenicity.

Biosimilar development

The aim of development is not to establish patient benefit per se as this has already been done for the originator.[2] The aim is to convincingly demonstrate high similarity to the reference product. This will then allow the biosimilar to rely on, in part, the existing efficacy and safety experience of the originator.[7] The biosimilar manufacturer must determine the acceptable level of product variability by assessing multiple batches of the originator. A process is then designed that allows the production of a product that falls within the existing product variability.[8]

The final product will then undergo an extensive comparability exercise to demonstrate "biosimilarity". This is the regulatory term used in the EU to denote comparability between a biosimilar and originator.

The type and extent of clinical data required to demonstrate biosimilarity vary and will depend on factors such as, the complexity of the active substance and how well it can be characterised. This assessment will be made on a case-by-case basis. However, a repetition of the entire development program of the reference product is scientifically not necessary and could even be considered unethical.[7]

The infliximab biosimilar comparability exercise

There were five key elements involved in the assessment process of biosimilar infliximab.

1. Analytical - e.g. primary structure, purity, charge variants, glycosylation
2. Binding studies - e.g. binding to TNFa and Fc receptors
3. Biological activity - e.g. apoptosis, Antibody Dependent Cellular Cytotoxicity (ADCC).
4. Non-clinical studies - e.g. Pharmacokinetic and toxicity studies in rats
5. Clinical studies - e.g. Phase 1 and 3 studies in specified indications.

Analytical studies identified lower levels of a type of glycosylation, termed "afucosylation", for the biosimilar. The difference in glycosylation led to lower levels of binding to one type of Fc receptor. The altered Fc binding appeared to result in a reduced effect on Antibody Dependent Cellular Cytotoxicity (ADCC). However, no differences in experimental models regarded as more relevant to the pathophysiological conditions in Crohn's Disease patients were detected.[9]

Two studies (PLANETAS and PLANETRA) were set up to assess the pharmacokinetics (PK) and pharmacodynamics (PD) of biosimilar infliximab vs Remicade (Appendix A, B). PK studies are ideally conducted in a healthy patient cohort, hence ankylosing spondylitis was selected. The PD study should be conducted in the most clinically sensitive endpoint which in this case was rheumatoid arthritis. These studies indicated comparable pharmacokinetics and efficacy for the biosimilar.

Both studies were extended at week 54 and at this point half the patients in each study receiving Remicade were switched to the biosimilar until the end of the trial period (week 102). In both studies the switched patients demonstrated continued efficacy and safety (Appendix C, D).

The human studies were required to examine the areas of residual uncertainty that analytics cannot assess, i.e. safety and immunogenicity. The overall rate of adverse effects was similar in both groups, as was the total rate of infections. Higher rates of pneumonia and TB were seen with the biosimilar but were felt by the regulator to be chance findings after closer examination of the data.

Over the 54 week treatment period a similar rate of immunogenicity was detected in both studies, i.e. anti-drug antibodies. This data was backed up by a recent cross-immunogenicity study comparing antibodies responses to Remicade and the biosimilar (Appendix E).

Extrapolation

This is the regulatory and scientific process of granting a clinical indication to a medicine without its own clinical efficacy and safety data to support that indication.[4] Additional data will be requested by the regulator where the mechanism of action is complex or may differ between indications, as was the case with biosimilar infliximab.[10]

Evidence was also provided to show that the difference in glycosylation had no clinically relevant impact on the efficacy and safety of the biosimilar, in particular in inflammatory bowel disease (IBD).[9]

Extrapolation principles apply equally to either originator biologics or biosimilars, and are already widely exercised. For originator biologics they are applied after a significant manufacturing process change or a product reformulation (e.g. trastuzumab IV to sub-cut) and they have also been applied to all the currently UK licensed biosimilars i.e. erythropoietin (EPO), granulocyte colony stimulating factor (GCSF), growth hormone (GH).

Terminology

“Interchangeability” means moving freely between the available infliximab products i.e. like a generic. This is not regulated by the EMA and it is not an option within the UK. “Substitution” involves changing products within pharmacy without informing the prescriber. This is also highly unlikely to occur within the UK. “Switching” means changing specific patients to the biosimilar following a mutually agreed local arrangement.[11,12]

Traceability and naming

The use of brand names in the prescribing, ordering and supply of infliximab will be essential to allow differentiation between the various forms of infliximab. This will allow traceability which is vital for accurate post-launch pharmacovigilance and will help assure patient safety, i.e. by reducing the chance of inadvertent switching.

Health Technology Appraisals (HTAs)

Both the All Wales Medicines Strategy Group and Scottish Medicines Consortium have issued positive HTAs in relation to biosimilar infliximab.[13,14] NICE has stated that it does not intend to routinely issue individual technology appraisals for each new biosimilar as it becomes available.[15] Since then the SMC has updated its position and in line with NICE “will no longer routinely assess biosimilar medicines”.[16]

British Society of Gastroenterology (BSG)

The BSG issued a statement regarding the biosimilars in late 2014. This was broadly positive and accepted the need to utilise the biosimilars. However, they noted the lack of published data in IBD and urged caution, i.e. avoidance of switching established patients at this stage (Appendix F).

Early published data in IBD

There are 3 large studies already underway that will provide additional data regarding the use of biosimilar infliximab in IBD and other licensed indications. However two small studies have already been completed and the results made available. (Appendix G, H)

- Clinical Experience of the Use of CT-P13, a Biosimilar to Infliximab in Patients with IBD: A Case Series
- The new era of biologic therapy in gastroenterology – case report.

Both studies are of small size but both show results that are comparable to those seen with the originator.

Commissioners' viewpoint

Savings of around 40% of the Remicade cost are likely with the biosimilar. This is obviously of interest to local primary care commissioners. There will be a variety of possible approaches they can take ranging from giving clinicians a free rein to use the biosimilars as they see fit, to capping the funding to the new price of the biosimilar. Ideally a middle ground approach using a commissioning incentive, e.g. gain-share, to encourage usage will be agreed and this will be the recommended approach. This will lay the foundations for the successful introduction of subsequent biosimilars in the future.

Conclusion

Clearly clinician support is vital in order for biosimilar infliximab to be successfully and safely adopted. However, a paradigm shift in thinking is required by prescribers. Regulatory approval for biosimilars centres on analytics and not clinical trials; for licensing approval similarity is the goal and not efficacy in isolation.

The infliximab biosimilar is the first of many biosimilars entering the UK market. It offers a significant opportunity to free up funds that could benefit both primary and secondary care. A joined up approach is required to maximise this opportunity and lay the foundations for successful adoption of further biosimilars in the future.

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Appendix A

Park W et al. A randomised, double-blind, multicentre, parallel-group, prospective study comparing the pharmacokinetics, safety, and efficacy of CT-P13 and innovator infliximab in patients with ankylosing spondylitis: The PLANETAS study. Annals of the Rheumatic Diseases 2013; 72 (10): 1605-1612.

Background

CT-P13 is a biosimilar product of infliximab (INX). Data up to week 30 has been reported at EULAR 2012.

Objectives

To assess the pharmacokinetic (PK), efficacy and safety of CT-P13 in patients with active ankylosing spondylitis (AS) up to week 54 and to compare this with INX, also in relation to the formation of anti-drug antibodies (ADAs).

Methods: Patients with active AS (1984 modified NY criteria) were randomised (1:1) to receive either CT-P13 (5mg/kg) or INX (5mg/kg) at weeks 0, 2, 6 and then every 8 weeks up to week 54.

Results

Of 250 patients randomised at baseline, 213 patients were treated up to week 54. Cmax of CT-P13 and INX were shown to be equivalent, since 90% CIs for the ratio of geometric means were within 80-125% at all doses (CT-P13, 128.1µg/mL-172.2µg/mL; INX, 123.0µg/mL-176.7µg/mL). At week 54, the proportion of patients testing positive for ADAs was comparable between CT-P13 and INX (22.9% [25/109] vs 26.7% [28/105]). ADAs had similar effects on PKs in both groups. Patients with negative ADA results had higher Cmax values (CT-P13, 134.5µg/mL-177.2µg/mL; INX, 131.9µg/mL-177.4µg/mL) compared with patients with positive results (CT-P13, 101.8µg/mL-160.4µg/mL; INX, 104.0µg/mL-175.2µg/mL). At week 54, Assessment in Ankylosing Spondylitis (ASAS) 40 and ASAS partial remission were comparable between groups (CT-P13, 54.7% and 19.8%; INX, 49.1% and 17.6%, respectively). More patients with negative ADA results achieved ASAS40 responses (CT-P13, 61.0%; IFX, 54.7%) compared with patients with positive results (CT-P13, 37.9%; IFX, 36.4%). The safety profiles of CT-P13 and INX were also comparable. Active tuberculosis (TB) was reported in 3 patients (CT-P13, 2; INX, 1) and there were no malignancies.

Conclusions

CT-P13 has similar PK values and a clinical efficacy comparable to INX up to week 54. CT-P13 was well tolerated with a safety profile comparable to that of INX up to 54 weeks. ADAs seem to diminish the clinical response to both agents in some patients.

Appendix B

Yoo DH et al. A randomised, double-blind, parallel-group study to demonstrate equivalence in efficacy and safety of CT-P13 compared with innovator infliximab when coadministered with methotrexate in patients with active rheumatoid arthritis: The PLANETRA study. Annals of the Rheumatic Diseases 2013; 72 (10):1613-1620.

Background

CT-P13 is a biosimilar product of infliximab (INX). Data up to week 30 has been reported at EULAR 2012.

Objectives

To compare the efficacy and safety of CT-P13 and INX in active rheumatoid arthritis (RA) patients up to week 54.

Methods

Patients with active RA (1987 ACR criteria) and inadequate response to methotrexate (MTX) were randomised (1:1) to receive either CT-P13 (3mg/kg) or INX (3mg/kg) at weeks 0, 2, 6 and then every 8 weeks up to week 54 in combination with MTX (12.5–25mg/week).

Results

Of 606 patients randomised at baseline, 457 patients were treated up to week 54. At week 54, ACR20 was highly similar between groups (CT-P13, 57.0% [172/302]; INX, 52.0% [158/304]; 95% CI: -0.03-0.13). ACR50 and ACR70 scores were also comparable between groups (CT-P13, 33.1% and 16.2%; INX, 31.6% and 15.1%, respectively). In the CT-P13 and INX groups respectively, 26.4% and 27.8% of patients reached remission with DAS28-CRP; additionally, 14.3% and 14.8% reached low disease activity compared to approximately 80% high disease activity in both groups at baseline. The proportion of patients testing positive for anti-drug antibodies (ADAs) was comparable between CT-P13 (52.3%) and INX (49.5%). More patients with negative ADA results achieved ACR20 responses (CT-P13, 73.9%; INX, 67.2%) compared with patients with positive results (CT-P13, 53.2%; INX, 48.1%). Total Sharp scores at baseline and week 54 were comparable (CT-P13, 104.6 and 70.4; INX, 103.6 and 73.0). Cmax of CT-P13 or INX at all doses ranged from 66.1µg/mL-112.2µg/mL and 60.3µg/mL-104.5µg/mL, respectively. The safety profiles of CT-P13 and INX were also comparable.

Conclusions

CT-P13 showed comparable efficacy and PKs to those of INX up to week 54. CT-P13 was well tolerated with a safety profile comparable to that of INX up to week 54.

Appendix C

Park W et al. Efficacy and safety of CT-P13 (infliximab biosimilar) over two years in patients with ankylosing spondylitis: Comparison between continuing with CT-P13 and switching from infliximab to CT-P13. Arthritis and Rheumatism 2013; 65(12):3326 (abstract).

Background/purpose

CT-P13 is an infliximab (INX) biosimilar recently approved by the European Medicine Agency. PLANETAS was a 54-week (wk) randomized double-blind parallel group multicenter Phase I study demonstrating pharmacokinetic equivalence of CT-P13 (5 mg/kg infusion every 8 wks) with INX, in patients (pts) with ankylosing spondylitis (AS) (Park W, ARD 2013;72(S3):516). Here we report results from the extension phase of the Phase I equivalence study, investigating long-term efficacy and safety of extended CT-P13 therapy and switching from INX to CT-P13 in pts with AS.

Methods

In this open-label extension study, a total of 174/210 pts who completed PLANETAS entered into the extension phase: 88 were continuously treated with CT-P13 (maintenance group) and 86 were switched from INX to CT-P13 (switch group) for 1 additional year.

Results

At wk 54 ASAS20/ASAS40 and ASAS partial remission rates were similar between groups (CT-P13, 70.5%/58.0% and 20.5%; INX, 75.6%/53.5% and 19.8%, respectively). During the extension, ASAS20/ASAS40 rates were similar in the maintenance group (70.1%/57.5% at wk 78 and 80.7%/63.9% at wk 102) and the switch group (77.1%/51.8% at wk 78 and 76.9%/61.5% at wk 102). ASAS partial remission rates were also similar between groups; 21.8% and 21.7% at wk 78, and 27.7% and 28.2% at wk 102, respectively. An overview of the efficacy data are shown in the Table. Anti-drug antibodies (ADA) were comparable between the two groups and positivity was maintained throughout the study (maintenance group, 22.2%, 24.4% and 25.0%; switch group, 26.2%, 31.3% and 30.7%, at wk 54, 78 and 102, respectively). ADA negative pts achieved higher ASAS40 responses (maintenance group, 62.9%/61.5%/66.1%; switch group, 58.1%/60.0%/71.2% at wks 54, 78 and 102, respectively) compared with ADA-positive pts (maintenance group, 38.9%/36.8%/55.0%; switch group, 41.7%/33.3%/45.8% at wks 54, 78 and 102, respectively) with no differences between the maintenance and switch groups. The proportion of pts with ≥1 treatment-emergent adverse event (TEAE) was lower in the maintenance group (48.9%) compared with switch group (71.4%) mainly due to fewer mild and moderate AEs. Serious TEAEs were identical between groups (4 vs 4 pts). Other tolerability and safety outcomes were similar in both groups. TEAEs due to hypersensitivity and infusion-related reactions were similar in both groups (5 pts in maintenance group vs 2 pts in switch group). There was 1 case of TB in each group and 1 report of prostate cancer in the maintenance group (considered unrelated to treatment).

Conclusion

CT-P13 was safe and efficacious over 2 years in pts with AS. Switching from INX to CT-P13 was efficacious and tolerable from wk 54 to wk 102. The comparable efficacy and tolerability profiles of CT-P13 and INX in pts with AS observed at wk 54 were maintained up to 102 wks in both groups with continued CT-P13 treatment in the extension study.

Appendix D

Hanyang D-HY et al. Efficacy and safety of CT-P13 (infliximab biosimilar) over two years in patients with rheumatoid arthritis: Comparison between continued CT-P13 and switching from infliximab to CT-P13. Arthritis and Rheumatism 2013; 65(12): 3319 (abstract).

Background/purpose

CT-P13 is a biosimilar of infliximab (INX), approved by the European Medicines Agency. The objective of this open-label Phase 3 extension study was to confirm long-term efficacy and safety of CT-P13 and to investigate switching from INX to CT-P13, in patients (pts) with rheumatoid arthritis (RA).

Methods

The PLANETRA Study was a 54-week (wk), randomized, double-blind, parallel-group study demonstrating efficacy and safety equivalence of CT-P13 (3 mg/kg) compared with INX when co-administered with methotrexate (12.5-25 mg/wk) and folic acid (≥5 mg/wk, oral dose) every 8 wks in pts with RA (Yoo DH ARD2013;72(S3):73). In total, 302/455 pts who completed the scheduled visits were entered into the open-label extension phase for an additional 48 wks: 158 pts were maintained with CT-P13 (maintenance group) and 144 pts switched from INX to CT-P13 (switch group). Efficacy (including ACR20/50/70) and safety assessments including immunogenicity were monitored throughout the study.

Results

At wk 54, ACR20/50/70 response rates were similar between groups (CT-P13: 76.8%/45.7%/21.9%; INX 77.5%/50.0%/23.9%, respectively). At wk 78, ACR20/50/70 response rates were comparable for the maintenance group (71.5%/48.3%/24.5%) and switch group (78.2%/47.9%/29.6%). Through wk 102, ACR20/50/70 response rates were maintained and were similar in each group; 72.2%/48.3%/24.5% and 71.8%/51.4%/26.1%, respectively. Good and moderate EULAR-CRP responses at wks 54, 78 and 102 were observed in 89.4%/79.5%/81.5% of pts in the maintenance group and 87.3%/85.9%/76.8% of pts in the switch group, respectively. Changes in DAS28-CRP from baseline were comparable between the two groups: −2.4/−2.4/−2.4 in the maintenance group; −2.4/−2.6/−2.5 in the switch group, at wks 54, 78 and 102 respectively). EULAR-ESR response rates and DAS28-ESR results were also comparable between groups. The proportion of pts positive for anti-drug antibody (ADA) was comparable between the two groups throughout the study and ADA positivity did not increase significantly during year 2 when both groups were receiving CT-P13: maintenance group, 49.1%, 50.4% and 46.4%; switch group, 49.3%, 49.6% and 49.6% at wk 54, 78 and 102, respectively. The number of pts with at least one AE or SAE was comparable (Table). Infusion-related reactions were seen in 10 pts (6.3%) in the maintenance group and in 4 pts(2.8%) in the switch group (p=0.1781). There were no reports of TB infections in either group. Malignancies were reported in 1 pt (ovarian cancer) in the maintenance group and in 4 pts (breast cancer, T-cell lymphoma, ovarian cancer and myeloproliferative disorder) in the switch group.

Conclusion

CT-P13 was well tolerated and effective over 2 years in pts with active RA. The efficacy and safety profiles of the maintenance group and the switch group were comparable during this extension study.

Appendix E

Ben-Horin S et al. Cross-immunogenicity: antibodies to infliximab in Remicade-treated IBD patients similarly recognize the bio-similar Remsima. Paper presented at the UEGW (United European Gastroenterology Week), Vienna Oct 2014.

Introduction

Remsima, an infliximab bio-similar, recently received European approval for use in IBD. However, the cross-immunogenicity of Remsima with the originator drug Remicade in IBD patients is unknown.

Aims and methods

Sera of Remicade-treated IBD patients with measurable antibodies to Remicade were tested by anti-lambda ELISA for their cross-reactivity to two batches of Remsima. Sera negative for anti-Remicade antibodies were tested in parallel as controls. Anti-Remicade antibodies were tested for their functional inhibition of TNFalpha-binding by either Remsima or Remicade using a competition assay. Cross-reactivity of anti-adalimumab antibodies with Remicade and Remsima was also investigated.

Results

In total, 124 sera were tested. All 68 positive anti-Remicade IBD sera were cross-reactive with Remsima. In negative controls (16 healthy individuals, 40 IBD patients), there was a slightly higher background signal in the ELISA assay for Remsima compared to Remicade, but all 56 control sera which were anti-Remicade negative also tested negative for anti-Remsima antibodies.

Moreover, the measured titers of anti-drug antibodies were very similar when reacted against Remicade or Remsima (rho values between 0.92 to 0.99, $p<0.001$ for all experiments, Spearman correlation test). Anti-Remicade antibodies of IBD patients (n=10) exerted a similar functional inhibition on Remsima and Remicade TNF alpha-binding capacity (P=not significant (NS) for all points on the inhibition curves). Antibodies to adalimumab in adalimumab-treated IBD patients (n=7) did not cross-react with neither Remicade nor Remsima.

Conclusion

Antibodies to Remicade in Remicade-treated IBD patients recognize Remsima to a similar extent, suggesting shared immuno-dominant epitopes on these two infliximab agents. In contrast, there is no cross-reactivity of anti-adalimumab antibodies to Remsima or Remicade.

Appendix F

IBD Section Statement on Biosimilar drugs

The BSG welcomes the introduction of new agents to treat patients with IBD. Drugs that increase treatment options and generate price competition that ultimately benefit patients are necessary and desirable: the healthcare economy is finite and patient access to biologics, in particular, is limited by the NICE models of cost effectiveness.

Anti-TNF biosimilar drugs appear to provide a new means of treating patients with agents that resemble drugs in current use: we note the position of EMA on the similarity.

It is noted that manufacturing processes have changed since infliximab (Remicade) was launched and the drug we use now is not necessarily identical to the one used in the original trials. Remicade may already be its own biosimilar.

Most anti-TNF mAbs have been shown to be effective in both Crohn's disease and ulcerative colitis.

It is reasonable to suppose that biosimilar anti-TNFs will also be effective. The target epitopes appear to be the same although the post translation modification by bacteria may differ: such details are not in the public domain.

There is evidence that biosimilar anti TNFs are effective in some rheumatological diseases.[1,2] There is no published evidence at all in IBD. The IBD Committee are aware of three studies that will begin to fill this void

ClinicalTrials.gov Identifier: NCT02066272 (SATIMOS),

ClinicalTrials.gov Identifier: NCT02148640 (Nor-Switch),

ClinicalTrials.gov Identifier: NCT02096861 - Demonstrate non-inferiority in Efficacy and to Assess Safety of CT-P13 in Patients With Active Crohn's Disease.

At present, we urge caution until we have more data. We recommend:

1. Prescribing by brand name, e.g. use Remicade rather than infliximab.
2. For patients already on therapy, avoidance of switching from parent drug to biosimilar, or vice versa, at least until we have safety data.
3. The use of a prospective registry of all biological use in IBD to capture safety data, rare and new side effects. We recommend the IBD Registry (www.ibdbiologicsaudit.org).
4. Discussion with patients about the choice of anti-TNF.
5. A substantial discount in line with Norway (39%) and Poland (31%)[3], to facilitate market access by the biosimilar in order to gain real-world experience. However, any apparent cost advantage must be balanced against the uncertain efficacy and unknown risk from the biosimilar. Product specific data (from IBD trials) will mitigate against this concern.

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Appendix G

Kang YS et al. Clinical Experience of the Use of CT-P13, a Biosimilar to Infliximab in Patients with Inflammatory Bowel Disease: A Case Series. Dig Dis Sci 2014 Oct 18. DOI 10.1007/s10620-014-3392-z [Epub ahead of print]

Abstract

Background CT-P13 is the first biosimilar monoclonal antibody to infliximab. However, the antibody was tested only in rheumatoid arthritis and ankylosing spondylitis, which demonstrated equivalence to the originator in efficacy, safety, and pharmacokinetic profile. Extrapolation of its efficacy and safety to other pathologies is tenuous. Interchangeability with its originator is another unclear area.

Aim

We aimed to describe the experience of CT-P13 use in inflammatory bowel disease at a tertiary center.

Methods

Seventeen subjects diagnosed with Crohn's disease (CD, n = 8) or ulcerative colitis (UC, n = 9) who were administered CT-P13 from November 2012 to October 2013 at Dongguk University Ilsan Hospital were retrospectively enrolled. Medical records analyzed included patients' characteristics, previous history of anti-tumor necrosis factor administration, response and remission to this biosimilar antibody, disease flare-up, and adverse drug reaction.

Results

Male-female ratio was 1.8. Mean age was 35.4 years (range 15-57). Mean number of CT-P13 administrations was 4.2 ± 1.9. Induction treatments were done in five UC and three CD patients. Clinical response and remission at 8 weeks were achieved in seven patients (five UC and two CD). One CD patient did not respond to CT-P13. Nine patients in maintenance with the originator were interchanged with CT-P13 (four UC and five CD patients). One UC patient experienced arthralgia and CTP13 was discontinued. One patient experienced loss of response during the study period.

Conclusions

CT-P13 may have biosimilarity and interchangeability with its originator in inflammatory bowel disease. A large, randomized, double-blind, prospective study is needed.

Appendix H

Jahnsen J. The new era of biologic therapy in gastroenterology – case report. Presented at an industry sponsored satellite symposium, UEGW (United European Gastroenterology Week), Vienna, Oct 2014.

New "real world" data suggests that the efficacy of Remsima® (infliximab), a biosimilar monoclonal antibody (mAb) anti-TNF-alpha agent approved by the European Commission, is similar to Remicade® (infliximab) in the treatment of IBD (Crohn's disease and ulcerative colitis).

Monoclonal antibodies are complex substances that bind to specific molecules, in the case of infliximab to tumor necrosis factor (TNF) alpha, a protein promoting the inflammatory response associated with auto-immune disorders.

Presenter Jørgen Jahnsen, MD, professor of gastroenterology at the University of Oslo in Norway, said, "Whilst biologics have become increasingly important as a treatment option for IBD, they are also expensive which may mean that some patients have limited access to them. The availability of a biosimilar anti-TNF-alpha could contribute to improving patient access to advanced biologic treatments."

Dr. Jahnsen reported on disease activity at week 14 in 46 IBD patients, following 3 infusions of Remsima.

Of the 26 Crohn's patients, 17 were women and 19 were men. Mean age was 37 years. Mean disease duration was 6.8 years.

Measures of disease activity for Crohn's were changes in HBI (Harvey Bradshaw Index), calprotectin (a marker in the feces of gastrointestinal inflammation) and CRP (C-reactive protein).

Of the 20 ulcerative colitis patients, 7 were women and 13 were men. Mean age at diagnosis was 33 years. Mean age at start of treatment was 39 years. Mean disease duration was 5.6 years.

Measures of disease activity for ulcerative colitis were changes in Partial Mayo Score, Simple Activity Index and calprotectin.

He reported that the Crohn's patients achieved significant improvements in HBI, calprotectin and CRP.

Likewise, the ulcerative colitis patients achieved significant improvements in Partial Mayo Score, Simple Activity Index and calprotectin.

No unexpected adverse events appeared during the 14 weeks of treatment and evaluation.

Dr. Jahnsen concluded that, "The efficacy and safety of Remsima in the treatment of IBD appears to be similar to Remicade."

http://www.medicalupdateonline.com/2014/10/remsima-a-biosimilar-infliximab-shows-efficacy-and-safety-in-real-world-analysis/

Information compiled by James Kent, PrescQIPP NHS Programme, April 2015 and reviewed by Katie Smith, East Anglia Medicines Information Service, May 2015.

Non-subscriber publication September 2015.