Golimumab (Simponi) for ulcerative colitis - second line

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The National Horizon Scanning Centre Research Programme is part of the National Institute for Health Research
Golimumab (Simponi) for ulcerative colitis - second line

Target group
- Ulcerative colitis (UC) in adults: moderate to severe - second line after failure of corticosteroids or immunomodulators.

Technology description
Golimumab (Simponi; CNTO-148) is a high affinity, fully humanised monoclonal antibody, directed against tumour necrosis factor-α (TNF-α). Golimumab inhibits the interaction between TNF-α and the p55 and p75 cell surface receptors, neutralising its biological effects\(^1\). In the phase III trial, golimumab was administered subcutaneously (SC) at doses of 50mg or 100mg every 4 weeks.

Golimumab is licensed in the EU for the treatment of moderate to severe active rheumatoid arthritis, active and progressive psoriatic arthritis and severe ankylosing spondylitis. Common reported side effects include upper respiratory tract infections.

Golimumab is in phase III development for juvenile rheumatoid arthritis and phase II development for sarcoidosis.

Innovation and/or advantages
Golimumab offers an alternative and potentially more convenient route of administration compared to infliximab (intravenous) providing an additional treatment option for this patient group.

Developer
MSD.

Availability, launch or marketing dates, and licensing plans
In phase III clinical trials.

NHS or Government priority area
None identified

Relevant guidance
- NICE technology appraisal in development. Ulcerative colitis (moderate to severe, second line) – adalimumab. Expected date of issue to be confirmed\(^3\).
- NICE technology appraisal. Infliximab for the treatment of acute exacerbations of ulcerative colitis. 2008\(^3\).
- NICE technology appraisal. Infliximab for subacute manifestations of ulcerative colitis. 2008\(^4\).
- NICE clinical guideline. Colonoscopic surveillance for prevention of colorectal cancer in people with ulcerative colitis, Crohn’s disease or adenomas. 2011\(^5\).
- NICE interventional procedure guidance. Leukapheresis for inflammatory bowel disease. 2005\(^6\).
- British Society of Gastroenterology. Guidelines for the management of inflammatory bowel disease in adults. 2011\(^7\).

Clinical need and burden of disease
UC is a form of chronic inflammatory bowel disease (IBD) affecting the colon and rectum. The most common symptoms are abdominal cramping, faecal urgency and bloody diarrhoea. Patients with IBD are at an increased risk of developing colorectal cancer, thought to be the result of chronic inflammation of the gastrointestinal mucosa. Patients with UC have approximately 20% lifetime risk of colorectal cancer, with the risk increasing with the duration of the disease. Colorectal cancer is rarely encountered in patients experiencing colitis for less than seven years. Thereafter the risk is estimated to increase at a rate of 0.5-1.0% per year.

The prevalence of UC in England and Wales is estimated to be around 120,000 to 150,000 people, with an incidence of 10-20 per 100,000 (approximately 5,400-10,800 new cases per year in England and Wales). The highest incidence of UC is observed between the ages of 10 and 40 years, although 15% of patients are over the age of 60 at diagnosis. The clinical course of UC is marked by exacerbation and remission, with around 50% of patients experiencing a relapse in any year. Flare-ups can significantly affect patients’ quality of life; around 55% of patients report flare-ups every few months, 9% have monthly flare-ups, and a further 9% experience weekly problems.

In 2009-2010 there were 34,096 admissions for UC in England, resulting in 80,584 bed days and 41,188 finished consultant episodes (ICD10 K51). UC has a slight excess of mortality in the first two years after diagnosis, but little subsequent difference from the general population thereafter. A severe attack of UC can be potentially life threatening, and in 2009 there were a total of 149 registered deaths in England and Wales.

Existing comparators and treatments
Treatment of UC involves induction of remission in patients with active disease and subsequent maintenance of remission.

Treatments include:

- Aminosalicylates – mild to moderate UC. Available as oral preparations, retention enemas, rectal foam preparation and suppositories (examples include mesalazine, balsalazide sodium and sulphasalazine).
- Corticosteroids – moderate to severe relapsing UC. Available as oral preparations, parenteral preparations, retention enemas and rectal foam preparations (examples include prednisolone, beclometasone dipropionate, hydrocortisone).
- Ciclosporin – severe UC, not responding to intravenous (IV) corticosteroids.
- Infliximab – moderate to severe UC refractory to corticosteroids and/or immunosuppressive agents (recommended by NICE as an option for treatment of acute exacerbations where ciclosporin is contra-indicated or inappropriate).
- Unlicensed immunosuppressants are sometimes used, including azathioprine, methotrexate and 6-mercaptopurine.
- Colectomy.

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* Expert personal communication
## Efficacy and safety

<table>
<thead>
<tr>
<th>Trial</th>
<th>NCT00487539, CR014176, C0524T17, 2006-003398-28; adults; golimumab vs placebo; phase II/III.</th>
<th>NCT00488631, CR014179, 2006-003399-37, C0524T18; adults; golimumab vs placebo; phase III extension.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>Centocor.</td>
<td>Centocor.</td>
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<tr>
<td>Status</td>
<td>Complete but unpublished.</td>
<td>Ongoing.</td>
</tr>
<tr>
<td>Source of information</td>
<td>Trial registry¹⁵.</td>
<td>Trial registry¹⁶.</td>
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<tr>
<td>Location</td>
<td>EU (inc UK), USA, Canada and other countries.</td>
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<tr>
<td>Design</td>
<td>Randomised, placebo-controlled.</td>
<td>Randomised, placebo-controlled.</td>
</tr>
<tr>
<td>Participants and schedule</td>
<td>n=676 (planned); adults; moderate to severely active UC; failure of corticosteroids or immunomodulators; history of or current corticosteroid dependency. Arm 1 Week 0 - 1 x golimumab 100mg SC plus 3 x placebo SC. Week 2 - 1 x golimumab 50mg SC plus 2 x placebo SC. Arm 2 Week 0 - 2 x golimumab 100mg SC plus 2 x placebo SC. Week 2 - 1 x golimumab 100mg SC plus 2 x placebo SC. Arm 3 Week 0 - 4 x golimumab 100mg SC. Week 2 - 2 x golimumab 100mg SC plus 1 x placebo SC. Arm 4 Week 0 - 4 x placebo SC. Week 2 - 3 x placebo SC.</td>
<td>n=1,350 (planned); completed trial NCT00487539. Arm 1 3 x placebo SC every 4 weeks through 52 weeks. Arm 2 1 x golimumab 50mg SC plus 2 x placebo SC every 4 weeks through 52 weeks. Arm 3 1 x golimumab 100mg SC plus 2 x placebo SC every 4 weeks through 52 weeks.</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Active treatment period 6 weeks.</td>
<td>Active treatment period 54 weeks.</td>
</tr>
<tr>
<td>Primary outcome</td>
<td>Safety and efficacy in inducing clinical response at week 6.</td>
<td>Safety and efficacy in maintaining clinical response at week 54.</td>
</tr>
<tr>
<td>Secondary outcome</td>
<td>Efficacy of different dosing regimens in inducing clinical remission, mucosal healing, improving disease-specific health-related quality of life at week 6.</td>
<td>Efficacy of different dosing regimens in maintaining clinical remission and mucosal healing at week 30 and 54; clinical remission; corticosteroid use at week 54.</td>
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<tr>
<td>Expected reporting date</td>
<td>Previously reported as October 2010.</td>
<td>Estimated study completion date October 2012.</td>
</tr>
</tbody>
</table>

## Estimated cost and cost impact

The cost of golimumab for this indication is not yet known. However, the cost of golimumab 50mg (pre-filled pen or pre-filled syringe) for its licensed indication is
The cost of infliximab (IV) at a dose of 5mg/kg at weeks 0, 2, 6 and every 8 weeks thereafter would be £13,428 in the first year.

Claimed or potential impact – speculative

Patients
- Reduced mortality or increased length of survival
- ✓ Reduction in associated morbidity or improved quality of life for patients and/or carers
- ◐ Quicker, earlier or more accurate diagnosis or identification of disease
- ◐ Other:
- ◐ None identified

Services
- ✓ Decreased use: SC administration.
- □ Increased use
- □ Service organisation
- □ Other:
- □ Staff requirements
- □ None identified

Costs
- □ Increased unit cost compared to alternative
- □ Increased costs: more patients coming for treatment
- □ Increased costs: capital investment needed
- □ New costs:
- ✓ Savings: Uncertain unit cost compared to alternative therapeutic options
- ◐ Other: dependent upon dosing regimen.

Other issues
- □ Clinical uncertainty or other research question identified:
- □ None identified

References


Based on average weight 76.9kg (men and women) and average surface area 1.7m².
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