The Ideal Management of Crohn’s Disease: Top Down Versus Step Up Strategies. A Prospective Controlled Trial in the Benelux.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27896

Source
Nationaal Trial Register

Brief title
N/A

Health condition

Crohn's disease.

Sponsors and support

Primary sponsor: Investigator Initiated Study.
Source(s) of monetary or material Support: N/A

Intervention

Outcome measures

Primary outcome

Remission (CDAI < 150) at 6 months starting at randomization. The treatment phase of the

study will last two years, but follow-up will be extended as long as feasible.

Secondary outcome

1. Remission (CDAI < 150) at 9, 12, 15, 18, 21 and 24 months following randomization;

2. IBDQ and EUROQoL measured every three months;

3. Number of draining fistulas at any point of evaluation;

4. Serious adverse events caused by medication with causality assessment (WHO criteria);

5. Prednisone/Budesonide/Prednisolone free days;

6. Number of days absent from work, school or normal daily activities due to disease related problems (should also be assessed for the month prior to randomization);

7. Number and type of surgeries for Crohn’s disease or related problems;

8. Number of days in the hospital for Crohn’s related problems and for any other problems;

9. Total cost of medication, surgeries and hospitalisation during the 2 year period and possibly beyond (pharmaco-economic evaluation) + visits to specialist/general practitioner.

Study description

Background summary

N/A

Study objective

Newly diagnosed Crohn's disease patients will benifit more from a 'top-down' approach where they receive the most potent therapy available, than from the current 'step-up' strategy where they start with the least potent treatment and build up to the most potent therapy if necessary.

Study design

N/A

Intervention

Randomization strategy 1:

TOP-DOWN Start infliximab 5 mg/kg three infusions at week 0, 2 and 6 + azathioprine 2 to 2.5 mg/kg day from day 0 onwards.

If patients improve and tolerate both drugs:
Conintue azathioprine, repeat infliximab 1 infusion 5 mg/kg if relapse.

If patients respond (decrease of CDAI >50 if CDAI 200-250 at start, or > 75 if CDAI 250-350 at start, or >100 if CDAI at start >350)but do not tolerate azathioprine, even when given as split dose, with meals or as an evening dose, or in case of pancreatitis: stop azathioprine, start MTX IM 25 mg/week for 12 weeks, then tapered to 15 mg/week IM together with folic acid 2 mg/day PO.
If symptoms flare (see section 8.1.4) in spite of MTX/azathioprine, repeat infliximab 1 infusion 5 mg/kg.

If patients do not improve on the above mentioned strategy:

Cross over to prednisone 40 mg/day or methylprednisolone 32 mg/day at least 4 weeks after the last infliximab infusion.
Continue azathioprine (or MTX)

Taper as outlined below.

Randomization strategy 2:

STEP-UP
First line treatment:

1. Entocort CIR/Budenofalk 9 mg per day OM for ileal or ileocolonic involvement OR Medrol 32 mg/Prednisone 40 mg per day for colonic involvement alone or in case of severe EIM, poor general well-being or fever.

2. Antibiotics (Flagyl or quinolones) to be added at the discretion of the investigator.

3. Initial therapy with IV methylprednisolone for up to 14 days allowed. TPN/enteral nutrition allowed as adjunctive therapy.

If improvement: tapering following guidelines.

Second line treatment:

1. if symptoms flare (increase of CDAI >50 and CDAI > 200) during corticosteroid tapering, go back to starting dose and try to taper again. Exclude complications such as abscesses or strictures.

2. if relapse during second attempt to taper, add azathioprine 2-2.5 mg/kg/day PO

3. if relapse within 4 months after steroid withdrawal, start steroids again, this time in combination with azathioprine.

4. if refractory to corticosteroids after 4 weeks, increase the dose to 80 mg of prednisone (64 mg methylprednisolone) and add azathioprine

Adding azathiopine: start 2 to 2.5 mg/kg/day, together full dose of corticosteroids. Try to taper the steroids again according to guidelines.

Third line treatment:

1. pts with severe adverse events on azathioprine:

Stop azathioprine, start MTX 25 mg/week. After three injections, start tapering corticosteroids again.

2. pts who cannot be withdrawn from steroids in spite of azathioprine for at least 4 months in optimal dose: Continue azathioprine, start Infliximab 5 mg/kg at weeks 0, 2 and 6 without increasing the steroids ! Continue to taper steroids after 3 infliximab infusions.

Fourth line treatment:
pts with severe relapse in spite of MTX or intolerant to azathioprine and MTX.
Start Infliximab 5 mg/kg at weeks 0, 2 and 6. One single 5 mg/kg infusion to be repeated upon relapse of symptoms. Continue MTX if tolerated.

Contacts

Public
Academic Medical Center (AMC),
Department of Gastroenterology,
P.O. Box 22660
M.J. Spek, van der
Meibergdreef 9
Amsterdam 1100 DD

The Netherlands
+31 (0)20 5666545
Scientific
Academic Medical Center (AMC),
Department of Gastroenterology,
P.O. Box 22660
M.J. Spek, van der
Meibergdreef 9
Amsterdam 1100 DD
The Netherlands
+31 (0)20 5666545

Eligibility criteria

Inclusion criteria

1. Men and women age 16 -75;

2. New diagnosis of Crohn's disease, endoscopically and histologically OR radiologically (in the case of small bowel disease) proven;

OR

- diagnosis of Crohn's disease in the previous 4 years but NEVER treated with corticosteroids/budesonide or immunomodulators (azathioprine/6-mercaptopurine / methotrexate / cyclosporine / FK 506 / Mycophenolate Mofetil) or biologics (Remicade or any other investigational drugs);

3. CDAI > 200 for more than four weeks (to exclude self-limited problems) in new patients or > 200 for more than two weeks for patients with known CD;

4. Symptoms do NOT improve with 5-ASA therapy in appropriate doses (Pentasa 4 grams per day for 6 weeks) or are considered too serious to be treated with 5-ASA alone. Antibiotics can be given at the discretion of the investigator;

5. Willing to sign the informed consent form;

6. Ability to comply with study visits and other protocol requirements;

7. Women of childbearing potential must be willing to use adequate birth control measures in the 6 month period following each infliximab infusion. If pregnant, they will be excluded from further Infliximab infusions.

Exclusion criteria

1. Need for surgery at diagnosis or in the immediate future: complications such as abdominal abscess or stricture with obstruction;

2. Current signs or symptoms of severe, uncontrolled or progressive renal, hepatic, hematologic, endocrine, pulmonary, cardiac, neurologic or cerebral disease;

3. Serious infections such as viral hepatitis, pneumonia, pyelonephritis in the last 3 months;

4. Recent or ongoing tuberculosis (< 2 years) or treatment for tuberculosis.
- Less serious infections should be treated appropriately, after which the patient can be included upon the discretion of the investigator;

5. Use of biologics, corticosteroids or immunemodulators for other diseases;

6. Documented HIV infection;

7. Any currently known malignancy or premalignant lesion or any history of malignancy in the last 5 years;

8. Active pregnancy or immediate pregnancy wish; pregnancy should be deferred until at least 6 months after the last infliximab infusion.
-Patient on azathioprine have to continue this medication should they become pregnant during the study;

9. Allergy to murine proteins

10. Known recent substance abuse (drugs or alcohol);

11. Symptomatic stenosis or ileal/colonic strictures with prestenotic dilatation;

12. Positive stool culture for enteric pathogens.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-05-2001
Enrollment:	130
Type:	Actual

Ethics review

Positive opinion

Date:	12-09-2005
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL341
NTR-old	NTR379
Other	: N/A
ISRCTN	ISRCTN61510219

Study results

Summary results
N/A