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

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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...

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON27896

Bron
Nationaal Trial Register

Verkorte titel
N/A

Aandoening

Crohn's disease.

Ondersteuning

Primaire sponsor: Investigator Initiated Study.
Overige ondersteuning: N/A

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

N/A

Doel van het onderzoek

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.

Onderzoeksopzet

N/A

Onderzoeksproduct en/of interventie

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.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-05-2001
Aantal proefpersonen:	130
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	12-09-2005
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten

Samenvatting resultaten
N/A