A randomized phase III study to evaluate the efficacy of chemoimmunotherapy with the monoclonal antibody Campath-1H (Alemtuzumab) given in combination with 2-weekly CHOP versus 2-weekly CHOP alone and consolidated by autologous stem cell transplant, in young patients with previously untreated systemic peripheral T-cell lymphomas

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To demonstrate in a phase III study that the addition of the monoclonal anti-T cell antibody alemtuzumab added to standard CHOP chemotherapy followed by autologous stam cell transplantation will increase the response, event-free survival,...

Ethical review	Approved WMO
Status	Pending
Health condition type	Lymphomas non-Hodgkin's T-cell
Study type	Interventional

Summary

ID

NL-OMON31642

Source
ToetsingOnline

Brief title
Alemtuzumab and CHOP in T-cell Lymphoma in young patients, The ACT-1 Trial

Condition

- Lymphomas non-Hodgkin's T-cell

Synonym
T cell lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: Nordic Lymphoma Group
Source(s) of monetary or material Support: HOVON + KWF (datamanagement)

Intervention

Keyword: Alemtuzumab, peripheral T cell lymphoma, phase III trial, T-cell non-Hodgkin's lymphoma

Outcome measures

Primary outcome

Event-free survival at 3 yr

Secondary outcome

overall survival at 3 yr

progression-free survival at 3 yr

responses (%CR and %PR), at the end of therapy

time to progression

relation CD52 expression and response-rate

safety addition of alemtuzumab to CHOP measured by incidences of infections

Study description

Background summary

The prognosis of patients with peripheral T cell lymphoma is poor despite optimal CHOP-like chemotherapy. In patients with B cell lymphoma, the addition of the B cell monoclonal antibody rituximab to CHOP chemotherapy resulted in a 10-15% survival improvement in both elderly and younger patients. Here, the efficacy and toxicity of the monoclonal anti-T cell antibody alemtuzumab will be studied in a randomized phase III trial. Alemtuzumab will be added to the standard therapy consisting of CHOP chemotherapy followed by consolidating autologous stem cell transplantation (standard arm), since several phase II studies consisting of the combination of alemtuzumab with CHOP showed promising responses with acceptable toxicity. If the addition of alemtuzumab is indeed successful as studied in this phase III setting, this monoclonal antibody will be added to all patients with T cell lymphoma who are candidate for intensive therapy.

Study objective

To demonstrate in a phase III study that the addition of the monoclonal anti-T cell antibody alemtuzumab added to standard CHOP chemotherapy followed by autologous stam cell transplantation will increase the response, event-free survival, progression-free survival and overall survival, without unacceptable additional toxicity.

Study design

Multicenter randomized phase III trial, see above

Intervention

the addition of alemtuzumab to standard CHOP-14 followed by autologous transplant

Study burden and risks

Standard induction treatment consists of CHOP, given at 2 weeks interval. The addition of alemtuzumab requires subcutaneous injections at day 1 and 2. The first 2 injections can cause transient painful infiltrates. The risk on infections is increased requiring additional antibiotics and blood controls, especially related to CMV re-activations. Blood products need to be irradiated.

Contacts

Public
Nordic Lymphoma Group

Aarhus University Hospital Tage Hansens Gade 2
8000
DK
Scientific
Nordic Lymphoma Group

Aarhus University Hospital Tage Hansens Gade 2
8000
DK

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Age: 18-65 years
2. All stages, including stage I with bulk (>= 7.5 cm)
3. Confirmed histological diagnosis of peripheral T cell NHL of the following types:
peripheral T-cell lymphoma PTCL-NOS
Angioimmunoblastic T cell lymphoma
Anaplastic large cell lymphoma, only if primary systemic and ALK-negative
intestinal T/NK-cell lymphoma (± enteropathy)
hepatosplenic gamma-delta lymphoma
subcutaneous panniculitis-like PTCL
extranodal NK/T cell lymphoma, nasal type
4. Performance status: ECOG 0 - 2 (Karnofsky index: 60 - 100%). ECOG 3 is acceptable, if lymphoma related.
5. Measurable disease
6. written consent of the patient
7. life expectancy of 3 months or longer

Exclusion criteria

1. Stage I with IPI 0 and without bulk
2. Already initiated lymphoma therapy
3. Serious accompanying disorder or impaired organ function, in particular:
- severe cardiac dysfunction (NYHA class II-IV; LVEF <45%)
- severe pulmonary dysfunction (FeV1<50% or DC <50%)
- Renal: creatinine >150 umol/l, unless related to NHL
- Hepatic: bilirubin >2.5 times the upper reference limit, unless related to NHL
- Uncontrollable diabetes mellitus (prephase treatment with prednisone!)
4. T-cell malignanies of other categories
5. CNS involvement
6. Known hypersensitivity to the medications to be used, especially murine or chimeric antibodies
7. uncontrolled asthma or allergy
8. Known HIV-positivity
9. Active hepatitis infection, active CMV infection, active systemic fungal infection, active infection with mycobacterium tuberculosis or atypical tuberculosis
10. Suspicion that patient compliance will be poor
11. Simultaneous participation in any other study protocol
12. Prior chemo- or radiotherapy for malignancy
13. Other concomitant malignant disease (history of active cancer during the past 5 years, except basal carcinoma of the skin or stage 0 cervical carcinoma)
14. Non-conformity to eligibility criteria

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL
Recruitment status: Pending

Start date (anticipated):	01-05-2008
Enrollment:	40
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Mabcampath
Generic name:	Alemtuzumab, Monoclonal antibody Campath-1H
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	06-06-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-06-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-11-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-06-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2006-006130-17-NL
CCMO	NL18525.042.08