

# AHOD0031

No registrations found.

<b>Ethical review</b>	Positive opinion
<b>Status</b>	Recruiting
<b>Health condition type</b>	-
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON25408

### Source

NTR

### Brief title

N/A

### Health condition

paediatric patients, intermediate risk hodgkin disease, Hodgkin.

## Sponsors and support

**Primary sponsor:** The Children's Oncology Group, USA

**Source(s) of monetary or material Support:** Dutch Childhood Oncology Group, The Hague

## Intervention

## Outcome measures

### Primary outcome

Efficacy endpoints.

The primary endpoint for efficacy analysis is event-free survival (EFS), which is the minimum time from study entry, time of response assessment, or randomization (as appropriate) until treatment failure (disease progression, disease recurrence, biopsy positive residual after completion of all protocol therapy), occurrence of a second malignant neoplasm, or death

from any cause.

The patients to be included in the analyses for Aim 1.12 (=To determine whether involved field radiation therapy (IFRT) can be eliminated based upon early and complete response to multiagent chemotherapy.)

are the cohort of all RER patients who are randomized. The patients to be included in the analyses for Aim 1.13 (=To determine whether the addition of an additional two cycles of chemotherapy (DECA) can improve outcome in those with a slow early response to standard chemotherapy.)

are the cohort of all SER patients who are randomized. These analyses will include randomized patients with protocol violations and randomized patients removed for protocol therapy. However, patients who are determined to be ineligible based on the study eligibility/entry criteria will be excluded.

Toxicity endpoints.

The primary endpoint for toxicity analysis will be occurrence of any key toxicity, which in this study is the occurrence of any Grade 4 non-haematologic toxicity, or Grade 3 non-haematologic toxicity that doesn't respond to treatment within 7 days despite recommended therapy modification, or toxic death, which is any death primarily attributable to treatment. Exceptions are Grade 3 nausea, vomiting or liver function abnormalities that return to Grade  $\leq$  2 within 7 days.

All treated patients will be included in the toxicity analyses.

## **Secondary outcome**

Secondary efficacy endpoints are overall survival (OS) and disease response.

# **Study description**

## **Background summary**

Cure rates for pediatric Hodgkin disease remain among the highest in pediatric oncology. However, cure often comes with a significant cost in the form of delayed effects of therapy. This protocol will evaluate a dose intensive regimen ABVE-PC in the treatment of intermediate risk Hodgkin disease. This protocol will combine dose intensity with response-based augmentation or reduction in therapy to

- 1) improve outcome for all intermediate risk pediatric patients with Hodgkin disease and
- 2) decrease the risk for delayed effects of treatment.

The standard arm for this protocol will be 4 cycles of ABVE-PC plus consolidative involved field radiation therapy. Slow early responders will be randomized to either the standard arm, or the augmented therapy arm, which will add 2 additional cycles of different chemotherapy (DECA) to the standard arm. Rapid early responders who then go on to a complete response following 4 cycles of chemotherapy will be randomized to the standard arm, or the reduced therapy arm, where consolidative radiation therapy will be omitted.

## **Study objective**

To determine whether involved field radiation therapy (IFRT) can be eliminated based upon early and complete response to multiagent chemotherapy

To determine whether the addition of an additional two cycles of chemotherapy (DECA) can improve outcome in those with a slow early response to standard chemotherapy.

## **Study design**

Every year : interim report for the overall-study,

Per patient:

Response will be assessed at the following time points:

In all patients after 2 cycles of ABVE-PC.

In all patients, after completion of 4 cycles of ABVE-PC.

In SER group, after completion of 2 cycles of DECA and if still not in CR, after all chemotherapy, prior to RT.

In all patients who receive IFRT, 6 weeks after completion of IFRT only if not in CR at start of radiotherapy.

In ALL patients, 12 weeks after completion of therapy (chemotherapy or radiation therapy whichever ended last).

## **Intervention**

The standard arm for this protocol will be 4 cycles of ABVE-PC plus consolidative involved field radiation therapy. Slow early responders will be randomized to either the standard arm, or the augmented therapy arm, which will add 2 additional cycles of different chemotherapy (DECA) to the standard arm. Rapid early responders who then go on to a complete response following 4 cycles of chemotherapy will be randomized to the standard arm, or the reduced therapy arm, where consolidative radiation therapy will be omitted.

## Contacts

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## Eligibility criteria

### **Inclusion criteria**

- Patients with newly diagnosed, pathologically confirmed Hodgkin disease (all histologies) are eligible for this protocol if they meet the following clinical stage guidelines:

1. All Stage IB regardless of bulk disease
2. All Stage IIB regardless of bulk disease
3. Stage IA only with bulk disease
4. Stage IIA only with bulk disease
5. All Stage IAE, IIAE regardless of bulk disease
6. All Stage IIIA, IIIAE, IIIS, IIIAE+S regardless of bulk disease
7. All Stage IVA, IVAE regardless of bulk disease

See Appendix I of the protocol for definitions of clinical staging, E criteria, B symptoms and bulk disease.

## Clinical Staging

Staging on this study will be determined by the clinical stage. Patients who have surgical staging (by laparotomy) alone are ineligible for entry on this protocol. Surgically staged patients may be entered on this study if they also have pre-surgical staging that meets the above criteria. Surgical staging is strongly discouraged.

8. Ages 0 - 21 years inclusive.

### 9. Organ Function Requirements

- Adequate renal function defined as:

\* Creatinine clearance or radioisotope GFR  $\geq 70\text{ mL/min/1.73m}^2$   
or

\* A serum/plasma creatinine calculation using the Schwartz formula

(Schwartz et al. J. Peds, 106:522, 1985)

Estimated Creatinine Clearance (in mL/min/1.73 m<sup>2</sup>)\*\* =  
 $(k)(L)/\text{Pcr}$

Where L = child's length in cm

Pcr = plasma (or serum) creatinine (in mg/dL)

k Values =

0.33 low birth weight infant

0.45 term infant

0.55 child

0.55 adolescent female

0.70 adolescent male

\*\*The conversion formula for serum/plasma creatinine when reported in  $\mu\text{Mol/L}$  units:

$(k \cdot \text{ht})/(\text{sCr in } \mu\text{Mol/L} \cdot 88.4)$

\* Adequate liver function defined as:

-Total bilirubin  $\leq 1.5 \times$  normal, and

- SGOT (AST) or SGPT (ALT)  $< 2.5 \times$  normal.

\*Adequate cardiac function defined as:

- Shortening fraction of  $\geq 27\%$  by echocardiogram, or if echocardiogram not feasible, ejection fraction of  $\geq 50\%$  by radionuclide angiogram (MUGA), unless due to large mediastinal mass from HD. Study chair approval required for entry onto protocol with shortening fraction  $< 27\%$  or ejection fraction  $< 50\%$ .

- No pathologic prolongation of QTc interval on 12-lead ECG

\* Adequate pulmonary function defined as:

- FEV1/FVC  $> 60\%$  by pulmonary function test, unless due to large mediastinal mass from HD. Study chair approval required for entry onto protocol with FEV1/FVC  $\leq 60\%$

- For children who cannot adequately perform PFTs, no evidence of dyspnea at rest, no exercise intolerance, and a pulse oximetry  $> 94\%$ . PFTs should not be attempted for children under the age of 7 years.

Patients with other pre-existing cardiac or pulmonary abnormalities require Study Chair approval prior to being placed on therapy.

10. Women who are pregnant or breast-feeding will not be eligible.

11. Previous therapies. Patients may not have received any previous chemotherapy, biological modifiers such as monoclonal antibody therapy or radiation therapy. Patients may not have received corticosteroids within 28 days of enrollment on this protocol, except as specified in Section 5.1 for emergent treatment for respiratory distress or spinal cord compression, or for treatment of contrast agent allergy required for CT scan.

12. Venous access.

Adequate venous access is required. An infusaport (portacath) is recommended, but not required.

13. Informed Consent.

The patient and/or the patient's legally authorized guardian must acknowledge in writing that consent to become a study subject has been obtained, in accordance with institutional policies approved by the U.S. Department of Health and Human Services.

14. Protocol Approval.

Approval for the use of this treatment protocol by the individual institution's Human Rights Committee must be obtained, in accordance with the institutional assurance policies of the

## Exclusion criteria

Criteria for case exclusion include:

1. Equivocal immunophenotyping results
2. Morphologically unclassifiable lymphoma
3. Pathology review diagnosis not included in this study

## Study design

### Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

### Recruitment

NL	
Recruitment status:	Recruiting
Start date (anticipated):	15-05-2006
Enrollment:	1700
Type:	Anticipated

## Ethics review

Positive opinion	
Date:	28-04-2008
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	NL1256
NTR-old	NTR1302
Other	METC : 2004/019
ISRCTN	ISRCTN wordt niet meer aangevraagd.

## Study results