Efficacy and feasibility of first-line treatment with risk-adapted dose-adjusted EPOCH-R (DA-EPOCH-R) in patients with Burkitt lymphoma. A phase II clinical trial.

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Primary objectives-Determine efficacy, defined as PFS and OS at 2 years of risk-adaptive DA-EPOCH-R in newly diagnosed Burkitt lymphoma patients 18-75 years.-Determine feasibility, defined as > 60% of cycles of the DA-EPOCH-R scheme on an out-...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lymphomas non-Hodgkin's B-cell
Study type	Interventional

Summary

ID

NL-OMON36941

Source
ToetsingOnline

Brief title
DA-EPOCH-R trial

Condition

- Lymphomas non-Hodgkin's B-cell
- Lymphomas non-Hodgkin's B-cell

Synonym
Burkitt lymphoma, highly aggressive B cell lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Burkitt Lymphoma

Outcome measures

Primary outcome

Primary endpoints

-2 years overall survival (OS; time from registration. Patients still alive or

lost to follow up are censored at the date they were last known to be alive)

and progression free survival (PFS; i.e. time from registration to progression

or death from any cause, whichever comes first).

-Number of cycles of the DA-EPOCH-R scheme completed on an out-patient *clinic

basis

Secondary outcome

Secondary endpoint

-Negative predictive value of low dose PET/CT scan after 2 cycles of DA-EPOCH-R

on OS and PFS

Study description

Background summary

The DA-EPOCH-R regimen represents a major paradigm shift for the treatment of BL. Whereas standard treatment relies on dose density and intensity based on methotrexate and cytarabin to achieve adequate cell kill, DA-EPOCH-R relies on a pharmacodynamic based infusional schedule to improve the therapeutic index of chemotherapy. Based on the pilot results presented by Dunleavy at ICML 2011,

DA-EPOCH- R appears to provide a high rate of cure with significantly lower treatment toxicity and tumor lysis syndrome compared to standard treatment. As such, DA-EPOCH-R may provide a major treatment advance in BL by lowering morbidity, mortality, and cost, while maintaining or possibly improving efficacy. The current protocol is aims to confirm the results obtained with DA-EPOCH-R in BL in Dutch general hematology practice, as this protocol has been conducted primarily by the NIH

Study objective

Primary objectives
-Determine efficacy, defined as PFS and OS at 2 years of risk-adaptive DA-EPOCH-R in newly diagnosed Burkitt lymphoma patients 18-75 years.
-Determine feasibility, defined as > 60% of cycles of the DA-EPOCH-R scheme on an out-patient-clinic basis

Secondary objective
-Assess negative predictive value of early FDG-PET/CT scans on PFS in BL.

Study design

Phase II, prospective, monocenter, open label, non-randomized clinical trial of risk adapted DA-EPOCH-R in BL:
* Low risk patients will receive 3 cycles of DA-EPOCH-RR
* High risk patients will receive 6 cycles of DA-EPOCH-R
* CSF cytology will be done in all patients.
* High Risk patients with CSF negative will receive prophylactic intrathecal treatment
* Low risk patients with CSF negative (1 normal LP and no clinical suspicion) will not receive prophylactic intrathecal treatment
* All patients with CSF positive will receive active intrathecal treatment
* FDG-PET/CT pre- and post-cycle 2 in all patients. Low risk patients with positive low-dose PET/CT (positive defined as a score * 3 according to Deauville criteria (appendix B1) after 2 cycles will receive 6 cycles of DA-EPOCH-R
* A total of 22 patients will be enrolled in the protocol.

Intervention

combination chemotherapy

Study burden and risks

The chemotherapy will be given by a portable pump system. Once a day, the patient is requested to visit the hospital for changing the bag.
For the patient is this less demanding than a hospital admission.

For the ward, its beneficial for the bed setting.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* First diagnosis of Burkitt lymphoma, histological confirmed according to the WHO classification 2008
* Patients * 18 years of age.
* No prior treatment except local radiation or short course steroids 1 mg/kg for acute symptoms.
* All disease stages.
* ECOG-WHO status 0-3; WHO status 4 will be allowed if Burkit Lymphoma related.
* Written informed consent obtained according to local guidelines.

Exclusion criteria

* Inadequate renal function or creatinine clearance < 50 ml/min unless lymphoma related.
* Inadequate hepatic function: bilirubin > 2 * ULN (total) except patients with Gilbert*s syndrome as defined by > 80% unconjugated.
* Inadequate hematological function ANC < 1x109/l and platelets < 75x109 /l unless lymphoma related.
* Female subject of child-bearing potential not willing to use an acceptable method of birth control (i.e., a hormonal contraceptive, intra-uterine device, diaphragm with spermicide, condom with
spermicide, or abstinence) for the duration of the study and one year beyond treatment completion.
* Female subject pregnant or breast-feeding.
* Male subject unwilling to use an acceptable method for contraception for the duration of the study and one year beyond treatment completion.
* History of a prior invasive malignancy in past 5 years.
* Active symptomatic ischemic heart disease, myocardial infarction, or congestive heart failure within the past year. If echo is obtained the LVEF should exceed 40%.
* Serious concomitant medical illnesses that would jeopardize the patient's ability to receive the regimen with reasonable safety.
* HIV positive patients not willing to suspend HAART therapy during the treatment period of the protocol.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-11-2012
Enrollment:	22
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cyclophosphamide
Generic name:	Cyclophosphamide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Doxorubicin
Generic name:	Doxorubicin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Etoposide
Generic name:	Etoposide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Prednisolon
Generic name:	Prednisolon
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Vincristine
Generic name:	Vincristine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	06-08-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-10-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	EUCTR2012-003141-16-NL
CCMO	NL41499.029.12
Other	NTR