June 2012

RATHL Trial

A Randomised Phase III Trial to assess response adapted therapy using FDG-PET imaging in patients with newly diagnosed, advanced Hodgkin Lymphoma

Chief Investigator: Professor Peter Johnson

Rationale

A multi-centre randomised trial comparing treatment outcome for patients with advanced Hodgkin lymphoma, using FDG-PET imaging after 2 cycles of ABVD to determine response and subsequent management decisions.

Objectives

Primary

3 year progression free survival

Secondary

Overall survival

Toxicity, both acute (during the treatment) and long term until 5 years from randomisation

Sample size

The plan is to recruit 1200 patients over a 4 year period.

It is anticipated that 800 patients will be recruited from the UK and 400 patients from International Sites.

Current recruitment is 980 (June 2011)

Exclusion

- Cardiac contra-indication to doxorubicin: abnormal contractility on echocardiography or nuclear medicine examination (MUGA)
- Neurological contra-indication to chemotherapy (e.g. pre-existing neuropathy)
- CNS or meningeal involvement by lymphoma
- Poorly controlled diabetes mellitus

Drug supply

Doxorubicin	Bleomycin
Vinblastine	Dacarabazine
Cyclophosphamide	Etoposide
Procarabazine	Prednisolone
Vincristine	

All drugs are to be supplied locally from hospital stock

Trial design (1)

All eligible patients will be given a baseline PET-CT scan and then given 2 cycles of ABVD at full dose and on schedule.

Patients will then have a Response PET-CT scan. PET negative patients will be randomised to either 4 cycles of ABVD or 4 cycles of AVD.

PET positive patients will be given either 4 cycles of BEACOPP-14 or

Eligibility (1)

- Newly diagnosed HL previously untreated
- Aged 18 or above
- Clinical stage IIB, IIIA, IIIB or IV, or Clinical Stage IIA with adverse feature:

o Bulk mediastinal disease

o Outside the mediastinum, lymph node or lymph node mass greater than 10cm

Baseline Assessments

- Laboratory assessment includes FBC, biochemistry, bone marrow function, hormone levels
- Imaging to include CT scan, and PET/CT scan
- Cardiac assessment to include Electrocardiogram and Echo cardiogram or MUGA
- Sperm counts recommended for men and cryopreservation should be discussed

PET Centres

See separate list

Trial design (2)

3 cycles of BEACOPP-escalated.

PET positive patients will then have a 3rd PET-CT Scan.

Patients with a negative score will then continue with either 2 cycles of BEACOPP-14 or 1 cycle of BEACOPP-escalated.

Patients with a positive score will receive radiotherapy or salvage therapy decided by the clinician.

Eligibility (2)

o More than 2 sites of disease

o Other poor risk feature which the clinician feels needs to be treated with a full course of combination chemotherapy

- Performance status 0-3
- Written informed consent
- Agree to take adequate precautions to avoid conception

Assessments & FU

- Prior to each cycle: Physical examination, toxicity and adverse event and Laboratory assessments
- After the final cycle of chemotherapy: Physical examination, toxicity and adverse event assessment, pulmonary function tests and bone marrow if initially involved. FBC and CT Scan.
- Follow up every 3 months during year 1, 4 months in year 2, 6 monthly in year 3, 4 and 5 and annually thereafter
- CT scan at 3 and 12 months and pulmonary function tests to be measured annually

Contact the RATHL trial team for further information:
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Cancer Research UK & UCL Cancer Trials Centre

NCRI National Cancer Research Institute

CANCER RESEARCH UK

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