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Brentuximab vedotin In patients with Hodgkin lymphoma

Submission date 16/10/2013	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 16/10/2013	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 28/05/2020	**Condition category** Cancer	[_] Individual participant data

Plain English summary of protocol
http://www.cancerresearchuk.org/cancer-help/trials/a-trial-looking-at-brentuximab-for-people-with-hodgkin-lymphoma-who-are-unable-to-have-chemotherapy-brevity

Contact information

Type(s)
Public

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT02567851

Clinical Trials Information System (CTIS)
2012-000214-11

Protocol serial number

14703

Study information

Scientific Title
BREVITY: A phase II study of brentuximab vedotin using a response adapted design in patients with Hodgkin lymphoma unsuitable for chemotherapy due to age, frailty or co-morbidity

Acronym
BREVITY

Study objectives
The aim of BREVITY is to assess the effectiveness of a new drug called brentuximab vedotin in patients with newly diagnosed Hodgkins Lymphoma for whom standard chemotherapy is not considered a good option due to age or frailty. Brentuximab vedotin is a new type of drug known as an antibody-drug conjugate and is made up of 2 parts linked together, an anti-body and a chemotherapy drug. The antibody acts like a homing device, and takes the chemotherapy drug directly to the lymphoma cells, where it causes them to die when they try to divide.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES committee East Midlands - Derby; 18/06/2013, ref: 13/EM/0159

Primary study design
Interventional

Study design
Non-randomised; Interventional; Design type: Treatment

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Lymphoma; Disease: Lymphoma (Hodgkin's)

Interventions
Brentuximab vedotin: Antibody-drug conjugate
30 patients will be recruited from hospitals across the UK and will receive a maximum of 16 doses over 48 weeks.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Brentuximab vedotin

Primary outcome(s)

Current primary outcome measure as of 18/05/2018:
Complete metabolic response rate (CMR) after 4 cycles of brentuximab vedotin defined as Deauville score of 1, 2 or 3 at PET 4; Timepoint(s): After 4 cycles (12 weeks)

Previous primary outcome measure:
Complete response rate (CR) after 4 cycles of brentuximab vedotin defined as Deauville score of 1, 2; Timepoint(s): After 4 cycles (12 weeks)

Key secondary outcome(s)

Current secondary outcome measures as of 18/05/2018:
1. Tolerability is defined in terms of absence of toxicities related to brentuximab vedotin quantified by the CTCAE v4 criteria and dose intensity. Dose intensity is defined as the total dose prescribed to each patient as a proportion of the planned protocol dose. Timepoint: 16 cycles
2. Overall objective response rate (ORR), including complete or partial response (CR/PR), after 4 cycles and 16 cycles of treatment with brentuximab vedotin according to the Recommendations for Initial Evaluation, Staging, and Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: The Lugano Classification; Timepoint: 4 and 16 cycles
3. Progression Free Survival (PFS) where progression is defined as the time from date of Cycle 1 Day 1 until documented progressive disease or death from any cause; Timepoint: censored at 2 years after day 1 cycle 1
4. Overall survival (OS) and cause of death. OS is defined as the time from Cycle 1 Day 1 to the date of death from any cause. Alive patients will be censored at their date of last follow-up. Timepoint: censored at 2 years after day 1 cycle 1
5. Deauville score after cycle 2 based on blinded PET2 scan, Timepoint: 2 cycles
6. Correlation of Deauville score after 2 cycles (blinded PET2) with Deauville score after 4 cycles (PET 4), response after 16 cycles, progression-free and overall survival, Timepoint: After 2, 4 and 16 Cycles, Progression or Death.
7. Co-morbidities satisfying eligibility criteria in the study population and documented throughout the study, Timepoint: During treatment and follow-up
8. CIRS-G profile in the study population assessed at baseline, Timepoint: Baseline
9. Any additional treatments administered following treatment with brentuximab vedotin (BV), Timepoint: In follow-up

Previous secondary outcome measures:
1. Tolerability is defined in terms of absence of toxicities related to brentuximab vedotin quantified by the CTCAE v4 criteria and dose intensity. Dose intensity is defined as the total dose prescribed to each patient as a proportion of the planned protocol dose. Timepoint: 4 cycles
2. Overall objective response rate (ORR), including complete or partial response (CR/PR), after 4 cycles and 16 cycles of treatment with brentuximab vedotin according to the Revised Response Criteria for malignant lymphoma. Timepoint: 4 and 16 cycles
3. Progression Free Survival (PFS) where progression is defined according to the Revised Response Criteria for malignant lymphoma [4] is defined as the time from date of Cycle 1 Day 1 until documented progressive disease or death from any cause. Timepoint: censored at 5 years after day 1 cycle 1
4. Overall survival (OS) and cause of death. OS is defined as the time from Cycle 1 Day 1 to the date of death from any cause. Alive patients will be censored at their date of last follow-up. Timepoint: censored at 5 years after day 1 cycle 1
5. Deauville score after cycle 2 based on blinded PET2 scan, Timepoint: 2 cycle

6. Correlation of Deauville score after 2 cycles (blinded PET2) with Deauville score after 4 cycles (PET 4), response after 16 cycles, progression-free and overall survival, Timepoint: After 2, 4 and 16 Cycles, Progression or Death.
7. Co-morbidities satisfying eligibility criteria in the study population and documented throughout the study, Timepoint: During treatment and follow-up
8. CIRS-G profile in the study population assessed at baseline, Timepoint: Baseline
9. Any additional treatments administered following treatment with brentuximab vedotin (BV), Timepoint: In follow-up

Completion date
20/04/2018

Eligibility

Key inclusion criteria
Current inclusion criteria as of 18/05/2018:
1. Histologically confirmed CD30 positive classical Hodgkin lymphoma
2. No previous treatment for classical Hodgkin lymphoma
3. Aged more than or equal to 16 years
4. Stages II (with B symptoms, extranodal disease, bulky disease, more than or equal to sites of nodal involvement, fewer than 3 sites of nodal involvement but unsuitable for radiotherapy because of anatomical distribution or ESR more than or equal to 50 mm/h), III and IV classical Hodgkin lymphoma
5. Any of the following:
At any age and with ECOG score of 0, 1, 2 or 3, for whom standard chemotherapy considered inappropriate because:
5.1. Impaired cardiac function defined either by an ejection fraction of < 50% assessed by echocardiogram or nuclear medicine scan (MUGA)
5.2. Left ventricular ejection fraction more than or equal to 50% measured by echocardiography or MUGA but in the presence of significant co-morbidities or cardiac risk factors such as diabetes mellitus, hypertension, peripheral vascular disease, ischaemic heart disease, previous myocardial infarction, obesity, stroke or transient ischaemic attacks (TIA) that make anthracycline-containing chemotherapy inadvisable as determined by the investigator.
5.3. Heart failure clinically determined by the presence of New York Heart Association (NYHA) heart failure grade II and III due to a cause other than Hodgkin lymphoma
5.4. Impaired respiratory function with DLCO and/or FVC/FEV1 ratio <75% of predicted due to a cause other than Hodgkin lymphoma
5.5. For patients aged 60 years or older, an ECOG score of 2 or 3 for any reason, before the start of permitted steroids and considered unsuitable for treatment with standard chemotherapy by the supervising physician.
6. FDG avid disease – proven by PET scan
7. Measurable disease with at least one lesion measuring >1.5 cm in long axis diameter (for nodal lesions) or >1.0cm in long axis diameter (for extra-nodal lesions)
8. Written informed consent
9. Able to comply with requirements of the protocol (including PET scans)
10. Agree and be able to use adequate contraception if required

Previous inclusion criteria:
1. Histologically confirmed CD30 positive classical Hodgkin lymphoma
2. No previous treatment for classical Hodgkin lymphoma
3. Aged more than or equal to 16 years

4. Stages II (with B symptoms, extranodal disease, bulky disease, =3 sites of nodal involvement, fewer than 3 sites of nodal involvement but unsuitable for radiotherapy because of anatomical distribution or ESR =50 mm/h), III and IV classical Hodgkin lymphoma
5. Any of the following:
At any age, standard chemotherapy considered inappropriate because:
5.1. Impaired cardiac function defined either by an ejection fraction of less than 50% assessed by echocardiogram or
nuclear medicine scan (MUGA)
5.2. Left ventricular ejection fraction =50% measured by MUGA or echocardiography but in the presence of significant comorbidities or cardiac risk factors such as diabetes mellitus, hypertension, peripheral vascular disease, ischaemicheart disease, previous myocardial infarction, obesity, stroke or transient ischaemic attacks (TIA) that make anthracyclinecontaining chemotherapy inadvisable as determined by the treating physician.
5.3. Heart failure clinically determined by the presence of New York Heart Association (NYHA) heart failure grade II and III due to a cause other than HL
5.4.Impaired respiratory function with DLCO and/or FVC/FEV1 ratio less than 75% of predicted due to a cause other than HL for patients aged 60 years or older,
5.5. an ECOG score of 2 or 3 for any reason, before the start of permitted steroids and considered unsuitable for treatment with standard chemotherapy by the supervising physician.
6. FDG avid disease
7. Measurable disease with at least one lesion measuring 1.5 cm in short axis diameter
8. Written informed consent
9. Able to comply with requirements of the protocol (including PET scans)
10. Agree and be able to use adequate contraception if required

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
38

Key exclusion criteria
Current inclusion criteria as of 18/05/2018:
1. Nodular lymphocyte predominant Hodgkin lymphoma
2. Grade 2 or worse peripheral neuropathy
3. Haemoglobin <90 g/l (transfusion allowed)
4. Unsupported neutrophil count <1.0 x 109/l and platelet count <100 x 109/l unless due to bone marrow infiltration by Hodgkin lymphoma demonstrated by trephine biopsy
5. Serum bilirubin more than 1.5 times upper limit normal unless due to Hodgkin lymphoma or

Gilberts syndrome
6. Creatinine clearance < 30 ml/min (calculated by the modified Cockroft-Gault formula) unless due to Hodgkin lymphoma. Patients with an eGFR < 30 ml/min but a measured GFR by another method (e.g. EDTA) of 30ml/min or greater would be eligible
7. Pregnant or lactating women
8. Any other cancer diagnosis within the last 24 months – except for:
8.1. Appropriately treated superficial melanoma, basal cell carcinoma and squamous cell carcinoma of the skin
8.2. Appropriately treated cervical intra-epithelial neoplasia
8.3. In situ or organ confined prostate cancer not currently requiring therapy
Previous cancers treated with curative intent and with no evidence of recurrence following a minimum of at least 2 years of follow-up are permitted.
9. The use of other investigational or anti-neoplastic agents within the previous 6 weeks or during the trial
10. Known to be HIV, Hep B positive (Hep B Core antibody positive allows inclusion providing surface / core antigen both negative) or Hep C positive (Hep C antibody positive allows inclusion providing PCR for viral RNA is negative)
11. Known hypersensitivity to recombinant proteins, murine proteins, or to any excipient contained in the drug formulation of brentuximab vedotin
12. Known cerebral or meningeal involvement by Hodgkin Lymphoma
13. Symptoms or signs of progressive multifocal leukoencephalopathy (PML)
14. Any active systemic viral, bacterial, or fungal infection requiring intravenous antimicrobials within 2 weeks prior to registration
15. Evidence of current uncontrolled cardiovascular conditions, including unstable angina and NYHA grade IV heart failure
16. ECOG score 4 at time of registration

Previous exclusion criteria:
1. Nodular lymphocyte predominant Hodgkin lymphoma
2. Grade 2 or worse peripheral neuropathy
3. Haemoglobin <9 g/dl (transfusion allowed)
4. Unsupported neutrophil count <1.0 x 109/l and platelet count <100 x 109/l unless due to bone marrow infiltration by Hodgkin lymphoma demonstrated by trephine biopsy
5. Serum bilirubin more than 1.5 times upper limit normal unless due to Hodgkin lymphoma or Gilberts syndrome
6. Creatinine clearance less than 30 ml/min (calculated by the modified CockroftGault formula, see appendix) unless due to Hodgkin lymphoma. Patients with a calculated GFR less than 30 ml /min but a GFR by EDTA clearance of 30 ml/min or greater would be eligible
7. Pregnant or lactating women
8. Concurrent metastatic or new diagnosis of malignancy within the last 24 months except appropriately treated superficial melanoma, basal cell carcinoma and squamous cell carcinoma of the skin, cervical intraepithelial neoplasia or in situ or organ confined prostate cancer not currently requiring therapy
9. The use of other investigational or antineoplastic agents within the previous 6 weeks or during the trial. Corticosteroids are allowable for immediate relief of symptoms
10. Known to be HIV, Hep B or C positive
11. Known hypersensitivity to recombinant proteins, murine proteins, or to any excipient contained in the drug formulation of brentuximab vedotin
12. Known cerebral or meningeal involvement by Hodgkin Lymphoma
13. Symptoms or signs of PML
14. Any active systemic viral, bacterial, or fungal infection requiring intravenous antibiotics within 2 weeks prior to cycle 1 day 1 of brentuximab vedotin

15. Evidence of current uncontrolled cardiovascular conditions, including unstable angina and NYHA grade IV

Date of first enrolment
10/02/2014

Date of final enrolment
20/10/2017

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Christie Hospital
Manchester
United Kingdom
M20 4BX

Study participating centre
Churchill Hospital
Oxford
United Kingdom
OX3 7LE

Study participating centre
Beatson West of Scotland Cancer Centre
Glasgow
United Kingdom
G12 0YN

Study participating centre
St James's University Hospital
Leeds
United Kingdom
LS9 7TF

Study participating centre
Southampton General Hospital
Southampton
United Kingdom
SO16 6YD

Study participating centre
The Queen Elizabeth Hospital
Birmingham
United Kingdom
B15 2TH

Study participating centre
Nottingham City Hospital
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Clatterbridge Cancer Centre
Liverpool
United Kingdom
L7 8XP

Study participating centre
Guy's Hospital
London
United Kingdom
SE1 9RT

Study participating centre
Freeman Hospital
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Leicester Royal Infirmary
Leicester
United Kingdom
LE1 5WW

Study participating centre
Norfolk and Norwich University Hospital
Norwich
United Kingdom
NR4 7UY

Study participating centre
University Hospital of Wales
Cardiff
United Kingdom
CF14 4XW

Sponsor information

Organisation
University of Birmingham (UK)

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
Leukaemia and Lymphoma Research

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location
United Kingdom

Funder Name
Millennium: The Takeda Oncology Company (USA)

Funder Name
Bloodwise

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results	results presented at 14th International Conference on Malignant Lymphoma Palazzo dei Congressi, Lugano (Switzerland):	01/06/2017	07/06/2019	No	No
Basic results			28/05/2020	No	No
HRA research summary			28/06/2023	No	No