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OPTIMAL: OPTimising renal outcome in Myeloma renal failure

Submission date 19/06/2014	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 19/06/2014	**Overall study status** Completed	
Last Edited 12/12/2022	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-bortezomib-and-thalidomide-in-people-with-myeloma-whose-kidneys-are-not-working-well-optimal

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2012-003947-31

ClinicalTrials.gov (NCT)
NCT02424851

Protocol serial number

26866138-MMY2070

Study information

Scientific Title
A study of Thalidomide, Bendamustine, and Dexamethasone (BTD) vs Bortezomib, Bendamustine, and Dexamethasone (BBD) in patients with renal failure defined as a GFR below 30 ml/min

Acronym
OPTIMAL

Study objectives
Renal impairment is a life-threatening complication of myeloma. Up to 20-25% of patients will present at myeloma diagnosis with renal dysfunction.
In this Phase II study, 120 newly diagnosed myeloma patients with eGFR less than 30 ml/min from approximately 20 centres will be randomised to receive either Thalidomide or Bortezomib; all patients will receive bendamustine and dexamethasone in three weekly cycles. All patients will receive a minimum of four cycles.

Aims:
1. Establish whether proteasomal inhibition (bortezomib) or IMiD (thalidomide) based therapy achieves threshold reduction of sFLC in a significant majority of patients
2. Establish whether sFLC response to the first two cycles (early responder) predicts haematological and renal response to the next two cycles of therapy
3. Establish an early time point for assessment of sFLC reduction as a biomarker for response

Ethics approval required
Old ethics approval format

Ethics approval(s)
Northeast Newcastle and North Tyneside2 (NNT2) Committee, 03/03/2014, ref:13-NE-0361;

Study design
Randomised; Interventional; Design type: Process of Care

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Cancer; Subtopic: Haematological Oncology; Disease: Myeloma

Interventions
BTD vs BBD, Thalidomide + Bendamustine + Dexamethasone (BTD) vs Bortezomib + Bendamustine + Dexamethasone (BBD); Follow Up Length: 12 month(s); Study Entry: Single Randomisation only

Added 16/02/2017:
Potential eligible participants are screened and baseline assessments undertaken including: medical history; treatment history; concomitant medications; bone imaging; local laboratory evaluations.
Eligible patients are randomised to one of two treatment groups, stratified by age and Chronic Kidney Disease (CKD) stage.

Group 1: Bortezomib, Bendamustine and Dexamethasone (BBD)
Participants receive Bortezomib 1.3 mg/m2 subcutaneous on days 1, 4, 8 and 11. They receive Bendamustine 60 mg/m2 intravenous infusion on days 1 and 8. They also take Dexamethasone 40 mg daily orally on days 1-2,4-5,8-9,11-12.

Group 2: Thalidomide, Bendamustine and Dexamethasone (BTD)
Participants take Thalidomide 100 mg daily p.o. preferably at night for 21 days. They receive Bendamustine 60 mg/m2 intravenous infusion on days 1 and 8. They also take Dexamethasone 40 mg daily orally on days 1-2,4-5,8-9,11-12.

Participants are randomised to receive up to 4 cycles of either Bortezomib (Arm A) or Thalidomide (Arm B) (21 days in each cycle). All participants receive Bendamustine and Dexamethasone as combination therapy. Participants not considered suitable for autologous stem cell transplant (ASCT) may be given a further two cycles of their allocated treatment (up to 6 cycles in total).

During treatment assessments are undertaken including: physical examination; concomitant medications, local laboratory evaluations and adverse event reporting.

All participants who have received at least 2 cycles of their allocated treatment are followed up at 1 month post end of treatment (approximately 30 days after last dose) and 12 months post randomisation. These assessments include physical examination, disease status, treatment efficacy, overall survival and local laboratory evaluations.

Participants are asked to complete a validated (EQ-5D- 3L) Quality of Life questionnaire at screening (baseline), on day 1 of each treatment cycle and at 1 month and 12 month follow-up.

Central laboratory samples are collected at screening (baseline), during treatment and at 1 month follow up and sent to both Oxford and Birmingham.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Thalidomide + Bendamustine + Dexamethasone (BTD), Bortezomib + Bendamustine + Dexamethasone (BBD)

Primary outcome(s)
Response defined as >50% reduction (from baseline) in sFLC week 6 (end of cycle 2)

Added 16/02/2017:
1. Serum free light chain response is measured as the proportion of participants with response defined as >50% reduction (from baseline) in sFLC week 6 (end of cycle 2).
2. Myeloma response is measured by the renal response (Modified IMWG Uniform Criteria Of Response and Progression) at the end of 4 cycles of therapy

Key secondary outcome(s))
Renal response at end of four cycles of therapy.

Added 16/02/2017:
1. Overall response and correlation with monoclonal protein the urine is measured by the sFLC response at week 1, 2, 3, 4, 5, 6, 9 and 12
2. Haematological and non-hameatological toxicity in both arms is preasured by haematological responses adverse Events (NCI CTCAE v4.0) criteria
3. Survival at 1 month post end of treatment and 12 months post randomisation
4. change in renal function between the two treatment regimens is assessed by the renal response (defined by the IMWG renal response criteria) at the end of cycle 2 and cycle 4
5. Treatment effects on other patient reported outcomes is measured by the EQ-5D-3L Quality of life questionnaire at baseline, start of each treatment cycle and at 1 and 12 months post follow-up

Completion date
01/06/2020

Eligibility

Key inclusion criteria
1. Patients attending NHS haemato-oncology centres
2. Patients with newly diagnosed symptomatic myeloma and renal failure
3. Patients willing and able to give written informed consent
4. Chronic kidney disease stage 4 or 5
5. GFR <30 ml/min
6. A number of patients with newly diagnosed myeloma and renal failure will have a pre-existing medical condition (hypertension, diabetes etc) causing renal damage. Where there is a medical condition (eg. hypertension, diabetes) which may cause renal damage, there must have been a further decline (=15 ml/min) between previous steady state and the study screening
7. Women of childbearing potential (WCBP) and male participants whose partner is a WCBP must be prepared to use contraception in accordance with (and consent) to the Celgene-approved process for thalidomide and lenalidomide Risk Management and Pregnancy Prevention Programme
8. WCBP must have a negative pregnancy test performed by a healthcare professional in accordance with the Celgene-approved process for thalidomide and lenalidomide Risk Management and Pregnancy Prevention
9. Free of prior malignancies for = 2 years with exception of currently treated basal cell, squamous cell carcinoma of the skin, localised prostate cancer or carcinoma 'in situ' of the cervix or breast
10. In the Investigator's opinion, is able and willing to comply with all trial requirements
11. Willing to allow his or her GP and consultant, if appropriate, to be notified of participation in the trial

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
31

Key exclusion criteria
1. Female patient who is pregnant, lactating or planning pregnancy during the course of the trial or the female partner of a male participant planning a pregnancy during the course of the trial
2. Age <18 years
3. Known allergy to investigational drugs
4. Any other significant disease or disorder which, in the opinion of the Investigator, may either put the participant at risk because of participation in the trial, or may influence the result of the trial, or the participant's ability to participate in the trial
5. Any of the following laboratory abnormalities:
5.1. Absolute neutrophil count (ANC) <1.0 x 10(9)/L
5.2. Platelet count <75 x 10(9)/L
5.3. Serum SGOT/AST or SGPT/ALT >3 x upper limit of normal
6. Use of any standard/experimental anti-myeloma drug therapy 14 days prior to trial entry
7. CKD <4
8. Intention to use a physical method of serum free light chain removal such as plasma exchange or high cut-off dialysis
9. Grade 2 neuropathy (NCICTCAE v 4.0) or more will preclude use of thalidomide and bortezomib
10. Participants who have participated in another research trial involving an investigational product in the past 12 weeks.

Date of first enrolment
21/03/2015

Date of final enrolment
31/03/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

Churchill Hospital, Oxford (lead site)
Oxford University Hospitals NHS Foundation Trust
Old Road
Oxford
United Kingdom
OX3 7LE

Study participating centre
St Helier Hospital
Epsom and St Helier University Hospitals NHS Trust
Wrythe Lane
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United Kingdom
SM5 1AA

Study participating centre
Queen Alexandria Hospital
Portsmouth Hospitals NHS Trust
Southwick Hill Road
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PO6 3LY

Study participating centre
Basingstoke and North Hampshire Hospital
Hampshire Hospitals NHS Foundation Trust
Aldermaston Road
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United Kingdom
RG24 9NA

Study participating centre
Kent and Canterbury Hospital
East Kent Hospitals University NHS Foundation Trust
Ethelbert Road
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CT1 3NG

Study participating centre
Royal Liverpool Hospital
Royal Liverpool Hospital and Broadgreen University Hospitals NHS Trust
Prescot Street
Liverpool
United Kingdom
L7 8XP

Sponsor information

Organisation
Oxford University Hospitals NHS Foundation Trust

ROR
https://ror.org/03h2bh287

Funder(s)

Funder type
Charity

Funder Name
Bloodwise

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
Janssen Cilag International NV

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	results	29/11/2022	12/12/2022	Yes	No
Basic results	EU Clinical Trials Register results	23/05/2021	20/05/2022	No	No
Basic results	ClinicalTrials.gov results	27/01/2022	23/05/2022	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 12.0	01/08/2017	07/07/2022	No	No