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Study of DTP3 in patients with relapsed or refractory multiple myeloma or diffuse large B-cell lymphoma

Submission date
18/03/2022

Recruitment status
Recruiting

Registration date
27/05/2022

Overall study status
Ongoing

Last Edited
09/12/2025

Condition category
Cancer

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
The aim of this study is to investigate a new drug called DTP3 in patients with multiple myeloma (bone marrow cancer) or diffuse large B cell lymphoma (a cancer that starts in white blood cells). This is a new drug and the researchers wish to determine if it is effective in treating the disease and to decide on the safest dose level of the drug to use in the future. DTP3 has been developed for the treatment of multiple myeloma and diffuse large B cell lymphoma. DTP3 can cause the death of myeloma/lymphoma cells, but not normal healthy cells in both laboratory and early human studies. During a recent first-in-human trial in a small number of multiple myeloma patients, there were encouraging signs of clinical benefit from DTP3 and no significant side effects were experienced by participants This study will further expand on this investigation of the DTP3 drug.

Who can participate?
Patients aged over 16 years with multiple myeloma or diffuse large B cell lymphoma

What does the study involve?
The initial stage will involve the first patient being given the study drug (DTP3) at a particular starting dose. If this is well tolerated for one treatment cycle (4 weeks), the next patient will be dosed at the next higher dose. This will help the investigators determine what the optimal dose is most effective, whilst balancing potential side effects. Once the optimal dose is known, the second part of the trial involves participants being given the study drug (DTP3) at this optimal dose. Each participant would continue with ongoing treatment cycles of the study drug until either unacceptable side effects, progression of their myeloma or lymphoma, or until the study ends. The researchers would also follow up the participants' survival status after their participation in the trial through their hospital/clinic, or otherwise their GP or nominated next of kin if they no longer attend the hospital. At the end of this trial, the researchers should know the optimal dose, potential side effects and how effective DTP3 is as a drug for treating cancer. This may lead to further larger studies into DTP3 as a possible new treatment for multiple myeloma and/or diffuse large B cell lymphomas.

What are the possible benefits and risks of participating?
The researchers do not know if DTP3 will be effective in myeloma or lymphoma which is why they are doing this study. It is possible that the study drug will help, but the researchers cannot give any assurance that it will do so. Information from the trial could also potentially help towards treating patients with myeloma, lymphoma, or other cancers in the future.
The study drug DTP3 has been tested on three previous patients prior to this study and it was found that there were no significant side effects experienced. However, side effects may occur as the dose is increased as the investigators determine what the optimal dose is to be most effective at treating the cancer whilst balancing minimal side effects.
The drug has also been given to animals and was well tolerated. To ensure the safety of all patients in the trial, an internal safety monitoring committee, consisting of all the doctors involved in the study and an independent expert will be regularly reviewing the patients throughout the study. The routine procedures to take blood and tissue samples are invasive and carry additional risks. These can include bleeding, pain, infection and tissue injury at the local site. In very rare circumstances they can cause serious and life-threatening events, such as bleeding and injury to organs. Participants may decline to have these invasive tests and still continue with their study participation. They may experience some soreness or bruising around the site where the drug is administered after each treatment course, similar to other treatments administered through the vein that they may have previously had. Participants should not experience any side effects from having the imaging tests but may feel some discomfort from having to stay still until the scan is complete. This may take up to 60 minutes. During a PET scan, participants may feel some discomfort from having a tracer injected into their vein. The tracer is a harmless solution which allows the doctors to see the cancer in the body. Participants will have either a CT, MRI or PET-CT exam. Participants with diffuse large B cell lymphoma will also have follow up PET-CT scans. All of these are part of routine care. Participants will not undergo any additional x-ray or nuclear medicine exams. These procedures use ionising radiation to form images of the body and provide the doctor with other clinical information. Ionising radiation may cause cancer many years or decades after the exposure. The chances of this happening are the same whether you take part in this study or not. As this drug has not yet been extensively tested in large scale clinical trials, some side effects may be unknown. To start with, the researchers do not know what dose level will be the best to use. This could be a high dose or it could be a low dose, which is why the study is examining a wide range of doses. The first group of patients will receive a low dose of the study drug. Although it is possible that the drug will work, even at the lowest doses being studied, it is more likely that it will work better at higher doses. The low dose of study drug might be less effective than a higher dose, but the researchers can’t know this for sure. However, the study doctor also has the option to slowly increase the dose of DTP3 that you start off with, if he/she believes it would be appropriate to do this. The study doctor will discuss this after the first 4 weeks of DTP3 treatment. It is possible that if the treatment is given to a pregnant woman it could harm the unborn child. Therefore, pregnant women should not take part in this study; neither should women who plan to become pregnant during the study. Women who are at risk of pregnancy may be asked to have a pregnancy test before taking part to exclude the possibility of pregnancy. Women who could become pregnant should use two types of contraception during the period of the study and for 90 days after ceasing treatment with DTP3. Any woman who finds that she has become pregnant while taking part in the trial should immediately tell the study doctor. It is also possible that the treatment could damage the sperm. For this reason, men in the study should use barrier methods of contraception (a condom plus spermicidal gel) during the study and for 90 days after ceasing treatment with DTP3 if there is any possibility that their partner might become pregnant.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
September 2021 to March 2027

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Ms Elizabeth Hadley, e.hadley@imperial.ac.uk (temporary leave)
Ms Elena Ferrer, e.ferrer@imperial.ac.uk

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-dtp3-for-lymphoma-or-myeloma

Contact information

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-004028-13

Integrated Research Application System (IRAS)
1004023

ClinicalTrials.gov (NCT)
Nil known

Central Portfolio Management System (CPMS)
CPMS 51116

Study information

Scientific Title
Treating multiple myeloma and diffuse large B cell lymphoma by targeting the NF-κB pathway with the first-in-class GADD45β/MKK7 inhibitor, DTP3

Acronym
DTP3

Study objectives
The study is designed to assess the safety and effectiveness of a new molecule, DTP3, in the treatment of patients with relapsed/refractory multiple myeloma (MM) and diffuse large B cell lymphoma (DLBCL).

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 02/12/2021, London - London Bridge Research Ethics Committee (postal address: not available; +44 (0)207 1048202, +44 (0)207 1048124; londonbridge.rec@hra.nhs.uk), ref: 21/LO/0794

Study design
Interventional non randomized

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Multiple myeloma and diffuse large B cell lymphoma

Interventions
The initial stage will involve the first patient being given the study drug (DTP3) at a particular starting dose. If this is well tolerated for one treatment cycle (4 weeks), the next patient will be dosed at the next higher dose. This will help the investigators determine what the optimal dose is most effective, whilst balancing potential side effects. Once the optimal dose is known, the second part of the trial involves participants being given the study drug (DTP3) at this optimal dose. Each participant would continue with ongoing treatment cycles of the study drug until either unacceptable side effects, progression of their myeloma or lymphoma, or until the study ends. The researchers would also follow up the participants' survival status after their participation in the trial through their hospital/clinic, or otherwise their GP or nominated next of kin if they no longer attend the hospital. At the end of this trial, the researchers should know the optimal dose, potential side effects and how effective DTP3 is as a drug for treating cancer. This may lead to further larger studies into DTP3 as a possible new treatment for multiple myeloma and/or diffuse large B cell lymphomas.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
DTP3

Primary outcome(s)
1. Incidence, nature, and severity of all adverse events (AEs), serious adverse events (SAEs) and dose-limiting toxicities (DLTs): Common Terminology Criteria for Adverse Events (CTCAE) V5.0 will be assessed at each clinic visit and other assessments, including laboratory parameters, ECGs, and vital signs will be assessed at designated intervals during each cycle of treatment
2. Overall Response Rate (ORR): response will be evaluated using IMWG 2016 (MM) and Lugano Criteria 2014 (DLBCL). MM disease evaluation will occur 4 weekly and DLBCL imaging evaluation will occur 8 weekly
3. MM: best overall response of stringent complete response (sCR), complete response (CR), very good partial response (VGPR) or partial response (PR); response will be evaluated using IMWG 2016 (MM) - MM disease evaluation will occur 4 weekly

4. DLBCL: best overall response of PR or CR; response will be evaluated using Lugano Criteria 2014 (DLBCL). DLBCL imaging evaluation will occur 8 weekly

Key secondary outcome(s))

Current secondary outcome measures as of 12/11/2024:

1. Laboratory parameters, ECGs, and vital signs assessed at designated intervals during each cycle of treatment
2. Extent of exposure to DTP3: relative DTP3 dose intensity (delivered dose versus intended dose) will be calculated for each patient and presented descriptively at the end of a patient's participation in the trial:
2.1. Dose intensity = Delivered dose / Intended dose (expressed as a percentage)
2.2. Delivered dose = cumulative total dose the patient actually received over the duration of the study participation (affected by dose reduction/delay)
2.3. Intended and delivered dose values are calculated at the end of a patient's participation in the trial - after the drug has been permanently withdrawn
3. Pharmacokinetic (PK) parameters of DTP3 will be examined on Day 1, Day 3, and Day 5 of Cycle 1. Derived PK parameters will include: Cmax, Tmax, t1/2, AUC 0-t, AUC 0-,àû, Vd, Vss
4. Pharmacodynamic (PD) biomarkers of pathway-specific response measured at screening and 24 hours (range 18-36 hours) after the 4th dose (C1W2D2).
Tissue collection for PD marker analysis (phospho-JNK and phospho-ERK, cleavedcaspase-3, propidium iodide nuclear staining, propidium iodide nuclear staining)
4.1 MM: 50 ml of blood and 10ml bone marrow aspirate
4.2 DLBCL: 50ml blood and tumour biopsy (if accesible), 28G core biopsy
5. Efficacy through disease evaluation with CT/FDG PET for MM (IMWG) and DLBCL (lugano criteria).

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Previous secondary outcome measures:

1. Laboratory parameters, ECGs, and vital signs assessed at designated intervals during each cycle of treatment
2. Extent of exposure to DTP3: relative DTP3 dose intensity (delivered dose versus intended dose) will be calculated for each patient and presented descriptively at the end of a patient's participation in the trial:
2.1. Dose intensity = Delivered dose / Intended dose (expressed as a percentage)
2.2. Delivered dose = cumulative total dose the patient actually received over the duration of the study participation (affected by dose reduction/delay)
2.3. Intended and delivered dose values are calculated at the end of a patient's participation in the trial - after the drug has been permanently withdrawn
3. Pharmacokinetic (PK) parameters of DTP3 will be examined on Day 1, Day 3, and Day 5 of Cycle 1. Derived PK parameters will include: Cmax, Tmax, t1/2, AUC 0-t, AUC 0-,àû, Vd, Vss
4. Pharmacodynamic (PD) biomarkers of pathway-specific response measured at screening and 24 hours (range 18-36 hours) after the seventh dose of DTP3 treatment (Cycle 1, Week 3, Day 2):
4.1. Correlation of GADD45 expression with pharmacodynamic and clinical response
4.2. Relative reduction in levels of M protein and free light chains (MM only)

Completion date

31/03/2027

Eligibility

Key inclusion criteria

Disease-specific inclusion criteria (MM):
1. Documented diagnosis of multiple myeloma (IMWG 2014 criteria)
2. Any R-ISS stage
3. Measurable disease as determined by at least one of:
3.1. Serum M-protein ≥500 mg/dL
3.2. Urine M-protein ≥200 mg/24 hour
3.3. Involved serum free light chain (sFLC) level ≥10 mg/dL, provided that serum sFLC ratio is abnormal
4. Has previously been treated with an ImiD, a proteasome inhibitor and an anti-CD38 antibody
5. Previous treatment with at least two prior regimens
6. Relapsed (after most recent regimen) or refractory disease [refractory defined as either best response of progression on previous regimen or progression within 6 months of achieving PR (or better) on previous regimen]
7. Requires active therapeutic intervention (in the judgement of the investigator)
8. Not currently a candidate for stem cell transplantation or CAR T-cell therapy

Disease-specific inclusion criteria [DLBCL]:
9. Documented diagnosis of DLBCL [WHO 2016 criteria]
9.1. Diffuse large B-cell lymphoma – de novo or transformed (from follicular lymphoma only)
9.2. High-grade B-cell lymphoma (MYC with BCL2 and/or BCL6); High-grade B-cell lymphoma (NOS)
9.3. Primary mediastinal B-cell lymphoma
10. Non-GCB by local IHC [Dose Expansion Only]
11. Measurable disease as determined by CT (or MRI) documentation of two or more clearly demarcated lesions/nodes with a long axis >1.5 cm and short axis >1.0 cm or one clearly demarcated lesion/node with a long axis >2.0 cm and short-axis ≥1.0 cm AND baseline FDG-PET scans must demonstrate positive lesion compatibility with CT (or MRI) defined anatomical tumour sites
12. No available standard of care therapeutic regimens in the opinion of the investigator
13. Relapsed (after most recent regimen) or refractory disease [refractory defined as either best response of progression on previous regimen or progression within 6 months of achieving PR (or better) on previous regimen]
14. Requires active therapeutic intervention (in the judgement of the investigator)
15. Not currently a candidate for stem cell transplantation or CAR T-cell therapy

General inclusion criteria:
16. Adequate hematologic function:
16.1. ANC ≥ 1 x 10e9/l (no restriction on prior growth factor support)
16.2. Platelet count ≥50 x 10e9/l (no platelet transfusions permitted in 7 last days prior to assessment). Platelet counts of <50 x 10e9/l may be considered, on a case by case basis, for patients with significant malignant bone marrow involvement, after discussion with the medical monitor
16.3. Hb ≥8 g/dl (no RBC transfusions permitted in 7 last days prior to assessment)
16.4. aPTT and PT within institutional normal range (unless the patient is on full-dose warfarin, in which case INR within normal institutional therapeutic range is acceptable)
17. No evidence of bleeding diathesis or coagulopathy
18. Adequate laboratory biochemical function:
18.1. Serum creatinine ≤1.5 x ULN OR creatinine clearance ≥30 ml/min (Cockcroft-Gault

calculation)
18.2. Bilirubin level <1.5 X ULN
18.3. AST and ALT <2.5 X ULN
19. ECOG performance status 0-2
20. Age >16 years
21. Written informed consent prior to admission into the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 years

Upper age limit
99 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Primary or secondary CNS lymphoma
2. T-cell rich B-cell lymphoma
3. Plasma cell leukaemia
4. POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes)
5. Primary amyloidosis
6. Clinically significant (in the opinion of the investigator) cardiovascular disease, such as:
• History of myocardial infarction, acute coronary syndromes (including unstable angina), coronary angioplasty/stenting/bypass grafting within the past 6 months prior to the date of consent
• Class III or IV heart failure as defined by the New York Heart Association (NYHA) functional classification system
• Severe cardiac arrhythmia requiring medication or severe conduction abnormalities
• Poorly controlled hypertension (resting diastolic blood pressure >100 mmHg)
• Clinically significant valvular disease, cardiomegaly, ventricular hypertrophy, or cardiomyopathy, QTc prolongation [defined as a QTc interval >450 msec (males) or >470 msec (females)] or other significant ECG abnormalities including 2nd degree (type II) or 3rd degree AV block or bradycardia (ventricular rate <50 beats/min)
7. Clinically significant (in the opinion of the investigator) cerebrovascular disorders or vascular dementia
8. Clinically significant (in the opinion of the investigator) intercurrent medical or psychiatric illness, including serious active infection

9. Significant neuropathy (Grade 3, Grade 4, or Grade 2 with pain)
10. Concurrent treatment with other experimental drugs
11. A daily requirement for prednisone at a dose of >10 mg/day (or steroid equivalent) at time of starting the first dose of study drug. Higher doses are permitted for primary disease symptomatic control during the screening period, after discussion with the medical monitor, but this must have been tapered to a dose of ≤10 mg/day by the time treatment with DTP3 starts
12. Sem cell transplant (autologous/allogeneic) or CAR T-cell regimen within 12 weeks of the date of consent
13. Participation in another clinical trial with any investigational drug within 28 days prior to the date of consent
14. Prior (non-experimental) MM or DLBCL therapy within 28 days of the date of consent. Concomitant bisphosphonate therapy is permitted
15. Prior radiotherapy within 28 days of the date of consent. Localised palliative radiation therapy to a single site for symptomatic control is acceptable within this period
16. Anticipated need for concurrent radiotherapy during the study
17. Past or current history of other neoplasms, except for:
17.1. Curatively treated non-melanoma skin cancer
17.2. Adequately treated in situ carcinoma of the cervix
17.3. Prostate adenocarcinoma with documented PSA value of <0.1 ng/ml within 6 weeks of the date of consent
17.4. Other cancer curatively treated and with no evidence of disease for at least 3 years before the date of consent.
18. Known HIV infection
19. Active hepatitis C virus (HCV) or hepatitis B virus (HBV). Patients who are positive for hepatitis B core antibody, hepatitis B surface antigen or hepatitis C antibody must have a negative polymerase chain reaction (PCR) result
20. Ability to become pregnant (or already pregnant or lactating). However, those female patients who have a negative serum or urine pregnancy test before enrolment and agree to use two highly effective forms of contraception:
20.1. Oral, injected or implanted hormonal contraception and condom
20.2. Have an intra-uterine device and condom
20.3. Vasectomised partner
20.4. Sexual abstinence during the trial and for 6 months after the last dose of DTP3 are considered eligible.
Where age appropriate, female patients must be given advice on potential germ cell donation and cryopreservation
21. Male patients with partners of child-bearing potential (unless they agree to take measures not to father children by using one form of highly effective contraception [condom plus spermicide] during the trial and for 90 days after the last date of DTP3). Where age appropriate, male patients must be given advice on potential germ cell donation and cryopreservation. Men with pregnant or lactating partners should be advised to use barrier method contraception (for example, condom plus spermicidal gel) to prevent exposure to the foetus or neonate.

Date of first enrolment
19/05/2022

Date of final enrolment
31/03/2027

Locations

Countries of recruitment
United Kingdom

England

Wales

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Hammersmith Hospital
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Study participating centre
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Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council; Grant Codes: MR/V027581/1

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type

Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	version 1.2	16/09/2021	20/05/2022	No	Yes
Protocol file	version 4.0	12/12/2023	12/11/2024	No	No