ISRCTN15438979 https://doi.org/10.1186/ISRCTN15438979

An early phase trial to test the safety and determine the appropriate dose of BTM-3566 in patients with mature B cell lymphoma and advanced solid tumors

Submission date
16/01/2025

Recruitment status
Recruiting

Registration date
20/01/2025

Overall study status
Ongoing

Last Edited
18/12/2025

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
The purpose of this study is to test how safe and effective the treatment BTM-3566 is for treating mature B cell lymphomas. This type of cancer affects certain white blood cells. The study will gradually increase the doses given to patients, starting from very low doses and moving to higher ones, to ensure safety at each level.

Who can participate?
Participants can be males or females aged 18 years or older who have relapsed or refractory B cell lymphoma. This means their cancer has returned or has not responded to previous treatments. They must have tried at least two other therapies without success and meet specific health criteria.

What does the study involve?
Participants will be assigned to different dose groups based on when they join the study. They will take BTM-3566 orally for seven days, followed by a seven-day break with no medication. This cycle will continue throughout the study. Participants must also be willing to follow the study visit schedule and undergo necessary tests and biopsies.

What are the possible benefits and risks of participating?
Possible benefits include the potential treatment of cancer, stabilization of the disease, or shrinking of tumors. Participants will also contribute to knowledge about the safety and effects of BTM-3566 for future use. However, there are risks, including side effects like loss of appetite, nausea, weight loss, and potential damage to skeletal or heart muscles.

Where is the study run from?
The study is being conducted across various hospitals in Canada.

When is the study starting and how long is it expected to run for?
July 2024 to December 2026.

Who is funding the study?
Bantam Therapeutics (USA).

Who is the main contact?
Lori McDermott, Lmcdermott@bantampharma.com
Sarah Young, syoung@scimega.com

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Ms Sarah Young

Contact details
3055 Boulevard Saint-Martin West, Suite T500
Laval, Quebec
Canada
H7T 0J3
+1 450 629-2200 ext 250
syoung@scimega.com

Additional identifiers

Protocol serial number
BTM-3566-001-CA

Study information

Scientific Title
A Phase I Trial of BTM-3566 in Relapsed/Refractory Mature B Cell Lymphomas and Advanced Solid Tumors

Study objectives
To determine the dose-limiting toxicity and safety of BTM-3566

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 11/04/2025, Ontario Central Research Ethics Board (661 University Avenue, Suite 510, Toronto, M5G 0A3, Canada; +1 416-673-6649; Natascha.Kozlowski@oicr.on.ca), ref: Reference number not provided

2. approved 27/03/2025, Nova Scotia Health Research Ethics Board (5790 University Avenue, Halifax, B3H 1V7, Canada; +1 844-483-3344; researchethics@nshealth.ca), ref: 1031500

Study design
Multicenter interventional non randomized dose-escalation trial

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Relapsed/refractory mature B cell lymphoma or advanced solid tumors

Interventions
Current interventions as of 18/12/2025:

Dose escalation will be done separately and in parallel with two separate dose escalations: one in lymphoma and one in solid tumor patients. Dose-escalations of BTM-3566 will be done using single patient cohorts followed by traditional 3+3 methodology. The starting dose level is 0.9mg /kg and will be increased in 33% increments up to a total of 12.1mg/kg or until the maximum tolerated dose or recommended phase 2 dose is established. Dose de/escalations are determined by the Safety Review Committee which assesses after each dose escalation cohort completes the dose-limiting toxicity period (ie. 28 days), at minimum, to evaluate the data available. BTM-3566 will be administered as an liquid oral medication with dose based on each patient's weight (mg/kg). Treatment is given as two-week cycles, with BTM-3566 taken daily during the first week (ie 7 days) and no treatment on the second week.

_____

Previous interventions:

Dose-escalations of BTM-3566 will be done using single patient cohorts followed by traditional 3+3 methodology. The starting dose level is 0.9mg/kg and will be increased in 33% increments up to a total of 12.1mg/kg or until the maximum tolerated dose or recommended phase 2 dose is established. Dose de/escalations are determined by the Safety Review Committee which meets after each dose escalation cohort completes the dose-limiting toxicity period (ie. 28 days), at minimum, to evaluate the data available. BTM-3566 will be administered as an liquid oral medication with dose based on each patient's weight (mg/kg). Treatment is given as two-week cycles, with BTM-3566 taken daily during the first week (ie 7 days) and no treatment on the second week.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
BTM-3566

Primary outcome(s)

Dose limiting toxicity of BTM-3566 using the incidence and severity of adverse events measured using Common Terminology Criteria for Adverse Events (CTCAE) v5.0 at every study visit for the first 28 days on treatment (i.e. C1D1, C1D2, C1D3, C1D7, C1D9, C2D1, C2D3)

Key secondary outcome(s))
1. The maximum tolerated dose (MTD) and/or recommended phase 2 dose (RP2D) of BTM-3566 using the incidence and severity of adverse events experienced during the first 4 weeks of treatment measured using Common Terminology Criteria for Adverse Events (CTCAE) v5.0 at every study visit for the first 28 days on treatment (i.e. C1D1, C1D2, C1D3, C1D7, C1D9, C2D1, C2D3)
2. The pharmacokinetic properties of BTM-3566 measured via plasma concentrations of BTM-3566 at C1D1, C1D2, C1D7, C1D9, C2D1
3. The clinical activity of BTM-3566 measured through Objective Response Rate and Duration of Response by Revised Lugano Criteria at C3D1, and every 12 weeks thereafter, and Progression-Free Survival and Overall Survival measured using length of survival at each study visit and every 3 months post-treatment for up to 5 years or until death

Completion date
31/12/2026

Eligibility

Key inclusion criteria
Current key inclusion criteria as of 18/12/2025:

1. Patients aged ≥18 years with a diagnosis of relapsed or refractory mature B cell lymphoma* or advanced, unresectable and/or metastatic solid tumors.
2. Patients with non-Hodgkin's lymphoma (NHL) must have received at least 2 lines of prior therapy and have no available therapies in the investigator's opinion with known clinical benefit; patients with advanced solid tumors should be refractory to or relapsed after all standard therapies known to provide proven clinical benefit, unless the patient is not a candidate for standard treatment, there is no standard treatment, or the patient refuses standard treatment after expressing an understanding of all available therapies with proven clinical benefit. For subjects who have refused standard treatment, a rationale for refusal to receive the treatment will be captured in the case report form (CRF) and the medical record. There is no limit to the number of prior treatment regimens.
3. For lymphoma, patient must have measurable disease at screening per Lugano classification. For advanced solid tumors, patient must have non-measurable and/or measurable disease at screening per the revised RECIST guideline (version 1.1).
4. Patient must have an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 – 2
5. Patient must have a predicted life expectancy of >3 months
6. Patient must have the following laboratory values (obtained ≤21 days prior to enrollment):
6.1. High sensitivity cTnI <99% ULN for the local assay
6.2. NT-proBNP < age-adjusted "rule in" value for CHF (450 pg/mL or ng/L for age <50; >900 pg /mL or ng/L for 50-75; >1800 pg/mL or ng/L for age >75)
6.3. Serum CK < ULN
6.4. Serum creatinine <1.5 × ULN or if creatinine higher than normal range, calculated creatinine clearance (CrCL) must be ≥60 mL/min; actual body weight must be used for CrCL unless BMI >30 kg/m²; lean body weight must be used if BMI >30 kg/m²
6.5. Total bilirubin ≤1.5 × ULN unless has known history of Gilbert's syndrome (in which case,

total bilirubin must be ≤3 × ULN)
6.6. AST and ALT ≤2.5 × ULN, or ≤5 × ULN if due to liver involvement by tumor
6.7. Hemoglobin ≥8.0 g/dL
6.8. Platelets ≥ 75 × 10^9 cells/L
6.9. Absolute neutrophil count ≥1.0 ×10^9 cells/L (without the use of hematopoietic growth factors)
6.10. Corrected QT interval (QTc) <470 ms for females and <450 ms for males (as calculated by the Fridericia correction formula)
6.11. LVEF ≥ 50% or ≥ LLN for their institution, whichever is higher
6.12. Women of child-bearing potential (WOCBP) must have a negative urine pregnancy test within 72 hours prior to first administration of BTM-3566
7. WOCBP and males with female partners of child-bearing potential must agree to use adequate birth control throughout their participation and for 90 days following the last dose of BTM-3566.
8. Patient must be willing to adhere to the study visit schedule and the prohibitions and restrictions specified in this protocol.
8.1. Patient should have a site of disease amenable to biopsy and be a candidate for tumor biopsy according to institutional guidelines. Patients should be willing to undergo a new tumor biopsy at baseline and after dose 2 to 4 in either Cycle 1 or 2 of this study. Note: Patients with sites of disease not amenable to biopsy, or unwilling to undergo biopsies, will be considered for enrollment after discussion with the study PI.
8.2. Patients must not be enrolled in any other clinical trial and must not be receiving other therapy directed at their malignancy.

*Includes the following subtypes defined by WHO (Swerdlow et al 2016):
- Splenic Marginal Cell Lymphoma
- Splenic diffuse red pulp small B-cell lymphoma
- Lymphoplasmacytic lymphoma
- Nodal Marginal Zone Lymphoma
- Follicular Lymphoma (including in situ and duodenal-type)
- Large B-cell lymphoma with IRF4 rearrangement
- Primary cutaneous follicle center lymphoma
- Mantle cell lymphoma
- Primary mediastinal (thymic) large B-cell lymphoma
- Intravascular large B-cell lymphoma
- Anaplastic lymphoma kinase (ALK) + large B-cell lymphoma
- Plasmablastic lymphoma
- Primary effusion lymphoma
- Burkitt lymphoma
- Burkitt-like lymphoma with 11q aberration
- High-grade B cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangement
- High-grade B cell lymphoma, Not otherwise specified (NOS)
- B-cell lymphoma unclassifiable, with features intermediate between diffuse large B cell lymphoma (DLBCL) and classical Hodgkin lymphoma
- DLBCL, NOS
- Germinal center B-cell type DLBCL
- Activated B-cell type DLBCL
- Primary cutaneous DLBCL
- T-cell/histiocyte-rich large B-cell lymphomas
- Epstein-Barr Virus (EBV)+ DLBCL, NOS
- HHV8+ DLBCL, NOS
- DLBCL associated with chronic inflammation

———

Previous key inclusion criteria:

1. Patients aged ≥18 years with a diagnosis of relapsed or refractory mature B cell lymphoma*
2. Patients with non-Hodgkin's lymphoma (NHL) must have received at least 2 lines of prior therapy and have no available therapies with known clinical benefit
3. Patient must have measurable disease at screening per Lugano classification
4. Patient must have an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 – 2
5. Patient must have a predicted life expectancy of >3 months
6. Patient must have the following laboratory values (obtained ≤21 days prior to enrollment):
6.1. High sensitivity cTnI <99% ULN for the local assay
6.2. NT-proBNP < age-adjusted "rule in" value for CHF (450 pg/mL for age <50; >900 pg/mL for 50-75; >1800 pg/mL for age >75)
6.3. Serum CK < ULN
6.4. Serum creatinine <1.5 × ULN or if creatinine higher than normal range, calculated creatinine clearance (CrCL) must be ≥60 mL/min; actual body weight must be used for CrCL unless BMI >30 kg/m²; lean body weight must be used if BMI >30 kg/m²
6.5. Total bilirubin ≤1.5 × ULN unless has known history of Gilbert's syndrome (in which case, total bilirubin must be ≤3 × ULN)
6.6. AST and ALT ≤2.5 × ULN, or ≤5 × ULN if due to liver involvement by tumor
6.7. Hemoglobin ≥8.0 g/dL
6.8. Platelets ≥ 75 × 10^9 cells/L
6.9. Absolute neutrophil count ≥1.0 ×10^9 cells/L (without the use of hematopoietic growth factors)
6.10. Corrected QT interval (QTc) <470 ms for females and <450 ms for males (as calculated by the Fridericia correction formula)
6.11. LVEF ≥ 50% or ≥ LLN for their institution, whichever is higher
6.12. Women of child-bearing potential (WOCBP) must have a negative urine pregnancy test within 72 hours prior to first administration of BTM-3566
7. WOCBP and males with female partners of child-bearing potential must agree to use adequate birth control throughout their participation and for 90 days following the last dose of BTM-3566.
8. Patient must be willing to adhere to the study visit schedule and the prohibitions and restrictions specified in this protocol.
8.1. Patient should have a site of disease amenable to biopsy and be a candidate for tumor biopsy according to institutional guidelines. Patients should be willing to undergo a new tumor biopsy at baseline and after dose 2 to 4 in either Cycle 1 or 2 of this study. Note: Patients with sites of disease not amenable to biopsy, or unwilling to undergo biopsies, will be considered for enrollment after discussion with the study PI.
8.2. Patients must not be enrolled in any other clinical trial and must not be receiving other therapy directed at their malignancy.

*Includes the following subtypes defined by WHO (Swerdlow et al 2016):
- Splenic Marginal Cell Lymphoma
- Splenic diffuse red pulp small B-cell lymphoma
- Lymphoplasmacytic lymphoma
- Nodal Marginal Zone Lymphoma
- Follicular Lymphoma (including in situ and duodenal-type)
- Large B-cell lymphoma with IRF4 rearrangement

- Primary cutaneous follicle center lymphoma
- Mantle cell lymphoma
- Primary mediastinal (thymic) large B-cell lymphoma
- Intravascular large B-cell lymphoma
- Anaplastic lymphoma kinase (ALK) + large B-cell lymphoma
- Plasmablastic lymphoma
- Primary effusion lymphoma
- Burkitt lymphoma
- Burkitt-like lymphoma with 11q aberration
- High-grade B cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangement
- High-grade B cell lymphoma, Not otherwise specified (NOS)
- B-cell lymphoma unclassifiable, with features intermediate between diffuse large B cell lymphoma (DLBCL) and classical Hodgkin lymphoma
- DLBCL, NOS
- Germinal center B-cell type DLBCL
- Activated B-cell type DLBCL
- Primary cutaneous DLBCL
- T-cell/histiocyte-rich large B-cell lymphomas
- Epstein-Barr Virus (EBV)+ DLBCL, NOS
- HHV8+ DLBCL, NOS
- DLBCL associated with chronic inflammation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
110 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current key exclusion criteria as of 18/12/2025:

1. Patient has received the therapies/interventions listed below within the specified timeframe, or has ongoing toxicity from prior therapy > Grade 1 according to the CTCAE v5.0, with the exception of alopecia, vitiligo, Grade ≤2 neuropathy, well-controlled hypo/hyperthyroidism or other endocrinopathies that are well controlled with hormone replacement. Such exceptions must be assessed by the investigator (and approved by the sponsor) as not placing the patient at

undue safety risk from participating in this study.
1.1. Patient has undergone a major surgery (excluding minor procedures, e.g., placement of vascular access) <3 months prior to administration of BTM-3566.
1.2. Time since the last dose of prior therapy to treat underlying malignancy (including other investigational therapy):
i. Systemic cytotoxic chemotherapy: ≥ the duration of the most recent cycle of the previous regimen (with a minimum of 2 weeks for all, except 6 weeks for systemic nitrosourea or systemic mitomycin-C);
ii. Biologic therapy (eg, antibodies): ≥3 weeks;
iii. Small molecule therapies: ≥5 × half-life, no longer than 21 days, whichever is shorter.
1.3. Patient has received radiation therapy <28 days prior to administration of BTM-3566. Exception: limited (e.g., pain palliation) radiation therapy is allowed prior to and during study treatment as long as there are no acute toxicities and the patient has measurable disease outside the radiation field.
2. Patient has primary CNS lymphoma, primary brain tumor, breast cancer, pheochromocytoma, fibrolamellar
carcinoma, prostate cancer, pancreatic cancer, adrenocortical carcinoma, cutaneous melanoma, or ocular
melanoma.
3. Patient has previously received a total anthracycline dose ≥ 360mg/m² doxorubicin or equivalent.
4. Patient has a history of any of the following ≤6 months before first dose: congestive heart failure New York Heart Association Grade ≥2, unstable angina, myocardial infarction, unstable symptomatic ischemic heart disease, uncontrolled hypertension despite appropriate medical therapy, ongoing symptomatic cardiac arrhythmias of Grade >2, pulmonary embolism, or symptomatic cerebrovascular events, or any other serious cardiac condition (e.g., pericardial effusion or restrictive cardiomyopathy). Chronic atrial fibrillation on stable anticoagulant therapy is allowed.
5. Patients with history of statin-associated myopathy within 6 months of enrollment who is still taking a statin.
6. Patient has symptomatic or uncontrolled neurologic disease (brain metastases, leptomeningeal disease, or spinal cord compression) not definitively treated with surgery or radiation. Note: Symptomatic or uncontrolled neurologic disease is defined as patient has active CNS metastases (including evidence of cerebral edema by MRI, or progression from prior imaging study, or any requirement for steroids, or clinical symptoms of/from CNS metastases) within 28 days prior to study treatment. Patients with known CNS metastases must have a baseline MRI scan within 28 days of study treatment.
7. Patient has current second malignancy at other sites (exceptions: non-melanomatous skin cancer, adequately treated in situ carcinoma, or indolent prostate cancer under observation). A history of other malignancies is allowed at the discretion of the PI and medical monitor as long as patient has been free of recurrence for ≥2 years, or if the patient has been treated with curative intent within the past 2 years and, in the opinion of the investigator, is unlikely to have a recurrence.
8. Patient has active and clinically significant bacterial, fungal, or viral infection, including known Hepatitis A, B, or C or HIV (testing not required).
9. Patient requires prolonged use of a moderate or strong CYP3A4 inhibitor or inducer. Moderate or strong CYP3A4 inhibitors or inducers must be stopped 14 days or 5 half-lives, whichever is longer, prior to the administration of BTM-3566.
10. Women who are pregnant or breastfeeding.
11. Patient has any contraindications to the imaging assessments or other study procedures that patients will be undergoing.
12. Patient has any medical or social condition that, in the opinion of the investigator, might

place a patient at increased risk, affect compliance, or confound safety or other clinical study data interpretation.
13. Patient cannot avoid use of OAT3 substrates with narrow therapeutic windows (cefaclor, cefonicid, cefoxitin, cephradine, cidofovir, furosemide, and zidovudine).
14. A family history of long QT syndrome.
15. Patient cannot avoid drugs that prolong the QT interval (such as antipsychotic medications (e.g., chlorpromazine, haloperidol, thioridazine, ziprasidone), antibiotics (e.g., moxifloxacin), Class 1A (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications or any other medications known to prolong the QT interval) from 7 days prior to the first dose of study drug and throughout the study.

_____

Previous key exclusion criteria:

1. Patient has received the therapies/interventions listed below within the specified timeframe, or has ongoing toxicity from prior therapy > Grade 1 according to the CTCAE v5.0, with the exception of alopecia, vitiligo, Grade ≤2 neuropathy, well-controlled hypo/hyperthyroidism or other endocrinopathies that are well controlled with hormone replacement. Such exceptions must be assessed by the investigator (and approved by the sponsor) as not placing the patient at undue safety risk from participating in this study.
1.1. Patient has undergone a major surgery (excluding minor procedures, e.g., placement of vascular access) <3 months prior to administration of BTM-3566.
1.2. Patient has received any anti-cancer therapy <28 days prior to administration of BTM-3566.
1.3. Patient has received radiation therapy <28 days prior to administration of BTM-3566. Exception: limited (e.g., pain palliation) radiation therapy is allowed prior to and during study treatment as long as there are no acute toxicities and the patient has measurable disease outside the radiation field.
2. Patient has primary CNS lymphoma.
3. Patient has previously received a total anthracycline dose ≥ 360mg/m² doxorubicin or equivalent.
4. Patient has a history of any of the following ≤6 months before first dose: congestive heart failure New York Heart Association Grade ≥2, unstable angina, myocardial infarction, unstable symptomatic ischemic heart disease, uncontrolled hypertension despite appropriate medical therapy, ongoing symptomatic cardiac arrhythmias of Grade >2, pulmonary embolism, or symptomatic cerebrovascular events, or any other serious cardiac condition (e.g., pericardial effusion or restrictive cardiomyopathy). Chronic atrial fibrillation on stable anticoagulant therapy is allowed.
5. Patients with history of statin-associated myopathy within 6 months of enrollment who is still taking a statin.
6. Patient has symptomatic or uncontrolled neurologic disease (brain metastases, leptomeningeal disease, or spinal cord compression) not definitively treated with surgery or radiation. Note: Symptomatic or uncontrolled neurologic disease is defined as patient has active CNS metastases (including evidence of cerebral edema by MRI, or progression from prior imaging study, or any requirement for steroids, or clinical symptoms of/from CNS metastases) within 28 days prior to study treatment. Patients with known CNS metastases must have a baseline MRI scan within 28 days of study treatment.
7. Patient has current second malignancy at other sites (exceptions: non-melanomatous skin cancer, adequately treated in situ carcinoma, or indolent prostate cancer under observation). A history of other malignancies is allowed at the discretion of the PI and medical monitor as long as patient has been free of recurrence for ≥2 years, or if the patient has been treated with curative intent within the past 2 years and, in the opinion of the investigator, is unlikely to have a

recurrence.
8. Patient has active and clinically significant bacterial, fungal, or viral infection, including known Hepatitis A, B, or C or HIV (testing not required).
9. Patient requires prolonged use of a moderate or strong CYP3A4 inhibitor or inducer. Moderate or strong CYP3A4 inhibitors or inducers must be stopped 14 days or 5 half-lives, whichever is longer, prior to the administration of BTM-3566.
10. Women who are pregnant or breastfeeding.
11. Patient has any contraindications to the imaging assessments or other study procedures that patients will be undergoing.
12. Patient has any medical or social condition that, in the opinion of the investigator, might place a patient at increased risk, affect compliance, or confound safety or other clinical study data interpretation.
13. Patient cannot avoid use of proton pump inhibitor (PPI) from 7 days prior to the first dose and throughout the study. H2 antagonists are permitted if they are not taken within 10 hours prior to dosing or 2 hours after dosing.
14. Patient cannot avoid use of CYP2C19 substrates with narrow therapeutic windows (e.g., clopidogrel) or OAT3 substrates with narrow therapeutic windows (cefaclor, cefonicid, cefoxitin, cephradine, cidofovir, furosemide, and zidovudine).
15. A family history of long QT syndrome.
16. Patient cannot avoid drugs that prolong the QT interval (such as antipsychotic medications (e. g., chlorpromazine, haloperidol, thioridazine, ziprasidone), antibiotics (e.g., moxifloxacin), Class 1A (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications or any other medications known to prolong the QT interval) from 7 days prior to the first dose of study drug and throughout the study.

Date of first enrolment
25/04/2025

Date of final enrolment
01/09/2026

Locations

Countries of recruitment
Canada

Study participating centre
Princess Margaret Hospital
610 University Ave
Toronto
Canada
M5G 2M9

Study participating centre
QEII Health Sciences Centre
5820 University Avenue
Halifax

Canada
B3H 1V7

Sponsor information

Organisation
Bantam Pharmaceuticals

Funder(s)

Funder type
Industry

Funder Name
Bantam Pharmaceuticals

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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes