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Cell therapy clinical trial of BOXR1030 in GPC3 positive liver, squamous lung, Merkel cell cancer, and myxoid/round cell liposarcoma

Submission date
10/05/2022

Recruitment status
Recruiting

Registration date
29/09/2022

Overall study status
Ongoing

Last Edited
16/01/2025

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
This study is to test the safety of giving BOXR1030 to participants with cancer expressing GPC3. It will test BOXR1030, referred to as a chimeric antigen receptor (CAR) T cell therapy, a type of cellular therapy made up of immune cells that normally fight infection. BOXR1030 is made using white blood cells (WBCs), which are removed from participants' peripheral blood. The WBCs are sent to a manufacturing facility, where they will be grown outside of the body with ingredients added to help expand T cells. While they grow a retrovirus will be used to introduce genetic material into the cells which will become a permanent part of the participants T cells' genetic material and creates a new protein on the cells. This protein on the outside surface of the participants T cells, a so-called T cell receptor (TCR), is designed to recognise GPC3 which is being expressed on tumour cells. A second protein will be produced within the participants cells (GOT2) to enhance fitness of these T cells to combat cancer. BOXR1030 is infused back into participants once manufacturing is complete. The BOXR1030 T cells can then target and attack tumour tissues that express GPC3. It is thought that as healthy cells do not express GPC3, BOXR1030 T cells will selectively recognise the tumour cells. To increase the chance of the participants body accepting BOXR1030, participants will receive 2 chemotherapy medicines approved by the MHRA, for other uses in patients with cancer, called fludarabine and cyclophosphamide. These medications are not intended to treat cancer directly but may change the immune system to help BOXR1030 work. This is called lymphodepleting chemotherapy.

Who can participate?
Patients aged 18 – 80 years with GPC3 positive liver, squamous lung, Merkel cell cancer, or myxoid/round cell liposarcoma

What does the study involve?
This study has 2 parts. The 1st part is the dose escalation phase. The 2nd part is the expansion phase. Participants will be in either the first or second part. Up to 20 study sites in the US and UK will enrol about 110 participants. The study is expected to run for approximately 60 months, participants will continue in long-term follow-up for up to 15 years after BOXR1030 administration; assessments will be performed throughout.

What are the possible benefits and risks of participating?
Benefits:
The potential benefits of BOXR1030 and taking part in this clinical study are unknown. However, the knowledge gained from this study may help the study doctor and other physicians participating in this clinical study determine what treatment to provide other cancer patients in the future.
We cannot and do not guarantee or promise that participants will receive any benefits from this study.

Risks:
The potential risks and burdens for this study are provided in the Participant Information Sheet and Informed Consent Form(s) (PIS-ICF(s)). The participants will understand associated risks and burdens prior to taking part in the study. Due to the character limit for this question please refer to the PIS-ICF(s) for the risks and burdens and the management of these risks and burdens.

Safety will be evaluated by assessment of clinical laboratory tests, physical examinations, vital signs measurements at various time points during the study, and by the documentation of AEs.

Where is the study run from?
SOTIO Biotech Inc (USA)

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

Who is funding the study?
SOTIO Biotech Inc (USA)

Who is the main contact?
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Additional identifiers

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2021-005086-41

IRAS number
1005273

ClinicalTrials.gov number
NCT05120271

Secondary identifying numbers
B1030-101, IRAS1005273, CPMS 52312

Study information

Scientific Title
A first-in-human, phase 1/2, dose escalation study of BOXR1030 T cells in subjects with advanced GPC3-positive solid tumors

Study objectives
- To characterize the safety of BOXR1030 in the first 6 months after dosing in subjects with GPC3+ advanced malignancies
- To determine the RP2D of BOXR1030 in GPC3+ solid tumors
- To assess short-term antitumor activity of BOXR1030 in GPC3+ tumors, using RECIST 1.1 criteria

- To characterize BOXR1030 T-cell population, as well as expansion and persistence, in blood
- To evaluate increases from baseline in inflammatory markers and cytokines as potential correlates of safety and/or antitumor activity
- To characterize the long-term safety of BOXR1030 up to 15 years after administration

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/08/2022, North East - York Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 (0)207 104 8079; york.rec@hra.nhs.uk), ref: 22/NE/0096

Study design
Interventional dose escalation study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Patients with advanced, unresectable liver, squamous lung, and Merkel cell cancer, and myxoid /round cell liposarcoma that have tumor that is positive for GPC3 protein

Interventions
Current interventions as of 16/01/2025:
All study participants will receive a one time i.v. administration of BOXR1030 after completion of cyclophosphamide and fludarabine lymphodepleting chemotherapy (LD chemotherapy). Both the participant and their study doctor will know that they are receiving these medications.

After signing informed consent and completing all screening assessments, eligible participants will be enrolled and undergo leukapheresis to obtain T cells for BOXR1030 manufacturing. Participants will receive a 3-day LD chemotherapy regimen with fludarabine and cyclophosphamide, administered according to institutional standard practice for these medications at this dosage, including inpatient administration as appropriate. Participants must be hospitalised for BOXR1030 administration and will remain hospitalised for 10 days after the infusion. For 28 days after BOXR1030 administration, all participants must stay within a distance that requires no more than 2 hours of travel to the study site. During the Post-treatment Evaluation Period (within 6 months after BOXR1030 administration), study visits will occur daily for the first week, twice in the second week, and then once weekly at Weeks 3, 4, 6, 9, 12, 15, 18, and 24. Safety (targeted physical examination, adverse event assessment, and clinical labs) will

be evaluated and samples will be collected for endpoint analyses. For 28 days after BOXR1030 administration, participants will be required to monitor their temperature and complete neurological evaluation via the immune effector cell-associated encephalopathy (ICE) assessment tool every day (to be administered by site staff during clinical visits and by a caregiver at home on non-clinic days). At regular intervals, antitumour activity will be assessed per RECIST 1.1 and iRECIST criteria. After 6 months of follow-up from BOXR1030 administration, participants will enter the Long-term Follow-up Period for a total duration of 15 years after BOXR1030 dosing. Study visits are scheduled at Months 7, 9, 11, 13, 15, 18, 21, and 24, every 6 months thereafter until Year 5, and then annually through Year 15. Long-term follow-up assessments will focus on long-term safety and disease status.

Previous interventions:
All study participants will receive a one time i.v. administration of BOXR1030 after completion of cyclophosphamide and fludarabine lymphodepleting chemotherapy (LD chemotherapy). Both the participant and their study doctor will know that they are receiving these medications.

After signing informed consent and completing all screening assessments, eligible participants will undergo leukapheresis to obtain T cells for BOXR1030 manufacturing. Participants will receive a 7-day LD chemotherapy regimen with fludarabine and cyclophosphamide, administered according to institutional standard practice for these medications at this dosage, including inpatient administration as appropriate. Participants must be hospitalised for BOXR1030 administration and will remain hospitalised for 10 days after the infusion. For 28 days after BOXR1030 administration, all participants must stay within a distance that requires no more than 2 hours of travel to the study site. During the Post-treatment Evaluation Period (6 months after BOXR1030 administration), study visits will occur daily for the first week, twice in the second week, and then at Weeks 3, 4, 6, and Months 2, 3, 4, 5, and 6. Safety (targeted physical examination, adverse event assessment, and clinical labs) will be evaluated and samples will be collected for endpoint analyses. For 28 days after BOXR1030 administration, participants will be required to monitor their temperature and complete neurological evaluation via the immune effector cell-associated encephalopathy (ICE) assessment tool every day (to be administered by a caregiver at home on non-clinic days). At regular intervals, antitumour activity will be assessed per RECIST Version 1.1 and iRECIST criteria. After 6 months of follow-up from BOXR1030 administration, participants will enter the Long-term Follow-up Period for a total duration of 15 years after BOXR1030 dosing. Study visits are scheduled every 3 months from Month 9 to Month 24, every 6 months thereafter until Year 5, and then annually through Year 15. Long-term follow-up assessments will focus on long-term safety and disease status.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
BOXR1030

Primary outcome measure
Current primary outcome measures as of 16/01/2025:
1. Variable: Dose-limiting toxicities (DLTs)
Method of measurement: Selected adverse events (AEs) defined by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.0 or American Society

for Transplantation and Cellular Therapy (ASTCT) criteria for cytokine release syndrome or immune effector cell-associated neurotoxicity syndrome
Duration and time points: From the time of BOXR1030 administration (Study Day 1) through 28 days after BOXR1030 administration (Study Day 28/Week 4); daily for the first week, twice in the second week, and then once weekly at Weeks 3 and 4
2. Variable: Maximum tolerated dose (MTD)
Method of measurement: Defined as the dose that maximizes the probability of targeted toxicity among doses that satisfy the escalation with overdose control criterion
Duration and time points: From the time of BOXR1030 administration (Study Day 1) through 28 days after BOXR1030 administration (Study Day 28/Week 4); daily for the first week, twice in the second week, and then once weekly at Weeks 3 and 4
3. Variable: Recommended phase 2 dose (RP2D)
Method of measurement: The RP2D may be the same as the MTD, a previously tested dose, or an intermediate/alternative dose below the MTD that is yet unexplored. Alternatively, the RP2D may be selected on the basis of observed safety and activity in dose escalation before the MTD is reached.
Duration and time points: From the time of BOXR1030 administration (Study Day 1) through 28 days after BOXR1030 administration (Study Day 28/Week 4); daily for the first week, twice in the second week, and then once weekly at Weeks 3 and 4
4. Variable: Treatment-emergent AEs (TEAEs)
Method of measurement: Type, frequency, and severity of TEAEs; clinically significant abnormal safety laboratory findings; and vital signs. TEAEs and laboratory findings according to NCI CTCAE version 5.0 and ASTCT criteria.
Duration and time points: From the time of BOXR1030 administration (Study Day 1) through Week 24; daily for the first week, twice in the second week, and then once weekly at Weeks 3, 4, 6, 9, 12, 15, 18, and 24

Previous primary outcome measures:
1. Occurrence of dose-limiting toxicity DLT measured using Common Terminology Criteria for Adverse Events version 5.0 (CTCAEv5) criteria during the first 28 days
2. RP2D measured using CTCAEv5 during the first 28 days and recommendations of the Dose Escalation Committee (DEC)
3. Incidence of treatment-emergent AEs measured using CTCAEv5 during the first 28 days
4. Incidence of adverse events of special interest measured using CTCAEv5 during the first 28 days

Secondary outcome measures

Current secondary outcome measures as of 16/01/2025:
1. Variable: Objective response rate
Method of measurement: Radiologic scans for disease assessment (CT, MRI); response defined according to RECIST 1.1 criteria
Duration and time points: From the time of BOXR1030 administration (Study Day 1) every 6 weeks (±2 weeks) or more frequently if clinically indicated until disease progression/recurrence or start of new anti-cancer therapy, whichever came first, assessed up to approximately 15 years / end of study visit
2. Variable: Best overall response
Method of measurement: Radiologic scans for disease assessment (CT, MRI); defined as the best response recorded from the date of treatment to disease progression or death
Duration and time points: From the time of BOXR1030 administration (Study Day 1) every 6 weeks (±2 weeks) or more frequently if clinically indicated until disease progression/recurrence or start of new anti-cancer therapy, whichever came first, assessed up to approximately 15 years

/ end of study visit
3. Variable: Duration of response
Method of measurement: Radiologic scans for disease assessment (CT, MRI); defined as the time from the first achieved response (complete or partial) to the first date of radiological progression
Duration and time points: From the time of BOXR1030 administration (Study Day 1) every 6 weeks (±2 weeks) or more frequently if clinically indicated until disease progression/recurrence or start of new anti-cancer therapy, whichever came first, assessed up to approximately 15 years / end of study visit
4. Variable: Progression-free survival
Method of measurement: Radiologic scans for disease assessment (CT, MRI); defined as the time from the date of treatment to the first date of radiological progression or death
Duration and time points: From the time of BOXR1030 administration (Study Day 1) every 6 weeks (±2 weeks) or more frequently if clinically indicated until disease progression/recurrence or start of new anti-cancer therapy, whichever came first, assessed up to approximately 15 years / end of study visit
5. Variable: Clinical benefit rate
Method of measurement: Radiologic scans for disease assessment (CT, MRI); defined as the total number (or percentage) of patients who achieved a complete response, partial response, or had stable disease for 6 months or longer
Duration and time points: From the time of BOXR1030 administration (Study Day 1) every 6 weeks (±2 weeks) or more frequently if clinically indicated until disease progression/recurrence or start of new anti-cancer therapy, whichever came first, assessed up to approximately 15 years / end of study visit
6. Variable: Time to response
Method of measurement: Radiologic scans for disease assessment (CT, MRI); defined as the time from the date of treatment to the first objective tumor response
Duration and time points: From the time of BOXR1030 administration (Study Day 1) every 6 weeks (±2 weeks) or more frequently if clinically indicated until disease progression/recurrence or start of new anti-cancer therapy, whichever came first, assessed up to approximately 15 years / end of study visit
7. Variable: Time to progression
Method of measurement: Radiologic scans for disease assessment (CT, MRI); defined as the time from the date of treatment to disease progression
Duration and time points: From the time of BOXR1030 administration (Study Day 1) every 6 weeks (±2 weeks) or more frequently if clinically indicated until disease progression/recurrence or start of new anti-cancer therapy, whichever came first, assessed up to approximately 15 years / end of study visit
8. Variable: BOXR1030 T-cell levels in blood
Method of measurement: Analysis of blood samples
Duration and time points: From the time of BOXR1030 administration (Study Day 1) until the end of the study, assessed up to approximately 15 years; Days 2, 4, 6, 8, 10, and 14, once weekly at Weeks 3, 4, 6, 9, 12, 15, 18, and 24, every 3 months from Month 9 to Month 24, every 6 months thereafter until Year 5, and then annually through Year 15 / end of study visit
9. Variable: BOXR1030 T-cell characterization in blood
Method of measurement: Analysis of blood samples
Duration and time points: From the time of BOXR1030 administration (Study Day 1) until the end of the study, assessed up to approximately 15 years; Days 2, 4, 6, 8, 10, and 14, once weekly at Weeks 3, 4, 6, 9, 12, 15, 18, and 24, every 3 months from Month 9 to Month 24, every 6 months thereafter until Year 5, and then annually through Year 15 / end of study visit
10. Variable: Levels of inflammatory markers
Method of measurement: Analysis of blood samples

Duration and time points: From the time of BOXR1030 administration (Study Day 1) until the end of the study, assessed up to approximately 15 years; daily for the first week, twice in the second week, once weekly at Weeks 3, 4, 6, 9, 12, 15, 18, and 24, every 3 months from Month 9 to Month 24, every 6 months thereafter until Year 5, and at the end of study visit

Previous secondary outcome measures:
Short-term antitumour activity measured using Response Evaluation Criteria in Solid Tumours (RECIST) 1.1 Criteria for overall response rate at 6 weeks

Overall study start date
05/05/2021

Completion date
31/10/2027

Eligibility

Key inclusion criteria
Current inclusion criteria as of 16/01/2025:
1. Aged 18 to 80 years at time of enrollment.
2. Body weight of ≥50 kg at time of enrollment. Note: For dose level 1, subjects must have a minimum body weight of 65 kg.
3. Able to provide a recent tumor specimen taken within 6 months prior to signing consent and after the initiation of the subject's most recent systemic anticancer therapy, for GPC3 expression assessment by IHC.
Note: Subjects with available, previously collected tumor tissue older than 6 months at the time of GPC3 IHC testing or collected prior to the initiation of their current or last systemic therapy may be permitted for GPC3 prescreening. If prescreening sample is found to be GPC3 positive, a new tumor biopsy will be needed to confirm tumor remains GPC3 positive in order to proceed with the subsequent main Protocol ICF signing and screening.
4. Histologically confirmed advanced unresectable or metastatic hepatocellular carcinoma (HCC), SCC of the lung, myxoid/round cell liposarcoma, or MCC with GPC3 overexpression by IHC, with a cytoplasmic/membranous H-score >30 for study eligibility. (In the event of a tumor-agnostic expansion cohort, other indications may be investigated.) Subjects must consent to IHC testing in a separate informed consent.
Note: Tumor samples will be sent to a central laboratory for GPC3 expression analysis.
5. Documentation of disease progression or refractory disease or intolerance to all existing prior lines of SoC therapies for advanced or metastatic disease. Subjects with tumors with genetic alterations and mutations (e.g., breast cancer gene [BRCA], EGFR mutations, and anaplastic lymphoma kinase [ALK] translocation) who have approved targeted therapies available for their cancer will need to have been treated with all such approved therapies, or are intolerant to such approved targeted therapy for their cancer prior to enrolling in this study.
6. Life expectancy >16 weeks.
7. Have adequate organ function (renal/hepatic/pulmonary).
8. Left ventricular ejection fraction (LVEF) ≥50% by multiple-gated acquisition (MUGA) scan or echocardiogram (ECHO).
9. Eastern Cooperative Oncology Group performance status of 0 to 1.
10. For subjects with HCC:
10.1. Child-Pugh Score of A.
10.2. No fibrolamellar carcinoma or mixed hepatocellular cholangiocarcinoma histology.
10.3. No grade 2 or grade 3 ascites based on the European Association for the Study of Liver

guidelines.
11. A minimum of 2 sites of disease, including at least 1 site that is measurable by RECIST 1.1 criteria to ensure sufficient disease for response assessment. At least 1 of the other lesions must be considered adequate for Protocol-required tumor biopsy. Consider prioritization of percutaneous lesions that are palpable, or guided by imaging if necessary, and exclude biopsies of any lesions that are in proximity to vital visceral, cardio-pulmonary, or any neurovascular structures. A single site of disease is considered adequate to allow for response assessment and Protocol-required tumor biopsies if it measures at least 2 cm in the shortest axis).
12. Adequate wash-out of prior systemic therapy for underlying malignancy, relative to leukapheresis:
12.1. Last dose of any antineoplastic treatment must be at least 2 weeks before leukapheresis.
12.2. Last dose of any investigational agent must be at least 3 half-lives of the treatment, or 28 days, before leukapheresis (whichever is shorter).
Adequate wash-out of prior systemic therapy for underlying malignancy, relative to LD chemotherapy:
Note: Subjects may receive an additional dose of their last received form of therapy at the same dose and dosing schedule following leukapheresis as bridging therapy; however, the required wash-out period prior to start of LD chemotherapy must be adhered to:
12.3. The last dose of systemic nitrosourea or systemic mitomycin-C must be at least 6 weeks before the first dose of LD chemotherapy in this study.
12.4. For all other systemic cytotoxic chemotherapy, the wash-out must be the duration of a full cycle of that therapy. For example, if the prior therapy is given in 3-week cycles, there must be at least 3 weeks between the last dose of that therapy and the first dose of LD chemotherapy in this study. If the prior therapy is administered more frequently than every 2 weeks, a minimum 2-week wash-out is required.
12.5. For biologic therapy (e.g., antibodies) the wash-out must be either the duration of the biologic agent dosing interval, or 3 weeks, whichever is shorter.
12.6. For small molecule therapies, the wash-out must be 5 half-lives of the drug.
12.7. For any investigational agent, the wash-out must be 3 half-lives of the investigational agent, or 4 weeks, whichever is shorter.
Note: Local radiation of lesions is allowed if indicated for palliation requiring 1 week wash-out prior to start of BOXR1030 dosing if ≤2 weeks of radiotherapy for non-central nervous system (CNS) disease; locally treated lesions will be considered non-target lesions. Hormone ablation is also allowed as clinically indicated.
13. Subjects or their legally acceptable representative must be able and willing to:
13.1. Provide Institutional Review Board/Independent Ethics Committee (IRB/IEC/EC)-approved written informed consent in accordance with regulatory and institutional guidelines. This must be obtained before the performance of any Protocol-related procedures that are not part of normal patient care.
13.2. Comply with the study Protocol and with the planned biopsy procedures.
14. Willing and able to commit to study assessments and visit schedule, including availability of a caregiver to conduct daily neurological assessments for 28 days after BOXR1030 administration.
15. For women of childbearing potential (defined as physiologically capable of becoming pregnant), confirmation of a negative serum pregnancy test and agreement to use of highly effective contraception per Clinical Trials Facilitation and Coordination Group (CTFG) criteria from screening though a period of 12 months after the last cyclophosphamide dose. For men with partners of childbearing potential, agreement to use effective barrier contraception from screening through a period of 6 months after the last cyclophosphamide dose.

Previous inclusion criteria:
1. Aged 18 to 80 years at time of enrollment
2. Able to provide a recent tumor specimen taken since the time of the subject’s most recent

systemic anticancer therapy, for GPC3 expression assessment by IHC.
3. Histologically confirmed advanced unresectable or metastatic hepatocellular carcinoma (HCC), squamous cell carcinoma (SCC) of the lung, myxoid/round cell liposarcoma, or MCC with GPC3 overexpression by IHC, with a cytoplasmic/membranous H-score >30 for study eligibility.
4. Documentation of disease progression or refractory disease or intolerance to prior lines of standard-of-care (SOC) therapies. Patients with tumors with genetic alterations and mutations who have approved targeted therapies available for their cancer will need to have been treated with such approved therapies or refused such approved targeted therapy for their cancer prior to enrolling in this study.
5. Life expectancy >16 weeks
6. Have adequate organ/renal function as defined by the protocol
7. Left ventricular ejection fraction (LVEF) ≥50% by multiple-gated acquisition (MUGA) scan or echocardiogram (ECHO)
8. Eastern Cooperative Oncology Group performance status of 0 to 1
9. For subjects with HCC:
9.1 Child-Pugh Score of A
9.2 No fibrolamellar carcinoma or mixed hepatocellular cholangiocarcinoma histology
9.3 No moderate or severe ascites
10. A minimum of 2 sites of disease, including at least 1 site that is measurable by RECIST Version 1.1 criteria to ensure sufficient disease for response assessment. At least 1 of the other lesions must be considered adequate for protocol-required
tumor biopsy. Consider prioritization of percutaneous lesions that are palpable, or guided by imaging if necessary, and exclude biopsies of any lesions that are in proximity to vital visceral, cardio-pulmonary, or any neurovascular structures. A single site of disease is considered adequate to allow for response assessment and protocol-required tumor biopsies if it measures at least 2 cm in the shortest axis.
11.1 Adequate wash-out of prior systemic therapy for underlying malignancy, relative to leukapheresis:
11.1.a Last dose of any antineoplastic treatment must be at least 2 weeks before leukapheresis.
11.1.b Last dose of any investigational agent must be at least 3 half-lives of the treatment, or 28 days, before leukapheresis (whichever is shorter).
11.2 Adequate wash-out of prior systemic therapy for underlying malignancy, relative to LD chemotherapy:
11.2.a The last dose of systemic nitrosourea or systemic mitomycin-C must be at least 6 weeks before the first dose of LD chemotherapy in this study.
11.2.b For all other for systemic cytotoxic chemotherapy, the wash-out must be the duration of a full cycle of that therapy.
11.2.c For biologic therapy (eg, antibodies) the wash-out must be either the duration of the biologic agent dosing interval, or 3 weeks, whichever is shorter.
11.2.d For small molecule therapies, the wash-out must be 5 half-lives of the drug.
11.2.e For any investigational agent, the wash-out must be 3 half-lives of the investigational agent, or 4 weeks, whichever is shorter.
Note: Local radiation of lesions is allowed if indicated for palliation; locally treated lesions will be considered non-target lesions. Hormone ablation is also allowed as clinically indicated.
12. Subjects or their legally acceptable representative must be able and willing to:
12.1 Provide Institutional Review Board/Independent Ethics Committee (IRB/IEC)-approved written informed consent in accordance with regulatory and institutional guidelines. This must be obtained before the performance of any protocol-related procedures that are not part of normal patient care.
12.2 Comply with the study protocol and with the planned biopsy procedures.
13. Willing and able to commit to study assessments and visit schedule, including availability of a caregiver to conduct daily neurological assessments for 28 days after BOXR1030 administration.

14.1 For women of childbearing potential (defined as physiologically capable of becoming pregnant), confirmation of a negative serum pregnancy test and agreement to use of highly effective contraception per Clinical Trials Facilitation and Coordination Group (CTFG) criteria from screening through the first 12 months after BOXR1030 administration.
14.2 For men with partners of childbearing potential, agreement to use effective barrier contraception from screening through the first 12 months after BOXR1030 administration.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
80 Years

Sex
Both

Target number of participants
110

Key exclusion criteria
Current exclusion criteria as of 16/01/2025:
1. Prior treatment with adoptive cell therapy (e.g., CAR T-cell therapy, natural killer cell therapy, engineered T-cell receptor therapy).
2. History of allogenic hematopoietic stem cell transplant (HSCT).
3. Known untreated CNS tumors or brain metastasis. Subjects are eligible if CNS metastases are asymptomatic, have been treated with radiotherapy for at least 1 month prior to informed consent, are off corticosteroids and have neurologically returned to baseline (residual signs or symptoms related to the CNS treatment are permitted). Imaging obtained for the purpose of CNS metastases management performed during screening must document radiographic stability of CNS lesions for at least 1 month prior to leukapheresis and be performed after completion of any CNS directed therapy. If brain scans are performed, magnetic resonance scans are preferred; however, CT scans are acceptable if MRI is medically contraindicated. CNS evaluation for subjects with no suspicion of brain tumors in their history is not required for the study. Subjects with known leptomeningeal metastases are excluded.
4. Subjects who have not recovered to grade ≤1 or baseline from all AEs due to previous therapies (subjects with grade ≤2 peripheral neuropathy that has been stable for at least 4 weeks or grade ≤2 endocrine-related AEs that has been stable for at least 4 weeks on replacement therapy).
5. Planned use of any antineoplastic treatment or investigational agent from the time of the first dose of LD chemotherapy through the end of study participation, except for allowed local radiation of lesions for palliation (to be considered non-target lesions after treatment) and hormone ablation.
6. Uncontrolled or life-threatening symptomatic concomitant disease including clinically significant gastrointestinal bleeding or pulmonary hemorrhage within 4 weeks before screening, known symptomatic human immunodeficiency virus (HIV) positive with an acquired

immunodeficiency syndrome (AIDS)-defining opportunistic infection within the past 12 months prior to screening, or a current CD4 count <350 cells/μL, symptomatic active hepatitis B or C checked at screening, or active tuberculosis therapy.
Subjects with HIV are eligible if:
6.1. They have received antiretroviral therapy (ART) as clinically indicated for at least 12 months prior to starting LD therapy and have an HIV viral load less than 40 copies/mL prior to start of LD therapy
6.2. They continue on ART as clinically indicated while enrolled on study
6.3. CD4 counts ≥350 cells/μl and CD4 counts and viral load are monitored per standard of care by a local health care provider
6.4. They are fully vaccinated against SARS-CoV-2
7. Has undergone a major surgery within 3 weeks of starting study treatment or has inadequate healing or recovery from complications of surgery prior to starting study treatment.
8. Has received prior radiotherapy within 2 weeks of the start of BOXR1030 treatment. Subjects must have recovered from all radiation-related toxicities, not require corticosteroids, and not have had severe radiation pneumonitis. A 1-week wash-out is permitted for palliative radiation (≤2 weeks of radiotherapy) to non-CNS disease.
9. Potentially life-threatening second malignancy requiring systemic treatment within the last 3 years (i.e., subjects with a history of prior malignancy are eligible if treatment was completed at least 3 years before entering the Treatment Period and the subject has no evidence of disease) or which would impede evaluation of treatment response. Hormone ablation therapy is allowed within the last 3 years. Subjects with history of prior early stage basal/squamous cell skin cancer or non-invasive or in situ cancers that have undergone definitive treatment at any time are eligible.
10. Clinically significant (i.e., active) cardiovascular disease: cerebral vascular accident/stroke (<6 months prior to enrollment), myocardial infarction (<6 months prior to enrollment), unstable angina, congestive heart failure (New York Heart Association Classification Class ≥II), or the presence of any condition that can increase proarrhythmic risk (e.g., hypokalemia, bradycardia, heart block) including any new, unstable, or serious cardiac arrhythmia requiring medication, or other baseline arrhythmia that might interfere with interpretation of electrocardiograms (ECGs) on study (e.g., bundle branch block). Subjects with QTcF >450 msec for males and >470 msec for females on screening ECG are excluded, except subjects with a known right bundle branch block who will be excluded with QTcF >480 msec.
11. Has an active infection excluding controlled HIV
12. Has an active autoimmune disease requiring systemic (immunosuppressive) therapy.
13. Has received any live vaccines against infectious disease within 6 weeks before start of LD chemotherapy and/or from start of screening through the end of the study treatment period. Note: the full series (e.g., both doses of a two-dose vaccination series) should be completed prior to leukapheresis when feasible and when a delay in enrollment would not put the study subject at risk).
14. A woman of child-bearing potential (WOCBP) who has a positive pregnancy test prior to enrollment.
15. Is breastfeeding or expecting to conceive or father children within the projected duration of the study, starting with the Screening visit through 6 months after the last dose of study treatment.
16. Unable to receive any of the agents used in this study due to history of severe immediate hypersensitivity reaction (e.g., hypersensitivity to dimethyl sulfoxide [DMSO]).
17. Known allergy or contraindication to any of the LD chemotherapy tocilizumab, or other prophylaxis medications required during the study.
18. Any other significant co-morbid disease or condition which, in the judgment of the Investigator, would put the subject at undue risk (e.g., cirrhotic liver disease).

Previous exclusion criteria:
1. Prior treatment with adoptive cell therapy
2. History of allogenic hematopoietic stem cell transplant (HSCT).
3. Untreated central nervous system (CNS) tumors or brain metastasis unless they are asymptomatic, were treated and patients have neurologically returned to baseline. Imaging obtained for the purpose of CNS metastases management performed within 28 days prior to Day 1 must document radiographic stability of CNS lesions and be performed after completion of any CNS directed therapy. CNS evaluation for asymptomatic patients is not required for the study. Patients with leptomeningeal metastases are excluded.
4. Patients who have not recovered to ≤ Grade 1 or baseline from all AEs due to previous therapies (patients with ≤ Grade 2 neuropathy that has been stable for at least 4 weeks or ≤Grade 2 endocrine-related AEs that has been stable for at least 4 weeks on replacement therapy).
5. Planned use of any antineoplastic treatment or investigational agent from the time of the first dose of LD chemotherapy through the end of study participation, except for allowed local radiation of lesions for palliation (to be considered non-target lesions after treatment) and hormone ablation.
6. Uncontrolled or life-threatening symptomatic concomitant disease including clinically significant gastrointestinal bleeding or pulmonary hemorrhage within 4 weeks before screening, known symptomatic human immunodeficiency virus (HIV) positive with an acquired immunodeficiency syndrome (AIDS)-defining opportunistic infection within the last year, or a current CD4 count <350 cells/uL, symptomatic active hepatitis B or C checked at screening, or active tuberculosis. Patients with HIV are eligible if:
6.1 They have received antiretroviral therapy (ART) as clinically indicated for at least 4 weeks prior to starting study treatment
6.2 They continue on ART as clinically indicated while enrolled on study
6.3 CD4 counts and viral load are monitored per standard of care by a local health care provider
7. Has undergone a major surgery within 3 weeks of starting study treatment or has inadequate healing or recovery from complications of surgery prior to starting study treatment.
8. Has received prior radiotherapy within 2 weeks of start of study treatment. Subjects must have recovered from all radiation-related toxicities, not require corticosteroids, and not have had severe radiation pneumonitis. A 1-week wash-out is permitted for palliative radiation (≤2 weeks of radiotherapy) to non-CNS disease.
9. Potentially life-threatening second malignancy requiring systemic treatment within the last 3 years (ie, patients with a history of prior malignancy are eligible if treatment was completed at least 3 years before entering the Treatment Period and the patient has no evidence of disease) or which would impede evaluation of treatment response. Hormone ablation therapy is allowed within the last 3 years. Patients with history of prior early stage basal/squamous cell skin cancer or non-invasive or in situ cancers that have undergone definitive treatment at any time are eligible.
10. Clinically significant (i.e. active) cardiovascular disease: cerebral vascular accident/stroke (<6 months prior to enrollment), myocardial infarction (<6 months prior to enrollment), unstable angina, congestive heart failure (≥ New York Heart Association Classification Class II), or the presence of any condition that can increase proarrhythmic risk (eg, hypokalemia, bradycardia, heart block) including any new, unstable, or serious cardiac arrhythmia requiring medication, or other baseline arrhythmia that might interfere with interpretation of electrocardiograms (ECGs) on study (eg, bundle branch block). Patients with QTcF >450 msec for males and >470 msec for females on screening ECG are excluded. Any patients with a bundle branch block will be excluded with QTcF >450 msec. Males who are on stable doses of concomitant medication with known prolongation of QTcF (eg, selective serotonin re-uptake inhibitor antidepressants) will only be excluded for QTcF >470 msec.
11. Has an active infection requiring systemic therapy.

12. A woman of child-bearing potential (WOCBP) who has a positive pregnancy test prior to treatment.
13. Is breastfeeding or expecting to conceive or father children within the projected duration of the study, starting with the Screening Visit through 6 months after the last dose of study treatment.
14. Unable to receive any of the agents used in this study due to history of severe immediate hypersensitivity reaction (eg, hypersensitivity to dimethyl sulfoxide [DMSO]).
15. Known allergy or contraindication to any of the LD chemotherapy or prophylaxis medications required during the study.
16. Any other significant co-morbid disease or condition which, in the judgment of the Investigator, would put the subject at undue risk (eg, cirrhotic liver disease).

Date of first enrolment
26/10/2022

Date of final enrolment
30/04/2027

Locations

Countries of recruitment
England

Scotland

United Kingdom

United States of America

Study participating centre
The Royal Marsden Hospital (london)
Fulham Road
London
United Kingdom
SW3 6JJ

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre

Beatson Institute for Cancer Research
Wolfson Wohl Cancer Research Centre
Switchback Rd
Bearsden
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G61 1BD

Study participating centre
University of Texas MD Anderson Cancer Center
1515 Holcombe Blvd
Houston
United States of America
TX 77030

Study participating centre
Froedtert and Medical College of Wisconsin
9200 W. Wisconsin Ave
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Study participating centre
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Sponsor type
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Funder(s)

Funder type
Industry

Funder Name
SOTIO Biotech Inc

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Internal report
Conference presentation
Publication on website
Other publication
Submission to regulatory authorities
The Sponsor may share pseudonymised data (in coded form) collected during this study. The data will not include information that identifies the participant.

Intention to publish date
31/10/2028

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No