Trial record **1 of 1** for: ct7001

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Modular Study to Evaluate CT7001 Alone in Cancer Patients With Advanced Malignancies

ClinicalTrials.gov Identifier: NCT03363893

Recruitment Status : Active, not recruiting
First Posted : December 6, 2017
Last Update Posted : April 14, 2021

Sponsor:
Carrick Therapeutics Limited

Information provided by (Responsible Party):
Carrick Therapeutics Limited

Study Description

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Brief Summary:

This is a modular, Phase I/II, multicentre study to investigate **CT7001** monotherapy in advanced solid malignancies and to further investigate **CT7001** as monotherapy or in combination with standard therapy in specific participant groups with Triple Negative Breast Cancer (TNBC), Castrate Resistant Prostate Cancer (CRPC) and in combination with fulvestrant for patients with hormone receptor-positive (HR+ve) / human epidermal growth factor-2 negative (HER2-ve) breast cancer.

Condition or disease	Intervention/treatment	Phase
Advanced Solid Malignancies	Drug: **CT7001**	Phase 1
	Drug: **CT7001** in combination with fulvestrant	Phase 2
	Drug: **CT7001** (in original vs enteric capsule)	

Detailed Description:

Module 1 comprises two sequential parts:

- Part A: First-in-human (FiH) dose escalation investigating the safety and tolerability of CT7001 to identify the minimum biologically active dose (MBAD) and maximum tolerated dose (MTD). Part A also includes a cohort expansion for breast cancer participants only: this includes sequential tumour biopsies for evaluation of pharmacokinetic (PK), pharmacodynamic (PD) and tumour responses. Recruitment is completed.
- Part B: To refine the safety, tolerability, and PK and PD profiles of CT7001 monotherapy in participants with advanced solid malignancies from up to four tumour- specific cohorts, which may include, but is not limited to, triple-negative breast cancer, ovarian cancer, small-cell lung cancer and prostate cancer.
  - Part B, Cohort 1, Triple-Negative Breast Cancer (M1B-1 TNBC) treated with CT7001 as monotherapy. Recruitment is currently closed.
  - Part B, Cohort 2, Prostate Cancer (M1B-2 CRPC) treated with CT7001 as monotherapy. Recruitment is currently closed.
  - Additional Module 1B Cohorts of up to 25 participants each may be added in the future.
- Module 4 is a study investigating the effect of food on the PK of CT7001 monotherapy in participants with advanced solid malignancies. Recruitment is completed.
- Module 2 is a Phase Ib/II, 3-part safety and efficacy study in participants with hormone-receptor positive (HR+ve) and human epidermal growth factor-2 negative (HER2-ve) breast cancer. This module will dose CT7001 in combination with fulvestrant. Module 2 consists of 3 parts - Part A, Part B and Part C. Module 2 Part A recruitment is completed.Part B is double-blind, randomized and placebo-controlled Part C will be a crossover from Part B.
- Module 6 is a Phase 1 study to explore the tolerability of, and the total and peak exposure of, an enteric capsule formulation of CT7001 [CT7001(EC)], when given as monotherapy to patients with advanced solid malignancies.

Study Design

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Study Type : Interventional (Clinical Trial)
Estimated Enrollment : 250 participants

Allocation:	Randomized
Intervention Model:	Parallel Assignment
Intervention Model Description:	Modular design
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	A Modular, Multipart, Multiarm, Open-label, Phase I/II Study to Evaluate the Safety and Tolerability of **CT7001** Alone and in Combination With Anti-cancer Treatments in Patients With Advanced Malignancies
Actual Study Start Date :	November 14, 2017
Estimated Primary Completion Date :	March 2023
Estimated Study Completion Date :	March 2023

Resource links provided by the National Library of Medicine

Drug Information available for: Fulvestrant

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: Module 1 Part A Participants with advanced solid tumours receive **CT7001** (samuraciclib) as oral monotherapy, in ascending dose cohorts, to identify the maximum tolerated dose (MTD), minimally biologically active dose (MBAD) and recommended dose for Phase II testing (RP2D). This module includes a cohort expansion of participants with breast cancer who provide paired biopsy samples.	Drug: **CT7001** Cyclin-dependent kinase 7 (CDK7) inhibitor given orally once daily until disease progression Other Name: Samuraciclib
Experimental: Module 1 Part B Participants with advanced solid tumours that may include, but is not limited to, triple negative breast cancer (TNBC), castrate-resistant prostate cancer (CRPC), small cell lung cancer (SCLC) or ovarian cancer, will receive **CT7001** (samuraciclib) as oral monotherapy at the dose, frequency and schedule recommended from Module 1 Part A. To date Module 1 Part B Arm has recruited a cohort of CRPC participants.	Drug: **CT7001** Cyclin-dependent kinase 7 (CDK7) inhibitor given orally once daily until disease progression Other Name: Samuraciclib
Experimental: Module 1 Part B-1 TNBC Expansion Participants with locally advanced or metastatic triple-negative breast cancer (TNBC) will receive **CT7001**(samuraciclib) as oral monotherapy at the dose, frequency and schedule recommended from Module 1 Part A.	Drug: **CT7001** Cyclin-dependent kinase 7 (CDK7) inhibitor given orally once daily until disease progression Other Name: Samuraciclib
Experimental: Module 2 Part A Participants with locally advanced or metastatic HR+ve and HER2-ve breast cancer will receive **CT7001** (samuraciclib) oral monotherapy in combination with fulvestrant.	Drug: **CT7001** in combination with fulvestrant Cyclin-dependent kinase 7 (CDK7) inhibitor given orally once daily until disease progression in combination with fulvestrant given as 2 x 250mg intramuscular (IM) gluteal injections on Day 1, Day 15, Day 28 and every 28 days thereafter Other Name: Samuraciclib
Experimental: Module 2 Part B Participants with locally advanced or metastatic HR+ve and HER2-ve breast cancer will be randomized to receive **CT7001** (samuraciclib) or matching placebo as oral monotherapy at the dose determined in Module 2 Part A, in combination with fulvestrant.	Drug: **CT7001** in combination with fulvestrant Cyclin-dependent kinase 7 (CDK7) inhibitor given orally once daily until disease progression in combination with fulvestrant given as 2 x 250mg intramuscular (IM) gluteal injections on Day 1, Day 15, Day 28 and every 28 days thereafter Other Name: Samuraciclib
Experimental: Module 2 Part C Participants with locally advanced or metastatic HR+ve and HER2-ve breast cancer who were enrolled to the placebo arm in Module 2 Part B will, on progression of disease, receive **CT7001** (samuraciclib) oral monotherapy in combination with fulvestrant.	Drug: **CT7001** in combination with fulvestrant Cyclin-dependent kinase 7 (CDK7) inhibitor given orally once daily until disease progression in combination with fulvestrant given as 2 x 250mg intramuscular (IM) gluteal injections on Day 1, Day 15, Day 28 and every 28 days thereafter Other Name: Samuraciclib
Experimental: Module 4 Participants with advanced solid tumours will receive **CT7001**(samuraciclib) oral monotherapy in a randomized, balanced, single-dose, two-treatment (fed v fasting), two-period, two-sequence crossover study followed by once daily continuous dosing.	Drug: **CT7001** Cyclin-dependent kinase 7 (CDK7) inhibitor given orally once daily until disease progression Other Name: Samuraciclib

Experimental: Module 6 Participants with advanced solid malignancies will receive **CT7001** (samuraciclib) and a new enteric capsule **CT7001** (EC) (samuraciclib) oral monotherapy in a randomized, single blind, balanced, two treatment two period, two sequence crossover with one wash out period in between, followed by once daily continuous dosing.	Drug: **CT7001** (in original vs enteric capsule) Cyclin-dependent kinase 7 (CDK7) inhibitor given orally once daily until disease progression Other Name: Samuraciclib

Outcome Measures

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Primary Outcome Measures :

1. Treatment-Emergent Adverse Events and Laboratory Abnormalities (Safety and Tolerability) [Time Frame: Screening to end of study]

   Type, incidence and severity

Secondary Outcome Measures :

1. Maximum Plasma Concentration of **CT7001** (and Fulvestrant, where applicable) (Cmax) [Time Frame: After the first dose and during the dosing period]
2. Area Under the Curve (AUC) [Time Frame: After the first dose and during the dosing period]
3. Biological Activity Parameters (Biomarkers) in Peripheral Blood [Time Frame: Screening to end of treatment]
4. Anti-tumour Activity according to RECIST v1.1 [Time Frame: Baseline until disease progression or withdrawal from the study]
5. Objective Response Rate (ORR) [Time Frame: Baseline until disease progression or withdrawal from the study]
6. Progression-Free Survival (PFS) [Time Frame: Baseline until disease progression or withdrawal from the study]

Eligibility Criteria

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Information from the National Library of Medicine NIH NLM

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years and older (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Core Inclusion Criteria:

1. ECOG performance status 0 or 1 with no deterioration over the previous 2 weeks
2. Estimated life expectancy of greater than 12 weeks
3. Ability to swallow and retain oral medication
4. Women either of non-childbearing potential or of childbearing potential willing to practice effective contraception for the duration of the study and for 6 months (Module 1, Module 4) and 24 months (Module 2) after the last dose of CT7001
5. Sexually active male patients must be willing to use condoms with all sexual partners for the duration of the study and for 3 months after the last dose of CT7001.
6. Provision of signed and dated, written informed consent

Core Exclusion Criteria:

1. Any other malignancy that has been active or treated within the past 3 years, with the exception of cervical intraepithelial neoplasia and non-melanoma skin cancer
2. Any unresolved toxicity (except alopecia) from prior therapy of ≥ CTCAE Grade 2
3. Spinal cord compression or brain metastases, unless asymptomatic, stable, and not requiring steroids for at least 4 weeks before the first dose of investigational product (IP)
4. Refractory nausea and vomiting, chronic gastrointestinal (GI) disease or previous significant bowel resection, with clinically significant sequelae that would preclude adequate absorption of CT7001
5. Uncontrolled seizures
6. Active infection requiring systemic antibiotic, antifungal, or antiviral medication
7. Severe or uncontrolled medical condition or psychiatric condition
8. Active bleeding diatheses
9. Renal transplant
10. Known hepatitis B, hepatitis C, or human immunodeficiency virus infection

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11. Breastfeeding or pregnancy
12. Receipt of systemic cytotoxic treatment for the malignancy within 28 days or ≤ 5 half-lives, whichever is shorter before the first dose of IP
13. Receipt of non-cytotoxic treatment for the malignancy within 5 half-lives of the drug before the first dose of IP
14. Receipt of corticosteroids (at a dose > 10 mg prednisone/day or equivalent) within 14 days before the first dose of IP
15. Receipt of any small-molecule investigational medicinal product (IMP) within 28 days or ≤ 5 half-lives, whichever is shorter before the first dose of IP
16. Receipt of any biological IMP (e.g., immune checkpoint blockers, antibodies, nanoparticles) within 42 days before the first dose of IP
17. Receipt of St John's Wort within 21 days before the first dose of IP or of another concomitant medication, herbal supplement, or food that is a strong inhibitor or inducer of CYP3A4, CYP2C19, CYP2D6, or P-glycoprotein (PGP) activity within 14 days before the first dose of CT7001
18. Receipt of a blood transfusion (blood or blood products) within 14 days before the first dose of IP
19. Known hypersensitivity to CT7001 or any excipient of the product
20. Impaired hepatic or renal function as demonstrated by any of the following laboratory values:
    a. Albumin < 30 g/L
    b. Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 2.5 × the upper limit of normal (ULN)
    c. > 5.0 × ULN for patients with liver metastases
    d. Total bilirubin > 1.5 × ULN
    e. Serum creatinine > 1.5 × ULN
21. Liver function deteriorating in a manner that would likely make the participant meet the AST, ALT, or bilirubin levels specified above at the time of the first dose of IP
22. Other evidence of impaired hepatic synthesis function
23. Inadequate bone marrow reserve or organ function as demonstrated by any of the following laboratory values:
    a. Absolute neutrophil count (ANC) < 1.5 × 10^9/L
    b. Platelet count < 100 × 10^9/L
    c. Haemoglobin < 90 g/L
24. Persistent (> 4 weeks) severe pancytopenia due to previous therapy rather than to disease (ANC < 0.5 × 10^9/L or platelets < 50 x 10^9/L)
25. Cardiac dysfunction (defined as myocardial infarction within 6 months of study entry, New York Heart Association Class II/III/IV heart failure, unstable angina, unstable cardiac arrhythmias, or left ventricular ejection fraction < 55 percent)
26. Mean resting QT interval corrected for heart rate by the Fridericia formula (QTcF) > 470 msec obtained from 3 electrocardiograms (ECGs) obtained within 5 minutes of each other prior to the first dose
27. Any clinically important abnormalities in rhythm, conduction, or morphology on resting ECG (e.g., complete left bundle branch block, third degree heart block). Controlled atrial fibrillation (AF) is permitted
28. Any factor that increases the risk of QTc prolongation or of arrhythmic events (e.g., heart failure, hypokalaemia, congenital long QT syndrome, immediate family history of long QT syndrome or unexplained sudden death under 40 years of age)
29. In the opinion of the Investigator, unlikely to comply with study procedures, restrictions, or requirements
30. A history of haemolytic anaemia or marrow aplasia
31. Has received a live-virus vaccination within 28 days or less of planned treatment start

Additional Module 1A Inclusion Criteria:

1. Histological, radiological or cytological confirmation of an advanced non-haematological malignancy not considered to be appropriate for further standard treatment
2. Module 1A biopsy cohort only : at least one tumour suitable for repeat biopsy

Additional Module 1A Exclusion Criteria:

1. International normalised ratio (INR) ≥1.5

Additional Module 1B Inclusion Criteria

1. Histological or cytological confirmation of metastasis or locally advanced tumour
2. At least one line of systemic anti-cancer therapy
3. Disease measurable by RECIST v1.1

Additional Module 1B-1 (TNBC Expansion) Inclusion Criteria:

1. Histologically-confirmed carcinoma of breast not expressing oestrogen receptor (ER) or progesterone receptor (PR) and negative for human epidermal growth factor receptor 2 (HER2)
2. Documented disease progression on or within 6 months of most recent cytotoxic prior cytotoxic chemotherapy
3. Disease measurable by RECIST v1.1
4. Must have received at least one cytotoxic chemotherapy for metastatic/locally advanced disease

Additional Module 1B-1 (TNBC Expansion) Exclusion Criteria:

1. No more than three lines of cytotoxic chemotherapy for metastatic/locally advanced disease
2. No advanced, symptomatic visceral metastases
3. No known symptomatic central nervous system (CNS) metastases, carcinomatous meningitis or leptomeningeal disease
4. Prior exposure to CT7001
5. Patients who are investigational site staff members directly involved in the conduct of the trial and their family members, site staff members otherwise supervised by the

5. Patients who are investigational site staff members directly involved in the conduct of the trial and their family members, site staff members otherwise supervised by the Investigator, or patients who are Carrick employees directly involved in the conduct of the trial

Additional Module 2 Inclusion Criteria:

1. Women only
2. Pre- or peri-menopausal women must have initiated LHRHa at least 28 days prior to first dose of CT7001/placebo
3. Histologically-confirmed, metastatic or locally advanced, ER+ve and/or PGR+ve and HER2-ve breast cancer
4. Part A only: Disease measurable by RECIST v1.1
5. Documented objective disease progression while on, or within 6 months after the end of, the most recent therapy
6. Must have received an aromatase inhibitor together with a CDK4/6 inhibitor in the same line of therapy for locally advanced or metastatic disease or for treatment of early breast cancer if the disease-free interval was <12 months.
7. For Part B only: patients must have received at least 6 months clinical benefit with the CDK4/6 as a line of therapy immediately preceding study entry. Patients who received CDK4/6 inhibitor < 6 months due to tolerability issues when at least 6 months aromatase inhibitor was received.
8. Ability to receive intramuscular injections.

Additional Module 2 Exclusion Criteria:

1. Prior therapy with fulvestrant
2. More than 2 lines of endocrine treatment for locally advanced or metastatic disease
3. Part A Only: Prior treatment with more than one line of cytotoxic chemotherapy for locally advanced or metastatic breast cancer.
4. Part B Only: Prior treatment with cytotoxic chemotherapy for locally advanced or metastatic breast cancer or treatment with a mammalian target of rapamycin (mTOR) inhibitor including, but not limited to, everolimus.
5. Patients with liver metastasis will be limited to approximately 30-40% of the enrolled patients. I
6. Known hypersensitivity to CT7001, fulvestrant or any excipient of the investigational products
7. Patients who are investigational site staff members directly involved in the conduct of the trial and their family members, site staff members otherwise supervised by the Investigator, or patients who are Carrick employees directly involved in the conduct of the trial

Additional Module 4 Inclusion Criteria:

1. Patients must be able to eat a high-fat meal, as provided by the study site, within a 30-minute period
2. Histological, radiological or cytological confirmation of an advanced non-haematological malignancy not considered to be appropriate for further standard treatment

Additional Module 4 Exclusion Criteria:

1. Patients who were unable to fast for at least 10 hours

Additional Module 6 Inclusion Criteria:

1. Histological, radiological or cytological confirmation of an advanced non- haematological malignancy not considered to be appropriate for further standard treatment.

Additional Module 6 Exclusion Criteria:

1. Any concurrent gastrointestinal conditions, not covered in Core Protocol Exclusion Criteria #4
2. Patients whom has received an agent that increases gastric pH (i.e. proton pump inhibitors (PPI), H2 antagonists) within 2 days or 5 half-lives, whichever is shorter, prior to PK Period Day 1.

Contacts and Locations

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Information from the National Library of Medicine NIH NLM

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT03363893***

Locations

▸ Show 32 study locations

Sponsors and Collaborators

Carrick Therapeutics Limited

Investigators

Principal Investigator: Matthew Krebs, MBChB PhD The Christie Hospital, Manchester, UK

More Information

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Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Sava GP, Fan H, Coombes RC, Buluwela L, Ali S. CDK7 inhibitors as anticancer drugs. Cancer Metastasis Rev. 2020 Sep;39(3):805-823. doi: 10.1007/s10555-020-09885-8. Review.

Responsible Party:	Carrick Therapeutics Limited
ClinicalTrials.gov Identifier:	NCT03363893 History of Changes
Other Study ID Numbers:	**CT7001**_001
	2017-002026-20 (EudraCT Number)
First Posted:	December 6, 2017 Key Record Dates
Last Update Posted:	April 14, 2021
Last Verified:	April 2021

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD:	No

Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No

Keywords provided by Carrick Therapeutics Limited:

Neoplasms

Additional relevant MeSH terms:

- Neoplasms
- Fulvestrant
- Antineoplastic Agents, Hormonal
- Antineoplastic Agents
- Estrogen Receptor Antagonists
- Estrogen Antagonists
- Hormone Antagonists
- Hormones, Hormone Substitutes, and Hormone Antagonists
- Physiological Effects of Drugs

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