A Phase 1 Study of JNJ-78278343, a T Cell Redirecting Agent Targeting Human Kallikrein 2 (KLK2), for Advanced Prostate Cancer

Published: 20-05-2021
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This study has been transitioned to CTIS with ID 2023-506585-31-00 check the CTIS register for the current data. The study contains 2 parts: Part 1 is the dose escalation part. Part 2 is the dose expansion part.The primary objective of part 1 is to…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON53995

Source
ToetsingOnline

Brief title
78278343PCR1001

Condition

- Reproductive neoplasms male malignant and unspecified

Synonym
Prostate cancer, prostate carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag

Source(s) of monetary or material Support: Janssen-Cilag BV

Intervention

Keyword: First-in-Human, Prostate Cancer, Recommended phase 2 dose, Safety

Outcome measures

Primary outcome

The primary objective of part 1 is to determine recommended Phase 2 dose(s) (RP2Ds) of JNJ-78278343 by investigating the incidence and severity of AEs, including dose-limiting toxicity.

The primary objective of part 2 is to determine the safety at the RP2D(s) by investigating the incidence and severity of AEs

Secondary outcome

The secondary objectives are:

-Assess the pharmacokinetics by looking at the serum concentration-time profiles and pharmacokinetic parameters for JNJ-78278343 including but not limited to Cmax, Tmax, AUC(t1-t2), AUCtau, Cmin, and accumulation ratio (RA)

- Assess the pharmacodynamics by looking at the pharmacodynamic markers including, but not limited to, systemic cytokine concentrations and serum PSA

- Assess the immunogenicity by looking at the presence of anti-JNJ-78278343 antibodies

-Assess preliminary antitumor activity by looking at the objective response rate, PSA response, and duration of response according to response criteria of the Prostate Cancer Working Group 3 (PCWG3).

Study description

Background summary

JNJ-78278343 is a humanized immunoglobulin (Ig)G1-based bispecific antibody designed to direct T lymphocytes (T cells) to human kallikrein 2 (hK2or KLK2) positive target tumor cells. One arm of JNJ-78278343 binds to the cluster of differentiation (CD)3 receptor complex present on T cells and the other arm binds to KLK2 present on target tumor cells leading to the activation of the T cells and T-cell-mediated lysis of the KLK2 bearing tumor cells. JNJ-78278343 is being developed for the treatment of metastatic castration-resistant prostate cancer (mCRPC). KLK2 expression is highly restricted in normal tissues and highly enriched in prostate adenocarcinoma and its expression is mostly maintained throughout disease progression, making KLK2 an attractive target for therapy.

Study objective

This study has been transitioned to CTIS with ID 2023-506585-31-00 check the CTIS register for the current data.

The study contains 2 parts: Part 1 is the dose escalation part. Part 2 is the dose expansion part.
The primary objective of part 1 is to determine recommended Phase 2 dose(s) (RP2Ds) of JNJ-78278343 by investigating the incidence and severity of AEs, including dose-limiting toxicity.
The primary objective of part 2 is to determine the safety at the RP2D(s) by investigating the incidence and severity of AEs. The secondary objectives are:
-Assess the pharmacokinetics by looking at the serum concentration-time profiles and pharmacokinetic parameters for JNJ-78278343 including but not limited to Cmax, Tmax, AUC(t1-t2), AUCtau, Cmin, and accumulation ratio (RA)
- Assess the pharmacodynamics by looking at the pharmacodynamic markers including, but not limited to, systemic cytokine concentrations and serum PSA
- Assess the immunogenicity by looking at the presence of anti-JNJ-78278343 antibodies
- Assess preliminary antitumor activity by looking at the objective response rate, PSA response, and duration of response according to response criteria of the Prostate Cancer Working Group 3 (PCWG3).

Study design

This study will be conducted in 2 phases: a Screening Phase (up to 30 days), a Treatment Phase (start of study drug administration) with an end of treatment (EOT) visit (up to 30 plus 14 days after last dose of study drug or prior to the start of a new anticancer therapy), whichever comes first). The total

duration of the study is up to 1 year and 10 months. Safety assessment will include adverse events (AEs) including dose-limiting toxicity (DLT), serious adverse events (SAEs), physical examination, vital signs, electrocardiogram, clinical safety laboratory assessments, Eastern Cooperative Oncology Group (ECOG) performance status, and neurologic examination.

Intervention

Participants will receive JNJ-78278343 subcutaneously (SC). The dose levels will be escalated based on the dose limiting toxicities (DLT) evaluation by the study evaluation team (SET) in Part 1 (dose escalation). In Part 2 (dose expansion), participants will receive JNJ-78278343 SC at recommended phase 2 dose (RP2D) as determined in Part 1.

Study burden and risks

This is the first clinical study of JNJ-78278343. The potential risks and mitigation strategies are based on the target expression data, known mechanism of action (ie, T cell activation and tumor cell lysis), and route of administration (Table 6 in the protocol).
It is unknown if there is clinical benefit associated with treatment with JNJ-78278343. JNJ-78278343 has the potential to lead to effective killing of target cells that express KLK2 such as those in mCRPC and could possibly result in an increase in progression-free survival (PFS) survival for patients with advanced disease and limited treatment options.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Each potential participant must satisfy all of the following criteria to be enrolled in the study:
Age
1. 18 years of age or older.

Disease Characteristics
2. Confirmed adenocarcinoma of the prostate which has spread to other body parts.
3. Measurable or evaluable disease
4. Prior treatment with at least 1 prior novel androgen receptor (AR)-targeted therapy or chemotherapy.
5. Prior surgical removal of testicles; or, for participants who have not undergone surgical removal of testicles, must be receiving ongoing androgen deprivation therapy (ADT) with a gonadotropin releasing hormone analog.
6. Concurrent use of any other anticancer treatment.
7. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.

Exclusion criteria

Any potential participant who meets any of the following criteria will be excluded from participating in the study:

Disease Conditions
1. Active central nervous system (CNS) involvement.
2. Toxicity related to prior anticancer therapy has not adequately recovered.

Prior/Concomitant Therapy

3. Prior treatment with KLK2-targeted therapy.
4. Received, or are receiving, medications that suppress the immune system within 3 days prior to the first dose of study drug.
5. Received or plans to receive any live, attenuated vaccine within 4 weeks prior to the first dose of study drug.

Prior/Concurrent Medical Conditions
6. Diagnosis of cancer other than prostate cancer within 2 years prior to the first dose of study drug.
7. Solid organ or bone marrow transplantation.
8. Major clotting diseases within one month prior to the first dose of study drug.
9. Active autoimmune disease within 12 months prior to the first dose of study drug.
10. Active infection.
11. Major diseases of heart and blood vessels within 6 months prior to the first dose of study drug.
12. Clinically significant lung diseases.
13. Active or chronic hepatitis B or hepatitis C infection.
14. Known positive test result for human immunodeficiency virus (unless stable on antiretroviral therapy with undetectable viral load).
16. Any serious underlying medical conditions or other issue that would impair the ability of the participant to receive or tolerate the planned treatment.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-10-2021
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	JNJ-78278343
Generic name:	JNJ-78278343

Ethics review

Approved WMO Date:	20-05-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	06-08-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	17-09-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-03-2022
Application type:	Amendment
Review commission:	METC NedMec

Approved WMO Date:	12-04-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-04-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-08-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-10-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-10-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-12-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-02-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	07-03-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-04-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-05-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-08-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-506585-31-00
EudraCT	EUCTR2020-005970-83-NL

Register	ID
ClinicalTrials.gov	NCT04898634
CCMO	NL76980.031.21