Phase 2b Clinical Study Evaluating Efficacy and Safety of TAR-200 in Combination with Cetrelimab, TAR-200 Alone, or Cetrelimab Alone in Participants with High-Risk Non-Muscle Invasive Bladder Cancer (NMIBC) Unresponsive to Intravesical Bacillus Calmette-Guerin (BCG) who are Ineligible for or Elected Not to Undergo Radical Cystectomy

Published: 15-12-2020
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This study has been transitioned to CTIS with ID 2023-506146-23-00 check the CTIS register for the current data. Cohorts 1, 2, and 3 only:The purpose of this study is to evaluate the overall complete response (CR) rate in participants treated with...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON54181

Source
ToetsingOnline

Brief title
SunRISe-1

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
Bladder cancer

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Janssen-Cilag International N.V.

Intervention

Keyword: Bladder cancer, Cetrelimab, NMIBC, TAR-200/Gemcitabine

Outcome measures

Primary outcome

Cohorts 1, 2, and 3:

Overall Complete Response (CR) Rate

Up to 5 years

Overall CR rate, is defined as the percentage of participants achieving a CR at any time post-treatment. It will be measured by determining the percentage of participants without presence of high-grade disease using results from cystoscopy and centrally read urine cytology at any time point.

Cohort 4:

Disease-free surivival (DFS) rate

DFS rate is defined as the time from treatment to recurrence, progression or death due to any reason. Twelve-month DFS rate will be determined.

Secondary outcome

Duration of Response (DOR) - Up to 5 years

DOR is defined from the date of first CR achieved to the date of first evidence of recurrence or progression or death (whichever is earlier) for participants who achieve a CR.

Overall Survival (OS) - Up to 5 years

OS, defined as the time from the date of first dose of study treatment to death; if a participant has not died at the time of analysis, the participant will be censored at the date last known alive.

Cohort 1, 2 and 4: Concentrations of Gemcitabine and 2*,2* difluorodeoxyuridine (dFdU) in Urine and Plasma - Up to Week 21

Concentrations of gemcitabine and its metabolite dFdU in urine and plasma will be assessed.

Cohort 1 and 3: Serum Concentration of Anti-cetrelimab Antibodies - Predose, up to 3 years

Serum concentration of anti-cetrelimab antibodies will be assessed using a validated immunoassay for anti-drug antibody (ADA) analysis.

Number of Participants with Anti-cetrelimab Antibodies - Predose, up to 3 years

Number of participants with anti-cetrelimab antibodies will be reported.

Change from Baseline in European Organisation for Research and Treatment of Cancer Quality-of-life Questionnaire (EORTC QLQ) -C30 Scores - Baseline, up to 3 years and 4 months

EORTC QLQ-C30 is a core 30-item questionnaire for evaluating the health-related quality of life (HRQoL) of participants participating in cancer clinical studies. It incorporates 5 functional scales (physical, role, cognitive, emotional, and social functioning), 3 symptom scales (fatigue, pain, and nausea or vomiting), and a global health status or HRQoL scale. Ratings for each item range from 1 (not at all) to 4 (very much).

Change from Baseline in EORTC QLQ- Non-Muscle-Invasive Bladder Cancer (NMIBC) 24 Scores - Baseline, up to 3 years and 4 months

EORTC QLQ-NMIBC24 is a 24-item questionnaire for evaluating the HRQoL of participants with superficial (non-muscle-invasive) bladder cancer. The questionnaire is designed to supplement the QLQ-C30 and incorporates 6 multi-item scales and 5 single items. Ratings for each item range from 1 (not at all) to 4 (very much).

Number of Participants with Adverse Events (AEs) by Severity Grades - Up to 5 years

An AE is any untoward medical occurrence in a participant participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. Severity grades ranges from Grade 1 (Mild) to Grade 5 (Death). Grade 1= Mild, Grade 2= Moderate, Grade 3= Severe,

Grade 4= Life-threatening and Grade 5= Death related to adverse event.

Number of Product Quality Complaints (PQC) - Up to 3 years and 1 month

A PQC is defined as any suspicion of a product defect related to manufacturing,

labeling, or packaging, that is, any dissatisfaction relative to the identity,

quality, durability, reliability, or performance of a distributed product,

including its labeling, drug delivery system, or package integrity.

Study description

Background summary

Bladder cancer is the tenth most common type of cancer worldwide. The natural history of high-risk Non-Muscle Invasive Bladder Cancer (NMIBC) is unpredictable; rates of recurrence vary from 15 percent (%) to 78%, and rates of progression to muscle invasion and metastasis vary from less than (<) 1 to 45%. The gemcitabine 225 milligrams (mg) intravesical delivery system (JNJ-17000139) product (hereafter, TAR-200) is an investigational product that is comprised and device components. Cetrelimab (JNJ-63723283) is a fully human immunoglobulin G4 (IgG4) kappa monoclonal antibody (mAb) that binds programmed-cell death protein 1 PD-1.

Study objective

This study has been transitioned to CTIS with ID 2023-506146-23-00 check the CTIS register for the current data.

Cohorts 1, 2, and 3 only:
The purpose of this study is to evaluate the overall complete response (CR) rate in participants treated with TAR-200 in combination with cetrelimab (Cohort 1), or TAR-200 alone (Cohort 2), or cetrelimab alone (Cohort 3) with Carcinoma in Situ (CIS), with or without concomitant high-grade Ta or T1 papillary disease.

Cohort 4 only:
The purpose of this study is to evaluate disease-free survival (DFS) in participants treated with TAR-200 alone with papillary disease only.

Study design

This is an open-label, parallel-group, multi-center study of the efficacy and safety of intravesical TAR-200 in combination with cetrelimab, TAR-200 alone, or cetrelimab alone in participants with high-risk NMIBC unresponsive to prior intravesical Bacillus Calmette-Guerin (BCG) therapy who are either ineligible for or have elected not to undergo radical cystectomy (RC). All enrolled participants must have received adequate BCG and confirmed CIS [with or without papillary disease] or confirmed papillary disease only (high-grade Ta or any T1, without CIS) at enrollment. There are 4 cohorts in this study: Cohort 1 TAR-200 in combination with cetrelimab in participants with CIS with or without papillary disease; Cohort 2 TAR-200 alone in participants with CIS with or without papillary disease; Cohort 3 cetrelimab alone in participants CIS with or without papillary disease and, Cohort 4 TAR 200 alone in participants with papillary disease only. This study consists of 3 periods: screening phase (up to 30 days); treatment phase (up to 2 years); follow up phase (up to 5 years). Total duration of study is up to 6 years and 7 months. Efficacy, safety, pharmacokinetics (PK), and biomarkers will be assessed at specified time points during this study.

Intervention

Cohort 1: TAR-200 and Cetrelimab
Type: Experimental
TAR-200 is placed into the bladder through a urinary placement catheter on Day 0 and will be dosed every 3 weeks (Q3W) for up to the first 24 weeks (6 months), then every 12 weeks through Week 99 (Year 2). In addition, Cetrelimab will be dosed Q3W through Week 78 (18 months).

Cohort 2 and 4: TAR-200
Type: Experimental
TAR-200 is placed into the bladder through a urinary placement catheter on Day 0 and will be dosed Q3W for up to the first 24 weeks (6 months), then every 12 weeks through Week 99 (Year 2).

Cohort 3: Cetrelimab
Type: Experimental
Participants will receive Cetrelimab which will be dosed Q3W through Week 78(18 months).

Study burden and risks

The systemic and local delivery of gemcitabine is known to be active in transitional cell carcinoma of the upper and lower genitourinary tract. There has been broad human experience with intravesical gemcitabine in the management of patients with all-risk non-muscle invasive transitional cell carcinoma.

These trials have shown that prolonged dwell-time and repeated exposure to intravesical gemcitabine results in meaningful responses. Ongoing clinical studies of TAR-200 in over 60 patients with various stages of organ-confined urothelial carcinoma have demonstrated good tolerability of intravesical dosing. The safety and efficacy of cetrelimab in immune-sensitive advanced cancers was found to be consistent with those of other known anti-PD-1 antibodies. Accounting for the measures taken to minimize risk to participants of this study, the potential risks identified in association with TAR-200 in combination with cetrelimab are justified by the anticipated benefits that may be afforded to participants with NMIBC unresponsive to BCG who are ineligible for or refusing radical cystectomy.

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

1. Age >=18 years male or female (or the legal age of consent in the jurisdiction in which the study is taking place) at the time of informed consent 2. Histologically confirmed diagnosis of persistent or recurrent CIS (or Tis), with or without papillary disease (T1, high-grade Ta) or papillary disease only (high-grade Ta or any T1 and absence of CIS), within 12 months of completion (last dose) of adequate BCG therapy, in patients who have received adequate BCG 3. All visible papillary disease must be fully resected (absent) prior to randomization (residual CIS acceptable for participants eligible for Cohorts 1, 2, and 3 only) and documented in the eCRF at Screening cystoscopy. For patients with papillary disease only (Cohort 4), local urine cytology at screening must be negative or atypical (for HGUC). 4. Participants must be willing to undergo all study procedures (e.g., multiple cystoscopies from Screening through the end of study and TURBT/bladder biopsy for assessment of recurrence/progression) 5. Participants must be ineligible for or have elected not to undergo radical cystectomy 6. BCG-unresponsive high-risk NMIBC after treatment with adequate BCG therapy defined as a minimum of 5 of 6 full doses of an induction course (adequate induction) plus 2 of 3 doses of a maintenance course, or at least 2 of 6 doses of a second induction course 7. All AEs adverse events associated with any prior surgery and/or intravesical therapy must have resolved to CTCAE version 5.0 Grade <2 prior to screening 8. Participants must sign the informed consent form ICF indicating that he or she understands the purpose of, and procedures required for, the study and is willing to participate in the study and agree to store samples when applicable 9. Eastern Cooperative Oncology Group ECOG performance status Grade 0, 1, or 2 10. Adequate bone marrow, liver, and renal function (creatinine clearance >30 mL/min) 11. Contraceptive use by participants should be consistent with local regulations regarding the use of contraceptive methods for participants participating in clinical studies. Investigators will advise both male and female participants on the options for banking of sperm and ova, respectively for reproductive conservation a. A female participant must be either of the following: i. Not of childbearing potential ii. Of childbearing potential and practicing true abstinence, or have a sole partner who is vasectomized, or practicing at least 1 highly effective user independent method of contraception Participant must agree to continue the above throughout the study and for 6 months after the last dose of study treatment. Note: If a women becomes of childbearing potential after start of the study, the woman must comply with point ii, as described above. A female participant must also agree to not donate eggs (ova, oocytes) or freeze for future use for the purposes of assisted reproduction during the study and for at least 6 months after the last dose of study drug, and not be breastfeeding (including participants temporarily withholding breastfeeding) and not planning to become pregnant during the study and for at least 6 months after the last dose of study drug. Female participants should consider preservation of eggs prior to study treatment as anti-cancer treatments may impair fertility. Investigators will

advise female participants on the options of banking of ova for reproductive conservation. b. A male participant must wear a condom (with or without spermicidal foam/gel/film/cream/suppository) when engaging in any activity that allows for passage of ejaculate to another person during the study and for a minimum of 6 months after receiving the last dose of study treatment. His female partner, if of childbearing potential, must also be practicing a highly effective method of contraception. If the male participant is vasectomized, he still must wear a condom (with or without spermicidal foam/gel/film/cream/suppository), but his female partner is not required to use contraception. Male participants should consider preservation of sperm prior to study treatment as anticancer treatments may impair fertility. Investigators will advise male participants on the options for banking of sperm for reproductive conservation. A male participant must also agree to not donate sperm for the purpose of reproduction during the study and for at least 6 months after the last dose of study drug, and not plan to father a child while enrolled in this study or within 6 months after the last dose of study drug 12. A female participant of childbearing potential must have a negative serum test at screening and a negative urine test within 72hours of the first dose of study treatment and must agree to further serum or urine pregnancy tests during the study, that may exceed those listed in the Schedule of Activities 13. Participants must be willing and able to adhere to the lifestyle restrictions specified in this protocol

Exclusion criteria

1. Presence or history of histologically confirmed, muscle-invasive, locally advanced, nonresectable, or metastatic urothelial carcinoma (ie,T2,T3,T4, and/or Stage IV).
2. Must not have had urothelial carcinoma or histological variant at any site outside of the urinary bladder. Ta/T1/CIS of the upper urinary tract (including renal pelvis and ureter) is allowable if treated with complete nephrouretrectomy more than 24 months prior to randomization.
3. Active malignancies (ie progressing or requiring treatment change in the last 24 months prior to randomization) other than the disease being treated under study:
a. skin cancer (non-melanoma or melanoma) that is considered completely cured
b. non-invasive cervical cancer that is considered completely cured
c. adequately treated lobular carcinoma in situ (LCIS) and ductal CIS
d. history of localized breast cancer and receiving antihormonal agents
e. history of localized prostate cancer (N0M0) and receiving androgen deprivation therapy
f. Localized prostate cancer (N0M0)
4. Presence of any bladder or urethral anatomic feature (eg. urethral stricture) that may prevent the safe insertion, indwelling use, or removal of TAR-200, or passage of a urethral catheter for intravesical chemotherapy, or

administration of intravesical BCG. Participants with tumors involving the prostatic urethra in men will be excluded.
5. Evidence of bladder perforation during diagnostic cystoscopy.
6. Bladder post-void residual (PVR) volume >350mL at Screening after second voided urine.
7. No history of acute ischemic heart disease within 30 days of cohort assignment, or history of uncontrolled cardiovascular disease.
8. A history of clinically significant polyuria with recorded 24-hour urine volumes greater than 4000 mL.
9. Received a live virus vaccine within 30 days of planned start of study treatment. Inactivated (non-live or non-replicating) vaccines approved or authorized for emergency use (eg, COVID-19) by local health authorities are allowed.
10. Active infection requiring systemic IV therapy within 14 days prior to randomization.
11. Currently participating or has participated in a study of an investigational agent and received study therapy or investigational device within 4 weeks prior to screening.
12. Indwelling catheters are not permitted; however, intermittent catheterization is acceptable.
13. Received serial intervening intravesical chemotherapy or immunotherapy from the time of pre-screening or screening cystoscopy/TURBT to starting study treatment. Peri-operative intravesical chemotherapy prior to study is allowed per institutional guidelines.
14. Prior therapy with an anti-programmed -cell death 1, anti-PD-ligand 2 agent, or with an agent directed to another co-inhibitory T-cell receptor.
15. Not recovered from toxicity of prior anticancer therapy (except toxicities which are not clinically significant such as alopecia, skin discoloration).
16. No clinically significant liver disease that precludes participant treatment regimens prescribed on the study.
17. Human immunodeficiency virus (HIV) infection, unless the participant has been on a stable anti-retroviral therapy regimen for the last 6 months or more prior to randomization and has had no opportunistic infections and a CD4 count of >350 in the last 6 months.
18. Active hepatitis B or C infection (for example, participants with history of hepatitis C infection but undetectable hepatitis C virus PCR test and participants with history of hepatitis B infection with positive HBsAg antibody and undetectable PCR are allowed).
19. Concurrent urinary tract infection, defined as a symptomatic infection with a positive urine culture with a bacterial count of >=10^5 colony forming units (CFU)/mL in urine voided from women, or >10^4 CFU/mL in urine voided from men, or in straight-catheter urine from women.
20. Known hypersensitivity to gemcitabine (or other drug excipients) or chemically-related drugs.
21. Known hypersensitivity to the TAR-200 device constituent or the (TAR-200) UPC materials.
22. Evidence of radiographic features associated with pulmonary

fibrosis/advanced interstitial lung disease or active non-infectious pneumonitis
23. Participants must not have active tuberculosis.
24. Major surgery within 4 weeks before screening (TURBT is not considered major surgery).
25. Any condition for which participation would not be in the best interest of the participants or that could prevent, limit, or confound the protocol-specified assessments.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-10-2021
Enrollment:	9
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Cetrelimab
Generic name:	Cetrelimab
Product type:	Medicine
Brand name:	Cetrelimab (new formulation 360mg/vial)
Generic name:	Cetrelimab (new formulation 360mg/vial)

Product type:	Medicine
Brand name:	TAR-200
Generic name:	TAR-200

Ethics review

Approved WMO Date:	15-12-2020
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-02-2021
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-03-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	11-03-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-03-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-03-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-05-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-05-2021

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-07-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	01-09-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-09-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-10-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-11-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-11-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	08-05-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-05-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-09-2022

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-10-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-11-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	13-12-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-05-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-05-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-08-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-10-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-11-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	11-01-2024

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-02-2024
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	CTIS2023-506146-23-00
EudraCT	EUCTR2020-002646-16-NL
ClinicalTrials.gov	NCT04640623
CCMO	NL75604.028.20