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A phase 3, randomized study evaluating the efficacy and safety of TAR-210 Erdafitinib intravesical delivery system versus single agent intravesical chemotherapy in participants with intermediate-risk non-muscle invasive bladder cancer

Submission date 15/03/2024	**Recruitment status** Recruiting	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 03/05/2024	**Overall study status** Ongoing	
Last Edited 04/06/2024	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Intermediate-risk non-muscle invasive bladder cancer (IR-NMIBC) is an early stage of bladder cancer that is limited to the inner lining of the bladder.

The standard treatment for this type of bladder cancer is removal of cancer by surgery followed by treatment administered directly into the bladder, such as chemotherapy, Bacillus Calmette-Guerin therapy, or other treatments. Even after surgical removal and additional treatments there is a high risk of the cancer coming back or worsening.

The study treatment, TAR-210, is a drug delivery system that is temporarily placed in the bladder. It continuously delivers erdafitinib, a medicine being investigated to treat the bladder cancer.

In this study, researchers want to compare the length of time participants are alive and free of any signs or symptoms of the cancer (disease-free survival), when treated with TAR-210 or intravesical chemotherapy* with mitomycin C (MMC) or gemcitabine in participants with IR-NMIBC with an alteration in a gene called fibroblast growth factor receptor (FGFR).

*Treatment in which anticancer drugs are put directly into the bladder through a thin, flexible tube inserted into urethra.

Who can participate?
Patients aged 18 years or older, with bladder cancer, who meet all of the inclusion criteria.

What does the study involve?
Participants will be randomly allocated to receive one of two treatments for one year.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
The participant information sheet(s) (PISs) will contain full information on the potential side effects of study interventions.

TAR-210:

There is limited information available on the possible discomforts, side effects, and risks related to TAR-210 treatment. Possible risks based on information available from participants treated with TAR-210 in the first in human (FIH) Phase 1 study, testing of TAR-210 in animals, the risks associated with intravesical delivery systems similar to TAR-210, and oral erdafitinib are described in the PIS.

There is a possibility that TAR-210 may be damaged when passing through the Urinary Placement Catheter. If the study doctor believes that the TAR-210 may be damaged, it will be removed immediately. However, a damaged TAR-210 may be placed into the bladder if the damage is not visible to the study doctor. If this happens, the damaged TAR-210 may remain inside the bladder for the duration of 90 days and it may have no effect, may not work as intended, or may be expelled.

If TAR-210 becomes damaged or if it is accidentally voided, the study doctor may have to perform some additional tests or procedures, including but not limited to an abdominal x-ray and additional cystoscopy.

It is very unlikely that TAR-210 will be expelled from the bladder during this study. In the unlikely event that TAR-210 is expelled during voiding, it can be safely handled with gloves. TAR-210 should be placed in a double plastic bag that will be provided by a member of the study team.

It is essential for participants to return to the study site to have their TAR-210 removed. There are rare potential risks associated with the same TAR-210 in the bladder for greater than the planned placement period. The potential risks may include, but are not limited to:
• Encrustation (the formation of a hard outer layer) of TAR-210
• Urinary tract infection
• Bladder stone formation
• Blood infection
• Extensive cystoscopy or surgery to remove TAR-210 and/or bladder stone

Participants may experience some discomfort when the cystoscope or urinary placement catheter is passed into the bladder for the cystoscopic examination, during insertion/removal of TAR-210, and possibly during the time between TAR-210 insertion and removal while TAR-210 remains in the bladder. Perforation of the bladder could also occur, which could require urgent surgery.

There may be discomfort, side effects and risks with the use of TAR-210 that are not yet known.

Potential Discomforts, Side Effects, and Risks Associated with Gemcitabine and Mitomycin C (MMC) are detailed in the PIS.

Bladder Biopsy/Transurethral Resection of Bladder Tumour:
There are some risks associated with this procedure such as pain, bleeding, infection, or damage to the bladder. Urinary tract infections may also occur, but these risks are low. Antibiotics will be given in advance of this procedure. There is a small risk associated with the anaesthesia that is administered.

Cystoscopy:
Participants may experience side effects for a short time following a cystoscopy procedure, such as blood in urine, urinary urgency, frequent urination, pain during urination, bladder infection, discomfort as the cystoscope is passed into the bladder for the cystoscopic examination, and discomfort during removal of the TAR-210. Tear of the bladder tissue could also occur.

ECG:
There is generally no risk with having an ECG. The sticky patches may pull skin or cause redness or itching.

CT Urography/MR Urography Scan with Contrast:
Full risk information for imaging is detailed in the PIS.

Blood draw/tests:
Participants may get a bruise or irritation. Some participants may faint and, in rare cases, can get an infection.

Where is the study run from?

When is the study starting and how long is it expected to run for?

Who is funding the study?

Who is the main contact?
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Contact information

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Scientific

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Clinical Trials Information System (CTIS)
2023-507684-19

Integrated Research Application System (IRAS)
1009589

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
42756493BLC3004, IRAS 1009589, CPMS 60694

Study information

Scientific Title
A phase 3, randomized study evaluating the efficacy and safety of TAR-210 Erdafitinib intravesical delivery system versus single agent intravesical chemotherapy in participants with intermediate-risk non-muscle invasive bladder cancer

Acronym
MoonRISe-1

Study objectives
The primary objective of the study is to compare disease-free survival (DFS) between Group A and Group B.

The secondary objectives for this study are:
1. To compare time to next treatment (TTNT) (local or systemic) between study treatments.
2. To compare high grade (HG) recurrence-free survival (RFS) between study treatments.
3. To compare progression-free survival (PFS) between study treatments.
4. To compare the rate of diagnostic and therapeutic invasive urological interventions after study treatment.
5. To assess safety and tolerability.
6. To compare overall survival (OS) between study treatments.
7. To compare participant-reported disease- and treatment-related symptoms and impacts on functioning between study treatments.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/05/2024, NorthWest Liverpool Central REC (2 Redman Place, Stratford, E20 1JQ, United Kingdom; +44 (0)207 104 8340; liverpoolcentral.rec.@hra.nhs.uk), ref: 24/NW/0105

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Intermediate-risk Non-muscle Invasive Bladder Cancer (IR-NMIBC)

Interventions
Group A
Participants will receive TAR-210 (500 mg erdafitinib intravesical drug delivery system) every 12 weeks (+/- 1 week window) over a treatment duration of approximately 1 year. TAR-210 drug delivery system containing 500 mg Erdafitinib (release rate approximately 3 mg/day) will be administered to the participant intravesically.

Group B
For participants in Group B, Mitomycin C (MMC) or gemcitabine will be dosed once weekly for 4-6 induction doses followed by a maintenance phase for a minimum of 6 months and up to 1 year within a minimum dose of 6 treatment cycles.
Gemcitabine (2000 mg) or MMC (40 mg) will be administered to the participant intravesically

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
TAR-210 [ERDAFITINIB], mitomycin, gemcitabine

Primary outcome(s)
The primary endpoint for the study is disease-free survival (DFS). DFS will be measured as the time from randomisation to the date of the first documented recurrence of NMIBC of any grade, disease progression, or death due to any cause, whichever occurs first

Key secondary outcome(s))
1. Time to next treatment (TTNT). Randomisation to the date of first documented subsequent treatment for bladder cancer.
2. High grade (HG) recurrence-free survival (RFS). Randomisation to the date of HG NMIBC or death.
3. Progression-free survival (PFS). Randomisation to the date of disease progression or death.
4. The rate of diagnostic and therapeutic invasive urological interventions after study treatment.
5. Safety and tolerability: Frequency/grade of AEs and other measures.

6. OS. Randomisation to the date of death from any cause.
7. Proportion of participants with meaningful change in EORTC QLQ-C30 and EORTC QLQ-NMIBC24 scores between study treatments.

Completion date
28/04/2032

Eligibility

Key inclusion criteria
1. Be 18 or more years of age at the time of informed consent.
2. Have a histologically confirmed diagnosis (within 90 days of randomisation) of intermediate-risk non-muscle invasive bladder cancer (IR-NMIBC) with at least one of the protocol-defined criteria fulfilled.
3. Have a susceptible fibroblast growth factor receptor (FGFR) mutation or fusion either by urine testing or tumour tissue testing (from transurethral resection of bladder tumour [TURBT] tissue), as determined by central or local testing.
4. Participants must be willing to undergo all study procedures (e.g., multiple cystoscopies from Screening through the end of study and TURBT for assessment of recurrence/progression) and receive the assigned treatment, including intravesical chemotherapy if randomised into that arm.
5. Visible papillary disease must be fully resected prior to randomisation and absence of disease must be documented at Screening cystoscopy. The same method for visualising disease at Screening cystoscopy should be used throughout for the participant (white light versus enhanced assessment method).
6. Can have a prior or concurrent second malignancy (other than the disease under study) which natural history or treatment is unlikely to interfere with any study endpoints of safety or the efficacy of the study.
7. Have an Easter Cooperative Oncology Group (ECOG) performance status of 0 to 2.
8. Have an estimated glomerular filtration rate (eGFR), based on the Modification of Diet in Renal Disease (MDRD) 4-variable formula of greater than 30 millilitres (mL) per minute (min).
9. Meet the protocol-defined hepatic function criteria.
10. Participants should have adequate bone marrow function, as defined within the protocol.
11. While on study treatment and for 6 months after the last dose of study treatment, a participant must not breastfeed or be pregnant, not donate gametes (i.e., eggs or sperm) or freeze for future use for the purposes of assisted reproduction, and wear an external condom, as applicable. If of childbearing potential, participants must have a negative highly sensitive pregnancy test at Screening and within 24 hours before the first dose of study treatment, and agree to further pregnancy tests, and practice at least 1 highly effective method of contraception (if oral contraceptives are used, a barrier method of contraception must also be used). If a participant’s partner is of childbearing potential, the partner must practice a highly effective method of contraception unless the participant is vasectomised.
12. Must sign an informed consent form (ICF; or their legally acceptable representative must sign) indicating that the participant understands the purpose of, and procedures required for, the study and is willing to participate in the study and agree to store samples for research when appropriate.
13. Be willing and able to adhere to the lifestyle restrictions specified in the protocol.

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Known allergies, hypersensitivity, or intolerance to any study component or its Excipients.
2. Presence of any bladder or urethral anatomic feature that, in the opinion of the investigator, may prevent the safe insertion, indwelling use, removal of TAR-210 or passage of a urethral catheter for intravesical chemotherapy.
3. Polyuria with recorded 24-hour urine volumes greater than 4000 millilitres (mL).
4. Current indwelling urinary catheters, however, intermittent catheterisation is acceptable.
5. Had major surgery or had significant traumatic injury and/or not fully recovered within 4 weeks before first dose (transurethral resection of bladder tumour [TURBT] is not considered major surgery).
6. Has active bladder stones or persistent risk of bladder stones.
7. Concurrent urinary tract infection (UTI) as defined in the study protocol.
8. Any cardiovascular dysfunction as defined in the study protocol.
9. Histologically confirmed diagnosis of high-risk (HR) non-muscle invasive bladder cancer (NMIBC) or muscle-invasive bladder cancer (MIBC), locally advanced, non-resectable, or metastatic urothelial carcinoma at any time prior to enrolment.
10. Has or had urothelial carcinoma (UC) outside of the urinary bladder or has a histological variant of UC.
11. HIV-positive participants with AIDS-related symptoms.
12. Received an investigational treatment for bladder cancer after TURBT for the current NMIBC diagnosis or within 4 weeks or the agent/therapy washout period, whichever is longer, before the planned first dose of study treatment, or is currently enrolled in an investigational study.
13. Received adjuvant induction intravesical chemotherapy within 6 months of current diagnosis.
14. Received prior intravesical treatment with immunotherapy including BCG within 2 years prior to randomisation.
15. Received prior treatment with an fibroblast growth factor receptor (FGFR) inhibitor.
16. Not recovered from adverse events (AEs) associated with any prior surgery or prior anticancer therapy (except toxicities which are not clinically significant).
17. Symptomatic, active infection requiring systemic therapy.
18. Evidence of current bladder perforation by cystoscopy or imaging.
19. Any condition for which, in the opinion of the investigator, participation would not be in the best interest of the participant or that could prevent, limit, or confound the protocol-specified assessments.
20. The participant is unable to comply with the requirements of the protocol, including any factors that are likely to affect the participant’s return for scheduled visits and follow-up.

Date of first enrolment
29/04/2024

Date of final enrolment

27/07/2026

Locations

Countries of recruitment
United Kingdom

Argentina

Austria

Belgium

Brazil

Canada

China

Denmark

France

Germany

Hong Kong

Ireland

Israel

Italy

Poland

Spain

Türkiye

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Sponsor information

Organisation
Janssen-Cilag International NV

Funder(s)

Funder type
Industry

Funder Name
Janssen-Cilag N.V

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing policy of the Janssen Pharmaceutical Companies of Johnson and Johnson is available at www.janssen.com/clinical- trials/transparency. As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access (YODA) Project site at yoda.yale.edu

IPD sharing plan summary
Available on request