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A phase 3, randomized, open-label, multicenter study evaluating the efficacy and safety of TAR-210 erdafitinib intravesical delivery system versus investigator's choice of intravesical chemotherapy in participants with high-risk non-muscle-invasive bladder cancer with susceptible FGFR alterations who had received intravesical Bacillus Calmette-Guérin (BCG)

Submission date
02/07/2025

Recruitment status
Recruiting

Registration date
11/09/2025

Overall study status
Ongoing

Last Edited
03/10/2025

Condition category
Cancer

[_] 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
High-risk non-muscle invasive bladder cancer (HR-NMIBC) is an early-stage bladder cancer, limited to the inner lining of bladder but has a considerable high chance of cancer coming back or worsening.
Available treatment options include having treatments administered directly into the bladder such as intravesical chemotherapy* or repeat Bacillus Calmette Guerin (BCG) treatment or removing the bladder to treat the cancer (radical cystectomy [RC]). However, there is a high risk of cancer worsening or coming back and removal of bladder can have potentially serious short and long-term complications. Therefore, there is a need for better treatment options.
*Anticancer drugs put directly into the bladder through a thin, flexible tube inserted in urethra.
TAR-210 is an intravesical drug releasing system in which a thin tube is temporarily placed into the bladder. It continuously releases erdafitinib, a medicine being investigated to treat HR-NMIBC in participants with alteration in a gene for fibroblast growth factor receptor (FGFR) present in cancer cells.
In this study, researchers want to compare the length of time participants are alive and without the recurrence of their bladder cancer (disease-free survival), when treated with TAR-210 or single agent intravesical chemotherapy with either mitomycin C (MMC) or gemcitabine.

Who can participate?
Participants aged 18 years or older with HR-NMIBC with alteration in gene for FGFR, who have previously received BCG treatment.

What does the study involve?
Screening Phase (Up to 60 days)
Treatment Phase (approximately up to 2 years)- Participants will be randomly (by chance) assigned to either:
Group A: TAR-210
Group B: MMC or gemcitabine
Follow-up Phase (Up to 5 years from first dose of study treatment): Participants will be followed-up for their health.
Participants will undergo study assessments including blood and urine tests, medical history, physical examination, vital signs, and laboratory tests. The overall duration of the study is around 5 years.

What are the possible benefits and risks of participating?
There is no established benefit to participants of this study. Based on scientific theory, taking TAR-210 may improve HR-NMIBC. However, this cannot be guaranteed because TAR-210 is still under investigation as a treatment and it is not known whether it will work.
If participants are put in the comparator group, they will not receive TAR-210 but treatment already available in the market.
Participants may experience some benefit from participation in the study that is not due to receiving study drug, but due to regular visits and assessments monitoring overall health.
Participation may help other people with HR-NMIBC in the future.
Participants may have side effects from the drugs or procedures used in this study that may be mild to severe and even life-threatening, and they can vary from person to person. The most common, known risks are getting symptoms such as local and systemic (in blood) adverse events (AEs; side effects as a result of study treatment), fetal (unborn baby) harm, infections (for example, urinary tract infection), urinary disorders and risks associated with insertion/ removal of TAR-210 from urethra (a tube that carries urine out of the body). Risks associated with MMC, or gemcitabine include bladder or urinary disorders, dermatological (skin) disorders, infections (lung or urinary and reproductive system infections), abnormalities in laboratory values, gastrointestinal disorders (conditions affecting digestive system), pain (above pelvic region, sexual pain and pain not related to urinary or digestive system) and other risks such as fatigue (tiredness), headache, heavy legs, chills, hot flashes and sweating. There are other, less frequent risks. The participant information sheet and informed consent form, which will be signed by every participant agreeing to participate in the study, includes a detailed section outlining the known risks to participating in the study.
Not all possible side effects and risks related to TAR-210 are known at this moment. During the study, the sponsor may learn new information about TAR-210. The study doctor will tell participants as soon as possible about any new information that might make them change their mind about being in the study, such as new risks.
To minimise the risk associated with taking part in the study, participants are frequently evaluated for any side effects and other medical events. Participants are educated to report any such events to their study doctor who will provide appropriate medical care. Any serious side effects that are reported to the sponsor are thoroughly reviewed by a specialist drug safety team.
There are no costs to participants to be in the study. The sponsor will pay for the study drug and tests that are part of the study. The participant will receive reasonable reimbursement for study related costs (for example, travel/parking costs).

Where is the study run from?
Janssen-Cilag International NV (Netherlands)

When is the study starting and how long is it expected to run for?
June 2025 to May 2027

Who is funding the study?
Janssen-Cilag International NV (Netherlands)

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)
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Integrated Research Application System (IRAS)
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ClinicalTrials.gov (NCT)
NCT06919965

Protocol serial number
42756493BLC3005, CPMS 68919

Study information

Scientific Title
A phase 3, randomized, open-label, multicenter study evaluating the efficacy and safety of TAR-210 erdafitinib intravesical delivery system versus investigator's choice of intravesical chemotherapy in participants with high-risk non-muscle-invasive bladder cancer with susceptible FGFR alterations who had received intravesical Bacillus Calmette-Guérin (BCG)

Acronym
MoonRISe-3

Study objectives
Main objectives
• To compare the length of time participants are alive and without the recurrence (coming back) of their bladder cancer (disease-free survival).

Secondary objectives
1. To further assess how well the treatment works (efficacy).
2. To assess how safe the treatments are and how well participants tolerate them.
3. To compare the participant-reported symptoms (disease and treatment related symptoms), their impact on daily activities, and how well participants tolerate them.

Ethics approval required
Ethics approval required

Ethics approval(s)
notYetSubmitted, TBC, ref: 25/LO/0546

Study design
Interventional randomized controlled trial

Primary study design

Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
High-risk non-muscle-invasive bladder cancer

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 2 years. 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; 40mg) or gemcitabine (2000 mg) 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.

Intervention Type
Drug

Phase
Phase III

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

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

Key secondary outcome(s))
1. Recurrence-Free Survival (RFS). The time from randomisation to the date of the first recurrence of HR-NMIBC or death due to any cause
2. Time to Next Intervention (TTNI). The time from randomisation to the date of next intervention (localised or systemic) for the treatment of UC
3. Time to Disease Worsening (TTDW). The time from randomisation to the date of cystectomy, systemic therapy, or radiation therapy, whichever occurs first
4. Time to Progression (TTP). The time from randomisation to the date of first documented evidence of disease progression, or distant disease, or death due to disease progression, whichever occurs first
5. Overall Survival (OS). The time from randomisation to death due to any cause
6. Safety and tolerability of TAR-210 and investigators choice of intravesical chemotherapy through assessing frequency and grade of AEs
7. Comparison of patient reported symptoms through proportion of participants with meaningful change in EORTC QLQ-C30 and EORTC QLQ-NMIBC24 scores, and frequency of response of EORTC Q168, global side effect impact

Completion date
28/05/2027

Eligibility

Key inclusion criteria
1. Be 18 years of age or more at the point of informed consent.
2. Histologically confirmed diagnosis by local histopathology of papillary-only high-risk non-muscle-invasive bladder cancer (HR-NMIBC).
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. All visible tumour completely resected prior to randomisation. Urine cytology must not be positive or suspicious for high-grade (HG) urothelial carcinoma (UC) before randomisation. For participants with lamina propria invasion (T1) on the screening biopsy/TURBT, muscularis propria must be present to rule out muscle-invasive bladder cancer (MIBC).
5. Participants must have had an adequate induction course of Bacillus Calmette-Guérin (BCG; 5 of 6 doses) and meet additional protocol specific treatment criteria.
6. For participants with BCG-unresponsive or BCG-experienced disease:
- Diagnosis of recurrence must be within 90 days prior to screening.
- Participants with BCG-unresponsive disease (recurrence) must have HG T1 disease at first disease assessment after Induction or HG Ta/any T1 disease within 6 months after last BCG.
- Participants with BCG-experienced disease (recurrence) must have HG Ta/any T1 disease within 12 months after last BCG.
For BCG-intolerant participants:
- For participants without recurrence after BCG: qualifying diagnosis must be within 180 days prior to screening and most recent BCG instillation was within 90 days prior to start of screening.
- For participants with recurrence: must have HG Ta/any T1 disease within 12 months after the last BCG instillation, and diagnosis of recurrence must be within 90 days prior to screening.
7. Participants must be ineligible for or refusing radical cystectomy (RC).
8. All adverse events (AEs) associated with any prior surgery and intravesical therapy must have resolved to Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 Grade less than or equal to 2 prior to Screening.
9. Have an Eastern Cooperative Oncology Group (ECOG) performance status Grade of 0, 1, or 2.
10. Adequate bone marrow, liver, and renal function, as defined in the study protocol.
11. While on study treatment and for 6 months after the last dose of study treatment (i.e., 3 months after last TAR-210 removal in Group A), 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; wear an external condom. If of childbearing potential, a participant 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; 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. Participants must sign all applicable Informed Consent Forms (ICFs; or their legally designated representative must sign, if applicable) indicating that the participant understands the purpose of, and procedures required for, the study and is willing to participate in the study and agreement to store samples when applicable.
13. Participants must be willing to comply with and able to undergo all study procedures and 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. Presence of carcinoma in situ (CIS) at any point from time of diagnosis of papillary-only high-risk non-muscle-invasive bladder cancer (HR-NMIBC) recurrence to randomisation. Additionally, presence or history of histologically confirmed, muscle-invasive, locally advanced, nonresectable, or metastatic urothelial carcinoma (UC).
2. Must not currently have UC or histological variant at any site outside of the urinary bladder. UC of the upper urinary tract (including renal pelvis and ureter) is allowable if treated with complete nephroureterectomy more than 24 months prior to randomisation with no evidence of recurrence.
3. N+ and/or M+ per Blinded Independent Central Review (BICR) of CT/MR Urography.
4. Active malignancies (i.e., progressing or requiring treatment change in the last 24 months) other than the disease being treated under study. Allowed recent second or prior malignancies are specified in the study protocol.
5. Presence of any bladder or urethral anatomic feature that, in the opinion of the investigator, may prevent the safe placement, indwelling use, or removal of TAR-210. Participants with tumours involving the prostatic urethra in men will be excluded.
6. A history of clinically significant polyuria with recorded 24-hour urine volumes higher than 4,000 millilitres (mL).
7. History of uncontrolled cardiovascular disease.
8. Pyeloureteral tube externalised to the skin is exclusionary. Unilateral nephrostomy tube or ureteral stent is permitted if it does not interfere with either insertion of TAR-210 into (or retention in) the bladder.
9. Participants who have not recovered from the effects of major surgery or significant traumatic injury at least 14 days before randomisation (transurethral resection of bladder tumour [TURBT] is not considered major surgery).
10. Indwelling catheters are not permitted; however, intermittent catheterisation is acceptable.
11. Concurrent urinary tract infection (UTI) as defined within the protocol.
12. Uncontrolled intercurrent illness including ongoing or active infection, or psychiatric illness /social situation that would limit compliance with study requirements.
13. As determined by the investigator, contraindications to the use of TAR-210, mitomycin C (MMC), or gemcitabine per local prescribing information. Known hypersensitivity to any study component.
14. Received a live virus vaccine within 30 days prior to randomisation. Inactivated (non-live or non-replicating) vaccines approved or authorised for emergency use (e.g., COVID-19) by local health authorities are allowed.
15. Received serial intravesical therapy or systemic therapy from the time of histologic diagnosis

of recurrent HR-NMIBC to date of randomisation. Immediate post-TURBT single-dose per-operative intravesical chemotherapy is allowed in accordance with institutional guidelines.
16. Prior application of TAR-210 within 6 months of randomisation or prior intravesical chemotherapy with gemcitabine or mitomycin within 6 months of randomisation.
17. Currently participating or has participated in a study and received an investigational agent or investigational device within 4 weeks prior to screening.
18. Evidence of bladder perforation which has not resolved prior to randomisation.
19. Bladder post-void residual (PVR) volume greater than 350 mL at screening after second voided urine.
20. Any condition for which, in the opinion of the investigator, participation would not be in the best interest of the participant (e.g., compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments.

Date of first enrolment
07/09/2025

Date of final enrolment
29/03/2027

Locations

Countries of recruitment
United Kingdom

Argentina

Belgium

Brazil

China

France

Germany

Greece

Israel

Italy

Japan

Netherlands

Spain

Study participating centre

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Sponsor information

Organisation
Janssen-Cilag International NV

Funder(s)

Funder type
Industry

Funder Name
Janssen-Cilag International NV

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