Health Technology Briefing
April 2024

Sasanlimab with Bacillus Calmette-Guérin for treating high-risk non-muscle invasive bladder cancer

Company/Developer	Pfizer Limited (UK)

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 28717	NICE ID: Not available	UKPS ID: 656642

Licensing and Market Availability Plans

Sasanlimab in combination with Bacillus Calmette-Guérin is currently in phase III clinical development.

Summary

Sasanlimab in combination with Bacillus Calmette-Guérin (BCG) is in clinical development for BCG-naïve, high-risk non-muscle invasive bladder cancer (NMIBC). Bladder cancer is when cancerous cells develop in the lining of the bladder. NMIBC is the most common type of bladder cancer and is categorised by risk (low, medium and high). High-risk NMIBC is when cancerous cells are more likely to persist or return after treatment, this means people with this type might require additional treatment and monitoring. Symptoms of NMBIC include but are not limited to blood in urine and urination problems. There remains unmet need in the treatment of high-risk NMIBC as recurrence and progression remains common.

Sasanlimab is a monoclonal antibody (type of protein) that blocks the interaction between PD-1 (a protein found on immune cells) and PD-L1 (a protein found on the surface of tumours). Blocking PD-1 activates natural killer cells and cytotoxic T-lymphocytes (immune cells), which can attack tumour cells. This can slow down or stop the growth of these cells. When PD-1 is activated, it dampens T-cell activity. In cancer, tumours exploit this to evade the immune system. Sasanlimab is administered by subcutaneous injection (under the skin). If licensed, sasanlimab in combination with BCG will offer an additional treatment option for patients with high-risk NMIBC.

Proposed Indication

Treatment, in combination with Bacillus Calmette-Guérin (BCG), of BCG naïve, high-risk, non-muscle invasive bladder cancer (NMIBC).[1]

Technology

Description

Sasanlimab (PF-06801591) is a humanized, hinge region-stabilized IgG4 monoclonal antibody antagonist specific for human PD-1 that can selectively bind to human PD-1 receptor and block the interaction between PD-1 and PD-L1/PD-L2.[2] This prevents the activation of PD-1 and its downstream signalling pathways. This may restore immune function through the activation of natural killer (NK) cells and cytotoxic T-lymphocytes against tumour cells. PD-1, an inhibitory receptor belonging to the B7-receptor family, is expressed on activated T-lymphocytes, B-cells and NK cells; it functions as an immune checkpoint that negatively regulates T-cell activation and effector function when activated by its ligands, and plays an important role in tumour evasion from host immunity.[3]

Sasanlimab is in clinical development in combination with BCG to treat high risk NMIBC. In the phase III clinical trial (CREST; NCT04165317), participants in the experimental arms of the trial will be administered sasanlimab alongside BCG induction only (first 6 weeks), or induction and maintenance.[1]

Key Innovation

Patients with high-risk NMIBC often experience a poor prognosis with a high chance of recurrence and progression, in addition to experiencing a reduced quality of life.[4] In a phase I dose expansion study, sasanlimab was administered subcutaneously at 300 mg every 4 weeks to patients with advanced urothelial carcinoma and non-small cell lung cancer. It was found to have an acceptable safety profile and durable antitumour activity, while offering the convenience of subcutaneous administration compared with intravenous chemotherapy such as pembrolizumab.[5,6] If licensed, sasanlimab in combination with BCG will offer an additional treatment option for patients with high-risk NMIBC.

Regulatory & Development Status

Sasanlimab does not currently have marketing authorisation in the EU/UK for any indication.

BCG currently has marketing authorisation in the EU/UK for treatment of primary or concurrent carcinoma-in-situ of the urinary bladder and for the prevention of recurrence of high grade and/or relapsing superficial papillary transitional cell carcinoma of the urinary bladder (Stage Ta (grade 2 or 3) or T1 (grade 1, 2 or 3)) after transurethral resection.[7]

Patient Group

Disease Area and Clinical Need

Bladder cancer is the growth of cancerous cells within the bladder. If the growth of these cells is contained within the lining of the bladder, this is described as NMIBC, whereas if the cells spread beyond the lining into the surrounding bladder muscle, this is muscle-invasive bladder cancer.[8] NMIBC is divided into three risk groups: low, intermediate (medium) and high. High risk NMIBC means the cancer is more likely to spread or return after treatment, so may require more treatment and closer monitoring.[9] Most cases of bladder cancer appear to be caused by exposure to harmful substances, which lead to abnormal changes in the bladder's cells over many years; contact with certain chemicals previously used in manufacturing is

also known to cause bladder cancer.[8] Tobacco smoking is the most important risk factor for bladder cancer, causing 50% of the cases.[10] The most common symptom of bladder cancer is blood in urine also known as haematuria.[11]

In England in 2017, there were 8,686 newly diagnosed cases and 4,736 death registrations for malignant neoplasm of bladder (ICD-10 code C67) and a crude total death rate of 11.8 per 100,000 in men, and 5.3 per 100,000 in women.[12] The age-standardised 1-year and 5–year survival for patients diagnosed with bladder cancer in England in 2017 was 74.1% and 52.6% respectively.[13] In England, 2022-23, there were 66,634 finished consultant episodes (FCE) and 62,831 admissions for malignant neoplasm of bladder (ICD-10 code C67) which resulted in 87,622 FCE bed days and 41,531 day cases.[14]

Recommended Treatment Options

The current treatment options recommended by NICE for adults with high risk NMIBC are:[15]

- Bacille Calmette-Guérin
- Cystectomy
- Adjuvant chemotherapy may be offered following cystectomy

Clinical Trial Information

Trial	**CREST**, NCT04165317, EudraCT 2019-003375-19; A Phase 3, Multinational, Randomized, Open-Label, Three Parallel-Arm Study of PF-06801591, an Anti-PD-1 Antibody, in Combination With Bacillus Calmette-Guerin (BCG Induction With or Without BCG Maintenance) Versus BCG (Induction and Maintenance) in Participants With High-Risk, BCG-Naïve Non-Muscle Invasive Bladder Cancer or PF-06801591 as a Single Agent in Participants With BCG-Unresponsive NMIBC **Phase III:** Active, not recruiting **Location(s):** 6 EU countries, UK, USA, Canada and other countries **Primary completion date:** June 2024
Trial Design	Randomised, open-label, parallel assignment
Population	N=1070 (actual); subjects with non-muscle invasive bladder cancer; aged 18 years and older
Intervention(s)	• Sasanlimab in combination with BCG induction and maintenance (arm A) • Sasanlimab in combination with BCG induction only (arm B)
Comparator(s)	BCG induction and maintenance (arm C)
Outcome(s)	Primary outcomes: - Event free survival (arm A compared to arm C) [time frame: 55 months after first participant randomised] - Event free survival (arm B compared to arm C) [time frame: 55 months after first participant randomised] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of sasanlimab is not yet known.

The NHS indicative price for one vial of BCG (12.5mg) is £71.61.[16]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Pembrolizumab with BCG for treating high-risk non-muscle-invasive bladder cancer (ID6271). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Durvalumab with BCG for treating high-risk non-muscle-invasive bladder cancer after resection of papillary tumours in people previously untreated with BCG (ID5080). Expected date of issue to be confirmed.
- NICE clinical guideline. Bladder cancer: diagnosis and management (NG2). Feb 2015.
- NICE quality standard. Bladder Cancer (QS106). December 2015
- NICE interventional procedures guidance. Transurethral laser ablation for recurrent non-muscle-invasive bladder cancer. (IPG656). July 2019.
- NICE interventional procedures guidance. Electrically stimulated intravesical chemotherapy for non-muscle-invasive bladder cancer (IPG638). January 2019.
- NICE interventional procedure guidance. Intravesical microwave hyperthermia and chemotherapy for non-muscle-invasive bladder cancer (IPG628). September 2018.
- NICE medical technologies guidance. Synergo for non-muscle-invasive bladder cancer (MTG61). November 2021.

NHS England (Policy/Commissioning) Guidance

- NHS England. Guidelines for the Management of Bladder Cancer. December 2016.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a.

Other Guidance

- Holzbeierlein J, Bixler BR, Buckley DI, Chang SS, Holmes R, James AC,et al. Diagnosis and treatment of non-muscle invasive bladder cancer: AUA/SUO guideline: 2024 amendment.[17]
- European Association of Urology (EAU). EAU Guidelines on Non–muscle-invasive Bladder Cancer. 2022.[18]
- Powles T, Bellmunt J, Comperat E, De Santis M, Huddart R, Loriot Y, et al., Bladder cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. 2021[19]

Additional Information

On August 31, 2022, the Sponsor announced the discontinuation of enrolment to Part B, which enrolled patients with BCG unresponsive NMIBC. The decision to discontinue enrolment to Part B was not made for safety reasons.[1]

References

1 Clinicaltrial.gov. *A Study of Sasanlimab in People With Non-muscle Invasive Bladder Cancer (CREST)*. *Trial ID: NCT04165317*. 2019. Status: Active, not recruiting. Available from: https://clinicaltrials.gov/study/NCT04165317 [Accessed 28 February 2024].

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