WHAT TO KNOW ABOUT BLADDER CANCER AND BCG

medac

DEAR PATIENT,

Your doctor has diagnosed you with a non-muscle-invasive bladder cancer (NMIBC). This type of tumour can generally be removed surgically because the muscle layer of your bladder is not affected. After the surgical removal, your doctor has recommended treatment with BCG.

In this leaflet, we would like to answer as many questions as possible about your disease and the treatment with BCG. If you have any unanswered questions after reading this, do not hesitate to ask your doctor or care team.

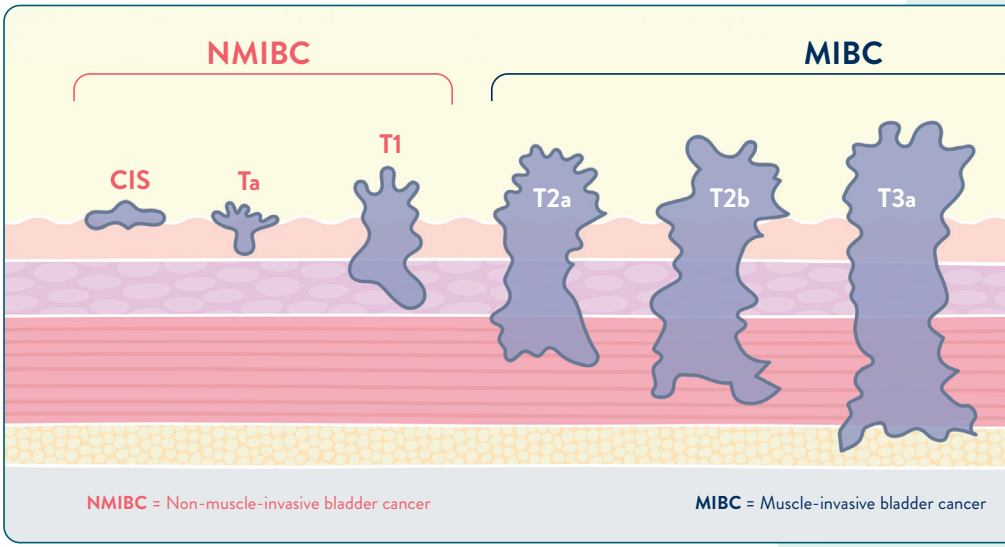
BLADDER CANCER & NON-MUSCLE-INVASIVE BLADDER CANCER (NMIBC)

Worldwide, bladder cancer is the 10th most common cancer. Almost all bladder cancers are urothelial carcinomas. Urothelial carcinoma is a cancer that develops from the cells of the mucosa of the bladder wall – called the urothelium.

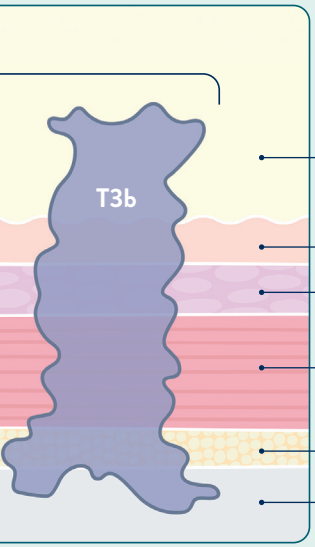
If urothelial carcinomas are detected at an early stage, they belong to the group of non-muscle-invasive bladder carcinomas (NMIBC, labelled as CIS, Ta, and T1 in the figure).

Stages of growth of urothelial carcinoma

Illustration of urothelial carcinoma (bladder cancer) at different stages. Early stages, such as **CIS**, **Ta** and **T1**, are tumours that have not yet grown into the muscle tissue (Muscularis propria).



NMIBC occur only in the tissue lining the inner surface of the bladder. These tumour stages must be treated in the bladder (also called intravesical or instillation treatment) to prevent the tumour(s) from either recurring or progressing, the latter meaning that the cancer is growing into the muscle layer of the bladder.



Bladder interior (Lumen)

Bladder mucosa (Urothelium)

Subepithelial tissue (Lamina propria)

Muscle tissue (Muscularis propria)

Perivesical tissue

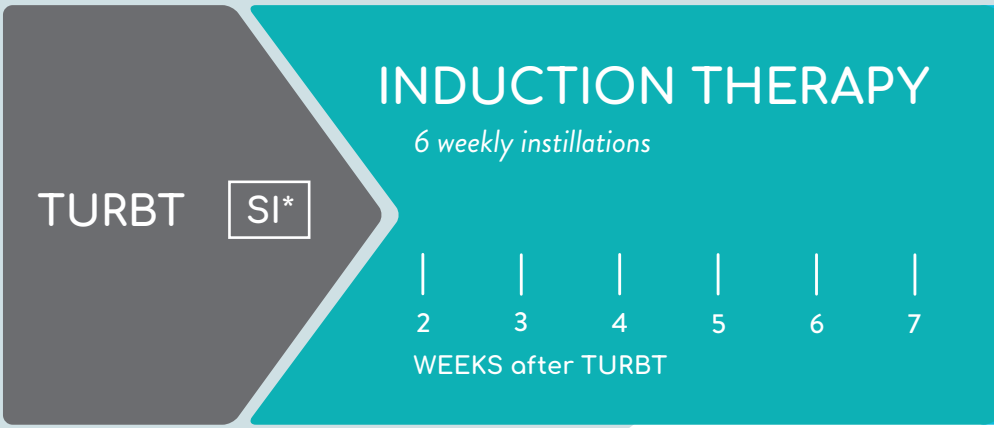
Bladder exterior

HOW IS NON-MUSCLE-INVASIVE BLADDER CANCER TREATED?

1. Surgical removal of the tumour(s)

The first step in your treatment is the transurethral resection of the bladder tumour(s), abbreviated as TURBT. Under general anesthesia, your doctor inserts an endoscopic instrument through the urethra into the bladder and removes the tumour(s). Afterwards, the chemotherapeutic agent Mitomycin C will be instilled into your bladder once (single immediate instillation). After the surgical removal, the tumour tissue is analyzed, and further therapy is selected while also taking other (risk) factors into account.

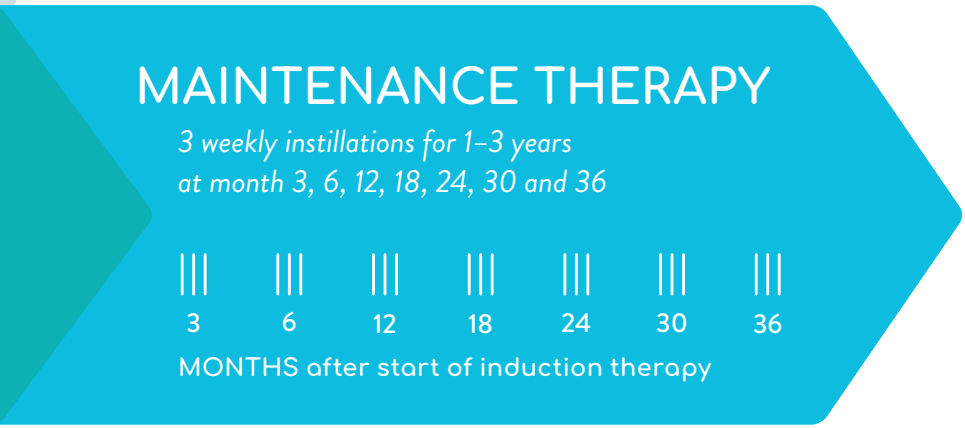
BCG treatment schedule



* Single immediate instillation of 40mg Mitomycin C

2. Instillation therapy with BCG

After the surgical removal, few tumour cells may remain in the bladder. If these are not treated, a new tumour may grow from them and the bladder cancer may recur (disease recurrence). Therefore, your doctor has recommended treatment with BCG as the next step of therapy. Over a period of 1 to 3 years, a liquid containing BCG will be instilled into your bladder at regular intervals. The therapy is divided into two stages: Induction therapy and maintenance therapy. Both are required for optimal efficacy.



Lamm et al., 2000

HOW DOES BCG WORK?

BCG is a liquid with live bacteria (Bacillus Calmette-Guérin). These bacteria are modified (weakened, resp. attenuated) to train your immune system without causing an infection – similar to a vaccination.

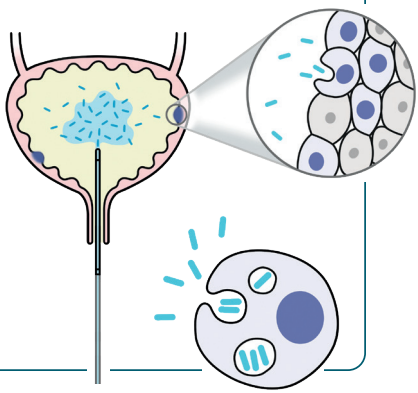
The BCG instilled into the bladder cause a local inflammation. This is intentional and is used therapeutically because it activates the body‘s immune defenses. The BCG-induced inflammation enables your immune system to recognize and specifically eliminate remaining tumour cells. This can markedly reduce the risk of bladder cancer recurrence and progression (worsening of the disease).

Since the body‘s own immune system is activated to specifically combat residual tumour cells, treatment with BCG is called an immunotherapy. Adherence to the therapy regimen of induction therapy and maintenance therapy over 1 to 3 years plays an important role in training your immune system and controlling the course of the disease in the long term.

BCG – MODE OF ACTION

1

After instillation into the bladder the BCG bacteria are taken up (internalized) by the tumour cells.



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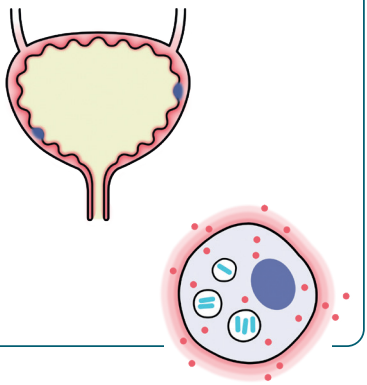
The bacteria trigger an inflammatory reaction. In this process, immunostimulatory messenger substances are produced, which enable the immune recognition of tumour cells as foreign.



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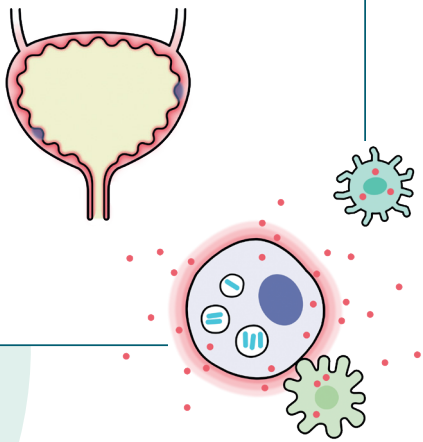
Cytokines are released and attract respectively activate different types of immune cells that cooperate to facilitate immune recognition of the tumour cells as foreign.



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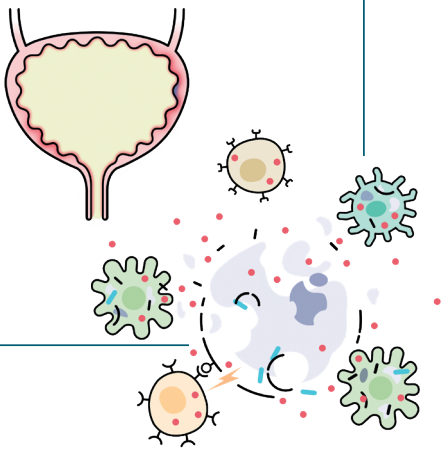
Among others, T-cells, natural killer cells and macrophages now attack the labelled tumour cells, which leads to their elimination as well as an enhancement of the immune response against the tumour.



POSSIBLE SIDE EFFECTS

The most common side effects include cystitis (bladder inflammation), more frequent, unpleasant or painful bladder emptying, nausea and fever under 38.5 °C, accompanied by flu-like symptoms. These side effects may arise after the first treatment, or after later treatments. They are generally mild and transient.

Symptoms suggestive of an infection in the bladder are positive signs for the therapy taking effect and the body's immune reaction!

Talk to your doctor, pharmacist or the medical staff if you find the side effects worrying. They will be able to help you.

WHAT YOU SHOULD DO IF YOU NOTICE UNWANTED SIDE EFFECTS

In addition to the intended inflammatory reaction of the bladder, systemic infection may occur in rare cases, which manifests as symptoms outside the bladder. This unwanted side effect must be treated. **Signs and symptoms may be:**

- **Fever above 39.5 °C over at least 12 hours**
- **Fever above 38.5 °C over at least 48 hours**
- **Increasing discomfort**
- **Weight loss of unknown cause**
- **Various signs of inflammation such as difficulty breathing or cough, which do not feel like a normal cold, a feeling of pressure in the right upper abdomen in the liver area and pain or reddening in the eye to conjunctivitis, visual impairment or blurred vision**

Please consult your doctor, pharmacist or the medical staff immediately if signs of such unwanted side effects occur or if you notice unexpected symptoms.

WHAT CAN I DO AS A PATIENT?

- It is important that you attend to your treatments and check-ups. Regular treatments according to the therapy plan are necessary for BCG therapy to be effective. Always have your treatment plan with you during doctor visits to keep it up to date. Plan your treatments on a long term and advise your doctor in advance of any vacation or other absence.
- Smoking is the most significant risk factor in the development and treatment of bladder tumours. Avoid this risk factor at all costs.
- Make sure you drink enough fluids every day.
- Support your immune system with a healthy lifestyle. A healthy diet and exercise contribute to a well-functioning immune system.

NOTES

HOW TO OBTAIN FURTHER INFORMATION

You can obtain detailed information on bladder cancer and your BCG therapy in the patient information leaflet on bladder cancer from medac. Simply speak to your urology team about it, they will be able to help you.

The opportunity to exchange with other bladder cancer patients may support you during and after treatment. Patient organizations can be a valuable way to network.

medac is a privately owned international pharmaceutical company specialising in the treatment of diseases in the fields of oncology, haematology, autoimmune diseases and urology. In the field of NMIBC, medac has built its urological expertise over more than 40 years. medac is committed to delivering high-quality therapies that make a positive difference in the lives of NMIBC patients.

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