

GRANT DISICK, M.D. U R O L O G Y

What is BCG?

BCG (Bacillus Calmette-Guerin) is a weakened bacteria that was first created as a vaccine for tuberculosis. Although BCG is ineffective as a vaccine, it can stimulate your immune system and help your body fight bladder cancer. There are several reasons your doctor may choose to give you BCG. BCG is used to decrease the chance of having another bladder tumor, to prevent the cancer from invading the muscle wall of the bladder, and to cure a variant of bladder cancer called carcinoma-in-situ ("CIS"). Your urologist can help you understand the reason BCG is indicated in your case.

How is BCG given?

The standard initial ("Induction") is one treatment per week for 6 weeks. BCG is given in your urologist's office. A catheter is placed into your bladder to deliver the BCG, in liquid form, directly into your bladder. Once the BCG liquid is instilled into your bladder through the catheter, the catheter is removed. You will hold this BCG liquid in your bladder for 2 hours (you do not stay in the office for these 2 hours). BCG is a weakened – not dead – bacteria. It is important that we minimize any exposure for others who are not receiving this medicine. You must be careful about where, when, and how you empty your bladder after the 2 hours is up (instructions below).

What are the side effects of BCG and what can I do about them?

- Burning and frequency with urination: increase your fluid intake, avoid caffeine and alcohol. Sometimes medications like Pyridium and Uribell can be given.
- Low grade fevers (up to 100), fatigue, aches, flu-like symptoms: Tylenol can help relieve these symptoms within 48 hours. Drink fluids to keep urine clear and rest. These symptoms are occurring because BCG stimulated the immune system.
- Blood in the urine: BCG can cause irritation to the bladder and may cause bleeding. Drink fluids to keep your urine clear and rest. Ask your doctor if you should stop any blood thinners you are taking.
- If you have a fever over 101, chills, rash, joint pain, or any symptoms last longer than 48 hours, call your urologist. Some specific medications may be required.

What happens on the day I get BCG?

1. Do not drink too much fluids on the morning of your treatment because you will have to hold the BCG in your bladder for 2 hours; we advise only 1 glass of fluid (or 1 cup of coffee) at breakfast. You can eat any food you like.
2. You will be given a medication called Ciprofloxacin, which is an antibiotic, to prevent infection. You will take the first tablet in the morning and the last tablet in the evening.
3. You will be asked to give a urine specimen to test for infection or blood. If an infection or a large amount of blood is detected, you may not receive BCG that day.

4. You will lie down on an exam table and a catheter will be placed in your bladder to remove any residual urine. The BCG liquid is then injected into the catheter and the catheter is removed.
5. You will be allowed to leave the office after the catheter is removed. You are able to drive yourself. You are allowed to walk around while you hold in the BCG and you may be shown to rotate from side to side to ensure the BCG covers the entire inside of the bladder.
6. You should try to hold the BCG in your bladder for 2 hours for best results. If you must urinate before 2 hours, please let us know at your next visit how long you were able to hold in the BCG in.
7. Men should SIT on the toilet to urinate so the BCG doesn't splash. DO NOT FLUSH THE TOILET AT THIS POINT.
8. Wash your hands and genitals with soap and water after urinating
9. After urinating and washing your skin, pour 2 cups of household bleach (Clorox or equivalent) into the toilet. Let the bleach mix with the BCG in the toilet for 15 minutes before flushing. Flush the toilet with the lid closed. (Remember: BCG is weakened – not dead – bacteria; it is important to kill the bacteria so it won't affect others.)
10. Repeat steps 7-9 each time you urinate for the 6 hours following the treatment. It is best if you stay at home and use the same toilet for these 6 hours. Ensure that no one else uses. Drink 8oz of liquid every other hour for those 6 hours to help flush the bladder out.

Can I have sex?

Do not have sexual intercourse for at least 48 hours after each BCG treatment. Men receiving BCG are advised to wear condoms the entire course of the 6 week treatment and for 6 additional weeks after the treatment has ended. Women receiving BCG should avoid vaginal contact for one week following each treatment and for 6 additional weeks after treatment has ended.

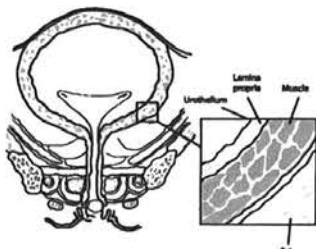
What else should I know?

You cannot receive BCG if you are bleeding, have a urinary tract infection, have active TB, are breast feeding, or are immunocompromised and taking immunosuppressive medications.

You are able to carry out your normal activities during the 6 week treatment. There are no restrictions on work, driving, etc.

Introduction

A large majority of patients who develop bladder cancer have what is known as 'non muscle invasive bladder cancer' or 'NMIBC'. This terminology comes from the fact that the tumor has not yet invaded into the true muscle layer of the bladder. When detected at this relatively early stage it is often possible, with the appropriate combination of treatments, to save the patient's bladder.



The first step is complete removal of all visible disease within the bladder. This is achieved with a transurethral resection of the tumor, also called TURBT. For some patients, this may require more than one surgery, especially if the tumor is high grade and involving more than the very first layer of the bladder. After this has been achieved and the bladder has healed, the appropriate treatment may be with intravesical instillation of Bacillus Calmette-Guerin or BCG. BCG is a form of the tuberculosis bacteria and originated as a vaccination against tuberculosis. After decades of detailed investigation including large trials in multiple countries that have tested BCG against various other agents, it currently remains the most effective therapy for NMIBC. However, as with any treatment, it works best when used appropriately – i.e for the right patient in the right manner.

It is instilled into the bladder with a urethral catheter (intravesical) in the office for several treatments. BCG works locally in the bladder to stimulate the body's own immune

system to fight off the cancer cells in the bladder. Because it stimulates the immune system, it is considered an immunotherapy (as opposed to chemotherapy). It works to activate the body's immune system to kill cancer cells without harming the normal cells. In addition, BCG is instilled locally in the bladder cannot reach other cells in the body.

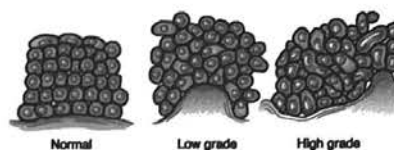


Who is eligible for BCG?

Intravesical immunotherapy with BCG is effective if the tumor is non-muscle invasive. These tumors are often divided into risk groups (low-risk, intermediate-risk and high-risk) based on the risk of recurrence (the likelihood the tumor will return) and the risk of progression (the likelihood the tumor will get worse

and potentially become invasive or spread).

[1] There are various factors that your urologist will consider when making this risk assessment – such as on how big the tumor is, if it is a first time tumor or a tumor that has



regrown, the length of time it took for the tumor to regrow, if the bladder cancer is pure urothelial cancer, as well as as the location of the tumor and the grade of the tumor.

In general, bladder cancer tumors can be low grade and high grade. Low grade cancers can recur often, but are less likely to progress. Thus the goal of therapy with these tumors is mainly to reduce the frequency of recurrence. The high grade tumors can progress and become muscle invasive or metastasize. In treating this type of tumor the goal is to not only prevent recurrence but especially to prevent progression.

Most patients with the intermediate-risk and high-risk non-muscle invasive bladder cancers will be candidates for immunotherapy with BCG. However, based on individualized risk assessment, other intravesical treatments or even bladder removal (cystectomy) may be recommended.

What are the benefits of BCG for patients?

BCG is relatively non-invasive and used to directly treat the bladder lining. BCG intravesical treatment for non-muscle invasive bladder cancer is the most effective treatment that exists for reducing the recurrence and progression of bladder tumors. [1] In patients who respond appropriately, BCG can be a life-saving treatment that reduces death from bladder cancer. Over half of patients have a complete response to BCG

without tumor recurrence for an extended period of time. In order to achieve this, it is crucial that patients received at least one course of induction BCG (6 weeks) and at least one course of maintenance BCG (at least 3 weeks) to allow the immune response to reach its peak.

BCG treatments do not require any additional adjunct medications such as urinary alkalization. Although BCG has some side effects, under the guidance of a diligent urologist the incidence of severe side effects are uncommon and most patients are able to successfully complete their therapy course. When mild BCG side effects do occur, they are often treated with over the counter medications.

After BCG treatment, patients must be followed closely with regular cystoscopy surveillance to detect any cancer recurrence or development of a new primary tumor in the bladder or elsewhere within the urogenital tract (ureters, bladder, urethra).

What are the risks?



BCG often causes some burning with voiding after the treatments. It can also cause some urgency and frequency. These often resolve a few days after the treatment, but the symptoms can increase in intensity after each instillation.

It is important to note that there may be no correlation of side effects with the dose and duration of the BCG maintenance. [2] Most patients do well with BCG and a small minority discontinue treatment because of side effects. [3]

It is normal for patients who receive a BCG instillation to have some transient flu-like symptoms (fever <101.5F, chills, malaise, joint aches, and fatigue). However, if BCG gets into the blood stream it can cause a bad infection or even sepsis. Symptoms of sepsis are flu-like symptoms for greater than 72 hours or a fever greater than 101.5F. With the appropriate precautions, such as delaying instillation if you see visible blood in the urine, making sure there is no trauma during instillation, etc, it is very rare for BCG to get in the blood stream.

BCG can cause infections in the other parts of the genitourinary system that are connected to the bladder such as the prostate and testicles. This can cause prostatitis or orchitis, but these are usually managed conservatively.

The other risk is that the BCG may not work. After BCG other treatments may be needed. If the BCG does work it will often be recommended to continue with maintenance BCG treatments.

What can be done for symptoms associated with BCG?

Make sure your bladder is emptied right before the BCG instillation.

Limitation of fluids before the instillation can be helpful. Limiting fluids will decrease urine production during the time you are holding the treatment in your bladder. This will decrease your discomfort while you are being treated.



You can ask your doctor for antispasmodic medication if you are having a lot of bladder and urethral irritation symptoms known as lower urinary tract symptoms. These symptoms are common, but are an uncommon cause of BCG discontinuation.

If you have a mild fever or flu-like symptoms it is okay to take medication to reduce fever, such as acetaminophen.

What factors can influence BCG effectiveness?

Some antibiotics may weaken effects of BCG. If you are given antibiotics it is recommend you do not take them in the 24 hours before or within 6 hours after BCG unless specifically instructed by your doctor.

Too much lubricating jelly that is used to insert the catheter should be avoided. Excess jelly can trap the BCG and keep it from treating the cancer. [4]

In addition lidocaine and lidocaine jellies should be avoided with the administration of BCG. The lidocaine can degrade the BCG and this can decrease the effectiveness of the BCG. [4]

What is the maintenance schedule for BCG?

In addition to the induction course of BCG, BCG maintenance is important in reducing bladder tumor recurrence and progression. With BCG induction and maintenance 60% of patients with an upfront tumor response will be tumor free for more than 5 years. [1] Also, the addition of maintenance decreases the risk of disease progression by 35%. [5] After the first six weeks of BCG treatments if there is no tumor on the follow up cystoscopy it is likely BCG maintenance treatments will be recommended. The most effective schedule would be BCG maintenance administered at months 3, 6, 12, 18, 24, 30, 36. At each of these time points of BCG is instilled once a week for three weeks (i.e. at 3 months there would be 3 weekly instillations). The table on the next page shows the schedule of BCG induction,



maintenance and the cystoscopies that are needed to stay on the treatment plan. The follow up schedule of treatments is continued based on the risk category of the bladder cancer (for at least 1-year in intermediate-risk patients and the full 3-years in high-risk patients). If you are not offered BCG after the initial 6-week induction period, it is prudent to ask your provider if BCG maintenance would be beneficial in your case.



**Sex after BCG: Is there a risk to my partner?
How long should I wait?**

Both men and women undergoing BCG treatments

are advised not to engage in sexual activity for 48 hours after the treatment. At other time points during the treatment it is recommend you use a barrier, such as a condom, be used to prevent BCG transmission to your partner. Women are advised not to become pregnant while on BCG therapy.

Why do I have to hold it in so long? How long does BCG need to be held in the bladder?

BCG should stay in the bladder for 90 mins to 2 hours after it is administered. This allows time for the BCG to make adequate contact with the tumor cells and initiate the immune response.



[5]

Intravesical BCG Treatment/Cystoscopy Schedule

Month	BCG Introduction		
	BCG #1		
	BCG #2		
	BCG #3		
	BCG #4		
	BCG #5		
	BCG #6		
3	Approximately 6-8 weeks from 6th BCG		Cystoscopy
	BCG Maintenance #1 - start within 0 to 3 weeks		
	BCG #1		
	BCG #2		
	BCG #3		
6	Approximately 9-12 weeks from last BCG		Cystoscopy
	BCG Maintenance #2 - start within 0 to 3 weeks		
	BCG #1		
	BCG #2		
	BCG #3		
9	Approximately 9-12 weeks from last BCG		Cystoscopy
12	~3 months from last Cystoscopy		Cystoscopy
	BCG Maintenance #3 - start within 0 to 3 weeks		
	BCG #1		
	BCG #2		
	BCG #3		

How does changing positions while the BCG is in my bladder help the BCG work?

Rotating positions when BCG is instilled was previously recommended. However, there is no current evidence to support the practice of changing positions with intravesical BCG. [5]

Copy and cut out this Intravesical BCG Treatment/Cystoscopy Schedule to keep track of your treatments.

Note: Your doctor may modify schedule based on your individual needs.



Intravesical BCG Treatment/Cystoscopy Schedule

15	Approximately 9-12 weeks from last BCG	Cystoscopy	
18	~3 months from last Cystoscopy	Cystoscopy	
	BCG Maintenance #4 - start within 0 to 3 weeks		
	BCG #1		
	BCG #2		
	BCG #3		
21	Approximately 9-12 weeks from last BCG	Cystoscopy	
24	~3 months from last Cystoscopy	Cystoscopy	
	BCG Maintenance #5 - start within 0 to 3 weeks		
	BCG #1		
	BCG #2		
	BCG #3		
30	Approximately 21-24 weeks from last BCG	Cystoscopy	
	BCG Maintenance #6 - start within 0 to 3 weeks		
	BCG #1		
	BCG #2		
	BCG #3		
36	Approximately 21-24 weeks from last BCG	Cystoscopy	
	BCG Maintenance #7 - start within 0 to 3 weeks		
	BCG #1		
	BCG #2		
	BCG #3		

Note: Your doctor may modify schedule based on your individual needs.

BCG TREATMENT



► What is *BCG*?

BCG (Bacille Calmette-Guerin) is a weak form of tuberculosis bacteria. It stimulates the body's immune system attack cancer cells. The initial BCG treatment is inserted directly into the bladder as a topical rinse. It does not enter your bloodstream. BCG is a common treatment for bladder cancer that has not invaded the muscle wall of the bladder. It is often used for patients who have high-grade tumors.

► What happens during BCG treatment?

BCG is a type of *intravesical immunotherapy*. Your health care provider puts a liquid containing the BCG directly into the bladder using a catheter. This is called "instillation." Medicines that are given this way affect the cells lining the inside of the bladder. There is little to no effect on cells in other parts of the body. Immunotherapy causes the body's immune system to attack the cancer cells.

- BCG remains in your bladder for up to two hours
- BCG treatment is usually given once a week for six weeks
- Additional series of BCG treatments referred to as "maintenance BCG," may be recommended



ASK YOUR HEALTHCARE TEAM

» *Why is BCG treatment a good option for me?*

- *What is the success rate of BCG for my age, tumor type, and stage?*
- *When might I know that the treatment is working?*

» *What's involved in having this treatment?*

- *How many treatments will I have and how often?*
- *Where will I get the treatment? Will I stay there for the whole treatment or can I go home for the time I hold the BCG in my bladder?*
- *Who can I talk to if I have questions or need help?*

» *What is your experience with BCG treatment?*

» *What options do I have if BCG does not work?*

Always consider
a 2nd opinion



TERMS TO KNOW

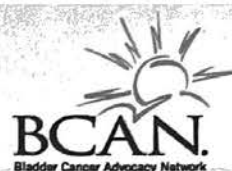
Catheter: A flexible tube inserted through a narrow opening into a body cavity, particularly the bladder.

Immunotherapy: The prevention or treatment of disease with substances that stimulate the immune response.

Intravesical: Within a bladder, especially the urinary bladder.

TURBT: A transurethral resection of the bladder tumor (TURBT) is a surgical procedure used to diagnose, stage, and treat visible bladder cancer tumors.

BCG TREATMENT



WHAT YOU SHOULD KNOW: Advice from bladder cancer patients who have experience with BCG

BEFORE BCG TREATMENT



- If you grew up outside of the United States it is possible you received BCG as a vaccine. Let your healthcare team know before starting BCG treatments.
- Try to schedule your appointment at a day and time that is convenient for you.
- Bring music or books to distract you during the time you must hold the BCG in your bladder.
- BCG will not be given until your bladder has healed from any TURBT procedures. This reduces the risk of BCG getting into your blood stream.
- Be prepared to provide a urine sample before your BCG treatment. If this urine sample shows signs of infection, you will not be treated with BCG until the infection clears up.
- You might be asked not to eat or drink for a period of time before the treatment.
- Bring a friend or family member to keep you company and to take notes on what the doctor tells you.

DURING BCG TREATMENT



- A **catheter** instills the liquid drug into your bladder.
- Some doctors ask patients to lie down and rotate around so that the drug coats the entire bladder.
- Medications are available to help you relax during the treatment.

AFTER BCG TREATMENT



- Tell your medical team if you experience any side effects. BCG can cause side effects, such as:
 - flu-like symptoms
 - fever
 - chills
 - fatigue
 - the urge to urinate
 - painful urination
 - symptoms of a urinary tract infection
 - blood or clots in your urine

- Ask about prescription or over-the-counter therapies, such as medications, creams, or heating pads that can help with possible side effects.
- Ask your doctor or nurse to give you instructions about safety procedures (such as using bleach in your toilet) to follow when you urinate after BCG treatment.
- Drink plenty of water and other non-caffeinated liquids after each treatment.
- Plan to rest for the day following your BCG treatment.
- Call your medical team if you have questions or something seems wrong.

NEXT STEPS:

- You will still need regular cystoscopies to make sure the tumors have not recurred.
- After the initial cycle of BCG, your doctor might recommend maintenance cycles of BCG.
- It can be helpful to talk to someone who has experienced BCG. Call the BCAN Survivor 2 Survivor program to connect with a volunteer who knows about having BCG treatment. Dial 888-901-BCAN.

The Bladder Cancer Advocacy Network (BCAN)

BCAN's mission is to increase public awareness about bladder cancer, advance bladder cancer research, and provide educational and support services for the bladder cancer community.



www.bcan.org

