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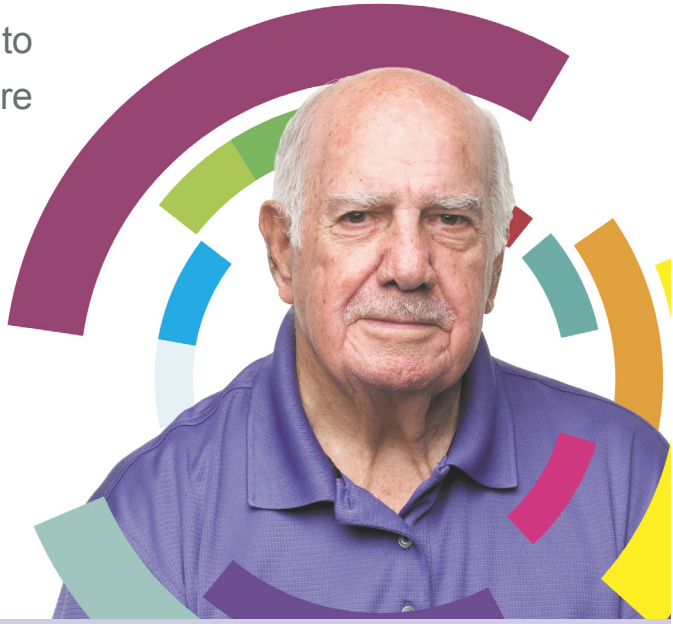
Keynote B15

A Clinical Trial for
Muscle Invasive Bladder Cancer

In this brochure, you will learn about **Muscle Invasive Bladder Cancer (MIBC)** and a clinical trial for this disease. This clinical trial is trying to find out if study drugs given together, before and after surgery, can help to improve the treatment of MIBC compared to chemotherapy before surgery.



What is Bladder Cancer?

Bladder cancer begins in the cells which make up the bladder, a hollow elastic organ that holds urine made by the kidneys until it is emptied from the body through the urethra. Most commonly, bladder cancer develops in the cells which line the inner surface of the bladder – these cells are called urothelial cells. This means that the most common kind of bladder cancer is called urothelial cancer. Urothelial cancer can develop anywhere along the urinary tract (e.g. inner lining of kidneys, ureters, bladder, urethra), but most frequently occurs in the bladder itself.

What is Muscle Invasive Bladder Cancer (MIBC)?

MIBC are tumors located in the bladder. These tumors have grown from the inner surface lining of the bladder into the deeper muscle layers, which is why they are called “Muscle Invasive.”

How is Muscle Invasive Bladder Cancer (MIBC) treated?

After diagnosis, the tumor is removed by a procedure called a Transurethral Resection of Bladder Tumor (TURBT), if it was not already removed during the initial biopsy to determine the diagnosis. Chemotherapy may then be used to treat any cancer cells which may have spread beyond the bladder and to prevent the cancer from coming back. A surgery called a Radical Cystectomy (RC) and Pelvic Lymph Node Dissection (PLND) will follow chemotherapy. In males, a Radical Cystectomy includes the removal of the bladder, prostate, and seminal vesicles. In females, a Radical Cystectomy includes the removal of the bladder along with the uterus, fallopian tubes, ovaries, and anterior vaginal wall.

Deciding to join a clinical trial is something only you, those close to you, and your doctors and nurses can decide together.

What is a clinical trial?

Clinical trials are research studies that help doctors find out if study drugs (alone or with other treatments) are safe and if they can help prevent or treat diseases or other conditions.

All about this clinical trial

Why is this clinical trial being done?

This clinical trial is trying to find out if study drugs given together, before and after surgery, are safe and work to help improve the treatment of patients with MIBC compared to chemotherapy before surgery. It is not known if these study drugs will work to treat MIBC in this setting.

What treatments are being studied?

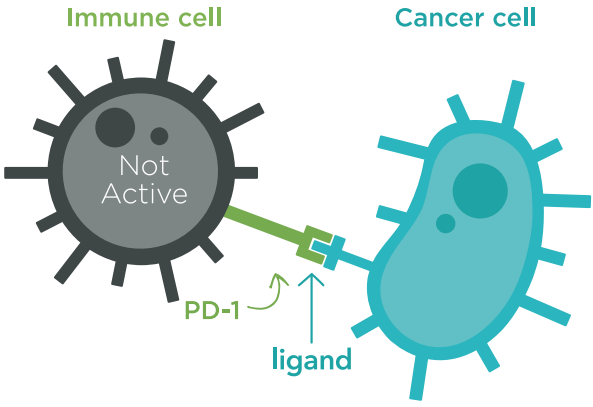
One drug being studied is an investigational medication (study drug) called pembrolizumab (also known as MK-3475). Pembrolizumab is a type of immunotherapy, which may help the body's immune system attack cancer cells.

The other drug being studied is an investigational medication (study drug) called enfortumab vedotin (also known as EV). Enfortumab vedotin is an antibody-drug conjugate (ADC) and it is designed for the treatment of cancer cells by delivering drug directly to the tumor.

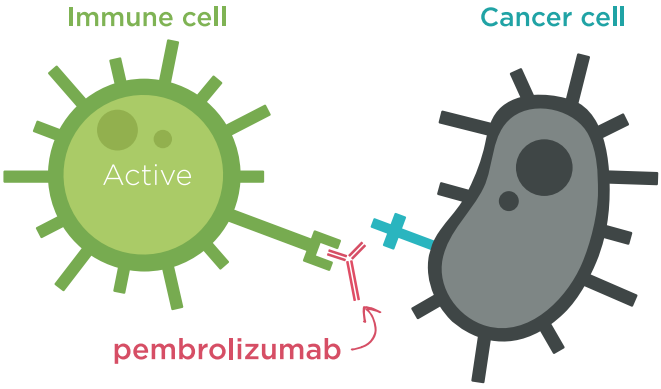
About Pembrolizumab:

1. A protein called PD-1 (on some of your immune system cells) sometimes binds with certain molecules called ligands (on some cancer cells)
2. When these two bind, it “turns off” the immune system cell, which means it can’t do its work to help protect you and attack cancer cells
3. This is where pembrolizumab comes in; this study drug binds with PD-1 and blocks PD-1 from binding with ligands
4. By blocking PD-1 from binding with ligands, pembrolizumab may help the immune system stay “on” so it can find and attack cancer cells

Another way to think about the treatment



When PD-1 and ligands bind, it's like turning off the immune cell. This means that the immune cell will not do its work to attack cancer cells.



This clinical trial is studying whether pembrolizumab can block PD-1 and ligands from binding so that the immune system cell stays on and can start working.

About Enfortumab Vedotin

Enfortumab vedotin is a type of drug called an antibody drug conjugate or ADC. ADCs usually have 2 parts:

Antibody: Antibodies are part of your immune system. Usually they help protect you from getting sick. In enfortumab vedotin, we are using an antibody designed to find and stick to the cancer cells in your body.

Drug: The drug is the part of the ADC that kills cells. The cell-killing part of enfortumab vedotin is a chemotherapy drug called monomethyl auristantin E (MMAE).

In enfortumab vedotin, the antibody part is designed to stick to cancer cells so that the drug part can kill them. It may also stick to some non-cancer cells in your body.

Who can join this study?

There are certain requirements that you must meet in order to join. Your study team will perform certain tests that will help them determine if you are eligible to join.

This study will include people with MIBC who are:

• Eligible to receive cisplatin-based chemotherapy;

AND

• Planning to have a Radical Cystectomy and PLND surgery

You and your study doctor will discuss the requirements to decide if this study is a good option for you, as well as the possible benefits and risks of joining this study.

Before deciding to participate, you should make sure you understand the potential side effects or risks of participating in the study. These will be explained to you by the study doctor. If there is anything you do not understand, you are encouraged to ask the study doctor.

Ask your doctor any questions about what happens in the study visits and how often they will happen

If I join, what will happen during the study visits?

You will visit the study site on a regular schedule so that your doctors can see how the study drug is working for you.

During your study visits, you might get:

- Blood and urine tests
- Physical exams
- Eye exams
- Imaging such as CT or MRI scans
- Questionnaires to complete about how you feel and function

What drug will I get?

You will be randomly assigned to one of two groups. You will have an equal chance (similar to flipping a coin) of being assigned to either group.

Group 1 (about 392 people)
If you are assigned to Group 1, you will receive: enfortumab vedotin and pembrolizumab before and after surgery

Group 2 (about 392 people)
If you are assigned to Group 2, you will receive: chemotherapy before surgery, and then follow with clinical observation

If you join the study, your doctor will need to stay in contact with you even after your study treatments and visits are over

This is very important because this clinical trial is studying how well the study drug works over time.

To learn more

Talk to your study doctor or contact:

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