

INTerpath 005

A Clinical Trial For **High-Risk Muscle-Invasive Urothelial Carcinoma (HR MIUC)**

In this brochure, you will learn about:

- High-risk muscle-invasive urothelial carcinoma (HR MIUC), a type of bladder cancer and a clinical trial for this disease.
- This clinical trial is trying to find out if an investigational combination of study drugs can help stop your high-risk muscle-invasive urothelial carcinoma (HR MIUC) from coming back or from spreading to other areas of your body.



What is high-risk muscle-invasive urothelial carcinoma (HR MIUC)?

High-risk muscle-invasive urothelial carcinoma (HR MIUC) is a type of bladder cancer.

This type of cancer is often called bladder cancer because it most often happens in the bladder, but it can happen in other parts of the urinary tract too.

It begins in the **urothelial cells**, which are cells that line the urinary system. The urinary system is several organs that work together to remove urine (pee) from our bodies, including the:

- Kidneys – organs that remove waste and extra water from your blood as urine
- Ureter- the tube that carries urine from your kidney to the bladder
- Bladder – an organ that stores urine
- Urethra- the tube that carries urine from your bladder to out of your body

Muscle-invasive means the cancer has grown into the muscle layers of the urinary system and **high-risk** means the cancer has a high chance of coming back and getting worse.

About 9 in 10 MIUC cases are in the lower urinary system (bladder and urethra). About 1 in 10 MIUC cases are in the upper urinary system (kidneys and ureters).

Your treatment options?

If you have HR MIUC, your cancer care team will discuss your treatment options with you and those close to you. Your options will depend on several things including:

- The stage of your cancer, which tells you if it has spread and if so, how far
- Your overall health and age
- Side effects you may have from prior treatment



Your care team may offer you one or more of these options:

- **Targeted therapy** - treatments that works on specific cells to stop them from growing
- **Immunotherapy** - medicines that help your immune system fight the cancer
- **Chemotherapy** - medicine to kill cancer cells or stop them from growing
- **Radiation therapy** - treatment that uses beams of intense energy (like X-rays) to shrink or get rid of tumors. This would only be used to treat symptoms related to tumor growth
- **Radical Surgery** - surgical removal of all or part of the bladder or kidney, or ureter to stop the cancer from spreading more
- **Clinical trials**, such as this one

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, find, or treat diseases or conditions. Clinical trials are carefully controlled research studies that are done to get a closer look at investigational treatments and procedures.

This clinical trial may include people:

- Who have had their MIUC removed and are at risk for it coming back
- Have had a radical surgery

What is an adjuvant clinical trial?

Adjuvant treatments are given after surgery to help lower the chance of the cancer coming back. Adjuvant therapies may include:

- Chemotherapy
- Radiation therapy
- Immunotherapy

In an adjuvant clinical trial, researchers learn about the safety of adjuvant treatments and how they work. The V940-005 study is an adjuvant clinical trial.

All about this clinical trial

Why is this study being done?

This trial is trying to find out if an investigational combination of study drugs is safe and works to prevent HR MIUC from coming back or spreading to other areas of the body in patients who have already had surgery to remove their HR MIUC. Researchers will also see what side effects may happen.

Who can join this trial?

There are certain rules and tests that you must meet to join, such as:

- Having HR MIUC that has been surgically removed
- Tests to make sure you qualify
- Other rules to decide if this trial is a good option for you

There may be other reasons why you cannot be in this trial. The trial doctor or staff will discuss these with you as well the possible benefits and risks of joining the trial.

What treatments are being studied?

This trial is studying an investigational combination of study drugs. The treatments being studied are:

- V940 (also known as mRNA-4157), in combination with pembrolizumab, both of which are types of immunotherapy
- Placebo with pembrolizumab

Immunotherapy is a treatment that works with a person's immune system to fight disease, including some cancers. A **placebo** is something that looks like the study medicine but has no actual study medicine in it.

If I join the trial, what study treatment will I get?

You will have an equal chance of being in 1 of 2 groups:

- **Group 1:** Will get V940 with pembrolizumab
- **Group 2:** Will get placebo with pembrolizumab

You and your trial doctor won't know which group you are in or which drugs you are getting.

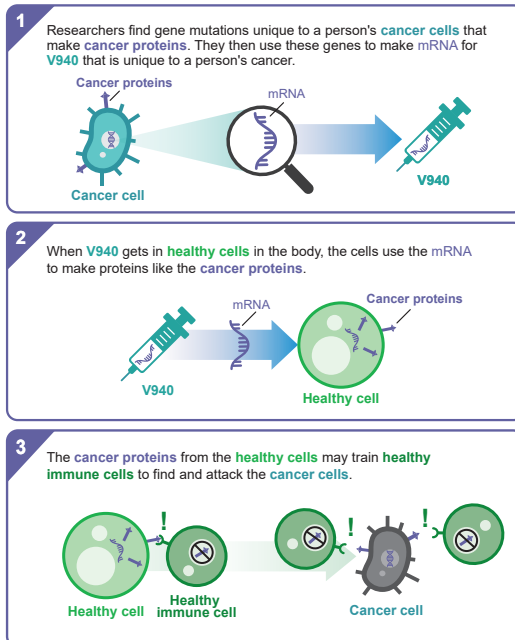
Here is what researchers know or assume about how each study drug works on its own.

How does V940 work?

V940 is a cancer therapy that has not been approved.

1. Every person's cancer has different mutations (changes) in their genes. V490 is made specifically for each person based on their gene mutations - in other words, it is individualized for each person.
2. Before a person gets V940, researchers find their cancer mutations. They then make mRNA to use in a dose of V940 made just for them (mRNA is genetic material that tells your body how to make proteins). The mRNA makes proteins that look like the person's specific cancer mutations.
3. When the person gets V940 as an injection into their muscles, the mRNA tells their body to make proteins that looks like their cancer mutations.
4. These proteins may help the immune system recognize and attack cancer cells with these mutations.

Another way to think about V940

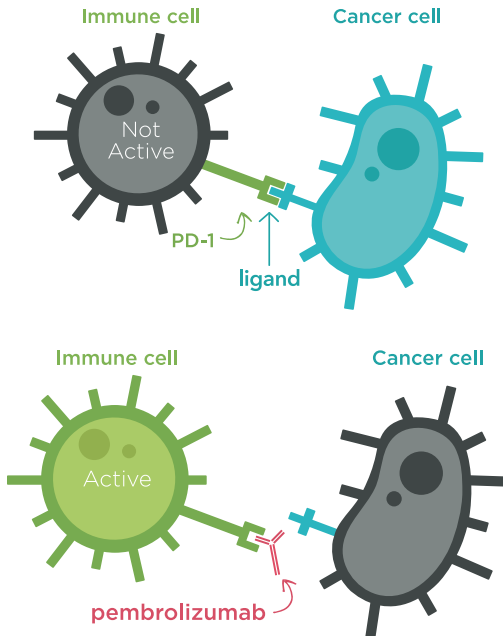


About Pembrolizumab

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 your 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 pembrolizumab

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.



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

You will visit the trial site on a regular schedule so that your doctor can see how the trial drug is working for you. During your trial visits, you might get:

- Blood and urine (pee) tests
- Physical exams
- Trial drugs
- Imaging scans, such as CT scans or MRIs
- Cystoscopy - a procedure that allows your doctor to look at the lining of your bladder and the tube that carries urine (pee) out of your body (urethra)

What happens when the trial is over?

If you join the trial, your trial doctor will need to stay in contact with you even after your trial visits are over. This is called the follow-up period. This is very important because this clinical trial is studying how well the trial drugs work overtime.

Thank you for learning about bladder cancer and this clinical trial.

To learn more

Talk to your study doctor or contact:



www.merckoncologyclinicaltrials.com