

Full trial title: Phase III, Randomized, Open-label, Global, Multicenter Study of Rilvegostomig or Durvalumab in Combination With Chemotherapy as a First-line Treatment for Patients With Advanced Biliary Tract Cancer (ARTEMIDE-Biliary02)

Lay language title: A trial to learn how safe the combination of rilvegostomig and chemotherapy is and how well it works compared to durvalumab and chemotherapy in adults with advanced biliary tract cancer

EU trial number: 2025-523085-24-00

Trial Background: Researchers are looking for a better way to treat **advanced biliary tract cancer**.

The **biliary tract** creates and sends a fluid called **bile** to the stomach to help with digestion. In people with biliary tract cancer, the body is not able to control the growth of some cells in the biliary tract. The extra cells can form tumors, which can affect the normal function of organs and the body. “Advanced” means that the cancer has spread from where it started to other parts of the body and cannot be treated with surgery.

Some cancers, including biliary tract cancer, have a protein called **PD-L1** on their surface. When a tumor has a certain amount of PD-L1, it is said to have **positive PD-L1 expression**. The PD-L1 protein acts like a shield, helping cancer cells hide from the immune system. They interact with immune system proteins like **TIGIT** and **PD-1**, to send a “don’t attack” signal. The trial drug **rilvegostomig** is designed to help the immune system to recognize and kill tumor cells by blocking **PD-1** and **TIGIT**.

The current standard treatment for biliary tract cancer is the combination of a drug called durvalumab and chemotherapy. **Durvalumab** helps the immune system kill tumor cells by blocking **PD-L1**. But, the standard treatment does not work well enough for all people.

In this trial, researchers want to learn how safe the combination of rilvegostomig and chemotherapy is and how well it works compared to durvalumab combined with chemotherapy in adults with advanced biliary tract cancer. They also want to learn if they can identify people with biliary tract cancer who may be more likely to benefit from the trial treatment based on the amount of PD-L1 protein in a sample of their tumor.

Objectives Questions the researchers want to answer during the trial	Endpoints How the researchers plan to answer their questions during the trial
Primary	
For participants with positive PD-L1 expression in their tumor sample, does the combination of rilvegostomig and chemotherapy help them live longer than durvalumab combined with chemotherapy?	For participants with positive PD-L1 expression, researchers will keep track of how long they live during the trial after starting treatment, also called overall survival (OS). People with positive PD-L1 expression are more likely to respond well to rilvegostomig.
Key Secondary	
How well does the combination of rilvegostomig and chemotherapy work compared to durvalumab combined with chemotherapy, as measured by participants’ lifespan and time to tumors growing?	Researchers will evaluate the following: - OS for all participants - For participants with positive PD-L1 expression, how long they live during the trial without their tumors growing or spreading after starting treatment, also called progression-free survival (PFS) - PFS for all participants The trial doctors will take scans of the participants’ tumors before, during, and after treatment.
Secondary	
How well does the combination of rilvegostomig and chemotherapy work compared to durvalumab combined with chemotherapy as measured by how much the tumor shrinks and how long the benefit lasts?	Researchers will evaluate the following for the participants with positive PD-L1 expression in their tumor sample, and for all participants: - The percentage of participants whose tumors disappear completely or shrink by at least 30% - How long the participants’ tumors continue to respond to trial treatment before growing or spreading - PFS after participants begin a new cancer treatment if they stop benefiting from their assigned treatment The trial doctors will take scans of the participants’ tumors before, during, and after treatment.

continued on next page

How does the overall health and safety of the participants change during the trial?	Researchers will keep track of any medical problems (adverse events) that happen during the trial. They will also look at the results of different tests and measurements to see if there are any changes to the participants' health after starting trial treatment.
How does rilvegostomig move throughout the body over time?	Researchers will measure the levels of rilvegostomig in the participants' blood at different times throughout the trial.
How do the participants' immune systems respond to rilvegostomig?	Researchers will measure the levels of anti-drug antibodies in the participants' blood that target rilvegostomig. Anti-drug antibodies can stop drugs from working and can also cause medical problems.
Does the combination of rilvegostomig and chemotherapy improve the participants' quality of life and symptoms more than durvalumab combined with chemotherapy?	The participants will complete questionnaires about their quality of life and symptoms before, during, and after treatment. Then, researchers will compare the results between the participants receiving rilvegostomig and chemotherapy and those receiving durvalumab and chemotherapy.

Trial Design: This is a Phase 3, randomized, open-label trial. **Randomized** means that a computer program will randomly assign the treatment each participant receives. **Open-label** means the participants, researchers, trial doctors, and other trial staff will know what each participant is receiving. The participants will continue to receive treatment unless their cancer gets worse, they have significant medical problems, or they leave the trial for another reason.

Trial Population: This trial will include up to about 1,100 participants. To join this trial, people must be at least 18 years old and have advanced biliary tract cancer.

Treatments and Procedures: Rilvegostomig, durvalumab, and chemotherapy are given through a needle directly into a vein over a period of time, also known as an IV infusion. Doses of rilvegostomig and durvalumab are measured in milligrams (mg). Chemotherapy doses are given based on the participants' body size on Day 1 and Day 8 of each cycle for the first 8 cycles. The chemotherapy drugs given in this trial are gemcitabine and cisplatin. The treatments will be given in 3-week or 4-week treatment periods called **cycles**.

	Group 1	Group 2
	550 participants	550 participants
	750 mg of rilvegostomig and chemotherapy every 3 weeks for the first 8 cycles then 750 mg of rilvegostomig every 3 weeks	1,500 mg of durvalumab and chemotherapy every 3 weeks for the first 8 cycles then 1,500 mg of durvalumab every 4 weeks

During the trial, the doctors will do the following:

- ▶ Test the participants' blood and urine
- ▶ Perform physical exams
- ▶ Check the participants' vital signs
- ▶ Perform a biopsy on some of the participants' tumors
- ▶ Take CT and/or MRI scans
- ▶ Test the participants' heart function using an electrocardiogram (ECG) and other tests
- ▶ Ask about the participants' medications and any medical problems
- ▶ Ask the participants to fill out questionnaires about their symptoms and quality of life

Ethical Considerations: All participants will help researchers learn more about biliary tract cancer. A possible **benefit** of receiving rilvegostomig is the improvement of a participant's biliary tract cancer.

Some possible **risks** of receiving rilvegostomig are below:

- ▶ Problems with the skin, including rashes
- ▶ Problems with the lungs or breathing
- ▶ Inflammation of the brain caused by the body's immune system attacking normal tissue
- ▶ Medical problems caused by the immune system overreacting to treatment
- ▶ A potentially life-threatening overreaction by the immune system after getting an IV infusion
- ▶ Problems and inflammation of the stomach or intestines
- ▶ Changes in the levels of certain hormones in the body (Endocrinopathies)
- ▶ Problems and inflammation of the liver, kidneys, and pancreas
- ▶ Inflammation of the heart muscles (Myocarditis)

The procedures done in this trial, as well as durvalumab and chemotherapy, also have risks. The trial doctor or staff may have more information on these risks.

The tests, procedures, and actions from the participants are needed to make sure the trial results are accurate.

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