ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

Summary of Clinical Study Results for Participants

A study to compare standard chemotherapy treatment alone or in combination with atezolizumab after surgery in people with a type of colon cancer called "stage III colon cancer with deficient DNA mismatch repair"

Definitions of key medical terms can be found at the end of this summary in the Glossary.

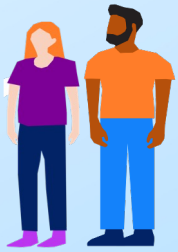
Title of the Study:	Randomized trial of standard chemotherapy alone or combined with atezolizumab as adjuvant therapy for patients with stage III colon cancer and deficient DNA mismatch repair
Protocol Number:	A021502 (ATOMIC)
Study Identifier:	2019-003562-40 (EUCT) and NCT02912559 (ClinicalTrials.gov)
Medicine(s) Studied:	**mFOLFOX6 plus Atezolizumab, mFOLFOX6**
Study Start and End Date:	October 16, 2017 - still ongoing
Date of Summary:	June 1, 2025
Status of This Study:	Primary Outcomes Analysis: This study started on October 16, 2017, with completion of primary outcome data through February 4, 2025. This summary includes the complete results of one part of the study that were collected and analyzed with presentation on June 1, 2025. At the time of writing this summary, all study patients have completed study treatment, the study has completed primary analysis and is ongoing for collecting follow-up information from study patients. This summary will be updated with additional information when the study ends.
Disease Studied:	This study involved people with a type of colon cancer called **stage III colon cancer with deficient DNA mismatch repair**. Stage III colon cancer means the cancer has spread to the nearby lymph nodes but has not spread to distant parts of the body. Deficient DNA mismatch repair means that the system in the body that fixes mistakes in the DNA is not working.
Type of Study:	This study is a Phase 3 randomized study of mFOLFOX6 plus Atezolizumab, and mFOLFOX6. A Phase 3 is a step in the research process that involves lots of people who have a certain disease. The purpose is to test how well a new treatment works and how safe it is. Randomized means it is a way to use chance to place study participants into different study treatment groups like flipping a coin, to protect against bias.

Thank you to our participants

We would like to thank all the individuals who took part in this study and their families, as well as carers who supported their participation.

Study participants belong to a large community of individuals around the world who have made it possible for researchers to answer important health questions and discover new medicines. We hope you feel proud of the critical role you have played in medical research.

We believe it is important for you, and people like you, to know the results of this study. If you have questions about the information in this summary, please speak with the doctor or nurse at the clinic where you participated in the study.



It is important to note that the information presented in this summary is from one study. Remember that one study cannot tell us everything about the possible effects of a study medicine and how well it may or may not work. It takes a lot of people, participating in many studies to learn as much as we can about new medicines. This is why the results of this study may be different from the results of other studies of the same medicine.

Why was this study needed?

In the United States, colon cancer is the fourth most common cancer and the second most frequent cause of cancer death. Surgery is the preferred way of treating colon cancer that has not spread to other parts of the body, including stage III colon cancer. In people who have a good chance to be cured of the disease, the stage of the disease is important in predicting how the disease will progress and if a medicine that kills cancer cells called “chemotherapy” is necessary.

About 35 to 40% of people have stage III colon cancer at diagnosis, which is about 50,000 people every year in the United States. About 15% of colon cancers have tumors that cannot fix mistakes in the DNA and are called “deficient DNA mismatch repair.” Despite surgery and treatment after surgery that kills cancer cells (called “adjuvant chemotherapy”), the cancer will come back in 3 years in about 25% of people with stage III colon cancer.

Cancer immunotherapy is a type of medicine that helps a person’s own defense (immune system) attack cancer cells. Patients with deficient DNA mismatch repair may have good responses to cancer immunotherapy.

A combination of three medicines called mFOLFOX6, is the standard adjuvant chemotherapy treatment for stage III colon cancer. There is a need to find new treatments to get better results in the treatment of people with stage III colon cancer and deficient DNA mismatch repair. Combining cancer immunotherapy with mFOLFOX6 may work better than standard treatment for people with stage III colon cancer and deficient DNA mismatch repair.

What was the main purpose of the study? What did researchers want to find out?

The main question researchers wanted to find out was whether adding atezolizumab to the standard mFOLFOX6 adjuvant chemotherapy treatment increased the length of time alive without the disease coming back, which is called “disease-free survival” in people with stage III colon cancer and deficient DNA mismatch repair.

The researchers did this study by comparing the combination atezolizumab plus standard mFOLFOX6 adjuvant chemotherapy to the standard mFOLFOX6 adjuvant chemotherapy alone.

The researchers wanted to find out if the combination treatment was better, the same, or worse than the standard treatment.

Who took part in the study?

712 people living with stage III colon cancer and deficient DNA mismatch repair

At 312 centres

In the United States and Germany

55% were women

45% were men

No prior medical (chemotherapy, immunotherapy, biologic or targeted therapy) or radiation therapy for colon cancer <u>except</u> for possibly one dose of mFOLFOX6

Participants were between 13 to 91 years of age

Additionally, people had:

- Stage III colon cancer confirmed by a technique that analyzes tissue or cell sample under a microscope (called “histology”)
- Deficient DNA mismatch repair confirmed by histology
- Performed activities almost as well as before the illness based on the “Eastern Cooperative Oncology Group” (ECOG) performance status of less than or equal to 2
- No pregnancy and no nursing for women

The following people could not take part in this study:

- People with evidence of cancer remaining in lymph nodes after surgery or cancer that has spread to other places in the body
- People with active known autoimmune diseases, hepatitis B or C, pulmonary disease with hypoxia
- People who have other planned experimental medications or other anti-cancer therapy
- People with known history of severe allergies to mFOLFOX6

What medicines were used in this study?

The main question of this study was to find out if the combination of atezolizumab plus standard mFOLFOX6 adjuvant chemotherapy lowered the risk of colon cancer from coming back better than standard mFOLFOX6 adjuvant chemotherapy alone.

mFOLFOX6

mFOLFOX6 is a modified version of FOLFOX6, a combination of three medicines, leucovorin, 5-fluorouracil and oxaliplatin, which is the standard chemotherapy, a type of treatment that kills cancer cells, for stage III colon cancer.

Atezolizumab

Atezolizumab, also known as Tecentriq, is a cancer immunotherapy medicine that works by blocking a protein called “PD-L1" found on the surface of cancer cells. PD-L1 stops the immune system from working properly and attacking cancer cells. Blocking PD-L1 helps to make the immune system find and kill cancer cells.

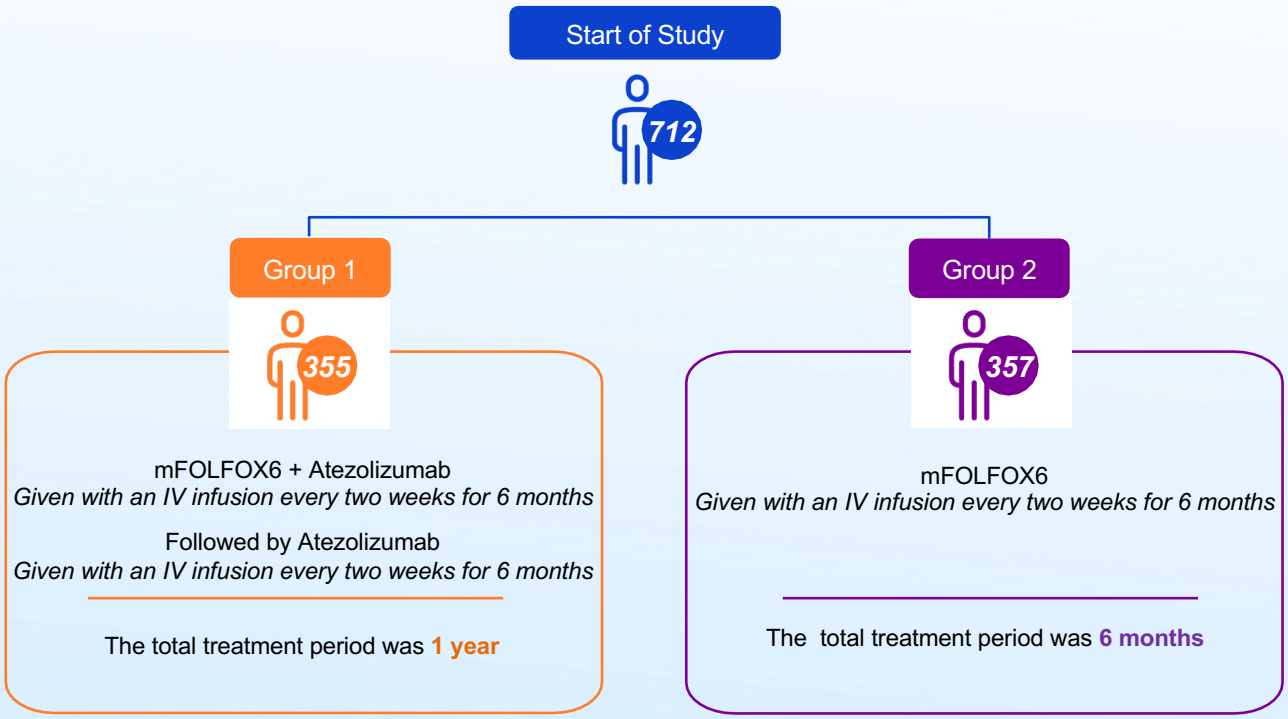
How was the study conducted?

People were assigned by chance into one of two study treatment groups by a computer. This is called randomization.

The study had two study groups: Group 1 and Group 2

- **Group 1**: Chemotherapy mFOLFOX6 plus atezolizumab were given slowly as a drip into a vein (called “IV infusion”) every two weeks for 6 months, then atezolizumab alone was given as an IV infusion every two weeks for an extra 6 months. The treatment had 25 doses in total.
- **Group 2**: Chemotherapy mFOLFOX6 alone was given as an IV infusion every two weeks for 6 months. The treatment had 12 doses in total.

For Group 1 and Group 2: Participants were cared for by their doctors for up to 8 years even if they did not finish study treatment.



What were the results of the study?

The main question researchers wanted to find out was whether adding atezolizumab to the standard mFOLFOX6 adjuvant chemotherapy treatment increased the length of time alive without the disease coming back, which is called “disease-free survival” in people with stage III colon cancer and deficient DNA mismatch repair.

The researchers did this study by comparing the combination atezolizumab plus standard mFOLFOX6 adjuvant chemotherapy to the standard mFOLFOX6 adjuvant chemotherapy alone.

The researchers wanted to find out if the combination treatment was better, the same, or worse than the standard treatment.

1. The study has shown that:

- The combination of atezolizumab plus mFOLFOX6 treatment lowered the chance of cancer from coming back or death by 50% compared to mFOLFOX6 treatment alone.
- Atezolizumab and mFOLFOX6 resulted in unwanted effects as expected. There were more serious unwanted events of low white blood cells that help fight infections (also called “neutrophils”) in the group of people who were given atezolizumab, but this was manageable.
- The data showed the combination of atezolizumab plus mFOLFOX6 treatment can be a new standard of care for people with stage III colon cancer and deficient DNA mismatch repair.

2. What unwanted effects did the participants experience?

Unwanted effects (also called "adverse reactions") are medical problems that happen during a study. They are described in this summary because the study doctor believes the unwanted effects were related to the medicine(s) used in the study. Unwanted effects may be mild to very serious and can be different for each person. **Not all the people in this study experienced all the unwanted effects noted below**.

Common unwanted effects are those that are experienced by at least 434 in every 680 participant (64% of participants). Mild unwanted effects are medical problems that do not impact a participant's daily routine. Moderate unwanted effects are those that are not life threatening, but that may impact a participant's day-to-day life. In these cases, the participant may need to have their study medicine dose adjusted or may need additional treatment. Serious unwanted effects are those that may result in death, may require a participant to be hospitalized, or may extend a participant's time in hospital.

In this study, the safety of **mFOLFOX6 plus atezolizumab and mFOLFOX6** is evaluated by measuring the unwanted effects experienced by some participants in the study. This information is listed below.

Group 1: mFOLFOX6 plus atezolizumab	
Effect	**346 of Participants Impacted**
Serious Unwanted Effects	
Low levels of a type of white blood cells that help the body fight infections (called "neutrophils")	137 out of 346 (40%)
Damage to the nerves	60 out of 346 (17%)
Diarrhea	37 out of 346 (11%)
Fatigue	32 out of 346 (9%)
Low levels of white blood cell	27 out of 346 (8%)
Common Unwanted Effects (including mild and moderate)	
Fatigue	298 out of 346 (86%)
Damage to the nerves	256 out of 346 (74%)
Wanting to throw up	246 out of 346 (71%)
Low levels of a type of white blood cells that help the body fight infections (called "neutrophils")	237 out of 346 (68%)
Low levels of small cells in the blood that help the blood to clot (called "platelets")	224 out of 346 (65%)
Diarrhea	238 out of 346 (69%)

Group 2: mFOLFOX6	
Effect	**334 of Participants Impacted**
Serious Unwanted Effects	
Low levels of a type of white blood cells that help the body fight infections (called "neutrophils")	116 out of 334 (35%)
Damage to the nerves	51 out of 334 (15%)
Diarrhea	26 out of 334 (8%)
Fatigue	11 out of 334 (3%)
Low levels of white blood cell	7 out of 334 (2%)
Common Unwanted Effects (including mild and moderate)	
Fatigue	267 out of 334 (80%)
Damage to the nerves	232 out of 334 (69%)
Wanting to throw up	220 out of 334 (66%)
Low levels of a type of white blood cells that help the body fight infections (called "neutrophils")	219 out of 334 (66%)
Low levels of small cells in the blood that help the blood to clot (called "platelets")	218 out of 334 (65%)
Diarrhea	196 out of 334 (59%)

How has this study helped research?

At this point in time, the study is still ongoing. However, the research has shown that the combination of mFOLFOX6 plus atezolizumab lowered the cancer from coming back and death by half compared to mFOLFOX6 alone in people with stage III colon cancer and deficient DNA mismatch repair. As a result, the combination treatment can represent a new standard treatment for stage III colon cancer and deficient DNA mismatch repair.

Where can I find more information about this study?

More information about this study can be found at:

Stage III Colon Cancer and Deficient DNA Mismatch Repair: https://clinicaltrials.gov/study/NCT02912559 – ClinicalTrials.gov Explore official registration details, eligibility criteria, and study updates.

Stage III colon adenocarcinoma with deficient MMR: https://euclinicaltrials.eu/search-for-clinical-trials/?lang=en&EUCT=2024-517269-18-00 – EU Clinical Trials Register View the EU listing with regulatory and trial data.

If you want to read more about the results of this study, the full title of the scientific publication is: <<Randomized trial of standard chemotherapy alone or combined with atezolizumab as adjuvant therapy for patients with stage III deficient DNA mismatch repair (dMMR) colon cancer (Alliance A021502; ATOMIC)>>. The first author is: <<Frank A. Sinicrope>>. The abstract is published in the American Society of Clinical Oncology for the 2025 Annual Meeting with a link at https://meetings.asco.org/abstracts-presentations/245969

What other studies are being conducted for this medicine?

At the time of writing this summary, no other studies with atezolizumab and mFOLFOX6 in stage III colon cancer are planned.

Sponsor(s):

This study was Sponsored and paid for by the National Cancer Institute (NCI) and conducted by the Alliance for Clinical Trials in Oncology with participation from the NCI-funded national clinical trials network (NCTN), in partnership with the German group Arbeitsgemeinschaft Internistische Onkologie (AIO).
Genentech, a member of the Roche Group, participated in this study as a pharmaceutical collaborator by providing financial support and atezolizumab as the investigational medicinal product.

Contact details:

If you have any further questions after reading this summary, please contact Alliance Communications at Communications@AllianceNCTN.org.

If you took part in this study and have questions about the results, please speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment, please speak with the doctor in charge of your treatment.

Glossary of key medical terms

Adjuvant therapy: a type of medicine given after their main treatment, such as surgery or ablation (ablation is a method of removing cancer cells using heat). This may help to slow down or stop cancer from coming back

Atezolizumab: a medicine that blocks PD-L1, allowing the immune system to attack the cancer cells. PD-L1 stops the immune system from working properly and attacking cancer cells. Blocking PD-L1 helps to make the immune system find and kill cancer cells

Autoimmune disease: a disease that makes the body attack healthy cells by mistake

Biologic therapy: biologic therapy is a medicine made by living organisms grown in a laboratory e.g., vaccines, blood components and living cells used in cell therapy

Chemotherapy: a medicine that kills cancer cells

Deficient DNA mismatch repair: a cell's ability to fix mistakes in its DNA is broken or not working

Disease free survival: the time between no signs of the disease on scans or tests after treatment and the signs that it has come back or death

Eastern Cooperative Oncology Group (ECOG) performance status: a measurement that describes people's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (walking, working)

Immune system: the body's natural defense, which protects the body from foreign or harmful substances such as bacteria and viruses

Immunotherapy: a type of medicine that helps a person's own immune system attack cancer cells

Intravenous infusion, or IV infusion: drip into a vein given slowly

Lymph nodes: small, bean-sized structures in the body that help fight infections

mFOLFOX6: a type of chemotherapy that is a combination of three medicines: leucovorin, 5-fluorouracil and oxaliplatin

Pulmonary disease with hypoxia: lung disease that damage the body's ability to sufficiently oxygenate the blood leading to not enough oxygen in the body

Radiation therapy, also called radiotherapy: a type of treatment where high energy rays are used to destroy cancer cells

Side effect: an unwanted effect which may or may not be caused by study treatment(s)

Stage III cancer: stage III cancer is a cancer that has spread to the nearby lymph nodes (small, bean-sized structures in the body that help fight infections), but that has not spread to distant parts of the body

Standard of care: the accepted standard treatment usually given to people with the disease

Targeted therapy: targeted therapy is a type of treatment that selects for specific features on cancer cells in the body to kill them. It causes less harm to the normal cells