PUBLICATION PLAIN LANGUAGE SUMMARY

RATIONALE-305: Final results of a study comparing tislelizumab plus chemotherapy versus placebo plus chemotherapy for people with untreated advanced gastric or gastroesophageal junction adenocarcinoma

FULL TITLE

Tislelizumab (TIS) plus chemotherapy (Chemo) vs placebo (PBO) plus chemo as first-line (1L) treatment of advanced gastric or gastroesophageal junction adenocarcinoma (GC/GEJC): Final analysis results of the RATIONALE-305 study

SUMMARY DATE

October 2023

KEY TAKEAWAYS

- In this study, people with untreated advanced gastric or gastroesophageal junction adenocarcinoma who received tislelizumab plus chemotherapy lived longer than people who received placebo plus chemotherapy
- The side effects of tislelizumab plus chemotherapy were considered to be manageable
- The results from this study support tislelizumab plus chemotherapy as a first treatment option for people with advanced gastric or gastroesophageal junction adenocarcinoma

PHONETICS

How to say medical terms used in this summary

Adenocarcinoma
<a-duh-noh-kaar-suh-NOH-muh>

Chemotherapy
<KEE-moh-THAYR-uh-pee>

Gastroesophageal
<ga-strow-uh-saa-fuh-JEE-uhl>

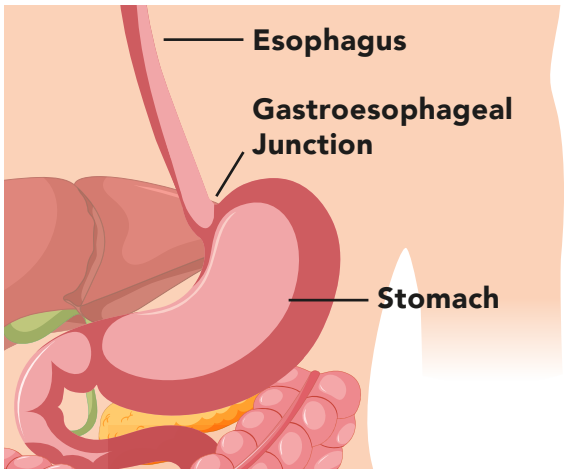
Immunotherapy
<IH-myoo-noh-THAYR-uh-pee>

Placebo
<pluh-SEE-boh>

Tislelizumab
<tis-le-LIZ-ue-mab>

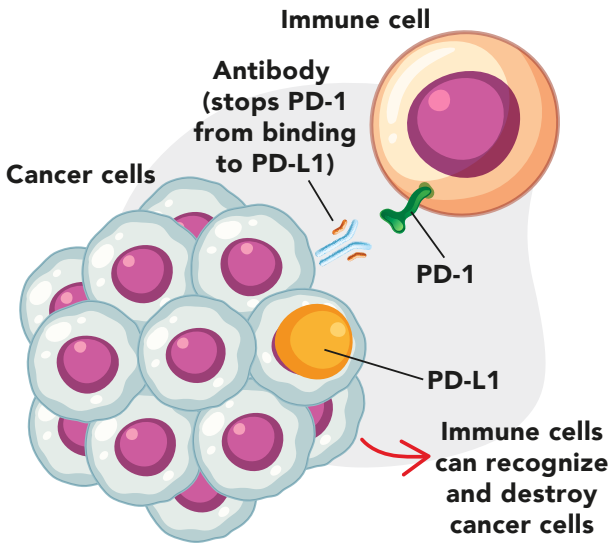
What is advanced gastric or gastroesophageal junction adenocarcinoma?

- Adenocarcinoma is a type of cancer that affects the cells surrounding the body's internal organs
- Gastric or gastroesophageal junction adenocarcinoma (GC/GEJC) is the fifth most commonly diagnosed cancer worldwide
- GE/GEJC affects the stomach or the junction between the stomach and the esophagus (the tube that carries food taken in by mouth and connects to the stomach)
  - Advanced can mean that the cancer has grown deeper into the stomach wall, may have spread to nearby areas or lymph nodes, and cannot be fully removed by surgery
    - Lymph nodes act as filters for damaged or abnormal cells
    - Cancer cells that break away from the main tumor can become trapped in lymph nodes
  - Advanced can also mean that the cancer has spread to distant parts of the body



What is immunotherapy?

- Immunotherapy is a type of cancer treatment that works by helping a person's immune system recognize and kill cancer cells
  - The immune system is the body's defense system
- The immune system can find and destroy cancer cells; however, these cells have ways to avoid detection
- One way cancer cells can avoid being detected by the immune system is by producing a protein called programmed death ligand 1 (PD-L1) on their surface
- White blood cells are a type of blood cell in the immune system that scans the body for unhealthy cells. White blood cells have a protein on their surface called programmed cell death protein-1 (PD-1) that can attach to the PD-L1 on cancer cell surfaces. When the white blood cells recognize and bind to cancer cells that have PD-L1 on their surface, they are tricked into not killing the cancer cells
- Anti-PD-1 antibodies are a type of protein that stops PD-1 on white blood cells from binding to PD-L1 on the cancer cells. This removes the cancer cells' 'disguise' and allows the immune system to kill cancer cells



What is tislelizumab?

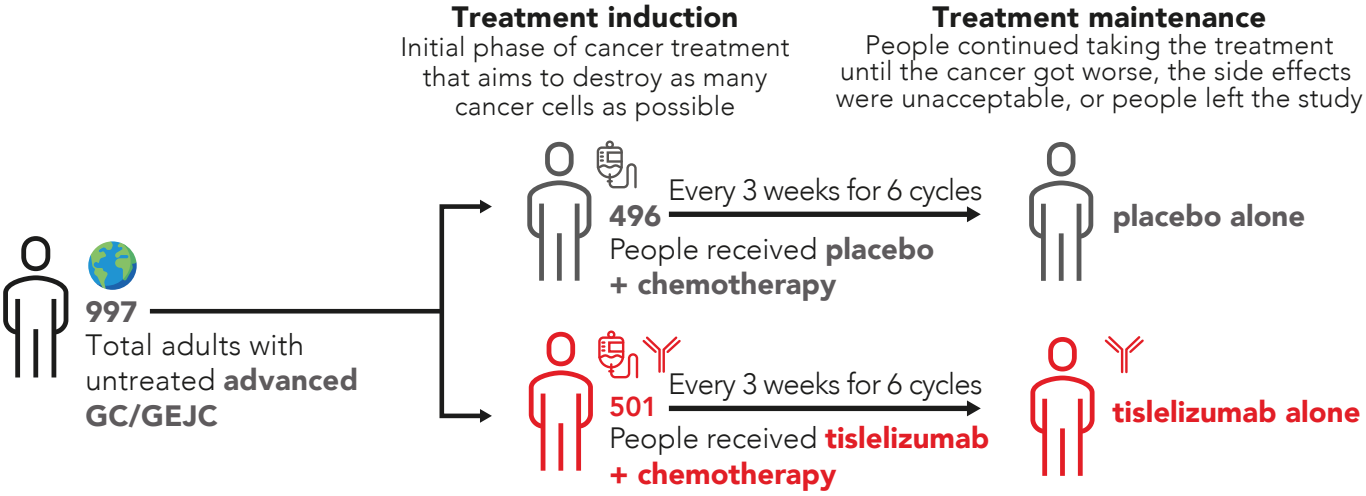
- Tislelizumab is an antibody that is designed in the laboratory. It works by binding specifically to PD-1, allowing the immune system to recognize and kill the cancer cells
  - Tislelizumab is given as an intravenous injection directly into the bloodstream
- In the RATIONALE-305 study, researchers compared the effects of tislelizumab plus chemotherapy versus placebo plus chemotherapy
  - A placebo looks and is given like the study drug (i.e., like tislelizumab) but does not contain any active ingredients

What does this summary describe?

- This summary describes the effects of tislelizumab plus chemotherapy versus placebo plus chemotherapy in people with advanced GC/GEJC
- In this study, researchers wanted to know:
  - How long people lived after they started the study treatment
  - How long people lived without their cancer growing or spreading after starting treatment
  - The proportion of people whose cancer got smaller or disappeared after starting treatment
    - How long people's cancer remained smaller or disappeared, on average, after starting treatment
  - The number and severity of side effects
    - A side effect is something that people feel is caused by the treatment they take
    - Researchers grade side effects on a scale from 1 to 5. The higher the grade, the more severe they are:
      - Grade 3 side effects are severe or medically significant but not life-threatening, Grade 4 side effects are life-threatening, and Grade 5 side effects are fatal

STUDY DETAILS

Who took part in the study?



What were the results of the study?

How well did the treatments work?

- After a minimum of 24.6 months (approximately 2 years) of follow-up, people who received **tislelizumab plus chemotherapy** lived longer than people who received **placebo plus chemotherapy**
  - Follow-up means seeing a health care provider regularly after treatment is done to check whether the cancer has come back
- People who received **tislelizumab plus chemotherapy** also lived longer without their cancer growing or spreading than people who received **placebo plus chemotherapy**

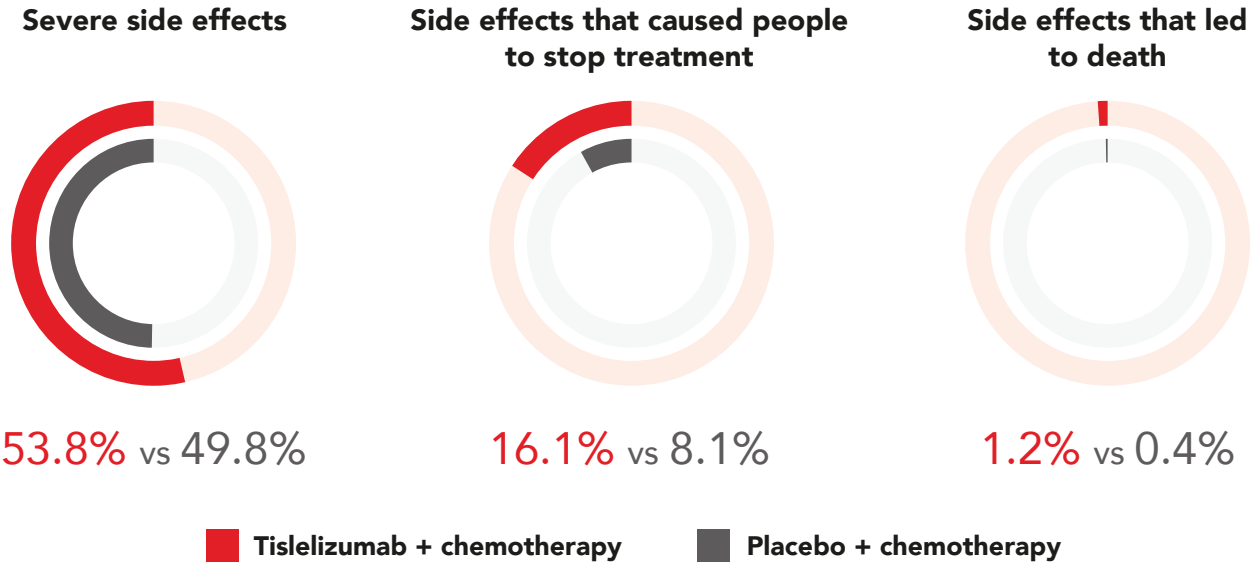
	Tislelizumab + chemotherapy	Placebo + chemotherapy
How long people lived, on average, after starting treatment	15.0 MONTHS	12.9 MONTHS
How long people lived, on average, without their cancer getting worse after starting treatment	6.9 MONTHS	6.2 MONTHS

- A greater proportion of people who received **tislelizumab plus chemotherapy** had cancers that got smaller or disappeared versus those who received **placebo plus chemotherapy**
  - The time period over which the cancers remained smaller or disappeared was longer in people who received **tislelizumab plus chemotherapy** versus those who received **placebo plus chemotherapy**

	Tislelizumab + chemotherapy	Placebo + chemotherapy
The proportion of people whose cancer got smaller or disappeared after starting treatment	47.3%	40.5%
How long people's cancer remained smaller or disappeared, on average, after starting treatment	8.6 MONTHS	7.2 MONTHS

What side effects did people have in the study?

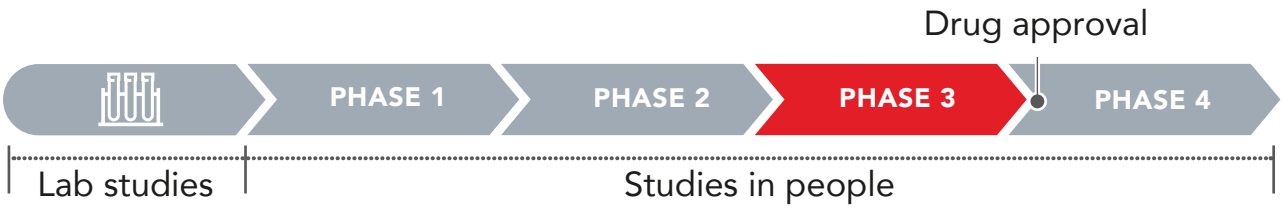
- A similar proportion of people who received **tislelizumab plus chemotherapy** and **placebo plus chemotherapy** had severe side effects
- More people who received **tislelizumab plus chemotherapy** stopped treatment because of side effects versus people who received **placebo plus chemotherapy**
- Side effects that led to death were rare for both treatments



Who sponsored the study?

This study was sponsored by BeiGene Ltd. BeiGene would like to thank the trial investigators, site support staff, and especially the people who took part in the study. This summary was prepared by Steven Moore, PhD, and Smitha Reddy, PhD, of Envision Pharma Group and was funded by BeiGene Ltd.

Whereabouts is tislelizumab in the drug development timeline?



Are there plans for additional studies?

This study started on December 13, 2018, is ongoing, and has not yet been completed. Other tislelizumab studies are currently ongoing and can be viewed by going to https://www.beigene.com/our-science-and-medicines/pipeline

Additional study information

For detailed study information, go to:
https://clinicaltrials.gov/study/NCT03777657

For more information about scientific studies done by specialist doctors in clinics and hospitals on new medicines in general, go to:
https://www.clinicaltrials.gov/ct2/about-studies/learn

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