PUBLICATION PLAIN LANGUAGE SUMMARY

RATIONALE-312: A study comparing tislelizumab plus chemotherapy versus chemotherapy alone for people with untreated extensive-stage small cell lung cancer

FULL TITLE

First-line chemotherapy with or without tislelizumab for extensive-stage small cell lung cancer: RATIONALE-312 phase 3 study

SUMMARY DATE

September 2023

KEY TAKEAWAYS

In this study, more people with untreated extensive-stage small cell lung cancer who received tislelizumab plus chemotherapy were alive without their cancer growing or spreading compared with people who received placebo plus chemotherapy. The researchers considered that the side effects of both treatments were manageable.

PHONETICS

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

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

Placebo
<pluh-SEE-boh>

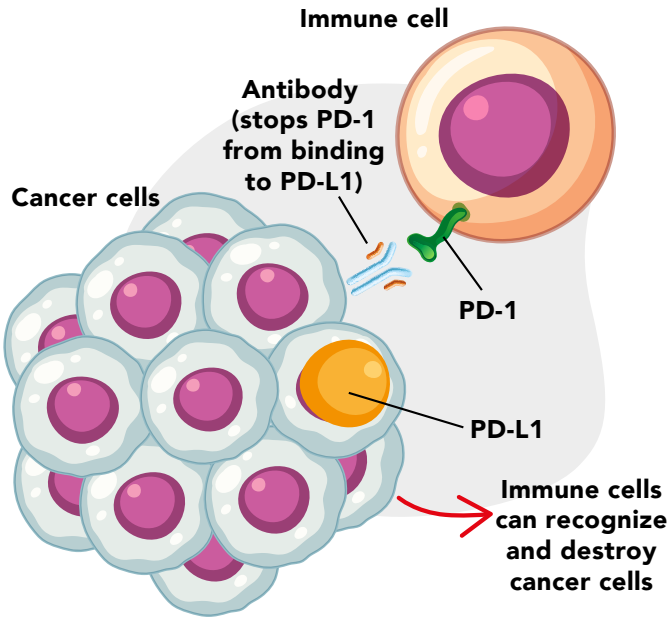
Tislelizumab
<tis-le-LIZ-ue-mab>

What is extensive-stage small cell lung cancer?

- Small cell lung cancer (SCLC) is the second most common type of lung cancer
  - Extensive-stage (ES) means that the cancer has spread either:
    - Throughout the lung
    - To the other lung
    - To lymph nodes on the other side of the chest
    - To other parts of the body (including the bone marrow)

What is immunotherapy?

- Immunotherapy is a type of cancer treatment that works by helping the patient'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 by the immune system
- 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



- 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?

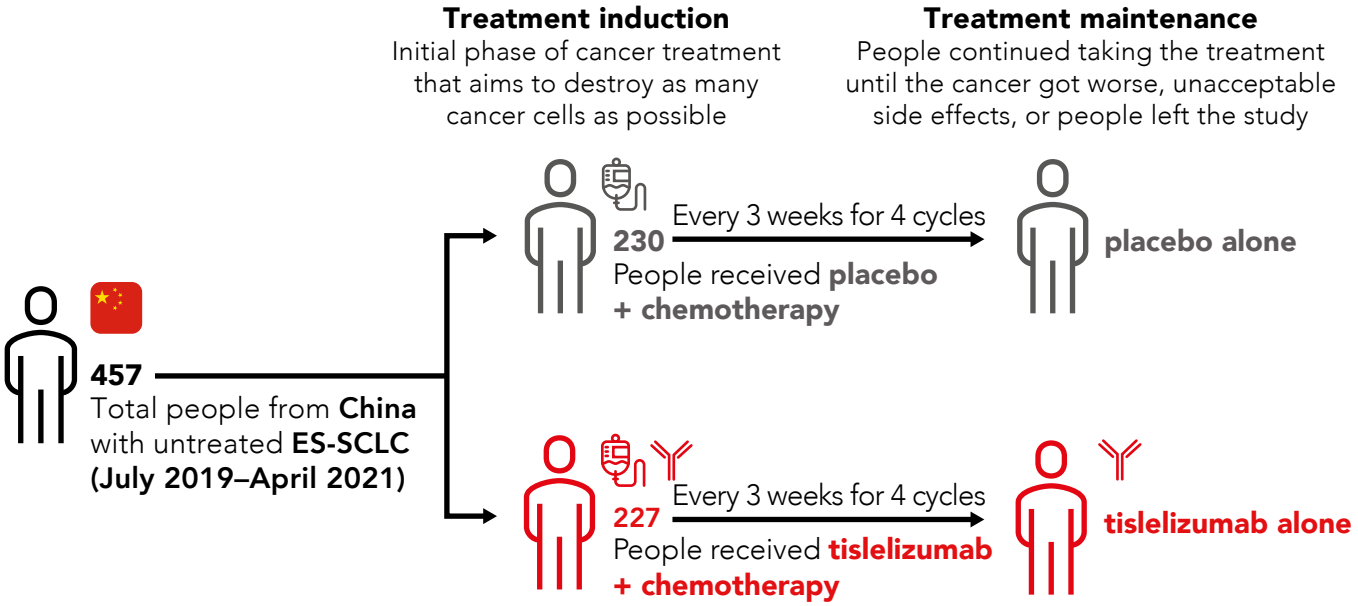
- Tislelizumab is an antibody that is artificially designed in the laboratory. It works by binding specifically to PD-1, allowing the immune system to recognize and kill the cancer cells
  - Tislelizumab is given as an intravenous injection directly into the bloodstream
- RATIONALE-312 was a study that looked at the effects of combining tislelizumab with chemotherapy versus combining a placebo with chemotherapy in people with ES-SCLC in China
  - 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 ES-SCLC in the RATIONALE-312 study. In this study, researchers wanted to know:
  - How long people lived after they started the study treatment
  - How long people lived without their cancer getting worse after they started the study treatment
  - The proportion of people whose cancer stopped growing or got smaller after receiving treatment
    - How long it took for people's cancer to stop growing or get smaller after receiving treatment
  - The number, severity, and type of side effects
    - A side effect is something that you feel was caused by the treatment you take
    - A side effect is considered "severe" when it limits daily activities, is disabling, could result in hospitalization, is potentially life threatening or may require urgent medical intervention
    - A side effect is considered "serious" when it is life threatening, requires hospital care or causes lasting problems for a patient

STUDY DETAILS

Who took part in the study?



What were the results of the study?

How well did the treatments work?

- After an average of 14.2 months of follow-up (in the maintenance part of the study), people who had received **tislelizumab plus chemotherapy** at induction lived longer without their cancer getting worse versus people who received **placebo plus chemotherapy**
  - Follow-up means seeing a health care provider regularly after treatment is done to check if the cancer has not come back

	Tislelizumab + chemotherapy	Placebo + chemotherapy
How long people lived after they started treatment	15.5 MONTHS	13.5 MONTHS
The proportion of people who were alive 1 year after treatment	62.7 %	58.4 %
The proportion of people who were alive 2 years after treatment	33.2 %	22.4 %
The proportion of people who were alive 3 years after treatment	25.0 %	9.3 %
How long people lived without their cancer getting worse after they started treatment	4.8 MONTHS	4.3 MONTHS

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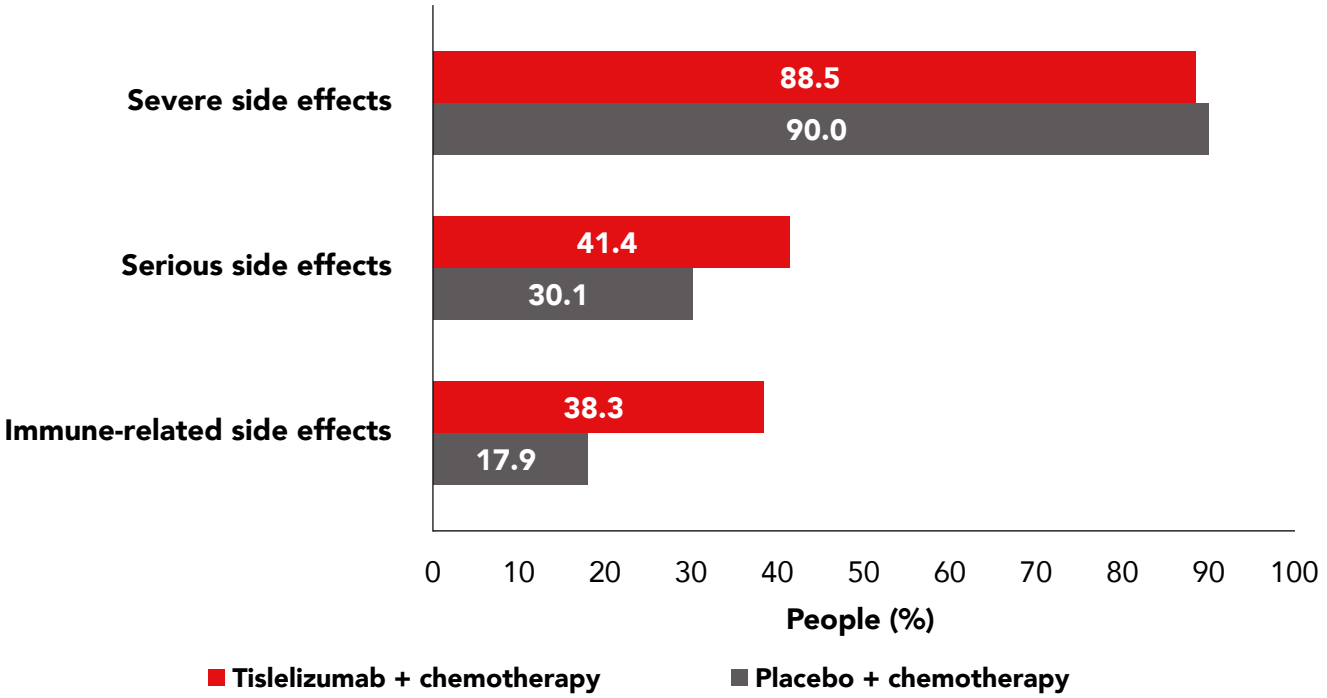
- A greater proportion of people who received **tislelizumab plus chemotherapy** had cancers that stopped growing or got smaller versus those that received **placebo plus chemotherapy**
  - The time period over which the cancers stopped growing or got smaller was longer in people who received tislelizumab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

	Tislelizumab + chemotherapy	**Placebo + chemotherapy**
The proportion of people whose cancer stopped growing or got smaller after receiving treatment	68.3 %	61.7 %
How long people's cancer stopped growing or got smaller after receiving treatment	4.3 MONTHS	3.7 MONTHS

What side effects did people have in the study?

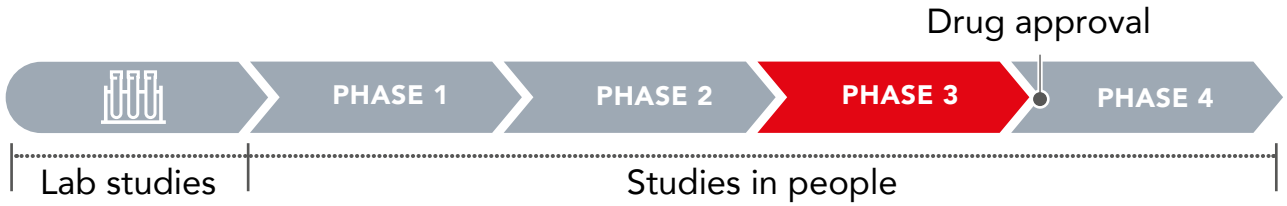
- The most common side effects in people who received **tislelizumab plus chemotherapy** or **placebo plus chemotherapy** were reductions in the numbers of different types of blood cells in their bloodstream



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, CMPP, and Camile S Grubor, 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 July 22, 2019, 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/NCT04005716

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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