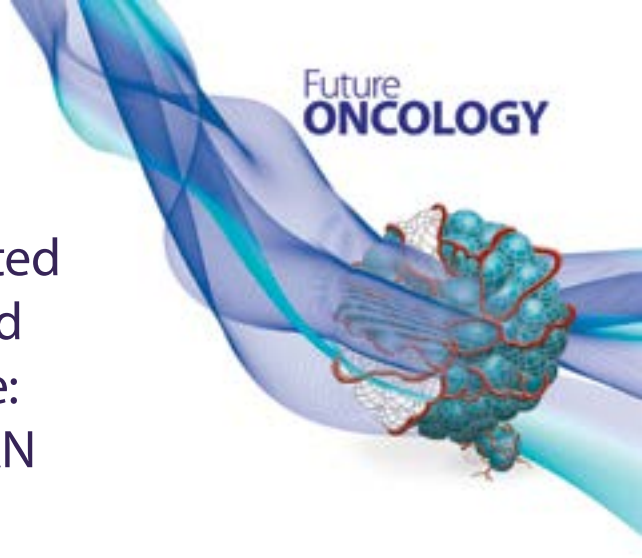
Plain Language Summary of Publication



Prostate-specific antigen and health-related quality of life in individuals with advanced prostate cancer treated with apalutamide: a plain language summary of the SPARTAN and TITAN studies

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Where can I find the original article on which this summary is based?

You can read the original article for a fee at: https://euoncology.europeanurology.com/article/S2588-9311(23)00280-8/fulltext ('**Post-hoc** analysis of rapid and deep prostate-specific antigen decline and patient-reported health-related quality of life in SPARTAN and TITAN patients with advanced prostate cancer').

Post hoc: An additional analysis that researchers perform after the main study is complete.

Summary

Castration-resistant means the cancer does not respond efficiently to treatments that lower the amount of testosterone in the body. In individuals with castration-resistant prostate cancer, lowering the amount of testosterone in the body does not effectively slow the growth of prostate cancer cells.

What is this sum
This is a summa TAN studies, which looked at whether a treatment called apalutamide can help treat individuals with advanced prostate cancer.

The SPARTAN study included 1207 participants with nonmetastatic castration-resistant prostate cancer (or nmCRPC). The TITAN study included 1052 participants with metastatic castration-sensitive prostate cancer (or mCSPC). Treatment with apalutamide w participants we een used for many y

ADT is part of the treatment plan for individuals with metastatic prostate cancer and for some individuals with nonmetastatic prostate cancer. ADT works by decreasing the amount of testosterone in the body.

The results showed that treatment with apalutamide plus ADT increased participants' ed the same, compared with sed the length of time that the tastasize) or did not continue to grow. In both studies, treatment with apalutamide plus ADT was associated with a deep decline in blood prostate-specific antigen (or PSA) levels (called a deep PSA decline).

Health-related quality of life consists of how an individual feels and how they function. It includes physical, social, emotional, and functional wellbeing.

How to say (download PDF and double click sound icon to play sound)...

- **Androgen deprivation therapy:** AN-droh-jen DEH-prih-VAY-shun THAYR-uh-pee
- **Apalutamide:** Ap-ah-LOO-tuh-mide
- **Castration:** kas-TRAY-shun
- **Metastatic:** meh-tuh-STA-tik
- **Placebo:** pluh-SEE-boh
- **Prostate-specific antigen:** PROS-tayt-speh-SIH-fik AN-tih-jen
- **Testosterone:** tes-TOS-teh-rone

Pronunciations are taken from the National Cancer Institute Dictionary of Cancer Terms available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/

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This additional analysis of the SPARTAN and TITAN studies was performed to understand whether the deep PSA decline in participants who received apalutamide plus ADT was linked to their overall health-related quality of life.

What were the results of the additional analysis?
In participants who received apalutamide plus ADT, those who achieved a deep PSA decline after the start of treatment had a greater chance that their health-related quality of life would remain stable. When participants achieved a deep PSA decline at 3 months after the start of treatment, the benefit to their health-related quality of life, including physical wellbeing, was even greater.

What do these results mean for individuals with advanced prostate cancer?
For individuals with advanced prostate cancer, it is important to monitor both PSA decline and any impacts on health-related quality of life. These results will help doctors and other healthcare professionals have a better understanding of patients' cancer experience and the impact of their treatment.

Who is this summary for?

This summary is intended for individuals with advanced prostate cancer and their family members or caregivers, patient advocates and healthcare professionals, including those who are trying to help individuals find the best treatment for advanced prostate cancer.

What is the purpose of this plain language summary?

The purpose of this plain language summary is to help you to understand the findings from recent research. The results of this study may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence not on the results of a single study.

Who sponsored the study?

The SPARTAN and TITAN studies were **sponsored** by Janssen Research & Development.

Sponsor: A company or organization that oversees and pays for a clinical research study. The sponsor also collects and analyzes the information that was generated during the study.

About prostate cancer

Prostate cancer is the result of abnormal cells in the prostate that grow and form tumors.

Participants in the SPARTAN study had nmCRPC and participants in the TITAN study had mCSPC.

ADT is part of the treatment plan for individuals with metastatic prostate cancer and for some individuals with nonmetastatic prostate cancer and is often used in combination with other treatments. ADT works by decreasing the amount of **testosterone** in the body. Decreasing the amount of testosterone in the body can slow the growth of prostate cancer cells.

Testosterone: A hormone (a chemical in the body that affects the function of specific cells, organs, and tissues) that can increase the growth of prostate cancer cells.

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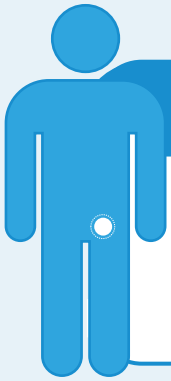
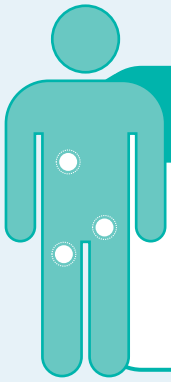


nmCRPC or nonmetastatic castration-sensitive prostate cancer in SPARTAN

Nonmetastatic means that the cancer has NOT spread to other parts of the body (besides **lymph nodes** in the pelvis)

Castration-resistant means the cancer does not respond efficiently to treatment with ADT. Therefore, even when the level of the hormone testosterone in the body is kept low with ADT, the prostate cancer cells keep growing



mCSPC or metastatic castration-sensitive prostate cancer in TITAN

Metastatic means that the prostate cancer has spread to other parts of the body

Castration-sensitive means that the cancer responds efficiently to treatment with ADT. Therefore, lowering the amount of the hormone testosterone in the body with ADT can slow the growth of prostate cancer cells

Lymph nodes: A part of the immune system located throughout the body, such as in the armpits and neck. Lymph nodes are also located in the pelvic area, which is close to the prostate.

What is health-related quality of life?

Health-related quality of life is how an individual feels and how they function on a day-today basis. It includes the individual's perception of physical, social, emotional and functional wellbeing. When cancer grows or spreads to other parts of the body, this can have a negative impact on an individual's health-related quality of life.

A variety of factors affect an individual's health-related quality of life. These include the ability to:

- Engage in desired activities, such as gardening, reading, walking the dog, taking a bath or shower
- Get in contact with family and friends and socialize with others
- Live independently

Health-related quality of life is also affected by an individual's experience of symptoms, such as pain and extreme tiredness, also known as fatigue.

The goals of treatment for individuals with advanced prostate cancer focus on increasing the length of survival while keeping the same health-related quality of life.

How is health-related quality of life studied?

An individual's health-related quality of life can be measured using specific questionnaires, sometimes called patient-reported outcome (PRO) questionnaires.

Different types of PRO questionnaires are used in studies of individuals with cancer and other diseases, including individuals with

prostate cancer. In the SPARTAN and TITAN studies, a PRO questionnaire called the Functional Assessment of Cancer Therapy-Prostate (or FACT-P) was used. The FACT-P questionnaire is specifically designed to study health-related quality of life in individuals with prostate cancer.

The FACT-P questionnaire allows individuals to report how they feel about their physical, social, emotional, and functional wellbeing.

Areas of health-related quality of life included in the FACT-P questionnaire

Physical wellbeing

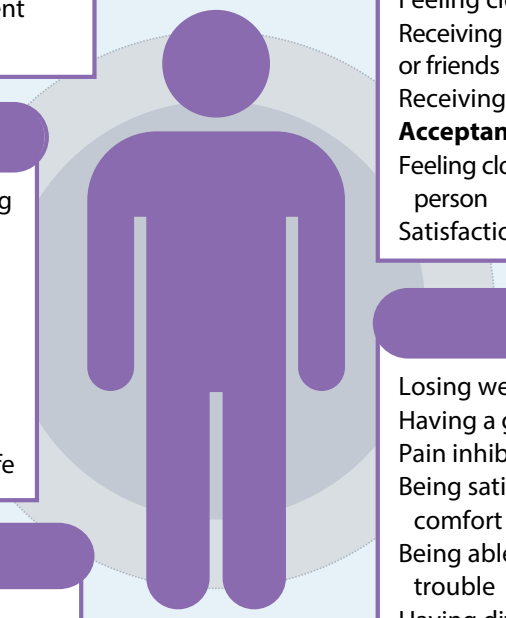
Not having energy
Having nausea
Not meeting needs of your family
Having pain
Feeling ill
Being bothered by side effects (unwanted or undesirable effects) of treatment
Spending time in bed

Functional wellbeing

Ability to work (including working from home)
Feeling that work is fulfilling
Enjoying life
Acceptance of illness (accepting medical condition)
Quality of sleep
Ability to experience joy
Feeling content with quality of life

Emotional wellbeing

Having feelings of sadness
Being satisfied with coping with illness
Losing hope in fight against illness
Feeling nervous
Worrying about dying
Worrying that condition will get worse



Social/Family wellbeing

Feeling close to friends
Receiving emotional support from family or friends
Receiving support from friends
Acceptance of illness by family
Feeling close to partner or main support person
Satisfaction with sex life

Additional concerns

Losing weight
Having a good appetite
Pain inhibits activities
Being satisfied with present level of comfort
Being able to move bowels without trouble
Having difficulty urinating
Difficulty urinating inhibits activities
Being able to have and maintain an erection

Acceptance of illness: Prostate cancer impacts patients and their families. Family members' acceptance of their loved one's illness is a gradual process during which people come to terms with their family members' illness and its impact on the both the patient and the family as a whole.

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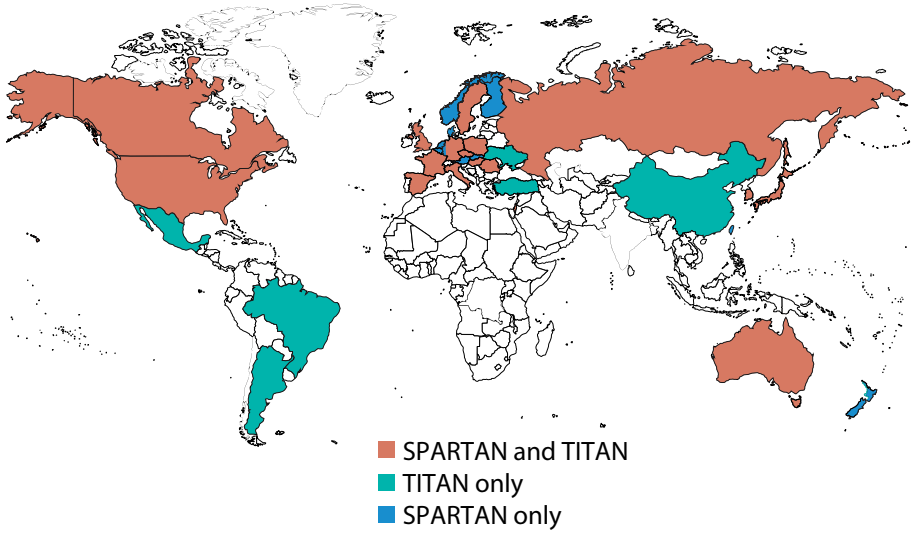
Participants in the SPARTAN and TITAN studies completed a FACT-P questionnaire to report how they were feeling about their health and overall quality of life. Participants filled in the questionnaire at the start of the study before receiving the first study treatment, at regular intervals according to each study schedule until the end of study treatment and then up to 1 year after **disease progression**. The information from the FACT-P questionnaires was collected directly from the study participants, not doctors' notes or diagnostic tests. This helped ensure that the information captured reflects the participants' unique and important point of view.

Disease progression: The cancer is growing or has spread to other parts of the body.

About the SPARTAN and TITAN studies

The SPARTAN and TITAN studies included participants from 32 countries:



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Norway
Poland
Romania
Russia
Slovakia
South Korea
Spain
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Taiwan
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United Kingdom
United States

The SPARTAN and TITAN studies included participants with advanced prostate cancer from 32 countries in North America, South America, Europe, Asia and Oceania.

In the SPARTAN study, participants had nmCRPC and in the TITAN study, participants had mCSPC.

Traditional tests for obtaining images of the inside of the body were used to confirm that the prostate cancer was nonmetastatic for the SPARTAN study, or metastatic for the TITAN study.

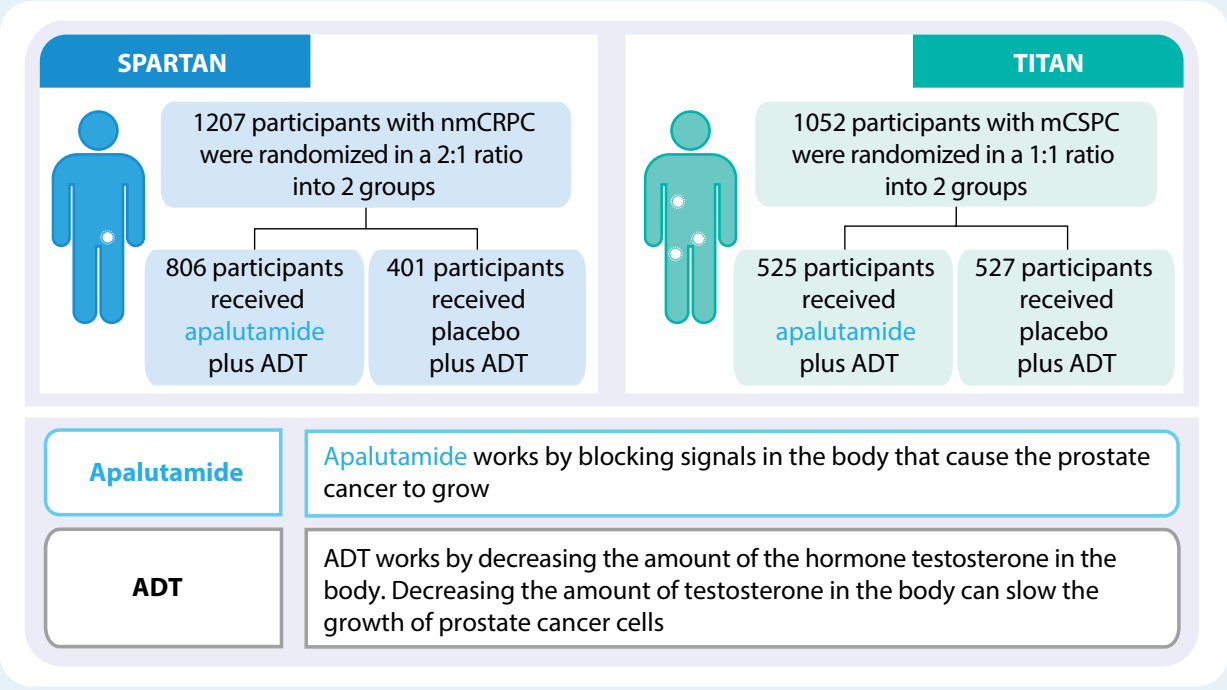
Traditional imaging tests	
Bone scan	A bone scan is a nuclear radiology procedure used to examine bones for bone diseases, including cancer
Computed tomography (CT) scan	A CT scan uses a series of x-rays to take detailed pictures of the inside of the body. An x-ray is a type of radiation used to make a digital image of the inside of the body
Magnetic resonance imaging (MRI)	An MRI uses radio waves and magnets to take detailed pictures of the inside of the body

Both SPARTAN and TITAN were placebo-controlled, double-anonymized double-blind, randomized studies

Placebo-controlled	A placebo looks exactly like the study drug but does not contain active medicine
Double-anonymized	Participants and doctors did not know which participants received apalutamide plus ADT or placebo plus ADT
Randomized	Participants were randomly selected to receive either apalutamide plus ADT or placebo plus ADT

The aim of the SPARTAN and TITAN studies was to find out whether combining apalutamide with ADT was more effective in treating individuals with advanced prostate cancer compared with placebo plus ADT.

Apalutamide plus ADT has been approved in the United States, Europe and other countries as a treatment for individuals with nmCRPC and mCSPC.



Participants in the SPARTAN and TITAN studies had their blood PSA levels measured throughout the study. High or increasing levels of PSA in the blood indicate that prostate cancer cells may be growing. PSA levels were measured before the start of study treatment and then again at 3 months and at 6 months of study treatment to identify participants whose PSA declined.
A PSA decline was defined as "deep" if:

- The blood PSA level decreased to 0.2 nanograms (ng) per milliliter (ml) or less.
- The blood PSA level decreased by at least 90% compared with the blood PSA level before the start of study treatment.

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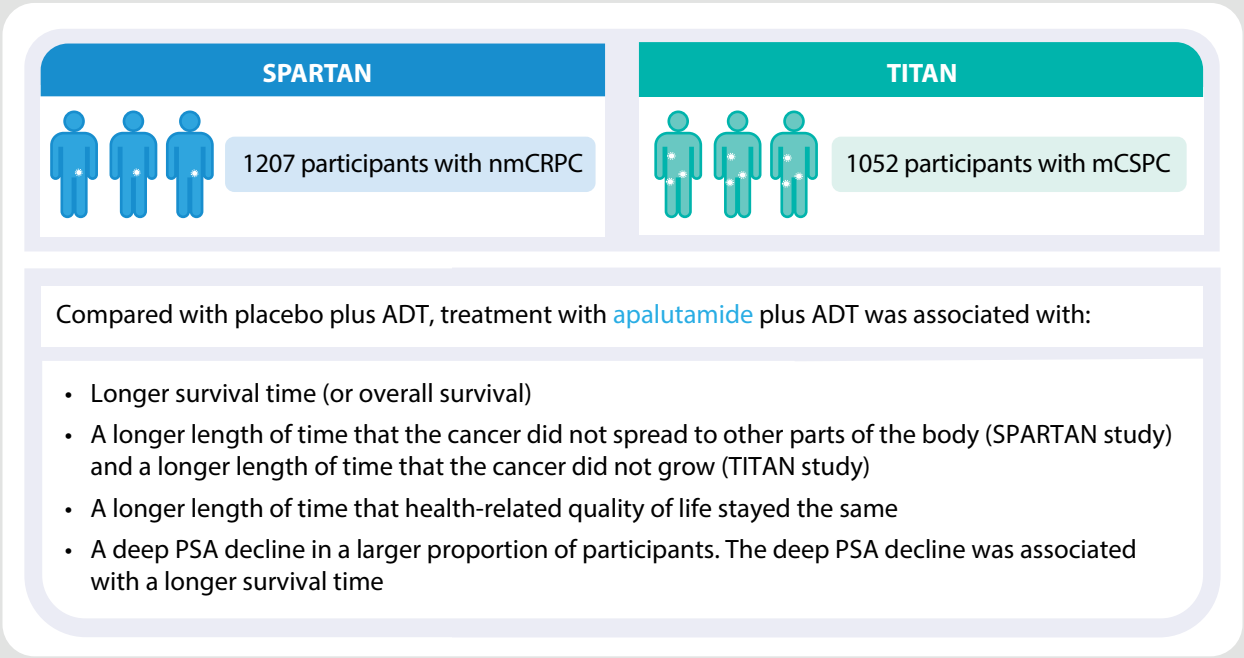
What were the main conclusions from the SPARTAN and TITAN studies?

The researchers found that treatment with apalutamide plus ADT was associated with improved outcomes in participants in both studies.



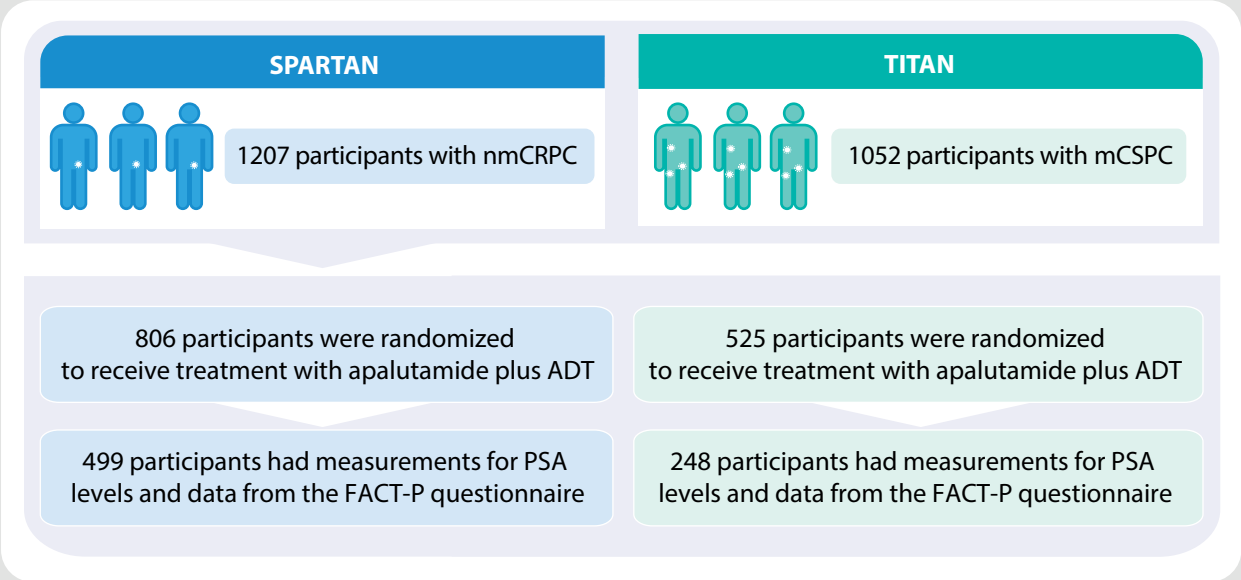
Health-related quality of life and PSA decline

In the additional (post hoc) analysis, researchers wanted to find out if the length of time that health-related quality of life stayed the same with apalutamide plus ADT was associated with a deep PSA decline or a rapid and deep PSA decline. A PSA decline was considered "deep" if the blood PSA level decreased to 0.2 ng/ml or less or by at least 90% compared with the blood PSA level before the start of study treatment. A PSA decline was considered rapid and deep if the deep PSA decline was achieved at 3 months of study treatment. A deep PSA decline achieved after 3 months of study treatment was not considered a rapid PSA decline.

In the SPARTAN and TITAN studies, a participant's PSA levels and information from their FACT-P questionnaire were collected before treatment started and then throughout treatment. The **median** duration of study treatment with apalutamide plus ADT was 32.0 months in the SPARTAN study and 39.3 months in the TITAN study.

Median: The middle number in a list of numbers organized from lowest to highest.

A total of 499 participants treated with apalutamide plus ADT from the SPARTAN study had measurements available for PSA levels and data from the FACT-P questionnaire. From the TITAN study, 248 participants treated with apalutamide plus ADT had measurements available for PSA levels and data from the FACT-P questionnaire.

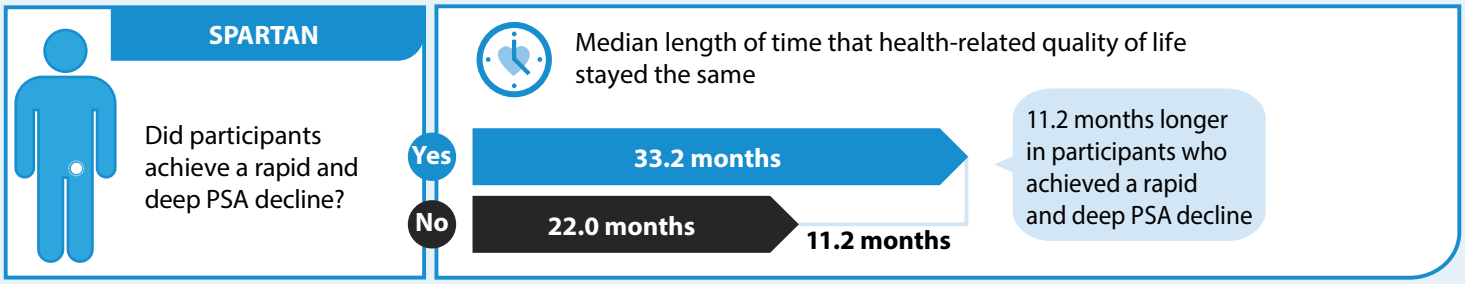


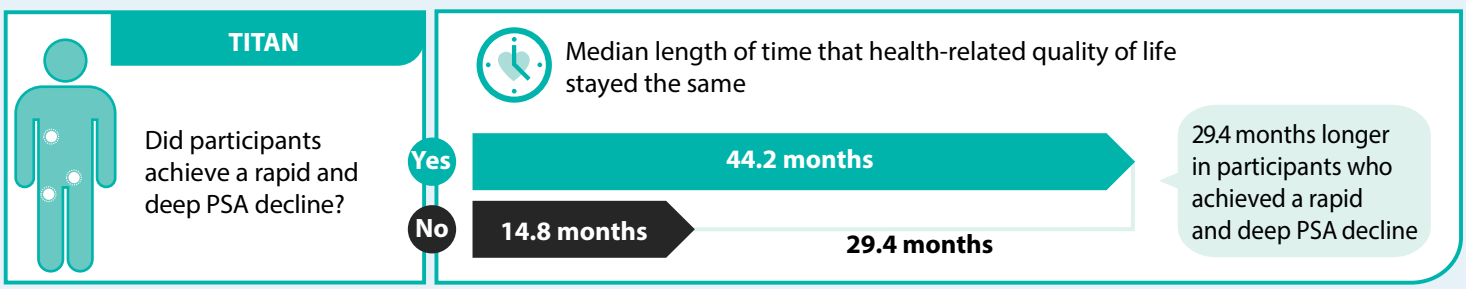
The researchers then compared results from the FACT-P questionnaires between participants who achieved a deep PSA decline and those who did not.

What were the main conclusions from the additional analysis?

The researchers found that, for participants who received apalutamide plus ADT, health-related quality of life was more likely to stay the same when there was a rapid and deep PSA decline compared to patients in whom there was no rapid and deep PSA decline. The median length of time that health-related quality of life stayed the same was greatest among participants treated with apalutamide plus ADT who achieved a rapid and deep PSA decline.

Rapid and deep PSA decline was defined as a PSA level of 0.2 ng/ml or less at 3 months of study treatment.





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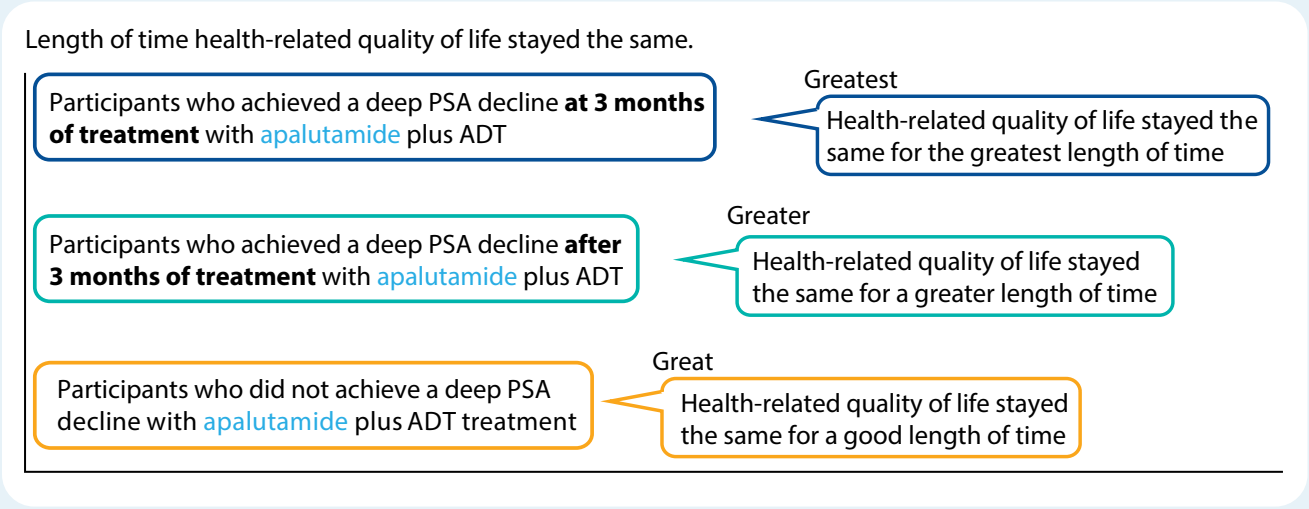
The researchers then used another type of analysis (called Kaplan-Meier) to confirm these findings. The researchers confirmed that in both the SPARTAN and TITAN studies, health-related quality of life stayed the same for the greatest length of time among participants who achieved a rapid and deep PSA decline with apalutamide plus ADT.



What do these results mean?

The results showed that health-related quality of life stayed the same for the greatest length of time among participants who achieved a rapid and deep PSA decline.

This means that for individuals with advanced prostate cancer, it is important to monitor the impacts of treatment on both PSA decline and health-related quality of life.

This will help doctors and other healthcare professionals have a better understanding of patients' response to treatment.

Where can readers find more information about the SPARTAN and TITAN studies?

The SPARTAN study start date was 14 October 2013, and the primary completion date was 19 May 2017. The TITAN study start date was 27 November 2015, and the primary completion date was 7 September 2020. The publication discussed in this summary is titled 'Post-hoc analysis of rapid and deep prostate-specific antigen decline and patient-reported health-related quality of life in SPARTAN and TITAN patients with advanced prostate cancer'. This publication is available to read for a fee at: https://euoncology.europeanurology.com/article/S2588-9311(23)00280-8/fulltext.

Small, et al. 'Post-hoc analysis of rapid and deep prostate-specific antigen decline and patient-reported health-related quality of life in SPARTAN and TITAN patients with advanced prostate cancer.' *Eur. Urol. Oncol.* 2024;7(4):844-852.

You can read more about the SPARTAN and TITAN studies on the following websites:

- Enter the study number NCT01946204 (SPARTAN) or NCT02489318 (TITAN) into the "Other terms" search field at: https://clinicaltrials.gov/

- Enter the EudraCT identifier 2012-004322-24 (SPARTAN) or 2015-000735-32 (TITAN) into the search field at: https://www.clinicaltrialsregister.eu. Click "Home & Search" to find the search option.

If you were a study participant and have questions about the results of this study and apalutamide, please speak with the doctor or staff at your study site.

Educational resources

- Read more about prostate cancer on the Prostate Cancer Foundation website at: https://www.pcf.org/guide/prostate-cancer-patient-guide/.
- Most countries throughout the world have dedicated national prostate cancer agencies and foundations. These organizations provide explanations, treatment options, educational resources, support for people interested in maintaining prostate health and assistance for those who have received a prostate cancer diagnosis. Ask your doctors and nurses or community support group to direct you to these organizations.

Acknowledgments

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Competing interests disclosure

LI Karsh reports serving as a speaker for AstraZeneca, Astellas, Bayer, Janssen, Merck and Pfizer. The authors have no other competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript apart from those disclosed.

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