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Plain Language Summary of Publication

Enzalutamide in metastatic hormone-sensitive prostate cancer: A plain language summary of the ARCHES and ENZAMET follow-up studies

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

You can read the ARCHES follow-up study in the *Journal of Clinical Oncology*. This article is available for free.

- The article was published in 2022 and is called 'Improved survival with enzalutamide in patients with metastatic hormone-sensitive prostate cancer'. It can be read at: https://ascopubs.org/doi/full/10.1200/JCO.22.00193

You can read the ENZAMET follow-up study in *The Lancet Oncology*. There is a fee to read this article.

- The article was published in 2023 and is called 'Testosterone suppression plus enzalutamide versus testosterone suppression plus standard antiandrogen therapy for metastatic hormone-sensitive prostate cancer (ENZAMET): an international, open-label, randomised, phase 3 trial'. It can be read at: https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(23)00063-3

Summary

What is this summary about?

This summary includes information from the ARCHES and ENZAMET **follow-up studies**. Both studies looked at enzalutamide treatment for people with metastatic hormone-sensitive prostate cancer (known as mHSPC). In ARCHES, researchers compared the medications enzalutamide + androgen deprivation therapy (known as ADT) with **placebo** + ADT. In ENZAMET, researchers compared enzalutamide + ADT with **standard treatment** + ADT. Some people in ENZAMET also took enzalutamide with docetaxel (a **chemotherapy** treatment). In both studies, researchers wanted to find out if enzalutamide helps people with mHSPC live longer.

How to say (double click sound icon to play sound)...

- **Androgen:** AN-droh-jen
- **Antigen:** AN-tih-jen
- **Docetaxel:** doe-se-TAKS-el
- **Enzalutamide:** EN-zuh-LOO-tuh-mide
- **Hormone:** HOR-mown
- **Metastatic:** meh-tuh-STA-tik
- **Nonsteroidal:** NON-steh-ROY-dul
- **Placebo:** pluh-SEE-boe
- **Prostate** PROH-stayt

Follow-up study: Follows each patient group for longer, after the initial report.
Placebo: Something that looks like the treatment being studied but doesn't contain any medicine. It is used to help find out if the results are because of the study treatment or another factor.
Standard treatment: A treatment that is already approved and used in this setting.
Chemotherapy: A type of medical treatment designed to kill cancer cells.

What are the key takeaways?

In both studies, researchers found that people with mHSPC who took enzalutamide lived longer than people who did not. People who took enzalutamide also lived longer without their cancer getting worse. The results were mostly similar in groups of people dependingon when and where their cancer was found. Researchers did not find any new safety concerns.

What were the main conclusions?

People with mHSPC may benefit from long-term treatment with enzalutamide + ADT. They may also benefit from taking enzalutamide with other treatments, like docetaxel. It may be better for people with mHSPC to have enzalutamide treatment before their cancer gets worse, rather than waiting. These people and their doctors should carefully consider the benefits and risks of each treatment to make a joint decision for treating mHSPC.

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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.

Enzalutamide is used to treat the condition that is discussed in this summary. Approval varies by country. Please check with your local provider for more details.

The results of these studies may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence.

Who is this plain language summary for?

This plain language summary is for anyone interested in finding out more about how enzalutamide treatment affects people with metastatic hormone-sensitive prostate cancer.

Who sponsored these studies?

ARCHES was **sponsored** by Astellas Pharma Inc. and Pfizer Inc., the developers of enzalutamide.

ENZAMET was an academic study led by the Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP), sponsored by the University of Sydney. The study drug and financial support were provided by Astellas Pharma Inc.

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.

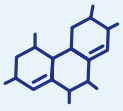
What is metastatic hormone-sensitive prostate cancer?

Everyone in these studies had **metastatic** **hormone-sensitive** **prostate cancer**, known as **mHSPC**.

Metastatic

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

Hormone-sensitive



Most prostate cancers need male sex hormones to grow. Hormones are chemical messengers in the body. Male sex hormones are called androgens. People can have surgery or take medicines to lower androgen levels. This is known as androgen deprivation therapy (ADT).

For most people with prostate cancer, ADT will stop or slow down the growth of prostate cancer cells. This is known as **hormone-sensitive** prostate cancer.

Prostate cancer

The **prostate** is a part of the body that helps make semen. It is in the pelvis, between the penis and the bladder.
Semen is the fluid that contains sperm.

Cancer is a disease where abnormal cells grow to form a tumor.

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What treatments did this study look at?

Androgen deprivation therapy (ADT)

- ADT is when people take medicines to lower androgen levels or have surgery to remove the testicles. This may stop or slow down prostate cancer growth.

Standard anti-androgen medication

- Standard anti-androgens can stop androgens from reaching prostate cancer cells. This may stop or slow down prostate cancer growth.
- Standard anti-androgens are also known as first-generation nonsteroidal anti-androgens.
- Examples of standard anti-androgens are bicalutamide, nilutamide, and flutamide. These are taken as a pill.

Enzalutamide

- Enzalutamide can stop androgens from reaching prostate cancer cells. This may stop or slow down prostate cancer growth.
- Enzalutamide is a newer type of hormonal treatment for prostate cancer than ADT or standard anti-androgens.
- Enzalutamide is taken as a tablet or capsule.

Docetaxel

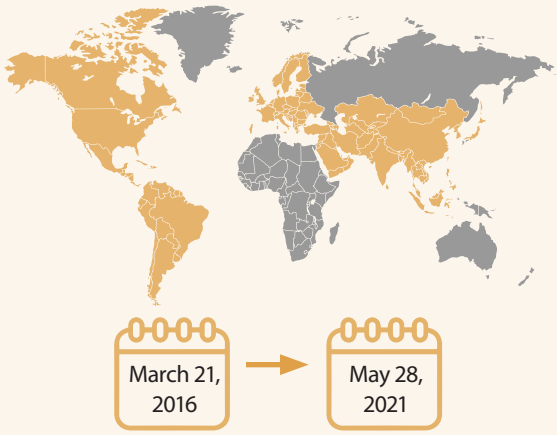
- Docetaxel can destroy cancer cells or slow cancer cell growth.
- Docetaxel is a type of chemotherapy.
- Docetaxel is given as a drip into the bloodstream (intravenously).

Placebo

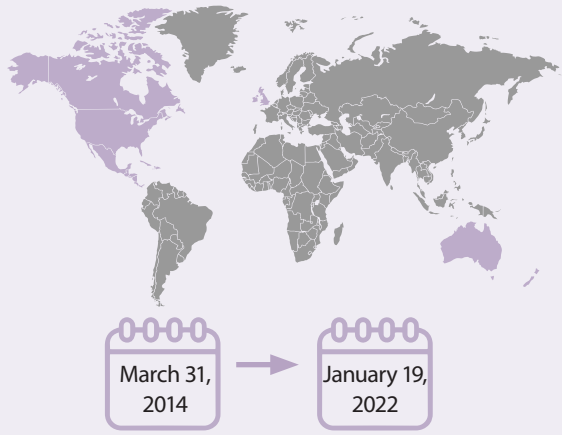
- A placebo is used in clinical studies to help find out if the results are because of the study treatment or another factor.
- The placebo looked like enzalutamide, but did not have any medicine in it.

Where and when did the studies take place?

The **ARCHES** study took place across 202 centers in North America, Latin America, Europe, and Asia. The follow-up study looked at information collected between March 21, 2016 and May 28, 2021.



The **ENZAMET** study took place across 83 centers in North America, Australia, New Zealand, Ireland, and the United Kingdom. The follow-up study looked at information collected between March 31, 2014 and January 19, 2022.



What did the ARCHES and ENZAMET studies look at?

In **ARCHES**, people with metastatic hormone-sensitive prostate cancer (known as mHSPC) took either enzalutamide + ADT or placebo + ADT.

People were put randomly into 2 groups. This means the group in which they were placed was decided by chance, like tossing a coin. This process ensures that each treatment group had similar numbers of people who:

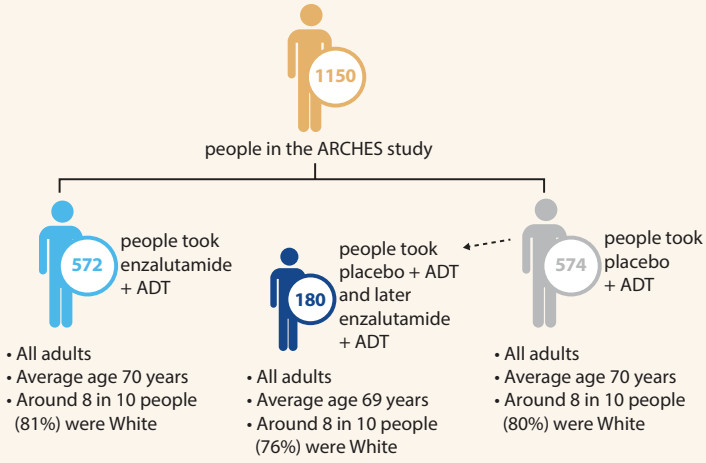
- Had smaller or bigger amounts of cancer that had spread in the body
- Previously had docetaxel treatment

The first part of the **ARCHES** study was blinded.

- Blinded means that researchers and people taking part did not know who took enzalutamide and who took placebo.

The second part of the **ARCHES** study was unblinded.

- If appropriate, people who first took placebo could then take enzalutamide instead.



In the ARCHES follow-up study, researchers wanted to find out:

- Does enzalutamide help people live longer overall?

Researchers also looked at:

- Does enzalutamide help people live longer without their cancer getting worse?
- Does enzalutamide give people more time before they need another cancer treatment?
- What are the results in different groups based on age, where they live, and when and where the cancer was found?
- What **side effects** did people in the study have?

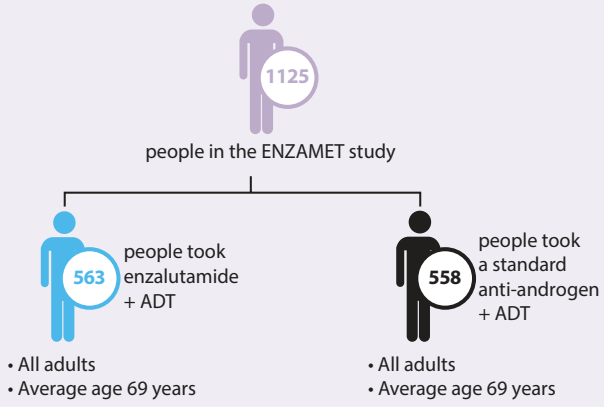
In **ENZAMET**, people with mHSPC took either enzalutamide + ADT or a standard anti-androgen + ADT.

People were put randomly into 2 groups. This process ensures that each treatment group had similar numbers of people who:

- Had smaller or bigger amounts of cancer that had spread in the body
- Planned with their doctor to have docetaxel treatment for their prostate cancer as well as the study treatment
- Planned with their doctor to have treatment to strengthen bones
- Had other health conditions
- Were at each study center

The **ENZAMET** study was not blinded.

- This means that researchers and people taking part knew which treatment the people received.



In the ENZAMET follow-up study, researchers wanted to find out:

- Does enzalutamide help people live longer overall?

Researchers also looked at:

- Does enzalutamide help people live longer without their cancer getting worse?
- What are the results in different groups based on when and where the cancer was found?
- Does it make a difference if people also have docetaxel treatment?
- What **side effects** did people in the study have?

Side effect: Something unexpected and unwanted that happens to someone in a study. It is not necessarily caused by the treatment that they take.

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What were the main differences between the designs of the ARCHES and ENZAMET studies?

The **ARCHES** study was blinded.
People in **ARCHES** took either enzalutamide or placebo.
People in **ARCHES** could not have treatment with docetaxel while receiving enzalutamide.

The **ENZAMET** study was not blinded.
People in **ENZAMET** took either enzalutamide or a standard anti-androgen.
People in **ENZAMET** could have additional treatment with docetaxel while receiving enzalutamide.

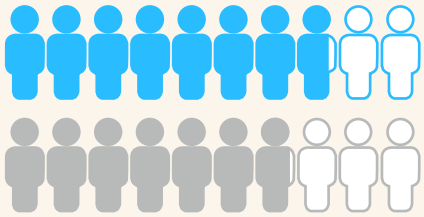
The **ARCHES** and **ENZAMET** studies used slightly different ways to measure if prostate cancer was getting worse.

What were the main results?

Enzalutamide + ADT helped people with mHSPC live longer

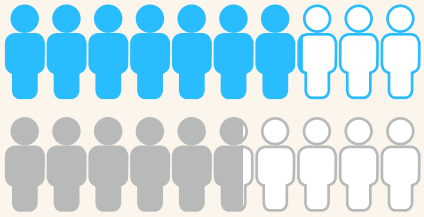
After 3 years in the **ARCHES** study:

- 78% of people who took enzalutamide + ADT were alive
- 69% of people who took placebo + ADT were alive



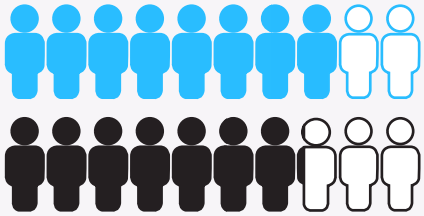
After 4 years in the **ARCHES** study:

- 71% of people who took enzalutamide + ADT were alive
- 57% of people who took placebo + ADT were alive



After 3 years in the **ENZAMET** study:

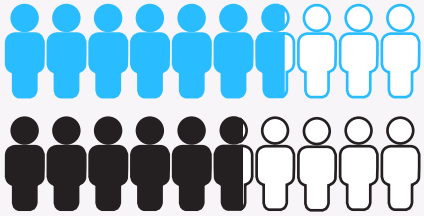
- 80% of people who took enzalutamide + ADT were alive
- 72% of people who took standard anti-androgen + ADT were alive



These data are from an earlier ENZAMET publication.

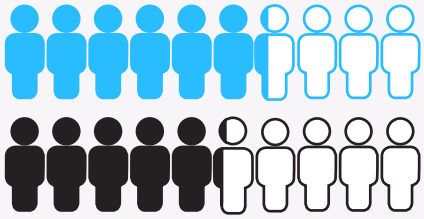
After 5 years in the **ENZAMET** study:

- 67% of people who took enzalutamide + ADT were alive
- 57% of people who took standard anti-androgen + ADT were alive



This stage of the **ENZAMET** follow-up study lasted for 7 years and 10 months. At this time:

- 63% of people who took enzalutamide + ADT were alive
- 52% of people who took a standard anti-androgen + ADT were alive



People in the **ENZAMET** study continue to be followed up. Researchers plan to publish more data in the future.

Enzalutamide + ADT helped people with mHSPC live longer without their cancer getting worse

In **ARCHES**, researchers used **CT** or bone scans to look at the spread of cancer. They found that, at 2½ years into the study:

86% of people who took enzalutamide + ADT did not have cancer that had grown or spread to additional parts of the body.

67% of people who took placebo + ADT did not have cancer that had grown or spread to additional parts of the body.

These data are from an earlier ARCHES publication.

At 5 years into the **ARCHES** study, researchers found that:

80% of people who took enzalutamide + ADT did not have **PSA progression**.

55% of people who took placebo + ADT did not have PSA progression.

In **ENZAMET**, researchers used **CT** or bone scans to look at the spread of cancer. They found that, at 5 years into the study:

56% of people who took enzalutamide + ADT did not have cancer that had grown or spread to additional parts of the body.

28% of people who took a standa rd anti-androgen + ADT did not have cancer that had grown or spread to additional parts of the body.

At 5 years into the **ENZAMET** study, researchers found that:

54% of people who took enzalutamide + ADT did not have **PSA progression**.

25% of people who took a standa rd anti-androgen + ADT did not have PSA progression.

CT scan: A scan that gives detailed information about the interior of the body.
Prostate-specific antigen (PSA): A protein made by normal prostate cells. Prostate cancer cells that are growing can lead to more PSA in the blood. When blood tests show that someone's PSA level is rising quickly, this is known as **PSA progression**. This may mean that a person's prostate cancer is getting worse.

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Enzalutamide + ADT benefited different groups of people with mHSPC

In **ARCHES**, researchers found that people whose cancer had spread to their **soft tissue** only, **lymph nodes** only, or **organs** were less likely to benefit from enzalutamide. However, the numbers of people in these groups were very small.

Researchers did not find that enzalutamide worked differently for people based on their age or where they lived.

Researchers found that enzalutamide benefited people in **ENZAMET** regardless of when and where the cancer was found.

Soft tissue: Parts of the body that are not bones.

Lymph nodes: Part of the body's immune system.

Organ: Part of the body that carries out a particular function. Examples of organs are liver, lungs, and kidneys.

Enzalutamide + ADT benefited people with mHSPC regardless of docetaxel treatment

Researchers found that enzalutamide benefited people in **ARCHES** regardless of whether they previously had docetaxel treatment. However, people were not treated with docetaxel during the study.

Researchers found that enzalutamide benefited people in **ENZAMET** if they were treated with docetaxel or if they were not treated with docetaxel during the study.

Enzalutamide + ADT gave people with mHSPC more time before they needed another cancer treatment

People who took enzalutamide + ADT were **62% less likely** to need another cancer treatment during the study compared with people who took placebo + ADT.

In **ENZAMET**, researchers did not look at how long it took for people to need another cancer treatment.

Researchers did not find any unexpected side effects for enzalutamide + ADT

	ARCHES 2019 results These data are from an earlier ARCHES publication		ARCHES follow-up results		ENZAMET 2019 results These data are from an earlier ENZAMET publication		ENZAMET follow-up results	
	The adverse events reported below use definitions from the Medical Dictionary for Regulatory Activities, version 21.0, except for hot flush and nausea		The adverse events reported below use definitions from the Medical Dictionary for Regulatory Activities, version 23.0, except for hot flush and nausea				The adverse events reported below have not been adjusted for how long people took each treatment for	
	Enzalutamide + ADT	Placebo + ADT	Enzalutamide + ADT	Placebo + ADT	Enzalutamide + ADT	Standard anti-androgen + ADT	Enzalutamide + ADT	Standard anti-androgen + ADT
Broken bones (fractures)	1 in 10 people (7%)	Less than 1 in 10 people (4%)	1 in 10 people (14%)	1 in 10 people (5%)	Less than 1 in 10 people (4%)	Less than 1 in 10 people (2%)	1 in 10 people (8%)	Less than 1 in 10 people (3%)
Falls	Less than 1 in 10 people (4%)	Less than 1 in 10 people (3%)	1 in 10 people (10%)	Less than 1 in 10 people (3%)	1 in 10 people (10%)	Less than 1 in 10 people (4%)	2 in 10 people (16%)	1 in 10 people (5%)
Feeling sick (nausea)	1 in 10 people (7%)	1 in 10 people (5%)	1 in 10 people (6%) Only includes people who felt sick because of the study medicines, not for other reasons	Less than 1 in 10 people (3%)	2 in 10 people (24%)	1 in 10 people (15%)	3 in 10 people (26%)	2 in 10 people (16%)
Fitting (seizures)	Less than 1 in 10 people (less than 1%)	Less than 1 in 10 people (less than 1%)	Less than 1 in 10 people (less than 1%)	Less than 1 in 10 people (less than 1%)	Less than 1 in 10 people (1%)	No one (0%)	Less than 1 in 10 people (1%)	No one (0%)
Heart problems (cardiac disorders)	Less than 1 in 10 people (2%) Only includes **ischemic heart disease**	Less than 1 in 10 people (1%)	Less than 1 in 10 people (5%) Only includes **ischemic heart disease**	Less than 1 in 10 people (2%)	2 in 10 people (20%)	1 in 10 people (14%)	2 in 10 people (22%)	1 in 10 people (13%)
High blood pressure (hypertension)	1 in 10 people (9%)	1 in 10 people (6%)	1 in 10 people (14%)	1 in 10 people (7%)	2 in 10 people (21%)	1 in 10 people (13%)	3 in 10 people (26%)	2 in 10 people (15%)
Hot flush	3 in 10 people (27%)	2 in 10 people (22%)	3 in 10 people (30%)	2 in 10 people (23%)	7 in 10 people (68%)	6 in 10 people (62%)	7 in 10 people (70%)	6 in 10 people (64%)
Problems with memory (memory impairment)	Less than 1 in 10 people (5%)	Less than 1 in 10 people (2%)	1 in 10 people (7%)	Less than 1 in 10 people (3%)	1 in 10 people (11%)	Less than 1 in 10 people (4%)	1 in 10 people (13%)	1 in 10 people (5%)
Tiredness (fatigue)	2 in 10 people (24%)	2 in 10 people (20%)	3 in 10 people (32%)	2 in 10 people (21%)	8 in 10 people (83%)	7 in 10 people (65%)	9 in 10 people (85%)	7 in 10 people (68%)

There were more adverse events in follow-up than in the 2019 results because these events naturally add up over time.

Ischemic heart disease: The heart is not getting enough blood and oxygen.

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Nobody in the **ARCHES** or **ENZAMET** studies died because of enzalutamide.

Researchers thought these **adverse events** were the most interesting. People also had other adverse events.

Researchers did not find any unexpected safety concerns for enzalutamide + ADT.

You can find more details on safety concerns and side effects in other articles listed in the 'Where can I find more information?' section.

Adverse event: Something unexpected and unwanted that happens to someone in a study. It is not necessarily caused by the treatment that they take.

What were the researchers' main conclusions?

In **ARCHES**, researchers compared enzalutamide + ADT with placebo + ADT in people with mHSPC. In **ENZAMET**, researchers compared enzalutamide + ADT with a standard anti-androgen + ADT in people with mHSPC.

In both studies, researchers found that:

- People who took enzalutamide lived longer

Researchers also found that:

- People who took enzalutamide lived longer without their cancer getting worse
- The results were mostly similar in groups of people depending on when and where their cancer was found
- There were no new safety concerns

What does this mean for people with metastatic hormone-sensitive prostate cancer?

People with mHSPC may benefit from:

- Long-term treatment with enzalutamide + ADT
- Taking enzalutamide with other treatments, like docetaxel
- Having enzalutamide treatment before their cancer gets worse, rather than waiting

These people and their doctors should make a joint decision when choosing treatments for mHSPC. They should carefully consider the benefits and risks of each treatment.

Where can I find more information?

This publication summarizes information from the **ARCHES** follow-up study: Armstrong AJ, Azad AA, Iguchi T, et al. *Journal of Clinical Oncology* 2022;40(15):1616–1622.

- You can read the original article for free at: https://ascopubs.org/doi/full/10.1200/JCO.22.00193

This publication summarizes information from the **ENZAMET** follow-up study: Sweeney CJ, Martin AJ, Stockler MR, et al. *The Lancet Oncology* 2023;24(4):323–334.

- There is a fee to read this article. You can find the original article at: https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(23)00063-3
- Request this article for free from the authors: https://www.researchgate.net/publication/369696560

The **ARCHES** study began in March 2016. This study is ongoing. For more information on the **ARCHES** study:

- ARCHES primary study: https://ascopubs.org/doi/10.1200/JCO.19.00799
- Clinicaltrials.gov: https://clinicaltrials.gov/study/NCT02677896

The **ENZAMET** study began in March 2014. This study is ongoing. For more information on the **ENZAMET** study:

- Find out about quality of life for people in the ENZAMET study: https://ascopubs.org/doi/10.1200/JCO.21.00941
- ENZAMET interim (ongoing) study: https://www.nejm.org/doi/full/10.1056/nejmoa1903835
- ANZUP summary: https://anzup.org.au/clinical-trial/enzamet-trial/
- Clinicaltrials.gov: https://clinicaltrials.gov/study/NCT02446405

For more information on clinical studies in general:

- https://www.clinicaltrials.gov/ct2/about-studies/learn
- http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/what-clinical-trials-are

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Declaration of interests

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