

# Immuno-Oncology Therapies to Treat Lung Cancer

What you need to know






## Introduction:

**Immuno-oncology** represents an innovative approach to cancer research that seeks to harness the body's own **immune system** to fight tumour cells. Today, we are at the forefront of this science as several new therapies hold promise for patients impacted by numerous types of cancer, and may have the potential to improve survival rates in a number of tumour types<sup>1</sup>.

Recent trials<sup>2,3</sup>, have resulted in positive data in a number of tumour types, and have also demonstrated that the safety profile is different compared to other treatments, and that side effects are manageable.

It is important therefore that patients impacted by cancer seek out, in partnership with their healthcare team, all options available to them, including **immuno-**



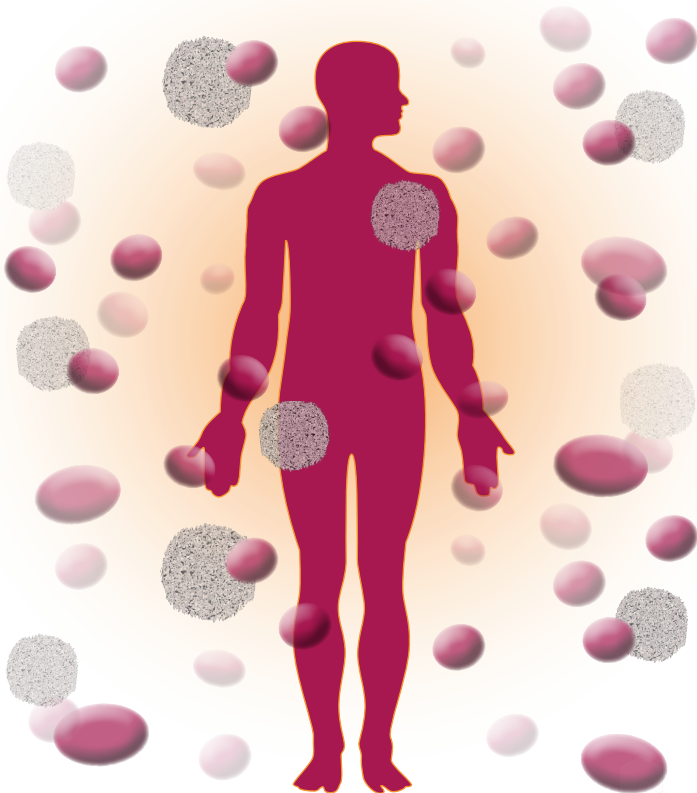
**oncology** therapies, to determine which treatment will work best against their cancer.

This resource has been designed to provide an overview of the **immune system** and **immuno-oncology** therapies, including how they work, and how they can potentially meet the needs of patients battling lung cancer.

<sup>1</sup><http://www.bms.com/careers/immuno-oncology-opportunities/Pages/default.asp>

<sup>2</sup>Longest follow-up of largest number of melanoma patients treated with ipilimumab shows some survive up to ten years. European Cancer Congress. 2013

<sup>3</sup>Additional Survival Data on Nivolumab, an Investigational PD-1 Immune Checkpoint Inhibitor, from Lung Cancer Cohort of a Phase 1 Study Presented at 15th World Conference on Lung Cancer - See more at: <http://news.bms.com/press-release/rd-news/additional-survival-data-nivolumab-investigational-pd-1-immune-checkpoint-inhi#sthash.X6mopghL.dpuf>

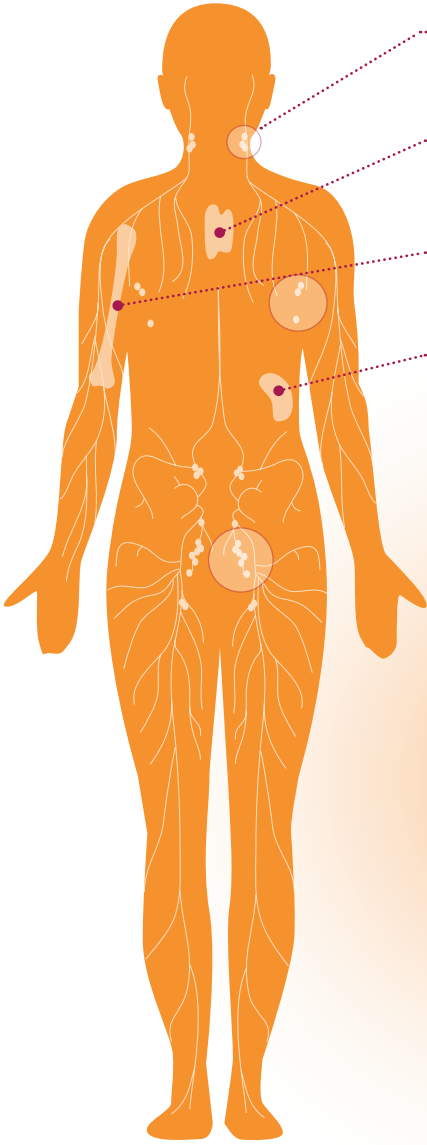




# The Immune System:

To be immune means to be protected, and the system that helps the body fight off sickness is called the **immune system**. The **immune system** is the body's natural defence system against viruses, bacteria, germs and other micro-organisms that can cause disease (known as pathogens). The **immune system** can also recognise a tumour as foreign, and help fight cancer by identifying and destroying tumour cells, just as it detects foreign particles that enter the body and cause harm. The **immune system** is made up of a network of cells, tissues and organs that work together to protect the body.

When the **immune system** detects a pathogen, it activates a process of creating cells that work to destroy the invading disease. White blood cells, also known as leukocytes or **B-cells** and **T-cells**, are part of this defence system. **T-cells** are found in many places in your body, including your **spleen**, your **thymus** gland and your **bone marrow**. Additionally, **T-cells** can be found in your **lymphatic system**. You've encountered your **lymphatic system** if you've ever had swollen glands on the sides of your neck, like when you have a sore throat. Although we often refer to them as "glands", they are actually **lymph nodes** and they produce and store **T-cells**. Normally, **lymph nodes** are small and round and you don't notice them, but when they're swollen, it means your **immune system** is at work.



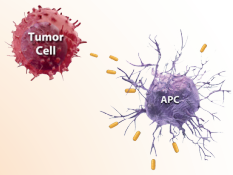
**Lymph nodes:**  
Produce and store T-cells

**Thymus:**  
Where T-cells mature

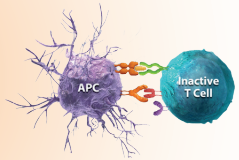
**Bone marrow:**  
Produces white blood cells

**Spleen:**  
Largest lymphatic organ  
containing white blood cells

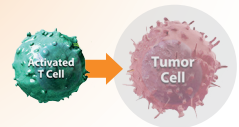
**Antigen-presenting cells (APCs)** detect bacteria, virus, pathogen or other illness



**T-cells, powerful white blood cells, are produced**







**T-cells eliminate or neutralise disease-causing cell or infectious agent**





# How Does the Immune System Work?<sup>4</sup>

We have a special team  inside our bodies that protects  us from disease.

This team  is our **immune system**.

 It's a team with many players, each one with a specific role. **B-cells**  make immunoglobulins,  or **antibodies**, which act as a barrier  against any kind of disease.



They kill germs, such as viruses and bacteria  that get into our bodies and make us sick .

The IgM  is the first immunoglobulin to rush  to our aid.

Its job is to protect  our blood and other parts of our body. Another team

member  is the **T-cell**. There are 3

kinds of **T-cells**:

First, is the Killer **T-cell** , which attacks and kills the infected cells .

Second, is the Helper **T-cell**,

which calls in more Killer

**T-cells** to kill germs .



Third, is the Regulator **T-cell**,  which tells the

**B-cells** and other **T-cells** when the body is better

and they can stop making **antibodies** .

<sup>4</sup><http://www.iocomunico.it/chiedilo%20a%20francesca/sistema%20immunitario.htm>





# Cancer and the Immune System

Cancer cells and normal cells have very few differences, so the **immune system** may not always recognise cancer cells as foreign. If cells become cancerous, they start to divide uncontrollably and don't die when they should. Over time, tumours can develop, which have the ability to adapt and avoid destruction by the **immune system**. This process of adapting and avoiding the **immune system's** defence mechanisms is called **immune evasion**, and leads to continued tumour growth, allowing cancer to continue to spread.

The **immune system** may not see cancer cells as foreign because cancer cells are not different enough from normal cells. Sometimes the **immune system** recognises the cancer cells, but the response may not be strong enough to destroy them.

To overcome this, researchers have designed ways to help the **immune system** recognise cancer cells as foreign and strengthen its response, so that it can destroy them.



# What is Immuno-Oncology and Why is it Important?

**Immuno-oncology** is a type of cancer treatment that seeks to use the body's natural defence – the **immune system** – against a range of cancers. **Immuno-oncology** treatment falls under a broader category of medicines used to treat many types of illness called **immunotherapies**, which activate the **immune system** to fight various types of diseases.

While immunotherapies have a long history of being used across the globe to treat various infectious diseases, including cholera, poliomyelitis, diphtheria, measles and mumps, it has increasingly become a focus for researchers working to develop cancer treatments.

For patients diagnosed with cancer, **immuno-oncology** presents a new treatment option in addition to more established types of cancer treatments, such as surgery, radiotherapy, chemotherapy and targeted therapy. **Immuno-oncology** therapies are currently approved or under investigation for the treatment of a number of solid cancers including:

- **Prostate cancer**
- **Melanoma**
- **Lung cancer**
- **Renal cell carcinoma (kidney cancer)**

Additionally, immuno-oncology therapies are also being widely studied in other types of cancers, including chronic myeloid leukaemia, multiple myeloma and lymphoma.



# Immuno-oncology

As researchers continue to learn more about the body's **immune system**, we are beginning to understand how to target specific cancers and treat cancer more effectively with **immuno-oncology**.

For example, recent data presented at major medical meetings of scientists investigating immuno-oncology showed that a small number of patients treated with immuno-oncology therapies for melanoma are still alive up to 10 years after initiating treatment with the therapy<sup>2</sup>. Another study showed that a combination of two **immuno-oncology** treatments in patients with advanced melanoma resulted in a fast and long lasting response, thereby helping to extend survival further<sup>5</sup>.

An on-going area of immuno-oncology research includes investigating how tumours are able to adapt to evade destruction and go unrecognised by the **immune system** — something that affects the ability of **immunotherapy** treatments to effectively combat cancer.

Additionally, on-going widespread research is being conducted into a molecule named Programmed Cell Death Protein 1 (PD-1). A protein molecule present on many tumour cells, PD-1 works to reduce the ability of **T-cells** to attack tumours. Research is focusing on exploring therapies that target PD-1, aiming to reduce this ability to suppress the body's own immune response.

Similarly, scientists are also exploring pathways that can boost **T-cell** production, as well as pathways that inhibit **T-cell** proliferation and their ability to destroy cancer cells, leading to new therapies that can enhance the body's **immune system** to fight cancer.

In comparison to other cancer treatments, **immuno-oncology** therapies have a distinct safety profile that is tolerable to the patient but nevertheless requires close monitoring. The most common side effects experienced by patients using some approved **immuno-oncology** therapies include inflammation of the intestines, liver, skin, and hormone glands.

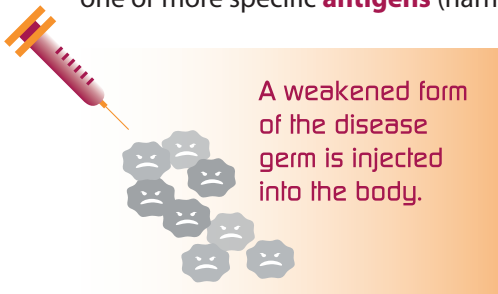
<sup>2</sup>Longest follow-up of largest number of melanoma patients treated with ipilimumab shows some survive up to ten years. European Cancer Congress. 2013

<sup>5</sup>Wolchock MD et al. N Engl J Med. 2013 Jul 11;369(2):122-33. doi: 10.1056/NEJMoa1302369. Epub 2013 Jun 2

# Cancer Vaccines

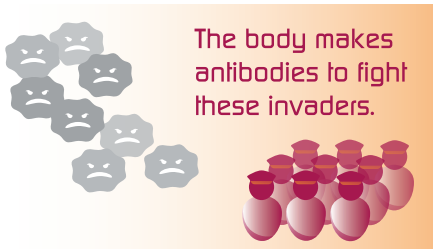
Vaccines have been used for many years as a way of preventing infectious illnesses like influenza, tuberculosis, measles, mumps, typhoid and rubella. Vaccines stimulate the body's **immune system** to recognise and fight abnormal or foreign cells in the body, such as viruses and bacteria.

Cancer vaccines trigger the body's **immune system** to respond to the presence of cancer cells. These vaccines don't just boost the **immune system** in general; they cause the **immune system** to produce proteins called **antibodies** to attack cells that contain one or more specific **antigens** (harmful substances that trigger the immune system to act).

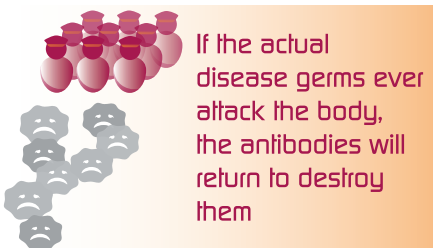


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A cancer vaccine contains cancer cells, parts of cells or pure **antigens**. The vaccine increases the immune response against cancer cells that are already present in the body.




Vaccines are not yet considered a major treatment for cancer, but there are many different types of vaccines now being studied to treat a variety of cancers and also prevent some types of cancer such as the Human Papilloma Virus (HPV). The HPV vaccine is licensed for use in women for the prevention of cervical cancer, caused by HPV types 16 and 18.



<sup>6</sup>[http://circsystemsunsig09r3b.wikispaces.com/\(c\)%09+Immunity+and+vaccination](http://circsystemsunsig09r3b.wikispaces.com/(c)%09+Immunity+and+vaccination)





# Looking to the Future of Immuno-Oncology Research & Development

Over the coming years, more **immuno-oncology** treatment options are expected to become available for multiple types of cancer, potentially improving the care of patients and increasing overall survival. The challenge will be to use these treatments effectively by selecting the most appropriate patients and tumour types for each.

In the future, research into these new therapeutic options through clinical trials will be essential to bring new **immuno-oncology** treatments into use. A number of resources exist within individual countries and across the EU to help patients find clinical trials in which they may be candidates to participate. Some of these include:

## **European Medicines Agency**

*EU Clinical Trials*

Register: <https://www.clinicaltrialsregister.eu/>

## **U.S. National Institutes of Health**

*Clinicaltrials.gov*

<https://www.clinicaltrials.gov/>

It is important that anyone interested in joining a clinical trial consults their health provider team (including their oncologist) to ensure the trial is appropriate for them based on their diagnosis, cancer type and overall health.

# Glossary of Terms



## Antibody

An antibody is a protein produced by the body's immune system when it detects harmful substances, called antigens<sup>7</sup>. Antibodies may be produced when the immune system mistakenly considers healthy tissue a harmful substance.



## Antigen

An antigen is any substance that causes your immune system to produce antibodies against it. An antigen may be a foreign substance from the environment such as chemicals, bacteria or viruses. An antigen may also be formed within the body, as with bacterial toxins or tissue cells<sup>8</sup>.



## B-cell

B-cells make antibodies, which act as a barrier against many kinds of disease.



## Bone Marrow

Bone marrow is the spongy tissue inside some bones, such as the hip and thigh bones. It contains immature cells, called stem cells. The stem cells can develop into red blood cells, which carry oxygen throughout the body, white blood cells, which fight infections, and platelets, which help to clot the blood<sup>9</sup>.



## Immune Evasion

The process of adapting and avoiding the immune system's defence mechanisms.

<sup>7</sup><http://www.nlm.nih.gov/medlineplus/ency/article/002223.htm>

<sup>8</sup><http://www.nlm.nih.gov/medlineplus/ency/article/002224.htm>

<sup>9</sup><http://www.nlm.nih.gov/medlineplus/bonemarrowtransplantation.html>



## Immune System

The immune response is how your body recognises and defends itself against bacteria, viruses and substances that appear foreign and harmful. Through a series of steps called the immune response, the immune system attacks organisms and substances that invade body systems and cause disease. The immune system is made up of a network of cells, tissues and organs that work together to protect the body<sup>10</sup>.



## Immuno-Oncology

Immuno-oncology is a type of cancer treatment that seeks to use the body's natural defences – the immune system – against a range of cancer types that someone may be diagnosed with throughout their lifetime.



## Immunotherapy

The prevention or treatment of disease with substances that stimulate the immune response.



## Lymphatic System

The lymphatic system is a network of organs, lymph nodes, lymph ducts and lymph vessels that make and move lymph from tissues to the bloodstream. The lymph system is a major part of the body's immune system<sup>11</sup>.



## Lymph Nodes

The lymph nodes are small glands that make white blood cells (lymphocytes), which fight infection. Lymph nodes may trap the germs that are causing an infection. Cancer often spreads to lymph nodes<sup>12</sup>.

<sup>10</sup><http://www.nlm.nih.gov/medlineplus/ency/article/000821.htm>

<sup>11</sup><http://www.nlm.nih.gov/medlineplus/lymphaticdiseases.html>

<sup>12</sup><http://www.nlm.nih.gov/medlineplus/ency/article/003933.htm>



### Monoclonal Antibody

A monoclonal antibody, an antibody produced by a single clone of cells grown in the laboratory, is used as an immunoncology treatment to target tumours.



### Spleen

The spleen is an organ above the stomach and under the ribs on the left side. The spleen is part of the lymphatic system, which fights infection and keeps body fluids in balance. It contains white blood cells that fight germs. The spleen also helps control the amount of blood in the body and destroys old and damaged cells<sup>13</sup>.



### T-cell

T-cells are a type of lymphocyte, or white blood cell. They make up part of the immune system. T-cells help the body fight diseases or harmful substances. There are three types of T-cells: Killer T-cells, which attack and kill infected cells; Helper T-cells, which call in more Killer T-cells; and Regulator T-cells, which tell the B-cells and other T-cells when the body is better and they can stop making antibodies.



### Thymus

The thymus is a small organ in the upper chest, under the breastbone. Before birth and during childhood, the thymus helps the body make a type of white blood cell. These cells help protect against infections<sup>14</sup>.

<sup>13</sup><http://vsearch.nlm.nih.gov/vivisimo/cgi-bin/query-meta?v%3Aproject=medline-plus&query=spleen&x=0&y=0>

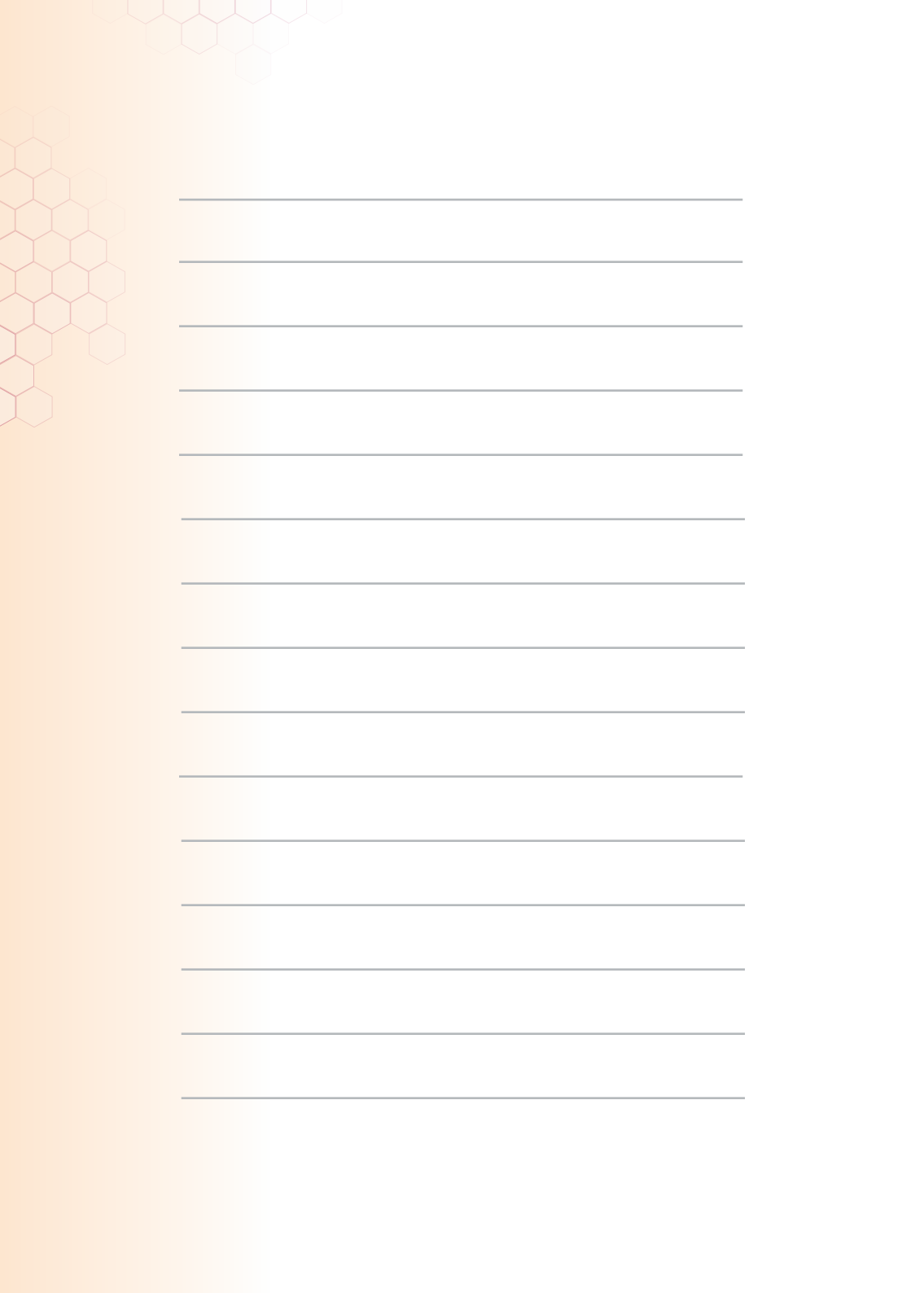
<sup>14</sup><http://www.nlm.nih.gov/medlineplus/thymuscancer.html>



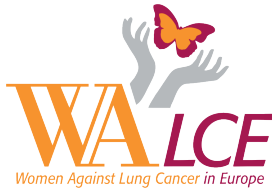












WALCE (Women Against Lung Cancer in Europe), is a non-profit organization founded in 2006 with the primary aim to raise women's awareness about the increased rate of lung cancer's incidence in female gender.

Our mission is to support and advocate for lung cancer patients, their families and caregivers and to educate and circulate information in terms of prevention, diagnosis and therapy.

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