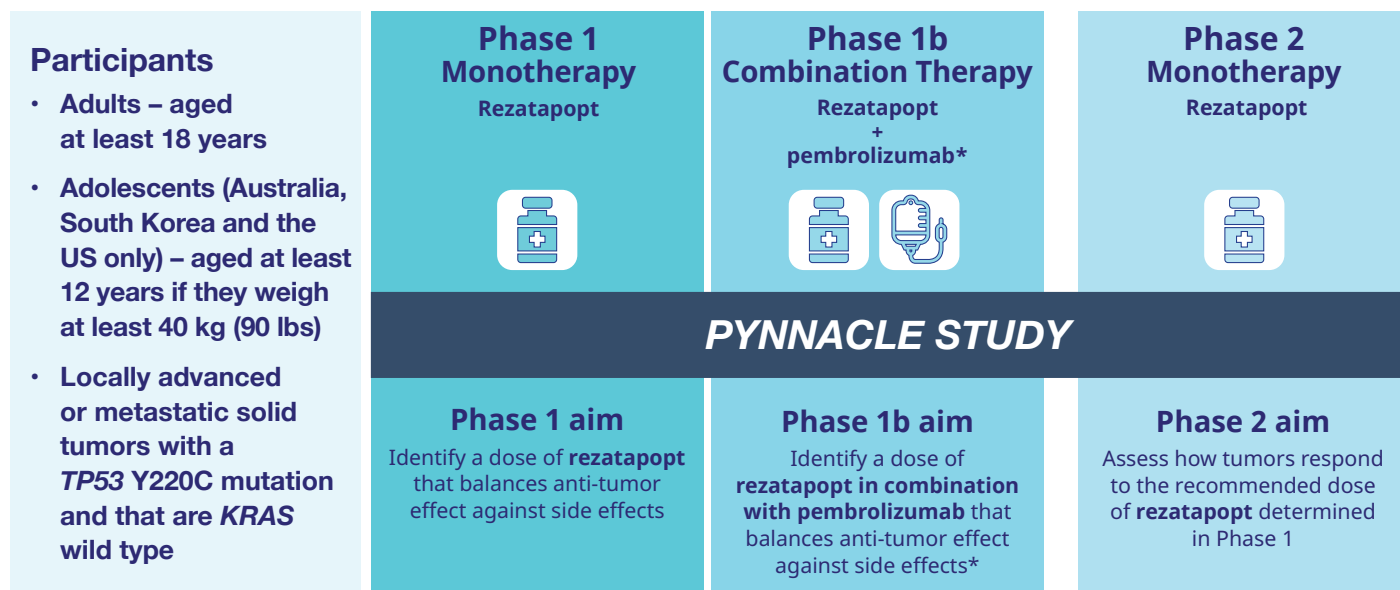


PYNNACLE: a study for patients with advanced solid tumors harboring a *TP53* Y220C mutation

What is PYNNACLE?

PYNNACLE (NCT04585750) is an ongoing registrational Phase 1/2 global study of the efficacy and safety of rezatapopt (also known as PC14586). The study is investigating rezatapopt first on its own and in combination with pembrolizumab.¹ You can visit [PYNNACLEstudy.com](https://www.PYNNACLEstudy.com) to find out if there is an available clinical trial site in your country. People taking part all have solid tumors, which **include but are not limited to** ovarian, lung, breast, and endometrial cancers, that have the *TP53* Y220C mutation.¹



*Pembrolizumab is a medicine for the treatment of several types of solid tumor.²

How do I join PYNNACLE?

To join Phase 2 of the PYNNACLE study, you must:

- Have a locally advanced or metastatic solid tumor that has the *TP53* Y220C mutation
- Have previously received anti-cancer therapy

In Australia, South Korea and the US only, adults and adolescents (aged at least 12 years) may take part if they weigh at least 40 kg (90 lbs)

Outside Australia, South Korea and the US, only adults (aged at least 18 years) can take part in the PYNNACLE study

You cannot join the PYNNACLE study if you have:

- Brain metastases, unless neurologically stable
- Primary central nervous system tumor
- History of leptomeningeal disease, spinal cord compression, organ transplant or gastrointestinal disease which may impact study drug absorption
- Heart conditions, including unstable angina, uncontrolled hypertension, heart attack within 6 months of screening, heart failure, and rhythm abnormalities
- A known *KRAS* mutation, defined as a single nucleotide variant

Find out more at www.PYNNACLEstudy.com

Where can I get more information?

If you are interested in taking part in a clinical trial, the Leal Health service can help find the right trial for you, for free.

Click [here](#) or scan this QR code for more information about Leal Health

You can also schedule time with a Leal Patient Support Specialist at <https://calendly.com/clinicalteam/exploring-clinical-trials-with-us> to see if PYNNACLE might be for you and receive answers to any questions you have.



Medical Information Request Form

For healthcare providers as well as patients and their caregivers to query PMV Pharmaceuticals for additional Medical Information.

Click [here](#) or scan the QR code for the Medical Information Request Form



You can find about more about *TP53* Y220C, biomarker testing, and rezatapopt on the next page

What is TP53 Y220C?

If cells start to multiply out of control, it can be a sign that they have become cancerous.³ One way your body naturally stops this from happening involves the p53 tumor suppressor protein.⁴ The p53 protein monitors your DNA for damage that might lead to growth of a tumor and instructs cells to self-destruct and die if there is a risk that they might become cancerous later.^{4,5}

Sometimes a mutation appears in the *TP53* gene: the part of your DNA that explains how to build the p53 tumor suppressor protein.³ In that case, the p53 protein will not work properly, and any affected cells that are damaged may become cancerous.⁶⁻⁹

The *TP53* gene can mutate in a number of ways. One of the variants is called *TP53* Y220C. This variant contains instructions to build the mutated p53 Y220C protein, which no longer functions normally.^{7,10-13}



Normal p53

In normal, healthy cells, p53 binds to DNA and monitors for damage to help prevent cancer

p53 Y220C

The mutated p53 Y220C protein has a different shape and cannot bind to DNA



The *TP53* Y220C mutation has been found in **1%** of all solid tumors. The mutation appears in around **3%** of ovarian tumors and around **1%** of lung, breast, and endometrial tumors.¹⁴

What is biomarker testing, and how does it work?

Biomarkers are measurable signs in your body, such as specific gene mutations or raised levels of hormones in your blood. By using biomarker testing, it's possible to find specific mutations that are linked to cancer growth and to choose treatments or design clinical trials on investigational treatments that target them.^{15,16}

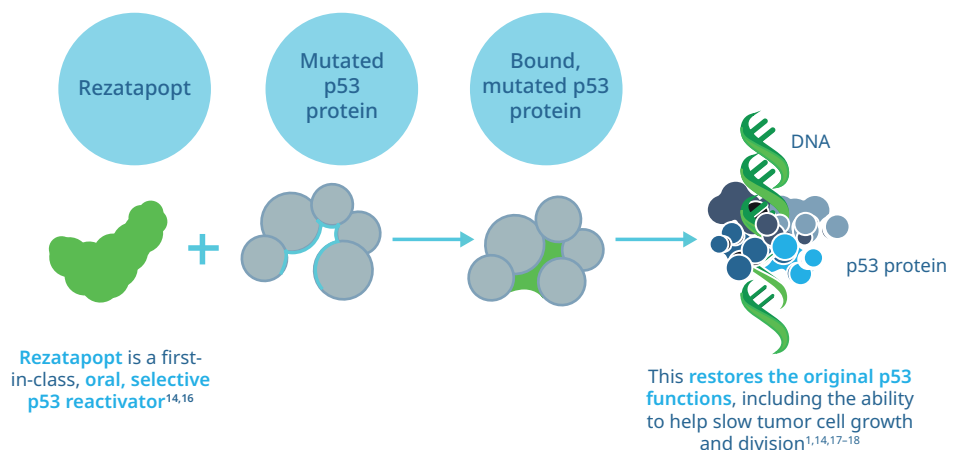
Advances in genetic research and technology mean that it is now possible to create a map of your DNA from a blood or tissue sample. This process, called 'next-generation sequencing', or NGS, allows doctors to search for mutations that are known to be associated with cancer, such as the *TP53* Y220C mutation.^{3,15}

What is rezatapopt?

Rezatapopt (also known as PC14586) is a new investigational treatment being evaluated for the treatment of people with locally advanced or metastatic solid tumors harboring a *TP53* Y220C mutation.^{1,14,17}

Rezatapopt reactivates the mutated p53 Y220C protein so that it regains its normal anti-cancer function.^{14,16} It is the first investigational treatment that can reactivate this specific mutated protein.¹

Rezatapopt selectively binds to the small pocket within the p53 Y220C mutated protein and corrects the shape of the protein to the normal p53 structure and function^{1,14,17}



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Rezatapopt (PC14586) is an investigational treatment that has not been approved by the US Food and Drug Administration (FDA), European Medicines Agency (EMA), or any other regulatory agency for the treatment of cancer.