Future Oncology

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/ifon20

Treatment of the blood cancer polycythemia vera with ruxolitinib in the MAJIC-PV study: a plain language summary

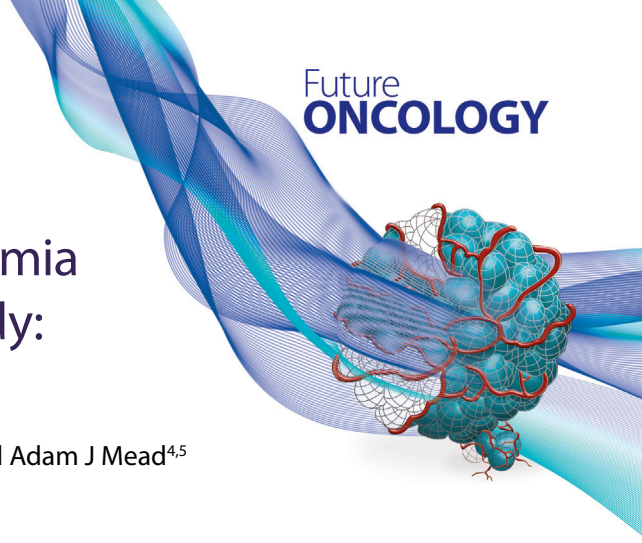
Claire N Harrison, Sonia Fox, Rebecca Boucher, Mary Frances McMullin & Adam J Mead

To cite this article: Claire N Harrison, Sonia Fox, Rebecca Boucher, Mary Frances McMullin & Adam J Mead (01 Oct 2024): Treatment of the blood cancer polycythemia vera with ruxolitinib in the MAJIC-PV study: a plain language summary, Future Oncology, DOI: 10.1080/14796694.2024.2406597

To link to this article: https://doi.org/10.1080/14796694.2024.2406597

Published online: 01 Oct 2024.

Plain Language Summary of Publication



Treatment of the blood cancer polycythemia vera with ruxolitinib in the MAJIC-PV study: a plain language summary

Claire N Harrison[1], Sonia Fox[2], Rebecca Boucher[2], Mary Frances McMullin[3] and Adam J Mead[4,5]
Full affiliations can be found at the end of this article

First draft submitted: 27 June 2024; Accepted for publication: 13 September 2024

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

You can read the original article titled 'Ruxolitinib Versus Best Available Therapy for Polycythemia Vera Intolerant or Resistant to Hydroxycarbamide in a Randomized Trial,' which was published in the *Journal of Clinical Oncology*, for free at: https://ascopubs.org/doi/10.1200/JCO.22.01935

Summary

What is this summary about?
This is a summary of an article describing the main results of the MAJIC-PV study. This study looked at using the cancer drug ruxolitinib to treat a type of blood cancer called polycythemia vera. People with polycythemia vera make too many red blood cells in their body. This can make their blood thicker and can increase the chances of **blood clots** forming in their blood vessels.

Researchers wanted to find out how well ruxolitinib worked compared with the best available therapy as a treatment for people with polycythemia vera who were at risk of developing blood clots that could lead to a heart attack or stroke. Specifically, the study looked at people who had already taken the **chemotherapy hydroxycarbamide** (also known as **hydroxyurea**) for their polycythemia vera, but it either didn't work for them or gave them **side effects** that they could not tolerate.

What were the results?
In the study, researchers divided 180 adults with polycythemia vera who were at high risk of developing blood clots that could lead to a stroke into two groups: 93 people who took ruxolitinib twice a day, and 87 people who took the best available therapy. 43% of people who took ruxolitinib and 26% of people who had the best available therapy had normal blood counts and **spleen** size within 1 year of treatment. 84% of people who took ruxolitinib and 75% of people who had the best available therapy lived for at least 3 years without their polycythemia vera becoming a more advanced type of blood cancer.

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

- **Hemorrhage:** HEH-muh-rij
- **Hydroxycarbamide:** HI-drox-ee-CAR-bo-mide
- **Myeloproliferative neoplasm:** MY-eh-loh-proh-LIH-feh-ruh-tiv NEE-oh-PLA-zum
- **Polycythemia vera:** PAH-lee-sy-THEE-mee-uh VAYR-uh
- **Ruxolitinib:** RUX-oh-LI-ti-nib
- **Thrombosis:** throm-BOH-sis

Blood clots: Gel-like clumps of blood that can form in your arteries and veins to help control bleeding, but they may also block blood flow in your vessels and may cause serious medical issues.
Chemotherapy: A type of medicine that is used to treat cancer by stopping fast-growing cancer cells from multiplying.
Hydroxycarbamide: A drug that is commonly used to treat polycythemia vera. Hydroxycarbamide works by lowering the number of blood cells made in the body and is also used to treat other cancers.
Side effects: An effect of a medicine that is beyond its desired effect. Some side effects can be harmful.
Spleen: An organ that helps to produce and remove blood cells as part of the body's immune system, which is the body's natural defense system.

Taylor & Francis
Taylor & Francis Group

10.1080/14796694.2024.2406597
Published by Informa UK Limited, trading as Taylor & Francis Group

ISSN 1744-8301

The most common side effects were disorders of the digestive system (stomach and gut), disorders of the blood vessels, and infections. This is similar to the side effects that doctors know about for ruxolitinib.

What do the results mean?
Compared with people who had the best available therapy for their polycythemia vera, people who took ruxolitinib were more likely to have normal blood counts and spleen size within 1 year of treatment, and were more likely to live longer without their polycythemia vera becoming a more advanced type of blood 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.

Ruxolitinib is approved to treat the condition in the study that is discussed in this summary. 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 is this article for?

This plain language summary may be helpful for people living with polycythemia vera, as well as their family and friends, and health professionals.

Who sponsored this research?

The MAJIC-PV study was **sponsored** by University of Birmingham (Birmingham, UK) and supported by Blood Cancer UK. An **unrestricted educational grant** was provided by Novartis to support the costs associated with running of the study and the associated scientific research.

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.
Unrestricted educational grant: A kind of funding provided by a company to an organization for educational purposes, such as conducting studies that aim to answer important clinical questions. The company has no control over and does not pose any conditions or limitations on how this funding is used by the recipient organization.

What is polycythemia vera?

Polycythemia vera is a type of blood cancer and it is one of the most common forms of **myeloproliferative neoplasm**.

People with polycythemia vera make too many red blood cells and other types of blood cells in their **bone marrow**.

Myeloproliferative neoplasms: A group of rare blood cancers that start in the bone marrow, which is the soft inner part of the bone where blood cells are made.
Bone marrow: The spongy tissue in the middle of certain bones. Most blood cells are made in the bone marrow.

This means that their blood is thicker than normal, increasing their risk of developing blood clots, which can lead to a heart attack or stroke.

People with polycythemia vera can also have an enlarged spleen.

Genes: Sections of DNA that have a set of instructions to make molecules called proteins. These proteins can then change how cells in the body work.

Nearly all people (i.e., over 96%) with polycythemia vera have a fault in the **gene** called JAK2.

The JAK2 gene makes a protein that controls how many blood cells the bone marrow makes.

A faulty JAK2 gene causes the bone marrow to start making red blood cells when it's not supposed to.

Treatments for polycythemia vera aim to lower the number of red blood cells and other types of blood cells in the body. This can reduce the risk of people having serious problems, such as blood clots.

Worldwide, hydroxycarbamide (hydroxyurea) is the most common treatment taken by people with polycythemia vera who are at high risk of developing a blood clot.

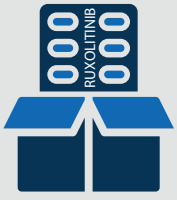
This is a type of chemotherapy that is taken as a capsule and slows down the multiplication of blood cancer cells in the body.

Hydroxycarbamide (hydroxyurea) often works for a while, but people may need to stop treatment because they are **resistant** or **intolerant**.

Resistant: The treatment has stopped working.
Intolerant: People have to stop treatment because of side effects.

More treatment options are needed for people with polycythemia vera who have to stop taking hydroxycarbamide (hydroxyurea).

What is the role of ruxolitinib in treating polycythemia vera?



Ruxolitinib is a type of targeted cancer treatment that is taken as a tablet. It works by blocking the effects of the faulty JAK2 gene in people with polycythemia vera.

In some people with polycythemia vera, ruxolitinib has been shown to:

Reduce levels of blood cells to normal levels seen in people without the disease

Reduce the size of the spleen

Improve the symptoms associated with polycythemia vera

10.1080/14796694.2024.2406597

What was the MAJIC-PV study?

The MAJIC-PV study was an **open-label randomized** study that looked at ruxolitinib as a treatment compared with the best available therapy for people with polycythemia vera.

Researchers wanted to find out if ruxolitinib worked well in people who became resistant or intolerant to hydroxycarbamide (hydroxyurea) treatment.

Open label: Participants and researchers knew who had taken ruxolitinib or the best available therapy.
Randomized: Researchers randomly divided people into two groups to take either ruxolitinib or the best available therapy.

What did the MAJIC-PV study look at?

The main aim of the study was to find out how many people had a **complete response** within 12 months of treatment with ruxolitinib or the best available therapy.

Complete response: Following treatment, a person had normal blood counts and spleen size, without needing to have a **blood draw** (venesection or phlebotomy) for more than 3 months.
Blood draw: A procedure where a specific amount of blood is removed from your body by withdrawing blood from one of your veins. For people with polycythemia vera, blood draw can be used to lower their red blood cell counts, which makes their blood flow more easily. Also known as venesection or phlebotomy.
Partial response: Following treatment, a person had partial improvement in blood counts or spleen size. For example, they might have a normal blood count except for higher-than-normal **platelet** counts, or their bone marrow might still show abnormal laboratory findings.
Platelets: Small, colorless cell fragments in our blood that form clots and stop or prevent bleeding.

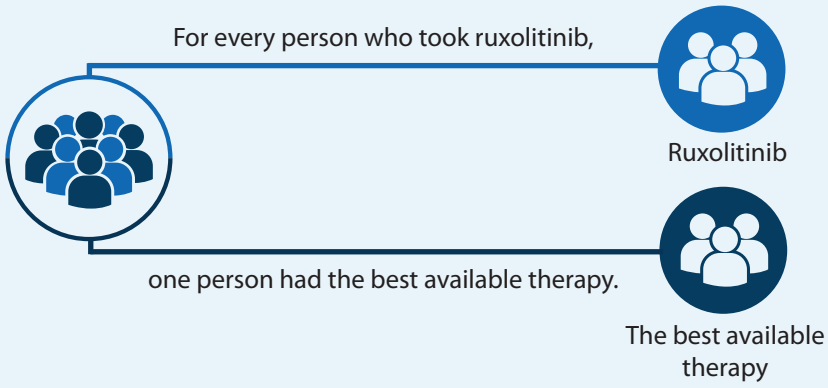
Other goals of the study were to find out:

- How many people had a **partial response** within 12 months of treatment with ruxolitinib or the best available therapy.
- How long people lived for after starting treatment with ruxolitinib or the best available therapy.
- How long people lived without their polycythemia vera becoming a more advanced type of blood cancer after treatment with ruxolitinib or the best available therapy.
- How many people lived without having a major problem caused by their polycythemia vera. This included:
  - » Having a major clot
  - » Having major bleeding
  - » Their disease progressing to a more advanced type of blood cancer, usually myelofibrosis or leukemia
  - » Death
- How many people had a reduction in the number of faulty JAK2 genes in their body with ruxolitinib or the best available therapy.
  - » If a reduction in someone's number of faulty JAK2 genes was linked to how they responded to treatment with ruxolitinib or the best available therapy.
- If the mental or physical health of people was impacted by treatment with ruxolitinib or the best available therapy.
- The side effects people had during or after treatment with ruxolitinib or the best available therapy.

How was the MAJIC-PV study carried out?

The people who took part in the study were from 38 sites across the United Kingdom between June 4, 2012, and March 28, 2022.

Researchers divided people into two groups to take either ruxolitinib or the best available therapy.



The kind of people who took part in the study were:

Adults who were at least 18 years old

People diagnosed with polycythemia vera who were at high risk of developing blood clots

People who started treatment with hydroxycarbamide (hydroxyurea), but were resistant or intolerant to it

Additional information about patients who were not eligible to take part in the study can be found in the supplementary material of the original article.

People who had the best available therapy mostly took:

Hydroxycarbamide (hydroxyurea)

Some people did not stop their hydroxycarbamide treatment and instead continued with hydroxycarbamide treatment rather than starting another standard treatment.

Interferon

An immunotherapy drug, which activates the body's immune system to attack cancer cells, which is also a common treatment, but many patients become resistant or intolerant to this drug too.

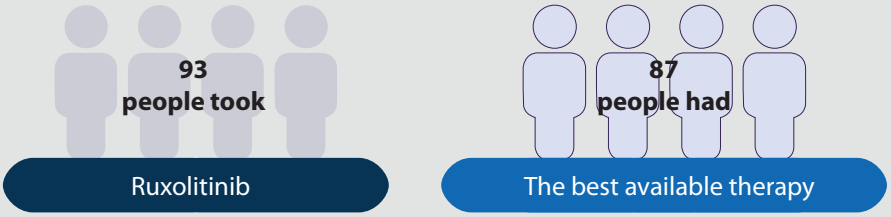
A combination of hydroxycarbamide and interferon

On average, people took ruxolitinib or the best available therapy for their polycythemia vera for approximately 3–4 years during the study.

10.1080/14796694.2024.2406597

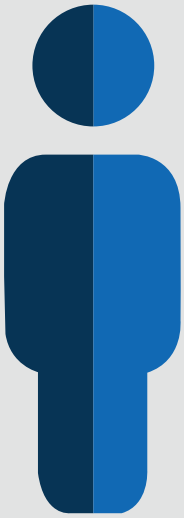
Who took part in the MAJIC-PV study?

Overall, **180 people** took part in the study



Characteristics were similar in the people who took ruxolitinib compared with standard treatment:

	Ruxolitinib	The best available therapy
Age	**67 years**	**66 years**
Gender	**40% women**	**44% women**
Median disease duration	**7.5 years**	**8 years**



Reason why hydroxycarbamide (hydroxyurea) became ineffective

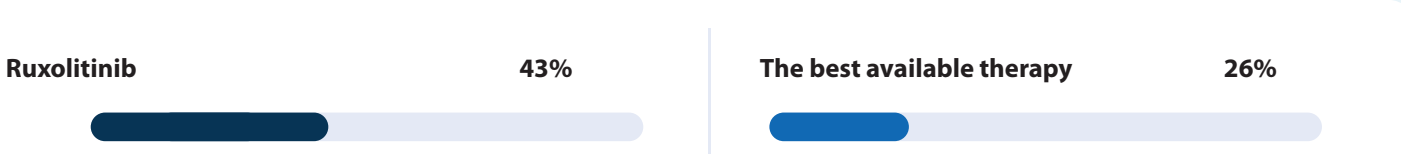
	Ruxolitinib	The best available therapy
Intolerant	**46%**	**43%**
Resistant	**33%**	**26%**
Intolerant and resistant	**20%**	**31%**

Median: The middle value in a set of measurements.

What were the results of the MAJIC-PV study?

Complete response within 12 months

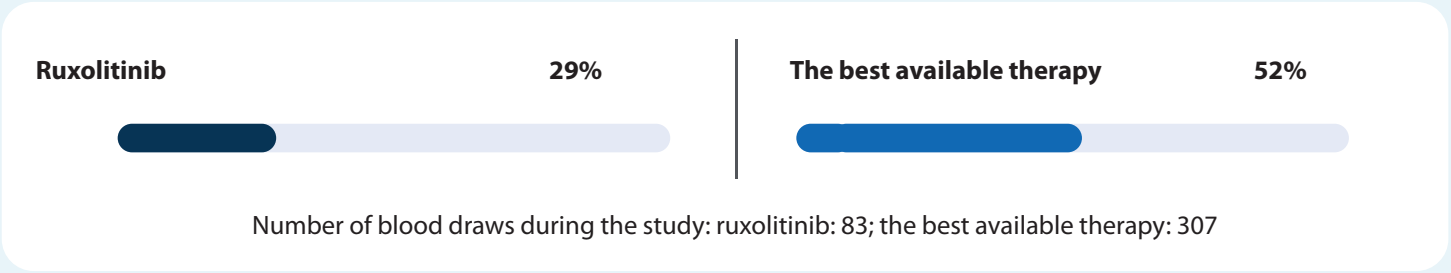
People who took ruxolitinib were more likely to have a complete response within 1 year of treatment compared with people who had the best available therapy.



People who took ruxolitinib were also more likely to have a longer response compared with people who had the best available therapy

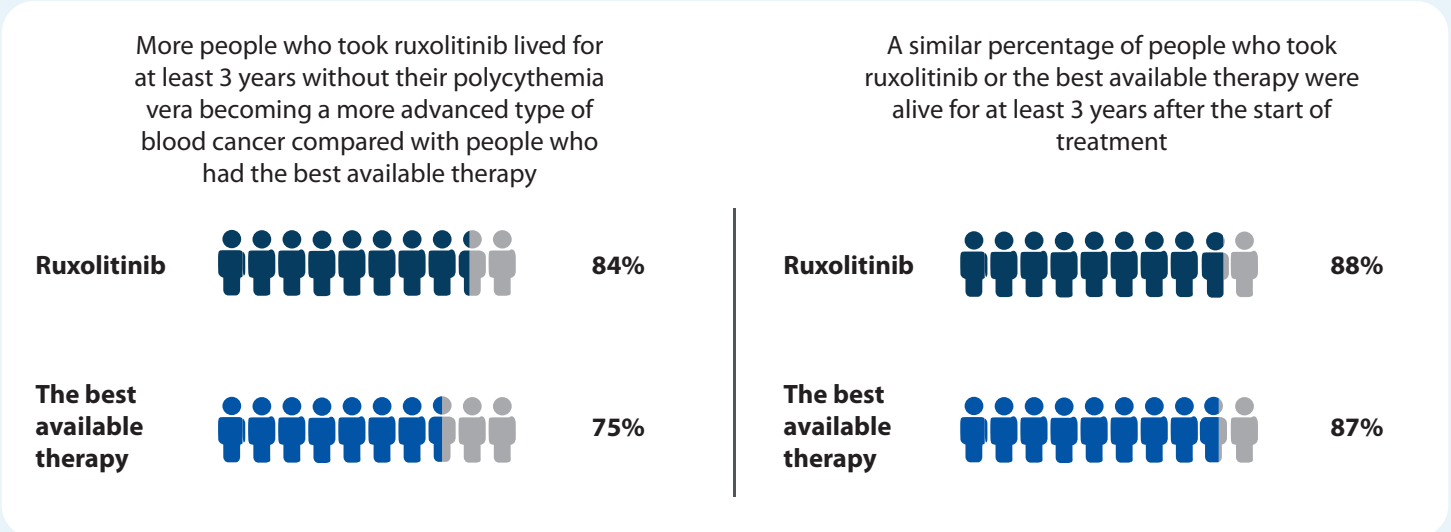
Partial response within 12 months
People who had the best available therapy were more likely to have a partial response within 1 year of treatment compared with people who took ruxolitinib.

Number of blood draws required during the study
People who took ruxolitinib were less likely to need a blood draw compared with people who had the best available therapy.



Survival
People who took ruxolitinib were more likely to live longer without having a major blood clot compared with people who had the best available therapy.

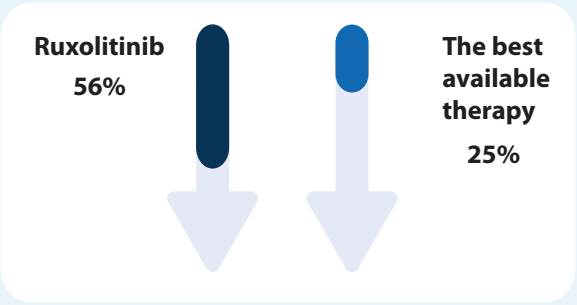
People who took ruxolitinib lived longer without having a major event compared with people who had the best available therapy.



10.1080/14796694.2024.2406597

Number of faulty JAK2 genes
A 50% reduction in faulty JAK2 genes was seen regardless of treatment.

More people who took ruxolitinib had a 50% reduction in the number of faulty JAK2 genes in their body compared with people who had the best available therapy.



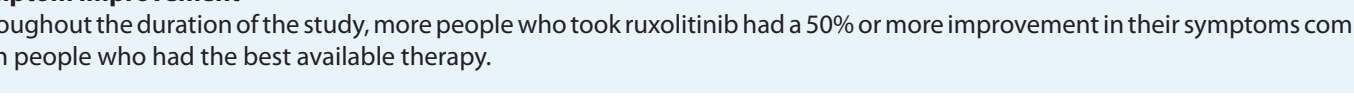
People who had a 50% reduction in the number of faulty JAK2 genes in their body were more likely to respond better to treatment, including:

- Living longer overall
- Living longer without their polycythemia vera becoming a more advanced type of blood cancer
- Living longer without having a major event (including a blood clot, major bleeding, their disease becoming a more advanced type of blood cancer, or death)

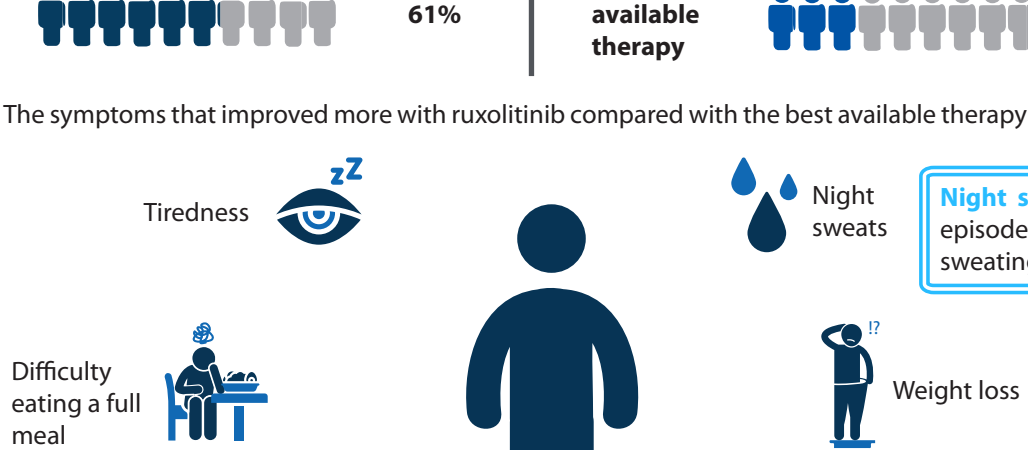
The number of faulty JAK2 genes decreased by over 90% in 3 patients who took ruxolitinib; the number of **stem cells** with a faulty JAK2 gene in their bodies decreased by 72–100% after 4 to 5 years.

Stem cells: A type of cell that develops into other types of cells, for example, blood cells or cells with a faulty JAK2 gene.

Symptom improvement
Throughout the duration of the study, more people who took ruxolitinib had a 50% or more improvement in their symptoms compared with people who had the best available therapy.



The symptoms that improved more with ruxolitinib compared with the best available therapy were:



Night sweats: Repeated episodes of very heavy sweating during sleep.

Taylor & Francis
Taylor & Francis Group

What were the most common side effects?

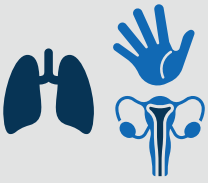
The most common **serious side effects** were:

Infections

Ruxolitinib
137 events

The best available therapy
99 events

Serious infections



Ruxolitinib
27 events

The best available therapy
12 events

Serious side effects: Any side effects that are life-threatening or require hospitalization, result in the formation of a new cancer, or cause long-term disability, birth defect, or death.
Events: Total number of times people had side effects during the study. Some people may have the same side effect more than once.

- Certain types of serious infections were more common in people taking ruxolitinib compared with people who had the best available therapy.
- These included respiratory infections, genital and urinary tract infections, and skin infections.
- Nobody died because of these infections.

Disorders affecting the digestive system:

Ruxolitinib
12 events

The best available therapy
12 events

Disorders affecting the blood vessels:

Ruxolitinib
14 events

The best available therapy
10 events

Although uncommon, a type of skin cancer called **squamous cell carcinoma** occurred more often in people who took ruxolitinib compared with people who had the best available therapy.

Ruxolitinib
11 events

The best available therapy
0 events

Squamous cell carcinoma: A type of cancer that develops on areas of skin that have been exposed to the sun. The main treatment for skin cancer is surgery to remove the cancer and a small amount of the skin around it. Most people don't need any more treatment after the surgery.

Side effects did not increase when people had treatment for a longer time

Side effects for people who took ruxolitinib in this study were similar to the side effects people had with ruxolitinib in other studies

10.1080/14796694.2024.2406597

Stopping treatment

A comparable number of people who took ruxolitinib or the best available therapy stopped treatment during the study:

Ruxolitinib	The best available therapy
30 patients	**23 patients**

- People who had the best available therapy were allowed to change to a different available therapy.
- Reasons for stopping treatment included:
  - » Polycythemia vera became a more advanced type of blood cancer
  - » Side effects
  - » No longer wanting to take part in the study
  - » Death
- People who had the best available therapy were more likely to switch treatments during the study than people who took ruxolitinib.
- A similar proportion of people who took ruxolitinib or the best available therapy died during the study (15 people who took ruxolitinib compared with 17 people who had the best available therapy).

For people for who took ruxolitinib, the most common causes of death were:

- Unrelated to their polycythemia vera or a different type of cancer
- Related to a different type of cancer
- Related to their polycythemia vera becoming a more advanced type of blood cancer

For people who had the best available therapy, the most common causes of death were:

- Unrelated to their polycythemia vera or a different type of cancer
- A major clot or major bleeding
- Related to a different type of cancer

Additional information about safety and deaths in the study can be found in the supplementary material of the original article.

What do the results of this study mean?

- In the MAJIC-PV study, people taking ruxolitinib were more likely to have normal blood counts and spleen size, without needing to have a blood draw for more than 3 months within 1 year of treatment, compared with people who took the best available therapy.
- People taking ruxolitinib were more likely to live longer without their polycythemia vera becoming a more advanced type of blood cancer, or without having a major problem caused by their polycythemia vera (including a major blood clot), compared with people who took the best available therapy.
- Fewer people taking ruxolitinib needed a blood draw to reduce the number of red blood cells in their blood compared with people who took the best available therapy.
- People taking ruxolitinib had greater improvements in their symptoms caused by polycythemia vera compared with people who took the best available therapy.
- People taking ruxolitinib had fewer stem cells with a faulty JAK2 gene after treatment than before they started therapy.

- More people taking ruxolitinib had a 50% reduction in their number of faulty JAK2 genes. This was associated with important clinical benefits such as:
  - » Having a complete response after treatment
  - » Living longer without polycythemia vera becoming a more advanced type of blood cancer
  - » Living longer without having a major problem caused by their polycythemia vera
  - » Living longer overall
- People had similar side effects with ruxolitinib as those reported in other studies. These included disorders of the digestive system or blood vessels, skin cancer, and infections.
- The study shows that ruxolitinib improved symptoms, people with polycythemia vera needed blood draws less often, and more people lived without their polycythemia vera becoming a more advanced type of blood cancer or without a major problem caused by their polycythemia vera compared with the best available therapy.

Limitations of the study

- During the study, people who had the best available therapy were allowed to change treatment.
- This could have made the differences between the two treatment groups smaller.
- A high proportion of people continued to take hydroxycarbamide (hydroxyurea) as the best available therapy for polycythemia vera, even though hydroxycarbamide (hydroxyurea) was not working for them or was giving them side effects that they could not tolerate.

Where can I find more information?

You can read the original article titled 'Ruxolitinib Versus Best Available Therapy for Polycythemia Vera Intolerant or Resistant to Hydroxycarbamide in a Randomized Trial,' which is free to access at the following link: https://ascopubs.org/doi/10.1200/JCO.22.01935. The full citation for the original article: Harrison CN, Nangalia J, Boucher R, et al. Ruxolitinib Versus Best Available Therapy for Polycythemia Vera Intolerant or Resistant to Hydroxycarbamide in a Randomized Trial. *J Clin Oncol.* 2023;41(19):3534-3544.

The supplementary material that was published with the original article and which includes additional information about the study, is available at the following link: https://ascopubs.org/doi/suppl/10.1200/JCO.22.01935/suppl_file/DS_JCO.22.01935.pdf.

The MAJIC-PV study started on June 4, 2012, and ended on March 28, 2022.

Further information on the MAJIC-PV study is available at: https://www.isrctn.com/ISRCTN61925716.

Readers may find useful resources on MPN on the MPN Voice website: https://www.mpnvoice.org.uk/

Funding

This manuscript was funded by Incyte Corporation. The funder contributed to the decision of the authors to develop and publish the manuscript.

Declaration of interest

CN Harrison has received honoraria from AbbVie, CTI BioPharma, Geron, Janssen, and Novartis; has acted in a consulting or advisory role for AOP Orphan Pharmaceuticals, Celgene, Constellation Pharmaceuticals, CTI BioPharma, Galecto, Geron, Gilead Sciences, Janssen, Keros Therapeutics, Novartis, Promedior,

Roche, Shire, and Sierra Oncology; has served on speakers' bureaus for AbbVie, Bristol Myers Squibb, CTI BioPharma, Geron, Novartis, and Sierra Oncology; and has received research funding from Bristol Myers Squibb, Constellation Pharmaceuticals, and Novartis. MF McMullin has acted in a consulting or advisory role for Bristol Myers Squibb, CTI BioPharma, Novartis, and Sierra Oncology; and has served on speakers' bureaus for AbbVie, Incyte, and Novartis. AJ Mead has stock and other ownership interests in Alethiomics; has received honoraria from AbbVie, Celgene/Bristol Myers Squibb, Constellation Pharmaceuticals, CTI BioPharma, Karyopharm Therapeutics, and Novartis; has received research funding from Alethiomics, Celgene/Bristol Myers Squibb, Galecto, and Novartis; and is a co-founder and equity holder in Alethiomics, a spinout company from the University of Oxford. AJ Mead has licensed a patent to Alethiomics. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Writing disclosure

Medical writing assistance was provided by Harriet Pike, PhD, and Emily Sun, PhD, of Envision Pharma Group, Fairfield, CT, USA, and funded by Incyte Corporation. Infographic icons designed by Freepik (www.freepik.com).

Acknowledgements

This study would not have been possible without the study teams, but most of all, without the participating patients and their families; we are very grateful to them, and all patients who kindly agree to take part in research.

Open access

Author affiliations

[1]Department of Haematology, Guy's and St Thomas' NHS Foundation Trust, London, UK; [2]Cancer Research UK Clinical Trials Unit, University of Birmingham, Birmingham, UK; [3]Queen's University, Belfast, UK; [4]Medical Research Council (MRC) Molecular Haematology Unit, MRC Weatherall Institute of Molecular Medicine, NIHR, Biomedical Research Centre, University of Oxford, Oxford, UK; [5]Cancer and Haematology Centre, Churchill Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, UK