

Vasculitis and azathioprine Summaries and decision aid

Should people with vasculitis who go into remission with cyclophosphamide change over to azathioprine?

To answer this question, scientists found 1 study and analysed it. People received cyclophosphamide and prednisone until they were in remission and then received pills of cyclophosphamide or azathioprine to stay in remission. This study provides the best evidence we have today.

What is vasculitis and how is it treated?

Vasculitis is a group of diseases, including Wegener's granulomatosis, Churg–Strauss syndrome, microscopic polyangiitis, and polyarteritis nodosa, in which blood vessels are inflamed. The inflammation or swelling can occur anywhere in the body causing the walls of blood vessels to thicken, weaken, narrow, scar or break. Blood clots may form and blood may not be able to flow well to the tissues and organs in the body. With low blood supply, the tissues may die and organs may not work well. When the disease is severe, cyclophosphamide and a corticosteroid (such as prednisone) are used to help people go into remission (a period of no symptoms) and stay in or maintain remission. Even though cyclophosphamide works to get people into remission, it has serious side effects that can permanently damage the body. It is thought that using cyclophosphamide for a short time until people are in remission and then changing to another drug (such as azathioprine or methotrexate) may decrease the chances of flare-ups in the future and the chances of permanent damage caused by cyclophosphamide.

Did taking cyclophosphamide and corticosteroids to go into remission and then changing to a different drug (azathioprine) for maintenance work well?

People went into remission with cyclophosphamide and corticosteroids and then to maintain the remission took azathioprine or kept on taking cyclophosphamide. After going into remission, the number of people who had flare-ups while taking azathioprine was about the same as the number of people who had flare-ups while continuing to take cyclophosphamide.

What were the side effects?

The study showed that both drugs caused side effects, such as temporarily decreasing the number of white blood cells that fight infection. Taking cyclophosphamide over a long period of time causes bladder cancer, but this does not happen with azathioprine. But cyclophosphamide and azathioprine are known to increase the chances of other cancers, such as lymphoma. The study included in this review was only 18 months long which is too short a time to determine the chances of cancer.

What is the bottom line?

There is “Silver” level evidence that after remission, cyclophosphamide should be stopped and other drugs such as azathioprine should be started to stop flare-ups in the future and to avoid the chances of serious side effects that cyclophosphamide over a long period might cause.

Based on Watts R, Scott DGI, Lane SE, Ottawa Methods Group. Primary systemic vasculitis. In: *Evidence-based Rheumatology*. London: BMJ Books, 2003.

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What is vasculitis and how is it treated?

Vasculitis is a group of diseases, including Wegener's granulomatosis, Churg–Strauss syndrome, microscopic polyangiitis, and polyarteritis nodosa in which blood vessels are inflamed. The inflammation or swelling can occur anywhere in the body and can cause the walls of blood vessels to thicken, weaken, narrow, scar or break. Blood clots may form and blood may not be able to flow well to the tissues and organs in the body. With low blood supply, the tissues may die and organs may not work well. Vasculitis can be mild or more severe and life-threatening.

Some types of vasculitis may only occur once and go away on their own, while others will need to be treated. Other types may occur in cycles, where there are flare-ups and then periods with no symptoms (remission). When the disease is severe, cyclophosphamide and prednisone are used to help people go into remission and stay in or maintain remission. Even though cyclophosphamide works to get people into remission, it may not maintain remission (stop flare-ups in the future) and it has serious side effects that can permanently damage the body. It is thought that using cyclophosphamide for a short time until people are in remission and then changing to another drug (such as azathioprine or methotrexate) may decrease the chances of flare-ups in the future and the chances of permanent damage caused by cyclophosphamide.

How did the scientists find the information and analyse it?

The scientists searched for studies and reviews of the medical literature that examined the treatment of vasculitis. Not all studies and reviews found were of a high quality and so only those studies that met high standards were selected.

The study selected was a randomised controlled trial – where one group of patients continued to receive cyclophosphamide and another group switched to azathioprine.

Which high quality studies were examined in this summary?

There was 1 study examined in this summary: 155 patients with vasculitis received oral (by mouth) cyclophosphamide and prednisolone and 144 went into remission. After remission, 73 patients continued to take cyclophosphamide and 71 patients stopped taking cyclophosphamide and received azathioprine instead. The study lasted for 18 months.

Did taking cyclophosphamide and corticosteroids to go into remission and then changing to a different drug (azathioprine) for maintenance work well?

People went into remission with cyclophosphamide and corticosteroids. Then to maintain the remission people took azathioprine or kept on taking cyclophosphamide. After going into remission, the number of people who had flare-ups while taking azathioprine was about the same as the number of people who had flare-ups while continuing to take cyclophosphamide after going into remission.

Specifically, the study showed that:

- 15 out of 100 patients who switched to azathioprine had a flare-up
- 13 out of 100 patients who continued to take cyclophosphamide had a flare-up

Were there side effects?

The study showed that both drugs caused side effects, such as temporarily decreasing the number of white blood cells that fight infection. Taking cyclophosphamide over a long period of time causes bladder cancer, but this does not happen with azathioprine. But cyclophosphamide and azathioprine are known to increase the chances of other cancers, such as lymphoma. The study included in this review was only 18 months long, which is too short a time to determine the chances of cancer.

The study showed that:

- about 10 out of 100 patients taking azathioprine or cyclophosphamide had serious side effects
- about 55 out of 100 patients taking azathioprine or cyclophosphamide had fewer white blood cells that fight infection
- 4 out of 100 patients who kept taking cyclophosphamide and 1 out of 100 patients who switched to azathioprine had blood in the urine caused by an infection in the bladder
- 7 out of 100 patients who switched to azathioprine had fevers, chills, and a rash that could have been due to a reaction to azathioprine.

What is the bottom line?

There is “Silver” level evidence that after remission, cyclophosphamide should be stopped and other drugs such as azathioprine should be started to stop flare-ups in the future and to avoid the chances of serious side effects that cyclophosphamide over a long period might cause.

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Information about vasculitis and treatment

What is vasculitis?

Vasculitis is a group of diseases, including Wegener's granulomatosis, Churg–Strauss syndrome, microscopic polyangiitis and polyarteritis nodosa, in which blood vessels are inflamed. The inflammation or swelling can occur anywhere in the body and can cause the walls of blood vessels to thicken, weaken, narrow, scar or break. Blood clots may form and blood may not be able to flow well to the tissues and organs in the body. With a poor blood supply, the tissues may die and organs may not work well. Vasculitis can be mild or more severe and life-threatening.

Some types of vasculitis may occur once and go away on their own, while others will need to be treated. Other types may occur in cycles, where there are flare-ups and then periods with no symptoms (remission). Treatment is used to stop flare-ups and to make sure blood vessels are not damaged. If vasculitis is not treated, inflammation or swelling in blood vessels can lead to permanent damage to tissues or organs and cause:

- loss of vision
- heart attack, kidney failure, lung damage
- gangrene
- death.

What can I do on my own to manage my disease?

- ✓ exercise when possible
- ✓ avoid alcohol
- ✓ rest and relax
- ✓ dress warmly in cold weather

What treatments are used for vasculitis?

Three kinds of treatment may be used alone or together. The common (generic) names of treatment are shown below:

1. *Oral or IV corticosteroids*
 - Prednisone
 - Prednisolone
 - Methylprednisolone
2. *Immunosuppressive agents (cytotoxics)*
 - Azathioprine
 - Cyclophosphamide
 - Ciclosporin
 - Methotrexate
3. *Other therapies*
 - Plasma exchange
 - Intravenous immunoglobulin

What about other treatments I have heard about?

There is not enough evidence about the effects of some treatments. Other treatments do not work. For example:

- Acupuncture
- Electropuncture
- Ultrasound
- Electrical stimulation
- Thermotherapy

What are my choices? How can I decide?

Treatment for your disease will depend on your condition. You need to know the good points (pros) and the bad points (cons) about each treatment before you can decide.

Vasculitis decision aid:

Should I switch to azathioprine after going into remission with cyclophosphamide?

This guide can help you make decisions about the treatment your doctor is asking you to consider.

It will help you to:

1. Clarify what you need to decide
2. Consider the pros and cons of different choices.
3. Decide what role you want to have in choosing your treatment.
4. Identify what you need to help you make the decision.
5. Plan the next steps.
6. Share your thinking with your doctor.

Step 1: Clarify what you need to decide What is the decision?

Should I continue to take cyclophosphamide or take a different drug (such as azathioprine) after going into remission?

Cyclophosphamide can be taken as a pill or as an infusion into the veins (IV); azathioprine is usually taken as a pill.

When does this decision have to be made? Check one

within days within weeks within months

How far along are you with this decision? Check one

- I have not thought about it yet.
- I am considering the choices
- I am close to making a choice
- I have already made a choice

Step 2: Consider the pros and cons of different choices

What does the research show?

Taking azathioprine after going into remission is classified as: **Likely beneficial**

There is “Silver” level evidence from 1 study of people with vasculitis who stopped taking cyclophosphamide and started another drug after going into remission. These studies found pros and cons that are listed in the chart below.

What do I think of the pros and cons of azathioprine?

1. Review the common pros and cons.
2. Add any other pros and cons that are important to you.
3. Show how important each pro and con is to you by circling from one (*) star if it is a little important to you, to up to five (*****) stars if it is very important to you.

PROS AND CONS OF AZATHIOPRINE TREATMENT	
PROS (number of people affected)	How important is it to you?
Less flare-ups and lower chances of dying than if stopped taking medications for vasculitis	* * * * *
Same number of people had a flare-up of vasculitis in the 18 months after going into remission with azathioprine or cyclophosphamide about 14 out of 100 people had a flare-up	* * * * *
No chances of bladder cancer with azathioprine	* * * * *
Less people have blood in urine 1 out of 100 people with azathioprine have blood in urine 4 out of 100 people with cyclophosphamide have blood in urine	* * * * *
Other pros:	* * * * *
CONS (number of people affected)	How important is it to you?
Side effects: lowers white blood cells in about 55 out of 100 people taking azathioprine or cyclophosphamide	* * * * *
Can cause fever, chills or rash 7 out of 100 people taking azathioprine	* * * * *
Personal cost of medicine	* * * * *
Other cons:	* * * * *

What do you think about taking azathioprine? Check one

Willing to consider this treatment
 Pros are more important to me than the Cons

Unsure

Not willing to consider this treatment
 Cons are more important to me than the Pros

Step 3: Choose the role you want to have in choosing your treatment

Check one

- I prefer to decide on my own after listening to the opinions of others
- I prefer to share the decision with: _____
- I prefer someone else to decide for me, namely: _____

Step 4: Identify what you need to help you make the decision

What I know	Do you know enough about your condition to make a choice?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you know which options are available to you?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you know the good points (pros) of each option?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you know the bad points (cons) of each option?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
What's important	Are you clear about which pros are most <i>important to you</i> ?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Are you clear about which cons are most <i>important to you</i> ?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
How others help	Do you have enough support from others to make a choice?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Are you choosing without pressure from others?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you have enough advice to make a choice?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
How sure I feel	Are you clear about the best choice for you?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you feel sure about what to choose?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure

If you answered No or Unsure to many of these questions, you should talk to your doctor.

Step 5: Plan the next steps

What do you need to do before you make this decision?

For example – talk to your doctor, read more about this treatment or other treatments for vasculitis.

Step 6: Share the information on this form with your doctor

It will help your doctor understand what you think about this treatment.

Decisional Conflict Scale © A O'Connor 1993, Revised 1999.

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