



Patient study guide

This guide has been developed to support your participation in the INTREPID study, and to help you understand a bit more about your condition.

The findings of this study will be used to help develop treatments for people with Crohn's disease in the future. The study team would like to extend their deepest gratitude to you for taking part in this study. Without participants like you, it would not be possible to conduct studies such as this or develop new treatments for disease.

Contents

1. Introduction

1. Introduction

INTREPID is a clinical study involving people with Crohn's disease. It is being carried out to see if a drug called brazikumab may help people with your condition.

*If any of the words in the guide are new or difficult to understand, there is a glossary and pronunciation guide **available here**. You can also ask your study doctor any questions you may have after reading this guide.*

This guide is to help you understand:

- ✓ Your disease
- ✓ Why you have been asked to take part in this study
- ✓ More about the study treatment, brazikumab
- ✓ What will be involved in the study
- ✓ Possible side effects of the study treatment
- ✓ The importance of attending clinic visits and answering electronic questionnaires (eDiaries)

2. Understanding Crohn's disease



2. Understanding Crohn's disease

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What is Crohn's disease?

It is a long-term medical condition which causes inflammation in your digestive system. It usually affects your large intestine (sometimes called the **colon**), and a part of your small intestine called the **ileum**.

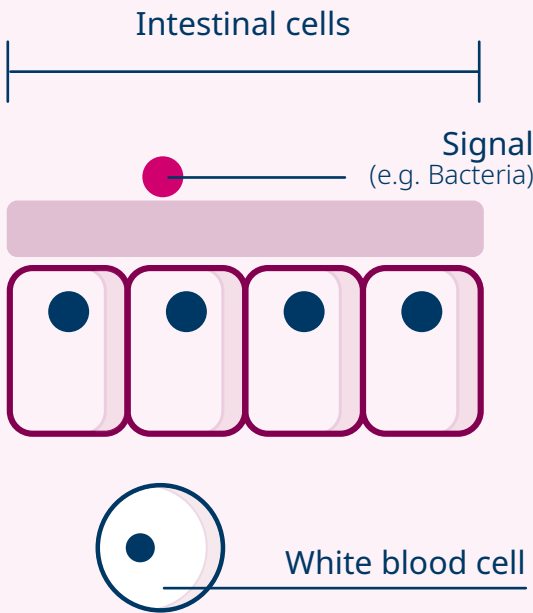
Usually, your immune system helps to protect your body from things like bacteria and viruses. However, your immune system can sometimes become overactive and start to attack healthy cells by mistake.

In Crohn's disease, your immune system mistakenly attacks healthy cells in your intestines. This causes damage, swelling, and inflammation in the colon, ileum, and other parts of the digestive system.

1

Healthy intestine

White blood cells respond to a signal, such as bacteria



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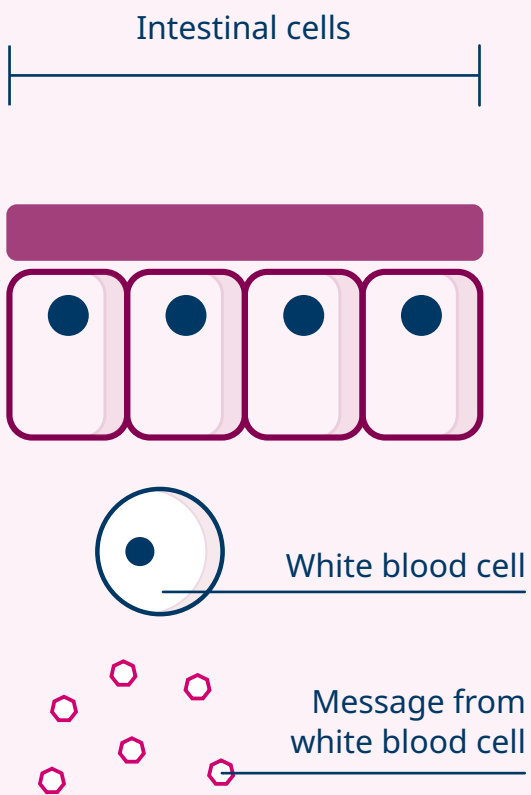
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In Crohn's disease, your immune system mistakenly attacks healthy cells in your intestines. This causes damage, swelling, and inflammation in the colon, ileum, and other parts of the digestive system.

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Inflamed intestine

White blood cells start to damage healthy cells and send messages to attract more white blood cells



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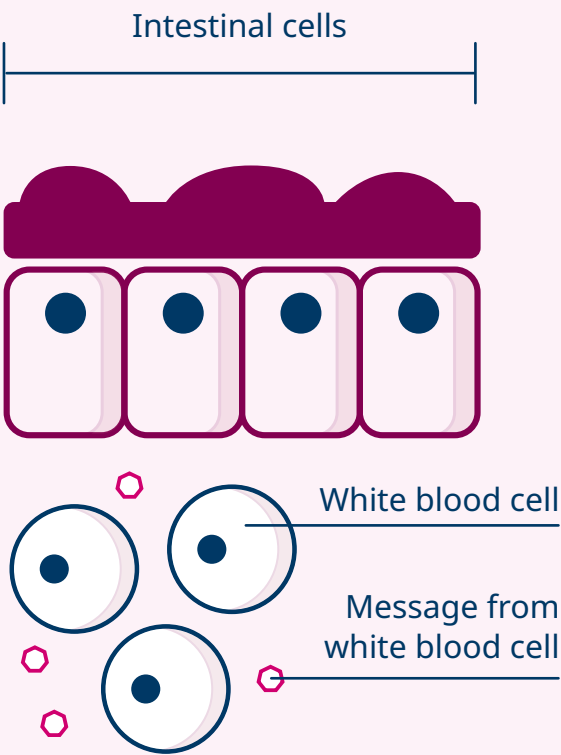
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3

Chronic inflammation in intestine

More white blood cells arrive, causing more damage and leading to the symptoms of Crohn's disease



Expand diagram

2. Understanding Crohn's disease

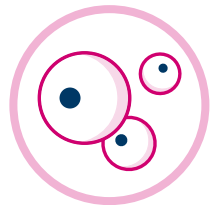
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What causes Crohn's disease?

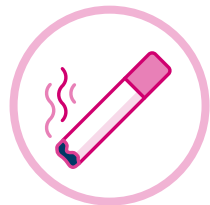
At the moment, the cause of Crohn's disease is still unknown, but scientists think it might be a combination of different things, including:



Your genes



Problems with your immune system



Smoking



A previous stomach bug



The types of bacteria in your digestive system

2. Understanding Crohn's disease

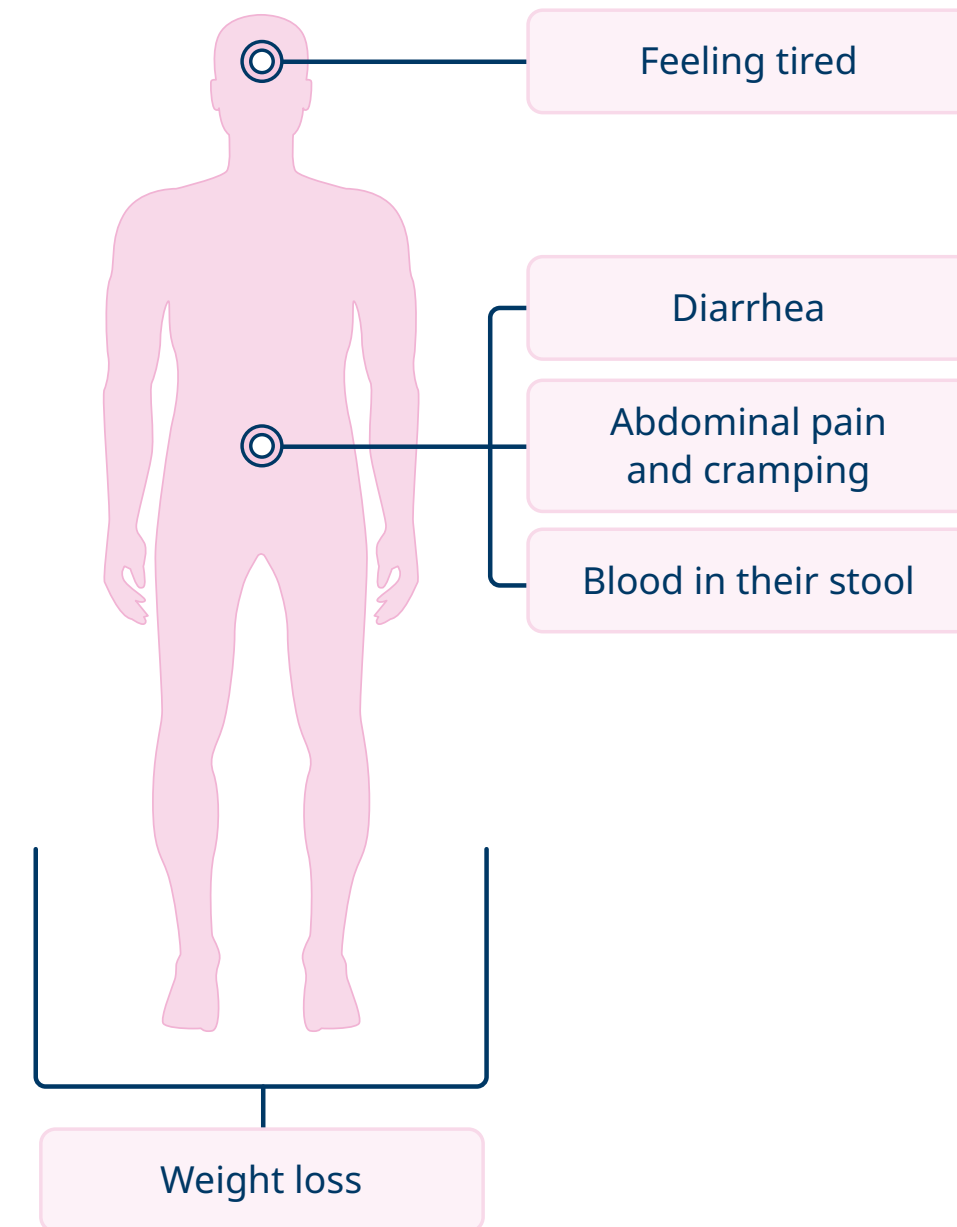
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What are the symptoms of Crohn's disease?

Depending on which part of the digestive system is affected, the symptoms of Crohn's disease may vary.

*People may experience periods of time with strong symptoms (**flares**) followed by periods of time with few symptoms or no symptoms at all (**remission**).*

People may experience none, some, or all of these symptoms:



2. Understanding Crohn's disease

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Current treatment options

Generally, treatments used to control symptoms of Crohn's disease aim to reduce, regulate, or normalize inflammation. You may also require medications to control any infections of your digestive system, or vitamins and minerals to improve your nutrition.

If symptoms do not improve with medication, some people with Crohn's disease have surgery to remove part of their intestines.

You can ask your doctor about treatments used to control symptoms of Crohn's disease and what treatments are best for you.

3. Why have I been asked to take part in this study?

3. Why have I been asked to take part in this study?

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You have been asked to take part in the INTREPID study because you:



Are aged between 18 and 80



Have been diagnosed
with Crohn's disease and
have been told you have
active disease



Have had no response
or an insufficient response
to previous treatment
for Crohn's disease



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4. What is the study treatment?



4. What is the study treatment?

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Brazikumab

Brazikumab is a type of protein called an **antibody** that may help prevent and reduce inflammation.

How does brazikumab work?

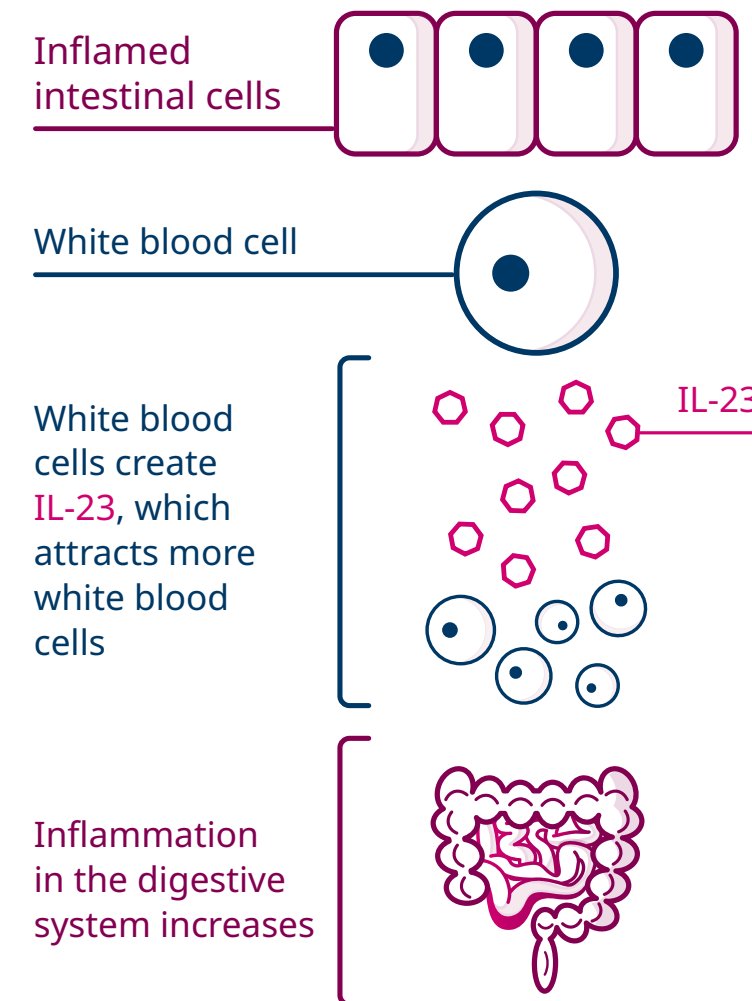
The white blood cells that make up your immune system use different types of proteins, called **interleukins**, to send messages to each other. These proteins help to organize immune responses.

In Crohn's disease, a particular type of interleukin, called interleukin-23 (**IL-23**), attracts new white blood cells to areas of inflammation, making it worse.

Brazikumab is designed to stick to IL-23. This helps to stop IL-23 from binding to white blood cells, meaning they can't get involved in inflammation.

Without brazikumab

With
brazikumab



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4. What is the study treatment?

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Brazikumab

Brazikumab is a type of protein called an **antibody** that may help prevent and reduce inflammation.

How does brazikumab work?

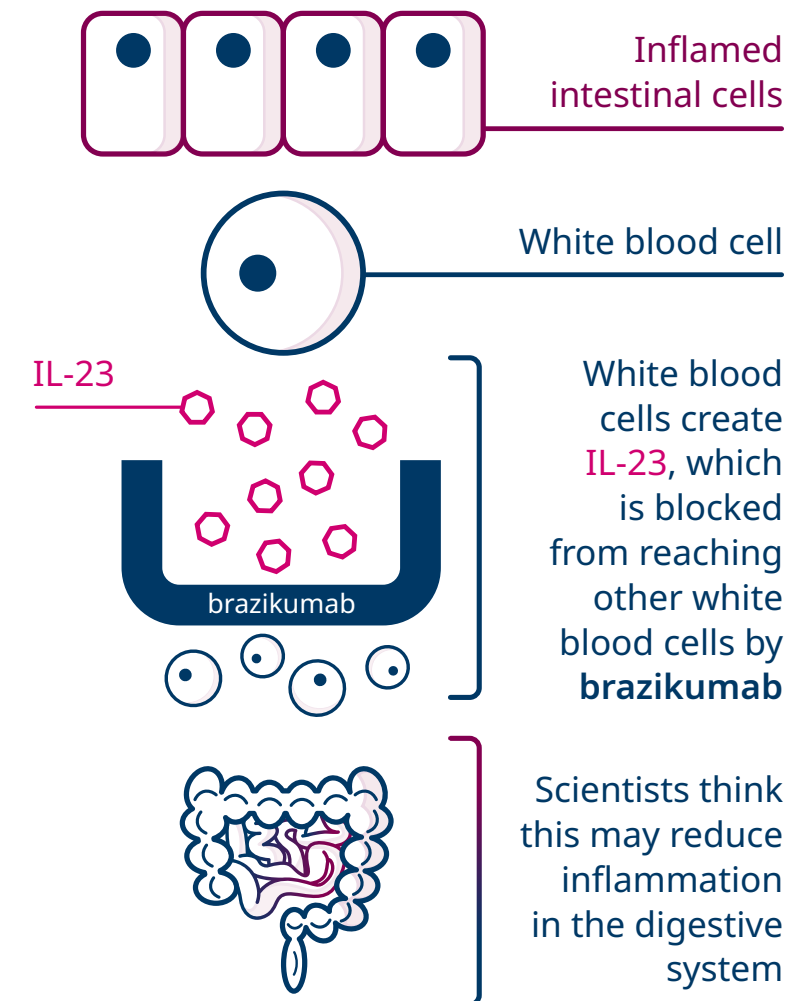
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Without
brazikumab

With brazikumab



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4. What is the study treatment?

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Why is brazikumab being investigated?

Previous clinical research has provided results showing that brazikumab may help in treating Crohn's disease. Scientists still need more information to make sure brazikumab is established as a safe and effective therapy option for people with Crohn's disease.



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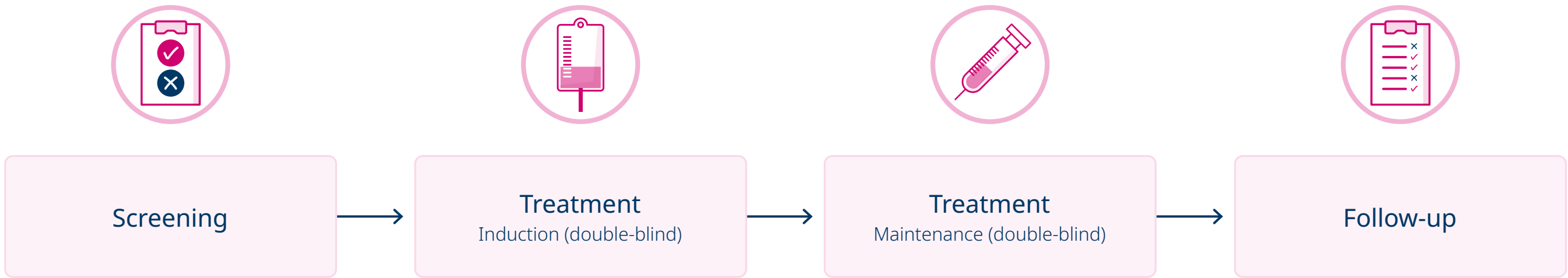


5. Study structure

5. Study structure

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Your study journey will be split into four parts: **screening**, **treatment (induction)**, **treatment (maintenance)**, and **follow-up**.



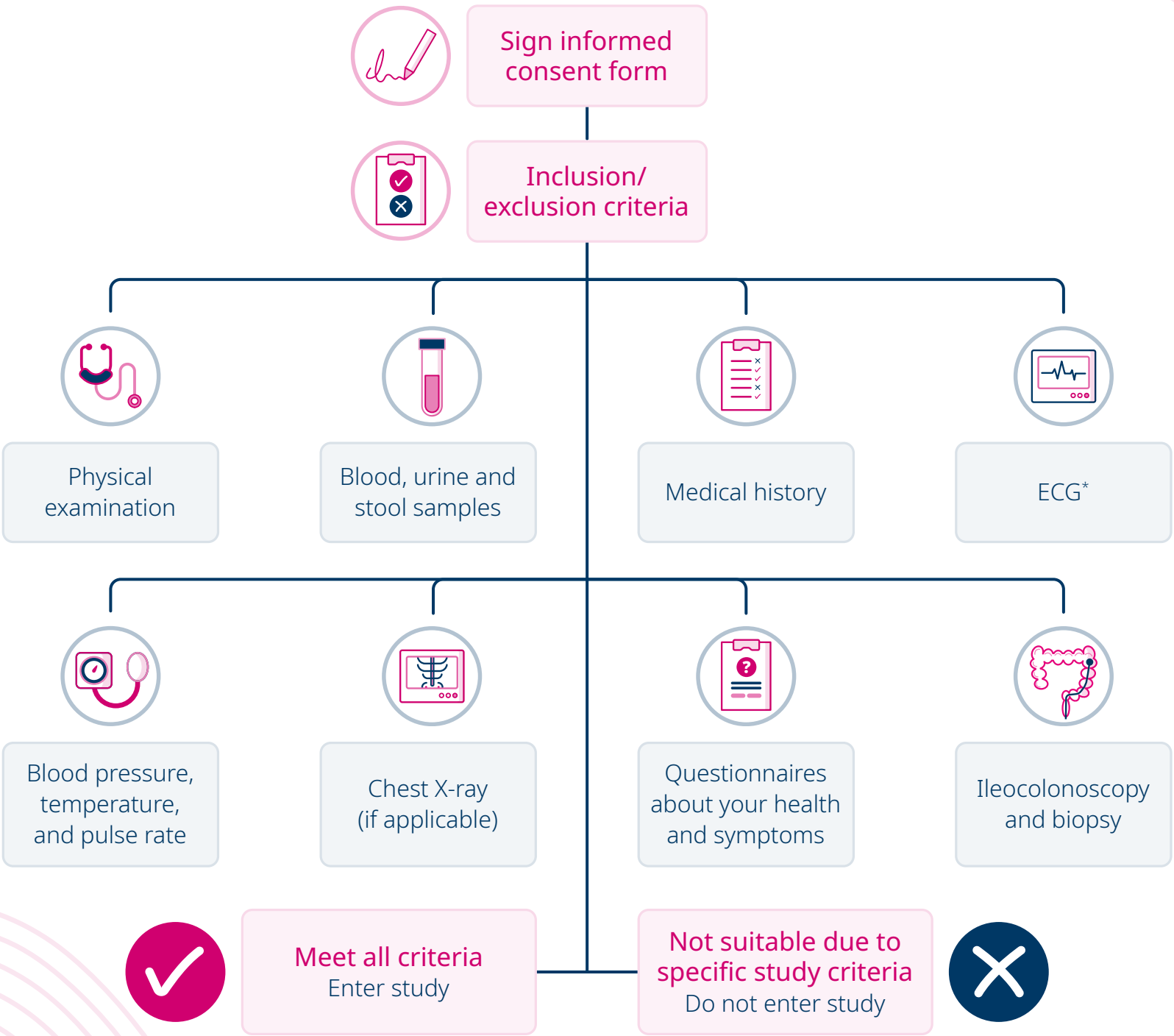
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Screening

During screening, the study team will check whether or not you can take part in the study. Screening may last up to **5 weeks** and you will be asked to attend a few appointments and undergo a number of tests. These tests will help the study team decide whether you can take part in the study.

If the study doctors decide you can take part in this study, you will be enrolled into the treatment period.



*ECG = electrocardiogram.

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Treatment

Treatment includes two periods: induction and maintenance. If you complete both, it will last **52 weeks**.

During the treatment period, you will be asked to come to the study clinic for appointments and receive various tests and assessments.

Alternative options for clinic visits may be available in case of study disruption. More information about this can be found in the **Appendix** section of this guide.

What will happen in the treatment phase?

In this study, brazikumab will be compared against a dummy treatment called a **placebo**. Placebos are used to find out if a treatment is actually working. The placebo will look like the study treatment and will be given in the same way.

The study will have three different treatment groups: a brazikumab high-dose group, a brazikumab low-dose group, and a placebo group. The group you are in will be chosen at random by a computer (**randomized**).

During treatment, neither you nor your study doctor will know which group you are in. That's why this part of the study is called **double-blind**.

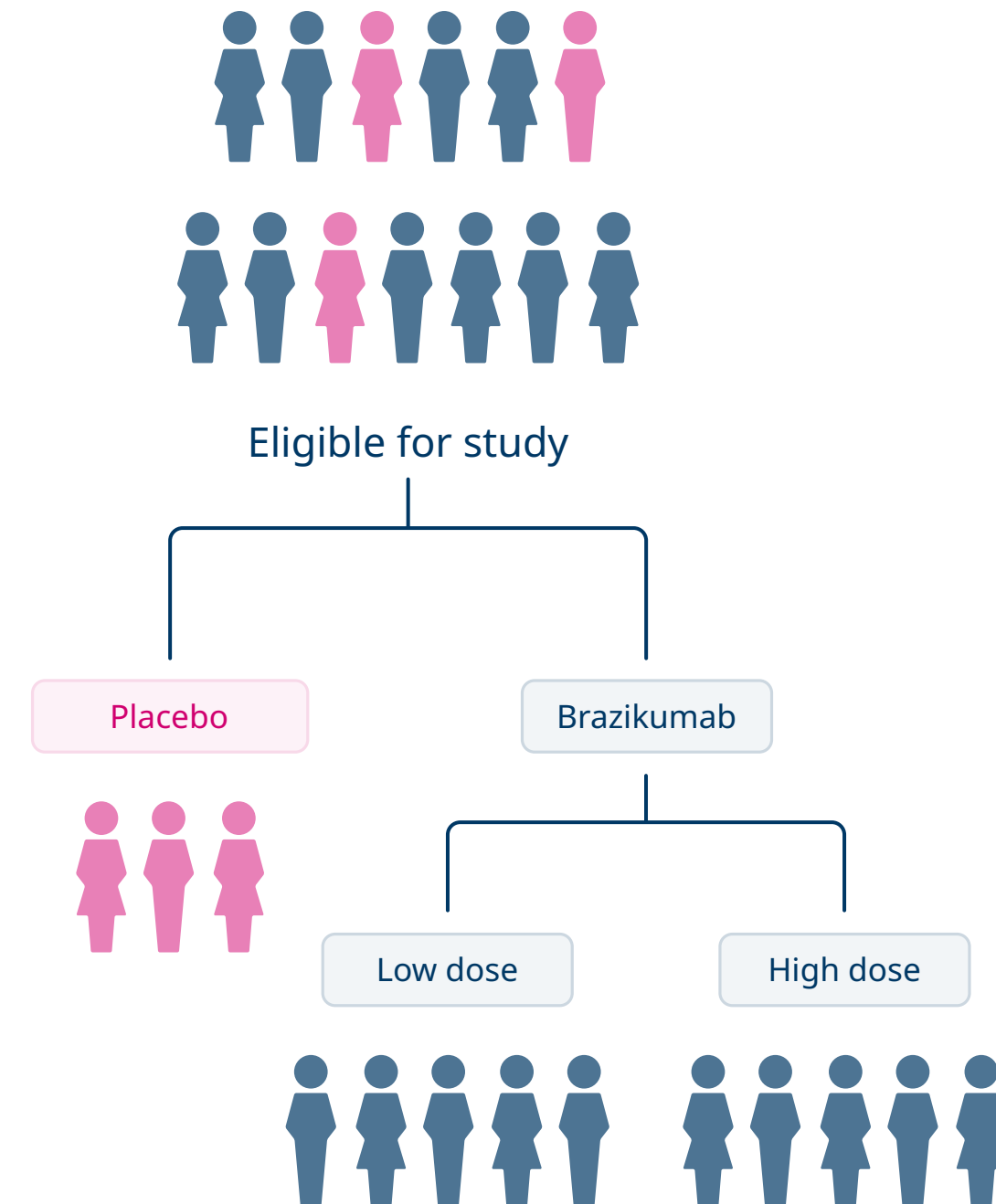
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You will have around a 75% chance of receiving brazikumab, and around a 25% chance of receiving placebo.

After the induction period, your study doctor will review whether your signs and symptoms have improved.

If you and your study doctor decide brazikumab is working for you, you will move into the maintenance period. If not, other treatment options will be discussed with you.



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How will my study treatment be given?

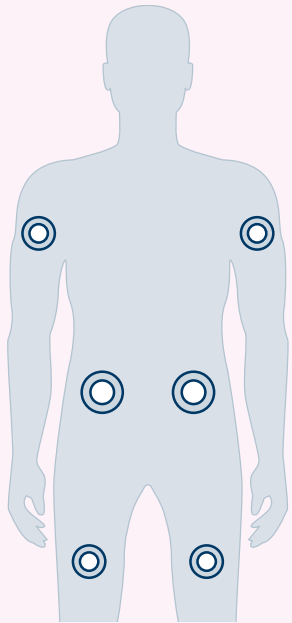
The study treatment will be given in two different ways at different times during the study.



By infusion into a vein (**intravenous**) during the induction period. Each intravenous infusion you receive will take around **60 minutes**



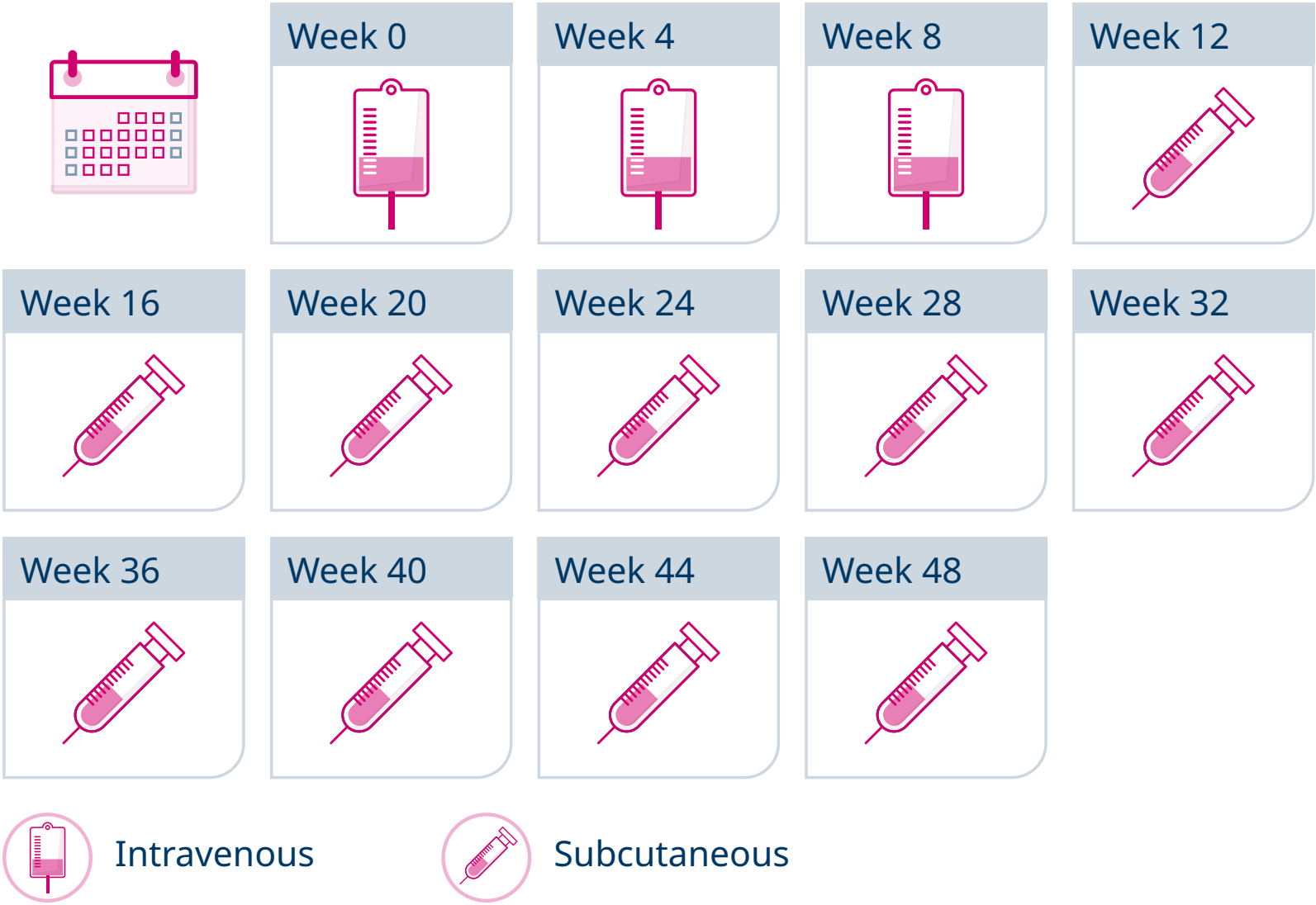
By injection into the fatty layer under your skin (**subcutaneous**) during the maintenance period. During clinic visits (or home visits if applicable) with subcutaneous injections, you will receive two injections, at least 2 cm apart. The injections will be given in a different area of your body (upper arm, thigh or abdomen) each time, as shown on the diagram. The total administration time for subcutaneous injections will be around **10 minutes**



5. Study structure

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You can find out more information about when you will receive intravenous infusions and subcutaneous injections in this calendar:



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What are the tests and assessments?

The tests and assessments you will have during clinic visits may include:



Patient-reported outcome (PRO) questionnaires

To understand any symptoms you may be experiencing. More information on PROs can be found later in this section



Ileocolonoscopy

A small flexible camera called an endoscope will be used to examine your colon and ileum to check for signs of inflammation in your digestive system



Biopsy

To study the inflammation in your digestive system



Physical examination

To check your overall health, measure your height and weight, and look at symptoms of Crohn's disease



Vital signs

To measure your blood pressure, temperature, and pulse rate



Electrocardiogram

To check that your heart is working properly



Blood tests

To check how your body is responding to the treatment and check your health



Urine tests

To check your health

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Stool sample tests
To check the level of inflammation in your intestines



Chest X-ray (if required)
If your tuberculosis test is positive or inconclusive, or if you have used certain medications to treat your Crohn’s disease. Your study doctor will let you know if you need a chest X-ray

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Using your eDiary device

One of the most important things you will be asked to do during the study is fill out questionnaires, called **patient-reported outcomes (PROs)**.

During the study, you will be given an electronic hand-held device, which you will be trained to use and will take home with you. This device will allow you to answer some questions about your health and about any symptoms you may be experiencing. Some of these questionnaires are to be completed at home, and some are to be completed during study visits.

- Daily questionnaires should take approximately **5–10 minutes**
- Periodic questionnaires during study clinic visits should take **10–20 minutes**
- You will receive icon reminders on the eDiary device when it is time for completion
- There are no right or wrong answers
- You should answer the questions yourself and not let anyone else alter them
- It is important to always keep your eDiary device charged
- If your eDiary device stops working, please contact the site for assistance as soon as possible
- Remember to bring your eDiary device to every study clinic visit as you will also be asked to complete questionnaires during your visits

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Some of the questionnaires you will fill out on your eDiary device will include:

- Daily questionnaires about each bowel movement you have had
- Daily questionnaires about your Crohn’s disease signs and symptoms
- Study clinic visit questionnaires related to your overall health



Completing the eDiary questionnaires is a very important part of this study. By completing the eDiary questionnaire you will help the study doctors understand, from your perspective, how the treatment is affecting your health and quality of life.

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Calendar of tests and assessments

You can find out more about what tests and assessments to expect during clinic visits in this calendar:



Weeks shown in pink will feature longer clinic visits

*Please collect your stool samples at home and bring them with you for clinic visits.

Week 0



- Vital signs
- Physical
- ECG
- Blood/urine samples
- Stool sample*

Week 2

- Vital signs
- Physical
- Blood/urine samples

Week 4



- Vital signs
- Physical
- Blood/urine samples

Week 8



- Vital signs
- Physical
- Blood/urine samples

Expand diagram

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Calendar of tests and assessments

You can find out more about what tests and assessments to expect during clinic visits in this calendar:



Weeks shown in pink will feature longer clinic visits

Week 12



- Vital signs
- Physical
- Ileocolonoscopy
- ECG
- Blood/urine samples
- Stool sample*

Week 16

- Vital signs
- Physical
- Blood/urine samples

Week 20

- Vital signs
- Blood/urine samples

Week 24



- Vital signs
- Physical
- ECG
- Blood/urine samples
- Stool sample*

*Please collect your stool samples at home and bring them with you for clinic visits.

Expand diagram

5. Study structure

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Calendar of tests and assessments

You can find out more about what tests and assessments to expect during clinic visits in this calendar:



Weeks shown in pink will feature longer clinic visits

*Please collect your stool samples at home and bring them with you for clinic visits.

Week 28

- Vital signs
- Blood/urine samples

Week 32

- Vital signs
- Blood/urine samples

Week 36

- Vital signs
- Physical
- Blood/urine samples

Week 40

- Vital signs
- Physical
- ECG
- Blood/urine samples
- Stool sample*

Expand diagram

5. Study structure

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Calendar of tests and assessments

You can find out more about what tests and assessments to expect during clinic visits in this calendar:



Weeks shown in pink will feature longer clinic visits

Week 44

- Vital signs
- Blood/urine samples

Week 48

- Vital signs
- Physical
- Blood/urine samples

Week 52



- | | |
|-----------------|---------------------|
| Vital signs | Blood/urine samples |
| Physical | Stool sample* |
| Ileocolonoscopy | |
| ECG | |
| Chest X-ray | |

*Please collect your stool samples at home and bring them with you for clinic visits.

Expand diagram

5. Study structure

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Lifestyle considerations

Please do not use any products containing nicotine (including nicotine patches) when you are receiving treatment at the clinic. You are also strongly encouraged not to eat or drink anything containing caffeine for a minimum of 1 hour before your clinic visit.



Tobacco



Coffee

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Follow-up

What happens after the study treatment is stopped?

Your study doctor will discuss further treatment options with you after you complete the study (Week 52 visit) or if you stop taking the study treatment and attend an **Early Termination Visit**. Further treatment options may include participating in an open-label extension study. Your study doctor will be able to provide you with more information about this.

If your doctor determines that you cannot take part in the extension study, or if you do not wish to, you will continue to have study visits to be evaluated for safety until 18 weeks after your last dose of the study drug. This is called **follow-up**.

During these appointments, your study doctor may conduct tests to check your health and follow up on any issues you may have experienced with the treatment.

You will have some similar tests to the ones you received during treatment, including physical examinations, blood tests, ECGs, and tests to measure your vital signs.

6. What kind of samples will be requested from me?

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During the study you will be required to:

- Have blood and urine samples collected at some study visits
- Collect stool samples at home and bring them to some of your study visits
- Have some tissue samples (biopsies) collected during the ileocolonoscopy

Your study doctor or nurse will let you know when these will take place. These samples are important to check your overall health, to monitor your Crohn's disease, and to collect information on brazikumab and how it works.

6. What kind of samples will be requested from me?

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Optional blood sample for genetic research

In addition to participating in the main study, you will also be asked if you are willing to donate an extra sample of your blood for DNA analysis. This sample will allow researchers to study how genes affect Crohn's disease.

You will be asked to sign a separate informed consent form (ICF) for this sample to be collected. You can still take part in the main study even if you do not agree to have this optional blood sample collected.



Future research

Some of your stored blood samples and images from your ileocolonoscopies may also be used in research to help find new ways to detect and treat diseases in the future.

To protect your privacy, none of your personal information will be included with the blood samples and images that are stored for these types of research.



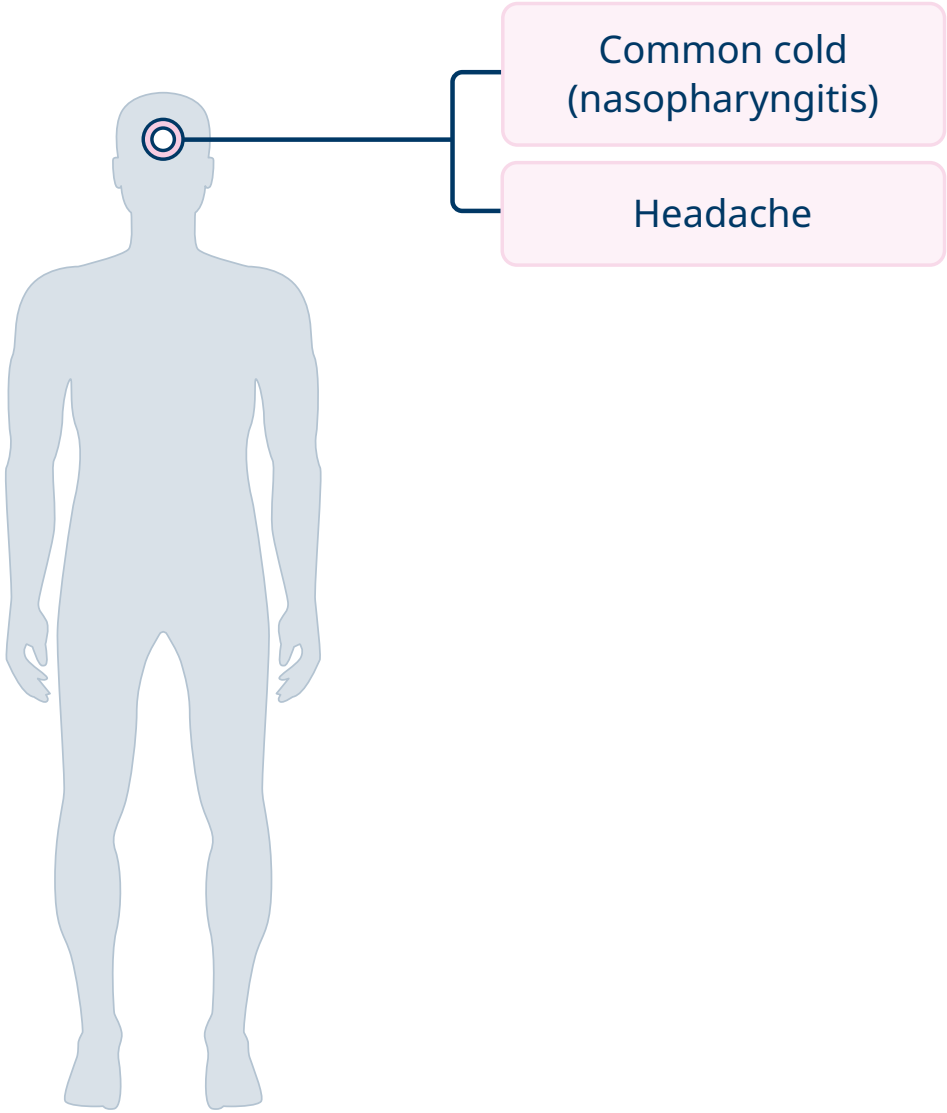
7. Does the treatment have any side effects?

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Contents

As with all medicines, there are side effects associated with the study treatment. Included here is a list of the most common side effects of brazikumab. You may experience none, some, or all of those listed. For a full list of side effects that may be associated with treatment, please ask your study doctor.

Very common side effects of brazikumab (affecting 1 in 10 people) include:

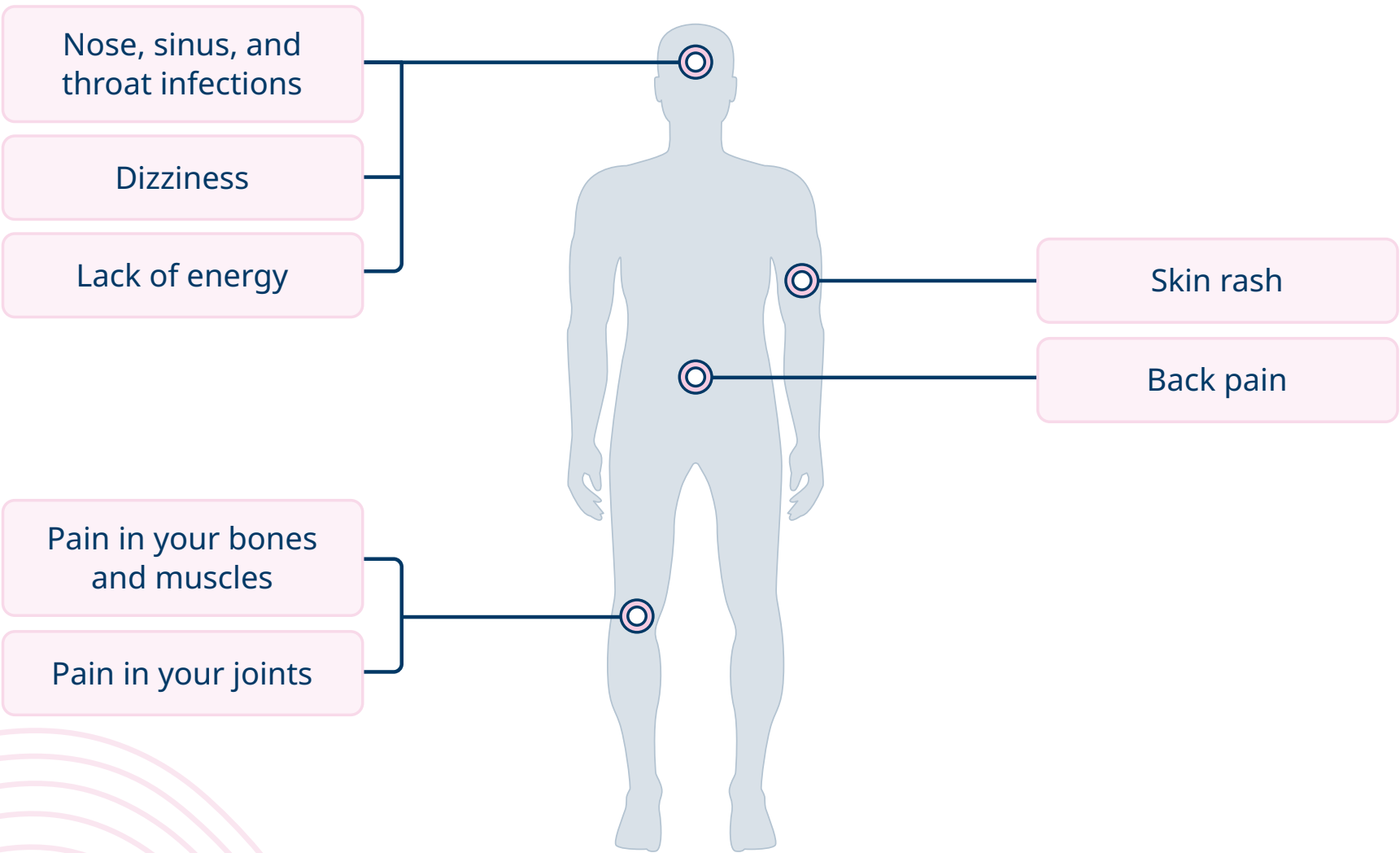


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Common side effects (affecting 1 in 100) include:



7. Does the treatment have any side effects?

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Infusion-related reactions and injection site reactions

You might experience a reaction at the area on your body used to give the study treatment.

This may include:



Itching



Swelling



Redness



Pain

Your study doctor will monitor you for any signs of this.



7. Does the treatment have any side effects?

Contents

Allergic reactions

Like with other medications, some people may have an allergic reaction to brazikumab, which may be severe. This can happen within hours or days after the injection, and you can recognize this by the following symptoms:



Swelling of the lips



Breathing problems



Fainting



Dizziness



Hives



Skin rash




Fast pulse



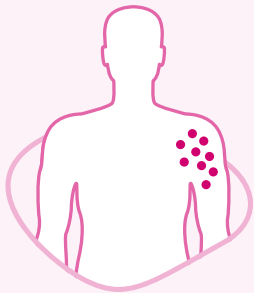
Sweating



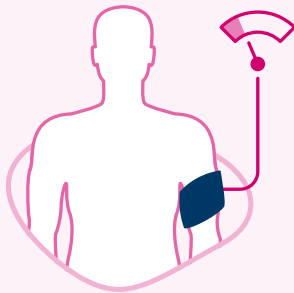
7. Does the treatment have any side effects?

 A serious type of allergic reaction known as **anaphylaxis** may occur and could be life-threatening.


Anaphylaxis can be indicated by these symptoms:



Rash



Drop in blood pressure



Difficulty in breathing

You will be observed in the clinic by the study doctor after each injection to monitor for any serious reactions. If you develop any of these symptoms after monitoring, or if you think you may be having a reaction to the study treatment, **please go to hospital immediately**.

For more information on these side effects, please see the ICF and ask your study doctor.

 **There is always a risk with taking a new medicine. If any side effects are troubling you, please report them to your study doctor.**

7. Does the treatment have any side effects?

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Study discomforts

Some of the tests may cause some discomfort.
You may experience none, some, or all of those listed.

Your study doctor will follow you closely throughout the entire study for side effects or discomfort. It is important to report any new illnesses, changes in medication, side effects or allergic reactions you may be experiencing to your study doctor as soon as possible.



Blood tests

You may feel lightheaded when having blood samples taken and experience some discomfort (such as pain or swelling) in the area where the needle will be inserted.



ECG

You may experience some redness and irritation in the areas where the electrodes are attached.



Ileocolonoscopy and biopsy

The ileocolonoscopy procedure may cause discomfort, and you may experience bleeding in areas where biopsies are taken. You may also experience reactions and side effects to the bowel prep medications, and to the medicine used to sedate you during the procedure.

8. What if I need further support or information?

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Please carefully read the information provided in your Informed Consent Form, which may contain additional details about the study and potential risks. If you have any questions or you are worried, you can call your study team at any time.

You will also be given a Patient Participation/Information Card which includes contact details about your clinic and study doctor/team in case of any medical problem you may encounter or if you need more information about the study.

For extra support:

If you would like some more information on your condition, your study team should be able to provide details of useful websites.

9. Can I change my mind?



9. Can I change my mind?

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YES – taking part in this study is entirely up to you.

You can stop at any time, whatever the reason,
and it will not affect your standard of care.

If you want to stop, you need to let your study doctor
know so that they can discuss the next steps with you.



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9. Can I change my mind?

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If you do stop, you can decide whether to:

Withdraw from treatment

OR

Withdraw your consent



You stop taking the study treatment



You will be encouraged to return for all regular clinic and phone call visits



The study clinic can still collect information on how safe and effective the treatment is



You stop taking the study treatment



You will need to attend a final safety evaluation appointment



You stop being part of the study, but will be contacted by a study doctor to check on your well-being, as part of standard medical care



You may request for your blood, urine, stool, and/or tissue samples to be destroyed



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10. Frequently asked questions

10. Frequently asked questions

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What are the costs of taking part in the study?

Participating in this study will not cost you anything. The study drug, study visits, tests and examinations are free of charge.

Will I be compensated for taking part in the study?

You will not be paid for taking part in the study. However, if applicable, you may be reimbursed for reasonable expenses incurred due to your participation in the study (for example: parking).

What happens if I become ill or have an injury during the study?

If you experience any side effect or injury, it is important to let your study doctor know immediately, so you can receive the appropriate medical treatment.

Where can I find out more information after the study?

A short summary of the study results will be added to www.trialssummaries.com after the study has ended. You can visit this website anytime to sign up to be notified when a summary of your study is available. You can also let your study doctor know if you would like a printed copy of the document.



It is very important to complete the study questionnaires and report any changes in your health or any changes in the medicine you are taking to your study doctor.

11. Glossary



11. Glossary

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Anaphylaxis	A serious type of allergic reaction that can be life-threatening.
Antibody	A protein in your blood that responds to bacteria, viruses, and other substances in the blood which your body identifies as foreign.
Colon	The large intestine.
Double-blind	A clinical trial in which neither you nor your study doctor know which treatment you are receiving.
ECG (electrocardiogram)	An assessment to check if your heart is working properly.
eDiary	A questionnaire about your well-being that is answered on an electronic handheld device. You will also be able to record any symptoms you may be experiencing.

Genetic testing	Genes are the instructions which allow a cell to produce a specific protein. Genetic testing uses tests to look at any possible differences in the make-up of your genes.
Ileocolonoscopy	An assessment with a device called an endoscope, which is a flexible camera used to examine your digestive system. An ileocolonoscopy uses an endoscope to examine your colon (large intestine) and ileum (final part of your small intestine).
Ileum	The final part of your small intestine, linked to your large intestine.
Infusion-related reaction	A type of reaction, which might be similar to anaphylaxis, and might occur after receiving an intravenous infusion.

11. Glossary

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Open-label	A clinical study in which both you and your study doctor know which treatment you are receiving.
Placebo	A harmless dummy treatment designed to look exactly like the real study treatment.
Randomize	Randomly select whether a person will receive treatment or placebo during a clinical study (usually done by a computer).

Pronunciation guide

Anaphylaxis	an-ah-fil-ax-is
Brazikumab	bra-zik-oo-mab



Appendix

Alternative options in case of study disruption

Due to unexpected circumstances leading to study disruption (for example, public health crises, civil crises, or natural disasters) you may not be able to or may not want to go to the clinic for study visits. Alternative options for certain study visits may therefore be made available to you.

The following options may be made available to you during the study:



A telemedicine visit

Contact between yourself and your study doctor using a smartphone, computer, or other device. Your doctor will use this call to discuss things like any symptoms and side effects you are having, and to answer your questions.



Home or remote visit

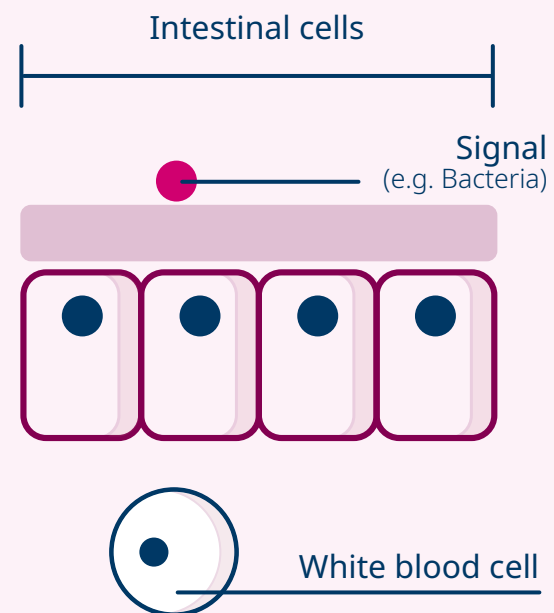
It may be possible to have brazikumab administered at home by a doctor or nurse. During these visits, the doctor or nurse can also perform most tests and assessments.



1

Healthy intestine

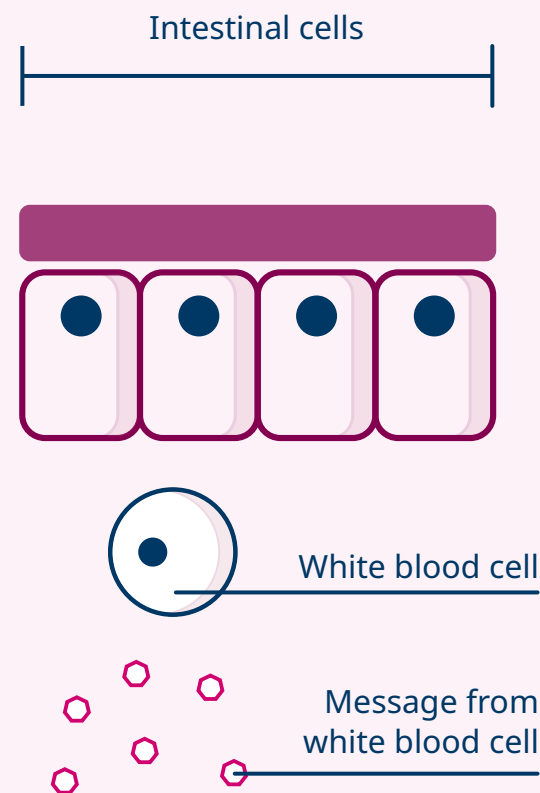
White blood cells respond to a signal, such as bacteria



2

Inflamed intestine

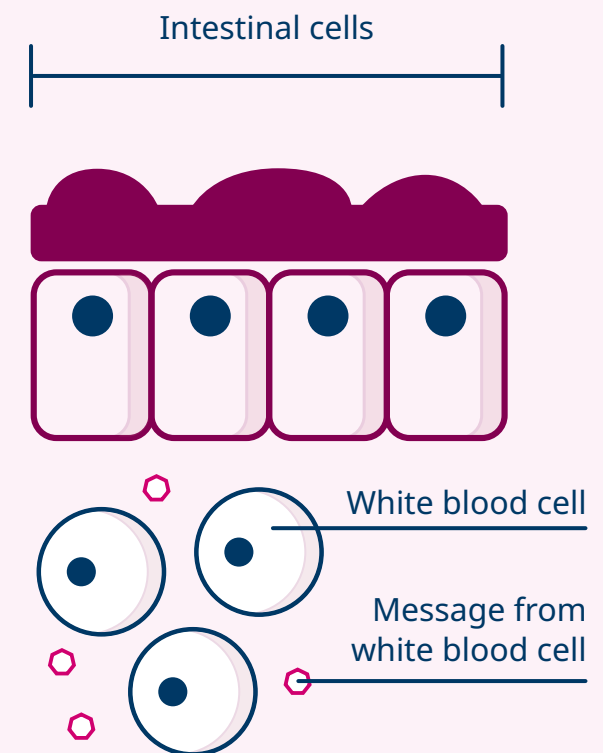
White blood cells start to damage healthy cells and send messages to attract more white blood cells



3

Chronic inflammation in intestine

More white blood cells arrive, causing more damage and leading to the symptoms of Crohn's disease



Close diagram

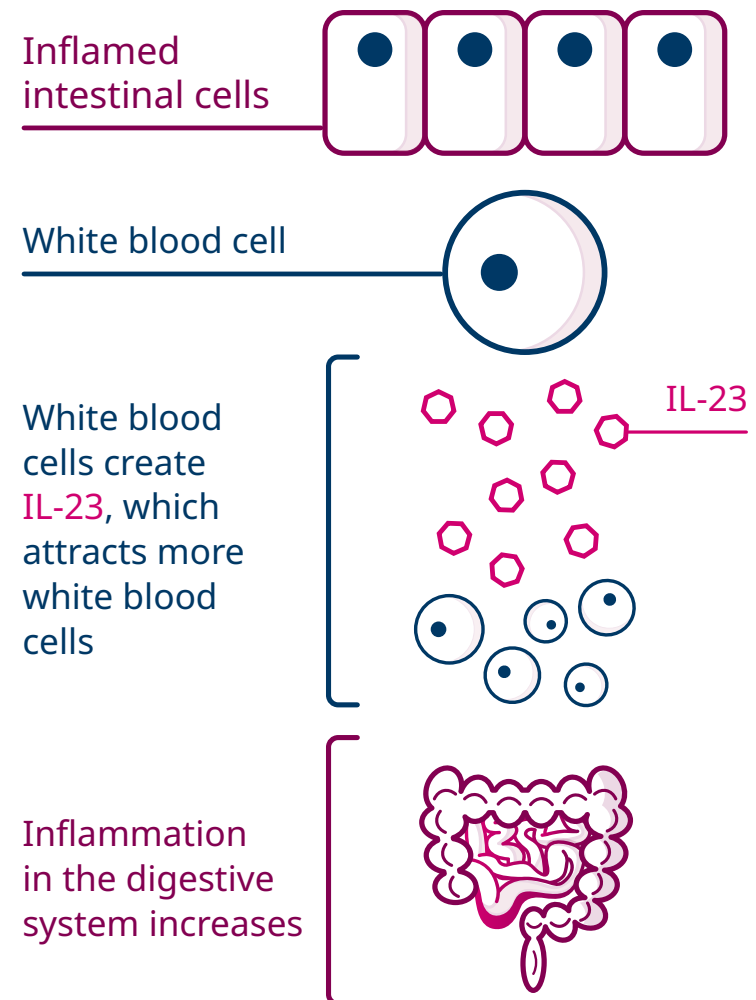


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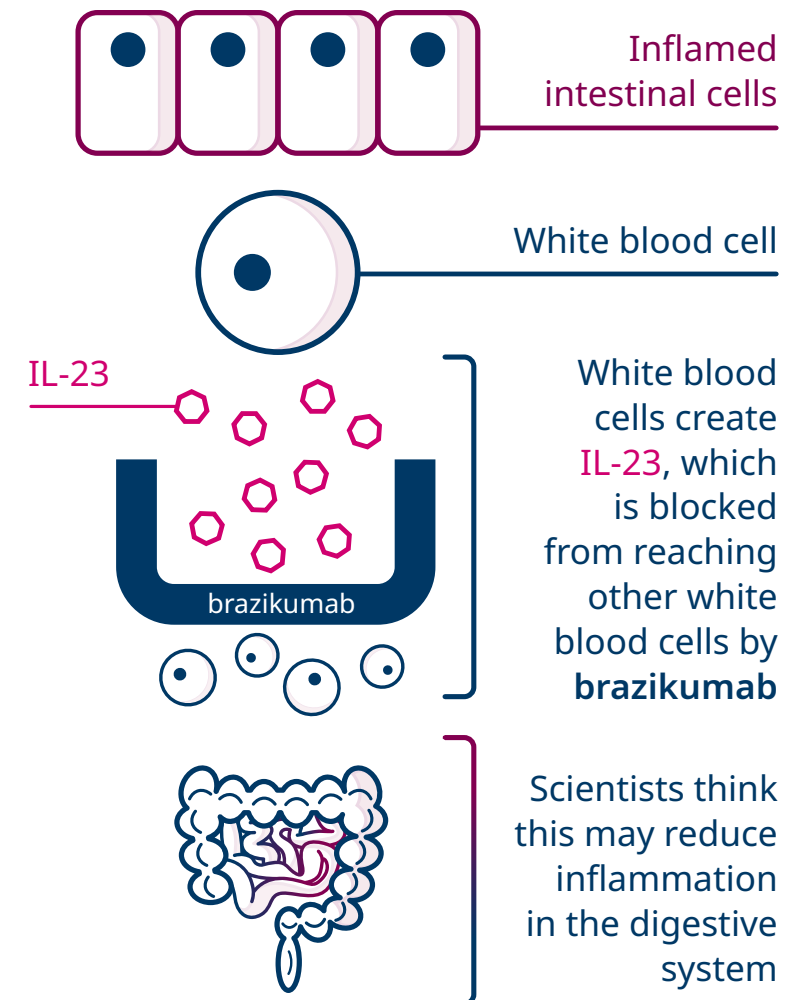


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Without brazikumab



With brazikumab





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Close
diagram



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