



## **Clinical Trial – Lay Summary**

A clinical trial that compared a new drug (zoliflodacin) with the standard drugs (a combination of ceftriaxone and azithromycin) for the treatment of gonorrhea.

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## 1. The purpose of this lay summary

This summary explains why and how this trial with zoliflodacin was done and what the results were. It has been written using plain language so that the general public can understand these results and what they mean. Researchers need to carry out many trials to work out how well a new drug works and if it is safe. This lay summary only describes the results of this one trial. The results may be different from other trials with zoliflodacin, or other trials in people with gonorrhea.

## 2. What did this trial set out to find?

Drugs that kill bacteria are known as “antibiotics.”

When antibiotics no longer kill bacteria, this is called “resistance.”

Because of resistance, we need new drugs to carry on treating diseases like gonorrhea.

Doctors are concerned that in a few years’ time, antibiotics will no longer kill the bacteria that cause some diseases. If a disease caused by a bacteria cannot be cured, then people may become very ill and large numbers of people could become infected. Doctors and scientists are looking for new antibiotic drugs that work in different ways so that they can replace the old drugs when they no longer work.

Gonorrhea is caused by a specific type of bacteria. A person catches gonorrhea by having sex with someone who already has it (known as a sexually transmitted infection, or STI). Because of resistance, we will need new antibiotic drugs in the next few years to stop gonorrhea spreading to more and more people.

Zoliflodacin is a new antibiotic that stops the gonorrhea bacteria from growing. This trial was done to see if zoliflodacin was no worse at treating gonorrhea than the drugs that doctors use today. The researchers also wanted to know what side effects people had when they took zoliflodacin and if they were similar to those with the drugs used today.

## 3. Where and when did the trial take place?

This trial is called “STI\_Zoli001”. It started in November 2019 and ended in March 2023.

This was the biggest trial ever done in people with gonorrhea around the world. In total, 930 people took part, and they came from the following countries:

Country	Number of people who took part
Belgium	9
Netherlands	69
South Africa	424
Thailand	270
USA	158
<b>TOTAL</b>	<b>930</b>

#### **4. Who could take part in the trial?**

A person could take part in the trial if they were:

- 12 years of age or older
- Had any of the following:
  - symptoms of gonorrhea in or on their genitals (penis or vagina), OR
  - a laboratory test found the gonorrhea bacteria in or on their genitals, OR
  - sex with someone who has gonorrhea

#### **5. What was done to people in the trial?**

At the start of the trial, everyone had a check-up. Swabs were used to take samples from the genitals, the rectum and the throat to test for the bacteria that causes gonorrhea.

Swabs were taken again 6 days and 30 days after the drugs were given to see if the bacteria was still there. If all the gonorrhea bacteria were dead, then the drug had worked, and this was called a cure.

Checks were made during the trial and at the end of the trial to see if anyone had any side effects. Blood samples were also taken to check if the drugs were safe.

#### **6. What drugs were given to people in the trial?**

People were placed by chance into one of two groups. Each group was given a single dose of antibiotic as follows:

Either

- The “new drug” (zoliflodacin) dissolved in a cup of water

Or

- “Standard drugs” used by doctors today to treat gonorrhea. These were given as an injection of ceftriaxone and a tablet of azithromycin.

Twice as many people were given the new drug as were given the standard drugs. This was done so that the researchers could get as much information as possible about the new drug.

#### **7. What kind of people took part in the trial?**

The trial included young people, adult men and women and people from a range of racial backgrounds. The groups of people that took the new drug (zoliflodacin) and those that took the standard drugs were very similar as shown in the table below.

In all, 930 people took part in the trial. The swabs at the start of the trial showed that 744 people had a gonorrhea infection in their genitals.

Characteristics	New drug	Standard drugs
<b>Age</b>		
Less than 18 years	2%	1%
18 years and older	98%	99%
<b>Sex at birth</b>		
Female	12%	12%
Male	88%	88%
<b>Race</b>		
White people	11%	15%
Black or African American people	56%	53%
Asian people	31%	30%
People of other races	2%	4%

## 8. What were the trial results?

### What was the main result?

The new drug (zofludacin), was as good as the standard drugs in getting rid of the gonorrhea bacteria from the genitals.

The table below shows that the percentage of people with a cure was similar, as there was only a 5% difference between the groups. The statistics confirmed that the new drug (zofludacin) worked as well as the standard drugs (you can read more about the statistics in the box below if you wish).

	New Drug	Standard Drugs
Number of people with a cure	460 out of 506 people <b>(91%)</b>	229 out of 238 people <b>(96%)</b>
Statistics	Difference between the new drug and the standard drugs is 5% (95% confidence interval: 1% to 9%)	

### What do the statistics tell us about the main result?

- The standard drugs used today cure most people, so the researchers designed the trial to see if zoliflodacin was no worse than the standard drugs.
- The results for the standard drugs and the new drug were compared by looking at the difference in the percentage of people cured. Before the trial, researchers and medicine regulators agreed that if the difference of percentage cured was less than 12%, this showed that zoliflodacin was no worse than the standard drugs.
- The “95% confidence interval” shows a range of how accurate the results are. It means that the researchers can be 95% confident that the result didn’t just happen by chance.
- In this trial, the 95% confidence interval was 1% to 9%, so well under the agreed limit of 12%. This means that the researchers are sure that the new drug is no worse than the standard drugs.

### What were the other results?

As this was such a large trial, the researchers analyzed the results in different ways to find out how well zoliflodacin works. The most important of these other analyses are shown below. In most of these analyses, the percentage of people whose gonorrhea was cured was similar for the new drug (zoliflodacin) and for the standard drugs.

Type of analysis	People with a cure in this trial		Difference in percent
	New drug	Standard drugs	
Only people who followed the trial instructions correctly*	434 out of 452 people (96%)	218 out of 219 people (100%)	4%
Only men	412 out of 456 people (90%)	213 out of 220 people (97%)	7%
Only women	48 out of 50 people (96%)	16 out of 18 people (89%)	-7%
Only Black or African American people	241 out of 278 people (87%)	125 out of 128 people (98%)	11%
Only White people	51 out of 57 people (90%)	34 out of 38 people (90%)	0%
Only Asian people	158 out of 161 people (98%)	65 out of 67 people (97%)	-1%
People who also had a gonorrhea infection in their rectum	69 out of 79 people (87%)	31 out of 35 people (89%)	2%
People who also had a gonorrhea infection in their throat	42 out of 53 people (79%)	22 out of 28 people (79%)	0%
Improvement in symptoms of gonorrhea in men**	375 out of 460 people (82%)	194 out of 220 people (88%)	6%
*People in the trial who took other antibiotics, missed the clinic appointment or had unprotected sex after taking the trial drug were not included here.			
**Rather than looking for the gonorrhea bacteria, the doctor looked to see if the signs or symptoms of gonorrhea had gone away following treatment.			

### What do the results mean?

- All the results from this trial showed that zoliflodacin is no worse than the standard drugs that doctors use today for treating people with gonorrhea.
- Like the standard drugs, zoliflodacin treats gonorrhea in:
  - men and women
  - people of different races
  - people who have gonorrhea infection in their rectum or in their throat

## **9. What were the side effects?**

### How many side effects were there?

A side effect is any change in a person's health after taking the drug, whether it is caused by the drug or something else. The number of people who had a side effect during the trial was the same for those who took the new drug (46%) and for those who took the standard drugs (46%). The percentage of people with side effects that the doctor thought were possibly caused by the drug was similar for the two treatment groups. None of the side effects were serious enough to need urgent treatment, or a visit to hospital, and nobody died.

Type of side effect	Number and percentage of people	
	New drug group	Standard drugs group
People with any side effects	286 out of 619 people (46%)	143 out of 308 people (46%)
People with a side effect possibly caused by the drug*	117 out of 619 people (19%)	76 out of 308 people (25%)
People with serious side effects**	0	0
People who died	0	0
*This was the opinion of the doctor at the clinic		
**Side effects that needed urgent treatment or a visit to hospital, etc.		

The researchers were not concerned that 46% of people had a side effect as everyone in the trial had check-ups during the month after taking the drug. In this time there would be many everyday illnesses such as coughs, colds, headaches, feeling sick, stomach upsets, period pains and so on. The important thing here is that the new drug (zoliflodacin) and the standard drugs had similar numbers of side effects.

### How bad were the side effects?

Most of the side effects were mild or moderate and did not affect the daily activities of the people in the trial. This was the same for both the new drug and the standard drugs used today.

### What were the common side effects?

Most side effects were as expected for people taking antibiotics and were only seen in a few people. The side effects that occurred in more than 2% of people are shown below.

Side effect	Number and percentage of people	
	New drug group	Standard drugs group
Low levels of white blood cells (all types)	66 out of 619 people (11%)	39 out of 308 people (13%)
Headache	61 out of 619 people (10%)	14 out of 308 people (5%)
Pain or soreness after injection	5 out of 619 people (1%)	38 out of 308 people (12%)
Diarrhea (loose or watery bowel movements)	15 out of 619 people (2%)	22 out of 308 people (7%)
Nausea (feeling sick)	16 out of 619 people (3%)	12 out of 308 people (4%)
Dizziness	21 out of 619 people (3%)	5 out of 308 people (2%)

Some people in both groups had low levels of white blood cells when measured in a blood test but there was no difference seen between the treatments. No one in the study had any health problems associated with low levels of white blood cells and the researchers were not concerned.

Pain or soreness after the injection was mainly seen in people who took the standard drugs. This was expected because one of these drugs (ceftriaxone) was given as an injection.

#### What do the results on side effects mean?

- When taken together, the results for the side effects showed that zoliflodacin was similar to the standard drugs used to treat gonorrhea (ceftriaxone in combination with azithromycin).
- Nobody had a side effect that made them seriously ill and nobody died, so the researchers think that the new drug (zoliflodacin) is as safe as the standard drugs.

#### **10. What are the next plans for zoliflodacin?**

The results of this trial were positive. Zoliflodacin was no worse than the combination of ceftriaxone and azithromycin for the treatment of gonorrhea and the side effects were similar.

The researchers will now give the results to the medicine regulators around the world.

The medicine regulators in each country will look at the trial results carefully. If they agree that the results are good and the drug is safe to give, they will let doctors in their countries use zoliflodacin to treat gonorrhea.



The health regulators may disagree and ask the researchers to provide more information or to do another trial.

These are the normal steps before a new drug can be used by doctors. This may take some time but the researchers will work with the health regulators to make zoliflodacin available as a new treatment for gonorrhea as soon as possible.

## **11. Further information**

### *What is the full title of this trial?*

“A Multi-center, Randomized, Open-label, Non-inferiority Trial to Evaluate the Efficacy and Safety of a Single, Oral Dose of Zoliflodacin Compared to a Combination of a Single Intramuscular Dose of Ceftriaxone and a Single Oral Dose of Azithromycin in the Treatment of Patients With Uncomplicated Gonorrhoea”.

### *What are the clinical trial identification numbers?*

- Protocol number: STI\_Zoli001
- EudraCT: 2019-0009900-22
- ClinicalTrials.gov: <https://classic.clinicaltrials.gov/ct2/show/NCT03959527>

### *What is the name of the research organization (Sponsor) and what are their contact details?*

This trial was organized and funded by the Global Antibiotic Research & Development Partnership (GARDP).

They can be contacted via their website at: <http://gardp.org>