

SUMMARY OF RESULTS



The Antibacterial Resistance Leadership Group (ARLG) funds, designs, and conducts clinical research that will help prevent, diagnose, and treat infections caused by bacteria that are resistant to antibiotics.

The ARLG, along with the team of study doctors, scientists, and researchers, are pleased to describe the results from a study focused on antibiotic review strategies in community hospitals to prevent overuse of antibiotics.

WHAT IS THE STUDY TITLE?

Targeted Reduction of Antibiotics using Procalcitonin in a multi-center, randomized, blinded, placebo-controlled, non-inferiority study of azithromycin treatment in outpatient adults with suspect Lower Respiratory Tract Infections (LRTI) and a procalcitonin level of < 0.1 ng/mL (TRAP-LRTI)



MANUSCRIPT OF PRIMARY RESULTS OR CLINICAL STUDY REPORT.

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(22\)00735-6/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00735-6/fulltext)

IS THE STUDY REGISTERED WITH CLINICALTRIALS.ORG?

[NCT03341273](https://clinicaltrials.gov/ct2/show/study/NCT03341273)



WHEN DID THE RESEARCH TAKE PLACE?

December 2017 to March 2020



WHAT IS THE PURPOSE OF THE RESEARCH? WHAT IS THE PRIMARY ENDPOINT?

When a patient has a lower respiratory tract infection (LRTI) such as bronchitis or exacerbations of COPD, it can be difficult for the doctor to know whether a bacterium or a virus is the cause. This diagnosis is important because doctors typically treat a bacterial infection with an antibiotic, but antibiotics will not work on an infection caused by a virus.

Another reason doctors try to avoid unnecessary use of antibiotics is that it contributes to the rise of antimicrobial-resistant bacteria. These bacteria, also called superbugs, develop resistance to certain antibiotics, which can cause infections in the general population that are very difficult to treat.

One method that can sometimes help doctors find what caused an LRTI is to measure the concentration of a

substance called procalcitonin in a patient's blood sample. Often, higher levels of procalcitonin can mean that the infection is caused by a bacterium and that antibiotics may be helpful. Likewise, low procalcitonin levels can mean there is no infection or that the LRTI is caused by a virus and the patient is not likely to benefit from antibiotics.

Although this method can be helpful, it cannot provide a definite answer on whether a doctor should withhold antibiotics for a patient with an LRTI and low procalcitonin level.

The purpose of the TRAP-LRTI Study was to help researchers learn more about whether a low procalcitonin measurement can be used to identify patients who will not benefit from antibiotic treatment. The study measured the safety and effectiveness of an antibiotic called azithromycin compared to placebo (which looks like the study drug but contains no active ingredients) in patients with LRTI who had low procalcitonin levels.

Changes to your healthcare should not be made based on information in this summary without first consulting a doctor. If you have questions about these results, speak with your doctor.





WHY WAS THIS RESEARCH CONDUCTED? WHAT IS THE RATIONALE?

Lower respiratory tract infections are among the most common reasons for frequent health-care visits. Patients with LRTI due to either a bacterial or a viral infection have similar symptoms, which makes it difficult for doctors to identify the cause.

This situation results in high rates of unnecessary antibiotic use, which contributes to the rise of antimicrobial resistance worldwide. Doctors need improved strategies to help identify which patients would not benefit from antibiotic treatment.

Doctors often measure the procalcitonin concentration in a patient's blood to determine whether to prescribe an antibiotic. High procalcitonin levels can mean a bacterial infection is present and therefore, antibiotic treatment may be helpful. However, some patients with low procalcitonin levels could still have bacterial infections. It is therefore unclear if doctors can safely withhold antibiotics for patients with LRTI and low procalcitonin levels.

Researchers conducted the TRAP-LRTI Study to help answer the question of whether a low procalcitonin level means doctors can safely withhold antibiotics to treat LRTI.



WHY IS THIS RESEARCH IMPORTANT TO PATIENTS, CLINICIANS, AND OTHER RESEARCHERS?

This goal of the study was to help clarify whether doctors can use low procalcitonin levels as a basis to identify patients who should not receive antibiotic treatment for LRTI.



WHO WAS INVOLVED?

The study took place at five U.S. health care systems. It included 499 adults over the age of 18 with:

- Suspected non-pneumonia LRTI,
- Symptoms lasting from 24 hours to 28 days, and
- Procalcitonin concentrations of 0.25 ng/mL or less.

During the study, 249 participants received azithromycin and 250 received the placebo.



WHAT HAPPENED DURING THE STUDY?

Within two hours of study en-rollment, researchers collected blood and measured procalcitonin levels.

Participants with a low procalcitonin concentration of 0.25 ng/mL or less were assigned at random (like flipping a coin) to receive either an oral dose of azithromycin or a matching placebo for five days.

Researchers evaluated the participants at day five and again on days 11 and 28 to check if:

- Their initial symptoms had improved,
- They developed any new or worsening symptoms requiring antibiotic treatment or hospitalization,
- They experienced any side effects of treatment.



WHAT WERE THE RESULTS?

At day five, participants who received the placebo did not do as well as the participants who received azithromycin.

The placebo group was the same at day 11 and the results showed mixed findings at day 28.

After factoring in possible antibiotic-related side effects, the placebo group was similar to the azithromycin-treated group at all time points.

Researchers also noted that patients with non-pneumonia LRTI typically show high rates of improvement by 28 days whether they receive an antibiotic treatment or not.

After considering all of these factors, researchers determined that low procalcitonin levels could be used to withhold antibiotics after accounting for the risks and benefits that individual patients might experience if antibiotics are prescribed.



HOW WILL THE RESULTS HELP PATIENTS AND DOCTORS?

Researchers can use the data obtained from the TRAP-LRTI Study to create additional clinical trials that will help answer the question of whether doctors should withhold antibiotics for patients with LRTI and low procalcitonin levels. The study only evaluated one antibiotic, azithromycin, so the results may not be relevant to other antibiotics. Researchers can also apply the TRAP-LRTI Study design to other trials to learn if other tests might be better at determining which patients need antibiotics and which do not.

Information from studies like TRAP-LRTI can help to limit nonessential antibiotic use, which would protect patients from unnecessary side effects and help prevent the global rise of antimicrobial-resistant bacteria.



WHAT'S NEXT?

Researchers are encouraging more clinical trials similar to TRAP-LRTI to gather data for other tests that might be better than procalcitonin to guide antibiotic use. It is also important to evaluate other types of study participants including those with other kinds of infections. Research that builds on this data and includes other age groups such as infants and children would also provide important information.