SUMMARY
OF RESULTS

PROOF
Antibacterial Resistance Leadership Group

The Antibacterial Resistance Leadership Group (ARLG) seeks to prioritize, design, and execute clinical research that will reduce the public health threat of antibacterial resistance. The ARLG, along with the team of doctors, scientists, and study coordinators, are pleased to describe the results from the **Phase I Study to Evaluate the Pharmacokinetics, Safety, and Tolerability of Two Dosing Regimens of Oral Fosfomycin Tromethamine in Healthy Adult Participants (PROOF)**.

We appreciate the time and commitment of the research participants who volunteered in the PROOF study and, in doing so, played such an important role in advancing medical science.

WHY WAS THIS STUDY CONDUCTED?

The drug investigated in this study is called fosfomycin tromethamine. The brand name is Monurol. In this document, the drug is referred to as fosfomycin.

Fosfomycin is approved for the treatment of urinary tract infections and cystitis, which is inflammation of the bladder.

The most recommended adult dose is three grams taken orally (by mouth) every other day, for a total of three doses. However, there are many different dosing regimens prescribed today that have not been studied or approved. In addition, based on activity observed in the lab, doctors are interested in prescribing this drug for its ability to treat infections caused by antibiotic-resistant bacteria (bacteria that are not controlled or killed by antibiotics). However, the drug has not been approved for this indication.

WHAT IS A PHASE 1 STUDY?

This is the first phase of clinical research studies.

Study participants are healthy volunteers or people with the disease/condition. The purpose of these studies is to find out if the drug is safe and to investigate an appropriate dose.

WHAT IS A DOSING REGIMEN?

A dosing regimen is a pattern of administering treatment.

WHAT IS THE PURPOSE OF THE STUDY?

This study gathered information on the pharmacokinetics (PK), safety, and side effects of two different oral dosing regimens of fosfomycin. The study results will help doctors identify alternative dosing regimens that:

- are appropriate and safe,
- may be helpful in treating infections involving resistant bacteria, or
- may be helpful when other oral antibacterial drugs are not available.

WHAT IS A PHARMACOKINETICS (PK) STUDY?

A PK study explores how a drug moves through and leaves the body. PK studies help doctors understand important information about a drug's dose, including route (by mouth or another method) and frequency (how many times per day the drug is taken).

WHEN WAS THE STUDY CONDUCTED?

January 2016 – August 2017

The National Institute of Allergy and Infectious Diseases of the National Institutes of Health through the Antibacterial Resistance Leadership Group provided funding for this study.

WHO WAS INVOLVED?

18 healthy participants enrolled at the University of Illinois at Chicago.

WHAT HAPPENED DURING THE STUDY?

Participants were randomly assigned (by chance) to one of two dosing regimens as described below.

	REGIMEN 1	REGIMEN 2
Dose	3-gram dose	3-gram dose
Frequency	Every other day	Once a day
Total Doses	3 doses	7 doses

After completion of the initial dosing regimen, each participant waited at least five days and then started the other dosing regimen. The following information was collected throughout the study:

- Blood and urine samples
- Time drug was taken
- How much drug was taken
- Side effects experienced

WHAT DID RESEARCHERS LEARN FROM THE STUDY?

- Participants who took fosfomycin every day experienced more days of diarrhea compared to participants who took the drug every other day.
- Important PK information was gathered on how the drug was absorbed, distributed, and eliminated from the body.
- PK information in participants was similar between the two dosing regimens.

This summary was completed on August 2018. Since this summary was written, newer information may exist.

WHERE CAN I LEARN MORE?

Visit: www.arlg.org

WHAT'S NEXT?

Researchers recommend additional studies to evaluate the safety and efficacy (how well it works) of different dosing regimens of oral fosfomycin tromethamine in patients with urinary tract infections.

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