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Plain Language Summary of Publication

A plain language summary of how lefamulin alone can be used to treat pneumonia caught outside of the hospital due to common bacterial causes, including drug-resistant bacteria

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Summary

What is this summary about?
Bacterial pneumonia is an infection of the lung caused by bacteria that is potentially deadly, costly, and affects millions of people worldwide every year. Treatment is becoming more challenging—many current treatments no longer work well because some strains of bacteria that cause pneumonia have become resistant to current **antibiotics**. Many of the antibiotics that do still work have undesirable **side effects**. Therefore, new antibiotics that work differently are needed to treat bacterial pneumonia.

Lefamulin (brand name, Xenleta®) is an antibiotic that was approved to treat bacterial pneumonia caught outside a hospital (also called community-acquired bacterial pneumonia, or CABP) based on results of two clinical studies. In both studies, participants started treatment with lefamulin before the type of bacteria causing the infection was known. Lefamulin was **well tolerated** and worked well in 5 to 7 days to kill the bacteria causing the infection and to improve symptoms in almost all participants with CABP.

What were the results?
After the studies were completed, the researchers looked back at what kinds of bacteria were identified from the study participants. Lefamulin worked well to kill bacteria and to improve CABP symptoms for most kinds of infecting bacteria, including bacteria resistant to many current antibiotics.

What do the results mean?
These results suggest that lefamulin, by itself, provides a much-needed treatment option for CABP that covers most of the key bacteria causing this infection.

How to say (double-click to play sound)...
- **Azithromycin:** uh-zith-row-MAI-sin
- **Amoxicillin:** uh-maak-suh-SIL-un
- **Ciprofloxacin:** sip-row-FLAAK-suh-sin
- **Clarithromycin:** kluh-rith-row-MAI-sin
- **Erythromycin:** uh-rith-row-MAI-sin
- **Lefamulin:** leh-FAM-yoo-lin
- **Levofloxacin:** lee-vo-FLAAK-suh-sin
- **Pleuromutilin:** plur-uh-MYOOT-uh-lin
- **Moxifloxacin:** maak-see-FLAAK-suh-sin
- **Pneumonia:** nuh-MOWN-yuh
- ***Streptococcus pneumoniae:*** strep-tuh-KAA-kuhs nuh-MOW-nee-ay
- ***Staphylococcus aureus:*** sta-fuh-luh-KAA-kuhs AW-ree-uhs
- ***Haemophilus influenzae:*** hee-MAW-fi-lus in-floo-EN-zay
- ***Mycoplasma pneumoniae:*** mai-ko-PLAZ-muh nuh-MOW-nee-ay
- ***Legionella pneumophila:*** lee-juh-NEH-luh noo-MAA-fee-luh
- ***Chlamydia pneumoniae:*** kluh-MI-dee-uh nuh-MOW-nee-ay

A **side effect** is an unintended effect of a medicine that can be beneficial or undesirable

An **antibiotic** is a type of medicine that kills bacteria or stops bacterial growth

Well tolerated means that a medicine has few side effects or has side effects that are manageable by the individual

Future Medicine part of fsg

Who is this article for?

This summary may be useful for non-specialist healthcare professionals (such as doctors, nurse practitioners, physician assistants, clinical pharmacists, etc.) who treat patients with a clinical diagnosis of CABP as well as patients with CABP and their families or caregivers. This article may be of particular interest to people who have had CABP or clinicians who have treated patients for CABP with previous recent antibiotic therapy, which may indicate a case of antibiotic resistance.

Who sponsored this study?

Nabriva Therapeutics funded the LEAP studies and was involved in study design, study oversight, data collection, and data analysis. The studies were approved by ethics committees at each participating health site or clinic.

What are pneumonia and CABP?

Pneumonia is an infection of the lung that can be caused by bacteria, viruses, or fungi. In the United States, pneumonia is one of the most common causes of hospitalization and a leading cause of death from infection:

Each year in the United States, pneumonia results in:

1.3 million	**740,000 to 1.6 million**	**74,000 to 160,000**
emergency department visits	hospital stays	deaths

Community-acquired bacterial pneumonia, shortened to CABP, is a type of pneumonia caused by a bacterial infection of the lung. It is called 'community acquired' because it is caught from the local community, not from within a hospital

Common symptoms of CABP include:

- cough
- the production of **phlegm**
- difficulty breathing
- chest pain
- tiredness
- fever
- chills

Phlegm is the thick mucus within the airways that is often produced in large quantities when a person has pneumonia

CABP can be caused by any kind of bacteria that infect the lung; however, the kinds of bacteria that most often cause CABP are:

- *Streptococcus pneumoniae* (shortened to *S. pneumoniae*)
- *Haemophilus influenzae* (shortened to *H. influenzae*)
- *Staphylococcus aureus* (shortened to *S. aureus*)
- *Chlamydia pneumoniae* (shortened to *C. pneumoniae*)
- *Mycoplasma pneumoniae* (shortened to *M. pneumoniae*)
- *Legionella pneumophila* (shortened to *L. pneumophila*)

People are at higher risk of getting CABP if they are:

- 65 years or older
- smoke
- have a weak immune system
- have other health conditions such as asthma, diabetes, or heart, kidney, liver, or chronic lung disease

What are antibiotics?

An **antibiotic** is a type of medicine that kills bacteria or stops bacterial growth

Antibiotics are grouped into **categories** according to their chemical structure or shape and how they kill bacteria or stop bacterial growth

Antibiotic categories that are discussed in this article include:

- **Macrolides**: antibiotics with a unique chemical structure that stop bacterial growth by blocking their ability to make proteins; common examples of **macrolides** include azithromycin, clarithromycin, and erythromycin
- **Penicillins**: antibiotics with a unique chemical structure that kill bacteria by blocking their ability to build a cell well; common examples of **penicillins** include amoxicillin, ampicillin, and penicillin
- **Fluoroquinolones**: antibiotics with a unique chemical structure that kill bacteria by blocking their ability to copy their genetic material; common examples of **fluoroquinolones** include ciprofloxacin, moxifloxacin, and levofloxacin
- **Pleuromutilins**: antibiotics with a unique chemical structure (but different from that of **macrolides**) that stop bacterial growth by blocking their ability to make proteins; lefamulin, the medicine discussed in this article, is a pleuromutilin

Why is antibiotic resistance a growing problem in CABP?

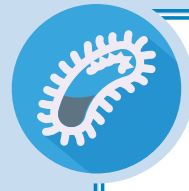
Antibiotic resistance means that:

- The bacteria are not killed and continue to grow
- The antibiotic no longer works as a medicine
- Infections caused by antibiotic-resistant bacteria are harder to treat

For a long time, antibiotics called macrolides have been a key medicine used for **empiric treatment** of CABP

However, *S. pneumoniae* and other bacteria that frequently cause CABP are becoming resistant to many of the antibiotics that are used to treat it, such as macrolides

When treating CABP, most recent guidelines that healthcare practitioners follow recommend avoiding macrolides if the local *S. pneumoniae* resistance to macrolides is 25% or greater (see text and map on next page for more details)



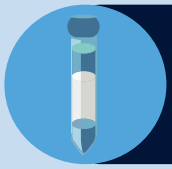
Over time, bacteria can develop pathways that block the antibiotics and make them ineffective in killing the bacteria; this is called **antibiotic resistance**

Empiric treatment is medical treatment, based on clinical experience or observation, that is given before the specific bacterium, virus, or fungus causing an infection has been identified

To understand what this means, let's take a closer look at resistance of *S. pneumoniae* bacteria to macrolide antibiotics:

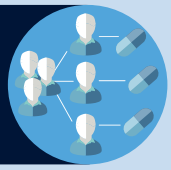
- When a person with a respiratory infection seeks medical attention, the healthcare practitioner wants to know what has caused that person's infection. To find that out, a sample that is coughed up (sputum) will usually be tested. Sometimes, if a patient is seen in the Emergency Room, a blood sample might also be tested
  - If bacteria are found in a patient's sample, then additional tests are done to find out what antibiotics those bacteria are resistant to, if any
  - Across the United States, many thousands of patient samples are tested in this way every year, and those test results can answer questions about patterns of infections and antibiotic resistance

- Two of the researchers who wrote this article and their colleagues published a study in 2021 in which they looked at airway and blood samples that tested positive for *S. pneumoniae*



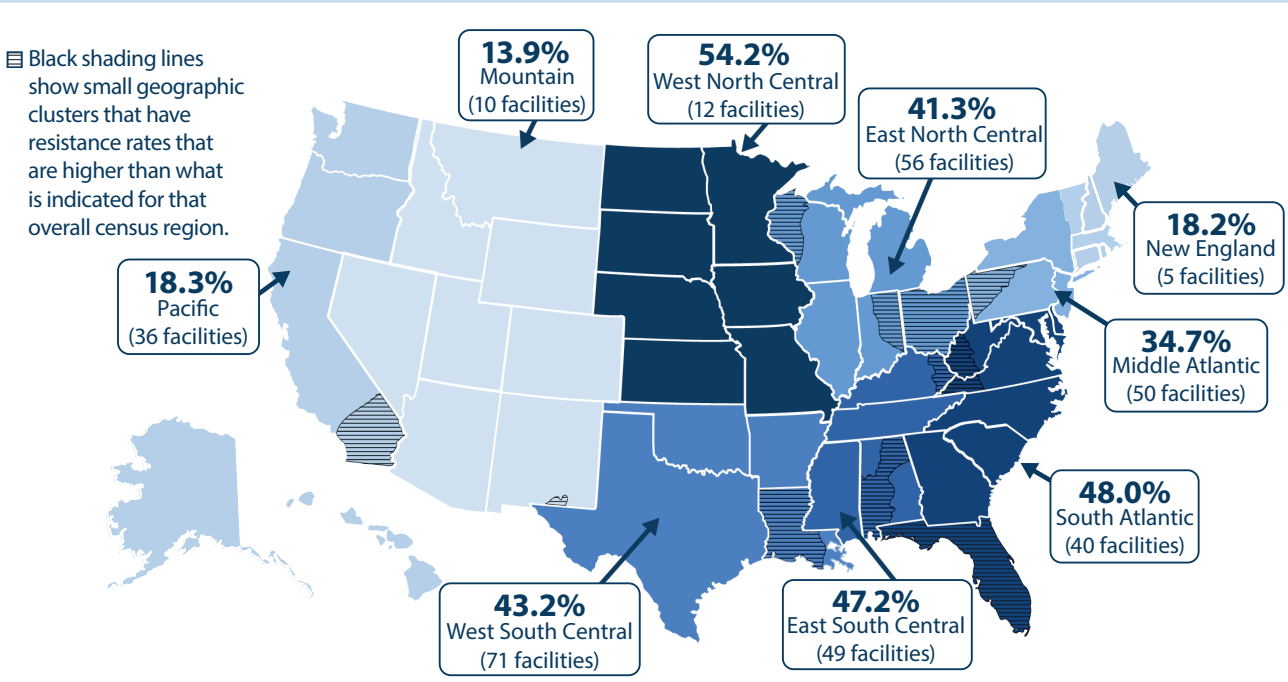
They took samples from **329** medical care facilities across the United States. *S. pneumoniae* was found and isolated **3626** independent times

Of the **3626** specimens, **39.5%** were resistant to the macrolide antibiotics azithromycin, clarithromycin, or erythromycin



Looking at the **9** individual census regions within the United States, resistance rates ranged from 14% to 54%

- This map shows that resistance rates to macrolide antibiotics are greater than 25% in many regions in the US
- Because resistance rates vary considerably even within US states, some states with lower overall resistance rates may still have a town or county with resistance rates that are higher than 25%



When conducting a census, the US Department of Health and Human Services divides the United States into 9 regions. *S. pneumoniae* macrolide resistance rates between October 2018 and September 2019 were measured for each census region and are shown in this map. The following 21 individual states did not have enough data to contribute to this analysis: Alaska, Arizona, Colorado, Connecticut, Delaware, Hawaii, Idaho, Kansas, Maine, Massachusetts, Montana, Nevada, New Hampshire, North Dakota, Oregon, Rhode Island, South Carolina, Tennessee, Utah, Vermont, and Wyoming.

- Follow this link to the original published article to see a detailed map of macrolide resistance rates by individual US zip codes: https://academic.oup.com/ofid/article/8/7/ofab063/6128791

Why are new antibiotics needed?

- Because *S. pneumoniae* rates of resistance to macrolides are so high, alternative antibiotics to macrolides are needed for empiric treatment (i.e., treatment given before a complete diagnosis is established). However, many of the currently available alternatives kill not only the types of bacteria that often cause pneumonia, but also the types of beneficial bacteria that help the body with other necessary functions such as maintaining gut health

- Many non-macrolide antibiotic alternatives may also have safety concerns:
  - **Penicillin antibiotics** such as amoxicillin are effective against many of the types of bacteria that cause CABP, but penicillin resistance is very common and up to 10% of the population reports some form of allergy to these drugs. Also, penicillins often require multiple pills per dose and 3 or more doses within 24 hours. These requirements might result in some patients taking only part of the prescribed treatment, which increases the risk of drug resistance because not all of the bacteria may be killed
  - **Fluoroquinolone antibiotics** such as moxifloxacin are active against a wider range of bacteria and are often used in more serious infections, or to treat infections thought to be resistant to penicillins. However, side effects involving tendons, muscles, joints, nerves, blood vessels, blood sugar, and mental health have been seen with these antibiotics

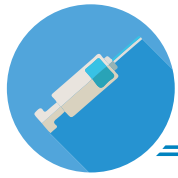
- The ability to take these antibiotics **orally** often allows patients to leave the hospital and complete treatment of pneumonia and other severe infections at home. As antibiotic resistance and safety concerns grow, however, some of these antibiotics will no longer be able to treat infections at home

- Therefore, new antibiotic options are needed for the types of bacteria that often cause CABP

An **oral** medication is one that is taken by mouth to be swallowed (eg, a pill or capsule)

What is lefamulin?

- Lefamulin is used to treat people with CABP and is the first pleuromutilin antibiotic for humans that can be taken by mouth or **IV infusion** twice a day for 5 to 7 days



An **intravenous (shortened to IV) infusion** is a medicine that is injected directly into a vein

- Pleuromutilin antibiotics such as lefamulin kill bacteria by blocking bacterial protein production, which prevents bacterial growth and reproduction

- Because lefamulin belongs to a new group of antibiotics and works in a unique way, bacteria are less likely to be resistant or to become resistant to lefamulin than to some other antibiotics

- Lefamulin works well against bacteria that are resistant to other antibiotics often prescribed in CABP

- Researchers have shown that lefamulin has a **narrow spectrum** of antibacterial activity, which means that it works well against the kinds of bacteria that often cause pneumonia but not against the kinds of good bacteria that help the body with necessary functions such as maintaining a healthy gut. This means that lefamulin does not kill most gut bacteria, so relevant gastrointestinal side effects may be minimized

A **broad-spectrum antibiotic** works against many different types of bacteria, while a **narrow-spectrum antibiotic** works against only a few types of bacteria

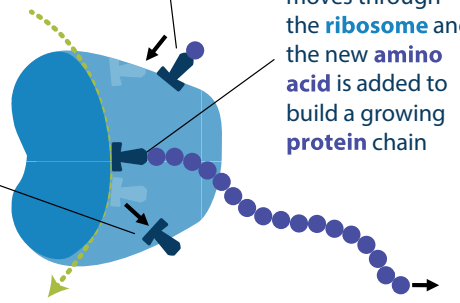
Function of the bacterial ribosome

1. **Messenger RNA** contains the *instructions* to build a **protein**, and a **ribosome** is the machinery that *reads* and carries out those instructions.

2. The ingredients needed to make a **protein** are called **amino acids**, which are carried to the **ribosome** by **transfer RNA**

3. **Transfer RNA** moves through the **ribosome** and the new **amino acid** is added to build a growing **protein** chain

4. Empty **transfer RNA** exits the **ribosome**



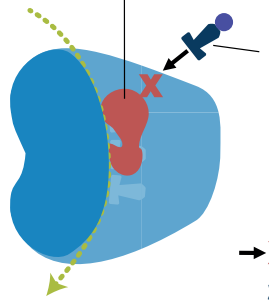
5. Newly created **proteins** go on to contribute to vital functions in bacteria such as growth and replication

- When a patient has CABP, the bacteria infecting their lungs are growing and multiplying
- Inside those bacteria, cellular machinery called **ribosomes** create **proteins**, which are vital building blocks that bacteria use to grow and multiply

Treatment with lefamulin

Bacterial ribosome blocked by lefamulin

1. **Lefamulin** binds to **ribosomes**, blocking binding of **transfer RNA**



2. **Transfer RNA** with **amino acid** is blocked and cannot bind to the **ribosome**

3. No new **proteins** can be created, vital functions such as growth and replication stop, and bacteria die

- When a patient with CABP is treated with **lefamulin**, **lefamulin** travels through the body until it finds the bacteria
- **Lefamulin** binds to **ribosomes** inside the bacteria and blocks the ability of those **ribosomes** to create **proteins**
- Without **proteins**, bacteria cannot grow or multiply and the infection is stopped
- Once the infection has been stopped, the patient's body can begin to recover

What was the purpose of the LEAP 1 and LEAP 2 clinical studies?

- LEAP is an abbreviation of the study name Lefamulin Evaluation Against Pneumonia. There were two studies, LEAP 1 and LEAP 2, that were standard clinical studies to investigate lefamulin as a treatment for patients with CABP
- The main aim of the studies was to see if lefamulin was at least as good as moxifloxacin (a fluoroquinolone antibiotic) in treating patients with CABP
  - In both studies, moxifloxacin was the **positive control**, which means that the researchers already knew before starting the study that it would likely work as a treatment for CABP

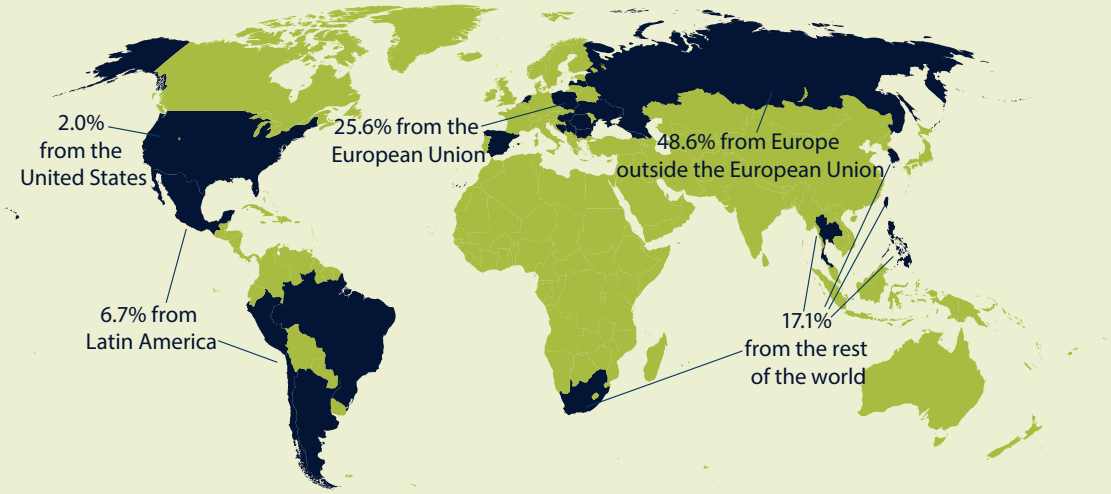
A **positive control group** in a study does not receive the experimental treatment but instead receives a treatment that is known to produce a positive result; the **positive control group** provides the basis for comparison to the **experimental group**

Who took part in the clinical studies?

- The LEAP 1 and LEAP 2 studies included 1289 participants (56% men, 44% women) who ranged in age from 19 to 97 years old

- The trials included participants from 23 countries:

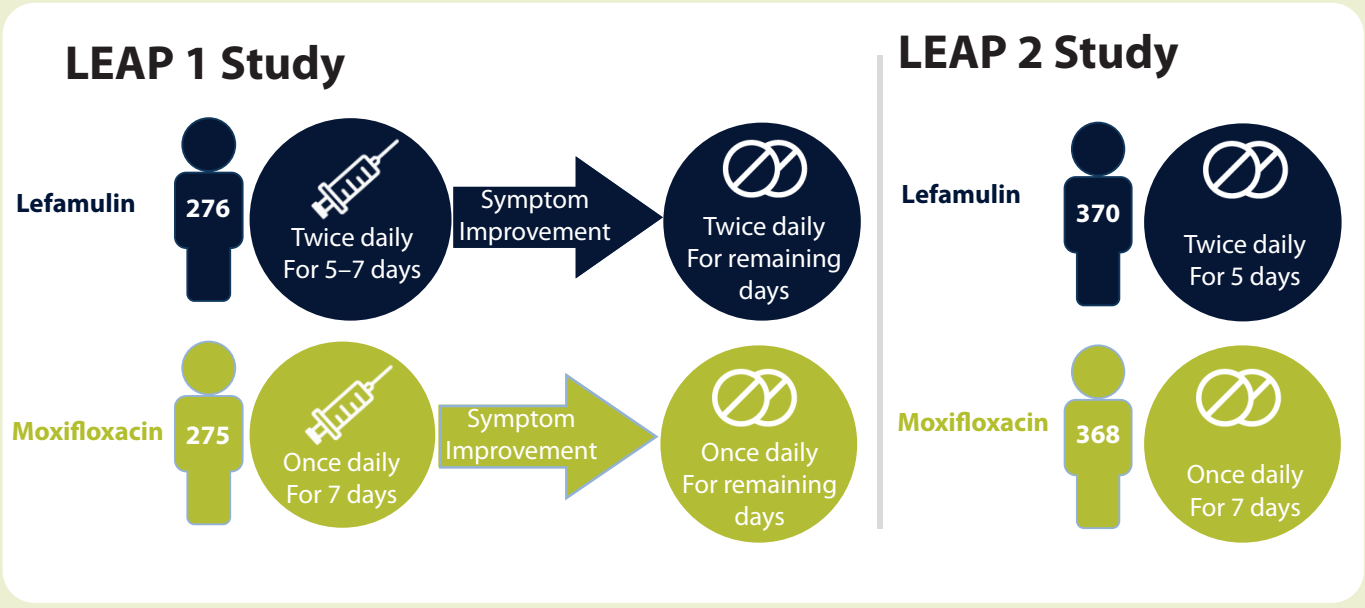
Argentina	Bosnia and Herzegovina	Brazil	Bulgaria	Chile	Georgia
Hungary	Latvia	Mexico	The Netherlands	Peru	Philippines
Poland	Romania	Russian Federation	Serbia	South Africa	South Korea
Spain	Taiwan	Thailand	Ukraine	United States	



- All participants had CABP, with the diagnosis confirmed by x-ray, and some or all of the following symptoms:
  - ✓ Fever
  - ✓ Low blood oxygen
  - ✓ Levels of white blood cells that indicate the body is fighting an infection
  - ✓ Difficulty breathing
  - ✓ New or increased cough
  - ✓ Chest pain
  - ✓ Production of phlegm
- Some key reasons why people were not allowed to participate in the studies were:
  - ✗ Had already received antibiotics for their current illness
  - ✗ Had already been hospitalized for their current illness
  - ✗ Had, or were at risk for developing, significant liver or heart disease

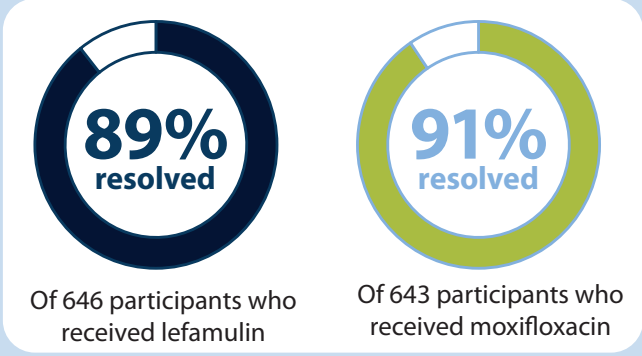
What happened during the clinical studies?

- These studies looked at how many participants responded to each treatment
- Researchers considered CABP to be resolved (i.e., successfully treated) if patients were alive and met 3 conditions:
  - At least 2 of 4 CABP symptoms (difficulty breathing, cough, chest pain, production of phlegm) improved, and
  - No CABP symptoms worsened, and
  - No extra antibiotics were needed to treat the infection

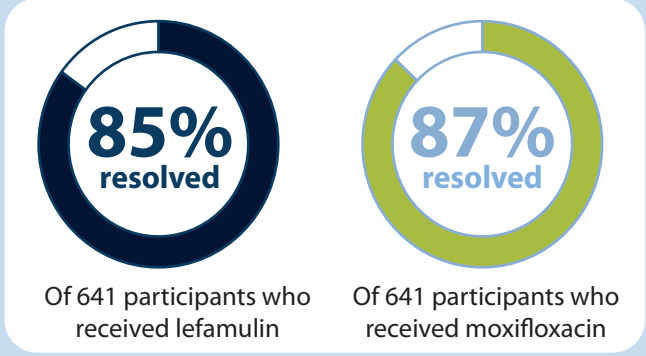


What were the overall study results?

After **3 to 5** days of treatment with lefamulin, symptoms were improved or CABP was resolved in most patients:



At **5 to 10** days after the last day of treatment, symptoms remained improved or CABP remained resolved in most patients:



Lefamulin improved symptoms and resolved CABP in most participants regardless of medical history or pre-existing conditions, including:


Advanced age


Diabetes


Heart disease


Smoking history


Lung disease


Kidney disease

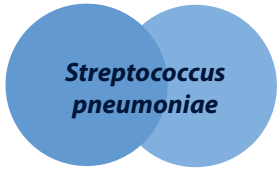

Liver disease

Lefamulin and moxifloxacin improved symptoms and resolved CABP in most participants regardless of whether given by IV infusion or by mouth

What bacteria were found in participants?

- In patients with pneumonia, identification of the underlying bacterial cause is difficult because of problems in obtaining a reliable sample to test. However, in the LEAP studies, bacteria were identified in 709 of 1289 (55%) participants. In these participants, the bacteria that were found included:

62% Of participants were infected with



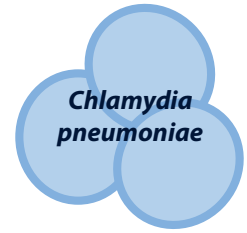
30% Of participants were infected with

5% Of participants were infected with

10% Of participants were infected with

9% Of participants were infected with

8% Of participants were infected with

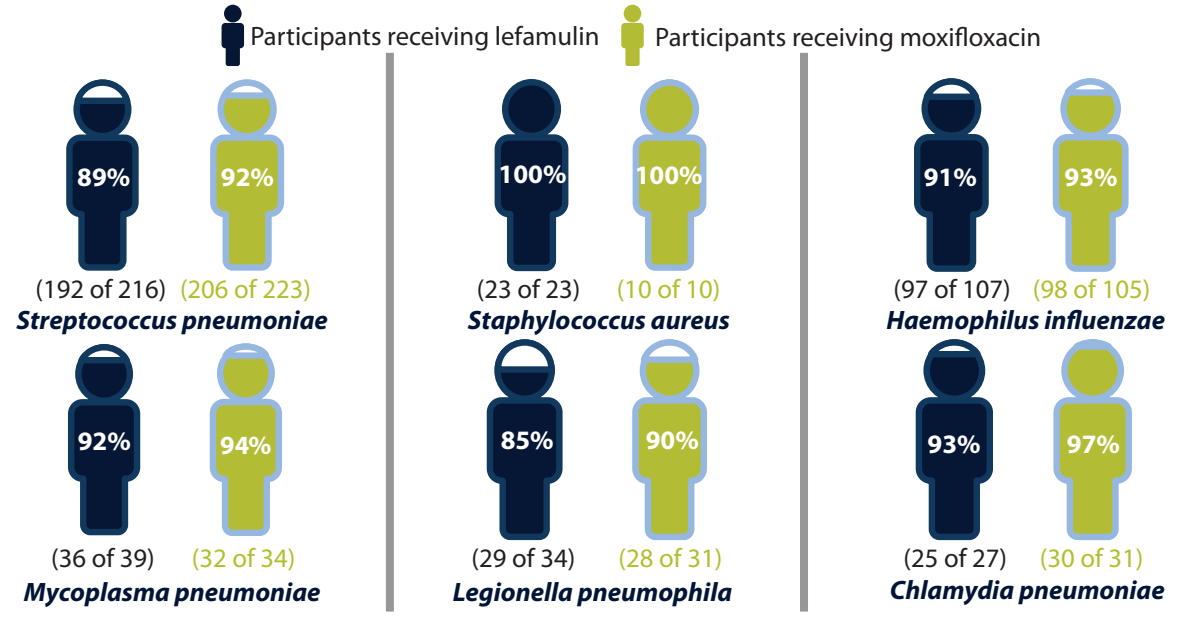


Did lefamulin work against each of these different kinds of bacteria?

Yes, both in the laboratory setting (where lefamulin was tested directly on the bacteria) and in study participants (who were treated with oral or IV lefamulin)

- Although participants were treated with lefamulin or moxifloxacin for 5 to 7 days, symptoms were improved or CABP was resolved within 3 to 5 days of treatment in 85% to 100% of participants, regardless of the bacterial cause
- For all bacterial types, symptoms were improved or CABP was resolved in similar percentages of patients, regardless of whether they were treated with lefamulin or moxifloxacin:

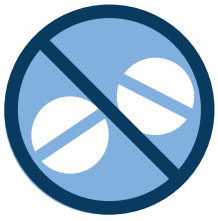
Percentages of patients with improved symptoms or resolved CABP by bacterial cause of infection



Were antibiotic-resistant bacteria found in the study participants?

Yes – among the 439 participants who were infected with *S. pneumoniae*, 3 categories of antibiotic resistance were found:

Penicillin resistant



In **14** participants, isolates were **PENICILLIN RESISTANT**, which means that the antibiotic penicillin **DOES NOT WORK** against these isolates

Macrolide resistant

In **31** participants, isolates were **MACROLIDE RESISTANT**, which means that antibiotics such as azithromycin or erythromycin **DO NOT WORK** against these isolates

Multidrug resistant

In **32** participants, isolates were **MULTIDRUG RESISTANT**, which means that at least 1 antibiotic in at least 3 antimicrobial categories* **DO NOT WORK** against these isolates

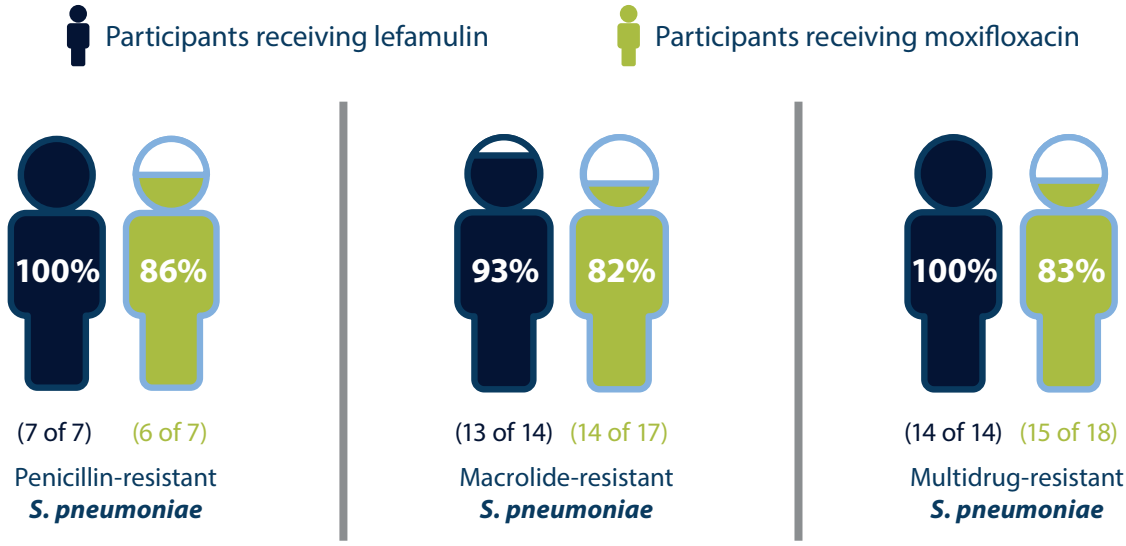
*Antibiotics that do not work might include: oral penicillin, moxifloxacin, ceftriaxone, clindamycin, azithromycin or erythromycin, doxycycline, or trimethoprim/sulfamethoxazole

Did lefamulin work against these antibiotic-resistant bacteria?

Yes, both in the laboratory setting (where lefamulin was tested directly on the bacteria) and in study participants (who were treated with oral or IV lefamulin):

- In the laboratory setting, the antibiotic resistance of these bacteria had no effect on how well lefamulin and moxifloxacin worked
- In the study participants who were infected with drug-resistant *S. pneumoniae*, symptoms were improved or CABP was resolved in 93% to 100% of those who received lefamulin and in 82% to 86% of those who received moxifloxacin, regardless of the type of antibiotic resistance of these bacteria:

Percentages of patients with improved symptoms or resolved CABP by type of *S. pneumoniae* antibiotic resistance

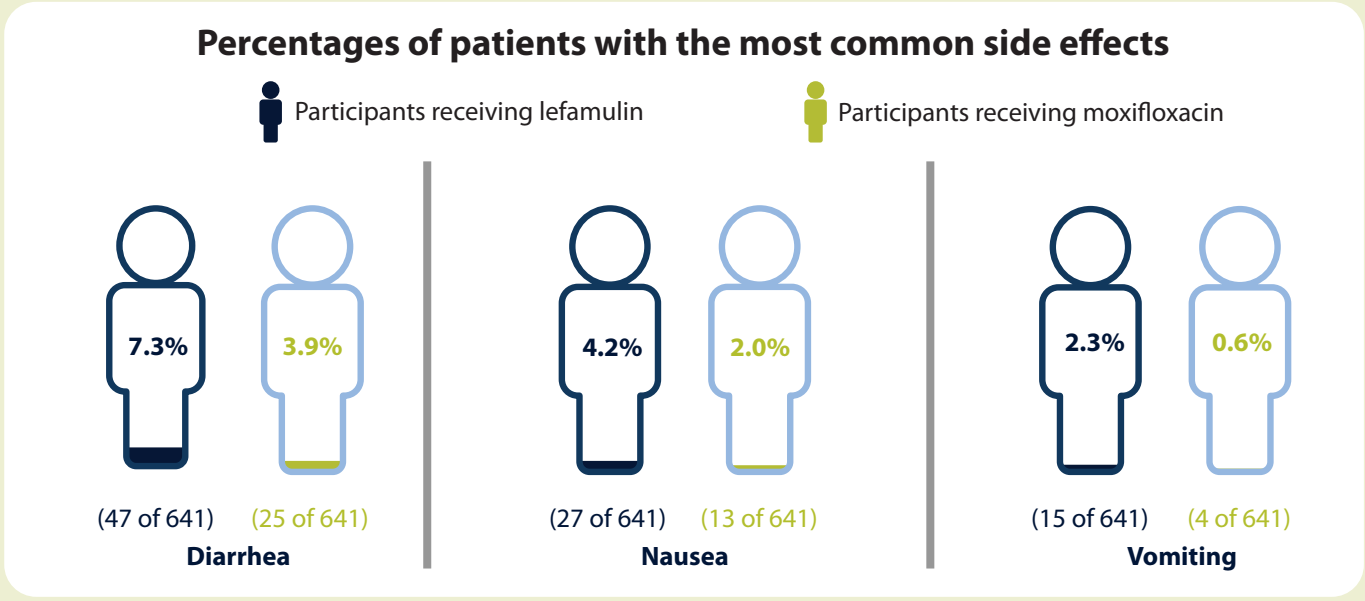


These results were observed after 3 to 5 days of treatment, and, in all but 2 patients, symptoms did not return and CABP remained resolved in most patients after completing the full 5 to 7 days of treatment

A full report of the combined LEAP 1 and LEAP 2 study results can be found on the websites listed at the end of this summary

What were the most common side effects?

- For both lefamulin and moxifloxacin, the most common side effects during the clinical studies were diarrhea, nausea, and vomiting; this is similar to many other antibiotic treatments
- In more than 95% of patients, side effects were mild to moderate in severity and did not lead to stopping the medication
- These side effects happened more often when medications were given by mouth than by IV infusion



- Lefamulin and moxifloxacin both have the potential to cause a disturbance in the normal rhythm of the heart. Treatment should therefore be avoided in patients taking medications known to have similar effects on the heart and in patients with certain heart conditions
- Findings from studies in animals suggest that lefamulin may cause fetal harm if given to pregnant women. Women of reproductive potential should be made aware of this possible risk

What do the results of these studies mean?

- The results from these studies showed that:
  - In almost all participants, 5 to 7 days of treatment with lefamulin was sufficient to improve symptoms and resolve CABP
  - Lefamulin worked well against the most common causes of CABP, including several types of infections that cannot be treated with other antibiotics due to resistance
  - Lefamulin worked at least as well as moxifloxacin to improve symptoms and resolve CABP and could be considered an alternative to fluoroquinolones
  - The total duration of treatment with lefamulin, 5 to 7 days, was the same as or shorter than treatment with moxifloxacin (7 days)
  - Lefamulin was well tolerated, and side effects were similar between treatment groups
  - Lefamulin can be taken as either an IV infusion or oral tablet and can be used in patients being treated either in or out of the hospital
- Because of growing concerns regarding the safety and tolerability of commonly used antibiotics, these results suggest that lefamulin, by itself, provides a much-needed treatment option for CABP without needing to identify the bacteria causing the infection

Based on the results of these studies, lefamulin was the first pleuromutilin antibiotic approved in the United States, Europe, and Canada as an empiric IV infusion and/or oral single-drug treatment for people with CABP.

Where can readers find more information?

- Lefamulin prescribing information can be accessed here: https://www.xenleta.com
- **The information summarized in this article about lefamulin for treatment of CABP** is from the article "Pooled Microbiological Findings and Efficacy Outcomes by Pathogen in Adults With Community-Acquired Bacterial Pneumonia from the Lefamulin Evaluation Against Pneumonia (LEAP) 1 and LEAP 2 Phase 3 Trials of Lefamulin Versus Moxifloxacin," which was published in the *Journal of Global Antimicrobial Resistance* in 2021. The original article is free to access and can be found at: https://www.sciencedirect.com/science/article/pii/S2213716521002459
- **The information summarized in this article about bacterial resistance to macrolide antibiotics in the United States** is from the article "A Multicenter Evaluation of the US Prevalence and Regional Variation in Macrolide-Resistant *S. pneumoniae* in Ambulatory and Hospitalized Adult Patients in the United States," which was published in *Open Forum Infectious Diseases* in 2021. The original article is free to access and can be found at: https://academic.oup.com/ofid/article/8/7/ofab063/6128791
- **Additional findings from the LEAP 1 and LEAP 2 studies of lefamulin for CABP can be found in the following articles:**
- The main results from the LEAP 1 study, entitled "Efficacy and Safety of Intravenous-to-Oral Lefamulin, a Pleuromutilin Antibiotic, for the Treatment of Community-acquired Bacterial Pneumonia: The Phase III Lefamulin Evaluation Against Pneumonia (LEAP 1) Trial," were published in *Clinical Infectious Diseases* in 2019. The original article is free to access and can be found at: https://academic.oup.com/cid/article/69/11/1856/5306243
- The main results from the LEAP 2 study, entitled "Oral Lefamulin vs Moxifloxacin for Early Clinical Response Among Adults With Community-Acquired Bacterial Pneumonia: the LEAP 2 Randomized Clinical Trial," were published in *JAMA* in 2019. The original article is free to access and can be found at: https://jamanetwork.com/journals/jama/fullarticle/2752331
- The results from the subgroup analysis of outpatients from the LEAP 2 study, entitled "Oral 5-Day Lefamulin for Outpatient Management of Community-Acquired Bacterial Pneumonia: Post-hoc Analysis of the Lefamulin Evaluation Against Pneumonia (LEAP) 2 Trial, " were published in the *Journal of Emergency Medicine* in 2021. The original article is free to access and can be found at: https://www.sciencedirect.com/science/article/pii/S0736467921001025?via%3Dihub
- The results from the LEAP 1 and LEAP 2 studies in subgroups of participants with CABP simultaneously with other common medical conditions such as advanced age, diabetes, chronic lung disease, heart disease, kidney disease, or liver disease, entitled "Lefamulin Efficacy and Safety in a Pooled Phase 3 Clinical Trial Population With Community-Acquired Bacterial Pneumonia and Common Clinical Comorbidities," were published in *BMC Pulmonary Medicine* in 2021. The original article is free to access and can be found at: https://bmcpulmmed.biomedcentral.com/articles/10.1186/s12890-021-01472-z

What other resources are available?

- Lefamulin: treatment of CABP and its place in therapy: https://www.youtube.com/channel/UCcXLVC0xsFEw16KA2s8NdVQ/videos
- Bacterial pneumonia: https://www.webmd.com/lung/bacterial-pneumonia
- Management of CABP: https://www.uptodate.com/contents/treatment-of-community-acquired-pneumonia-in-adults-in-the-outpatient-setting?topicRef=7027&source=see_link
- CABP Treatment Guidelines: https://www.atsjournals.org/doi/10.1164/rccm.201908-1581ST
- Antibiotic resistance: https://www.cdc.gov/drugresistance/index.html
- Drug-resistant *Streptococcus pneumoniae*: https://www.cdc.gov/Pneumococcal/Drug-Resistance.html
- Interactive dashboard for surveillance of bacterial infections in the United States: https://www.cdc.gov/abcs/bact-facts-interactive-dashboard.html
- Penicillin allergies: https://www.cdc.gov/antibiotic-use/clinicians/penicillin-allergy.html
- Risks associated with fluoroquinolone antibiotics: https://www.fda.gov/news-events/press-announcements/fda-updates-warnings-fluoroquinolone-antibiotics-risks-mental-health-and-low-blood-sugar-adverse

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