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Indirect Treatment Comparisons of Lefamulin Versus Omadacycline for the Treatment of Community-Acquired Pneumonia

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BACKGROUND & OBJECTIVE

Background:

- Community-acquired pneumonia (CAP) is one of the most common infectious diseases, defined as an infection of the lung parenchyma caused by the inhalation of respiratory pathogens outside of a hospital setting(1).
- Lefamulin (LEF) and Omadacycline (OMA) are two recently approved novel antibiotics in China for the treatment of CAP.

Objective:

- This study aims to indirectly compare the clinical efficacy and safety of LEF and OMA in the treatment of CAP in the absence of head-to-head trial data.

METHODS

Search strategy and selection criteria

- Electronic databases (including Pubmed, Cochrane, Clinical trials and Embase) were systematically searched from inception through March 2024. Studies meeting the following inclusion criteria were considered: (1) Population: adults with CAP; (2) Interventions: Lefamulin or Omadacycline; (3) Randomized clinical trial (RCT).
- The primary outcomes were early clinical response (ECR), investigator-assessed clinical response (IACR) at test of cure (TOC), and safety profile.
- Treatment effects are presented as relative risks (RRs) with 95% confidence intervals (CI). Moxifloxacin was the reference treatment.
- Outcomes were evaluated by indirect treatment comparison (ITC) using the Bucher method.

Data extraction and quality assessment

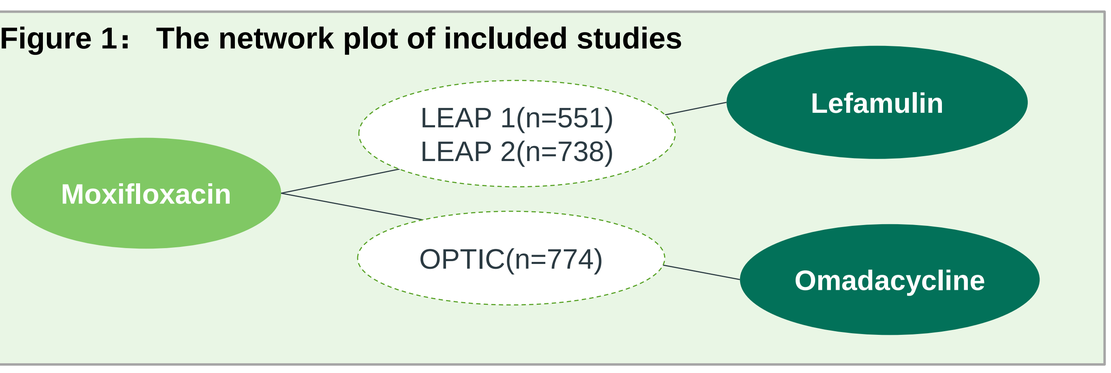
- Data were extracted by two independent investigators, and discrepancies were resolved by involving a third investigator.
- The qualities of the studies were evaluated following the *Cochrane Handbook Risk of Bias Assessment for Randomized Controlled Trials*.

RESULTS

Studies included in the ITC

- Three RCTs (LEAP 1, LEAP 2, OPTIC) with a total of 2,063 patients were identified **(Figure 1).** Intention-to-treat (ITT) population and subgroup population data were extracted from 8 articles(2-9) related to these three RCTs.

Figure 1： The network plot of included studies



Risk of bias

- All included RCTs were assessed as low risk of bias using the Cochrane risk-of-bias tool for randomized trials (RoB 2).

ITC results of efficacy endpoints

- Comparable efficacy of ECR (RR=1.01, 95%CI 0.93-1.09) and IACR at TOC (RR=0.95, 95%CI 0.88-1.02) was found between LEF and OMA **(Figure 2).**
- In subgroups analysis, LEF showed numerically superior to OMA regarding ECR **(Figure 3a)** and IACR at TOC **(Figure 3b)** in patients aged 65 years or older, a history of diabetes mellitus, and most of the CAP common and atypical pathogens, though these differences were not statistically significant. Additionally, LEF showed significantly superior to OMA regarding IACR in patients with Haemophilus influenzae (RR=1.28, 95% CI 1.03-1.60).

ITC results of safety profiles

- Both LEF and OMA were well tolerated in the treatment of CAP. The mortality rate in the LEF group was numerically lower than that in the OMA group (RR=0.67, 95% CI 0.15-3.02). No treatment-related deaths were observed in the LEF group, while no information was provided for the OMA group.
- In subgroup analysis, for patients aged 65 years or older, the LEF group was more likely to have a lower mortality risk than the OMA group (RR=0.74, 95% CI 0.15-3.66) **(Figure 4).**

Figure 2: ECR and IACR in ITT patients (LEF vs. OMA)

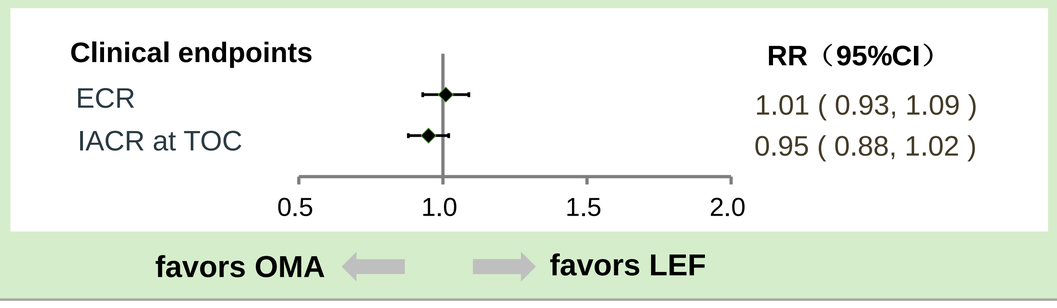


Figure 3a: Subgroup analysis of ECR (LEF vs. OMA)

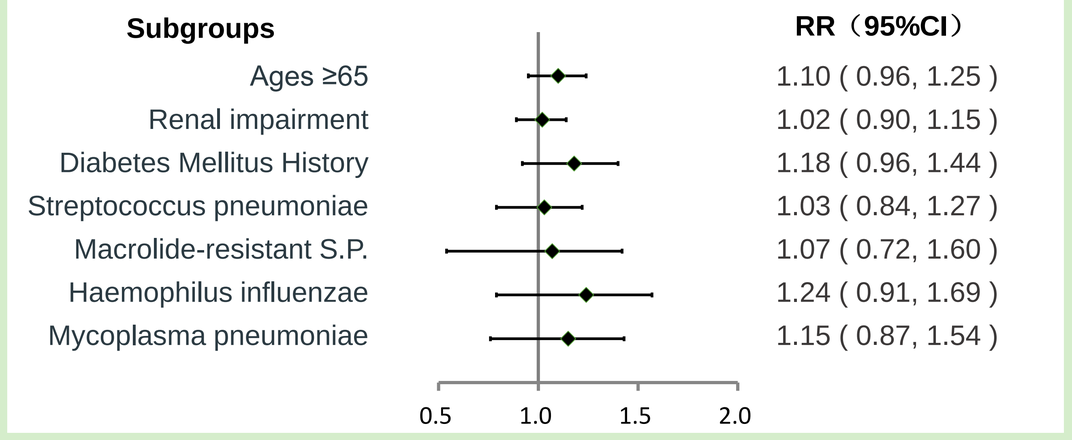
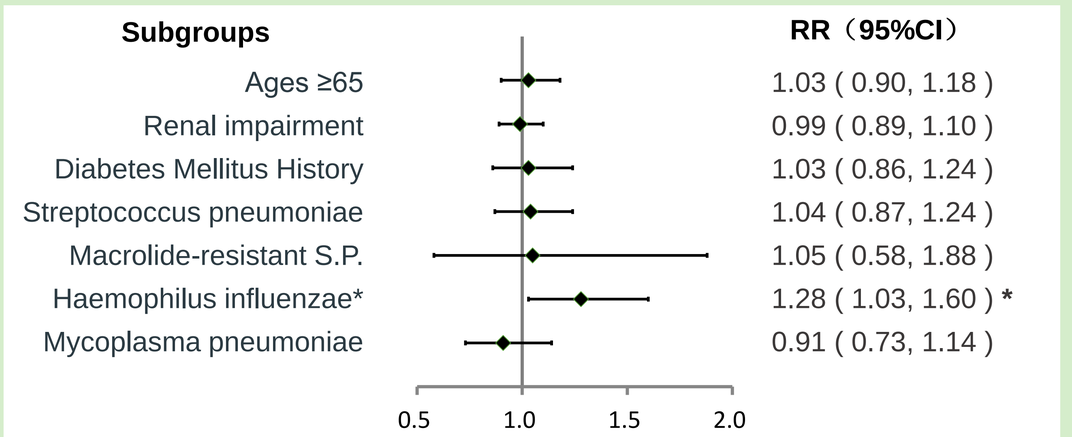
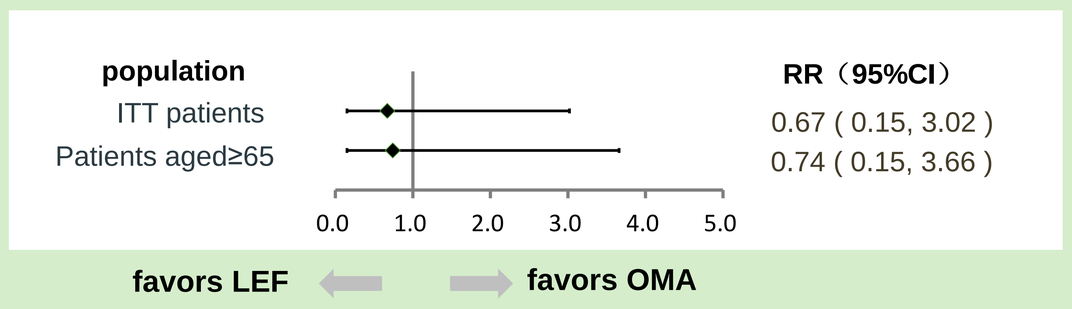


Figure 3b: Subgroup analysis of IACR at TOC (LEF vs. OMA)



*P＜0.05, showed statistically significant differences between the groups

Figure 4: Treatment emergent adverse events leading to death (LEF vs. OMA)



DISCUSSIONS

- Rising antibacterial resistance, coupled with the insufficient development of new antibiotics leads to a major global healthcare challenge.
- Lefamulin, a novel pleuromutilin antibiotic with a unique mechanism of action, meets the urgently need of new antibiotic classes. It shows promise in overcoming drug-induced resistance and cross-resistance, and it has potent in vitro activity against both common CAP bacteria and atypical pathogens(10).
- This study indirectly compared Lefamulin with Omadacycline, a new tetracycline-class antibiotic. The results demonstrate that Lefamulin is significantly superior to Omadacycline in terms of IACR in patients with Haemophilus influenzae. Additionally, compared to Omadacycline, Lefamulin shows potentially better outcomes in treating elderly patients, a history of diabetes mellitus, or with specific pathogens.
- However, not all subgroups were analyzed, such as patients with drug-resistant pathogens, due to a lack of relevant data. Further research is needed in the future.

CONCLUSIONS

- Lefamulin and Omadacycline have comparable efficacy and safety in treating CAP patients. Lefamulin appears to be a promising therapy option with a potentially lower risk of death. Further analysis of subgroups suggests that Lefamulin may improve clinical outcomes for elderly patients, those with comorbidities or specific pathogens.

REFERENCE

1. File TM Jr. Netter’s Infectious Diseases. 2012:127–36.
2. File Jr T M, et al. Clinical infectious diseases, 2019, 69(11): 1856-1867.
3. Alexander E, et al. Jama, 2019, 322(17): 1661-1671.
4. File Jr T M et al. BMC Pulmonary Medicine, 2021, 21(1): 154.
5. Cornely O A, et al, 2021, 57(2): 106263.
6. Pai M P, et al. Open Forum Infectious Diseases. 2019, 6.
7. Paukner S, et al. Journal of Global Antimicrobial Resistance, 2022, 29: 434-443.
8. Ramirez J, et al. 2018, 52: PA5465.
9. Stets R, et al. New England Journal of Medicine, 2019, 380(6): 517-527.
10. Shi Wu, et al. Front Microbiol. 2020 Sep 16;11:578824.

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