

Health-Related Quality of Life as Measured by the 12-Item Short-Form Survey Among Adults With Community-Acquired Bacterial Pneumonia who Received Either Lefamulin or Moxifloxacin in 2 Phase III Randomized, Double-Blind, Double-Dummy Clinical Trials

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Background. Interest in patient-reported outcomes (PROs) as part of benefit–risk assessment for new drug approvals is increasing. Lefamulin is the first intravenous (IV) and oral pleuromutilin antibiotic for treatment of adults with community-acquired bacterial pneumonia (CABP). Assessment of health-related quality of life (HRQoL) was prospectively incorporated in its CABP trials (Lefamulin Evaluation Against Pneumonia [LEAP] 1 and 2) via the 12-Item Short-Form Survey (SF-12), a widely used PRO that measures general health status in 8 domains.

Methods. HRQoL was evaluated by SF-12 at baseline and test of cure (TOC; 5–10 days after the last study drug dose) in patients who received lefamulin or moxifloxacin in LEAP 1 (IV/oral treatment) and LEAP 2 (oral-only treatment). SF-12 outcomes included the 8 domains, physical component and mental component summary scores, and the Short-Form Six-Dimension health utility score.

Results. Analysis included 1215 patients (lefamulin: n = 607; moxifloxacin: n = 608). At baseline, all mean SF-12 scores in both treatment groups were well below the United States reference mean. Clinically meaningful and significant improvements from baseline to TOC were observed in all SF-12 scores. No significant differences in mean score improvements from baseline to TOC between treatment groups were observed. SF-12 score improvements at TOC across predefined subgroups were comparable between treatment groups.

Conclusions. Results indicate that adults with CABP experienced comparable HRQoL improvements with lefamulin relative to moxifloxacin, and treatment with either agent resulted in returns to population norm HRQoL levels. These data suggest that lefamulin is a potential alternative to moxifloxacin for treatment of adults with CABP.

Keywords. lefamulin; patient-reported outcome measures; pneumonia; quality of life; SF-12.

Efficacy end points for most phase III antibiotic registrational trials have been based on clinician assessment of improvement/resolution of signs and symptoms of infection after completion of antimicrobial therapy (test-of-cure [TOC] visit) [1]. While this is a valuable assessment of a patient's response to treatment, it does not fully capture the patient's reported experience [2]. Across all therapeutic domains, there is increased interest in incorporating patient-reported outcomes (PROs) as part

of the benefit–risk assessment for new drug approvals [3–5]. According to the US Food and Drug Administration (FDA)–National Institutes of Health (NIH) Biomarkers, Endpoints, and other Tools (BEST) Working Group, a PRO is “a measurement based on a report that comes directly from the patient (ie, study subject) about the status of a patient's health condition without amendment or interpretation of the patient's response by a clinician or anyone else” [4]. Patient-centeredness is also a growing area of focus in the health care sector and is a major component of the person and community engagement quality domain in the Centers for Medicare & Medicaid Services Hospital Value-Based Purchasing Program [6, 7].

Lefamulin is a first-in-class intravenous (IV) and oral pleuromutilin antibiotic that is approved for the treatment of adult patients with community-acquired bacterial pneumonia (CABP). Lefamulin was shown to be noninferior to moxifloxacin based on the standard early and post-treatment clinical response end points in 2 phase III clinical trials,

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NAB-BC-3781-3101 (Lefamulin Evaluation Against Pneumonia [LEAP 1]; NCT02559310) and NAB-BC-3781-3102 (LEAP 2; NCT02813694) [8, 9]. Given the increasingly significant role of PROs in the development and evaluation of new medicines, health-related quality of life (HRQoL) measures [10], a type of PRO, were prospectively incorporated and evaluated in LEAP 1 and 2 via the acute form of the 12-item Short Form Survey (SF-12), version 2 [11]. The SF-12 is a general HRQoL survey that measures general health status in 8 domains (physical functioning, role limitations due to physical problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health) (Table 1). Although it has not been validated for patients with CABP, the SF-12 has been used extensively and is broadly demonstrated to be reliable and well-validated across most health and clinical contexts of use [12, 13]. The intent of this analysis was to describe and compare HRQoL outcomes as measured by the SF-12 administered to CABP patients who received either lefamulin or moxifloxacin using pooled data from LEAP 1 and 2.

METHODS

Study Design and Population

This analysis was performed using pooled data from 2 completed phase III clinical trials, LEAP 1 and 2 [8, 9]. The inclusion/exclusion criteria were similar, except that LEAP 1 included patients with greater disease severity (Pneumonia Outcomes Research Team [PORT] [14] risk class III–V compared with PORT risk class II–IV in LEAP 2), and patients with CABP due to known or suspected methicillin-resistant *Staphylococcus aureus* (MRSA) were excluded from LEAP 2. Other differences between the studies included the route of administration and duration of treatment. LEAP 1 involved IV administration followed by a possible switch to oral after 3 days in both treatment groups, whereas LEAP 2 involved the use of oral administration only. In LEAP 1, the lefamulin treatment duration was 5 or 7 days depending on protocol version vs

7 days for moxifloxacin; patients with MRSA were to receive 10 days in both groups. The moxifloxacin group in LEAP 1 also included treatment with adjunctive linezolid if MRSA was suspected at enrollment. In LEAP 2, the lefamulin treatment duration was 5 days vs 7 days for moxifloxacin.

The trial protocols and informed consent forms were approved by the ethics committee or institutional review board at each participating site. The trials were conducted in compliance with the ethical principles of the Declaration of Helsinki and the Good Clinical Practice guidelines of the International Conference on Harmonisation. All patients provided written informed consent before initiating any study-related procedures [8, 9].

Patients in the modified intent-to-treat (mITT) population (ie, all randomized and treated patients) from LEAP 1 and 2 were included in this analysis with the following additional requirements: (1) met CABP disease criteria, (2) were PORT risk II, III, or IV at baseline [14], and (3) received at least 24 hours of treatment (unless due to death).

Patient Data

Data elements in the LEAP trials included enrollment region, demographics, medical history and comorbidities, laboratory findings, prior antibiotic therapies, tobacco history and history of pneumococcal vaccination (if any), severity of illness based on the PORT scoring system [14], American Thoracic Society (ATS) minor severity criteria [15], modified ATS severity criteria [16], systemic inflammatory response syndrome (SIRS) criteria [17], CURB-65 (acronym for confusion, urea, respiratory rate, blood pressure, age ≥ 65 years) [18], and microbiological culture results. The full details of the patient data collected in LEAP 1 and LEAP 2 are described elsewhere [8, 9].

Health-Related Quality of Life

The acute form of the SF-12¹¹, used to measure HRQoL, was administered to patients in LEAP 1 and 2 at baseline, defined as within 24 hours before the first study drug dose, and at the

Table 1. SF-12 Items and Scales

Question No.	Description of Question	Response Options	Domain
2	General health	1–5	General Health
3a	Health affected moderate activities	1–3	Physical Functioning
3b	Health affected step climbing	1–3	Physical Functioning
4a	Physical health affected ability to accomplish	1–5	Role Physical
4b	Physical health affected kind of work or other activities	1–5	Role Physical
5a	Emotional health affected ability to accomplish	1–5	Role Emotional
5b	Emotional health affected kind of work or other activities	1–5	Role Emotional
6	Pain interfered with normal work	1–5	Bodily Pain
7a	Felt calm and peaceful	1–5	Mental Health
7b	Had a lot of energy	1–5	Vitality
7c	Felt downhearted or depressed	1–5	Mental Health
8	Amount of time physical or emotional problems interfered with social activities	1–5	Social Functioning

TOC visit, defined as 5–10 days after the last study drug dose. The TOC visit occurred between study days 12 and 17 for 95% of patients. The TOC visit occurred either before study day 12 or after study day 17 for the remaining 5% of patients.

The 12 items of the SF-12 and the 8 domains to which they correspond are detailed in [Table 1](#). The 8 individual domains and 2 component scores, the physical component summary (PCS) and mental component summary (MCS) scores, were evaluated using Optum's QualityMetric proprietary software, version 5.1 [19]. All scores were normalized against the 2009 US population reference scores. A score of 50 for any of the SF-12 domains or component summaries is equivalent to the reference population mean, and the standard deviation is set at 10. The minimum clinically important differences (MCIDs) for the PCS, MCS, and 8 domains are as follows: PCS: 2; MCS: 3; General Health: 2; Physical Functioning: 3; Role Physical: 3; Bodily Pain: 3; Vitality: 2; Social Functioning: 3; Role Emotional: 4; Mental Health: 3 [11].

The Short-Form Six-Dimension (SF-6D), a preference-based single utility measure of general health, was also derived from SF-12 items using Optum's QualityMetric proprietary software [20]. Utility values for SF-6D health states range between 0.0 and 1.0, where 0.0 represents death and 1.0 represents full health. US population norms for the SF-6D have been established as scores between 0.76 and 0.80, and a change of 0.03 points on the SF-6D has been established as the boundary for the MCID [21].

Data Analysis Plan

Analyses of SF-12 data were prespecified in the LEAP 1 and 2 statistical analysis plans and were conducted after study completion in the pooled population. Descriptive analysis of baseline patient characteristics included age, sex, race, weight, body mass index, renal status at baseline, severity of illness (ie, PORT [14], CURB-65 score [18], ATS severity criteria [15], and presence of SIRS [17]), presence of bacteremia, prior antibiotic use, microbiologic culture results, and all SF-12 scores (domain, PCS, MCS, and SF-6D). Treatment comparisons for all SF-12 domain scores, the PCS score, the MCS score, and the SF-6D score were performed at each visit (baseline and TOC). Changes from baseline to TOC (score at TOC – score at baseline) in SF-12 domain scores, the PCS score, the MCS score, and the SF-6D score were also compared between treatment groups. The overall difference in the change in SF-12 domain scores, the PCS score, the MCS score, and the SF-6D score between treatment groups was assessed using a linear model, adjusted for the corresponding baseline SF-12 score. Comparisons of all SF-12 scores were also conducted in following subgroups: PORT risk class (II, III, and IV), sex (male and female), age group (18 to <50 years, 50 to <65 years, and ≥65 years), number of comorbidities (0–2 and >2), and LEAP trial (LEAP 1 and

LEAP 2). The false discovery rate method was used to adjust for multiple comparisons [22].

RESULTS

There were 1215 patients (lefamulin: $n = 607$; moxifloxacin: $n = 608$) from the LEAP trials who met the selection criteria and were included in the study population, which represents 94% of the original randomized population (total: $n = 1289$; lefamulin: $n = 646$; moxifloxacin: $n = 643$). The most common reasons subjects were excluded from this analysis were not meeting CABP disease criteria ($n = 39$) and not receiving at least 24 hours of treatment ($n = 30$). Baseline characteristics were similar between lefamulin and moxifloxacin and are summarized in [Table 2](#). Overall, the average age was 59 years, 80% were white, the mean body mass index was 26.5 kg/m², 53% were PORT risk class III, and 96% met SIRS criteria. The proportion of males was slightly higher in the lefamulin group (58%) compared with moxifloxacin (53%). The median (interquartile range) number of comorbidities was 2 (1–4) in both the lefamulin and moxifloxacin groups. Comorbidities in >5% of patients overall included hypertension (38%), diabetes mellitus (13%), chronic obstructive pulmonary disease (10%), and asthma (6%). Prior use of a short-acting antibiotic within 72 hours before randomization was reported in 23% and 22% of patients in the lefamulin and moxifloxacin groups, respectively. Of the 1215 patients included, 3 patients (1 lefamulin and 2 moxifloxacin) were missing most of the baseline SF-12 scores, and 47 patients (25 lefamulin and 22 moxifloxacin) were missing most of the TOC SF-12 scores due to non- or partial completion of the SF-12 or a missed TOC visit. We were able to assess change in SF-12 scores in 1166 patients (582 lefamulin and 584 moxifloxacin).

At baseline, all mean SF-12 scores (domain, PCS, and MCS) were well below (>MCID) the US norm level of 50 in the lefamulin and moxifloxacin groups. This indicated a low level of HRQoL for patients with CABP, ranging from a mean of 31 for Role Emotional to a mean of 42 for Vitality ([Figure 1A](#)). At TOC, the mean SF-12 scores in both the lefamulin and moxifloxacin groups were generally close to the national norm of 50, indicating an average level of HRQoL ([Figure 1B](#)). Clinically meaningful and statistically significant improvements in all mean SF-12 scores were observed from baseline to TOC in both treatment groups ([Figure 1C](#)). The greatest magnitude of improvements was observed in the domain of General Health, which showed improvements of 15.6 for lefamulin and 15.8 for moxifloxacin. The least substantial improvement in HRQoL was seen in the domain of Mental Health, which showed improvements of 11.2 for lefamulin and 11.5 for moxifloxacin. There were no clinically or statistically significant differences in least squares mean score improvements in HRQoL from baseline to TOC between lefamulin and moxifloxacin. Similarly,

Table 2. Patient Characteristics

Characteristic	Lefamulin (n = 607)	Moxifloxacin (n = 608)	Total (n = 1215)
Age, mean (SD), y	58.8 (16.29)	58.4 (15.53)	58.6 (15.91)
Male, No. (%)	354 (58.3)	325 (53.5)	679 (55.9)
Race, No. (%)			
White	490 (80.7)	486 (79.9)	976 (80.3)
Black or African American	25 (4.1)	32 (5.3)	57 (4.7)
Asian	65 (10.7)	63 (10.4)	128 (10.5)
American Indian or Alaska Native	21 (3.5)	17 (2.8)	38 (3.1)
Native Hawaiian or other Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)
Other	6 (1.0)	10 (1.6)	16 (1.3)
Weight, mean (SD), kg	75.5 (19.22)	74.0 (18.34)	74.7 (18.79)
BMI, mean (SD), kg/m ²	26.5 (5.84)	26.4 (5.86)	26.5 (5.85)
Renal status, ^a No. (%)			
Severe impairment (CrCl <30 mL/min)	6 (1.0)	4 (0.7)	10 (0.8)
Moderate impairment (CrCl 30–<60 mL/min)	111 (18.3)	125 (20.6)	236 (19.4)
Mild impairment (CrCl 60–<90 mL/min)	190 (31.3)	181 (29.8)	371 (30.5)
Normal function (CrCl ≥90 mL/min)	299 (49.3)	298 (49.0)	597 (49.1)
Missing	1	0	1
PORT risk class, No. (%)			
II	174 (28.7)	181 (29.8)	355 (29.2)
III	327 (53.9)	322 (53.0)	649 (53.4)
IV	106 (17.5)	105 (17.3)	211 (17.4)
CURB-65 score, No. (%)			
0	106 (17.5)	106 (17.4)	212 (17.4)
1	308 (50.7)	303 (49.8)	611 (50.3)
2	162 (26.7)	163 (26.8)	325 (26.7)
3	31 (5.1)	32 (5.3)	63 (5.2)
4	0 (0.0)	4 (0.7)	4 (0.3)
5	0 (0.0)	0 (0.0)	0 (0.0)
Patients meeting minor ATS severity criteria, ^b No. (%)	80 (13.2)	78 (12.8)	158 (13.0)
Patients meeting modified ATS severity criteria, ^c No. (%)	47 (7.7)	53 (8.7)	100 (8.2)
Patients meeting SIRS criteria, ^d No. (%)	587 (96.7)	579 (95.2)	1166 (96.0)
Patients with bacteremia, No. (%)	12 (2.0)	12 (2.0)	24 (2.0)
Prior antibiotic use within 72 h before randomization, No. (%)	137 (22.6)	134 (22.0)	271 (22.3)
Comorbidities, median (IQR)	2 (1–4)	2 (1–4)	2 (1–4)

Abbreviations: ATS, American Thoracic Society; BMI, body mass index; CrCl, creatinine clearance; CURB-65, confusion, BUN >19 mg/dL, respiratory rate ≥30 breaths/min, blood pressure <90 mmHg systolic or ≤60 mmHg diastolic, and age ≥65 years; IQR, interquartile range; PORT, Pneumonia Outcomes Research Team; SIRS, systemic inflammatory response syndrome.

^aNational Kidney Foundation categories of renal impairment determined by Cockcroft-Gault [23] using baseline central laboratory serum creatinine. When baseline central laboratory serum creatinine was not available, local serum creatinine results were used.

^bDefined as presence of ≥3 of the following 9 criteria at baseline: respiratory rate ≥30 breaths/min, O₂ saturation <90% or PaO₂ <60 mmHg, BUN ≥20 mg/dL, WBC <4000 cells/mm³, confusion, multilobar infiltrates (defined as infiltrates present in any 2 locations; exception: lingula with left upper lobe was not considered multilobar), platelets <100 000 cells/mm³, temperature <36°C, systolic blood pressure <90 mmHg.

^cDefined as presence of ≥3 of the following 6 criteria at baseline: respiratory rate ≥30 breaths/min, SpO₂/FiO₂ <274 where SpO₂/FiO₂ = 64 + 0.84(PaO₂/FiO₂), BUN ≥20 mg/dL, confusion, age ≥65 years, multilobar infiltrates.

^dDefined as ≥2 of the following 4 symptoms at baseline: temperature <36°C or >38°C, heart rate >90 beats/min, respiratory rate >20 breaths/min, WBC <4000 or >12 000 cells/mm³, or immature PMNs >10%.

mean SF-6D scores of 0.58 in both groups at baseline were well below the US population norm range of 0.76–0.80 (Table 3). At TOC, the mean SF-6D scores of 0.74 and 0.75 in the lefamulin and moxifloxacin groups, respectively, approached the US population norm, reflecting clinically meaningful and statistically significant improvements in both treatment groups.

Results of the subgroup analyses are shown in the Supplementary Data. Patients with a lower PORT risk class, indicating lower disease severity, generally had slightly higher mean SF-12 scores at baseline, TOC, and greater improvement between baseline and TOC relative to patients with a higher

PORT risk class. Females and males generally had similar mean SF-12 scores at baseline and a similar level of improvement between baseline and TOC. Patients in younger age groups generally had slightly higher mean SF-12 scores at baseline and TOC and greater improvements between baseline and TOC relative to patients in older age groups. Patients with 0–2 comorbidities compared with patients with >2 comorbidities generally had similar mean SF-12 scores at baseline but had greater improvements between baseline and TOC. Patients from LEAP 1 compared with patients from LEAP 2 generally had slightly lower mean SF-12 scores at baseline and TOC but a similar

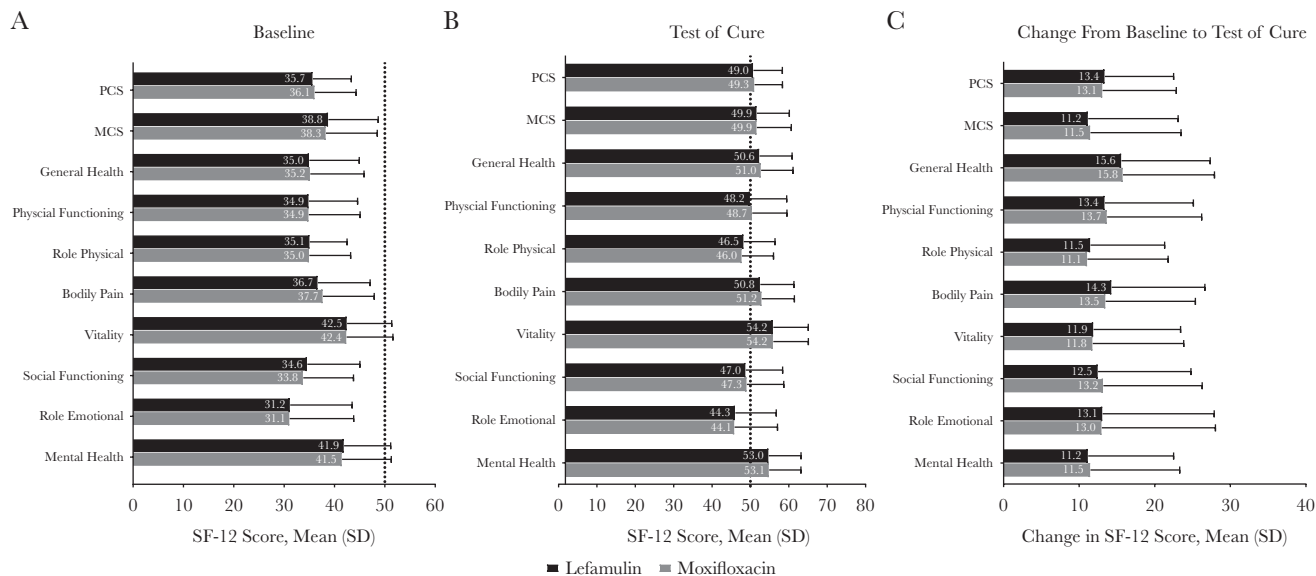


Figure 1. Summary of SF-12 scores. Higher SF-12 domain, PCS, and MCS scores indicate better health-related quality of life. Dotted line indicates the 2009 US population reference mean of 50. Abbreviations: MCS, mental component summary; PCS, physical component summary; SF-12, 12-item Short Form Survey.

level of improvement between baseline and TOC. No clinical or statistical differences, after adjustment for multiple comparisons, were noted in the least squares mean improvements in SF-12 scores from baseline to TOC between lefamulin and moxifloxacin in any subgroup analyses.

DISCUSSION

One of the fundamental goals of medical care is to improve the quality of life of those who require care. It is important to ensure that a patient is not only made well but feels well [24]. When quality of life is considered in the context of health and disease, it is commonly referred to as HRQoL and refers to the personal satisfaction expressed or experienced by individuals about their own physical, mental and emotional, and social functioning quality of life [10]. Evaluation of changes in HRQoL associated with health interventions is a public health priority [24], and there has been increasing interest in taking the “voice” of the patient into account during the development process [2–5]. PROs are now widely used in a number of therapeutic areas, mostly chronic diseases and oncology [3–5], and there has been a concerted effort to include PROs in the evaluation of antibiotics for acute infectious conditions [2], including

acute cystitis [25], community-acquired pneumonia [26, 27], and skin and skin structure infections [1, 28]. In the health care sector, there has been a growing movement to focus the evaluation of health care interventions and therapies on the assessment of changes in HRQoL and other end results in an effort to maximize the net health benefit derived from the use of finite health care resources [6, 7].

Given the interest across multiple stakeholders in incorporating patient experience data as part of the benefit–risk assessment for new drug approvals and formulary decisions [1–7, 28], an assessment of changes in HRQoL was included in the LEAP trials via the SF-12 survey. Overall, there were 3 major findings from the SF-12. First, all mean SF-12 and SF-6D scores were well below the US population norms at baseline. This is not surprising given the acuteness of illness among patients with CABP. Second, highly significant statistical and clinical improvements in all mean SF-12 and SF-6D scores were observed from baseline to TOC in both treatment groups, and all mean scores returned to near US population norms. This indicates that patients likely returned to pre-infection conditions. For the SF-12 scores, a 2- to 4-point improvement from baseline to TOC was considered clinically meaningful, and all domain

Table 3. Summary of SF-6D Scores

Score	Visit	Lefamulin (n = 607)	Moxifloxacin (n = 608)
SF-6D, mean (SD)	Baseline	0.58 (0.099)	0.58 (0.105)
	Test of cure	0.74 (0.130)	0.75 (0.127)
	Change from baseline to test of cure ^a	0.17 (0.142)	0.17 (0.147)

Abbreviation: SF-6D, Short-Form Six-Dimension.

^aA change of 0.03 points in the SF-6D has been established as the boundary for the minimum clinically important difference.

and component mean scores increased by 11–15. Similarly, a change of 0.03 points on the SF-6D was considered clinically meaningful, and mean SF-6D increased by 0.17 in both treatment groups. Of note, despite similar mean SF-12 scores at baseline, patients with 0–2 comorbidities had greater improvement between baseline and TOC relative to patients with >2 comorbidities. Although not assessed in this analysis, data indicate that CABP patients with multiple comorbidities are frequently readmitted within 30 days [29]. These collective findings suggest the importance of developing strategies to simultaneously manage patients' CABP and underlying comorbidities in order to maximize HRQoL and minimize the risk of readmission. Third, improvements in overall mean HRQoL scores were comparable between treatment groups. The totality of the above findings is notable considering that the treatment duration for lefamulin was 2 days less than moxifloxacin for all patients in LEAP 2 and for 25% of patients in LEAP 1 (before a protocol amendment for study logistics).

The comparable improvements in HRQoL outcomes between lefamulin and moxifloxacin have important implications for clinical practice. There are only a limited number of antibiotics with interchangeable IV and oral formulations approved for patients with CABP [15]. Fluoroquinolones are the most widely prescribed antibiotics, with interchangeable IV and oral formulations for patients with CABP, and their efficacy has been well documented across a large number of comparator studies. Despite their well-demonstrated efficacy in patients with CABP, there is increased recognition of their safety risks. The US FDA and European Medicines Agency (EMA) have updated the labeling of all fluoroquinolones, advising of the serious risk of multiple disabling and potentially irreversible adverse reactions associated with their use, including aortic aneurysm and rupture [30]. Both the FDA and EMA recommend prescribing fluoroquinolones to patients only when no other treatment options are available [30–33]. Combined with the phase III efficacy and safety data, the current HRQoL outcomes suggest that lefamulin is a potential fluoroquinolone replacement agent, especially in populations at an elevated risk for certain fluoroquinolone-associated adverse events.

Several issues should be taken into consideration when interpreting these findings. First, there is no FDA-approved HRQoL measure for patients with CABP. While CABP-specific PROs such as the Community-Acquired Pneumonia Symptom questionnaire (CAP-Sym), CAP Burden of Illness questionnaire (CAP-BIQ), and CAP Score (among others) have been developed and validated, they have been criticized as they fail to measure more global symptoms [26]. General HRQoL questionnaires such as the 36-item Short Form Survey (SF-36) and EuroQol EQ-5D-3L are widely used, well validated, and have been applied to patients with CAP [34, 35], but were considered potentially too burdensome for some patients enrolled in the LEAP trials. In light of this, we opted to administer the SF-12,

a widely used, validated generic PRO that has been translated into multiple languages, is comparable to the general population, and is associated with a smaller respondent burden than the larger generic SF-36 [12, 13, 26]. Although the SF-12 has not been specifically validated in adult patients with CABP, the parent SF-36 has been [26]. This study examined improvements in HRQoL and health utility outcomes in adult CABP patients from 2 pooled randomized, multicenter, double-blinded studies designed to assess efficacy. Data from real-world settings would help to affirm the findings, as this LEAP clinical trial population may not be representative of the patients likely to receive the medications in clinical practice. Similar to most CABP trials, the majority of patients enrolled in LEAP 1 and 2 were from non-North American countries. Given the potential cultural influence on HRQoL perception, data from additional patients in the United States would help to confirm the generalizability of the findings. However, the comparable improvements in HRQoL between the homogeneous treatment groups strongly suggest that lefamulin will produce a similar post-treatment HRQoL benefit as moxifloxacin.

In conclusion, there is an increased emphasis on incorporating the perspective of the patient when making medical decisions and assessing treatment impact. The findings from this analysis show that patients who received lefamulin had comparable improvements in HRQoL relative to those who received moxifloxacin. Combined with phase III efficacy and safety data, these findings have implications for clinical practice, as analyses suggest that lefamulin provides an effective new IV and oral monotherapy option for empiric treatment of adults with CABP. There is a clear clinical need for new antibiotics with interchangeable IV and oral formulations for patients with CABP that result in similar HRQoL improvements as fluoroquinolones without their inherent safety concerns. The methodology employed here also provides a framework to prospectively incorporate HRQoL assessments in phase III CABP efficacy trials. This examination of HRQoL data collected in 2 phase III clinical trials suggests that, in patients with CABP, lefamulin is associated with an improvement in patients' health-related quality of life and provides a potential alternative to respiratory fluoroquinolones; additional findings from the real-world setting will be important to confirm these conclusions.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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for Nabriva Therapeutics. Mr. Colman is an employee of Covance Market Access Services Inc., which Nabriva remunerated for the statistical analysis. Drs. Alexander, Stein and Fitts were employees of and held stock in Nabriva Therapeutics plc when the work was performed. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Author contributions. The SF-12 was prospectively incorporated in LEAP 1 and LEAP 2. T.L. and S.C. led completion of the data analysis plan, analysis and interpretation of the data, and drafting of the report. S.C. and D.F. were the study statisticians. All authors were responsible for data interpretation and drafting of the report. All authors provided critical reviews and final approval of the manuscript. The approval of the manuscript and decision to submit the manuscript for publication were the responsibility of the coauthors, led by T.L.

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Data availability. Data not publicly available.

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