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ORIGINAL ARTICLE

Comparison of hospitalization rates in patients with community-acquired pneumonia treated with telithromycin for 5 or 7 days or clarithromycin for 10 days

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SUMMARY

Aims: To compare the impact on hospitalization rates and the clinical efficacy of oral telithromycin and clarithromycin treatment in patients with community-acquired pneumonia (CAP).

Methods: A total of 581 patients with CAP were enrolled in this randomized, double-blind, parallel-group, multinational study, of whom 575 were evaluated for healthcare resource utilization from a payer perspective (intent to treat [ITT] population). Patients received telithromycin 800 mg once daily for 5 (n = 193) or 7 (n = 195) days, or clarithromycin 500 mg once daily for 10 days (n = 187). The primary efficacy endpoint was clinical outcome at test of cure (Days 17–24) in the per-protocol population. Frequency of CAP-related hospitalizations, physician visits/tests/procedures, and additional respiratory tract infection-related antibacterial use were compared by treatment group (ITT) up to late post-therapy (Days 31–36). Study investigators blinded to treatment assessed whether hospital admissions were CAP-related or not. CAP-related hospitalization costs (US$) for telithromycin and clarithromycin were compared.

Results: Clinical cure rates were similar in patients who received clarithromycin for 10 days and telithromycin for 5 or 7 days: 91.8% (134/146), 89.3% (142/159), and 88.8% (143/161), respectively, and both 5- and 7-day telithromycin were statistically equivalent to clarithromycin (difference: –2.5 and –3.0%, respectively; 95% CI: –9.7, 4.7 and –10.2, 4.3, respectively). There were 7 CAP-related hospital admissions among clarithromycin patients vs 3 (p = 0.283) and 1 (p = 0.021) admissions among 5- and 7-day telithromycin patients, respectively. The number of hospital days/100 patients was 40.1 for clarithromycin vs 17.1 and 7.2 for 5- and 7-day telithromycin, respectively. Projected hospitalization costs/100 patients were $86 205 for clarithromycin vs $37 930 (difference: –26 446; 95% CI: –66 654; 13 762) and $16 091 (difference: –37 847; 95% CI: –77 953; 2259) for 5- and 7-day telithromycin, respectively.

Conclusions: Data from this study demonstrate that telithromycin 800 mg once daily for 5 or 7 days is an effective treatment for CAP, and that telithromycin treatment of CAP may be associated with fewer hospital days and potentially lower hospitalization costs than clarithromycin treatment.

Introduction

In the USA, CAP is the sixth leading cause of death and the most common cause of death due to infection[1,2]. An estimated 2–5 million cases occur annually; consequently, the management of patients with this infection has significant financial implications for healthcare systems[1,3,4]. An estimated 20% of patients with CAP require hospitalization, while 80% of patients are treated in the outpatient setting[5,6]. The majority of CAP-related morbidity, mortality, and healthcare expenditure occurs among the 20% of persons hospitalized at some point during the course of their illness[5]. Outpatient mortality ranges from < 1 to 5% whereas inpatient mortality can be as high as 30–40% (average 14%)[1,6]. In the USA, direct annual outpatient treatment costs of US$1 billion have been estimated, while inpatient costs are in excess of US$8 billion[2,7–9]. Indirect costs – including days of bed confinement, restricted activity, and/or work loss – further add to the overall economic burden of the disease[7,10].

A large proportion of CAP cases are caused by bacterial infection. In the majority of outpatients, the etiology of CAP is not identified prior to the initiation of treatment[1]. Although microbiologic tests are usually performed for inpatients, the etiology of CAP cannot be identified for a significant proportion (40–60%) of these patients[1]. Antibacterial therapy for CAP – particularly in the outpatient setting – is, therefore, usually empiric and must cover the range of possible causative pathogens, including *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and atypical/intracellular pathogens such as *Chlamydia* (*Chlamydophila*), *Mycoplasma*, and *Legionella* spp.[11,12]. Current North American treatment guidelines recommend the use of doxycycline or oral macrolides, particularly newer agents such as azithromycin and clarithromycin, as first-line agents for the outpatient management of CAP[13–15]. This is because of their activity against atypical pathogens as well as *S. pneumoniae*. Antibacterial resistance among *S. pneumoniae* is now of major concern worldwide[16], and it may become increasingly difficult to provide optimum coverage for CAP with a single antibacterial agent[6,13–15]. Combination therapy with a macrolide and a β-lactam with good antipneumococcal activity is generally recommended for patients with risk factors for drug-resistant *S. pneumoniae* (DRSP)[6,13,14]. Treatment guidelines published by the Infectious Diseases Society of America[13] and the American Thoracic Society[6] advocate the use of fluoroquinolones as alternative agents for patients with risk factors for DRSP. Owing to concerns over the emergence and spread of pneumococcal fluoroquinolone resistance, the Centers for Disease Control and Prevention guidelines[14] recommend that these agents be restricted to patients who have failed previous therapy, are allergic to the preferred agents, or have documented infection with highly drug-resistant pneumococci.

Telithromycin is the first in a new class of antibacterials – the ketolides – related to the macrolides, but with a number of novel structural–functional features that confer enhanced antibacterial activity[17,18]. Telithromycin provides coverage of the common causative pathogens in CAP, including atypical/intracellular organisms and antibacterial-resistant strains of *S. pneumoniae*[17,18]. Results from eight Phase III/IIIb clinical studies confirm the clinical efficacy of oral telithromycin 800 mg once daily in the treatment of adolescent and adult outpatients with CAP of mild to moderate severity[17–21]. As clarithromycin is a commonly recommended first-line empiric therapy for the outpatient management of CAP in adults[6,13–15], two independent but similar studies assessed the efficacy of telithromycin vs clarithromycin in the treatment of CAP. In one study patients received telithromycin for 10 days[20], while in the second study patients received telithromycin for either 5 or 7 days[21]. The present *post hoc* analysis was performed to investigate whether there were any differences in overall healthcare resource utilization associated with telithromycin for 5 or 7 days vs clarithromycin for 10 days in adults with CAP. Cost analyses were performed from a payer perspective on hospitalization data collected prospectively in this randomized, double-blind, multicenter clinical study. An analysis of the overall healthcare resource utilization associated with 10 days of oral telithromycin vs 10 days of clarithromycin is reported separately[22].

Patients and methods

Patients and Study Design

Adult (aged ≥ 18 years) outpatients and inpatients considered suitable for oral therapy with a suspected diagnosis of CAP were enrolled in a randomized, double-blind, parallel-group Phase III clinical trial. This multicenter study was conducted at 77 investigational sites in 9 countries: Argentina (8 sites), Brazil (5 sites),

Canada (14 sites), Chile (2 sites), Germany (6 sites), South Africa (9 sites), Spain (4 sites), the UK (5 sites), and the USA (24 sites). The study was carried out in accordance with the ethical principles of the Declaration of Helsinki. Informed consent was obtained from all patients prior to the conduct of any study-related procedures.

A diagnosis of CAP was confirmed based upon the production of purulent sputum and new onset of at least two of the following clinical signs and symptoms: cough; auscultatory finding, such as rales and/or evidence of pulmonary consolidation; dyspnea or tachypnea, particularly if progressive in nature; fever and elevated total peripheral white blood cell count > 10 000/mm^3, or > 15% immature neutrophils (bands) regardless of total peripheral white blood cell count. Chest X-ray findings supportive of a clinical diagnosis of bacterial pneumonia were also required (e.g. presence of presumable new infiltrate). Respiratory/sputum and blood samples were collected from patients for bacteriologic documentation within the 48 h preceding enrollment. Based on their age, the presence of co-existing disease, and abnormal physical or laboratory findings, patients were stratified on the Fine scale (the Pneumonia Severity Index scoring system), with Class I being associated with the lowest risk of mortality, and Class V the highest[23]. Patients with severe CAP, CAP requiring immediate admission to an intensive care unit or parenteral antibacterial therapy, and those with infections attributable to sources other than community-acquired bacterial pathogens were excluded from the study. Also excluded were patients who had risk factors for DRSP – patients who had received more than 24 h of treatment with other antibacterials within the 7 days prior to enrollment, patients who had documented infection with a pathogen resistant to study medication prior to enrollment, patients with a history of alcohol abuse, and immunocompromised patients.

Patients were randomized (ratio 1:1:1) to receive oral telithromycin 800 mg once daily (two 400 mg tablets) for 5 or 7 days, or clarithromycin 500 mg twice daily for 10 days. Clinical, bacteriologic, and economic outcomes were followed for a 1-month period following randomization. Patient evaluations were undertaken at pre-therapy/entry (Day 1), on-therapy (Days 3–5), end of therapy (Days 11–13), post-therapy/test of cure (TOC) (Days 17–24), and late post-therapy (Days 31–36) visits.

The primary statistical hypothesis was equivalence in clinical efficacy at the post-therapy/TOC visit in the clinically evaluable per-protocol populations (PPc). Clinical outcomes were assessed on the basis of recognized signs and symptoms of CAP and chest X-ray findings. Outcomes were classified as cure (improvement with no subsequent antibacterial therapy required or return to pre-infection state), failure (unchanged or worsened symptoms, requirement for additional antibacterials, or an adverse event leading to treatment discontinuation), or indeterminate (missing post-treatment information or early discontinuation for reasons that were unrelated to the study drug, requirement for additional antibacterials for non-lower respiratory tract infection (RTI)-related reasons, or a laboratory measurement fulfilling exclusion criteria being identified after initiation of treatment that led to discontinuation of the study drug). Secondary efficacy variables included bacteriologic outcomes at the post-therapy/TOC visit and clinical and bacteriologic outcomes at the late post-therapy visit.

Safety and tolerability were assessed throughout the study based on measurements of laboratory safety parameters (including hematology, serum biochemistry, and urinalysis), electrocardiogram recordings (ECGs), and the emergence of adverse events (spontaneously reported by patients or observed by the study investigators, and assessed in terms of causality).

Healthcare Resource Utilization

Healthcare Resource Utilization Case Report Forms (HRU-CRFs) were used to collect healthcare resource utilization data. At the end of therapy, post-therapy/TOC, and late post-therapy visits, investigators collected information about the use of 'additional healthcare resources (beyond those required by protocol)'. Protocol-derived healthcare resources, as outlined in the clinical protocol, included:

- X-ray investigations
- ECGs
- physician visits, examinations, and tests/procedures
- microbiologic/bacteriologic tests
- measurement of safety parameters (hematology, biochemistry, and urinalysis).

Non-protocol related healthcare resource utilization data included:

- hospital emergency department visits
- additional contacts with general practitioner departments, pulmonary specialists, infectious disease specialists, community nurses, and other healthcare professionals
- healthcare-related home contacts
- additional ambulatory and inpatient tests/procedures
- hospitalizations related to CAP (also assessed at the pre-therapy/entry and on-therapy visits)
- concomitant medications related to RTI (information on additional antibiotic usage was obtained from Concomitant Medication Forms).

Healthcare resource utilization analyses were performed on the intent to treat (ITT) population of patients (randomized patients who received at least one dose of study medication) rather than the PPc population, as this population equates more closely to that seen in clinical practice.

Hospitalizations and Associated Costs

Hospitalizations were recorded on Serious Adverse Events Forms (SAEFs) up to the post-therapy/TOC visit as part of the clinical protocol, and on HRU-CRFs up to the late post-therapy visit as part of the healthcare resource utilization protocol. For the purposes of the healthcare resource utilization analysis, study investigators who were blinded to treatment group at the time of admission evaluated whether hospitalizations were CAP related (associated with the study indication based on clinical signs/symptoms) or not (signs/symptoms consistent with RTI other than the study indication, or any other non-respiratory related condition). Although hospitalizations due to all causes were recorded throughout the study – captured on the SAEFs or the HRU-CRFs (or both forms) – only those considered related to CAP by the blinded study investigators were included in subsequent cost analyses. Hospitalizations prior to the initiation of treatment (following randomization) were considered to be 'due to care' and were not included in the analyses. Length of stay was recorded for all patients admitted to hospital for CAP-related reasons.

Some inpatients were included in this multinational trial (due to inter-country differences in practice). Inpatients who failed on the study drug could still be captured in the hospitalization analysis (i.e. if discharged and re-hospitalized). Inpatients were deemed suitable for oral therapy and concomitant non-antibacterial treatments were kept to a minimum as part of the clinical protocol (i.e. there was no advantage of inpatient vs outpatient treatment in this clinical trial setting).

Total CAP-related hospitalization costs for telithromycin and clarithromycin patients were calculated in US dollars and compared by treatment group. Overall costs of inpatient hospitalization were derived by multiplying the total number of CAP-related hospital days per treatment group by the average *per diem* cost rate for short-term hospitals in 2000 (the year in which the clinical trial was performed), as published by the American Hospital Association (US$1149.40)[24].

Statistical Analysis

Healthcare resource utilization and hospitalization costs for each treatment group were compared. As two telithromycin treatments (5- and 7-day) were being compared with one control (clarithromycin), analysis of variance applying the Dunnett adjustment[25] was used to compare continuous variables between 5-day telithromycin and clarithromycin and 7-day telithromycin and clarithromycin, and to generate the 95% confidence intervals (CIs) for hospitalization costs. Fisher's exact test was used for comparison of categorical variables. Statistical analyses were performed at the 5% significance level. Statistical comparisons were not performed between 5- and 7-day telithromycin.

Results

Demographics

A total of 581 patients were enrolled in the study, of whom 575 were randomized and received at least one dose of study medication (ITT population): 5-day telithromycin, n = 193; 7-day telithromycin, n = 195; 10-day clarithromycin, n = 187. Six patients who were enrolled in the study were not randomized to treatment because of lack of chest X-ray findings consistent with bacterial CAP. There were no statistically significant differences across treatment groups in demographics, location of treatment initiation (No. of inpatients vs outpatients), or baseline clinical characteristics of the ITT populations (Table 1). The modified ITT (mITT) population (all ITT patients with clinical and radiologic confirmation of CAP) comprised 187 patients who received 5-day telithromycin, 191 patients who received 7-day telithromycin, and 181 patients who received clarithromycin.

Clinical Efficacy and Safety

Clinical cure rates in the PPc populations at post-therapy/TOC were similar in the three treatment arms: 89.3% (142/159) for 5-day telithromycin, 88.8% (143/161) for 7-day telithromycin, and 91.8% (134/146) for 10-day clarithromycin. Both 5- and 7-day telithromycin were statistically equivalent to 10-day clarithromycin (difference: –2.5 and –3.0%, respectively; 95% CI: –9.7, 4.7 and –10.2, 4.3, respectively). These results were supported by the analysis in the mITT population, which also showed statistical equivalence – 154/187 (82.4%) for 5-day telithromycin, 157/191 (82.2%) for 7-day telithromycin, and 147/181 (81.2%) for clarithromycin (difference: 1.1 and 1.0% for 5- and 7-day telithromycin, respectively; 95% CI: –7.3, 9.6 and –7.4, 9.4, respectively). Statistical comparisons were not performed between 5- and 7-day telithromycin.

Table 1. *Demographics and baseline clinical characteristics of the intent to treat population of patients who received telithromycin 800 mg once daily or clarithromycin 500 mg twice daily*

Characteristic	Treatment regimen		
	5-day telithromycin (n = 193)	7-day telithromycin (n = 195)	10-day clarithromycin (n = 187)
Gender, n (%)			
Male	121 (62.7)	103 (52.8)	97 (51.9)
Female	72 (37.3)	92 (47.2)	90 (48.1)
Age			
Mean (range), years	45.8 (18–87)	45.7 (19–87)	46.0 (15–88)
Aged < 65 years, n (%)	161 (83.4)	165 (84.6)	148 (79.1)
Aged ≥ 65 years, n (%)	32 (16.6)	30 (15.4)	39 (20.9)
Fine score, n (%)			
Class I	94 (48.7)	97 (49.7)	89 (47.6)
Class II	62 (32.1)	63 (32.3)	58 (31.0)
Class III	23 (11.9)	21 (10.8)	29 (15.5)
Class IV	13 (6.7)	14 (7.2)	11 (5.9)
Class V	1 (0.5)	0	0
Initial location of treatment, n (%)			
Outpatient	170 (88.1)	171 (87.7)	170 (90.9)
Inpatient	23 (11.9)	24 (12.3)	17 (9.1)

Table 2. *Non-protocol driven healthcare resource utilization by patients who received telithromycin 800 mg once daily or clarithromycin 500 mg twice daily (intent to treat populations)*

Resource	Treatment regimen			Probability	
	5-day telithromycin (n = 193)	7-day telithromycin (n = 195)	10-day clarithromycin (n = 187)	5-day telithromycin	7-day telithromycin
All-cause hospitalizations					
No. of patients	9	4	13	0.385	0.025
No. of events	9	4	13	0.283	0.021
Admissions/100 patients	4.7	2.1	7.0		
CAP-related hospitalizations					
No. of patients	3	1	7	0.214	0.034
No. of events	3	1	7	0.119	0.021
Admissions/100 patients	1.6	0.5	3.7		
CAP-related outpatient visits					
No. (%) of patients	23 (11.9)	26 (13.3)	30 (16.0)	0.300	0.473
No. of observations (observations/100 patients)	74 (38.3)	62 (31.8)	92 (49.2)	0.474	0.250
CAP-related laboratory tests					
No. (%) of patients	26 (13.5)	27 (13.8)	26 (13.9)	1.000	1.000
No. of observations (observations/100 patients)	139 (72.0)	127 (65.1)	185 (98.9)	0.490	0.385
RTI-related additional antibacterial agents					
No. (%) of patients	27 (14.0)	26 (13.0)	34 (18.0)	0.328	0.208
No. of observations (observations/100 patients)	46 (23.8)	32 (16.4)	54 (28.9)	0.492	0.089
Duration of IV antibacterial therapy (days)	79	56	119	0.434	0.223
Duration of oral antibacterial therapy (days)	256	169	241	0.921	0.257

Analysis of variance was used to compare continuous variables and Fisher's exact test was used to compare categorical variables.
CAP, community-acquired pneumonia; IV, intravenous; RTI, respiratory tract infection.

Bacteriologic outcome rates for telithromycin and clarithromycin were similar (bacteriologically evaluable per-protocol population) and the two agents had comparable tolerability profiles.

Health Outcomes and Healthcare Resource Utilization

As there were no significant differences in clinical efficacy between telithromycin (5- and 7-day) and 10-day clarithromycin, cost minimization analyses were performed. As treatment failure – particularly hospitalization – is the major driver of healthcare resource utilization in CAP, the cost comparison analysis focused on non-protocol-related healthcare resource utilization due to hospitalization.

Hospitalizations and Associated Costs

There were 13 hospital admissions (all causes) in the clarithromycin group vs 9 (p = 0.283) in the 5-day telithromycin group and 4 (p = 0.021) in the 7-day telithromycin group (Table 2). Of the total hospitalizations, 7 were considered CAP-related in the

Table 3. *Community-acquired pneumonia-related hospitalization listings for patients who received telithromycin 800 mg once daily or clarithromycin 500 mg twice daily (intent to treat populations)*

Treatment group	Patient characteristics				Length of stay, days	Reason for hospitalization
	Country	Age, years/ gender	Fine score	Study day		
5-day telithromycin	Brazil	20/M	1	4	13	Pleural effusion, worsening
	Germany	44/M	3	22	1	Relapse of pneumonia
	Germany	57/M	2	25	19	Pneumonia
7-day telithromycin	South Africa	39/M	3	24	14	Severe pneumonia, septic shock
10-day clarithromycin	USA	71/F	2	2	11	Pneumonia
	South Africa	64/F	4	2	7	Increased chest pain and bronchospasm
	USA	51/F	2	3	2	Possible sepsis
	Canada	51/F	2	6	9	Pneumonia aggravation; treatment failure
	USA	57/M	3	7	9	Worsening symptoms of pneumonia
	Canada	37/M	2	26	16	Increased shortness of breath
	Germany	69/M	3	33	21	Proteinuria

F, female; M, male.

Table 4. *Community-acquired pneumonia-related hospitalization data for patients treated with telithromycin 800 mg once daily vs clarithromycin 500 mg twice daily (intent to treat populations)*

Patient subset	Treatment regimen		
	5-day telithromycin (n = 193)	7-day telithromycin (n = 195)	10-day clarithromycin (n = 187)
No. of hospitalizations	3	1	7
Probability vs clarithromycin	0.119	0.021	–
Admissions/100 patients	1.6	0.5	3.7
ICU admissions; No. of patients (No. of observations)	0	1 (1)	0
Total length of hospital stay (range), days	33 (1–19)	14 (14–14)	75 (2–21)
Hospital days/100 patients	17.1	7.2	40.1
Probability vs clarithromycin	0.197	0.064	–
Total hospitalization costs	$37 930.20	$16 091.60	$86 205.00
Hospitalization costs per 100 patients	$19 653	$8252	$46 099
Probability vs clarithromycin	0.197	0.197	–
Difference vs clarithromycin per 100 patients	–$26 446	–$37 847	–
95% CI	–66 654; 13 762	–77 953; 2259	–

Analysis of variance was used to compare treatments and to generate the 95% CIs for hospitalization costs.
CI, confidence interval; ICU, intensive care unit.

clarithromycin group vs 3 (p = 0.119) among 5-day telithromycin recipients and 1 (p = 0.021) among 7-day telithromycin recipients. This equated to a CAP-related hospitalization rate of 3.7 hospitalizations per 100 patients treated with clarithromycin vs 1.6 and 0.5 hospitalizations per 100 patients receiving 5- and 7-day telithromycin, respectively (1.0 per 100 patients for 5- and 7-day combined; p = 0.026). Information regarding patients hospitalized for CAP-related reasons is presented in Table 3; treatment was initiated in the outpatient setting for all patients listed. The mean (median) length of CAP-related hospital stay was 11 (9) days for clarithromycin patients vs 14 (14) days for 5-day and 11 (13) days for 7-day telithromycin patients. The total number of CAP-related hospital days (all patients hospitalized for CAP-related reasons) was 40.1 days per 100 patients for clarithromycin vs 17.1 (p = 0.197) and 7.2 (p = 0.064) days per 100 patients for 5- and 7-day telithromycin, respectively (Table 4) (12.1 days per 100 patients for 5- and 7-day telithromycin combined; p = 0.07).

Similar rates of hospitalization were observed in the mITT population of patients, with 3.9, 1.6, and 0.52 hospitalizations per 100 patients receiving clarithromycin, 5-day telithromycin, and 7-day telithromycin, respectively (1.1 days per 100 patients for 5- and 7-day telithromycin combined; data not shown). The total number of CAP-related hospital days was 41.4 days per 100 patients for clarithromycin vs 17.6 and 7.3 days per 100 patients for 5- and 7-day telithromycin, respectively, (12.4 days per 100 patients for 5- and 7-day telithromycin combined).

Projected overall CAP-related hospitalization costs per 100 patients were $86 205 for clarithromycin vs

$37 930 (difference: –26 446; 95% CI: –66 654; 13 762) and $16 091 (difference: –37 847; 95% CI: –77 953; 2259) for 5- and 7-day telithromycin, respectively (Table 4). The difference in hospitalization costs did not achieve statistical significance due to the small effect size (very few patients hospitalized) and/or the large variance in cost.

Other Healthcare Resource Utilization

A summary of non-protocol driven resource utilization by patients who received telithromycin 800 mg once daily or clarithromycin 500 mg twice daily is presented in Table 2. The number of CAP-related unscheduled outpatient visits and laboratory tests for patients receiving telithromycin and clarithromycin were similar. A similar proportion of telithromycin and clarithromycin recipients required additional RTI-related antibacterial therapy (Table 2). The total duration of intravenous antibacterial treatment for clarithromycin-treated patients was 119 days (63.6 days per 100 patients) compared with 79 days (40.9 days per 100 patients) for 5-day telithromycin and 56 days (28.7 days per 100 patients) for 7-day telithromycin. In the mITT population, the duration of intravenous antibacterial treatment for clarithromycin-treated patients was 65.2 days per 100 patients compared with 38.5 and 28.8 days per 100 patients for 5- and 7-day telithromycin, respectively.

Discussion

Antibacterial prescribing for CAP is influenced by a number of issues, such as patient compliance, drug adverse-event profiles, and the local prevalence of resistance[4,26]. Combination therapy with a macrolide and a β-lactam with good antipneumococcal activity is generally recommended for the treatment of outpatients with risk factors for drug-resistant *S. pneumoniae*[6,13,14]. Monotherapy with a fluoroquinolone is a possible alternative, although controversy as to the suitability of fluoroquinolones for first-line therapy exists in current guidelines[6,13,14]. Antibacterial resistance may therefore play a role in increasing overall management costs through 'preventative use' of combination therapy, treatment of relapses, and hospitalizations. With increasing levels of antibacterial resistance among *S. pneumoniae*[16,27], empiric selection of an effective drug may become more challenging. Telithromycin provides coverage against the common causative agents of CAP – including atypical/intracellular pathogens and strains of *S. pneumoniae* that are resistant to currently available agents – and the clinical efficacy of telithromycin in CAP has been demonstrated in several studies[17–21].

The clinical data from the present randomized, double-blind study showed that the efficacy of telithromycin 800 mg once daily for 5 or 7 days and clarithromycin twice daily for 10 days in the treatment of patients with CAP was statistically equivalent. The data from the present patient outcome and hospitalization cost analyses showed that, compared with clarithromycin treatment, 5-day telithromycin treatment was associated with a trend towards numerically fewer hospitalizations and days required in hospital, and 7-day telithromycin treatment was associated with significantly fewer hospitalizations and a trend towards fewer days required in hospital. Projected CAP-related hospitalization costs were therefore numerically reduced for 5- and 7-day telithromycin recipients vs clarithromycin recipients. A comparison of indirect costs – such as days of reduced productivity and work loss – were beyond the scope of this analysis.

The direct healthcare resource utilization findings from this study are consistent with data from three separate studies involving patients with CAP (one study) and acute exacerbations of chronic bronchitis (AECB; two studies), respectively. Treatment with telithromycin 800 mg once daily for 5 (AECB studies) or 10 (CAP study) days was associated with a trend towards fewer hospitalizations and/or hospital days than treatment with clarithromycin 500 mg twice daily or amoxicillin–clavulanate 500/125 mg three-times daily for 10 days[22,28,29].

The present study was powered to demonstrate equivalence in clinical efficacy between treatments. However, the results suggest that antibacterial agents with similar clinical efficacies may potentially be associated with differences in the overall costs of treatment owing to differences in additional healthcare resources consumed during the course of care. This is due, in part, to the fact that several of the components associated with treatment failure, particularly hospitalization, are very expensive. Cost savings result from prevention of disease progression to the point where inpatient care is necessary or from reduction in length of stay in hospital.

The reasons for the lower rate of hospitalization among 7-day telithromycin recipients are currently unclear, given that clinical cure rates were equivalent to those of clarithromycin. A possible explanation is the favorable pharmacokinetic/pharmacodynamic profile of telithromycin for the treatment of RTIs. Telithromycin achieves a high area under the serum concentration–time curve to minimum inhibitory concentration ratios for key respiratory pathogens and maintains high concentrations in respiratory tissues and fluids[30]. Telithromycin also exhibits rapid bactericidal activity against *S. pneumoniae*,

the most frequent causative pathogen in CAP[31]. Such a profile may lead to a faster resolution of infection and more rapid symptom relief[32], although further studies would be required to support this theory.

This study had a number of limitations. The clinical trial was designed to demonstrate equivalence in clinical efficacy and was not statistically powered to demonstrate differences in healthcare resource utilization – there were very few patients hospitalized in either treatment group and there was a large variance in projected hospitalization costs. In addition, CAP-related hospitalizations were assessed in this study by investigators who were blinded to treatment group at the time of admission, in order to provide an unbiased reflection of CAP-related hospitalization rates for each treatment. Nevertheless, this approach could still be considered as somewhat subjective. Although this was a multinational study, the analysis was performed from a US managed care perspective and results of the hospitalization cost analyses are reported in US dollars. Hospitalization cost data presented here may not be directly applicable to other countries due to differences in reference prices, although this is unlikely to substantially affect the overall data trends observed. Furthermore, criteria for hospital admission (e.g. patients in some countries may be admitted for social rather than clinical reasons) and length of stay may also vary by country, potentially contributing to differences in treatment costs. Given that patients were randomized at the center level and given the overall spread of countries involved in the hospitalization analyses, international practice differences are also unlikely to substantially affect the overall data trends observed.

Because of the limitations of the study, the data from these patient outcome and cost analyses should be regarded as observational. That similar trends in requirement for hospitalizations/hospital days – translating into differences in consumption of healthcare resources – between patients receiving telithromycin and clarithromycin were observed in two other separate studies[22,29], however, adds support to the findings of the present study. Furthermore, statistically significant differences in CAP-related hospitalization rates were observed for 7-day telithromycin vs clarithromycin in the present study, despite the fact that the clinical trial was designed to demonstrate equivalence in clinical efficacy and was not statistically powered to demonstrate differences in healthcare resource utilization.

In summary, previous studies have demonstrated that telithromycin 800 mg once daily for 5–10 days is an effective therapy for adolescent and adult outpatients with CAP of mild to moderate severity[17–21]. Data from this patient outcomes analysis suggest that telithromycin 800 mg once daily for 7 days for the management of CAP is associated with significantly fewer hospitalizations and numerically fewer hospital days than clarithromycin 500 mg twice daily for 10 days, resulting in potentially lower projected hospitalization costs. That significant differences in hospitalization rates were observed for 7-day telithromycin vs clarithromycin is of interest, as the most likely dosing regimen for telithromycin in the treatment of CAP is 800 mg once daily for 7–10 days. Given the prevalence of CAP, potential reductions in additional direct healthcare resource consumption may have important implications for reducing annual treatment costs. Further studies to add support to the findings of these preliminary analyses are therefore warranted.

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