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Médecine et maladies infectieuses
Médecine et maladies infectieuses 39 (2009) 330–340

Original article

Cost-effectiveness of linezolid versus vancomycin for hospitalized patients with complicated skin and soft-tissue infections in France☆

Ratio coût-efficacité de l'utilisation en France du linézolide et de la vancomycine dans le traitement d'infections compliquées de la peau et des tissus mous

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Received 14 July 2008; accepted 30 January 2009
Available online 21 March 2009

Abstract

Studies have shown similar clinical cure rates and shorter length of hospitalization when using linezolid compared to vancomycin in patients with complicated skin and soft-tissue infections due to suspected or proven methicillin-resistant *Staphylococcus aureus* (MRSA).

Objective. – This study had for aim to compare the cost-effectiveness of linezolid versus vancomycin in French healthcare settings.

Method. – A decision-analytic model followed an average patient from the initiation of an empiric treatment until cure, death or second-line treatment failure. A clinical data probability was obtained from clinical trials, resource utilization data (including treatment duration and length of hospitalization) and prevalence of MRSA was obtained from a Delphi panel, and costs from published sources.

Results. – First-line cure rate for linezolid-treated patients was 90.7% versus 85.5% for vancomycin; the total cure rates after two lines of treatment were 98.5% and 98.0%, respectively. The average total cost was 7,778€ for linezolid versus 8,777€ for vancomycin. The mean estimated length of hospitalization after two lines of treatment was 10.7 days for linezolid versus 13.3 days for vancomycin. The increased effectiveness and reduced cost lead to more frequent prescription. This did not change after one-way sensitivity analyses.

Conclusion. – Linezolid may be considered as a cost-effective treatment for patients with complicated skin and soft-tissue infections suspected to be MRSA related in France.

Keywords: Complicated skin and soft-tissue infection; Cost-effectiveness; MRSA; Linezolid; Vancomycin

Résumé

Des études cliniques ont démontré pour les patients atteints d'infections compliquées de la peau et des tissus mous fortement suspectées à *Staphylococcus aureus* résistant à la méthiciline (SARM) et traités par le linézolide (versus la vancomycine), des taux de guérison similaires et des durées de séjour plus courtes.

Objectif. – Déterminer le ratio coût-efficacité du linézolide versus la vancomycine selon la perspective du système de santé français.

☆ Part of this manuscript was presented at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 10th Annual European Congress in Dublin, Ireland, 20–23 October 2007.

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doi:10.1016/j.medmal.2009.01.005

Méthodes. – Un modèle de décision analytique a été appliqué à un patient-type, de l'initiation du traitement empirique jusqu'à guérison, mort ou échec du traitement de deuxième ligne. Les probabilités cliniques provenaient des essais cliniques. Les données d'utilisation de ressources (incluant la durée de traitement et la durée de séjour) et les taux de prévalence SARM étaient fournis par un panel d'expert. Les coûts étaient appréciés à partir de publications.

Résultats. – Le taux de guérison en première ligne était de 90,7 % pour le linézolide versus 85,5 % pour la vancomycine (après deux lignes de traitement 98,5 % et 98 %, respectivement). Le coût total moyen était de 7778 € pour le linézolide versus 8777 € pour la vancomycine pour une durée de séjour moyenne de 10,7 jours et 13,3 jours, respectivement. La prescription de linézolide était la stratégie dominante. La conclusion ne changeait pas après réalisation des analyses de sensibilité.

Conclusion. – Le linézolide peut être considéré comme une stratégie coût-efficace en France dans le traitement des infections compliquées de la peau et des tissus mous suspectées à SARM.

Mots clés : Infection compliquées de la peau et des tissues mous ; Coût–efficacité ; SARM ; Linézolide ; Vancomycine

1. Introduction

Skin and soft-tissue infections (SSTI) are a common cause of morbidity in community settings and hospitals worldwide [1–3]. Complicated SSTI (cSSTI) may be defined by the presence of a major abscess requiring surgical drainage, an infected burn, deep extensive cellulitis, or an infected wound or ulcer. Hospitalization, surgery and intravenous (IV) antibiotic treatment are often required to treat cSSTI resulting in high treatment costs [4].

The most commonly implicated pathogens in cSSTI include Gram-positive bacteria, specifically *Staphylococcus aureus* which is often resistant to conventional therapy (methicillin/oxacillin), close to 60% in US hospitals [5]. Susceptibility data for bacteria causing a range of SSTI in hospitalized patients in France during 2001 showed that almost one-third of hospital SSTIs were *S. aureus*, and 34% of these were identified as methicillin-resistant *S. aureus*, or MRSA [6]. According to the European Antimicrobial Resistance Surveillance System (EARRS), resistance was detected in 26.7% of *S. aureus* isolates in France in 2005–2006, lower than the 33% reported in 2001–2002 and 29% in 2003–2004 [7]. Even though there seems to be a downward trend, the rate of MRSA remains high.

Various studies suggest that MRSA infection is associated with increased morbidity and mortality [8], and costs [9,10] compared with those for methicillin-susceptible *S. aureus* (MSSA) infection. Vancomycin has been the drug of choice for empirical treatment of MRSA-suspected infections. However, the emergence of Vancomycin-resistant *S. aureus* (VRSA) has highlighted the need for new agents to treat these infections [11–13]. Furthermore, any therapy targeting MRSA that could reduce hospital costs, while maintaining efficacy standards, could be a valuable tool in budget management.

Linezolid (Zyvox^{TM}) is an oxazolidinone antimicrobial agent that is effective against a broad spectrum of Gram-positive bacteria, including MSSA and MRSA [14,15]. It is not expected to develop cross-resistance with other antibiotics because of its unique mechanism of action. In addition to an IV formulation, linezolid is available in a 100% orally bioequivalent form which does not require the patient to remain in hospital for IV treatment [16]. Linezolid was given market approval for use in cSSTI caused by suspected MRSA in 2001. An update of the market approval in 2007 states the need to prove that Gram-positive resistant bacteria cause the infection before starting treatment.

In a recent multinational clinical trial by Weigelt et al. [17] in patients with cSSTI due to suspected or proven MRSA, the clinical cure rate was higher for linezolid than for vancomycin (92.2% versus 88.5%; $P = 0.057$). Within this trial, drug-related adverse events were reported in similar numbers in both the linezolid and the vancomycin arm. Results from a separate analysis based on the trial reported shorter hospital length of stay (LOS) in linezolid-treated patients versus vancomycin-treated patients (7.4 days versus 9.8 days; $P < 0.0001$) [18]. An economic analysis based on the trial indicated that treatment with linezolid resulted in lower costs compared with vancomycin, which the authors attributed to a switch from IV to oral treatment and earlier hospital discharge [19].

Health care systems in many countries are under increasing pressure to contain health care expenditures. In France, this lead to the introduction of Groupes Homogènes de Maladies (GHM), equivalent to Diagnosis Related Groups (DRG), as the main funding source for French hospitals. The GHM system aims at stimulating hospitals to become more efficient in its use of medical resources. This change in policy has certainly made decision makers, including hospital administrators and physicians, become more 'cost-conscious'. However, when introducing a novel and more costly drug, it is important that they not only consider cost, but also the full implications of drug, including efficacy, safety, and any impact on resource use patterns (eg, LOS). Economic modeling is a useful method to assess the cost-effectiveness of a new technology as it takes into consideration all the potential costs and consequences. Also, given that each country's health care system is unique, the generalizability of cost-effectiveness results from one country to another is limited. Hence, country-specific analyses using appropriate data are required to generate robust findings and allow informed decision-making on the use of novel drugs.

The aim of this study was to carry out a cost-effectiveness analysis in French healthcare settings, of linezolid versus vancomycin in the first-line empirical treatment of hospitalized patients with cSSTI, caused by suspected or proven MRSA. Those patients are the population in the randomized clinical trials from which the efficacy data was taken.