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CLINICAL RESEARCH

Cost-effectiveness of atorvastatin in the prevention of cardiovascular events in diabetic patients: A French adaptation of CARDS

Rapport coût/efficacité de l'atorvastatine dans la prévention des évènements cardiovasculaires chez le patient diabétique : adaptation française de l'étude CARDS

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Summary
Introduction. — We estimated the cost-effectiveness of atorvastatin in the primary prevention of cardiovascular events in patients with type 2 diabetes using data from the Collaborative AtoRvastatin Diabetes Study (CARDS).
Methods. — A total of 2838 patients aged 40—75 years with type 2 diabetes and no documented history of cardiovascular disease and without elevated low-density-lipoprotein cholesterol were recruited in the UK and in Ireland. Patients were randomly allocated to atorvastatin 10 mg daily ($n = 1428$) or placebo ($n = 1410$) and were followed up for a median of 3.9 years. Direct treatment costs and effectiveness were analysed to provide estimates of cost per event avoided and cost per life-year gained over the trial period and over a patient's lifetime.
Results. — The incremental cost-effectiveness ratio over the trial period was estimated to be €3862 per clinical event avoided. Over the patient's lifetime, the incremental cost per life-year gained was €2506 when considering cardiovascular deaths, and €1418 per year when considering all-cause death.
Conclusions. — Primary prevention of cardiovascular disease with atorvastatin is cost-effective in patients with type 2 diabetes, with the incremental cost-effectiveness ratio for this intervention falling within the current acceptance threshold.

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MOTS CLÉS
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Résumé
Introduction. — Nous avons estimé le ratio coût—efficacité de l'atorvastatine dans la prévention primaire des événements cardiovasculaires chez les patients diabétiques de type 2 au moyen des données de l'étude CARDS.
Méthodes. — Au total, 2838 patients, âgés de 40 à 75 ans avec un diabète de type 2, sans antécédent cardiovasculaire, ni élévation du LDL cholestérol ont été recrutés dans des centres britanniques et irlandais. Après tirage au sort, ils ont été traités par 10 mg quotidien d'atorvastatine ($n = 1428$) ou un placebo ($n = 1410$). La durée médiane de suivi de ces patients était de 3,9 ans. Les coûts directs et l'efficacité ont été analysés pour calculer des coûts par événement évité et des coûts par année de vie gagnée sur la période de l'essai et sur la vie entière des patients.
Résultats. — Sur la période de l'essai, le ratio coût—efficacité incrémental a été estimé à 3862 € par événement évité tel que défini dans le protocole de CARDS. Sur la vie entière, le coût par année de vie gagnée était estimé à 2506 € en considérant les décès d'origine cardiovasculaire et à 1418 € en considérant tous les décès.
Conclusion. — La prévention primaire des événements cardiovasculaires par atorvastatine chez les patients diabétiques de type 2 est une stratégie coût—efficace avec un ratio coût—efficacité incrémental inférieur au seuil considéré comme acceptable.

Introduction

Diabetic patients are at high risk of cardiovascular morbidity and mortality [1]. Since the introduction of statins 20 years ago, their indications have broadened with the emergence of data from numerous large randomized clinical trials. Now their approved indications include treatment of elevated low-density-lipoprotein (LDL) cholesterol, secondary prevention of cardiac events, and primary prevention of cardiac events in large subgroups of the population, including those with diabetes and at least one additional risk factor and without elevated LDL cholesterol. Atorvastatin was recently approved for the latter indication in France, based on the results of the Collaborative AtoRvastatin Diabetes Study (CARDS) [2—4]. This clinical trial was performed under the aegis of the UK Department of Health and was coordinated by University College London. The trial was designed to demonstrate the efficacy of atorvastatin in the primary prevention of cardiac events in patients presenting with diabetes and without elevated LDL cholesterol.

While there is no question as to the efficacy of atorvastatin in this group, it is important to evaluate its cost-effectiveness because of the large number of individuals who could benefit from the product. The French Transparency Commission estimated this target population to be approximately 600 000 in France [5]. The cost-effectiveness of atorvastatin has already been studied in Spain [6] and in the United Kingdom [7], but healthcare systems and medical expenses vary widely between countries. Therefore, the objective of the present study was to estimate its cost-effectiveness in the primary prevention of cardiac events in a French diabetic population without elevated LDL cholesterol.

Methods

This study is based largely on data from the CARDS clinical trial, which has been described in detail elsewhere [2—4]. In brief, a population of UK patients was randomly allocated to placebo or atorvastatin (10 mg daily). Patients were eligible for inclusion if they were diabetic, had no history of cardiac events, had an LDL cholesterol level lower than 4.14 mmol/L, and had at least one associated risk factor (retinopathy, albuminuria, current smoking or hypertension). The median duration of follow-up was 3.9 years in both groups. The risk reduction of cardiovascular events was estimated at 37% (95% confidence interval 17—52; $P < 0.001$) for atorvastatin, and treatment of 1000 patients could avoid 37 major events each year. Treatment was associated with a mortality reduction of 27% ($P = 0.059$) during the follow-up period. No significant side-effects were observed in either group and the trial was stopped prematurely because of the significance of efficacy in the second planned intermediary analysis.

The present cost-effectiveness study was carried out according to French guidelines [8,9]. The primary endpoints were the number of clinical events observed during the trial and the life expectancy of patients extrapolated to the lifetime of a similar population, comparing atorvastatin 10 mg daily to usual care without systematic atorvastatin treatment.

The number of cardiac events was extracted from the main article [4] and the clinical report. Owing to statistical considerations, the first event of one type was considered per patient in the article, which could lead to an underestimation of the economic difference between groups because patients with a first event are more likely to present with a second.

Life-expectancy estimates were calculated using the DEALE method [10]. This approach allows us to estimate the life expectancy of a particular population, taking into account the decrease in life expectancy of diabetic patients compared with that of the general population, and was based on data from Gu et al. [11]. In the UK Prospective Diabetes Study (UKPDS), the life expectancy of diabetic patients with a mean age of 54 was approximately 20 years [12,13].

The following calculations were performed as follows: