Cost-effectiveness of Pazopanib Versus Sunitinib as First-line Treatment for Locally Advanced or Metastatic Renal Cell Carcinoma from an Italian National Health Service Perspective

Stefano Capri, MSc[1]; Camillo Porta, MD[2]; and Thomas E. Delea, MSIA[3]

[1]School of Economics and Management, Università Cattaneo-LIUC, Castellanza, Italy; [2]Policlinico San Matteo, Pavia, Italy; and [3]Policy Analysis Inc, Brookline, Massachusetts, USA

ABSTRACT

Purpose: A prior randomized controlled trial (COMPARZ [Comparing the Efficacy, Safety and Tolerability of Pazopanib versus Sunitinib]) found non-inferior progression-free survival for pazopanib versus sunitinib as first-line therapy in patients with advanced or metastatic renal cell carcinoma. The present study evaluated the cost-effectiveness of pazopanib versus sunitinib as first-line treatment for patients with metastatic renal cell carcinoma from an Italian National Health Service perspective.

Methods: A partitioned-survival analysis model with 3 health states (progression-free survival, post-progression survival, and dead) was employed. The model time horizon was 5 years. For each treatment strategy, the model generated expected progression-free life years, post-progression life years, overall life years, quality-adjusted life years (QALYs), and costs. Results were reported as incremental costs per QALY gained and the net monetary benefit of pazopanib versus sunitinib. Probabilistic and deterministic sensitivity analyses were conducted to assess the impact on results of methodological and parameter uncertainty.

Findings: In the base case, pazopanib was associated with higher QALYs and lower costs and dominated sunitinib. Using willingness-to-pay thresholds of €30,000 and €50,000 per QALY, the net monetary benefits with pazopanib were €6508 and €7702 per patient, respectively, versus sunitinib. The probability that pazopanib is cost-effective versus sunitinib was estimated to be 85% at a cost-effectiveness threshold of €20,000, 86% at a threshold of €30,000, and 81% at a threshold of €50,000 per QALY. Results were robust to changes in key parameter values and assumptions.

Implications: These results suggest that pazopanib is likely to represent a cost-effective treatment option compared with sunitinib as first-line treatment for patients with metastatic renal cell carcinoma in Italy. (*Clin Ther*. 2017;39:567–580) © 2017 Published by Elsevier HS Journals, Inc.

Key words: cost-effectiveness analysis, partitioned survival analysis, renal cell carcinoma, utility values.

INTRODUCTION

Rates of kidney cancer are highest in Europe, North America, and Australia, with higher incidence and mortality rates in males.[1] Renal cell carcinoma (RCC) accounts for an estimated 85% of kidney cancer cases.[2] In 2012, Bosetti et al[3] projected that there would be approximately 7680 new RCC cases in Italy, yielding a nationwide prevalence of 25,740 new cases based on annual incidence and mortality data. About 25% to 30% of patients have metastatic disease at diagnosis, while another 40% who are initially diagnosed with localized cancer later develop metastases.[4]

Advances in understanding the biology and genetics of RCC have led to the development of novel targeted approaches for the treatment of metastatic RCC (mRCC).[2] Pazopanib is an antineoplastic agent that works by inhibiting multiple-receptor tyrosine kinases.[5] The efficacy and tolerability of pazopanib in treatment-naïve patients with locally advanced or mRCC was reported in COMPARZ (Comparing the Efficacy, Safety and Tolerability of Pazopanib versus Sunitinib), a Phase III, randomized, placebo-controlled trial.[6]

Accepted for publication January 9, 2017.
http://dx.doi.org/10.1016/j.clinthera.2017.01.017
0149-2918/$ - see front matter

The COMPARZ trial (protocol VEG108844, Clinical Trials.gov identifier NCT00720941) was powered to evaluate the non-inferiority of continuous doses of pazopanib (800 mg once daily) versus 6-week cycles of sunitinib (50 mg once daily for 4 weeks, followed by 2 weeks off treatment) as first-line therapy in patients with mRCC who had not received prior systemic therapy.[6] The primary end point was independent review committee (IRC)–assessed progression-free survival (PFS). Secondary end points included overall survival (OS), objective response rate, time to response, duration of response, incidence and severity of adverse events (AEs), health-related quality of life (HRQOL), and some selected measures of non-study medical resource utilization (MRU). The results from the COMPARZ trial demonstrated that pazopanib is non-inferior to sunitinib with respect to PFS. Longer-term follow-up of survival rates found no difference between pazopanib and sunitinib.[7] Rates of fatigue and hand-foot syndrome were higher in patients receiving sunitinib, while changes in hair color, alopecia, and weight loss occurred more frequently in patients receiving pazopanib. In 11 of 14 HRQOL domains, the mean change from baseline favored pazopanib, particularly those items related to fatigue or soreness in the mouth, throat, hands, or feet, during the first 6 months of treatment ($P < 0.05$ for all 11 comparisons). Based on these results, the COMPARZ investigators concluded the AE and HRQOL profiles favored pazopanib.[6,8]

While the COMPARZ trial provided evidence of the non-inferiority of pazopanib versus sunitinib as first-line treatment for mRCC,[6] it did not examine the cost-effectiveness of the 2 treatments. Economic analyses of treatment choices are increasingly important to both payers and prescribers in order to determine the most cost-effective treatments for patients. Drug costs are only one part of the overall treatment expenditures because side effects of drugs and their treatment can not only affect the overall costs, but also patients' quality of life. In the present analysis, we examine the cost–utility and net monetary benefit (NMB) analyses of pazopanib versus sunitinib as first-line treatment for patients with mRCC from an Italian National Health Service (NHS) perspective, based on the results reported in the COMPARZ trial.

METHODS

A partitioned-survival analysis model based on survival and disease progression was implemented to evaluate the cost-effectiveness of pazopanib versus sunitinib in patients with metastatic cancer, where a cure is not expected. In such a model, the proportion of patients in each of 3 health states (alive with no progression [pre-progression], alive with progression [post-progression survival; PPS], and dead) over the course of time was estimated based on survival functions for PFS and OS. Expected PFS and expected OS were calculated as the area under their respective survival curves. Expected PPS was defined as the area between the PFS and OS curves. Costs and quality of life were assumed to be conditioned on treatment and expected time in the given disease states. This approach is similar to a traditional Markov model, except that it does not require explicit calculation of transition probabilities between states. The population of interest was assumed to be the same as that in the COMPARZ trial and to represent a typical population of patients with mRCC.[6] A time horizon of 5 years (60 months) was used in the base case, consistent with the maximum duration of follow-up for OS in the final analysis of OS from the COMPARZ trial.[7]

Inputs

Survival Data

In the base case, the OS for pazopanib and sunitinib to 60 months (the last time point for which OS was available for both groups based on the September 30, 2013, data cut-off)[7] was based on Kaplan–Meier curves reported in the COMPARZ trial. Pazopanib was directly compared with sunitinib in the COMPARZ trial, and long-term PFS and OS data are available from the study. The PFS for pazopanib and sunitinib to 38.8 and 37.5 months, respectively (the last time point for which PFS was available for each group based on the May 21, 2012, data cut-off), were based on the Kaplan–Meier curves for investigator-assessed PFS.[6] Data on PFS were not updated in the final analysis of OS and therefore were not available to 60 months. The PFS from the end of the follow-up period to 60 months was estimated based on Weibull distributions fit to patient-level failure time data from the COMPARZ trial. Investigator-assessed rather than IRC-assessed PFS was used, as it is more likely to represent the assessment of progression in typical clinical practice. Additionally, it is less likely to be biased by informative censoring due to investigator-assessed progression before IRC-assessed progression.[9] The λ and γ values for PFS and OS are shown in Table I.