European Journal of Cancer 65 (2016) 102–108

Available online at www.sciencedirect.com

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journal homepage: www.ejcancer.com

Original Research

First-line sunitinib versus pazopanib in metastatic renal cell carcinoma: Results from the International Metastatic Renal Cell Carcinoma Database Consortium

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Received 16 May 2016; received in revised form 14 June 2016; accepted 16 June 2016

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http://dx.doi.org/10.1016/j.ejca.2016.06.016

KEYWORDS
Carcinoma;
Renal cell;
Sunitinib;
Pazopanib;
Vascular endothelial growth factor receptor

Abstract ***Background:*** Sunitinib (SU) and pazopanib (PZ) are standards of care for first-line treatment of metastatic renal cell carcinoma (mRCC). However, how the efficacy of these drugs translates into effectiveness on a population-based level is unknown.
Patients and methods: We used the International mRCC Database Consortium (IMDC) to assess overall survival (OS), progression-free survival (PFS), response rate (RR) and performed proportional hazard regression adjusting for IMDC prognostic groups. Second-line OS (OS2) and second-line PFS (PFS2) were also evaluated.
Results: We obtained data from 7438 patients with mRCC treated with either first-line SU (n = 6519) or PZ (n = 919) with an overall median follow-up of 40.4 months (95% confidence interval [CI] 39.2–42.1). There were no significant differences in IMDC prognostic groups (p = 0.36). There was no OS difference between SU and PZ (22.3 versus 22.6 months, respectively, p = 0.65). When adjusted for IMDC criteria, the hazard ratio (HR) of death for PZ versus SU was 1.03 (95% CI 0.92–1.17, p = 0.58). There was no PFS difference between SU and PZ (8.4 versus 8.3 months, respectively, p = 0.17). When adjusted for IMDC criteria, the HR for PFS for PZ versus SU was 1.08 (95% CI 0.981–1.19, p = 0.12). There was no difference in RR between SU and PZ (30% versus 28%, respectively, p = 0.15). We also found no difference in any second-line treatment between either post-SU or post-PZ groups for OS2 (13.1 versus 11 months, p = 0.27) and PFS2 (3.7 versus 5.0 months, p = 0.07).
Conclusions: We confirmed in real-world practice that SU and PZ have similar efficacy in the first-line setting for mRCC and do not affect outcomes with subsequent second-line treatment.

1. Background

The treatment of metastatic renal cell carcinoma (mRCC) is dominated with targeted therapies, and oncologists today have a number of options to offer their patients. With the use of these agents, today we are able to extend the survival of our patients.

Sunitinib (SU), an oral tyrosine kinase inhibitor (TKI), is approved as first-line treatment for mRCC. It demonstrated an improvement in progression-free survival (PFS) compared to interferon alpha and a trend in improvement in overall survival (OS) [1]. Pazopanib (PZ) is also approved as a first-line TKI-targeted therapy for mRCC, after a phase 3 trial that compared it to placebo. PFS was prolonged significantly with PZ in the overall study population, and a trend in a better OS [2,3].

The COMPARZ trial was a phase III non-inferiority study comparing SU to PZ in a first-line setting. PZ was non-inferior to SU with respect to PFS (hazard ratio [HR] for progression of disease or death from any cause, 1.05; 95% confidence interval [CI] 0.90–1.22), meeting the predefined non-inferiority margin. OS was similar (HR 0.91, 95% CI 0.76–1.08) [4]. Some criticisms of this trial include that the boundary to declare non-inferiority was too large with an HR of 1.25, non-inferiority was not reached in the per protocol analysis and whether this trial efficacy data translates into population-based effectiveness. In terms of subsequent second-line therapy in these patients, it is unknown whether the choice of SU or PZ affects the effectiveness of second-line therapy. This is important to study because the product monograph and US Food and Drug Administration (FDA) indication for second-line drugs such as everolimus include the provision that they be given after SU or sorafenib without mention of PZ [5].

In order to evaluate the previous results of the COMPARZ trial in a real-world setting, we compared SU versus PZ in a retrospective population-based analysis to confirm the outcomes in first-line therapy and subsequent second-line therapy.

2. Patients and methods

2.1. Study design and patients

In this retrospective population-based analysis, we included patients who received first-line targeted therapy, either SU or PZ for mRCC. These patients were derived from the International mRCC Database Consortium (IMDC) which is a collection of unselected consecutive patient series at 29 cancer centres in Canada, United States of America, Australia, Denmark, Belgium, Greece, Northeastern Italy, Poland (countrywide data), Japan, Singapore, South Korea and New Zealand between 1st January 2005 and 30th May 2015. The study was approved by the institutional review boards at each participating centre.

2.2. Procedures

We collected demographic, baseline patient characteristics and outcome data at each line of targeted therapy with