Research Report

Real-Word Experience of Cabozantinib in Metastatic Renal Cell Carcinoma (mRCC): Results from the Canadian Kidney Cancer information system (CKCis)

Hanbo Zhang\textsuperscript{a,*}, Naveen S. Basappa\textsuperscript{a}, Sunita Ghosh\textsuperscript{b}, Isaiah Joy\textsuperscript{a}, Aly-Khan A. Lalani\textsuperscript{c}, Aaron R. Hansen\textsuperscript{d}, Daniel Y.C. Heng\textsuperscript{e}, Vincent Castonguay\textsuperscript{f}, Christian K. Kollmannsberger\textsuperscript{g}, Eric Winquist\textsuperscript{h}, Lori Wood\textsuperscript{i}, Georg A. Bjarnason\textsuperscript{j}, Rodney H. Breau\textsuperscript{k}, Anil Kapoor\textsuperscript{l} and Jeffrey Graham\textsuperscript{m}

\textsuperscript{a} Cross Cancer Institute, University of Alberta, Edmonton, AB, Canada
\textsuperscript{b} Alberta Health Services, Cancer Control Alberta, Edmonton, AB, Canada
\textsuperscript{c} Juravinski Cancer Centre, McMaster University, Hamilton, ON, Canada
\textsuperscript{d} Princess Margaret Hospital, University of Toronto, Toronto, ON, Canada
\textsuperscript{e} Tom Baker Cancer Centre, University of Calgary, Calgary, AB, Canada
\textsuperscript{f} Centre Hospitalier Universitaire de Québec, Université Laval, Québec City, QC, Canada
\textsuperscript{g} BC Cancer-Vancouver Centre, Vancouver, BC, Canada
\textsuperscript{h} London Health Sciences Centre, Western University, London, ON, Canada
\textsuperscript{i} QEII Health Sciences Centre, Dalhousie University, Halifax, NS, Canada
\textsuperscript{j} Sunnybrook Odette Cancer Centre, Toronto, ON, Canada
\textsuperscript{k} University of Ottawa, Ottawa, ON, Canada
\textsuperscript{l} St. Joseph’s Health Centre, McMaster University, Hamilton, ON, Canada
\textsuperscript{m} CancerCare Manitoba, University of Manitoba, Winnipeg, MB, Canada

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Abstract.
BACKGROUND: Cabozantinib is an oral multitargeted tyrosine kinase inhibitor (TKI) that has demonstrated efficacy in metastatic renal-cell carcinoma (mRCC) randomized trials.
OBJECTIVE: To explore the real-world effectiveness of cabozantinib in pretreated patients with mRCC, including patients who progressed on immune-oncology checkpoint inhibitor (ICI) therapy.
METHODS: Using the Canadian Kidney Cancer information system (CKCis), patients with mRCC treated with cabozantinib monotherapy as second-line or later from January 1, 2011 to September 1, 2019 were identified. Patients were stratified based on line of cabozantinib received. We reported overall survival (OS), time to treatment failure (TTF) and disease control rate (DCR). Prognostic variables were analyzed using multivariable analysis.

\*Correspondence to: Hanbo Zhang, Cross Cancer Institute, 11560 University Avenue, Edmonton, Alberta, T6G 1Z2, Canada. Tel.: +1 780 432 8513; Fax: +1 780 432 8888; E-mail: hzhan59@gmail.com.

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RESULTS: 157 patients received cabozantinib (median TTF 8.0 months; median OS 15.8 months): 37 (24%) in the second line (median TTF 10.4 months; median OS 18.9 months) 66 (42%) in third line (median TTF 5.9 months; median OS 13.3 months) and 54 (34%) in either 4th or 5th line (median TTF 9.4 months; median OS 16.8 months). One hundred sixteen patients (74%) received cabozantinib after prior ICI therapy (median TTF of 7.6 months; median OS of 15.8 months). DCR in all patients was 63% with 46%, 65% and 72% in 2nd line, 3rd line and 4th/5th line patients respectively. DCR in patients who received cabozantinib after prior ICI therapy was 64%.

CONCLUSIONS: Cabozantinib is effective in a real-world, unselected population of mRCC patients, including in those who have progressed on prior ICI therapy, and in those exposed to multiple lines of therapy.

Keywords: Cabozantinib, renal cell carcinoma, metastatic, targeted therapy

INTRODUCTION

Renal-cell carcinoma (RCC) is the most common form of kidney cancer, with an estimated 403,000 new cases and 175,000 deaths worldwide in 2018 [1]. One third of patients present with metastatic RCC (mRCC) at diagnosis [2]. Relapse occur in about one third of patients treated with localized disease [3].

Treatments for mRCC have evolved significantly over the past decade. Multiple tyrosine kinase inhibitors (TKIs) directed against vascular endothelial growth factor receptors (VEGFRs) have been approved, including sunitinib, pazopanib, sorafenib and axitinib [4]. Immune checkpoint inhibitors (ICI) have revolutionized the treatment of mRCC. Specifically, single agent nivolumab has been shown to be beneficial for mRCC patients who were previously treated with other systemic therapies [5]. Combination nivolumab and ipilimumab has been shown to be superior to sunitinib in the first-line setting for mRCC patients with intermediate/poor risk disease as per International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) criteria [6]. Moreover, combination of the oral TKI axitinib and the ICI agents showed promising results for progression-free survival (PFS) and overall survival (OS) in the treatment of mRCC in the first-line setting [7, 8].

Cabozantinib is a TKI with activity against multiple kinases involved in the pathogenesis of RCC, including VEGFR-2, MET and AXL [9, 10]. Resistance to VEGF pathway inhibition is associated with activation of MET and AXL signaling, and preclinical models have demonstrated that cabozantinib may overcome sunitinib resistance [9]. As per the phase 3 METEOR trial, cabozantinib was found to be superior to everolimus in patients with mRCC following VEGFR TKI therapy, for both PFS (7.4 months versus 3.8 months) and OS (21.4 months versus 16.5 months) [11, 12]. Objective response rate (ORR) was 17% versus 3%. Based on this, cabozantinib was approved for treatment of patients with mRCC who progressed on prior VEGFR TKI therapy.

There is a paucity of prospective data with regard to the activity of cabozantinib in patients previously exposed to ICI. The majority of patients in the METEOR study were ICI-naïve [11]. Furthermore, as various treatment options exist, patients are often treated with multiple lines of systemic therapy. In this context, the effectiveness of cabozantinib in heavily-pretreated mRCC patients is unclear. To answer these questions, we explored the real-world effectiveness of cabozantinib in pre-treated mRCC patients across Canada, including those who had been previously treated with ICI.

MATERIALS AND METHODS

Study design

Data was retrieved from a prospectively maintained cohort in the Canadian Kidney Cancer Information System (CKCis) database, which consists of patients from 14 academic centres across Canada, from January 2011 to September 2019. The CKCis data from these centres has been shown to be representative of the Canadian kidney cancer population and thus felt to appropriately capture the national practice pattern. Key patient and tumour characteristics from CKCis are also in line with U.S. Surveillance, Epidemiology, and End Results (SEER) database, and the results from CKCis likely can be extrapolated to settings beyond Canadian academic centres [13]. All centres had research ethics board approval for CKCis projects. All research was conducted according to the principles of the Declaration of Helsinki. Included patients had to be >18 years old with mRCC treated with cabozantinib monotherapy as second-line or later.

Baseline demographic, clinical, and laboratory data were collected. For the analysis, patients were...
grouped based on line of cabozantinib (2nd line, 3rd line, and 4th and 5th line), and whether patients received prior ICI.

**Treatment outcomes**

OS was defined as the time from initiation of cabozantinib to death from any cause. Time to treatment failure (TTF) was defined as time from initiation of cabozantinib to date of discontinuation or death from any cause, whichever came first. Disease-control rate (DCR) is defined as summation of rates of best response to cabozantinib (investigator-assessed; complete response (CR) + partial response (PR) + stable disease (SD)). Per-protocol, patient information updates occurred at least every 3 months.

**Statistical analysis**

Descriptive statistics were reported for the study variables. Mean and standard deviations were reported for continuous variables. Frequencies and proportions were reported for categorical variables. The objectives were to assess OS, TTF and DCR in patients with mRCC treated with cabozantinib monotherapy in the second-line or later. Distribution of OS and TTF were calculated using the Kaplan-Meier method censoring at last follow-up. Median OS and TTF, along with 95% confidence intervals were reported. One and two-year estimated survival was reported for the entire cohort and the subgroups. Multivariable Cox regression analysis was performed for OS and TTF. The prognostic variables used in the multivariable analysis include line of systemic therapy treatment (>= 3 vs. < 3), IMDC risk group (poor vs. favorable; intermediate vs. favorable), presence of liver and/or brain metastases, clear cell histology vs. non-clear cell histology, and age (=< 65 years vs. >65 years). Hazard ratios and the corresponding 95% confidence intervals were reported. Variables significant at p < 0.05 were considered for the final multivariate model. IMDC risk factors include lower performance status (Karnofsky performance score [KPS] < 80%), low hemoglobin, elevated corrected calcium, elevated neutrophils, elevated platelets, and time from diagnosis to treatment < 1 year [14].

All statistical analysis were conducted using SAS (SAS Institute Inc., Cary, NC) version 9.3 software. A p-value ≤ 0.05 was used for statistical significance and two-sided tests were used. No adjustment was made for multiple testing.

**RESULTS**

**Patient demographic and baseline characteristics**

Our cohort consisted of 157 patients as shown in Table 1. The median age was 61 years and the majority of patients were male with good performance status (KPS >= 80%). Most patients had clear-cell histology (73%). Twenty-four percent of patients had liver metastases and 46% patients had bone metastases. Over half of patients (53%) had 3 or more metastatic organ sites. The majority of patients had nephrectomy (82%) and 29% of patients had metastatectomy. With regards to previous therapy, 74% received ICI prior to cabozantinib. Twenty-four percent of patients received cabozantinib in 2nd line, 42% of patients received cabozantinib in 3rd line and 34% of patients received cabozantinib as 4th or 5th line systemic therapy.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Variables</th>
<th>Value (n (%))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Median (range)</td>
<td>61 (21–84)</td>
</tr>
<tr>
<td></td>
<td>&lt;= 65</td>
<td>107 (68)</td>
</tr>
<tr>
<td></td>
<td>&gt;65</td>
<td>50 (32)</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>39 (25)</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>118 (74)</td>
</tr>
<tr>
<td>KPS</td>
<td>&gt;= 80</td>
<td>111 (71)</td>
</tr>
<tr>
<td></td>
<td>&lt;80</td>
<td>27 (17)</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>19 (12)</td>
</tr>
<tr>
<td>Pathology</td>
<td>Clear Cell</td>
<td>115 (73)</td>
</tr>
<tr>
<td></td>
<td>Papillary</td>
<td>12 (8)</td>
</tr>
<tr>
<td></td>
<td>Chromophobe</td>
<td>3 (2)</td>
</tr>
<tr>
<td></td>
<td>RCC Unclassified</td>
<td>12 (8)</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>15 (10)</td>
</tr>
<tr>
<td>Sarcomatoid Feature</td>
<td>Present</td>
<td>10 (6)</td>
</tr>
<tr>
<td></td>
<td>Not Present</td>
<td>69 (44)</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>78 (50)</td>
</tr>
<tr>
<td>Metastatic Locations</td>
<td>Brain</td>
<td>17 (11)</td>
</tr>
<tr>
<td></td>
<td>Lung</td>
<td>98 (62)</td>
</tr>
<tr>
<td></td>
<td>Liver</td>
<td>38 (24)</td>
</tr>
<tr>
<td></td>
<td>Bone</td>
<td>72 (46)</td>
</tr>
<tr>
<td></td>
<td>Lymph Node</td>
<td>86 (55)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>31 (20)</td>
</tr>
<tr>
<td>No. of Metastatic Organ Sites</td>
<td>1</td>
<td>27 (17)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>39 (25)</td>
</tr>
<tr>
<td></td>
<td>&gt;=3</td>
<td>83 (53)</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>8 (5)</td>
</tr>
<tr>
<td>Therapy Prior to Cabozantinib</td>
<td>Nephrectomy</td>
<td>129 (82)</td>
</tr>
<tr>
<td></td>
<td>Metastectomy</td>
<td>45 (29)</td>
</tr>
<tr>
<td></td>
<td>ICI</td>
<td>116 (74)</td>
</tr>
<tr>
<td>Received Cabozantinib</td>
<td>2nd Line</td>
<td>37 (24)</td>
</tr>
<tr>
<td></td>
<td>3rd Line</td>
<td>66 (42)</td>
</tr>
<tr>
<td></td>
<td>4th + 5th Line</td>
<td>54 (34)</td>
</tr>
</tbody>
</table>

Abbreviations: KPS = Karnofsky Performance Status; ICI = immune-checkpoint inhibitors.
IMDC risk groups by line of cabozantinib

A minority of patients (15%) in the entire cohort had IMDC favorable-risk disease upon initiation of cabozantinib as shown in Table 2. Almost half of all patients (48%) have IMDC intermediate-risk disease, and 18% have IMDC poor-risk disease. A minority of patients had missing IMDC risk group status (18%). Among patients who received cabozantinib in 2nd line, 35% of patients have IMDC favorable-risk disease whereas 11% have IMDC favorable-risk disease in 3rd line cabozantinib patients. More than half of 4th line and 5th line cabozantinib patients (63%) had either IMDC favorable-risk disease (7%) or IMDC intermediate-risk disease (56%).

Systemic therapy prior to cabozantinib

Among patients who received cabozantinib in 2nd line (n = 37), 6 patients received an ICI-based regimen prior. Specifically, 2 patients received ipilimumab + nivolumab, and 4 patients received axitinib + pembrolizumab. For patients who received 2nd line cabozantinib after TKI (n = 31), 42% received pazopanib and 58% received sunitinib.

Among patients who received cabozantinib in 3rd line (n = 66), 51 patients received single agent nivolumab in the 2nd line setting. Among these 51 patients, 82% received 1st line sunitinib and 18% received 1st line pazopanib. Seven patients who received cabozantinib in the 3rd line setting received 1st line ICI-based regimen, which include avelumab + axitinib (n = 3), pembrolizumab + axitinib (n = 2), and atezolizumab + bevacizumab (n = 2). Among these 7 patients, 2 received pazopanib and 5 received sunitinib prior to 3rd line cabozantinib. Among the 8 patients who received 2 lines of TKI prior to 3rd line cabozantinib, 6 received sunitinib and 2 received pazopanib in the 1st line setting. All of them received 2nd line axitinib.

Among patients who received cabozantinib in the 4th and 5th line, majority (96%) of patients have received ICI at one point during the previous lines of therapy.

Outcomes

In the overall cohort, the median time of follow-up was 9.6 months. The investigator-assessed DCR was 63%, with 44% of patients achieving SD, 17% achieving PR and 1% achieving CR as best response to cabozantinib, as shown in Table 3. Median TTF was 8.0 months (range 6.2 – 10.8 months) and median OS was 15.8 months (range 11.7 – 21.5 months) for the entire cohort. At two years, 33% of patients were alive. DCR for patients who previously received ICI prior to initiating cabozantinib was 64%, with 19% achieving PR and 1% achieving CR. In this group with prior ICI exposure, the median OS was similar to the overall cohort with a value of 15.8 months (range 10.3 – 20.7 months) and 28% of patients were alive at two years.

Median TTF of patients based on line of therapy is shown in Fig. 1 and Table 3, and median OS for these groups of patients is shown in Fig. 2 and Table 3. The sequence of systemic agents received is shown in Table 3.

The majority of patients (31/37) in the 2nd line cabozantinib group received TKI prior to cabozantinib, with a DCR of 48%, and a two-year OS rate of 43%. For the 6 patients in the 2nd line group (6/37) who received cabozantinib immediately after first-line ICI, the DCR was 33%. The DCR for 3rd line cabozantinib was 65%, with a median TTF (5.9 months vs. 10.4 months) and a median OS (13.3 months vs. 18.9 months) compared to 2nd line. One patient in the group who received cabozantinib immediately after ICI achieved a CR as best response. Fourth and 5th line cabozantinib patients had a DCR of 72% with an associated median TTF of 9.4 months (range 7.1 – 19.4 months) and median OS of 16.8 months (range 10.4 months – 27.8 months). The majority (52/54 or 96%) of patients in the 4th and 5th line group received ICI.
Table 3
Best Response to Cabozantinib, TTF and OS

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>CR (%)</th>
<th>PR (%)</th>
<th>SD (%)</th>
<th>PD (%)</th>
<th>DCR (%)</th>
<th>mTTF (mos)</th>
<th>mOS (mos)</th>
<th>One-year OS (%)</th>
<th>Two-year OS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>157</td>
<td>1</td>
<td>17</td>
<td>44</td>
<td>36</td>
<td>63</td>
<td>8.0 (6.2 – 10.8)</td>
<td>15.8 (11.7 – 21.5)</td>
<td>57%</td>
<td>33%</td>
</tr>
<tr>
<td>Prior ICI</td>
<td>116</td>
<td>1</td>
<td>19</td>
<td>42</td>
<td>35</td>
<td>64</td>
<td>7.6 (5.9 – 10.8)</td>
<td>15.8 (10.3 – 20.7)</td>
<td>56%</td>
<td>28%</td>
</tr>
<tr>
<td>2nd Line Cabozantinib</td>
<td>37</td>
<td>0</td>
<td>8</td>
<td>38</td>
<td>54</td>
<td>46</td>
<td>10.4 (5.7 – 13.6)</td>
<td>18.9 (11.1 – 36.6)</td>
<td>65%</td>
<td>40%</td>
</tr>
<tr>
<td>TKI - &gt; Cabozantinib</td>
<td>31</td>
<td>0</td>
<td>10</td>
<td>39</td>
<td>52</td>
<td>48</td>
<td>10.6 (5.9 – 19.5)</td>
<td>18.9 (11.8 – 36.7)</td>
<td>71%</td>
<td>43%</td>
</tr>
<tr>
<td>ICI - &gt; Cabozantinib</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>33</td>
<td>67</td>
<td>33</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3rd Line Cabozantinib</td>
<td>66</td>
<td>2</td>
<td>20</td>
<td>41</td>
<td>33</td>
<td>65</td>
<td>5.9 (4.5 – 8.8)</td>
<td>13.3 (8.3 – 22.6)</td>
<td>52%</td>
<td>21%</td>
</tr>
<tr>
<td>TKI - &gt; ICI - &gt; Cabozantinib</td>
<td>51</td>
<td>2</td>
<td>20</td>
<td>43</td>
<td>29</td>
<td>69</td>
<td>6.5 (4.9 – 12.0)</td>
<td>13.3 (8.3 – 20.7)</td>
<td>52%</td>
<td>27%</td>
</tr>
<tr>
<td>ICI - &gt; TKI - &gt; Cabozantinib</td>
<td>7</td>
<td>0</td>
<td>29</td>
<td>43</td>
<td>29</td>
<td>71</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>TKI - &gt; TKI - &gt; Cabozantinib</td>
<td>8</td>
<td>0</td>
<td>13</td>
<td>25</td>
<td>63</td>
<td>38</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>*4th + 5th Line Cabozantinib</td>
<td>54</td>
<td>0</td>
<td>18</td>
<td>53</td>
<td>27</td>
<td>72</td>
<td>9.4 (7.1 – 19.4)</td>
<td>16.8 (10.4 – 27.8)</td>
<td>58%</td>
<td>36%</td>
</tr>
</tbody>
</table>

*Majority (52/54) of patients in the 4th and 5th line group have received ICI at one point during the previous lines of therapy. Abbreviations: ICI = immune-checkpoint inhibitors; TKI = tyrosine-kinase inhibitor; CR = complete response; PR = partial response; SD = stable disease; DCR = disease-control rate; OS = overall survival; TTF = time to treatment failure. In multivariable analysis for TTF and OS shown in Fig. 3 and 4, initial IMDC poor-risk disease at one point during the previous lines of therapy. The DCR of cabozantinib in patients with bone metastases and in patients with non-clear cell histology were 56% and 40%, respectively. In multivariable analysis for TTF and OS shown in Fig. 3 and 4, initial IMDC poor-risk disease.
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Fig. 3. Forest Plots illustrating result of multivariable analyses of variables associated with TTF. Hazard ratio greater than 1 is associated with shorter TTF. Abbreviations: IMDC = International Metastatic Renal Cell Carcinoma Database Consortium.

Fig. 4. Forest Plots illustrating result of multivariable analyses of variables associated with OS. Hazard ratio greater than 1 is associated with shorter OS. Abbreviations: IMDC = International Metastatic Renal Cell Carcinoma Database Consortium.

was independently associated with shorter survival ($P = 0.0092$), and a trend towards shorter TTF which was not statistically significant ($P = 0.4272$).

DISCUSSION

In this study, we aimed to characterize the effectiveness of cabozantinib in the treatment of mRCC in a real-world setting. The CKCis database used in this analysis contains prospectively collected data and is a valuable resource for evaluating clinical characteristics and outcomes of kidney cancer. Real-world data in this space is important to confirm the efficacy of novel drugs in a less selective and more diverse patient population.

In this analysis of 157 patients, we demonstrated that patients with mRCC treated with cabozantinib in the second or later-line setting appear to derive clinical benefit in terms of DCR (63%) as well as TTF and OS. The median OS observed in this cohort who received cabozantinib in the 2nd line setting was 18.9 months, which is comparable to that of the METEOR study of 21.4 months [12]. Median TTF seen in those who received cabozantinib in the 2nd line setting was 10.4 months, which was longer than the median PFS observed in the METEOR study of 7.4 months [11]. However, 31% of the study population in the METEOR study were treated with two or more prior regimens [11, 12].

Similar findings were presented by Gan et al. in a retrospective analysis of the IMDC database of 413 mRCC patients who received cabozantinib in the 1st to 4th line setting. This study revealed a median TTF of 7.3 months and median OS of 17.8 months in the second-line setting and median TTF of 7.0 months and median OS of 12.6 months in the third-line [15]. CABOREAL is a real-world retrospective French multicentre study of 410 mRCC patients who received > 1 dose of cabozantinib. Nearly all patients (99%) received cabozantinib in the second or later-line setting with 41% of patients having had > 3 lines of prior therapy. Consistent with our results, this study revealed a median treatment duration of 7.6 months and a median OS of 14.4 months [16]. In contrast to our analysis, the CABOREAL study did not report response rates or TTF outcomes.

In patients who received 2nd line cabozantinib after a first-line TKI agent (pazopanib or sunitinib), survival outcomes were very similar to those reported in the subgroup analyses of the METEOR study [17]. Particularly, we saw a median TTF of 10.6 months and median OS of 18.9 months in this group of patients, compared to the METEOR study of 9.1 months median PFS and 21.4 months median OS in those who received sunitinib first-line, and 7.4 months median PFS and 22.0 months median OS in those who received pazopanib first-line. Our results support the hypothesis that cabozantinib can overcome resistance to first-line VEGFR TKIs by combined inhibition of VEGFRs and additional targets including MET and AXL [9].

We saw impressive response rates and survival in the heavily pre-treated group who received cabozantinib as 4th or 5th line systemic therapy, with DCR of 72%, median TTF of 9.4 months (range 7.1 – 19.4 months) and median OS of 16.8 months (range 10.4 – 27.8 months). Similarly, the IMDC retrospective analysis also reported long median TTF of 8.0 months (range 5.0 – 9.4 months) and median OS of 14.9 months (range 10.2 – 21.7 months) in patients who received cabozantinib in the 4th line setting [15]. We postulate that this could be impacted by selection bias, as RCC is a heterogenous disease in which
some tumours display a more indolent natural history which may allow patients to receive multiple lines of treatment [18]. Based on these data, caboza

As ICI based therapies enter clinical treatment algorithms, an area of active investigation is determining the optimal treatment strategy in those who progress on ICI. We observed activity of caboza

Bone metastases are common in mRCC (approximately 30% of patients), and are associated with high morbidity and a poor prognosis [22]. There is evidence to suggest that bone metastases do not respond well to VEGF inhibitors [23]. However, the CABO-SUN study suggested that caboza

In summary, we demonstrated that caboza

CONCLUSIONS

In summary, we demonstrated that caboza

0
and longer follow-up is needed in order to assess differences in effectiveness and survival between these different sequencing strategies. Toxicities of cabozantinib as well as dosing strategies are topics of interest for future studies within this cohort.

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AUTHOR CONTRIBUTIONS

Project development: HZ, NSB, JG. Data collection or management: HZ, IJ, SG. Data analysis: HZ, SG, JG. Manuscript writing/editing: HZ, NSB, SG, AAL, ARH, DYH, VC, CKK, EW, LW, GAB, RHB, AK, JG.

CONFLICT OF INTERESTS

All authors have no conflicts of interest to declare related to this manuscript. For COI unrelated to this manuscript: HZ: Hororarium - Merck. NSB: Honoraria - Astellas Pharma; Eisai; Ipsen; Janssen; Merck; Pfizer. Consulting or Advisory Role - Astellas Pharma; AstraZeneca; Bristol-Myers Squibb; Eisai; Ipsen; Janssen; Merck; Pfizer; Roche Canada; Bayer. Travel, Accommodations, Expenses - Eisai; Janssen. SG: None. JG: None. AAL: Honoraria - Astellas Pharma; Bayer; Bristol-Myers Squibb; Merck; Novartis; Pfizer; Roche/Genentech; Tersera. Consulting or Advisory Role - Abbvie; Astellas Pharma; Bayer; Bristol-Myers Squibb; Eisai; Ipsen; Janssen; Merck; Pfizer; Roche/Genentech; Tersera. Research Funding - Bristol-Myers Squibb (Inst); Ipsen; Novartis; Roche. ARH: Honoraria - AstraZeneca/MedImmune; Bristol-Myers Squibb; GlaxoSmithKline/Novartis; Merck; Pfizer. Consulting or Advisory Role - Boehringer Ingelheim; Boston Biomedical; Bristol-Myers Squibb; Genentech/Roche; GlaxoSmithKline; Merck; Novartis. Research Funding - Boehringer Ingelheim; Bristol-Myers Squibb (Inst); GlaxoSmithKline (Inst); Janssen (Inst); Karyopharm Therapeutics (Inst); Merck (Inst); Novartis (Inst); Roche/Genentech (Inst). DYH: Consulting or Advisory Role - Astellas Pharma; Bristol-Myers Squibb; Eisai; Ipsen; Janssen; Merck; Novartis; Pfizer. Research Funding - Bristol-Myers Squibb (Inst); Exelixis (Inst); Ipsen (Inst); Novartis (Inst); Pfizer (Inst). VC: Consulting or Advisory Role - AstraZeneca; Bristol-Myers Squibb; Celgene; Janssen; Novartis. CCK: Honoraria - Bristol-Myers Squibb; Novartis; Pfizer. Consulting or Advisory Role - Astellas Pharma; Bristol-Myers Squibb; Eisai; Ipsen; Janssen; Novartis; Pfizer. Travel, Accommodations, Expenses - Eisai; Novartis; Pfizer. EW: Honoraria - Amgen; Bayer; Eisai; Merck; Roche. Research Funding - AstraZeneca/MedImmune (Inst); Bristol-Myers Squibb (Inst); Eisai (Inst); Merck (Inst); Pfizer (Inst); Roche/Genentech (Inst). LW: Research Funding - Aragon Pharmaceuticals (Inst); AstraZeneca (Inst); Bristol-Myers Squibb (Inst); Exelixis (Inst); Merck (Inst); Novartis (Inst); Pfizer (Inst); Roche Canada (Inst). GAB: Honoraria - Bristol-Myers Squibb; Eisai; Ipsen; Novartis; Pfizer. Consulting or Advisory Role - Bristol-Myers Squibb; Eisai; Ipsen; Novartis; Pfizer. Research Funding - Merck (Inst); Pfizer (Inst). Travel, Accommodations, Expenses - Novartis; Pfizer. RHB: None. AK: Consulting or Advisory Role - Amgen; Bristol-Myers Squibb; Eisai; Ipsen; Janssen Oncology; Novartis; Pfizer. Research Funding - Bristol-Myers Squibb (Inst), EMD Serrano. JG: Consulting or Advisory Role - Ipsen; Janssen Oncology.

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