Real-world study of cabozantinib in patients with advanced renal cell carcinoma after VEGF-targeted therapy (CASSIOPE): interim data for patients who had received prior nivolumab

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Background

- Cabozantinib is a vascular endothelial growth factor (VEGF) receptor tyrosine kinase inhibitor with multiple targets, including MET and AXL.[1]
- Cabozantinib is approved in Europe as monotherapy for advanced renal cell carcinoma (aRCC) in treatment-naive adults with intermediate or poor risk, or following prior VEGF-targeted therapy.[2]
- We report a subgroup analysis of data from a pre-planned interim analysis of CASSIOPE (ClinicalTrials.gov identifier NCT03419572),[3] describing the real-world use of cabozantinib in patients with aRCC after VEGF-targeted therapy who have received prior nivolumab.

Objective

- The aim of this analysis was to assess patient characteristics and real-world outcomes for patients with aRCC who received cabozantinib after VEGF-targeted therapy in CASSIOPE and who had also received prior nivolumab.

Methods

Study design

- CASSIOPE is an ongoing, real-world, non-interventional, prospective, European study evaluating the utilization, safety, and effectiveness of cabozantinib in patients with aRCC who are initiating cabozantinib after prior VEGF-targeted therapy.[3]
- The study follows the real-life management of patients in routine care; patient visits take place according to the study site's usual clinical practice.

Study population

- Patients are eligible for inclusion if they:
  - are aged 18 years or older and have received a diagnosis of aRCC
  - have received at least one prior VEGF-targeted therapy
  - have no previous exposure to cabozantinib
  - are not currently enrolled in an interventional study.

Data collection and follow-up

- Patients are observed for up to 30 days after discontinuation of cabozantinib, with a maximum follow-up from treatment initiation of 12 months per patient.

Interim data and subgroup analysis

- A pre-planned interim analysis was conducted when 50% of the population had completed at least 3 months of follow-up (data cut-off, 27 February 2020).[3]
- The following were assessed over the first 3 months after treatment: best overall response (BOR; based on Response Evaluation Criteria in Solid Tumours version 1.1), dose modifications, and tolerability.
- Analyses were descriptive only.

Results

Patient disposition

- At the time of the interim analysis, 337 patients across several European countries had received at least one dose of cabozantinib (full analysis set [FAS], **Table 1**); of these, 265 (78.6%) continued receiving treatment.[3]
- Of all first-line therapies, sunitinib (56.7%) and pazopanib (32.3%) were most common; nivolumab was the most common second-line (2L) therapy.

Table 1. Patient demographics and baseline characteristics (FAS[a])

	Prior nivolumab subgroup (n = 154)	All patients (N = 337)
Age, years, median (range)	67.5 (36–88)	66.0 (29–88)
Sex, male, n (%)	109 (70.8)	246 (73.0)
Time since diagnosis, months, median (range)	39.56 (5.4–341.3)	39.05 (1.9–341.3)
IMDC risk, n (%)		
Favourable	13 (16.7)	33 (17.8)
Intermediate	46 (59.0)	115 (62.2)
Poor	19 (24.4)	37 (20.0)
Missing	76	152
ECOG PS score, n (%)		
0	40 (32.0)	109 (37.1)
1	61 (48.8)	143 (48.6)
2	21 (16.8)	37 (12.6)
3	3 (2.4)	4 (1.4)
4	0	1 (0.3)
Missing	29	43
Predominant cancer histology at diagnosis, n (%)		
Clear-cell RCC	135 (87.7)	282 (83.7)
Non-clear-cell RCC	19 (12.3)	55 (16.3)
RCC stage at start of cabozantinib treatment, n (%)		
Locally advanced (III)	6 (3.9)	12 (3.6)
Metastatic (IV)	148 (96.1)	325 (96.4)
Prior surgery, n (%)		
Prior nephrectomy	135 (87.7)	281 (83.4)
Other prior surgery	49 (31.8)	101 (30.0)
Metastasis site, n (%)		
Any site	148 (96.1)	325 (96.4)
Lungs	91 (59.1)	193 (57.3)
Bones	63 (40.9)	142 (42.1)
Liver	37 (24.0)	81 (24.0)
Lymph nodes	72 (46.8)	137 (40.7)
Other visceral metastasis	39 (25.3)	68 (20.2)
Brain	17 (11.0)	35 (10.4)
Other	43 (27.9)	95 (28.2)

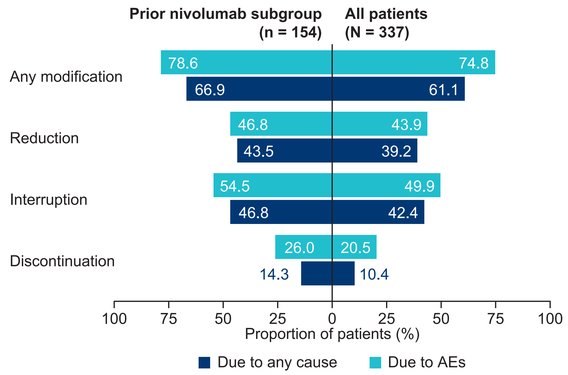
[a]Patients who received at least one dose of cabozantinib.
Percentages are subject to rounding.
ECOG PS, Eastern Cooperative Oncology Group Performance Status; FAS, full analysis set; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; RCC, renal cell carcinoma.

- In total, 154 patients (45.7%) had received prior nivolumab in any treatment line (**Table 1**).

Dosage and dose modifications among patients who received prior nivolumab

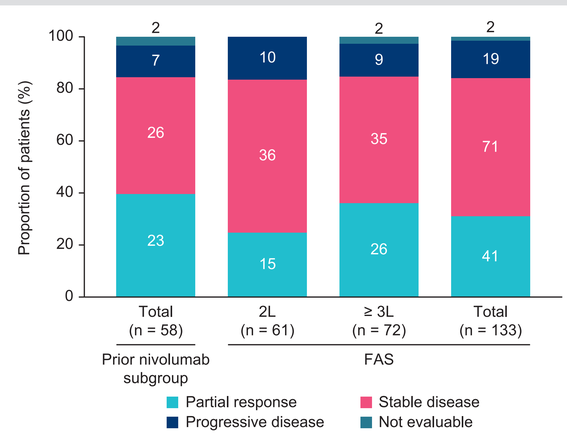
- One patient received 2L cabozantinib, and the remainder received cabozantinib in third-line (3L) or later-line settings.
- Overall, 58.4% and 37.7% of patients initiated cabozantinib at 60 mg/day and 40 mg/day, respectively; median daily dose during the study was 40 mg.
- One or more dose modifications occurred in 78.6% of patients, and these were due to adverse events (AEs) in 66.9% of patients (**Figure 1**).

Figure 1. Dose modifications (safety population[a])



[a]Patients who received at least one dose of cabozantinib and had a safety follow-up assessment.
AE, adverse event.

Figure 2. Best overall response based on RECIST v1.1 (FAS[a])



No patients had a complete response.
[a]Patients who received at least one dose of cabozantinib and a RECIST v1.1 assessment in the first 3 months after starting treatment.
2L, second-line; 3L, third-line; FAS, full analysis set; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1.

Adverse events

- The overall incidence of treatment-emergent AEs was similar for patients who received nivolumab and all patients included in the interim analysis (**Table 2**).

Tumour response

- During the first 3 months, 58 patients in the prior nivolumab subgroup had available BOR data, of whom 39.7% had a partial response, 44.8% had stable disease, 12.1% had progressive disease, and 3.4% were not evaluable (**Figure 2**).
  - These values are consistent with data reported for patients in the FAS who received 3L or later-line cabozantinib.

Table 2. TEAE frequency and intensity (safety population[a])

	Prior nivolumab subgroup (n = 154)	All patients (N = 337)
Any TEAEs, n (%)	146 (94.8)	312 (92.6)
Serious TEAEs, n (%)	58 (37.7)	112 (33.2)
Serious AEs leading to death, n (%)	17 (11.0)	29 (8.6)
TEAEs by intensity, n (%)		
Grade 1	118 (76.6)	250 (74.2)
Grade 2	116 (75.3)	245 (72.7)
Grade 3	59 (38.3)	126 (37.4)
Grade 4	10 (6.5)	18 (5.3)
Grade 5	17 (11.0)	29 (8.6)
Missing	9	13
Common TEAEs (reported in ≥ 10% of patients), n (%)		
Diarrhoea	56 (36.4)	153 (45.4)
PPE syndrome	39 (25.3)	79 (23.4)
Asthenia	35 (22.7)	77 (22.8)
Fatigue	33 (21.4)	69 (20.5)
Nausea	34 (22.1)	68 (20.2)
Decreased appetite	26 (16.9)	68 (20.2)
Hypertension	32 (20.8)	64 (19.0)
Mucosal inflammation	25 (16.2)	49 (14.5)
Stomatitis	23 (14.9)	43 (12.8)
Dysgeusia	17 (11.0)	36 (10.7)
Constipation	17 (11.0)	36 (10.7)
Hypothyroidism	17 (11.0)	36 (10.7)
Vomiting	17 (11.0)	35 (10.4)

[a]Patients who received at least one dose of cabozantinib and had a safety follow-up assessment.
AE, adverse event; PPE, palmar–plantar erythrodysaesthesia; TEAE, treatment-emergent adverse event.

Conclusions

- In this interim analysis of data from the real-world CASSIOPE study, cabozantinib used in routine care was broadly tolerable and may offer tumour response in patients previously treated with VEGF-targeted therapy and nivolumab.
- Consistent with previous observations, these data suggest that clinicians frequently use dose modifications to optimize cabozantinib use in routine clinical practice.[2]

Abbreviations

aRCC, advanced renal cell carcinoma; 2L, second-line; 3L, third-line; AE, adverse event; BOR, best overall response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FAS, full analysis set; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; PPE, palmar–plantar erythrodysaesthesia; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; RCC, renal cell carcinoma; TEAE, treatment-emergent adverse event; VEGF, vascular endothelial growth factor.

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