Data Supplement

Cabozantinib for previously-treated radioiodine-refractory differentiated thyroid cancer: Updated results from the phase 3 COSMIC-311 trial

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TABLE S1. Subsequent Therapy[a]

	Cabozantinib (n = 170)	**Placebo (n = 88)**
Systemic nonradiation anticancer therapy, No. (%)	19 (11)	10 (11)
Protein kinase inhibitors[b]	16 (9)	9 (10)
Lenvatinib	7 (4)	4 (5)
Cabozantinib	2 (1)	3 (3)
Dabrafenib	2 (1)	1 (1)
Sunitinib	2 (1)	0
Trametinib	2 (1)	1 (1)
Axitinib	1 (1)	0
Pazopanib	1 (1)	0
Vemurafenib	1 (1)	0
Repotrectinib	0	1 (1)

[a]Receipt of open-label cabozantinib was not considered a subsequent therapy. [b]Patients who received >1 protein kinase inhibitor were counted once.

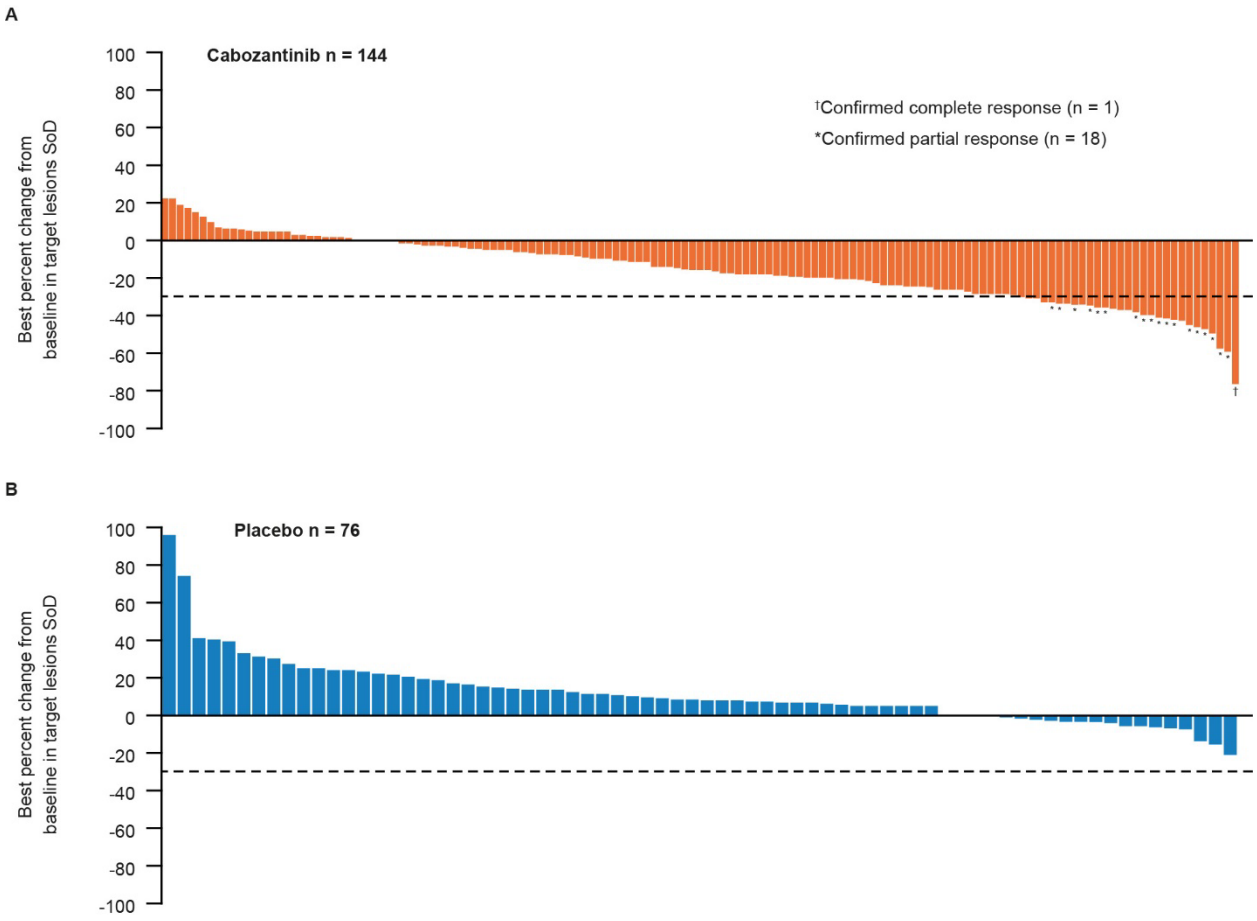
TABLE S2. Treatment Exposure and Dose Modification (Safety Population)

	Cabozantinib (n = 170)	**Placebo (n = 88)**
Duration of exposure, median (range), mo	6.0 (0.2–18.8)	2.6 (0.2–15.2)
Average daily dose, median (range), mg	39.5 (9.5–60.0)	59.9 (18.4–68.3)
Dose modifications due to adverse event, No. (%)	136 (80)	24 (27)
Dose holds due to adverse event, No. (%)	120 (71)	24 (27)
Duration, median (range), days	12.5 (1.0–112.0)	13.3 (1.0–63.0)
Dose reduction due to adverse event, No. (%)	114 (67)	3 (3)
Reduction to 40 mg	114 (67)	3 (3)
Reduction to 20 mg	54 (32)	0
Time to first dose reduction, median (range), days	57.0 (14.0–510.0)	85.0 (36.0–153.0)
Time to second dose reduction, median (range), days	127.5 (28.0–472.0)	NA
Discontinuation due to a treatment-emergent adverse event[a], No. (%)	15 (9)[b]	0
Discontinuation due to a treatment-related adverse event[a]	10 (6)	0

Abbreviations: mo, months; NA, not applicable; No., number.

[a]Unrelated to differentiated thyroid cancer. [b]Adverse events leading to discontinuation of cabozantinib (patients could have experienced more than 1 event): fatigue (3), diarrhea (2), arthralgia (1), abdominal pain (1), cardiorespiratory arrest (1), diverticular perforation (1), hypercalcemia (1), large-intestine perforation (1), increased liver function test (1), myalgia (1), myelodysplastic syndrome (1), neutrophil count decreased (1), pain (1), polyneuropathy (1), posterior reversible encephalopathy syndrome (1), proteinuria (1), renal impairment (1), stomatitis (1), stress cardiomyopathy (1), thrombocytopenia (1), urinary retention (1), weight decreased (1).

Figure S1. Waterfall plot for maximum percentage of tumor reduction from baseline in target lesions for individual patients**.** (A) Cabozantinib group. (B) Placebo group. Tumor response was assessed with Response Evaluation Criteria in Solid Tumors version 1.1 by blinded independent radiology committee. The waterfall plots show the maximum percentage of reduction or minimum increase from baseline in sum of diameters of target lesions before progressive disease or initiation of any nonprotocol anticancer medication. Only patients with at least 1 baseline and postbaseline assessment are shown. Any reduction in the sum of diameter in target lesion was observed in 115/144 (80%) evaluable patients assigned to cabozantinib and 18/76 (24%) assigned to placebo.



Abbreviation: SoD, sum of diameters.