

Genetic Testing, Treatment Patterns, and Clinical Outcomes Among Patients With Advanced/Metastatic Medullary Thyroid Cancer in the United States: A Retrospective Medical Record Review Study

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BACKGROUND

- The incidence of thyroid cancer has increased over the last 3 decades to an estimated 52,890 new cases in the United States (US) in 2020.¹
- Medullary thyroid cancer (MTC) accounts for approximately 1.6% of new cases.² Because more than half of MTCs are driven by mutation in the *RET* (rearranged during transfection) protooncogene,^{3,4} agents that target *RET* are recommended in the National Comprehensive Cancer Network treatment guidelines.⁵
 - Therefore, genetic testing should be part of the standard of care for patients with advanced/metastatic MTC.
- Real-world evidence on somatic/germline genetic testing, current treatment patterns, and associated clinical outcomes by each line of treatment is limited.

OBJECTIVE

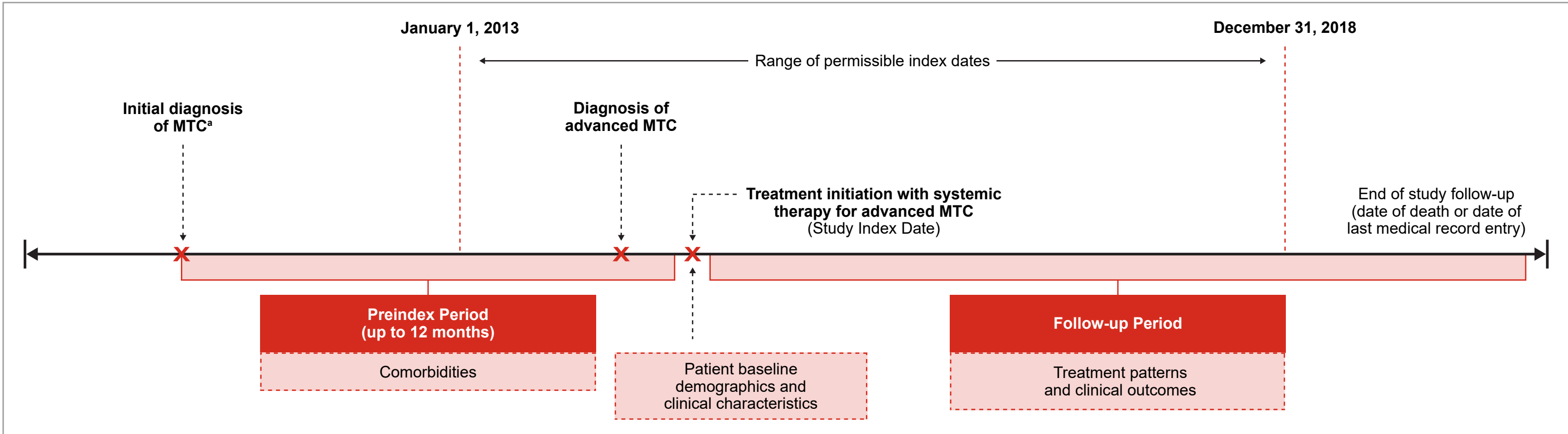
- This study was designed to describe patient characteristics, somatic/germline genetic testing, treatment patterns, and clinical outcomes among patients with advanced/metastatic MTC in a real-world setting in the US to understand patterns of care of these patients.

METHODS

Study Design

- Retrospective medical record abstraction was conducted by a convenience sample of selected physicians (medical or clinical oncologists, hematologist-oncologists, or pediatric oncologists) who treated > 1 patient with advanced/metastatic MTC during the year before medical record abstraction (Figure 1).
- Data were abstracted for a quasi-random sample of patients, drawn by asking participating physicians to select medical records for patients whose last names began with a randomly generated letter.
- Data abstraction was conducted from April 2020 through May 2020, allowing opportunity for at least 15 months of follow-up from the last permissible index date in December 2018; however, no minimum follow-up was required.

Figure 1. Study Design Schematic



* Only relevant for patients who were initially diagnosed with an earlier stage of the disease and subsequently experienced disease progression or recurrence with advanced disease between January 1, 2013, and December 31, 2018. Patient may have been diagnosed with earlier-stage MTC and/or advanced MTC before or during the preindex period (up to 12 months). Note: Figure is not to scale.

Patient Selection Criteria

Inclusion criteria	Exclusion criteria
Patients aged ≥ 12 years who were initially diagnosed with locally advanced or metastatic MTC or were initially diagnosed at an earlier stage and experienced progression to advanced/metastatic MTC. Patients could be living or deceased at the time of data abstraction.	Patients with evidence of other malignant neoplasms prior to initiation of the first systemic treatment for advanced MTC, except MEN2-associated pheochromocytoma that had been resected or was stable, nonmelanoma skin cancer, in situ cervical cancer, or other cancer from which the patient had been disease free for ≥ 5 years.
Initiated ≥ 1 systemic treatment (single agent or combination) for advanced/metastatic MTC from January 1, 2013, to December 31, 2018.	Patients who participated in a clinical trial involving an interventional drug as a first-line systemic treatment for advanced/metastatic MTC.

Data Collection & Analysis Plan

- Key patient demographics and clinical characteristics included: stage at initial diagnosis, *RET* mutation testing and associated results, site(s) of metastases at advanced/metastatic diagnosis, calcitonin and carcinoembryonic antigen (CEA) levels at advanced diagnosis and during each line of systemic treatment, and Eastern Cooperative Oncology Group (ECOG) performance status.
- Treatments received before and after advanced/metastatic diagnosis.
- Clinician-defined disease progression during each line of therapy and date of death, where applicable.
- Descriptive analysis was conducted for patient demographics, clinical characteristics, treatment patterns, progression-free survival (PFS), and overall survival.
- PFS and overall survival were estimated using the Kaplan-Meier method.
- All analyses were conducted using SAS, version 9.4.

CONCLUSIONS

- More than one-third of patients with advanced/metastatic MTC were not tested for *RET* mutations as recommended by the National Comprehensive Cancer Network guidelines throughout the study period.
- For the treatment of advanced/metastatic MTC, no specific preference of sequencing systemic agents was observed in the first- and second-line settings.
- The estimated overall survival is consistent with that observed from the Surveillance, Epidemiology, and End Results database for patients with de novo metastatic MTC.
- Considering the recent approval of selective *RET* inhibitors for patients with *RET*-mutant MTC, future research should investigate potential changes in these findings, particularly in the second-line setting.

RESULTS

- 75 oncologists (40 medical/clinical oncologists and 35 hematologist-oncologists) provided abstraction of 203 medical records of adult patients with advanced/metastatic MTC.
 - Data for a median of 2 patients were abstracted by each participating oncologist.
 - The 75 participating physicians represented all geographic regions (Northeast [25.3%], Midwest [16.0%], South [30.7%], and West [28.0%]).
 - Most physicians practiced in a cancer center or tertiary referral center (45.3%) or a private hospital or clinic (33.3%); 17.3% practiced in an academic or teaching hospital, and 4.0% practiced in another nonteaching hospital setting.
- The median age of patients at advanced/metastatic diagnosis was 53.0 years, and most patients (82.8%) were initially diagnosed with stage IV disease (Table 1).
- Among all patients, 125 (61.6%) had testing for *RET* mutations (somatic/germline), of whom 36.0% had *RET*-mutant MTC (somatic/germline) (Table 1).
 - The *RET* mutation type was reported for 28 patients; the most common mutations reported were M918T (64.3%) and C634R (32.1%).
- Of the 203 patients, 75.9% received only one line of systemic treatment for advanced disease, and for 44.3%, the last line of treatment was ongoing at the time of data extraction.
- The most common first- and second-line treatment regimens are shown in Figure 2, and treatment sequencing from first- to second-line treatment regimens is shown in Figure 3.
- The median PFS for first-line treatment was 26.6 months (95% confidence interval [CI], 20.8-60.8); for second-line treatment (n = 49), median PFS was 15.3 months (95% CI, 6.6-not estimable [NE]) (Table 2).
- The median overall survival from initiation of first- and second-line treatments was 63.8 months (46.3-NE) and 22.4 months (12.4-NE), respectively (Figure 4).

Figure 2. Common First- and Second-Line Treatment Regimens Among Patients With Advanced/Metastatic Medullary Thyroid Cancer

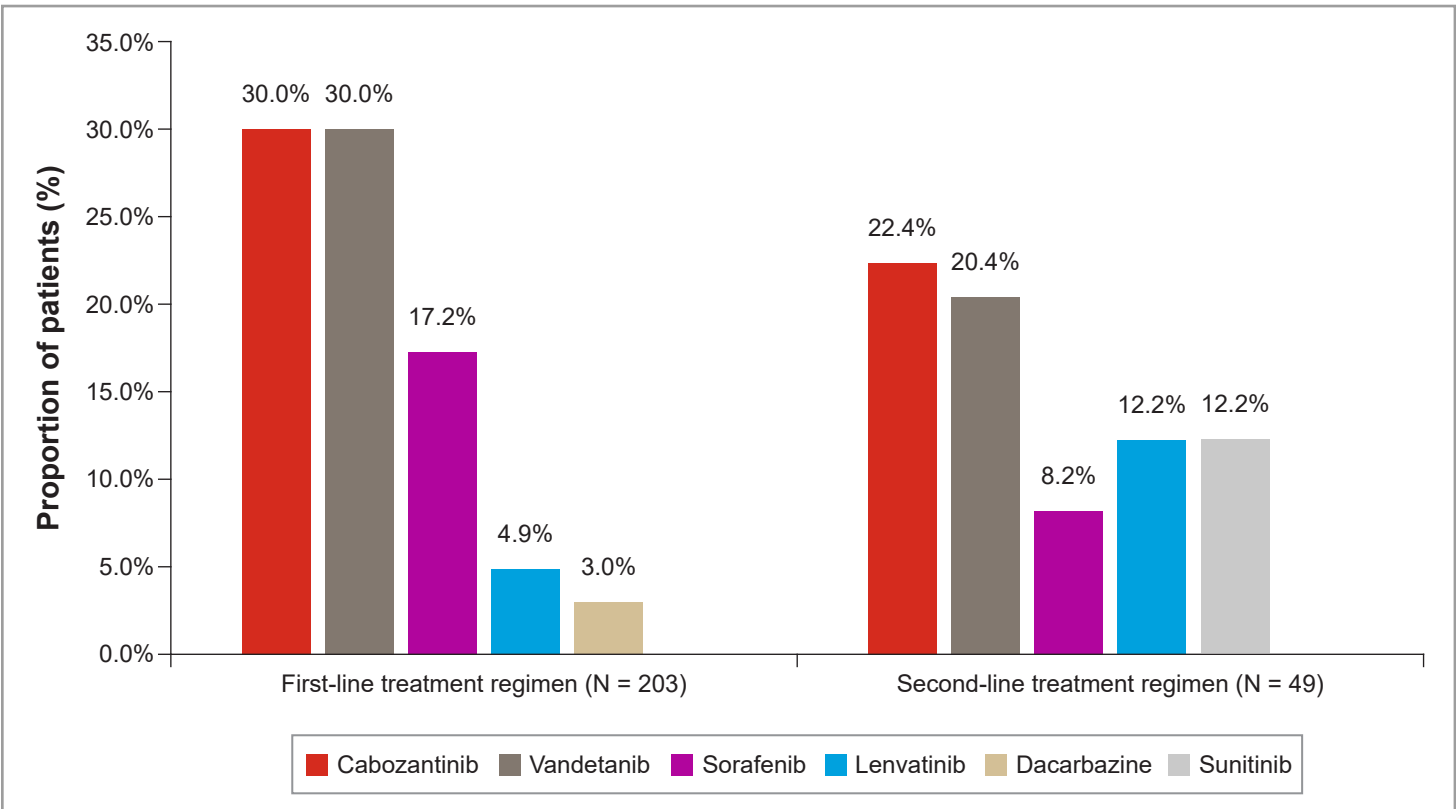


Table 1. Characteristics of Patients With Advanced/Metastatic Medullary Thyroid Cancer

	Overall	
Number of patients, N	203	
Age (years) at advanced/metastatic diagnosis of MTC (median, IQR)	53.0 (44.0, 59.0)	
Sex (n, %)		
Female	119	58.6%
Male	84	41.4%
Race (n, %)		
White	134	66.0%
Black/African American	45	22.2%
Asian, Native Hawaiian, or other Pacific Islander	18	8.9%
Other	1	0.5%
Hispanic (n, %)	25	12.3%
Tested for <i>RET</i> mutation (n, %)	125	61.6%
Patients with <i>RET</i> -mutant MTC	45	36.0%
<i>RET</i> mutation identified before initial MTC diagnosis	25	55.6%
<i>RET</i> mutation identified after initial MTC diagnosis	20	44.4%
Clinical stage at initial MTC diagnosis (n, %)		
Stage II	10	4.9%
Stage III	20	9.9%
Stage IVA	58	28.6%
Stage IVB	28	13.8%
Stage IVC	82	40.4%
Unknown or not reported	5	2.5%
Calcitonin level known at advanced/metastatic MTC diagnosis (pg/mL) (n, %)	117	57.6%
Mean (SD)	150.1 (138.9)	
CEA level known at advanced/metastatic MTC diagnosis (ng/mL) (n, %)	84	41.4%
Mean (SD)	30.0 (30.4)	
ECOG performance status at advanced/metastatic MTC diagnosis	173	85.2%
0 or 1	142	82.1%
Total duration of follow-up, months (mean [SD])	24.5 (16.0)	
Charlson Comorbidity Index (n, %)	197	97.0%
Mean (SD)	1.4 (1.8)	

IQR = interquartile range; SD = standard deviation.

Figure 3. Sankey Chart for First- and Second-line Treatment Regimens for Advanced/Metastatic MTC

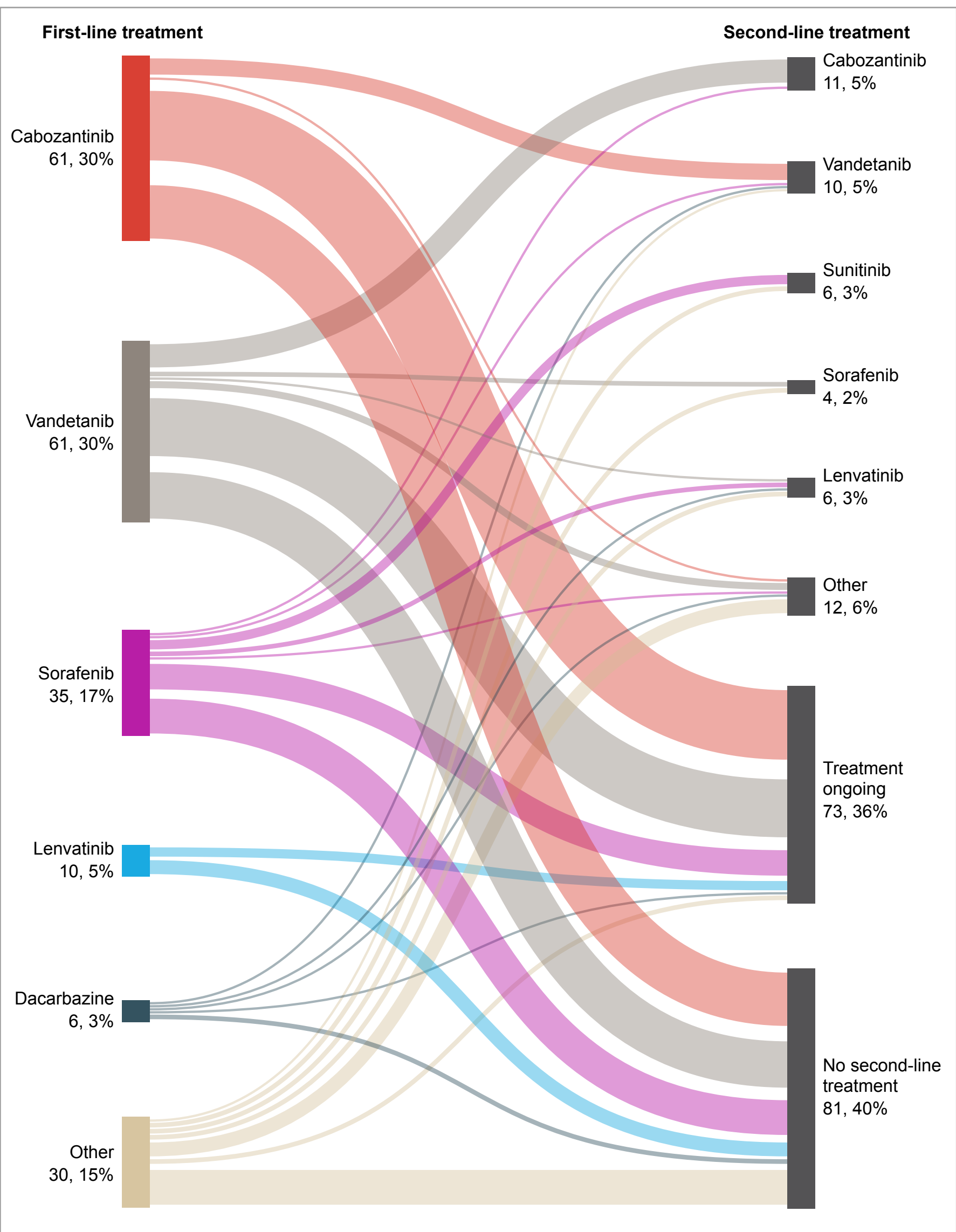


Table 2. Clinical Outcomes During First- and Second-Line Treatment

	First-Line Treatment		Second-Line Treatment	
Number of patients who initiated treatment line, N	203		49	
Best response to the treatment (n, %)				
Complete response	52	25.6%	7	14.3%
Partial response	77	37.9%	12	24.5%
Stable disease	48	23.6%	13	26.5%
Progressive disease	20	9.9%	13	26.5%
Response not assessed	5	2.5%	3	6.1%
Don't know	1	0.5%	1	2.0%
Objective response (complete or partial response)	129	63.5%	19	38.8%
Clinical benefit rate (complete response, partial response, or stable disease)	177	87.2%	32	65.3%
PFS (months)*				
Progressed or died (N, %)	97	47.8%	23	46.9%
Time from initiation of treatment (Kaplan-Meier estimate)				
Mean (SE)	34.3 (2.1)		13.4 (1.3)	
Median	26.6		15.3	
95% CI	20.8	60.8	6.6	NE
Censored (N, %)	106	52.2%	26	53.1%

SE = standard error.

* Physician-assessed disease progression, initiation of next line of treatment, and death were considered "progression events" for PFS calculation.

Figure 4A. Overall Survival From Initiation of First-Line Systemic Treatment

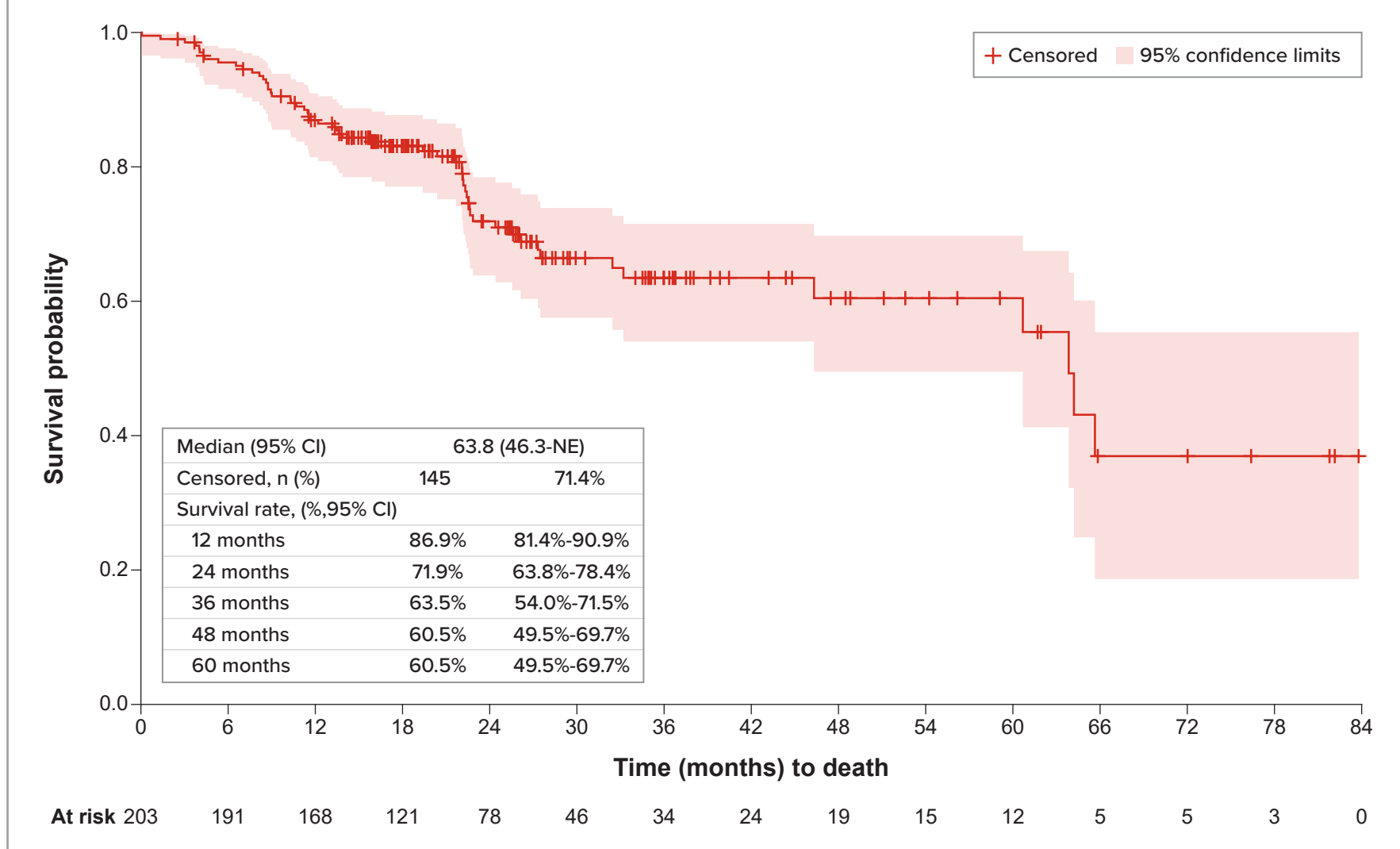
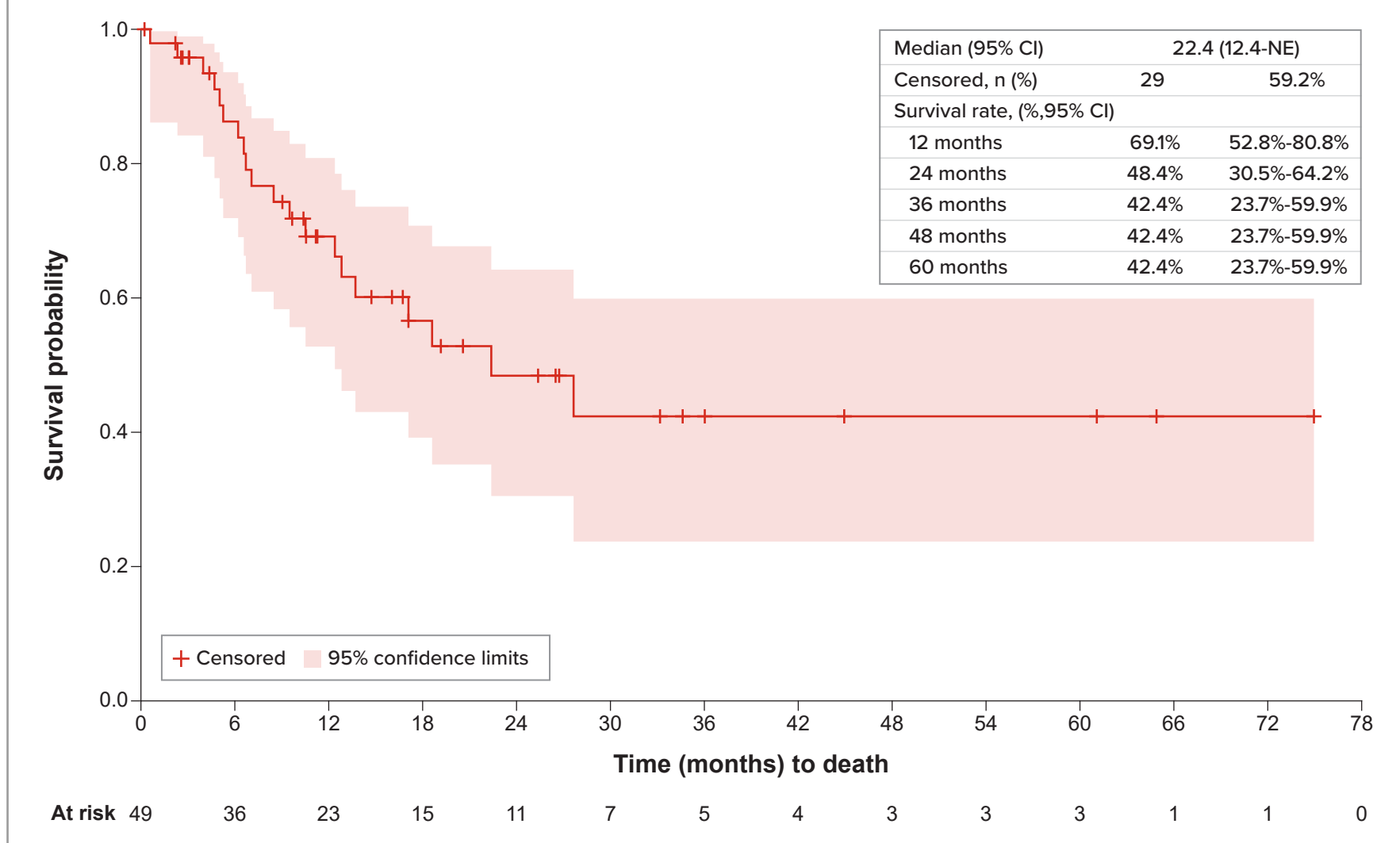


Figure 4B. Overall Survival From Initiation of Second-Line Systemic Treatment



LIMITATIONS

- Patients selected for study inclusion represent a convenience sample of medical records obtained from physicians who were willing to participate in the study. Therefore, study findings may not be generalizable to the overall population of US patients with advanced/metastatic MTC. To help mitigate this potential bias, we recruited physicians from a variety of geographic regions and practice types and instructed them to select patients by a quasi-random procedure. However, due to unequal distribution of names beginning with each letter, all medical records will not have an equal probability of inclusion in the study.
- Data available for the study were limited to those recorded in medical records. Although internal data consistency was improved by data checks and use of a customized data-collection form, the entered data were not validated against patients' medical records by independent review.
- Data on the source of the material that was genetically tested (somatic or germline) was not collected in this study.
- Finally, a considerable proportion of patients were undergoing first-line treatment or were alive at the time of data abstraction, and 52% and 71% of patients were censored for PFS and overall survival estimates, respectively; therefore, these estimates are based on immature data.

REFERENCES

- National Cancer Institute. 2020. <https://seer.cancer.gov/statfacts/html/thyro.html>.
- Howlader N, et al. SEER Cancer Statistics Review, 1975-2017. https://seer.cancer.gov/csr/1975_2017/.
- Moura MM, et al. Br J Cancer. 2009 Jun;100(11):1777.
- Moura MM, et al. Endocr Relat Cancer. 2015 Oct;22(5):R235-52.
- National Comprehensive Cancer Network. 2021. https://www.nccn.org/store/login/login.aspx?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf.

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