

Malignant Giant Cell Tumour of Bone: Clinicopathologic Characteristics, Treatment Outcomes, and Real-World Experience from a Tertiary Sarcoma Centre

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Abstract

Background: Giant cell tumor of bone (GCTB) is typically benign, but a small subset develops malignant GCTB (MGCTB), arising either de novo (primary) or after prior benign disease (secondary). This study presents real-world outcomes of systemic treatment in MGCTB.

Methods: We retrospectively analysed adults (≥ 18 years) with histologically confirmed primary or secondary MGCTB treated at our tertiary sarcoma clinic (2018–2025). Diagnosis was based upon expert pathology opinion and H3F3A IHC. Clinical, pathologic, treatment, and response data were collected and analysis was done using SPSS v.30.

Results: Twenty patients (median age 41 years, 65% male) were analysed: 7 (35%) PMGCTB and 13 (65%) SMGCTB (median latency 84 months). Tumours were mainly appendicular (70%), most often distal femur (45%). Around half (8/20; 40%) were metastatic at presentation, mostly to lung. Most common histology was osteosarcoma and UPS.

Local control was achieved with wide excision (12/15, 80%), amputation (1/15, 7%), intralesional surgery (2/15 13%). 18 patients (90%) received systemic therapy (median 5 cycles, predominantly doxorubicin-based (16/18, 88%). Neoadjuvant chemotherapy induced responses in 2/3 patients, allowing R0 resection. In the adjuvant group (n=6), only 2 patients remained disease free at the end of follow up. In the palliative chemotherapy cohort (n=7) responses were limited (2 PR, 1 SD). Pazopanib (n=8) produced clinical benefit in 4 patients (50%). Subsequent lines (gemcitabine–docetaxel, eribulin, cisplatin regimens, cabozantinib) showed modest, short-lived activity. The median overall survival was 60 months, with the estimated 12-month OS rate of 65%, and the 60-month OS rate of 42.6%.

Conclusions: This study represents one of the largest contemporary real-world evaluation of chemotherapy in MGCTB, providing novel real world insights into response and survival. Systemic therapy and targeted therapy offer modest benefit.

1. Introduction

Giant cell tumours (GCTs) are classified as intermediate-malignant neoplasms of bone, with locally aggressive behaviour. It comprises approximately 5% of primary bone tumours and up to 20% of benign skeletal tumours, with an estimated annual incidence of 1.2–1.7 cases per million individuals (1, 2). Malignant transformation can be primary or secondary. Primary MGCTB is defined by the presence of high-grade sarcomatous elements at initial diagnosis, whereas secondary MGCTB represents sarcomatous transformation in a previously treated benign lesion, most often following surgery and, less frequently, radiotherapy. In a retrospective analysis of more than 2,300 cases, the overall incidence was reported at $\sim 4\%$, comprising primary malignant GCTB (PMGCTB) in 1.6% and secondary malignant GCTB (SMGCTB) in 2.4%(3).

In the absence of prior therapy, the risk of secondary malignant GCT is lower, reported at $\sim 0.6\%$ (3). PMGCT is diagnosed at presentation, whereas SMGCT typically arises after a prolonged latency—averaging ~ 9 years following radiotherapy and up to ~ 20 years in spontaneous cases has been documented(4). The possible association between denosumab and secondary malignant transformation remains uncertain(3).

Diagnosis of malignant GCT is based on identification of high-grade sarcoma which commonly includes, osteosarcoma, undifferentiated pleomorphic sarcoma, fibrosarcoma, and leiomyosarcoma. Identification of H3F3A mutations, most commonly the H3.3 (p.G34W variant), by mutation-specific immunohistochemistry or sequencing on biopsy specimens is a sensitive and specific adjunct for confirming MGCTB. While most benign and primary malignant giant cell tumours of bone retain H3F3A mutations, a substantial minority of secondary malignant GCTB may be H3F3A-negative, reflecting clonal evolution or dedifferentiation(5).

The anatomical distribution of malignant GCTs mirrors that of benign GCTB, as seen in previous series and is most common in the meta-epiphyseal regions of long bones (85–90%). Most common sites are the distal femur (30%), proximal tibia (28%), distal radius (9%), and distal tibia (6%), whereas pelvic (2%), sacral (2%), and spinal (3%) locations are uncommon(6).

The malignant giant cell tumour (GCT) of bone, although rare, presents significant clinical challenges due to its aggressive behaviour, high risk of recurrence, and potential for metastasis. While advances in surgery and radiotherapy have improved local control, the role of systemic therapy, particularly chemotherapy, remains poorly defined. Evidence to date is largely confined to small series and anecdotal reports, with scarce data on regimens, dosing, or outcomes, leaving uncertainty regarding its true benefit. To address this gap, the present study reports real-world data on systemic treatment in malignant GCT of bone.

2. Materials and Methods

Study design and setting

This was a retrospective, observational study conducted at the Sarcoma Medical Oncology Clinic, All India Institute of Medical Sciences (AIIMS), New Delhi, a tertiary referral centre for bone and soft tissue sarcomas. The study included patients registered between January 2018 and June 2025. This study was approved by the Ethics Committee of the All India Institute of Medical sciences and was conducted in accordance with the Declaration of Helsinki and relevant local regulations. (Ref. No: AIIMSA4695/12.09.2025). The requirement for informed consent was waived owing to the retrospective nature of the study.

Study population and eligibility

Adult patients (≥ 18 years) with histologically confirmed malignant giant cell tumour of bone (MGCTB) were eligible for inclusion. Both primary malignant GCTB (PMGCTB) and secondary malignant GCTB (SMGCTB) arising from a previously diagnosed benign giant cell tumour of bone were included. All biopsy specimens were centrally reviewed by two expert sarcoma pathologists. Malignant histology was classified as osteosarcoma, undifferentiated pleomorphic sarcoma, fibrosarcoma, or malignant GCT NOS (not otherwise specified). Patients with incomplete clinical data or without confirmatory histopathology were excluded.

Assessment and follow-up

Baseline data collected included demographic characteristics, clinical presentation, tumour site, prior treatments for benign GCTB, latency period to malignant transformation (for SMGCTB), histological subtype, and extent of disease at diagnosis. Latency was defined as the interval between pathological diagnosis of benign GCT and malignant transformation.

Details of local treatment (surgery and radiotherapy), systemic therapy regimens, treatment intent (neoadjuvant, adjuvant, peri-operative, or palliative), and subsequent lines of therapy were recorded. Radiological assessment of response to systemic therapy performed using PET-CT imaging was evaluated according to Response Evaluation Criteria in Solid Tumours (RECIST), version 1.1. Patients were followed longitudinally until death or last documented follow-up. The cutoff for follow up was December 31, 2025.

Endpoints

The primary endpoint was overall survival (OS), defined as the time from diagnosis of malignant GCTB to death from any cause. Secondary endpoints included objective response rate (ORR), defined as the proportion of patients

achieving complete or partial response, clinical benefit rate (defined as ORR or stable disease), and patterns of disease recurrence or progression.

Sample size

Given the rarity of malignant giant cell tumour of bone, no formal sample size calculation was performed. All consecutive eligible patients treated during the study period were included to provide a comprehensive real-world assessment of clinical outcomes.

Statistical analyses

Descriptive statistics were used to summarise patient characteristics, treatments, and response outcomes. Categorical variables were reported as counts and percentages, and continuous variables as medians with interquartile ranges (IQR). Overall survival was estimated using the Kaplan–Meier method, and comparisons between groups were performed using the log-rank test. Statistical analyses were conducted using SPSS software (version 30.0). A p-value < 0.05 was considered statistically significant.

3. Results

Clinical features

A total of 20 patients with MGCTB were included in the analysis. The median age of the cohort at diagnosis of MGCTB was 40.5 years (IQR: 34–47), predominantly were males (13/20; 65%). All patients presented with pain and swelling, and one patient in addition, presented with cauda equina syndrome, due to a locally extensive sacral tumour. Appendicular involvement was more common than axial (14/20; 70% vs. 6/20; 30%). Distal femur was the most frequently affected site (9/20; 45%). Secondary malignant GCTB was more common (n=13/20; 65%). The median latency for malignant transformation in the SMGCT cohort was 84 months (IQR 48–120).

At diagnosis, 40% patients (n=8/20) were metastatic, including 8 SMGCT and 1 PMGCT. Lungs were the most frequent site for metastasis, seen in 6 of 8 patients (75%). Other sites included lymph nodes (5/8), skeletal metastases (3/8), and soft-tissue deposits (3/8). One case exhibited pericardial involvement, which was attributable to direct extension from pulmonary metastasis. The baseline characteristics have been summarised in Table 1.

Histologic characteristics

Among patients with PMGCT, tumour was composed of neoplastic cells consistent with high grade sarcoma, juxtaposed with a giant cell rich lesion. In contrast, SMGCTs, lacked a residual giant-cell-rich-lesion, and diagnosis was established based on the presence of a high-grade sarcoma with a prior history of benign GCT. H3F3A IHC was positive in 38.5% (n=5/13) of SMGCT and 100% (n=7/7) of PMGCT. The most frequent histology was Malignant GCT NOS (8/20; 40%).

Prior Treatment for benign disease in the SMGCT cohort

Among patients with secondary malignant GCTB (SMGCT; n = 13), initial local management of the antecedent benign lesion consisted of intralesional curettage with cementing or bone grafting in 8 patients (61.5%), wide local excision in 4 patients (30.7%), and definitive radiotherapy in 1 patient (7.6%). Local recurrence of benign GCTB occurred in 4 patients (31%) after a median interval of 49 months; all underwent repeat wide local excision with margin-negative (R0) resection. Prior exposure to denosumab and bisphosphonates was documented in 2 patients each.

Local treatment for malignant GCTB

Upfront local therapy for malignant disease was undertaken in 75% patients (n=15/20), including all 11 non-metastatic and 4 of 8 metastatic patients. Among those receiving upfront local treatment, wide local excision was the most common approach (12/15; 80%), followed by intralesional procedures (curettage or debridement; 2/15; 13%) and amputation (1/15; 7%). All surgically treated patients achieved margin-negative (R0) resections. Palliative radiotherapy was administered in 6 patients (30%), either as primary local therapy or for symptom control. Repeat local interventions were required in 5 patients during the disease course, including wide local excision (n=1) and amputation (n=2) for local recurrence, and lung metastatectomy (n=2) for distant recurrence. (Table 2)

Systemic therapy of malignant GCT

Systemic therapy was administered in 18 of 20 patients (90%) at some point during the disease course. It was given as a part of upfront treatment in 15 patients, while three initiated systemic therapy only at recurrence after initial local therapy. Two patients underwent surgical management only, during the entire follow-up period; curettage in 1 and amputation in 1.

First line systemic therapy

First-line systemic therapy was initiated with palliative intent in nine patients and curative intent (neoadjuvant, adjuvant, or peri-operative) in the remaining nine. Doxorubicin-based chemotherapy was the most commonly used first-line regimen, administered in 16 of 18 patients (88%), either as a single-agent (n=5) or in combination with ifosfamide, or cisplatin. Patients received a median of 5 cycles, with 50% patients completing all planned cycles.

In patients treated with first-line palliative systemic therapy (n = 9), 7 received chemotherapy and 2 received pazopanib. Among those who received chemotherapy, clinical benefit was observed in 43% (n=3/7), comprising two partial responses and one stable disease; the remaining patients progressed during treatment. In patients started on pazopanib, stable disease was seen in one, while progression in the other.

Neoadjuvant chemotherapy was administered in three patients; 66% (n=2/3) achieved a partial response and subsequently underwent surgical resection, and were disease free at the end of follow-up, while one patient developed progressive disease, and underwent excision, and developed local recurrence after 14 months managed by palliative radiotherapy. Among patients who received adjuvant chemotherapy (n = 6), only two remained disease-free at last follow-up.

Subsequent line systemic therapy and response

Disease progression following systemic therapy was observed in 12 of 18 patients (66.6%), including 8 patients who had metastatic disease and 4 who had localized disease at baseline. Patterns of failure included distant-only recurrence in 7 patients, local recurrence in 1 patient, and combined local and distant recurrence in 4 patients.

Second-line systemic therapy was administered to 5 of the 12 patients at first progression, while 5 patients received best supportive care. With further disease progression, third- and fourth-line systemic therapies were each administered in 4 patients, and fifth-line therapy in 2 patients.

Tyrosine kinase inhibitors (TKIs) were the most frequently used agents in subsequent lines. Pazopanib was used in 4 patients as second-line therapy and in 2 patients as third-line therapy, with objective responses in 50% (n=3/6) patients (Figure 1). Cabozantinib was used in two patients in the fourth-line setting, with one partial response; this patient remained alive at last follow-up. Subsequent-line chemotherapy regimens, including gemcitabine–docetaxel, eribulin,

cisplatin, and ifosfamide–etoposide, did not result in any objective responses. The different lines of systemic therapy have been detailed in Table 3.

Toxicities

Grade ≥ 3 adverse events associated with doxorubicin-based chemotherapy included febrile neutropenia ($n = 1$), grade 3 diarrhea ($n = 2$), grade 3 cytopenias ($n = 2$), and grade 3 nausea and vomiting ($n = 1$). No treatment-related mortality was observed. Pazopanib was generally well tolerated, with no grade ≥ 3 toxicities reported; treatment discontinuation occurred primarily due to disease progression rather than drug-related intolerance.

Survival Outcomes

Overall Survival (OS): At a median follow-up of 60 months, 10 of 20 patients (50%) were alive. The median OS for the overall cohort was 60 months (95% CI - 12 months to Not reached). The estimated 12-month and 60-month OS rates were 65% [47.1%-89.7%, 95% CI] and 42.6% [23.5%-77.0%, 95% CI], respectively, as demonstrated by Figure-2.

The median OS for Non-metastatic patients was not reached, while that for metastatic patients was 9.5 months, which was statistically significant on comparison by log rank ($p=0.02$) (Figure- 3). Patients with primary malignant GCT demonstrated numerically longer OS compared to those with secondary malignant SMGCTB (median OS not reached vs 28 months), though this difference was not statistically significant (log-rank $p = 0.32$) (Figure-4).

4. Discussion

This single-centre series of 20 patients with malignant giant cell tumour of bone (MGCTB) adds real-world data on clinicopathologic features, systemic therapy and outcomes in this rare entity. While prior reports have established the epidemiologic and pathologic spectrum of MGCTB, data describing modern systemic treatment patterns and outcomes remain sparse.

The clinical characteristics of this cohort were broadly consistent with established patterns. The median age was the fourth decade with a slight male predominance, consistent with earlier reports(7). Across different studies, the most common presenting symptoms include pain, swelling, functional limitation, or a pathological fracture, which are more common in SMGCTs where multiple recurrences precede transformation(8). The most common site of involvement was distal femur, which also mirrors the site distribution in benign GCTB, albeit with a slight enrichment in aggressive axial disease. Consistent with earlier reports, secondary malignant GCTB (SMGCTB) constituted the majority of cases (65%) and as in other series, the incidence of metastases was 40 percent, most commonly to lungs and more common with secondary MGCTB(7,9). The latency period to malignant transformation remains one of the defining clinical features of this entity. In our cohort, the median latent interval was 84 months (~ 7 years), closely approximating the 7.9-year mean reported by Liu et al(7) and 7.5 years by Verspoor et al(10). Longer intervals have been documented in other cohorts, viz, the 15-year median reported by Tsukamoto et al.(9), underscoring the protracted and unpredictable trajectory of malignant transformation.

The diagnostic complexity of malignant GCTB is further compounded by molecular heterogeneity. Recent molecular profiling studies have shown that malignant transformation is frequently accompanied by genomic instability, including complex copy-number alterations and TP53 pathway disruption, which may be associated with loss of H3F3A immunoreactivity in the malignant component(11). Published series of malignant GCTB report variable rates of H3F3A negativity: Yoshida et al. observed absence of the canonical G34 mutation in the sarcomatous component in 5/7 malignant GCTB cases, and Tsuda et al. found 4/8 malignant GCTB to be H3F3A-wildtype on genomic profiling. (12,13). In our cohort, similarly, a substantial proportion of secondary malignant GCTB cases lacked H3F3A

expression, supporting the concept of clonal evolution rather than diagnostic misclassification. These findings highlight the importance of integrating clinical history, morphology, and molecular features when evaluating suspected malignant transformation.

The biological heterogeneity of malignant GCTB is reflected in its variable but generally poor survival outcomes and given the aggressive natural history, the role of systemic therapy has been an area of ongoing debate. In a recent series published by Liu et al(7), improved pulmonary metastasis-free survival was observed among patients receiving perioperative chemotherapy (13 months vs 6 months; $P = 0.002$), but this did not translate into a statistically significant 5 year overall survival benefit (57.0% vs 33.3%, $P = 0.167$). In another study by Anract et al(14), chemotherapy did not improve 5-year survival, highlighting the absence of demonstrable long-term benefit. In our cohort, baseline metastatic disease was associated with markedly inferior overall survival, a finding consistent with prior reports identifying advanced stage and axial involvement as adverse prognostic factors(15). The relatively high proportion of metastatic disease at presentation in our cohort provides important context for the observed survival outcomes.

Prior studies are limited by heterogeneous treatment approaches and incomplete reporting of systemic therapy details including regimens, dosing, duration, or objective responses, precluding any meaningful assessment of efficacy. In contrast, our study provides regimen-specific real-world outcomes, demonstrating that anthracycline-based chemotherapy may offer context-dependent benefit, particularly in the neoadjuvant setting where radiologic response facilitated complete surgical resection. To our knowledge, no prior malignant GCTB series has explicitly reported the use or outcomes of non-anthracycline therapies including Gemcitabine-docetaxel, eribulin, or Ifosfamide-etoposide.

These limitations have prompted interest in alternative systemic approaches beyond conventional cytotoxic chemotherapy. Within this context, the activity observed with tyrosine kinase inhibitors in our cohort is noteworthy and it represents the largest reported experience with TKIs in malignant GCTB to date.

The only available evidence is a case report on pazopanib-induced regression and disease stabilisation of metastatic malignant giant cell tumour of soft tissue, maintained for ~11 months after treatment initiation, without severe toxicity, supporting potential activity in VEGFR-dependent sarcoma phenotypes(16). Preclinical data identify a c-Met-positive stromal subpopulation in GCTB and demonstrate that cabozantinib inhibits tumorigenic properties in vitro and in vivo, providing a biological rationale for targeting c-Met/VEGFR signalling(17), although clinical evidence in GCTB is lacking.

Several methodological considerations should be acknowledged. Given the rarity of malignant giant cell tumour of bone, this study represents a retrospective, single-centre experience with a limited sample size and expected variability in local and systemic treatment approaches, reflecting real-world practice. In addition, the study did not include a contemporaneous cohort managed without systemic therapy, which limits direct comparative assessment of treatment effect; however, this reflects prevailing clinical practice in advanced disease. The median follow-up of approximately 60 months was sufficient to characterise early disease behaviour and treatment response, though longer observation may be required to fully capture late events in the natural history of giant cell tumour of bone.

Despite these limitations, our study contributes valuable real-world evidence from an underrepresented population. Future efforts should focus on multicentre registries to overcome rarity, prospective evaluation of systemic regimens (including TKIs), and integration of molecular profiling to refine diagnosis, prognosis, and identification of novel therapeutic targets.

5. Conclusion

This study represents one of the largest contemporary real-world evaluations of systemic therapy in malignant giant cell tumor of bone. By providing regimen-level data on chemotherapy and targeted therapy, it demonstrates that systemic treatments confer modest, context-dependent benefit, with limited impact on long-term survival. Anthracycline-based chemotherapy showed limited efficacy in the adjuvant and palliative settings, but neoadjuvant use was associated with consistent radiologic responses that facilitated complete resection in selected patients. In advanced disease, tyrosine kinase inhibitors, particularly pazopanib and cabozantinib, exhibited modest yet clinically meaningful activity, representing the largest reported experience with these agents in malignant GCTB to date. These findings underscore the need for improved systemic strategies and collaborative efforts to advance care in this rare disease.

Abbreviations

CI – Confidence Interval

CR – Complete Response

GCT – Giant Cell Tumour

GCTB – Giant Cell Tumour of Bone

H3F3A - Histone 3, Family 3A

IE – Ifosfamide–Etoposide

IHC – Immunohistochemistry

IQR – Interquartile Range

MGCTB – Malignant Giant Cell Tumour of Bone

NOS – Not Otherwise Specified

ORR – Objective/Overall Response Rate

OS – Overall Survival

PD – Progressive Disease

PMGCTB – Primary Malignant Giant Cell Tumour of Bone

PR – Partial Response

RECIST – Response Evaluation Criteria in Solid Tumours

RT – Radiation therapy

R0 – Margin-negative resection

SA – Single Agent

SD – Stable Disease

SMGCTB – Secondary Malignant Giant Cell Tumour of Bone

TKI – Tyrosine Kinase Inhibitor

UPS – Undifferentiated Pleomorphic Sarcoma

VEGFR – Vascular Endothelial Growth Factor Receptor

WLE – Wide Local Excision

Declarations

Ethics approval and consent to participate: This study was approved by the Institutional Ethics Committee, All India Institute of Medical Sciences (AIIMS), New Delhi (Ref. No: AIIMSA4695/12.09.2025). The study was conducted in accordance with the ethical standards of the Institutional Research Committee and with the 1964 Declaration of Helsinki and its later amendments.

Given the retrospective nature of the study and use of anonymized data, the requirement for written informed consent was waived by the Institutional Ethics Committee.

Consent for publication:

Not applicable.

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Competing interests:

The authors declare that they have no competing interests.

Author Contribution

SR conceptualized and designed the study. ASH collected clinical data. ASH and KS performed the retrospective analysis. AB performed the histopathological evaluation and provided expert pathology review. ASi helped in data analysis. RP contributed radiotherapy-related clinical management. SASh provided support in PET-CT interpretation and imaging-based response evaluation. SAI and VC contributed to orthopedic management and surgical input. ASH and KS drafted the manuscript. SR critically revised the manuscript for important intellectual content and supervised the study. All authors contributed to interpretation of the data. All authors read and approved the final version of the manuscript.

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Sachin Sarcoma Society

DECLARATION OF INTEREST STATEMENT

☐ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Tables

Table 1. Baseline Clinicopathologic Characteristics

Characteristic	N = 20
Age (Median/IQR):	40.5 (IQR: 34 - 47) years
Sex:	
Male	13 (65%)
Female	7 (35%)
Type of malignant GCT:	
Primary malignant GCT (PMGCT)	7 (35%)
Secondary malignant GCT (SMGCT)	13 (65%)
Site of primary tumour:	
Distal femur	9 (45%)
Proximal femur	3 (15%)
Proximal humerus	1 (5%)
Proximal tibia	1 (5%)
Axial sites	6 (30%)
Metastatic sites at baseline presentation**	N= 8
Lung	6 (75%)
Nodal	5 (62.5%)
Skeletal	3 (37.5%)
Soft tissue	3 (37.5%)
Histology – malignant component:	
Malignant GCT NOS	8 (40%)
Osteosarcoma	6 (30%)
UPS	4 (20%)
Fibrosarcoma	1 (5%)
Epithelioid sarcoma	1 (5%)
Latency Period to malignant transformation (SMGCT)	84 months (IQR 48-120)

**Percentages exceed 100% as patients may have multiple metastatic sites; IQR- Interquartile Range

Table 2. Local treatment approaches for malignant GCTB

Local Treatment Type	N	Non-metastatic	Metastatic
Surgical Treatment-			
Wide local excision (WLE)*	12	10	2
Curettage/debridement	2	1	1
Amputation	1	1	0
Radiation therapy-			
Definitive RT	1	1	-
Salvage local procedures			
WLE/Amputation	3	2	1
Lung metastatectomy	2	0	2
Palliative RT	6	0	6
No local therapy	5	0	5

Note: * All resections were margin-negative (R0). Local treatment categories are not mutually exclusive; radiotherapy and salvage procedures may overlap with upfront surgical management.

TABLE 3. Systemic Therapy, and Response Rates

Type of systemic therapy	Treatment intent	Line of therapy	No. of patients (n)	CR	PR	SD	PD	ORR (%)
A. Anthracycline-based chemotherapy								
IAP -1 Ifosfamide-Doxo-1 Cisplatin-Doxo -1	Neoadjuvant	First line	3	0	2	0	1	66.0
SA doxo- 5 Ifosfamide-Doxo-1 Cisplatin-Doxo -1	Palliative	First line	7	0	2	1	4	28.5
Tyrosine kinase inhibitors (TKIs)								
Pazopanib	Palliative	First or later line	8	2	1	1	4	37.5
Cabozantinib	Palliative	Fourth line	2	0	1	0	1	50.0
Other chemotherapy regimens								
Gemcitabine–Docetaxel	Palliative	Later lines	3	0	0	0	3	0
Eribulin	Palliative	Later lines	1	0	0	0	1	0
Ifosfamide–Etoposide (IE)	Palliative	Later lines	2	0	0	0	2	0

Abbreviations: CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; ORR = objective response rate

Figures

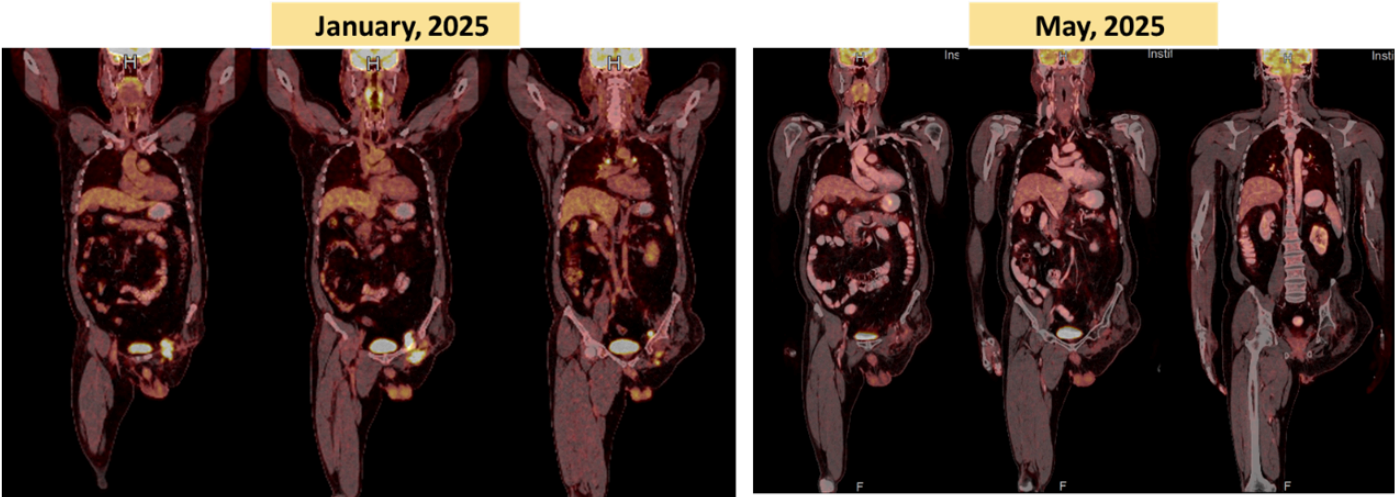


Figure 1

Objective response with Pazopanib in a nodal metastatic PMGCT, post amputation

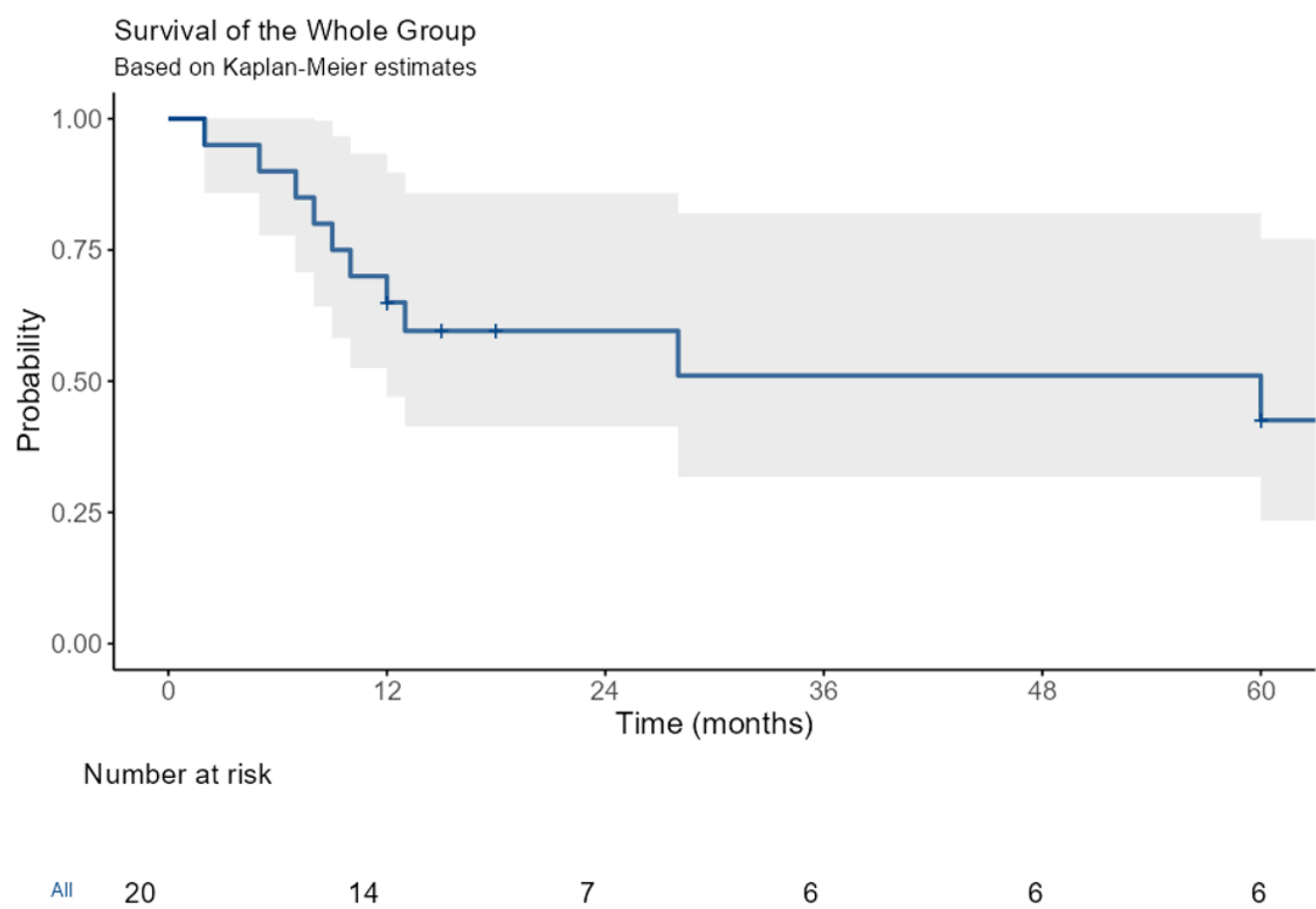


Figure 2

Kaplan–Meier Curve for Overall-Survival (OS).

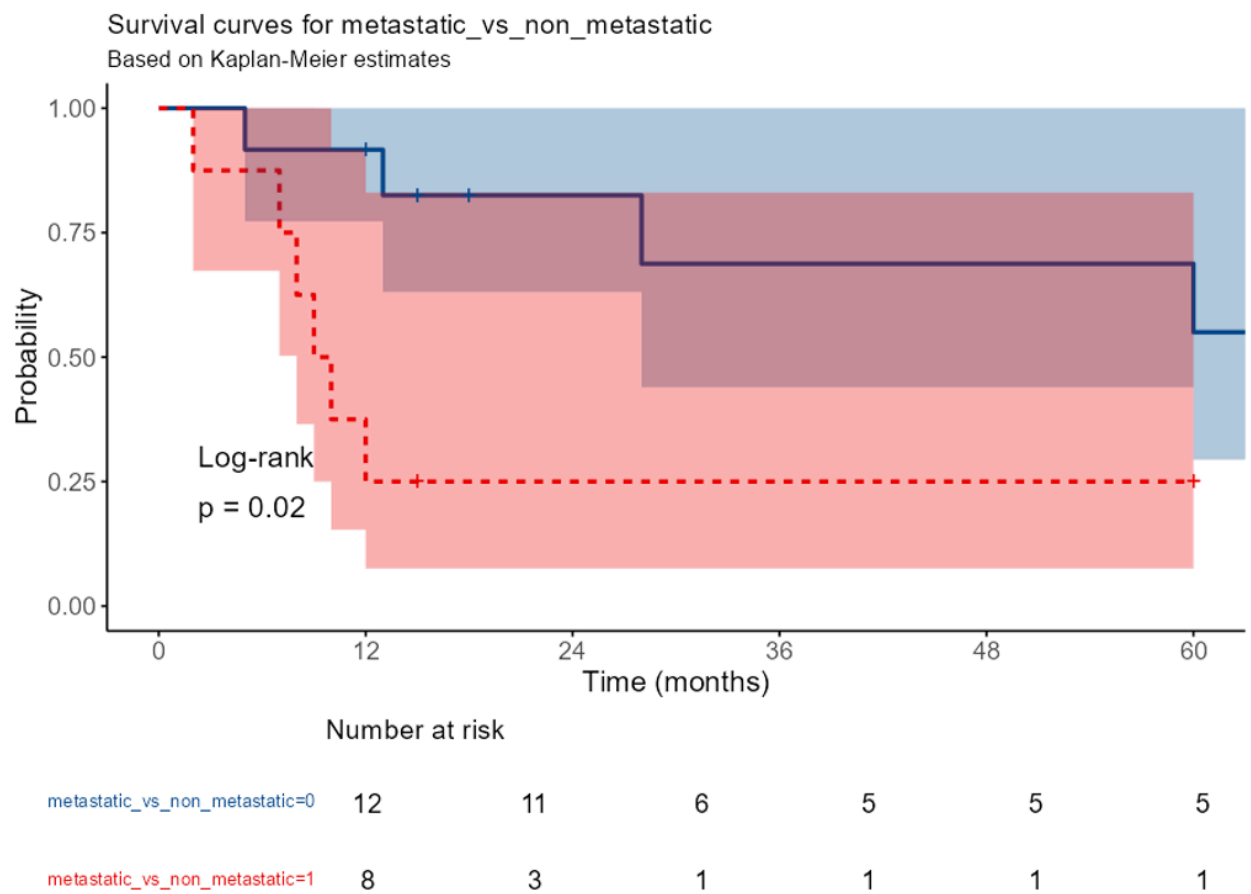


Figure 3

Overall survival by metastatic status at baseline

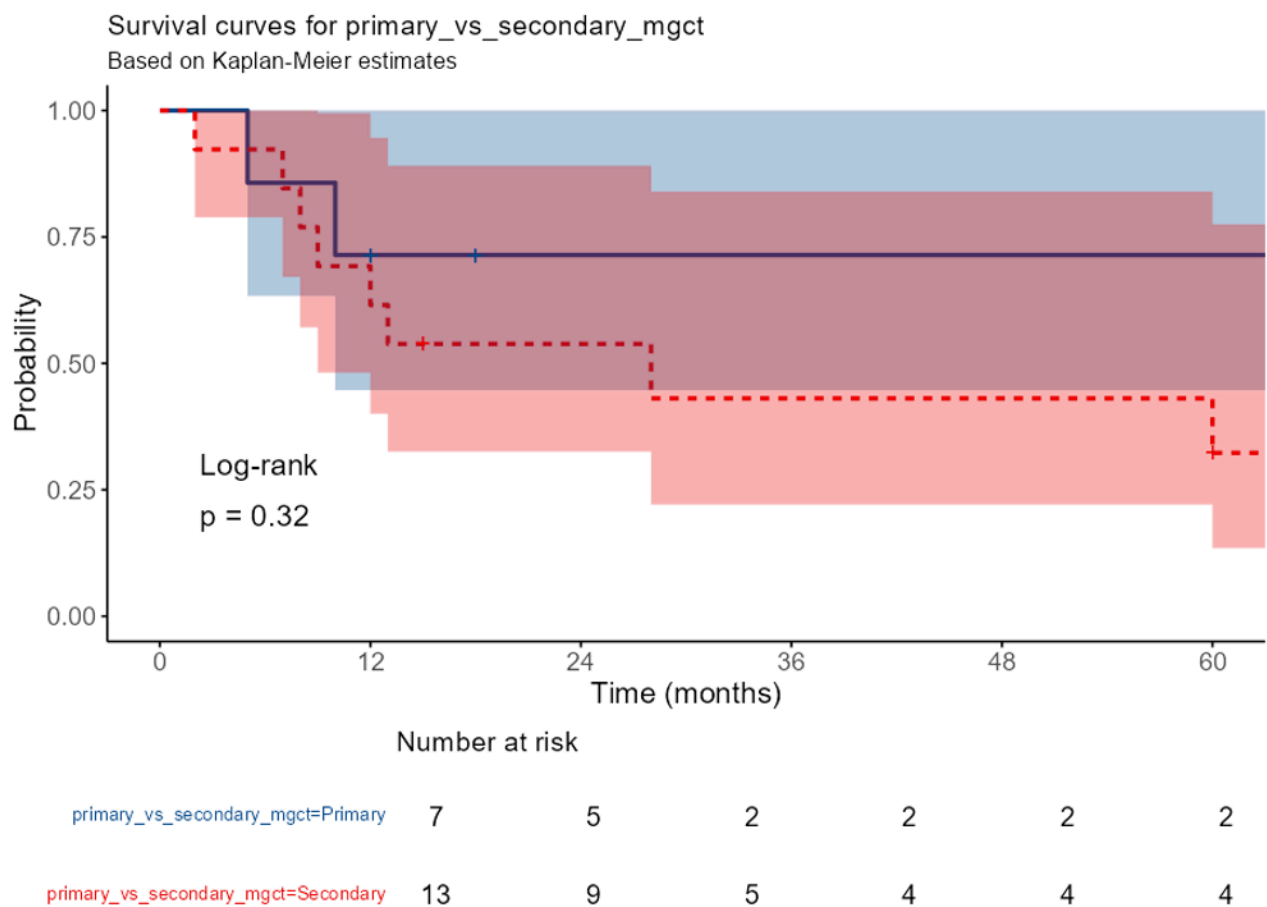


Figure 4

Overall Survival in PMGCT vs SMGCT