Research Square

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Biosimilar versus Original Denosumab in Giant Cell Tumour of Bone: Real World Outcomes from a Naturally Stratified Cohort

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Abstract

Background:
Denosumab is proven in the management of giant cell tumour of bone (GCTB), yet high cost of the original molecule was a barrier to wide acceptability in low- and middle-income countries (LMICs). A Biosimilar formulation available at half the cost offers a potential alternative; however comparative clinical data are scarce. This study presents real-world outcome of original denosumab (OD) versus biosimilar denosumab (BD) in a naturally stratified cohort.

Methods:
We conducted a retrospective cohort study of 77 patients with GCTB who received OD or BD in a tertiary cancer centre between 2020 and 2023. Molecule choice was influenced by affordability, resulting in a non-randomized naturally stratified cohort. Pre-operative dose was based on clinical need and external factors such as pandemic/financial related treatment disruptions. Primary outcomes were time-to-rim formation (RF) and time-to-intralesional-ossification (IO) on plain radiograph as a time to event. We used Kaplan–Meier survival-analysis and Cox proportional-hazards models adjusted for molecule type.

Results:
Among 77 patients, 64 had RF and 48 had IO. OD was associated with faster time to RF

(8 vs.11 weeks, p=0.03), higher proportion of RF (90% vs. 75%, p=0.04) and higher likelihood of achieving IO (70% vs. 54%, p=0.27) and time to IO (9.5 weeks to 11 weeks, p=0.02) even though the median tumour volume [OD 827.2cc (IQR: 484.08–1610.20) and BD 945 cc (IQR: 406.41–2230.02 cc)] was comparable in both arms. However, these differences may be confounded by treatment intent/duration. Stratified analysis revealed no significant difference in RF or IO in the short course groups. The observed superiority of OD was in the definitive group, where ossification and rim formation were more pronounced.

Conclusions:
While OD showed superior overall hazard ratios for RF and IO. It may be confounded by disease severity and treatment duration. In the short course setting, BD appears comparable in effectiveness to OD, there was no instance of BD to OD change, or change in time to treatment or intent based on molecule. This offers a cost-effective alternative in LMICs. These findings underscore the need for prospective validation and importance of individualized decisions in resource limited settings.

1. Introduction

GCTB is a rare, locally aggressive tumour that affects young adults (patients aged between 30 and 50 years) and involves epiphysis and metaphysis of long bones. It accounts for 4–10% of all primary bone tumours and often presents with extraosseous soft tissue, most commonly affecting distal femur, proximal tibia, and distal radius. Clinically, patients present with pain and joint dysfunction [1, 2]. Radiographically, there is progressive lucency and cortical expansion or destruction.

Denosumab is a fully humanised monoclonal antibody that binds and inhibits RANKL (Rank Ligand)[3], and is FDA (Food and Drug administration) approved for the treatment of patients with unresectable GCTB, or when surgery is likely to result in severe morbidity and in select cases as pre operative treatment to facilitate resection or curettage[4, 5]. Standard dosing is 120 mg, administered subcutaneously every 28 days with loading doses on days 8 and 15 (in the first month of therapy)[6, 7]. Off patent approval of a biosimilar was received in the year 2017.

The World Health Organization (WHO) defines a biosimilar as a biotherapeutic product that is similar in terms of quality, safety and efficacy to an already licensed reference product on the market (termed as originator or innovator). To ensure similar efficacy and safety, comparability studies for biosimilars should be carried out at quality, preclinical and clinical level[8].

Routine availability of biosimilar denosumab (BD)across world markets, the cost of treatment has come down. In the US self-pay market, innovator denosumab (120 mg/vial) is priced in the range of approximately USD 3,600 to USD 4,300. The UK NHS drug tariff lists the innovator drug at GBP 310 and recently launched biosimilars at GBP 273. In India, the market price varies relative to the MRP listed on the label, but most estimates benchmark the innovator at INR 26,000 and biosimilars at INR 13,000. Despite the certainty of price erosion in this competitive market, full HTA (health technology assessment) style price list with benchmark comparisons are not available. Crude standardisation for purchasing power parity (PPP) based on recent published World Bank estimates the price of denosumab biosimilar approximates to approximately 637 international dollars in India, 3,500–4,300 international dollars in the United States, and 414 international dollars in the United Kingdom suggesting, that in PPP terms, denosumab biosimilar remains expensive in India[9, 10]. The therapeutic efficacy equivalence promises to significantly drive down both institutional payer and out of pocket costs driving down health care costs.

Real world points of care studies comparing this efficacy for GCTB are lacking.

One phase III trial has compared efficacy, safety, and pharmacokinetics between biosimilar, QL1206 and denosumab in patients with bone metastasis from solid tumours, which showed similar results in terms of change in urinary N-telopeptide/creatinine ratio in both the drugs [11]. To our knowledge, there are no studies comparing the original molecule and its biosimilar for use in GCTB using real world data. This study presents real-world outcome of original (OD) versus biosimilar denosumab (BD), focusing on clinical and radiographic outcomes to determine efficacy.

2. Objectives

To compare the real-world radiological outcomes of original denosumab (OD) and biosimilar denosumab (BD) in patients with giant cell tumour of bone (GCTB).

3. Materials and methods

We conducted a retrospective analysis of a prospectively maintained database at a tertiary referral centre for bone and soft tissue tumours. We identified 247 patients of extremity GCT.

Of these, 77 patients received denosumab preoperatively to facilitate resection or curettage or for definitive management in inoperable cases. The following criteria were used for patient selection/exclusion

1.1. Inclusion criteria

- Histologically confirmed GCTB
- Age ≥ 16 years
- Received at least 2 doses of denosumab (original or biosimilar)
- Pre- and post-treatment radiographs available

1.2 Exclusion criteria

- Prior treatment with RANKL inhibitors
- Patients undergoing angioembolisation as an additional procedure
- Lost to follow-up before radiographic evaluation

1.3. Treatment protocol

Molecule choice in these 77 patients was influenced by patient affordability, resulting in a non-randomized but naturally stratified cohort. Patients received 2, 3, or 4 doses based on clinical need and external factors such as pandemic/financial related treatment disruptions. All patients had histologically proven giant cell tumour of bone; serum calcium, phosphorous and alkaline phosphatase levels were normal. All patients had pre Denosumab dental clearance to minimise risk of osteonecrosis of jaw. The standard dosing protocol was 0, 7, 14, 28 and then monthly dosing, accompanied by Vitamin D and calcium medications in doses of 60,000 IU weekly and 500 mg daily respectively. Modified doses at 0, 14 and evaluation for surgery at 6 weeks as a modified short course was employed in some patients as detailed below. All patients had baseline radiographs and MRI. Objective response assessment was done at 6 weeks and 10–12 weeks with radiographs.

1.4. Radiographic Assessment of Outcome measures

Radiographs were independently reviewed by two experienced orthopaedic oncologists blinded to treatment type and time to interpretation. Two outcomes were recorded:

1. **Rim Formation**: Defined as a continuous, sclerotic peripheral margin encasing the lesion.
2. **Intralesional Ossification (IO)**: Defined as ≥ 50% mineralization within the lesion on antero-posterior and lateral X-rays.

Both rim ossification and matrix mineralisation were treated as time to event to account for variation in doses / intervals and date of assessment.

We also stratified intent as pre-operative vs. definitive denosumab (inoperable setting) and type of drug (OD vs. BD) at baseline. Number of doses was captured as an integer and time to radiograph in weeks as a continuous variable. The patient selection and study cohort are shown in Fig. 1.

4. Measures to Minimize Bias

Patient self-selected original vs. biosimilar denosumab based on affordability as all payments were out of pocket. The indications &care protocol were uniform in both cohorts. We also compared both groups for potential outcome cofounders which include tumour size and volume. This cohort is not suitable for propensity score matching or similar techniques.

Flowchart showing the identification of 247 patients, application of the eligibility criteria and inclusion of 77 patients with GCTB who received original denosumab (OD) or biosimilar denosumab (BD). Radiographic outcomes were assessed by two experienced orthopaedic oncologists.

5. Statistical analysis

Categorical variables are presented as frequencies and percentages; continuous variables are presented as median with (SD). The rate of RF and IO were compared using chi-square or Fisher's test. Time-to-event analysis was performed using the Kaplan-Meier method to get the event-free survival probability. Volume distribution across both groups was compared using Mann-Whitney test. A multivariate Cox proportional hazard model was used to get the HR associated with molecule and dose for RF and IO. Log-rank test was used to compare the EFS across OD and BD.

6. Results

Out of 77 patients, 40 (51%) received OD and 37(49%) received BD. We evolved a pragmatic dosing pattern to suit clinical endpoints. The conventional dosing is at 0, 7, 14, 28 days. We modified the dose to 0, 14 days and evaluation at 6 weeks based on published articles cautioning regarding the difficulty of curetting lesions that were treated with denosumab[12–14].This also helped to halve the cost while still helping to achieve peripheral rimming or intralesional ossification adequate for safe surgery (reduced risk of tumour contamination, fracture and pain relief). As this pragmatic dosing pattern was evolving, we had 3 distinct dosing patterns in both groups, with 2, 3, 4 preoperative doses. As many of these patients were in the ‘pandemic era’, staggering surgery to optimise ‘cancer’ care, meant some patients received 1 or 2 additional preoperative doses. Since these groups were also non-random allocations, it allowed a dosing-group wise evaluation of outcomes in a time-to-event analysis.

The demographics of the study is mentioned in table 1. There were 41 males and 36 females, with median age being 29 in OD and 33 in BD group. We had 60 primary cases and 17 recurrent ones. The

median tumour volume of the study population was 850 cc with an IQR of 457.2 and 1715.4. The median tumour volume of OD arm was 827.2 (IQR: 484.08–1610.20) and in the BD arm was 945 (IQR: 406.41–2230.02 cc) showing no statistically significant difference between the two arms.

Table 1: Patient demographics

Variable	Level	BD (n=37)	OD (n=40)	Total (n=77)
Age	Mean (SD)	33.1 (11)	29.1 (10)	31 (10.6)
Sex	Female	17 (45.9)	19 (47.5)	36 (46.8)
	Male	20 (54.1)	21 (52.5)	41 (53.2)
Primary or Recurrent	P	29 (78.4)	31 (77.5)	60 (77.9)
	R	8 (21.6)	9 (22.5)	17 (22.1)
Tumour Volume (cc)	Median	945	827.2	-
	IQR	406.41-2230.02	484.08-1610.20	-

Abbreviations: BD Biosimilar Denosumab, OD Original Denosumab

6.1. Outcome measures:

The median time to first response evaluation radiograph in OD group was 7.8 weeks and that in BD group was 8.6 weeks. Out of total 77 patients, RF on radiographs was not accurately evaluable in 3 subjects (2 in OD group and 1 in BD group). RFwas noted amongst 74 patients. 36/40 (90%) patients in OD group and 28/37(75%) in BD group showed RF on radiographs (Table 2).

>50% intralesional ossification was seen in 28/40(70%) and 20/37(54%) patients amongst OD and BD group respectively. (Table 2)

Table 2: Overall events across brands

	Peripheral rim of bone			**Intralesional ossification >50%**		
molecule	Y	N	P-value	<50%	>50%	P-value
BD	28 (75.7%)	8 (21.6%)	0.044	17 (45.9%)	20 (54.1%)	0.227
OD	36 (90.0%)	2 (5.0%)		12 (30.0%)	28 (70.0%)	

Abbreviations: BD Biosimilar Denosumab, OD Original Denosumab

The dose wise distribution of events has been shown in Table 3.

Table 3: Number of events

Doses	Molecule	Total	Peripheral rim of bone N (%)	Intralesional ossification >50% N (%)
2	OD	8	7 (87.5%)	7 (87.5%)
2	BD	18	12 (66.67%)	9 (50%)
3	OD	10	8 (80%)	7 (70%)
3	BD	7	7 (100%)	4 (57.14%)
4	OD	22	21 (95.45%)	14 (63.64%)
4	BD	12	9 (75%)	7 (58.33%)

Abbreviations: BD Biosimilar Denosumab, OD Original Denosumab

Our results show that OD was associated with more consistent RF (Fig.2; 50% events see in 8 weeks in OD group vs 11 weeks in BD group p-0.029) and higher likelihood of achieving >50% IO (Fig.3; 9.5 weeks OD group vs. 11 weeks BD group, p-0.022).

6.2. Interpretation of outcomes

OD shows superior radiologic outcomes in both RF and IO. Table 4 and 5 show the hazard ratio (HR) for OD and BD; showing that OD nearly doubles the HR of achieving RF

(HR 1.94, 95% CI 1.15–3.24, p = 0.012) and more than double the HR of achieving intralesional ossification (HR 2.28, 95% CI 1.25–4.19, p = 0.007).

Table 4: Hazard ratio table for RF, rim formation

Variable	Units	Hazard Ratio (95% CI)	Pvalue
molecule	BD	Reference	
	OD	1.94 (1.15, 3.24)	0.012
Dose category	2	Reference	
	3	0.46 (0.23, 0.94)	0.033
	4	0.37 (0.2, 0.69)	0.002

Abbreviations: BD Biosimilar Denosumab, CI Confidence Interval,

OD Original Denosumab

Table 5: Hazard ratio table for Intralesional ossification IO

Variable	Units	Hazard Ratio (95% CI)	Pvalue
molecule	BD	Reference	
	OD	2.28 (1.25, 4.19)	0.007
Dose category	2	Reference	
	3	0.33 (0.15, 0.75)	0.008
	4	0.25 (0.12, 0.52)	0

Abbreviations: BD Biosimilar Denosumab, CI Confidence Interval, OD Original Denosumab

7. Discussion

Denosumab, a RANKL (receptor activator of nuclear factor κB Ligand) inhibitor, has transformed the management paradigm of giant cell tumour of bone (GCTB), particularly in unresectable lesions or when surgery would result in unacceptable morbidity. The landmark phase II studies by Thomas et al. [6] and Chawla et al. [7]established denosumab's efficacy in inducing tumour ossification, decreasing osteolytic activity, and enabling joint-sparing surgery in approximately 80–90% of patients

However, OD cost has limited access in LMICs, where health insurance coverage is limited and majority patients have catastrophic out of pocket expenditure[15].The introduction of biosimilars improved access, but real-world data on comparative clinical efficacy are limited[16,17].

Recent evidence regarding biosimilar denosumab in giant cell tumour of bone remains limited. A retrospective study bySingh et al.[18]found that encouraging clinical and radiological outcomes with biosimilar denosumab in a retrospective cohort of patients with aggressive GCTB, suggesting efficacy comparable to that reported in historical series of the originator product. However, the absence of direct head-to-head comparisons underscores the need for studies evaluating the relative effectiveness of biosimilar and innovator denosumab preparations. While studies designed for FDA approval typically use CT scores for documenting ossification, it is not used in routine practice due to its high-cost and low added value. Radiographs are routine, cost effective and provide optimal information guiding therapeutic response.

Radiological response assessment parameters published in existing literature, include appearance of an ossified rim around the soft-tissue component, improvement of the subchondral bone thickness, and presence of ossification within the lesion[19,20]. These correlated with clinical hardening of the lesion

and pain relief and thus considered as evidence of response to therapy[4,21]. We utilised rim formation (RF) and intralesional ossification (IO) as surrogate radiologic outcome measures. These reflect the clinical and radiographic feedback most orthopaedic oncologist's use for clinical decision making for therapeutic efficacy. This also correlates with reduction of pain and clinical benefit. We chose these endpoints as pragmatic, low cost, reproducible variables, commonly used across centres for assessing treatment response, de-escalating cost and treatment burden.

In our study, while OD demonstrated higher rates of rim formation and intralesional ossification across the cohort, BD also demonstrated rim formation and intralesional ossification adequate to serve the purpose it was intended for.

Martin-Broto et al.[22] emphasized the rapid ossification response to denosumab and its relevance in surgical planning; noting that ossification typically begins within 6–10 weeks of initiation. Similarly, Branstetter et al.[23] reported that the primary histologic effect of denosumab is the replacement of osteoclast-rich stroma with newly formed woven bone.

Our data support this timeline and radiologic pattern withbothODand BD achieving ossification in the reported timeframes.

The existing literature on biosimilar denosumab has demonstrated pharmacologic similarity and acceptable clinical outcomes, without increased adverse effects when used for metastatic bone disease or osteoporosis[11,24].The literature on OD versus BD for giant cell tumour of bone- in a neoadjuvant or definitive setting is lacking. Our study is one of the first studies to compare the two[25].

The use of blinded radiologic assessments, inclusion of a naturally stratified cohort reflective of real-world economic constraints, and alignment of findings with previous pharmacologic timelines lend credibility to our data. To our knowledge, this is the first study directly comparing BD and OD in GCTB, particularly in LMICs, and our findings provide valuable insights for resource-optimized clinical decision-making.A pragmatic approach using biosimilar molecules balancing cost concerns and efficacy expectationsin LMICs, may be beneficial to patients reducing dropout rates due to financial exhaustion.

Our study is limited by its retrospective nature and the lack of histological correlation with radiologic response. Prior studies, including those by van der Heijden et al.[26] , have shown that radiographic ossification does not always equate to eradication of tumour stromal cells, which are implicated in recurrence. Furthermore, the lack of long-term oncologic outcomes (e.g., recurrence-free survival) limits our ability to comment on the durability of response between OD and BD or make any comment with therapeutic predictive value of radiographic changes. Also, although we did not include a formal cost effectiveness analysis, our findings are likely to impact value driven care.

8. Conclusion

In summary, while OD may demonstrate superior radiologic response when administered in a definitive, long-course setting, BD appears non-inferior in neoadjuvant therapy, at a much lower cost.

In the neoadjuvant/short course setting, BD appears comparable in effectiveness to OD, offering a cost-effective alternative in LMICs. These findings underscore the need for further prospective validation and highlight the importance of individualized treatment decisions, particularly where access and affordability constrain therapeutic options. As biosimilar use continues to grow in oncology, prospective studies with histologic and functional endpoints will be essential to define their long-term role in GCTB management.

Abbreviations

GCTB: Giant Cell Tumour of Bone

LMIC: Low- And Middle-Income Countries

OD: Original Denosumab

BD: Biosimilar Denosumab

RF: Rim Formation

IO: Intralesional Ossification

RANKL: Rank Ligand / Receptor Activator of Nuclear Factor Kb Ligand

FDA: Food and Drug administration

WHO: World Health Organization

HTA: Health Technology Assessment

PPP: Purchasing Power Parity

SD: Standard Deviation

IQR:

HR: Hazard Ratio

Declarations

Ethics approval: This study was approved by Tata Memorial Centre, Institutional Ethics Committee, Mumbai (Reference number: OIEC/5224/2026/00001 or IEC Project No: 5224) on date 26.feb.2026.

This was a retrospective study conducted using anonymised patient data. Informed consent was waived by the ethics committee as no identifiable patient data was used. All procedures were performed in accordance with the Declaration of Helsinki and institutional ethical standards.

Consent to participate: Not Applicable

Consent for publication: Not Applicable

Availability of data and material: The data are not publicly available due to participant confidentiality and institutional ethical restrictions.

Conflicts of Interest/Competing Interests: The authors have no financial or personal conflicts of interest to declare in relation to the content of this article.

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Authors' contributions

PN conceptualized, supervised, administered, and validated the study and contributed to formal analysis, methodology, resources, and software. NT, PN, SC, DMK, AP, and KN contributed to data curation. SaC contributed to formal analysis. PN and DMK contributed to visualization. NT, PN, and DMK contributed to the original draft. PN, PH, MP, and AjP contributed to review and editing. All authors read and approved the final manuscript.

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References

1. Jagiello-Wieczorek E, Pieńkowski A, Rutkowski P. Denosumab for treating giant cell tumor of bone. Expert Opin Orphan Drugs. 2015;3:1219–29. https://doi.org/10.1517/21678707.2015.1086336.
2. Thomas DM, Skubitz KM. Giant cell tumour of bone. Curr Opin Oncol. 2009;21:338–44. https://doi.org/10.1097/CCO.0b013e32832c951d.
3. Bekker PJ, Holloway DL, Rasmussen AS, et al. A Single-Dose Placebo-Controlled Study of AMG 162, a Fully Human Monoclonal Antibody to RANKL, in Postmenopausal Women. J Bone Min Res. 2004;19:1059–66. https://doi.org/10.1359/JBMR.040305.
4. Puri A, Gulia A, Hegde P, et al. Neoadjuvant denosumab: its role and results in operable cases of giant cell tumour of bone. Bone Jt J. 2019;101–B:170–7. https://doi.org/10.1302/0301-620X.101B2.BJJ-2018-0907.R2.

5. Rutkowski P, Ferrari S, Grimer RJ, et al. Surgical Downstaging in an Open-Label Phase II Trial of Denosumab in Patients with Giant Cell Tumor of Bone. Ann Surg Oncol. 2015;22:2860–8. https://doi.org/10.1245/s10434-015-4634-9.
6. Thomas D, Henshaw R, Skubitz K, et al. Denosumab in patients with giant-cell tumour of bone: an open-label, phase 2 study. Lancet Oncol. 2010;11:275–80. https://doi.org/10.1016/S1470-2045(10)70010-3.
7. Chawla S, Henshaw R, Seeger L, et al. Safety and efficacy of denosumab for adults and skeletally mature adolescents with giant cell tumour of bone: interim analysis of an open-label, parallel-group, phase 2 study. Lancet Oncol. 2013;14:901–8. https://doi.org/10.1016/S1470-2045(13)70277-8.
8. Zimmermann K, Fido M, Roucka M. Insight into Biosimilars: Short Description, Analytical Assessment and Market. Med Res Arch 2020;8. https://doi.org/10.18103/mra.v8i3.2053
9. PPP conversion factor. GDP (LCU per international $) | Data n.d. https://data.worldbank.org/indicator/PA.NUS.PPP (accessed June 10, 2026).
10. International Comparison Program. (ICP) n.d. https://www.worldbank.org/en/programs/icp (accessed June 10, 2026).
11. Li H, Huang Y, Chen Z, et al. Efficacy and Safety of Denosumab Biosimilar QL1206 Versus Denosumab in Patients with Bone Metastases from Solid Tumors: A Randomized Phase III Trial. BioDrugs. 2023;37:259–69. https://doi.org/10.1007/s40259-023-00579-5.
12. Traub F, Singh J, Dickson BC, et al. Efficacy of denosumab in joint preservation for patients with giant cell tumour of the bone. Eur J Cancer. 2016;59:1–12. https://doi.org/10.1016/j.ejca.2016.01.006.
13. Errani C, Tsukamoto S, Leone G, et al. Denosumab May Increase the Risk of Local Recurrence in Patients with Giant-Cell Tumor of Bone Treated with Curettage. J Bone Jt Surg. 2018;100:496–504. https://doi.org/10.2106/JBJS.17.00057.
14. Gaston CL, Grimer RJ, Parry M, et al. Current status and unanswered questions on the use of Denosumab in giant cell tumor of bone. Clin Sarcoma Res. 2016;6:15. https://doi.org/10.1186/s13569-016-0056-0.
15. Hooley B, Afriyie DO, Fink G, et al. Health insurance coverage in low-income and middle-income countries: progress made to date and related changes in private and public health expenditure. BMJ Glob Health. 2022;7:e008722. https://doi.org/10.1136/bmjgh-2022-008722.
16. Tabernero J, Vyas M, Giuliani R, et al. Biosimilars: a position paper of the European Society for Medical Oncology, with particular reference to oncology prescribers. ESMO Open. 2016;1:e000142. https://doi.org/10.1136/esmoopen-2016-000142.
17. Indian Council of Medical Research. National Guidelines for Approval of Biosimilars. New Delhi: ICMR; 2021.
18. Singh RB, Jagannathan SK, Vineet K. Clinical Audit of Denosumab Biosimilar for Aggressive GCT of Bone: A Tertiary Care Center Retrospective Analysis. South Asian J Cancer. 2025;14:723–7. https://doi.org/10.1055/s-0045-1808094.

19. Alothman M, Althobaity W, Asiri Y, et al. Giant cell tumor of bone following denosumab treatment: assessment of tumor response using various imaging modalities. Insights Imaging. 2020;11:41. https://doi.org/10.1186/s13244-020-00845-y.
20. Engellau J, Seeger L, Grimer R, et al. Assessment of denosumab treatment effects and imaging response in patients with giant cell tumor of bone. World J Surg Oncol. 2018;16:191. https://doi.org/10.1186/s12957-018-1478-3.
21. Van Langevelde K, McCarthy CL. Radiological findings of denosumab treatment for giant cell tumours of bone. Skeletal Radiol. 2020;49:1345–58. https://doi.org/10.1007/s00256-020-03449-1.
22. Martín-Broto. Cleeland, Delgado. Patient-reported outcomes in GCTB patients treated with denosumab. Clin Cancer Res. 2019;25:6958–65.
23. Branstetter DG, Nelson SD, Manivel JC, et al. Denosumab Induces Tumor Reduction and Bone Formation in Patients with Giant-Cell Tumor of Bone. Clin Cancer Res. 2012;18:4415–24. https://doi.org/10.1158/1078-0432.CCR-12-0578.
24. Zhao M, Hu X, Zhuang P, et al. A multicenter, randomized, double-blind trial comparing LY01011, a biosimilar, with denosumab (Xgeva®) in patients with bone metastasis from solid tumors. J Bone Oncol. 2025;51:100661. https://doi.org/10.1016/j.jbo.2025.100661.
25. Boby JM, Rajappa S, Mathew A. Financial toxicity in cancer care in India: a systematic review. Lancet Oncol. 2021;22:e541–9. https://doi.org/10.1016/S1470-2045(21)00468-X.
26. van der Heijden L, Dijkstra P, van de Sande M. The effect of denosumab on recurrence in giant-cell tumor of bone. J Bone Joint Surg Am. 2014;96:e35.

Figures

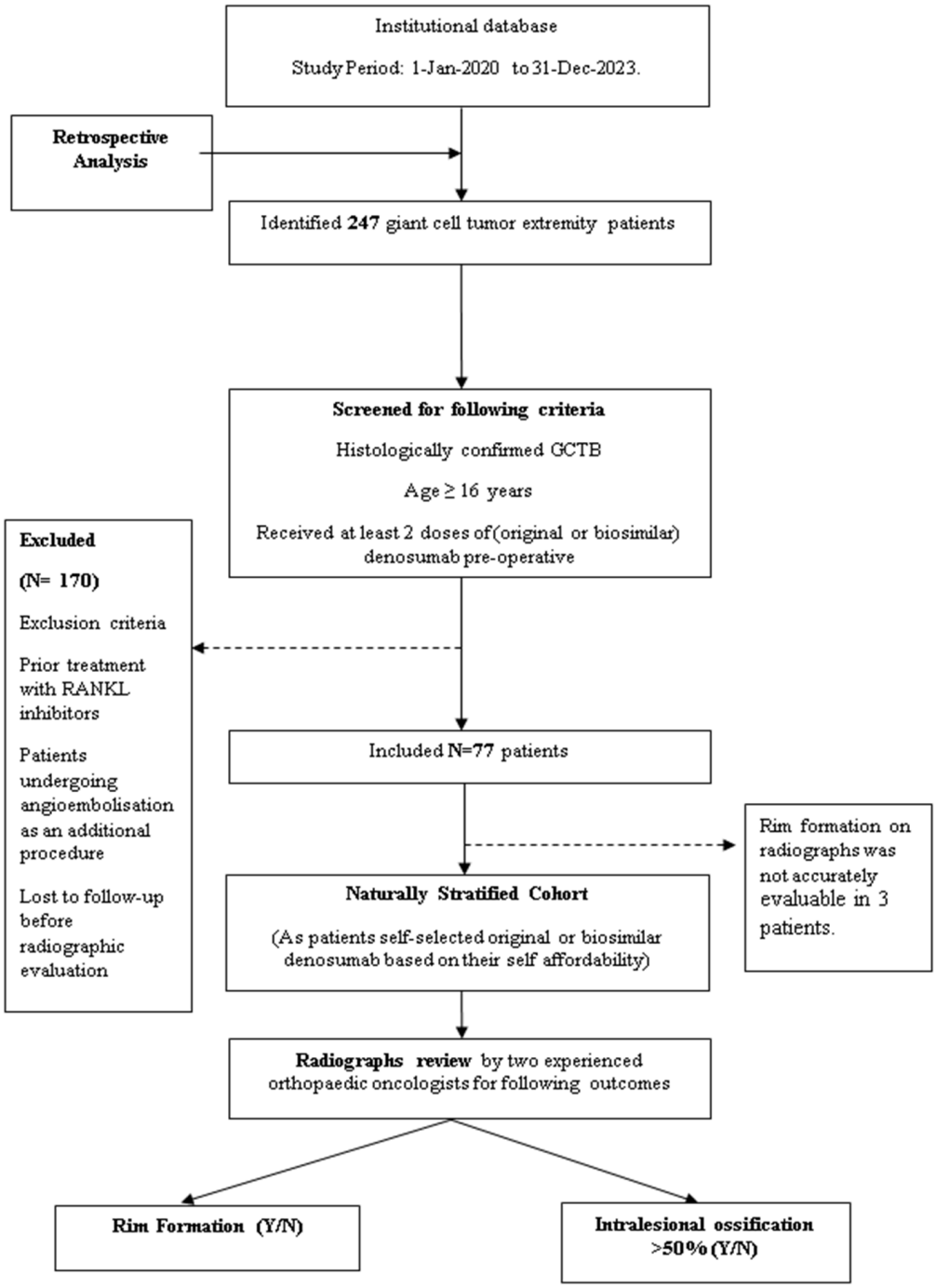

Figure 1

Study flowchart

Flowchart showing the identification of 247 patients, application of the eligibility criteria and inclusion of 77 patients with GCTB who received original denosumab (OD) or biosimilar denosumab (BD). Radiographic outcomes were assessed by two experienced orthopaedic oncologists.

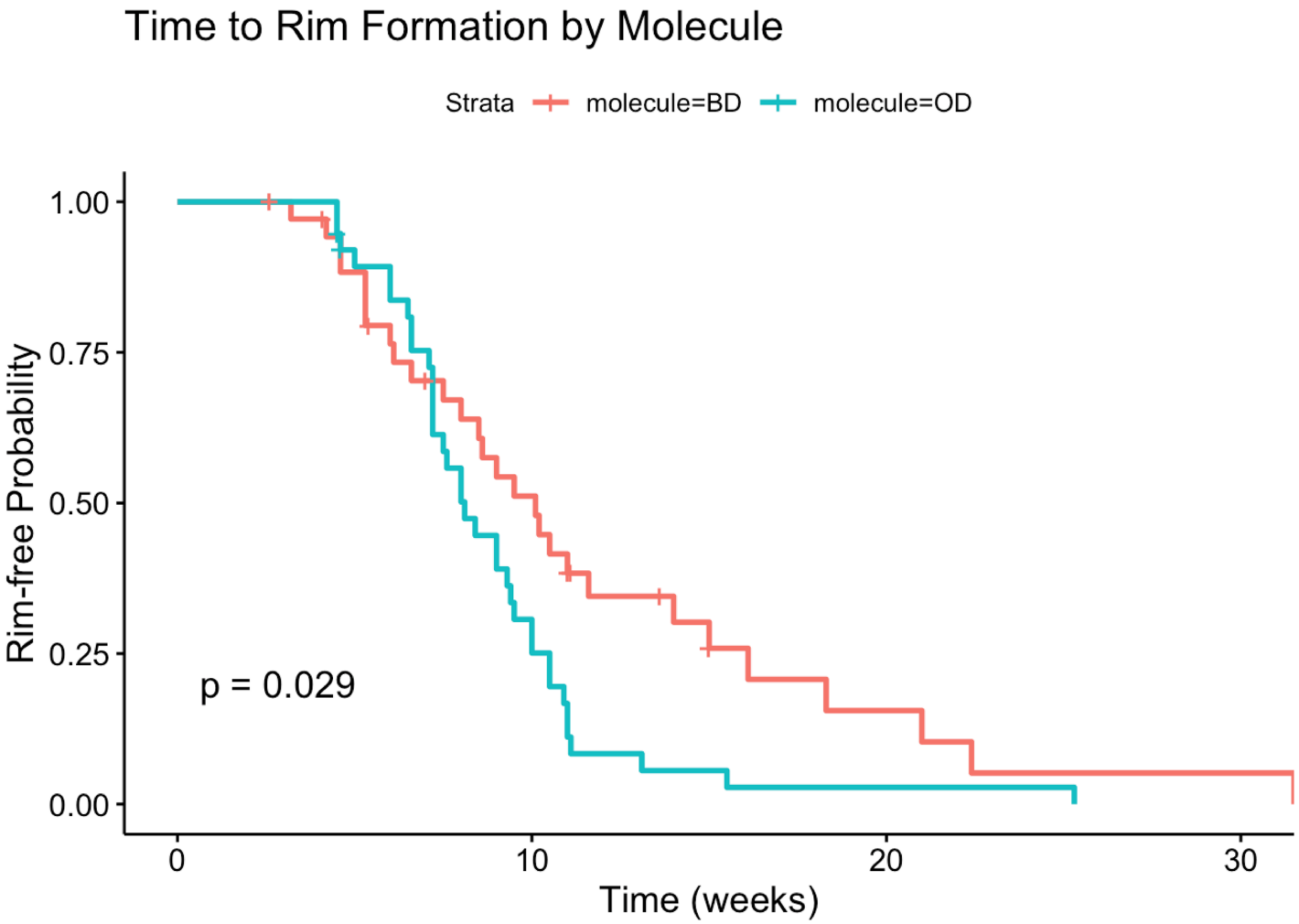

Figure 2

Time to Rim formation stratified by Denosumab Molecule

Kaplan–Meier curves showing time to rim formation in patients receiving original denosumab (OD) or biosimilar denosumab (BD).

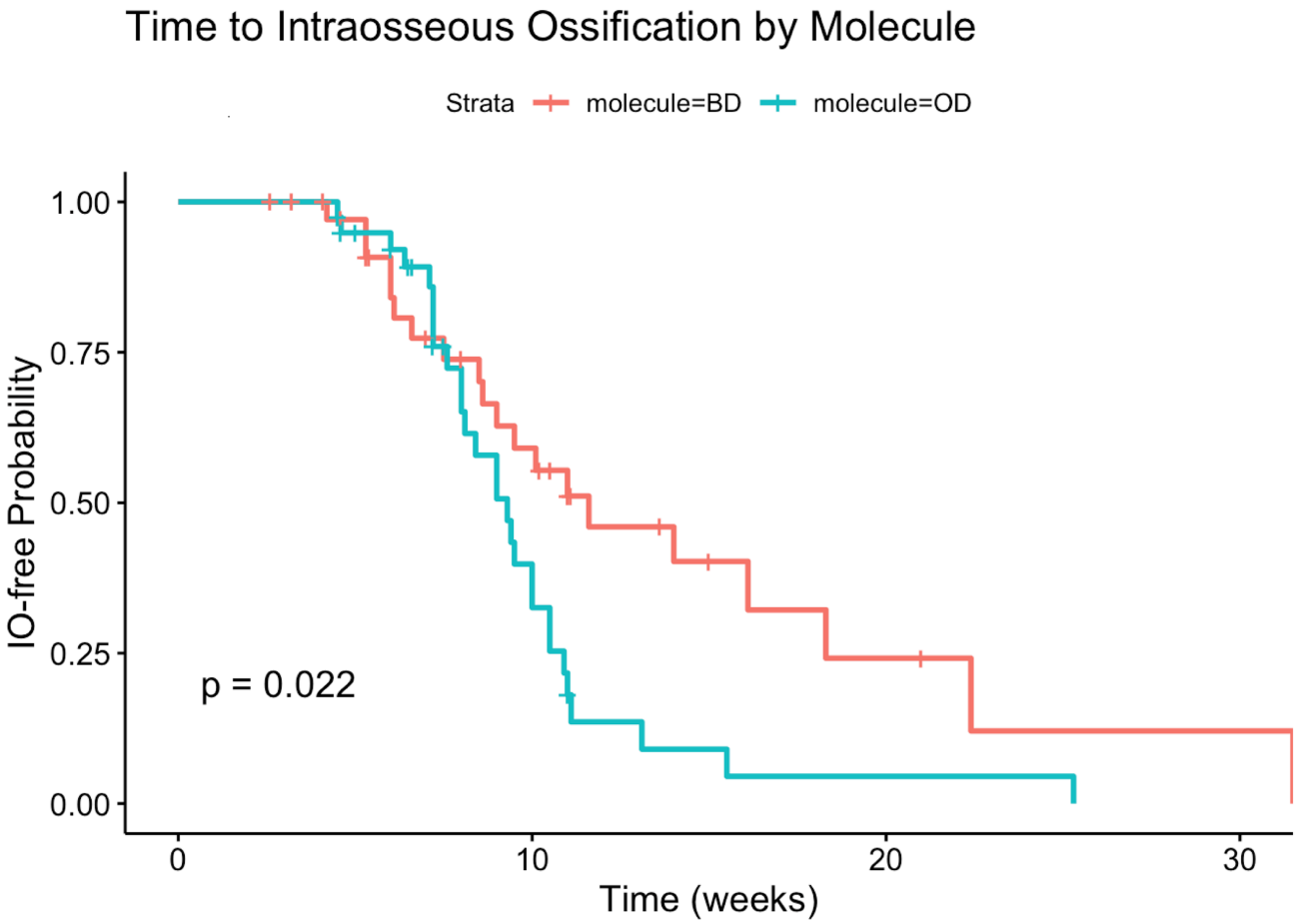

Figure 3

Time to Intralesional Ossification stratified by Denosumab Molecule

Kaplan–Meier curves showing time to intralesional ossification in patients receiving original denosumab (OD) or biosimilar denosumab (BD).