RWD168

DIAGNOSTIC PATHWAYS, HEALTHCARE RESOURCE USE, AND PREDIAGNOSTIC TREATMENT BURDEN IN TENOSYNOVIAL GIANT CELL TUMOUR: A REAL-WORLD COHORT STUDY IN JAPAN

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CONCLUSIONS

- **This observational claims-based study highlights the substantial diagnostic and healthcare burden experienced by patients with tenosynovial giant cell tumour (TGCT) in Japan.**
  - **Patients underwent a range of diagnostic procedures, most commonly biopsy, radiography/X-ray, histopathological confirmation, computed tomography (CT), and magnetic resonance imaging (MRI).**
  - **Patients were diagnosed across several different medical specialties, the most common being orthopaedics, further indicating variation in patients' diagnostic pathways.**
  - **The frequent use of non–TGCT-targeted systemic treatments (non-steroidal anti-inflammatory drugs [NSAIDs], corticosteroids) before definitive diagnosis is consistent with the clinical challenge of recognising TGCT, whose symptoms overlap with common musculoskeletal conditions.**
- **The varied use of diagnostic procedures and non-specific treatments prior to diagnosis suggests opportunities to further improve recognition and evaluation pathways for TGCT. Paired with the adoption of targeted treatment strategies for TGCT, this may help to optimise healthcare resource use and improve patient outcomes.**
- **The findings identify an unmet need for earlier recognition of TGCT in patients presenting with persistent musculoskeletal symptoms.**

PLAIN LANGUAGE SUMMARY

- **TGCT is a rare tumour that can cause pain, swelling, stiffness, and difficulty moving the affected joint.**
- **TGCT can be hard to diagnose because its symptoms can resemble more common conditions like arthritis and sports injuries.**
- **We used Japanese health insurance claims data to examine the tests, medical specialties, and treatments recorded before or at TGCT diagnosis.**
- **Many patients underwent several types of diagnostic testing, including biopsy and imaging, and diagnoses involved a range of medical specialties.**
- **Before diagnosis, most patients received treatments aimed at symptom management rather than TGCT-targeted therapy.**
- **Recognising TGCT earlier and having better access to TGCT experts may help patients to obtain an accurate diagnosis and appropriate treatment more quickly.**

INTRODUCTION

- TGCT is a rare, locally aggressive, soft-tissue tumour driven by colony-stimulating factor-1 (CSF-1) overexpression that affects an otherwise healthy adult population.[1–3]
- There are two major subtypes of TGCT[3–5]:
  - Localised TGCT (L-TGCT): a slow-growing and well-defined tumour typically found in smaller joints.
  - Diffuse TGCT (D-TGCT): a more invasive and extensive tumour that affects larger joints.
- TGCT can have a high symptom burden that includes pain, swelling, stiffness, reduced range of motion, and impaired physical function, which may substantially impact daily activities and quality of life.[3,4]
- Surgery is the primary treatment for symptomatic, resectable TGCT. However, treatment may be challenging when TGCT is diffuse, recurrent, or unresectable, or when surgery could cause considerable morbidity.[3,4]
- TGCT symptoms can resemble those of common musculoskeletal conditions, including rheumatoid arthritis, bursitis, osteoarthritis, and sports-related injuries, leading to misdiagnoses. Before TGCT is accurately identified, patients may face diagnostic delays, consult different medical specialists, and only receive symptomatic treatments that do not address the underlying disease.[2,3]
- Real-world evidence describing these diagnostic pathways, treatment patterns, and the associated healthcare burden in Japan is limited.

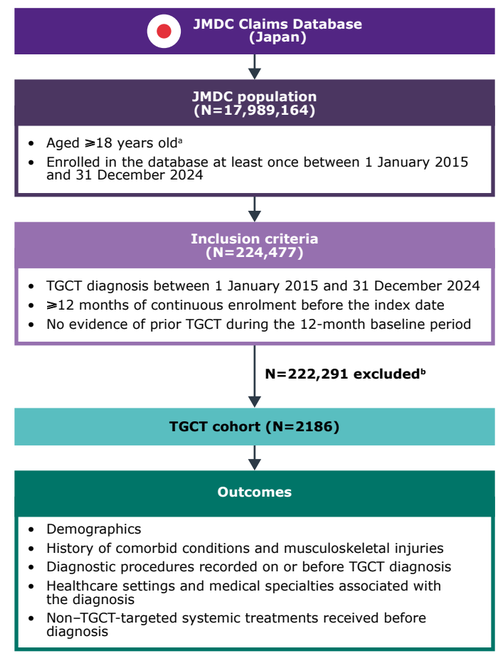
OBJECTIVE

- To characterise diagnostic pathways, healthcare resource utilisation, and systemic treatment patterns before and at diagnosis among adults with TGCT in Japan using real-world administrative claims data.

METHODS

- This non-interventional, non-comparative cohort study utilised claims data from the JMDC Claims Database.
  - The JMDC Claims Database is a large, comprehensive source of longitudinal claims data comprising approximately 19 million participants as of December 2024. The database primarily includes employed adults aged 18 to 74 years and their dependents. Individuals aged ⩾75 years are covered by Japan's separate Latter-Stage Elderly Healthcare System and are therefore not captured in the JMDC Claims Database.
  - Anonymised claims datasets from the JMDC Claims Database covering the period from 1 January 2014 to 31 December 2024 were extracted.
- Eligible patients were aged ⩾18 years at the index date (defined as the date of the initial TGCT diagnosis), were diagnosed with TGCT between 1 January 2015 and 31 December 2024, and had no TGCT-related claims during the 12 months before the index date (incident cases) (**Figure 1**).
- TGCT diagnosis required ⩾1 inpatient or outpatient claim indicating TGCT. TGCT was identified and categorised as L-TGCT or D-TGCT based on pre-specified International Classification of Diseases, 10th revision (ICD-10) diagnosis codes (D48.1 plus D21.X for L-TGCT; M12.2 for D-TGCT and associated combinations). Patients could also be identified by the use of CSF-1 receptor (CSF-1R) inhibitors (i.e., pexidartinib or vimseltinib used off-label).
- Study outcomes for patients with TGCT included demographics, clinical characteristics, and proxies for healthcare resource utilisation, including diagnostic modalities, healthcare settings and specialties at diagnosis, and systemic treatments used before diagnosis.
- All analyses for patients with TGCT, including D-TGCT and L-TGCT subtypes, were descriptive, and no formal hypothesis testing was performed.

Figure 1. Study design and patient identification



[a]The JMDC Claims Database does not include individuals aged 75 years and older as they are covered under Japan's separate Latter-Stage Elderly Healthcare System; [b]Exclusion criteria included diagnosis of a malignant soft tissue tumour on the date of TGCT diagnosis (n=451) and patients with chronic myeloid leukaemia or gastrointestinal stromal tumour receiving systemic therapy such as imatinib (n=9308). Patients with certain ICD-10 codes were excluded from the TGCT identification cohort at baseline (n=222,165). The exclusion criteria were not mutually exclusive; a patient could meet more than one exclusion criterion.

RESULTS

STUDY POPULATION AND BASELINE CHARACTERISTICS

- This analysis included 2186 newly diagnosed adult patients with TGCT, of whom 279 (12.8%) had D-TGCT and 1907 (87.2%) had L-TGCT (**Table 1**).
  - The median age at diagnosis was 48 years, and approximately half (51.6%) of patients were female.
  - Common musculoskeletal comorbidities included arthritis (30.4%), bursitis (20.5%), and osteoarthritis (19.0%). Spinal or limb injuries were also common (21.2%).

Table 1. Baseline patient characteristics

	Overall TGCT (N=2186)	D-TGCT (n=279)	L-TGCT (n=1907)
Age at diagnosis, median (Q1, Q3), years	48.0 (38.0, 56.0)	45.0 (32.0, 55.0)	49.0 (39.0, 56.0)
Female, n (%)	1128 (51.6)	137 (49.1)	991 (52.0)
History of chronic conditions[a] (⩾5% of overall patients with TGCT), n (%)			
Arthritis	665 (30.4)	270 (96.8)	395 (20.7)
Cardiovascular disease	463 (21.2)	51 (18.3)	412 (21.6)
Bursitis	449 (20.5)	56 (20.1)	393 (20.6)
Osteoarthritis	415 (19.0)	154 (55.2)	261 (13.7)
Any arthropathy (excluding arthritis)	333 (15.2)	156 (55.9)	177 (9.3)
Diabetes	230 (10.5)	31 (11.1)	199 (10.4)
Meniscal injuries	125 (5.7)	93 (33.3)	32 (1.7)
Depression	118 (5.4)	12 (4.3)	106 (5.6)
Chronic hepatic impairment	114 (5.2)	17 (6.1)	97 (5.1)
History of musculoskeletal injuries[a] (⩾5% of overall patients with TGCT), n (%)			
Spinal or limb injuries	464 (21.2)	154 (55.2)	310 (16.3)

[a]Not mutually exclusive, thus patients may have had multiple conditions.
Q, quartile.

DIAGNOSTIC PATHWAYS

- Patients frequently underwent multiple diagnostic modalities rather than a single confirmatory assessment (**Table 2**).
  - The most frequently used histological diagnostic procedures were biopsy (77.5%) and histopathology, excluding biopsy (70.8%).
  - The most frequently used imaging diagnostic procedures were radiography/X-ray (76.6%), CT (64.7%), and MRI (58.0%).

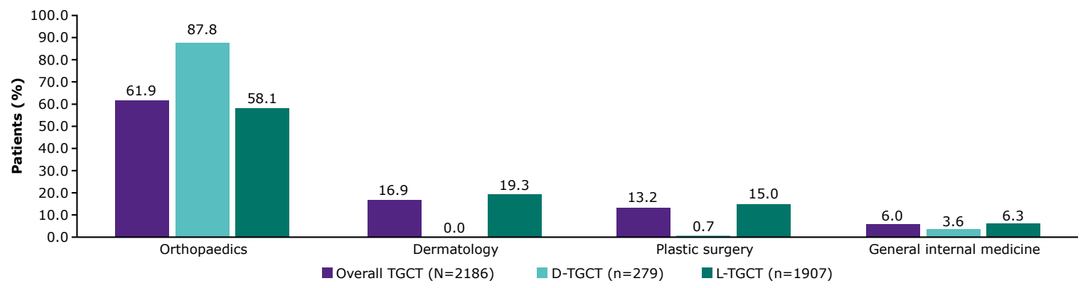
Table 2. Diagnostic modalities utilised prior to or at the time of TGCT diagnosis

	Overall TGCT (N=2186)	D-TGCT (n=279)	L-TGCT (n=1907)
Diagnostic modalities,[a] n (%)			
Biopsy	1695 (77.5)	270 (96.8)	1425 (74.7)
Direct radiography (plain X-ray)	1674 (76.6)	272 (97.5)	1402 (73.5)
Histopathological confirmation, excluding biopsy	1548 (70.8)	223 (79.9)	1325 (69.5)
Computed tomography	1414 (64.7)	253 (90.7)	1161 (60.9)
Magnetic resonance imaging	1267 (58.0)	244 (87.5)	1023 (53.6)
No diagnostic procedure	129 (5.9)	1 (0.4)	128 (6.7)
Arthroscopy (direct visualisation)	2 (0.1)	1 (0.4)	1 (0.1)
Other (not specified above)	1128 (51.6)	201 (72.0)	927 (48.6)

[a]Patients could have more than one modality recorded at the time of TGCT diagnosis.

- TGCT diagnosis involved multiple specialties, suggesting diverse routes to diagnosis within routine clinical practice (**Figure 2**).
  - Orthopaedics was the most frequently recorded specialty at TGCT diagnosis, accounting for the care of 61.9% of patients.
  - Additional specialties recorded at TGCT diagnosis included dermatology (16.9%), plastic surgery (13.2%), and general internal medicine (6.0%).
  - The involvement of several specialties may reflect differences in clinical presentation, tumour location, suspected diagnosis, and referral pathways.

Figure 2. Healthcare settings/medical specialties at TGCT diagnosis in ⩾5% of overall patients[a]

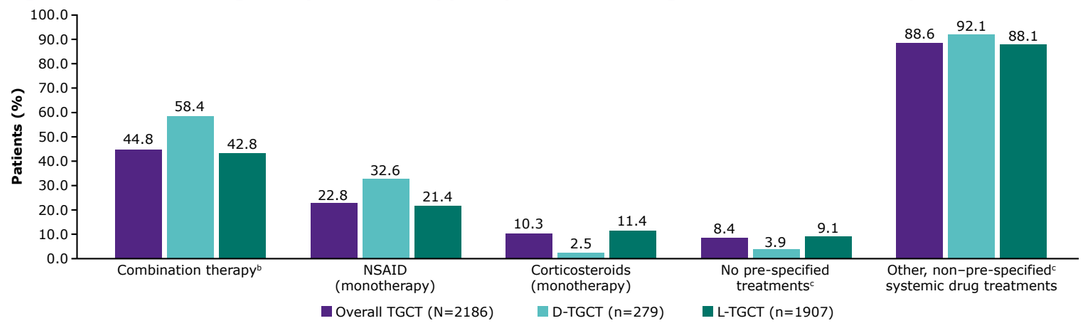


[a]Patients could have more than one medical specialty recorded at the time of TGCT diagnosis.

NON–TGCT-TARGETED SYSTEMIC TREATMENTS BEFORE TGCT DIAGNOSIS

- Overall, 91.6% of patients received at least one non–TGCT-targeted systemic treatment before diagnosis (**Figure 3**).
  - Notably, no patients received CSF-1R inhibitors prior to diagnosis.
- The most frequently recorded non–TGCT-targeted systemic treatments used before TGCT diagnosis were combination therapy (44.8%), most commonly NSAID/corticosteroids (23.1%), and cytochrome P450, family 3, (CYP3A) inhibitors/NSAID/corticosteroids (7.0%).
- Other common treatment patterns included NSAID monotherapy (22.8%) and corticosteroid monotherapy (10.3%).
- The high proportion of patients receiving systemic, non–TGCT-specific medications indicates substantial use for symptom management and repeated healthcare encounters before diagnosis.

Figure 3. Non–TGCT-targeted systemic therapy use prior to TGCT diagnosis in ⩾5% of overall patients[a]



[a]Non–TGCT-targeted systemic treatments used before diagnosis were not mutually exclusive, thus patients may have had multiple treatment modalities; [b]Combination therapy included NSAID/corticosteroids, CYP3A inhibitors/NSAID/corticosteroids, CYP3A inhibitors/NSAID, CYP3A inhibitors/corticosteroids, immunotherapy/NSAID/corticosteroids, PPARI/NSAID/corticosteroids, immunotherapy/CYP3A inhibitors/NSAID/corticosteroids, PPARI/NSAID, PPARI/corticosteroids, or other combinations; [c]Pre-specified systemic therapies included immunotherapy, CYP3A inhibitors, CSF-1R inhibitors (including tyrosine kinase inhibitors), monoclonal antibodies or anti-TNFs, PPARI, NSAID, vascular endothelial growth factor inhibitors, corticosteroids, chemotherapy, and combination therapy.
PPARI, peroxisome proliferator-activated receptor gamma inhibitor; TNF, tumour necrosis factor.

STUDY LIMITATIONS

- The JMDC Claims Database predominantly includes employed individuals aged 18–74 years and their dependents, limiting generalisability to the broader Japanese population, including adults aged ⩾75 years.
- Claims-based identification of TGCT, subtype, comorbidities, procedures, and treatments may be subject to coding errors and misclassification.
- The pathway to TGCT diagnosis involved multiple diagnostic modalities that were not mutually exclusive, and the terminology for 'no diagnostic procedure' was not defined.
- Information on symptom onset, disease severity, treatment intent, and actual medication use was not available; therefore, diagnostic delay and the reasons for treatment before TGCT diagnosis could not be assessed directly.

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AUTHOR DISCLOSURES

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