Plain Language Summary

Expert Perspectives on TGCT and the Outcomes of the Phase 3 MANEUVER Study of Pimicotinib Presented at ASCO and ESMO 2025: A Podcast Discussion

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Abstract Plain Language Summary

Tenosynovial giant cell tumor (TGCT) is a rare, non-life threatening but locally aggressive tumor that arises from the joint. Patients with TGCT usually experience pain, stiffness, and loss of range of motion in the affected joint, making daily activities difficult. TGCT has two distinct subtypes, localized and diffuse. Surgery is often the main treatment. However, diffuse TGCT has a high recurrence rate, highlighting the need for alternative treatments to surgery. A growing treatment approach involves medications that target the underlying cause of TGCT. One such medication is pimicotinib, an oral pill, which was evaluated in 94 patients with symptomatic TGCT where surgery was unlikely to provide benefit. For 24 weeks, 63 patients were randomly assigned to pimicotinib and 31 to placebo (a pill with no active medicine). Thereafter, all patients, including those earlier on placebo, received pimicotinib. After the initial 24-week treatment (at week 25), 54% of patients who received pimicotinib experienced tumor shrinkage (≥30% reduction in size of the tumor), compared with 3.2% of patients who received placebo. After another 24 weeks, tumor shrinkage in patients who received pimicotinib had increased to 76.2%. Patients who received pimicotinib showed improvement in pain, stiffness, and physical function regardless of tumor shrinkage. Treatment with pimicotinib was generally well-tolerated, with most side effects being mild-to-moderate; 29% of patients had moderate-to-severe side effects. Also, there were no cases of liver toxicity, or hair or skin color changes. This podcast article shares these findings in more detail and the study's clinical importance.

Full Plain Language Summary

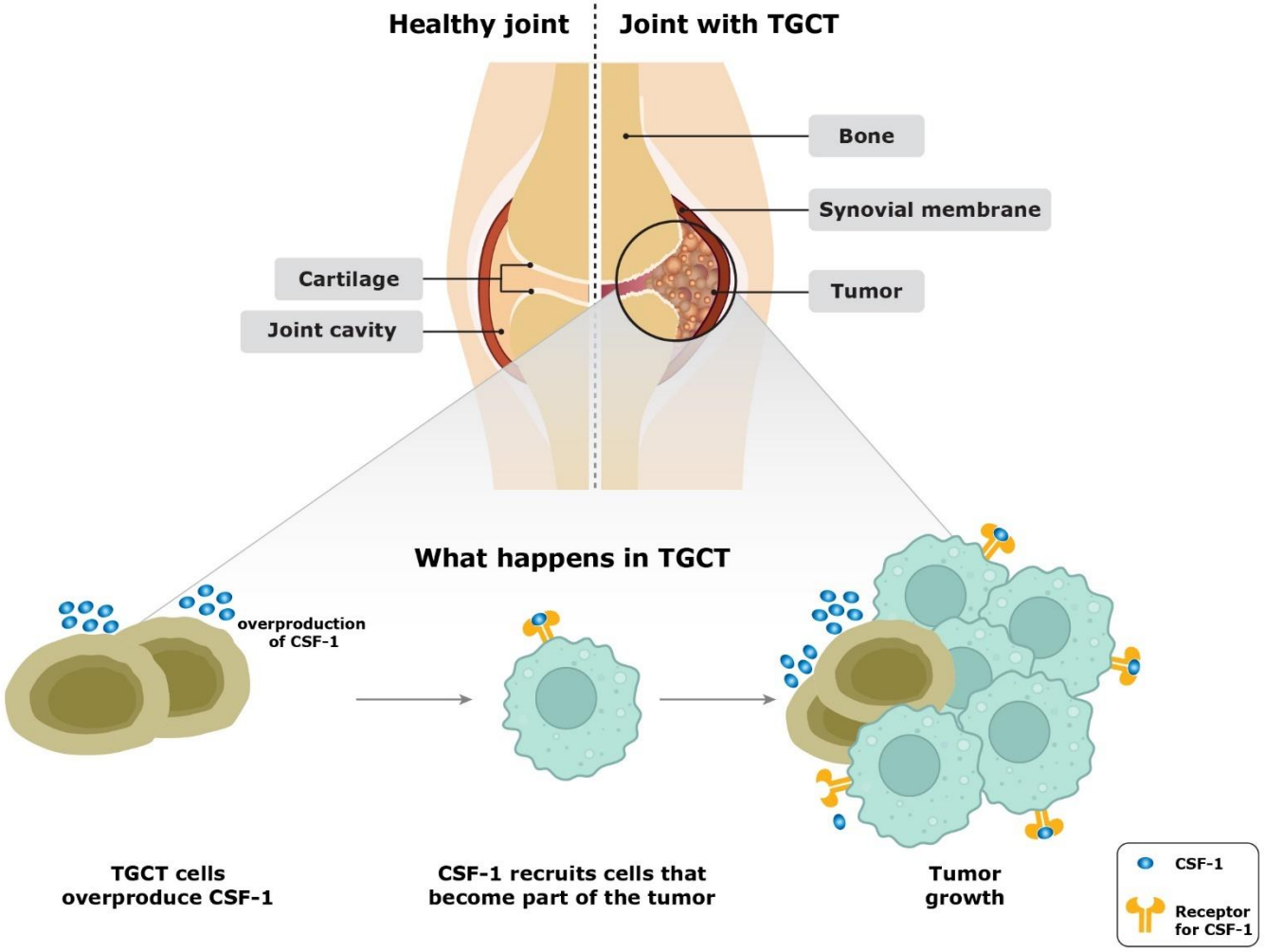
What is This Podcast Article About?

In this podcast article, the authors present an overview of tenosynovial giant cell tumor (TGCT), what symptoms lead to diagnosis, how it is diagnosed, current treatment options, and the patient journey through referral and treatment. In addition, they share their views on recently presented pimicotinib data from the MANEUVER trial.

What is TGCT?

TGCT is a rare, non-life threatening but locally aggressive tumor that arises in a single joint. Patients with TGCT usually experience pain, stiffness, and loss of range of motion in the affected joint, making it difficult to carry out their daily activities and impacting their quality of life, mental, emotional, and financial well-being. TGCT can happen at any age, but most often affects adults aged 25-50 years. Maintaining both mental and physical quality of life is a key factor when choosing appropriate treatment. [1-8]

TGCT occurs when the body produces too much of a protein called colony-stimulating factor-1 (CSF-1). Generally, cells in the human body use CSF-1 for tissue repair and healing, and bone maintenance. However, when the protein is overproduced by a minority of TGCT cells, it acts as a signal to recruit other cells. These recruited cells, even though harmless by themselves, contribute to tumor growth. Medications for TGCT directly block CSF-1 from acting as a signal to recruit cells that contribute to the tumor growth. [1,2,4-7]



The synovial membrane is a thin, protective tissue layer that lines the inside of joints. Often when we think of the inside of a joint, we think of everything inside this membrane.

Common symptoms of TGCT are [1-3,7,8]


Stiffness


Joint pain


Joint instability


Swelling


Limited movement

These symptoms can have substantial physical, psychological, financial, and social impact on patients.

What are the Types of TGCT?

TGCT has two main types: localized (also known as nodular) and diffuse.

Localized TGCT [2-4,6,7,9-11]	**Diffuse TGCT** [2-4,6,7,9-11]
• More common • Most often affects smaller joints (e.g., fingers, wrists, feet) but can impact ankles, knees; rarely affects the hips or elbows • Well-defined mass(es) with clear borders • Lower risk of recurrence	• Less common • Mainly forms around large joints such as the knees, ankles, and hips • Not well-defined, infiltrative into healthy tissue, no clear borders • Higher risk of recurrence

How is TGCT Diagnosed?

Symptoms experienced by patients with TGCT are similar to symptoms observed in other prevalent diseases such as rheumatoid arthritis or in individuals with sports injuries. This, together with the rarity of the disease, and possible unfamiliarity among healthcare professionals (HCPs) usually results in delayed diagnosis and misdiagnoses. More than half of the patients with TGCT have been reported to wait longer than 1 year before receiving an accurate diagnosis. Patients navigate a complex healthcare system, often consulting multiple HCPs before receiving the correct diagnosis.

Better awareness of TGCT among HCPs, quick referral to specialist centers, and involvement of a care team that includes different specialists are necessary for a prompt and accurate diagnosis. [6,12]

TGCT diagnosis involves:

Physical examination, where doctors do a careful check-up to look for any lumps, swelling around the affected joint, or if there are any issues with movement of the affected joint. [13]

Imaging tests

Magnetic resonance imaging (MRI) is considered the best imaging test for diagnosing and monitoring TGCT as it provides detailed images of the joint and helps the doctors measure the size of the tumor and its effect on the joint. [4,6,14]

Some patients may initially be asked to get an X-ray. In some instances, an X-ray may show changes in the bone which may make doctors consider an MRI for the patient. However, X-rays do not detect TGCT unless the tumor is very large and is pushing structures in the joint. Overall, many experts have recommended MRI as the main imaging tool for diagnosing TGCT. In order to characterize the TGCT subtype, MRI is used to identify localized and diffuse TGCT, and to monitor patients for changes in the disease or recurrence. [4,6,7,11,14,15,23]

Biopsy, which is when a doctor takes several small samples of the tissue of interest from the affected joint, is an important step to confirm diagnosis and must be done before starting treatment with any medication. [4]

What are the Different Options for Managing TGCT?

Effective treatment of TGCT focuses on improving clinical outcomes, such as minimizing pain, stiffness, swelling, improving movement of the affected joint and reducing the tumor size. [16-20]

Current management strategies include active surveillance, surgery, or medications that prevent the tumor from growing and/or manage the symptoms of TGCT.

Active surveillance, which means actively monitoring a patient's TGCT with imaging scans and symptom assessment, is commonly used as a management approach when the patient has no symptoms, or when symptoms are not affecting their daily activities. As part of active surveillance, the doctor may ask the patient to visit at regular intervals for checkups and imaging scans and may prescribe medicines to manage any symptoms the patient may be experiencing. [4,21-23]

In some instances, depending on the type of TGCT a patient has and severity of symptoms the patient is experiencing, the HCP may decide either to remove the tumor through surgery or to prescribe a medication that targets the underlying disease biology. [4,6,21]

Surgery is usually the preferred treatment for symptomatic localized TGCT. As the tumor is well defined and often confined to one area, complete removal is frequently possible, and the risk of recurrence is generally low, though it can still occur. [4,6,7,21]

For people with diffuse TGCT, surgery is often considered, but complete removal of all tumor tissue is frequently not possible as the tumor may have spread to nearby tissues and there may be a risk of significant functional side effects. [4,6,7,21]

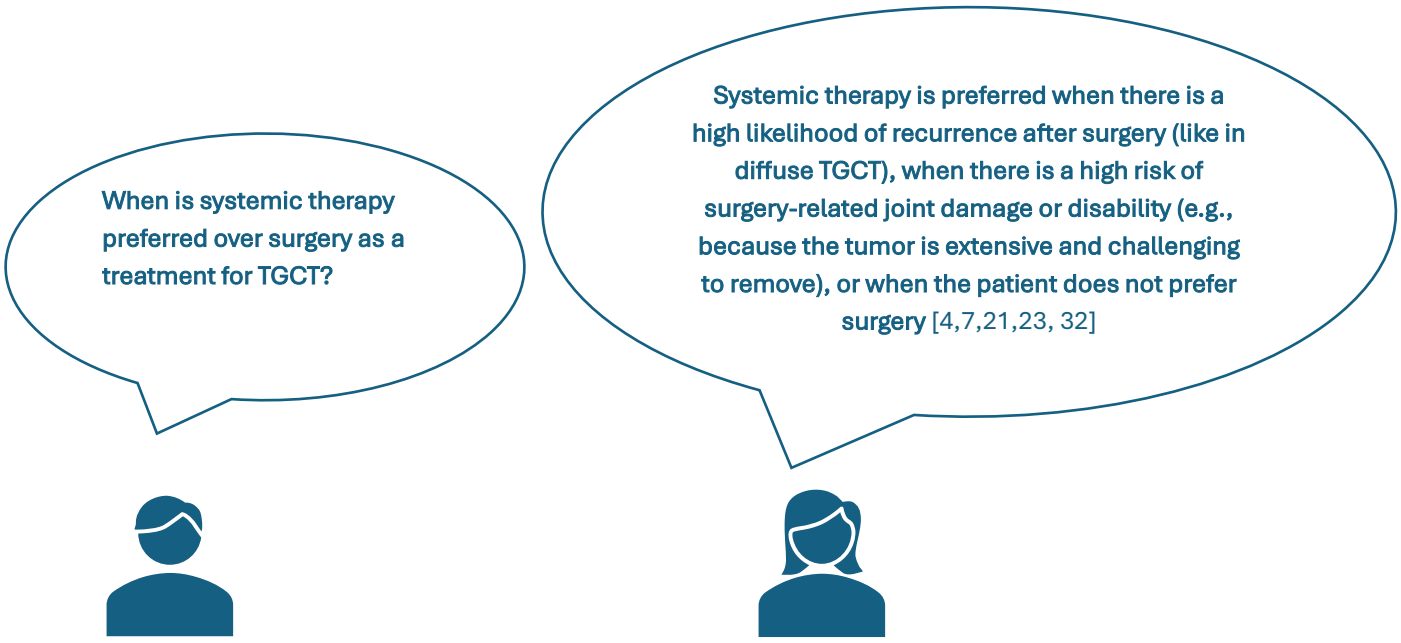
If surgery is unlikely to provide enough benefit, could cause substantial complications, or if the patient prefers another option, systemic therapy (medication that treats the disease throughout the body) is generally used instead. [4,21,23, 31]

What are Some Treatment Options for TGCT that Target the Mechanism of the Disease?

Pexidartinib, vimseltinib and pimicotinib are three oral TGCT medications that block CSF-1. Pexidartinib and vimseltinib are both approved by the US Food and Drugs Administration (FDA). Pexidartinib is also approved in Taiwan and South Korea, and vimseltinib is approved by the European Medicine Agency (EMA). Pimicotinib was approved by China's National Medical Products Administration (NMPA) in December 2025. [6,7,9,16,21,22,24-31]

Monitoring During Systemic Therapy

Systemic therapies are medications that absorb into the blood stream and circulate to find the drug target. During treatment with systemic therapy, the HCPs study the effect of the medications on the tumor using imaging scans (e.g. MRI), and by testing movement of the affected joints, and other physical functions and assess patients' pain and overall health. They also closely monitor side effects of the treatment.



The TGCT Care Journey

How Important is Awareness and Early Diagnosis in a Patient's Journey?

It is crucial that HCPs have a greater awareness and expertise of TGCT. An early diagnosis can improve a patient's quality of life in the long run. This is especially true for patients with diffuse TGCT, who benefit from referral to specialized centers which have experience in treating sarcoma and TGCT.

Many patients first experience joint pain or swelling and see a primary care doctor. They are often referred to sports medicine/orthopedic surgeons before they receive an accurate diagnosis. Specialists such as orthopedic oncologists, medical oncologists, pathologists, and radiologists usually help in confirming a patient's diagnosis. [4,6,12,19,23]

What is the Role of a Multidisciplinary Team in TGCT?

A well-coordinated multidisciplinary team (MDT) consists of various healthcare specialists and often includes orthopedic oncologists, medical oncologists, radiologists, pathologists, pain specialist, and other specialists who work together for an early and accurate diagnosis of TGCT. [4,6,12,19,23]

The multidisciplinary team works together to [4,6,12,19,23]

- ✓ **Diagnose TGCT**
- ✓ **Decide on the best treatment plan**
- ✓ **Coordinate treatment between specialists**
- ✓ **Manage side effects**

Better awareness of treatment options, easier access to specialized centers, and more effective and safer systemic therapies are some unmet needs of patients with TGCT

What is the MANEUVER Study?

MANEUVER - a global Phase 3 study in 94 patients with TGCT [33,34]

Patients enrolled in the MANUEVER study were at least 18 years of age, with symptomatic TGCT and for whom surgery was not expected to be beneficial. [33,34]

Of the 94 patients, 63 patients were randomly assigned to pimicotinib and 31 to placebo (a pill with no active medicine) for 24 weeks. This was a double-blind study, meaning that neither patients nor their doctors knew which treatment they received, so researchers could understand the safety and efficacy of pimicotinib in an unbiased manner. Thereafter, all patients, even those on placebo, could receive pimicotinib. This is called an open-label period. [33-35]

After the initial 24 weeks (at week 25), the MANEUVER trial met its main goal [33,34]

- **By week 25, more patients taking pimicotinib experienced a shrinkage of their TGCT tumors as compared to those taking placebo**
- While 54% of patients treated with pimicotinib experienced at least 30% shrinkage of their tumor, only 3.2% of patients who received placebo experienced a shrinkage in tumors
- Tumor shrinkage with pimicotinib began as early as week 13 of treatment
- Overall, by week 25, even patients whose scans did not show any tumor shrinkage, experienced an improvement in their pain, stiffness, range of motion, and daily physical functions.

Tumor shrinkage with pimicotinib was maintained over time [34]

- **After another 24 weeks in the open-label period (52 weeks total treatment with pimicotinib for some patients),** 76.2% of patients who continued pimicotinib had tumor shrinkage. No patients who remained on treatment experienced a worsening of their disease
- 64.5% of patients who switched from placebo to pimicotinib at week 25 also experienced tumor shrinkage after switching
- Improvements observed with pimicotinib lasted beyond 1 year, helping patients keep or further improve their movement, pain, stiffness, and overall physical functioning

What did the Study Show About the Safety of Pimicotinib?

The MANEUVER study found that pimicotinib was generally well-tolerated by patients.

Over the long term, only 6.3% of the patients completely stopped treatment due to side effects and 25.4% of patients required a reduction in pimicotinib dosage. A little over half (54%) of the patients had dose interruptions, where they temporarily stopped medication due to side effects. Despite occasional treatment interruptions, patients receiving pimicotinib still received nearly the full planned dose overall. In addition, there were no cases of serious liver injury or changes in skin or hair color.

Some common side effects that patients experienced were temporary increases in some liver enzymes, a muscle enzyme called creatine phosphokinase, itching, facial swelling, rash, swelling around the eyes, fatigue, nausea and headache. In most patients, these side effects were mild to moderate, and resolved with brief dose interruptions, where doctors temporarily stopped the medication. Notably, the temporary increases in muscle or liver enzymes were not associated with any symptoms. [33,35,36]

What are the Key Takeaways from this Podcast Article?

TGCT is a rare, non-life threatening but locally aggressive tumor that grows from the joint. It occurs in adults between the ages of 25 and 50, and can be managed by active surveillance, surgery or with medications that target the overproduction of CSF-1, the underlying abnormality in TGCT.

The Phase 3 MANEUVER study showed that pimicotinib significantly shrinks TGCT and improves pain, stiffness, joint range of motion, and physical function in patients with TGCT. The benefits were long-lasting, lasting more than 1 year in many patients, and pimicotinib was generally well-tolerated with mostly mild-to-moderate side effects.

The study findings suggest that pimicotinib may be an effective and durable oral treatment option for patients with symptomatic TGCT that is unlikely to benefit from surgery.

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