Expert perspectives on TGCT and the outcomes of the Phase 3 MANEUVER study of pimicotinib presented at ASCO and ESMO 2025

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1. TGCT disease overview, clinical presentation, and diagnosis

TGCT is a rare, locally aggressive neoplasm, affecting a joint, tendon sheath and/or bursae, and driven by CSF-1 overexpression[1–7]

TGCT disease subtypes

Localized: Presents as well-defined and encapsulated tumor, most commonly affecting smaller joins, e.g., digits and wrist[2–4]

Diffuse: Presents as infiltrative areas of disease with poorly defined boundaries, predominantly affecting large joints, e.g., knee, ankle, and hip[2–4]

Subtype and prevalence[8,9]

Localized:	80–90% of cases
Diffuse:	10–20% of cases

Recurrence rates post surgery[9,10,11]

Localized:	≤34%
Diffuse:	≤72%

A comprehensive diagnostic approach, is required due to TGCT's non-specific symptom profile, to avoid detrimental outcomes associated with misdiagnosis[4,6,7,12,13]

2. TGCT treatment landscape

The following treatment options are typically used

Active surveillance:
Patients with either localized or diffuse TGCT who have no symptoms or have **symptoms that are mild and well managed**[4,14,15]

Surgery:
Symptomatic patients with resectable TGCT, regardless of subtype

Systemic treatment:
In symptomatic patients who are unlikely to clinically benefit from surgery or where patients express preference for non-operative alternatives

CSF-1/CSF-1R targeting therapies

Pexidartinib	Available in US via REMS program (2019), South Korea (2021), and Taiwan (2022)
Vimseltinib	Approved by US FDA (2025) and EMA (2025)
Pimicotinib	Approved by the China NMPA in (2025)

Symptomatic improvements including reductions in pain, stiffness, and swelling, and improvements in overall quality of life are key drivers of treatment efficacy

3. Patient journey and role of multidisciplinary teams in managing patients with TGCT

Stage in typical patient journey	1 Symptoms: Joint pain/swelling[14]	2 Diagnosis	3 Referral to specialist centers[4,14,24]	4 Treatment[4,9,14,25]
HCP specialist involved	Primary care physician[14]	• Sports medicine physicians • Orthopedic oncologists • Orthopedic surgeons • Pathologists* • Radiologists*	Experienced sarcoma MDTs[4,14,24] including members[4] of the sarcoma MDT • Orthopedic surgeons/ oncologists • Medical oncologists • Pathologists • Radiologists	• Orthopedic surgeon (surgery) • Orthopedic oncologists[4,9,14] • Medical oncologists (systemic treatment)[4,14,25]

*May also be involved

A greater awareness of TGCT among healthcare professionals with prompt referral to a specialist center and involvement of multidisciplinary expertise where possible is needed for the timely and accurate diagnosis of patients with TGCT

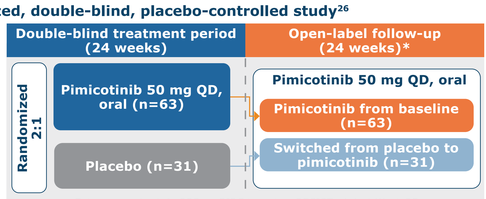
4. The MANEUVER study: Overview and key results presented at ASCO and ESMO 2025

A global Phase 3, randomized, double-blind, placebo-controlled study[26]

Key eligibility criteria[26]
- Aged ≥18 years
- Histologically-confirmed unresectable TGCT
- Measurable disease as defined by RECIST v1.1 with at least 1 lesion of ≥2 cm
- Symptomatic disease because of active TGCT

N=94

Study sites:
- China (23 sites),
- North America (10 sites),
- Europe (7 sites)



Primary endpoint: ORR by BIRC based on RECIST v1.1 at Week 25
Key secondary endpoints: ORR by BIRC based on TVS at Week 25; mean change from baseline in range of motion, worst pain NRS, worst stiffness NRS, PROMIS-PF T-score

*In a further follow-up open-label extension, all patients were eligible to continue to receive pimicotinib 50 mg QD

ASCO 2025: Efficacy outcomes – double-blind period (24 weeks)[17, 27]

Primary endpoint met
- ORR by BIRC at Week 25: 54.0% vs 3.2% (p<0.0001)
- Responses observed as early as Week 13
- 26/63 patients (41.3%) treated with pimicotinib achieved an objective tumor response

Pimicotinib demonstrated statistically significant and clinically meaningful improvements in all clinical outcome assessments, including range of motion, worst pain, worst stiffness and PROMIS-PF T-score

Parameter*	CFB, LS mean		Difference (95% CI)	p-value	Statistically significant	Clinically meaningful
	Pimicotinib (n=63)	Placebo (n=31)				
Relative ROM	15.64	−0.07	15.72 (7.33, 24.10)	0.0003	✓	✓
Worst stiffness NRS	−3.00	−0.57	−2.44 (−3.22, −1.65)	<0.0001	✓	✓
BPI worst pain NRS	−2.32	−0.23	−2.09 (−2.79, −1.39)	<0.0001	✓	✓
PROMIS-PF T-scores	5.63	2.23	3.40 (0.94, 5.86)	0.0074	✓	✓

*Estimated using mixed model for repeated measures with fixed effects for treatment, baseline, visit, stratification-factor of China versus non-China sites, and treatment-by-visit interaction, baseline-by-visit interaction, joint-type-category (knee, ankle, and others). An unstructured variance-covariance matrix is used.

Scan the QR code to access the full results here[27]

ESMO 2025: Efficacy outcomes – 24-week open-label follow-up[18]

ORR by BIRC per RECIST v1.1 and per TVS were both similarly improved over median follow-up of 435 days

ORR by BIRC per:
- RECIST v1.1: 76.2% (95% CI: 63.8, 86.0)
- TVS: 74.6 (95% CI: 62.1, 84.7)

Pimicotinib continued to demonstrate durable improvements in clinical outcome assessments beyond one year, with improvements in range of motion, worst pain, worst stiffness and PROMIS-PF T-score

	n	Mean (SD)
Active ROM	n=44	16.44 (21.84)
Worst Stiffness NRS*	n=46	−3.70 (1.91)
BPI worst pain NRS*	n=46	−2.56 (1.89)
PROMIS-PF*	n=49	6.55 (7.73)

*Patient-reported outcome.

ASCO and ESMO 2025: Safety outcomes[17,18]

Key safety profile details

Over both the primary and 24-week open-label follow-up, pimicotinib was generally well tolerated, with most TEAEs reported as Grade 1/2

Most frequent clinical TEAEs (>20%)
- Pruritus
- Facial edema
- Rash
- Periorbital edema
- Fatigue
- Nausea
- Headache

No evidence of: Cholestatic hepatotoxicity | Drug-induced liver injury | Hair/skin hypopigmentation

Dose reductions and treatment discontinuations over time

Primary analysis
- Dose reductions: 7.9%
- Discontinuations: 1.6%

24-week open-label follow-up
- Dose reductions: 25.4%
- Discontinuations: 6.3%

Blood CPK increased, blood LDH increased, AST increased, amylase increased, α-HBDH increased, and lipase increased were the key laboratory abnormalities observed.[17,18]

These findings suggest that pimicotinib may provide an effective, well tolerated, and convenient once-daily oral treatment option for patients with TGCT who require systemic therapy[17,18, 27]

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PEER-REVIEWED FEATURE

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