Pimicotinib in tenosynovial giant call tumor (TGCT): Long-term efficacy, safety, and patient-reported outcomes from the Phase 3 MANEUVER trial

Vinod Ravi; The University of Texas MD Anderson Cancer Center, Houston, TX, USA; vravi@mdanderson.org

Hans Gelderblom; Leiden University Medical Center, Leiden, Netherlands; a.j.gelderblom@lumc.nl

Javier Martin Broto; Medical Oncology Department, Fundación Jimenez Diaz University Hospital, Madrid, Spain; jmartin@atbsarc.org

Yong Zhou; Department of Orthopedics, West China Hospital, Sichuan University, Chengdu, China; zhouyonggk@163.com

Albiruni Ryan Abdul Razak; Princess Margaret Cancer Center; Toronto, ON, Canada; albiruni.razak@uhn.on.ca

Ramy Saleh; Cedars Cancer Center, McGill University Health Center, Montreal, QC, Canada; ramy.saleh@mcgill.ca

Jingnan Shen; Department of Musculoskeletal Oncology, the First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; shenjingnan@126.com

Tang Liu; The Second Xiangya Hospital of Central South University, Changsha, China; liutang1204@126.com

Silvia Stacchiotti; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; silvia.stacchiotti@istitutotumori.mi.it

Kamalesh K Sankhala; Precision NextGen Oncology and Research Center, Los Angeles, CA; sankhalak@nextgenonc.com

César Serrano; Medical Oncology Department, Hospital Universitario Vall d'Hebron, Vall d'Hebron, Institute of Oncology, Barcelona, Spain; cserrano@vhio.net

Jing Wang; Hunan Provincial People's Hospital, Changsha, China; wangj0405@163.com

Hairong Xu; Department of Orthopaedic Oncology Surgery, Beijing Ji Shui Tan Hospital, Peking University, Beijing, China; pagexu@126.com

Xiaohui Niu; Department of Orthopedic Oncology Surgery, Beijing Ji Shui Tan Hospital, Peking University, Beijing, China; niuxiaohui@263.net

Significance & Hypothesis/Techniques

TGCT is a rare, locally aggressive, and often debilitating synovial tumor driven by overproduction of colony stimulating factor-1 (CSF-1), highlighting the unmet need for effective systemic therapies. Pimicotinib is an oral, highly selective, potent CSF-1 receptor inhibitor. MANEUVER (NCT05804045) is the first global, Phase 3, randomized, placebo-controlled trial evaluating the efficacy and safety of pimicotinib in patients with TGCT from Asia, Europe, and North America. The primary endpoint (objective response rate [ORR] by blinded independent review committee per Response Evaluation Criteria in Solid Tumors [RECIST] v1.1) and all key secondary endpoints were met in Part 1 at Week 25.

Innovation

Although surgery is the standard of care treatment for TGCT, high recurrence rates, procedural risk, and morbidity remain a concern. Similarly, existing systemic treatments can be constrained by modest response, safety concerns, and limited global availability. Here we report efficacy, including clinical outcome assessments (COAs), and safety

outcomes with longer-term pimicotinib treatment at Week 49, which may help address these unmet needs for patients with TGCT.

Approach

In Part 1 (double-blind), patients received once-daily pimicotinib 50 mg or placebo (2:1) for 24 weeks; at Week 25, patients continued or switched to pimicotinib open-label for a further 24 weeks (Part 2), followed by an open-label extension phase.

Results

There were 94 patients randomized (pimicotinib: n=63; placebo: n=31). Median age was 40 years (range: 18–69); 68% were female and 50% had disease in the knee. At the final analysis data cutoff (Mar 12, 2025; median follow-up: 62 weeks), when all patients had completed Part 2, the ORR in patients randomized to pimicotinib was 76.2% (95% confidence interval [CI]: 63.8, 86.0) per RECIST v1.1 and 74.6% (95% CI: 62.1, 84.7) per tumor volume score; all COAs, including EuroQol visual analog scale, had ongoing improvement (**Table**). Patients switching from placebo to pimicotinib in Part 2 derived ORR and COA benefits. No new safety signals, or evidence of cholestatic hepatotoxicity or drug-induced liver injury, emerged. Treatment-emergent adverse events led to discontinuations in 4 (6.3%) patients randomized to pimicotinib and 2 (6.5%) patients randomized to placebo who switched to pimicotinib.

Discussion & Impact

Sustained treatment with pimicotinib in patients with TGCT demonstrated continued improvements in efficacy, enhanced patient outcomes, and an acceptable safety profile, reinforcing its potential for long-term use in eligible patients.

Data previously presented at the Connective Tissue Oncology Society 2025 Annual Meeting and the British Sarcoma Group Annual Conference 2026.

Funding: Merck KGaA, Darmstadt, Germany; Abbisko Therapeutics Co., Ltd.

Table. Clinical outcome assessments

Change from baseline, mean (SD)	**Randomized to pimicotinib**	
	Week 25	**Week 49**
Active Range of Motion	n=55 14.28 (20.407)	n=44 16.44 (21.840)
Worst Stiffness Numeric Rating Scale[a]	n=56 −2.98 (2.116)	n=46 −3.70 (1.914)
Brief Pain Inventory Worst Pain[a]	n=56 −2.32 (1.746)	n=46 −2.56 (1.893)
PROMIS-PF[a]	n=56	n=49

	5.59 (6.224)	6.55 (7.728)
EQ-VAS[a]	n=58 7.4 (10.58)	n=48 9.4 (10.88)

[a]Patient-reported outcome.

EQ-VAS, EuroQol visual analog scale; PROMIS-PF, Patient-Reported Outcomes Measurement Information System-Physical Function; SD, standard deviation.