2025 ASCO ANNUAL MEETING

Pimicotinib in tenosynovial giant cell tumor (TGCT): Efficacy, safety and patient-reported outcomes of Phase 3 MANEUVER study

June 1, 2025

Xiaohui Niu, Vinod Ravi, Javier Martín-Broto, Yong Zhou, Albiruni Ryan Abdul Razak, Ramy Saleh, Jingnan Shen, Tang Liu, Silvia Stacchiotti, Kamalesh K Sankhala, César Serrano, Jing Wang, Yingqi Hua, Piotr Rutkowski, Xiaojing Zhang, Yi Feng, Tao Li, Giacomo Giulio Baldi, Hairong Xu, Hans Gelderblom on behalf of the MANEUVER investigators

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Disclaimers

- Pimicotinib is being independently developed by Abbisko Therapeutics Co. Ltd., Shanghai, China. Merck KGaA, Darmstadt, Germany holds the commercial rights for pimicotinib globally.

- Data presented in this deck about pimicotinib are the property of Abbisko Therapeutics Co., Ltd.

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

MANEUVER met its primary and all key secondary endpoints

- Phase 3 MANEUVER, a randomized, placebo-controlled global study of patients with TGCT, met its primary endpoint:
  - Blinded independent review committee (BIRC)-assessed ORR at Week 25 per RECIST v1.1 was 54.0% with pimicotinib vs 3.2% with placebo
- BIRC-assessed ORR per TVS was significantly improved with pimicotinib (61.9% vs 3.2%)
- Pimicotinib significantly improved clinical outcome assessments (ROM, pain, stiffness, physical function) for patients with TGCT, regardless of achieving objective response per RECIST v1.1
- Treatment was well tolerated, with low incidence of treatment discontinuation and dose reductions, and no evidence of cholestatic hepatotoxicity, drug-induced liver injury, or hair/skin hypopigmentation
- Pimicotinib may offer an effective, well-tolerated, and convenient once-daily oral dosing option for patients with TGCT who require systemic therapy

ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumors; ROM, range of motion; TVS, tumor volume score

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Background

TGCT is a rare, benign, locally aggressive, soft-tissue tumor that can significantly impact patients' lives[1–6]

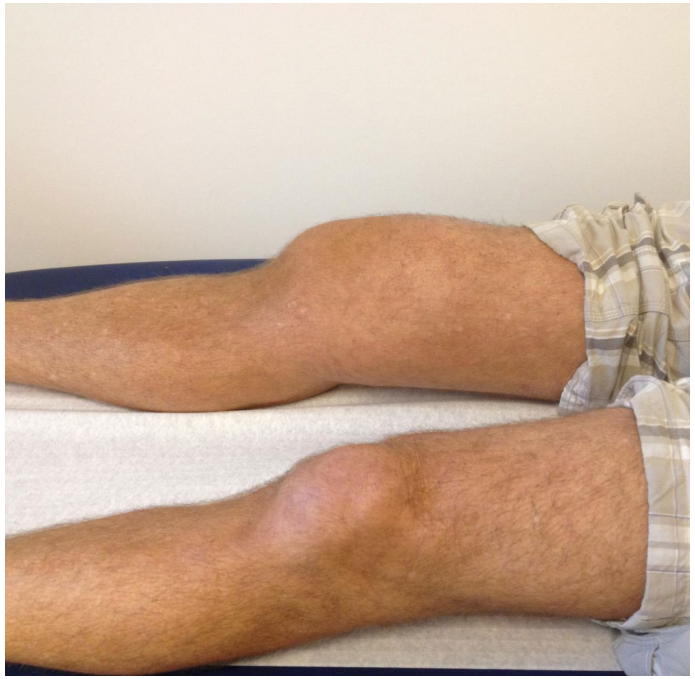


Image provided courtesy of Prof Dr M van de Sande (LUMC), with permission from the patient

- Aberrant CSF-1/CSF-1R signaling results in the accumulation of non-neoplastic inflammatory cells in the synovia and bursae of joints[7,8]
- Primarily affects younger adults (median age at diagnosis 33 years), causing chronic pain, stiffness, and functional impairments that significantly impact QoL[2–6]
- Incidence of 43 new cases (including 4 new D-TGCT cases) per 1 million people per year[9]
- Surgery is the standard treatment for symptomatic TGCT, but recurrence rates are high (up to 63%), potentially necessitating multiple surgeries and compromising joint function[1,2,3,10,11]
- Effective, well-tolerated, systemic treatment options that minimize treatment burden and improve patient outcomes are urgently needed[10]

CSF-1, colony-stimulating factor-1; CSF-1R; colony-stimulating factor-1 receptor; D-TGCT, diffuse TGCT; L-TGCT, localized TGCT; LUMC; Leiden University Medical Center; QoL, quality of life

1. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 2. Mastboom MJ et al. Interact J Med Res 2018;7:e4; 3. Ehrenstein V et al. J Rheumatol 2017;44:1476–83; 4. de Saint Aubain Somerhausen N, van de Rijn M. Tenosynovial giant cell tumour. In: Soft Tissue and Bone Tumours. WHO Classification of Tumours. 5th Edn, Vol 3, 2020; 5. Gelhorn HL et al. Clin Ther 2016;38:778–93; 6. Bernthal NM et al. Orphanet J Rare Dis 2021;16:191; 7. Spierenburg G et al. Expert Opin Ther Targets 2022;26:333–45; 8. Robert M et al. Front Immunol 2022;13:820046; 9. Mastboom MJ et al. Acta Orthopaedica 2017;88(6):688–94; 10. Stern S et al. Future Oncol 2025;1–10; 11. Assi T et al. Cancer Treat Rev 2025:134:102904

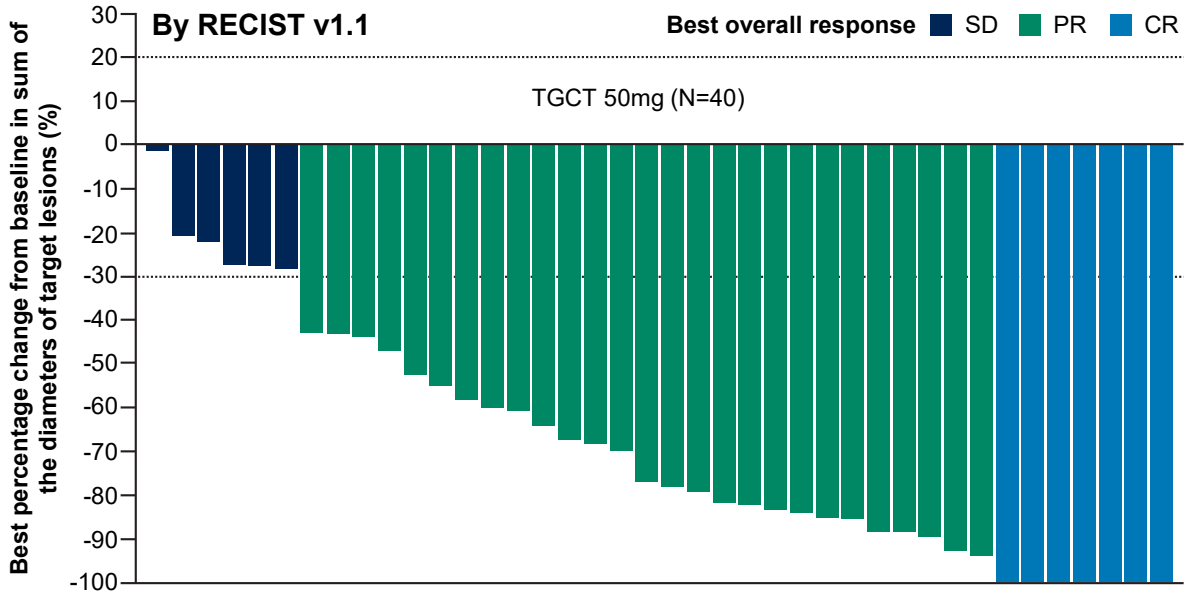
PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Background

Pimicotinib is a once-daily, oral, CSF-1R inhibitor under investigation for the treatment of patients with TGCT[1,2]

- Pimicotinib is thought to block CSF-1R signaling and disrupt inflammatory cell recruitment[1]
- Pimicotinib is highly specific for CSF-1R, potentially reducing off-target effects[1]
- In the Phase 1b study, at an RP2D of 50 mg once-daily, pimicotinib showed strong clinical activity in patients with TGCT (n=42)[3]
  - ORR by RECIST v1.1 at Week 25 was 67.5%[a]
  - ORR by RECIST v1.1 at 2-year follow-up was 85.0%[a]
  - Safety profile was tolerable, with mostly grade 1/2 TEAEs and no serious liver injuries or hair color changes

Best percentage change from baseline at 2 years in target lesions by IRC based on RECIST v1.1 from the Phase 1b study[3]



[a]As of June 30, 2024, 40 patients in the 50 mg QD pimicotinib group had completed at least one post-treatment tumor assessment by IRC based on RECIST v1.1
CR, complete response; IRC, independent review committee; PR, partial response; QD, once daily; RP2D, recommended Phase 2 dose; SD, stable disease; TEAE, treatment-emergent adverse event
1. Yang S et al. Cancer Res 2018;78(13_Suppl):LB-288; 2. Niu X et al. Future Oncol 2024;1–8; 3. Xu H et al. CTOS 2024 [P407]

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Methods

MANEUVER: A Phase 3, randomized, double-blind, placebo-controlled global study of pimicotinib in TGCT

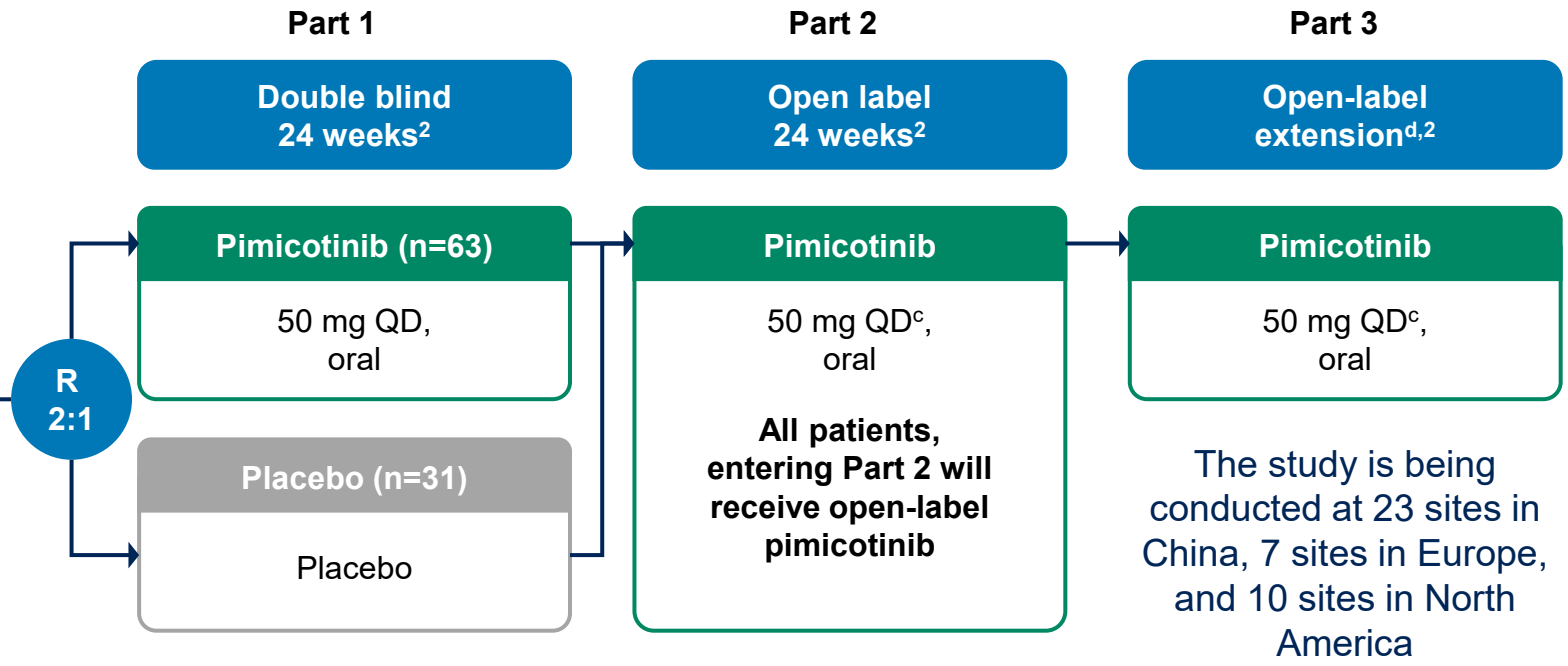
Study design

Key eligibility criteria[1]

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

N=94[b]

Stratification factor:
China vs non-China[2]



[a]Defined as one or more of the following: (i) a worst pain of ≥4 within 2 weeks prior to randomization (based on scale of 0 to 10, with 10 representing "pain as bad as you can imagine"), (ii) a worst stiffness of ≥4 within 2 weeks prior to randomization (based on a scale of 0 to 10, with 10 representing "stiffness as bad as you can imagine); [b]Between April 27, 2023 and March 29, 2024, 94 adults with TGCT underwent randomization: 63 were assigned to pimicotinib 50 mg QD and 31 to matching placebo; [c]If a patient has dose modification in Part 1/Part 2, the patient will continue to be administered at the modified dose in Part 2/Part 3; [d]All patients who complete 24 weeks of dosing in Part 2 will be eligible to enter the open-label extension treatment phase (ie, Part 3) for a longer treatment period and safety follow-up; R, randomization

1. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT05804045 [Accessed October 24, 2024]; 2. Niu X et al. Future Oncol 2024;1–8

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Methods
MANEUVER:
Primary and key secondary endpoints at Week 25[1]

	Endpoint	Definition and meaningful difference
Primary[1,2]	ORR by BIRC based on RECIST v1.1	Anatomic unidimensional assessment of tumor burden[3]
Key secondary[1,2]	ORR by BIRC based on TVS	The TVS is a semiquantitative scoring system designed specifically for TGCT to estimate tumor volume based on 10% increments; a response by TVS is defined as at least a 50% decrease in tumor volume[4]
	Mean change from baseline in clinical outcome assessments (tested in hierarchical order as listed):	
	Range of motion	Ability to move the affected joint assessed by goniometer under blinded conditions
	Worst pain NRS	Patient recollection of degree of worst pain over the past 24 hours from 0 (no pain) to 10 (worst imaginable)
	Worst stiffness NRS	Patient recollection of degree of stiffness over the past 24 hours from 0 (no stiffness) to 10 (worst imaginable)
	PROMIS-PF T-score	Function in upper and lower limbs, from 1 (unable to) to 5 (without any difficulty)

NRS, numeric rating scale; PROMIS-PF, Patient-Reported Outcomes Measurement Information System-Physical Function

1. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT05804045 [Accessed October 24, 2024]; 2. Niu X et al. Future Oncol 2024;1–8; 3. Aykan NF, Özatlı T. World J Clin Oncol. 2020;11:53–73; 4. Peterfy C et al. Future Oncol 2022;18:1449–59

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Results

Baseline characteristics were balanced between treatment groups

A total of 59 patients in the pimicotinib arm (93.7%) and 29 (93.5%) patients in the placebo arm completed the double-blind period[a]

Baseline characteristic	Pimicotinib (n=63)	Placebo (n=31)	Total (N=94)
Median age (range), years	41.0 (18–69)	36.0 (18–66)	40.0 (18–69)
Sex, n (%)			
Female	45 (71)	19 (61)	64 (68)
Geographic region, n (%)			
China	31 (49)	14 (45)	45 (48)
Europe	18 (29)	10 (32)	28 (30)
North America	14 (22)	7 (23)	21 (22)
Tumor location, n (%)			
Knee	33 (52)	14 (45)	47 (50)
Ankle	9 (14)	5 (16)	14 (15)
Hip	7 (11)	6 (19)	13 (14)
Other[b]	14 (22)	6 (19)	20 (21)
Prior surgery for TGCT, n (%)	37 (59)	19 (61)	56 (60)
Prior systemic therapy for TGCT (imatinib), n (%)	2 (3)	4 (13)	6 (6)

Data cutoff date Sep 23, 2024

[a]Between April 27, 2023 and March 29, 2024, 94 adults with TGCT were randomized; [b]Including 8 patients reported as foot, 7 patients reported as wrist, 2 patients reported as elbow, and one patient each reported as shoulder, right foot (big thumb) and left jaw

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Results

Pimicotinib showed marked and significant antitumor efficacy per RECIST v1.1

At Week 25	Pimicotinib (n=63)	Placebo (n=31)
ORR using RECIST v1.1, n (%)		
CR	1 (1.6)	0
PR	33 (52.4)	1 (3.2)
SD	20 (31.7)	28 (90.3)
PD	2 (3.2)[a]	0
NE	7 (11.1)	2 (6.5)
ORR using RECIST v1.1, n (%)	**34 (54.0)**	**1 (3.2)[b]**
95% CI[c]	(40.9–66.6)	(0.1–16.7)
Groups' difference (95% CI)[d]	50.7 (37.0–64.5)	
p-value[e]	<0.0001	
Median duration of response (range)	Not reached (0.03+, 11.76+)	Not reached NA

- The primary endpoint was met:
  - ORR by BIRC (RECIST v1.1) was 54.0% vs 3.2% at Week 25 (p<0.0001)
- Early onset of response was observed at Week 13, with 26 of 63 (41.3%) pimicotinib-treated patients achieving an objective tumor response
- The effect of pimicotinib on ORR was consistent across all prespecified subgroups[f]

Data cutoff date Sep 23, 2024; [a]One patient initially experienced a decrease in tumor size of 52% (PR) by Week 13 and then a subsequent increase of 38% (PD) at Week 25; however, by Week 37 the tumor size had reduced by 62% (PR), and the patient was still on treatment; [b]The single placebo responder, who had been receiving imatinib from May 2022 until discontinuation in February 2024 (4 weeks prior to study treatment initiation), with stable disease as the best overall response, showed a partial response under placebo; the possibility of a spontaneous regression or a delayed effect from imatinib cannot be ruled out; [c]95% CIs for rates were calculated using the exact Clopper-Pearson method; [d]95% CI for ratio difference was derived using the Wilson method; [e]p-values were obtained using Fisher's exact test; [f]Prespecified subgroups were based on age, sex, region, race, ethnicity, tumor location, TGCT type, ECOG PS, number of prior surgeries and prior systemic therapy
CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; NA, not applicable; NE, not evaluable; PD, progressive disease

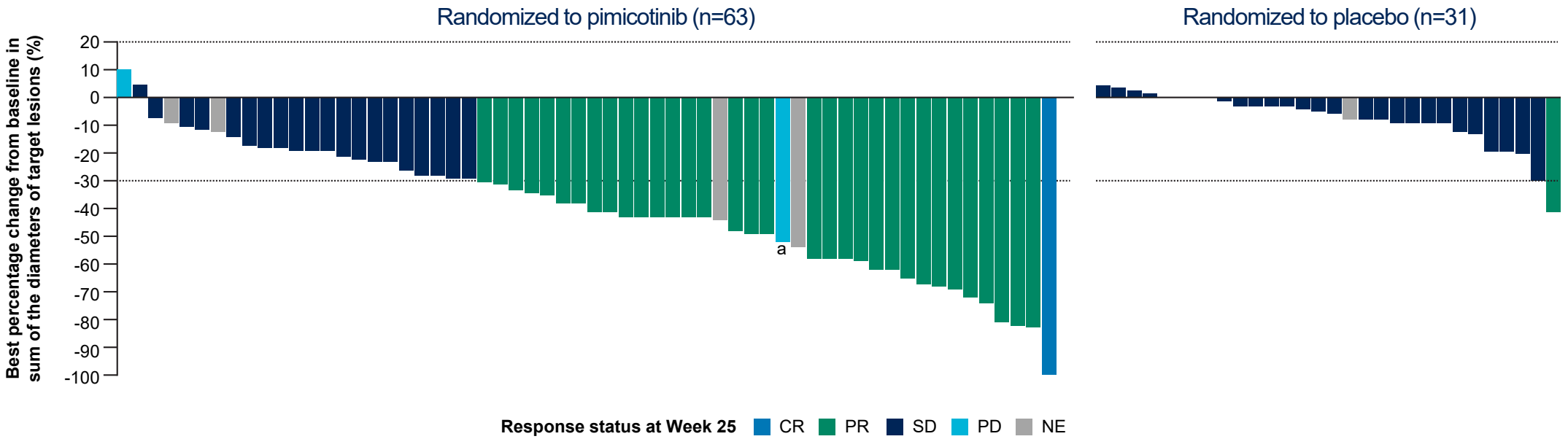
PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Results

Pimicotinib resulted in substantial reductions in tumor size

By the data cutoff, 58 of 63 patients (92.1%) in the pimicotinib group had a decrease in tumor size per BIRC based on RECIST v1.1

Best percentage change from baseline for individual patients



Data cutoff date Sep 23, 2024

[a]This patient initially experienced a decrease in tumor size of 52% (PR) by Week 13 and then a subsequent increase of 38% (PD) at Week 25; however, by Week 37 the tumor size had reduced by 62% (PR), and patient was still on treatment

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Results

Pimicotinib showed marked and significant antitumor efficacy by TVS

At Week 25	Pimicotinib (n=63)	Placebo (n=31)
ORR using TVS, n (%)		
CR	1 (1.6)	0
PR	38 (60.3)	1 (3.2)
SD	16 (25.4)	28 (90.3)
PD	1 (1.6)	0
NE	7 (11.1)	2 (6.5)
ORR using TVS, n (%)	**39 (61.9)**	**1 (3.2)**
95% CI[a]	(48.8–73.9)	(0.1–16.7)
Groups' difference, % (95% CI)[b]	58.7 (45.2–72.2)	
p-value[c]	<0.0001	
Median duration of response (range)	Not reached (0.03+, 14.13+)	Not reached (3.22+, 3.22+)

- ORR by BIRC (using TVS) at Week 25 was 61.9% vs 3.2% (p<0.0001)

The TVS is designed specifically for TGCT to estimate tumor volume;
a response by TVS is defined as at least a 50% decrease in tumor volume[1]

Data cutoff date Sep 23, 2024

[a]95% CIs for rates were calculated from the exact Clopper-Pearson method; [b]95% CI for ratio difference was derived from the Wilson method; [c]p-value was obtained from Fisher's exact test

1. Peterfy C et al. Future Oncol 2022;18:1449–59

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Results

Pimicotinib demonstrated statistically significant and clinically meaningful improvements in clinical outcomes

Parameter[a]	CFB, LS mean		Difference (95% CI)	p-value	Statistically significant	Clinically meaningful[1–6]
	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	✓	✓

- Improvements in ROM, stiffness, pain, and PROMIS-PF were observed in both patients with a response (PR or CR) to pimicotinib per RECIST v1.1, and also in those classified as non-responders
- COA findings were strengthened by consistently high questionnaire completion rates (>89% in the pimicotinib arm and >90% in the placebo arm completed baseline and Week 25 questionnaires)

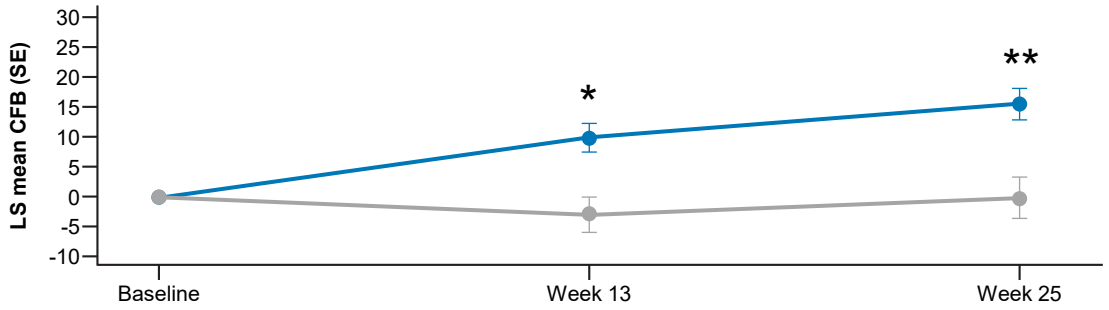
Data cutoff date Sep 23, 2024; [a]Estimated using mixed model for repeated measures with fixed effects for treatment, baseline, visit, stratification-factor of China versus non-China sites, and treatment-by-visit interaction, baseline-by-visit interaction, joint-type-category (knee, ankle, and others). An unstructured variance-covariance matrix is used; 1. Food and Drug Administration Center for Drug Evaluation and Research. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/211810Orig1s000MultidisciplineR.pdf; 2. Food and Drug Administration Center for Drug Evaluation and Research. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2025/219304Orig1s000MultidisciplineR.pdf; 3. Speck RM et al. J Patient Rep Outcomes 2020;4:61; 4. Van De Sande M et al. Acta Orthop 2021;92:493–9; 5. Blay JY et al. CTOS 2023 [P176]; 6. Dworkin RH et al. J Pain 2008;9:105–21; BPI, Brief Pain Inventory; CFB, change from baseline; COA, clinical outcome assessments; LS, least square

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

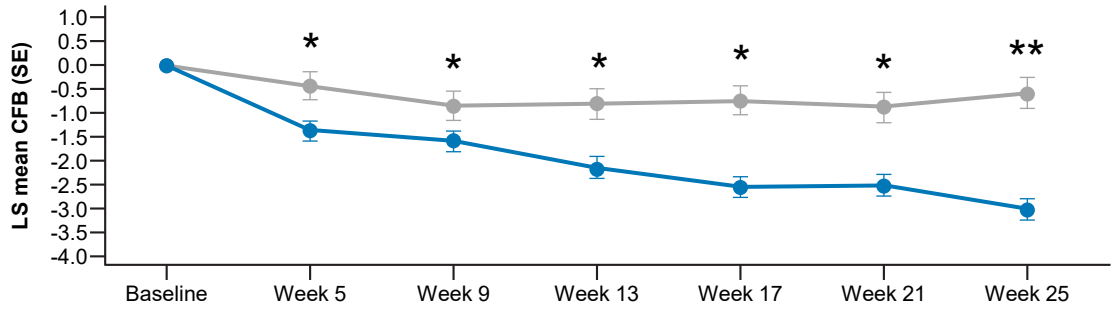
Results

Pimicotinib demonstrated early improvements in relative ROM, worst pain, worst stiffness, and PROMIS-PF T-score

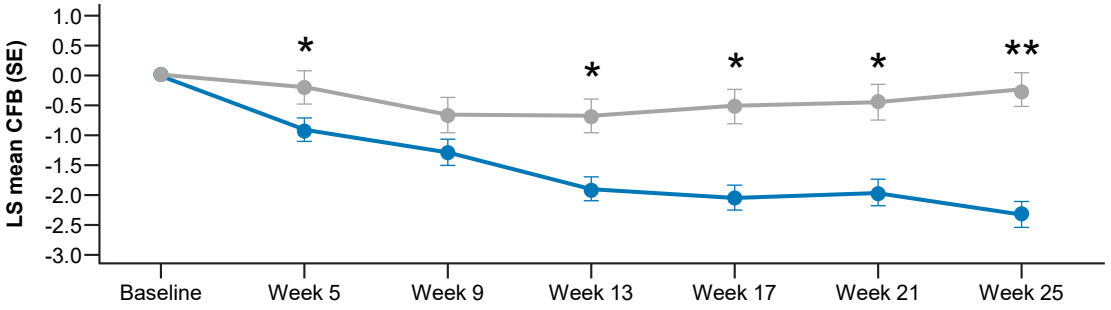
Relative ROM LS mean CFB by visit



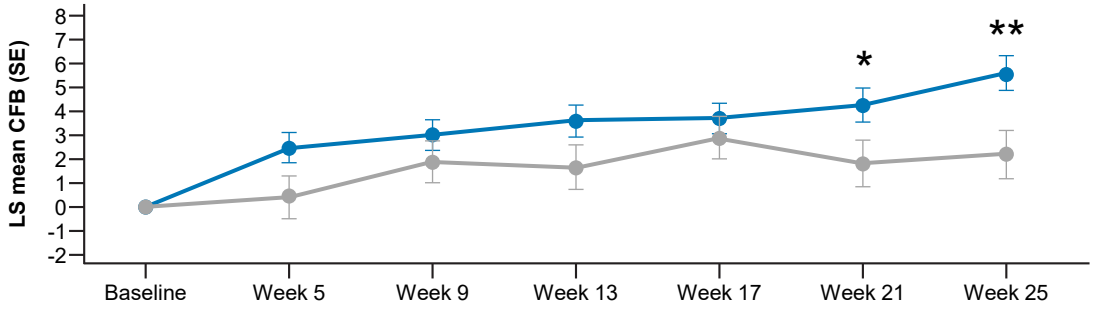
Worst stiffness NRS LS mean CFB by visit



BPI worst pain NRS LS mean CFB by visit



PROMIS-PF T-score LS mean CFB by visit



Treatment: Placebo Pimicotinib

Data cutoff date Sep 23, 2024

*p<0.05 for LS mean group difference at this timepoint; p-values are nominal; **p<0.05 for LS mean group difference at Week 25; p-values are significant (tested in hierarchical order)

CFB, change from baseline; SE, standard error

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Results

Pimicotinib was well tolerated, with a low rate of dose reductions and treatment discontinuations

TEAEs by week 25, n (%)	Pimicotinib n=63	Placebo n=31
Any TEAE	63 (100)	29 (93.5)
Any treatment-related TEAE	62 (98.4)	18 (58.1)
Any ≥Grade 3 TEAE	22 (34.9)	1 (3.2)
Any serious TEAE[a]	3 (4.8)	1 (3.2)
Any TEAE leading to dose reduction	5 (7.9)[b]	0
Any TEAE leading to dose interruption	34 (54.0)[c]	2 (6.5)
Any TEAE leading to treatment discontinuation	1 (1.6)[d]	0

Dose intensity[e] remained high (median 94.6%) despite treatment interruptions in the pimicotinib arm

Data cutoff date Sep 23, 2024

[a]Serious TEAEs in the pimicotinib arm included infectious enterocolitis, increased blood pressure, and erythema nodosum, and in the placebo arm included prostate cancer. Only increased blood pressure was considered related to pimicotinib by the investigator; [b]Dermatitis, rash, fatigue, headache, hypersomnia, and blood CPK increase each occurring in 1 patient, all Grade 1 or 2 TEAEs; [c]Including 14 Grade ≥3 TEAEs; [d]Grade 2 fatigue; [e]Percentage intended dose

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Results
Most frequent (≥20%) and class-specific TEAEs with pimicotinib

Most common TEAEs (≥20%) by Week 25, n (%)	Pimicotinib n=63		Placebo n=31	
Preferred term	**All grades**	**Grade 3/4**	**All grades**	**Grade 3/4**
Clinical AEs				
Pruritus	33 (52.4)	2 (3.2)	1 (3.2)	0
Face edema	30 (47.6)	0	0	0
Rash	22 (34.9)	2 (3.2)	0	0
Periorbital edema	20 (31.7)	0	3 (9.7)	0
Fatigue	18 (28.6)	0	7 (22.6)	0
Nausea	17 (27.0)	0	2 (6.5)	0
Headache	13 (20.6)	0	2 (6.5)	0

- There was no evidence of hair/skin hypopigmentation
- TEAEs of hypertension occurred in 14.3% of patients treated with pimicotinib (Grade 3, 3.2%)

Most common TEAEs (≥20%) by Week 25, n (%)	Pimicotinib n=63		Placebo n=31	
Preferred term	**All grades**	**Grade 3/4**	**All grades**	**Grade 3/4**
Laboratory AEs[a]				
Blood CPK increased	45 (71.4)	8 (12.7)	5 (16.1)	0
Blood LDH increased	36 (57.1)	0	0	0
AST increased	34 (54.0)	0	3 (9.7)	0
Amylase increased	22 (34.9)	0	0	0
α-HBDH increased	16 (25.4)	0	0	0
Lipase increased	15 (23.8)	2 (3.2)	1 (3.2)	0

- In the pimicotinib arm, AST/ALT elevations were mainly Grade 1 (50.8%/15.9%; Grade 2 3.2%/1.6%), and there was no evidence of cholestatic hepatotoxicity or drug-induced liver injury

Data cutoff date Sep 23, 2024; [a]Laboratory abnormalities were all asymptomatic and responded well to brief dose interruptions. Asymptomatic serum enzyme elevations were consistent with the known mechanism of action of CSF-1R inhibitors;
α-HBDH, alpha hydroxybutyrate dehydrogenase; AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; LDH, lactate dehydrogenase

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

MANEUVER met its primary and all key secondary endpoints

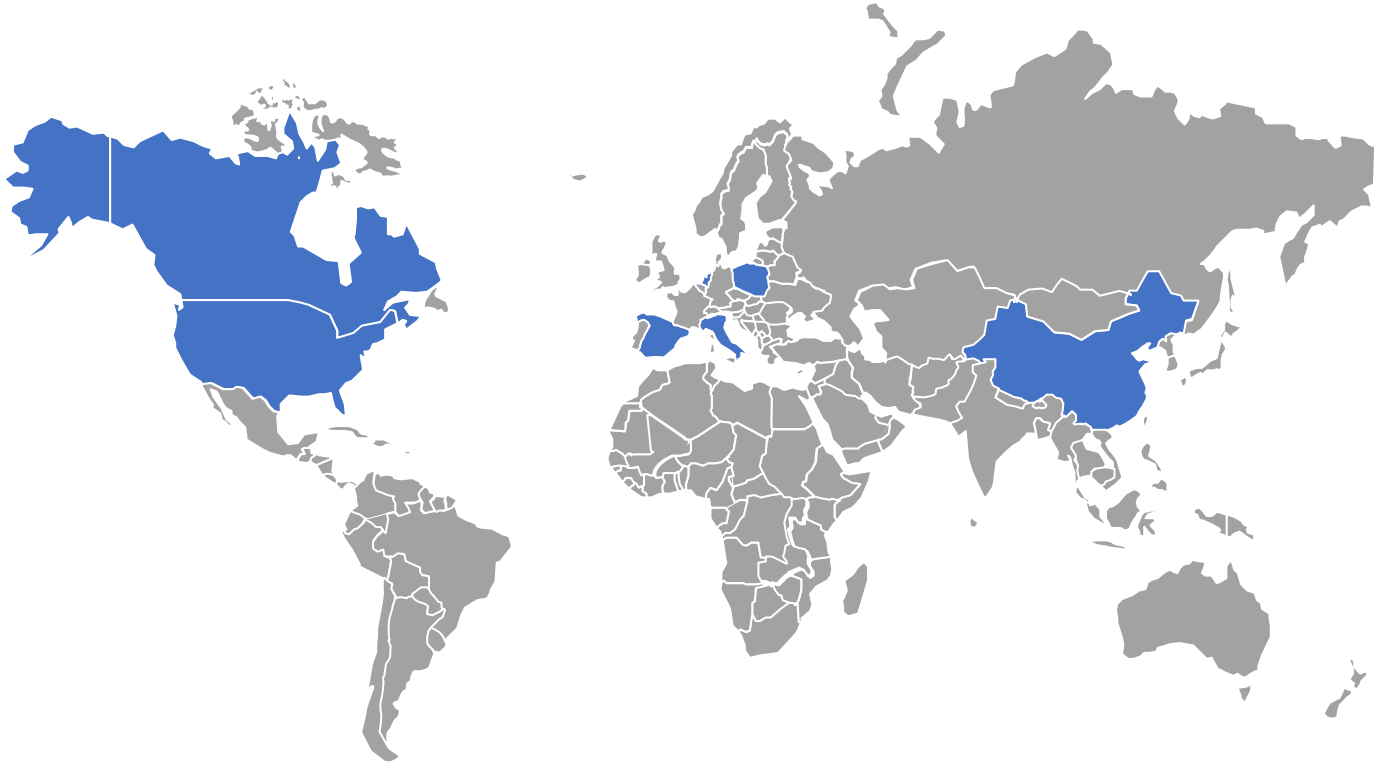
- Phase 3 MANEUVER, a randomized, placebo-controlled global study of patients with TGCT, met its primary endpoint:
  - BIRC-assessed ORR at Week 25 per RECIST v1.1 was 54.0% with pimicotinib vs 3.2% with placebo
- BIRC-assessed ORR per TVS was significantly improved with pimicotinib (61.9% vs 3.2%)
- Pimicotinib significantly improved clinical outcome assessments (ROM, pain, stiffness, physical function) for patients with TGCT, regardless of achieving objective response per RECIST v1.1
- Treatment was well tolerated, with low incidence of treatment discontinuation and dose reductions, and no evidence of cholestatic hepatotoxicity, drug-induced liver injury, or hair/skin hypopigmentation
- Pimicotinib may offer an effective, well tolerated, and convenient once-daily oral dosing option for patients with TGCT who require systemic therapy

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Acknowledgments

We would like to thank the patients who agreed to participate in the MANEUVER study, their families and caregivers, and the investigating teams at all participating sites

Scan to access a plain language summary of the presentation



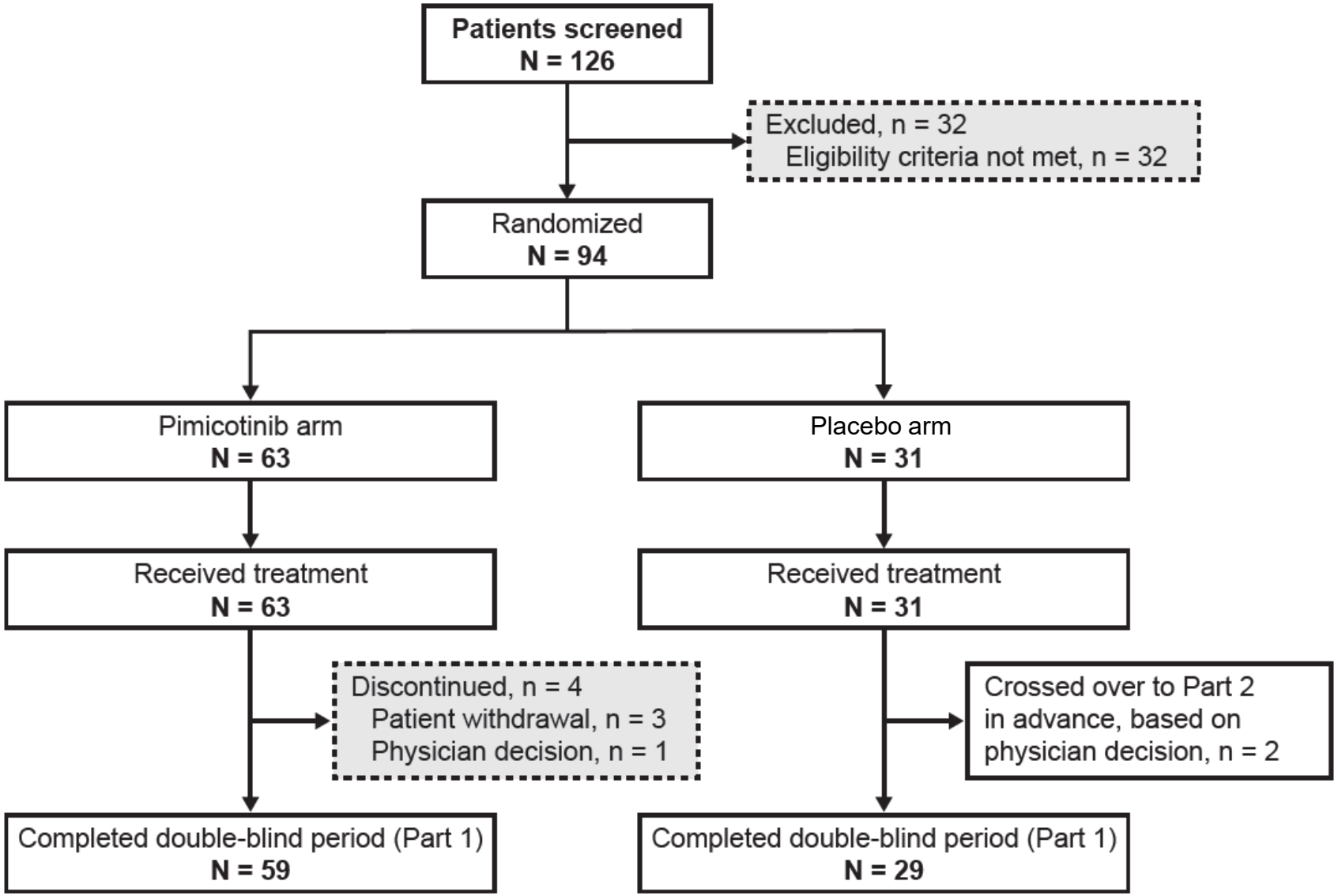
- Pimicotinib (ABSK021) is being developed by Abbisko Therapeutics Co. Ltd., Shanghai, China
- Merck KGaA, Darmstadt, Germany, holds the rights to commercialize pimicotinib worldwide
- Medical writing support was provided by Caudex, an IPG Health Medical Company, funded by Merck KGaA, Darmstadt, Germany

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Backup

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

CONSORT diagram



PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands