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Extended efficacy and safety from the Phase 3 MANEUVER trial of pimicotinib in patients with tenosynovial giant cell tumour (TGCT)

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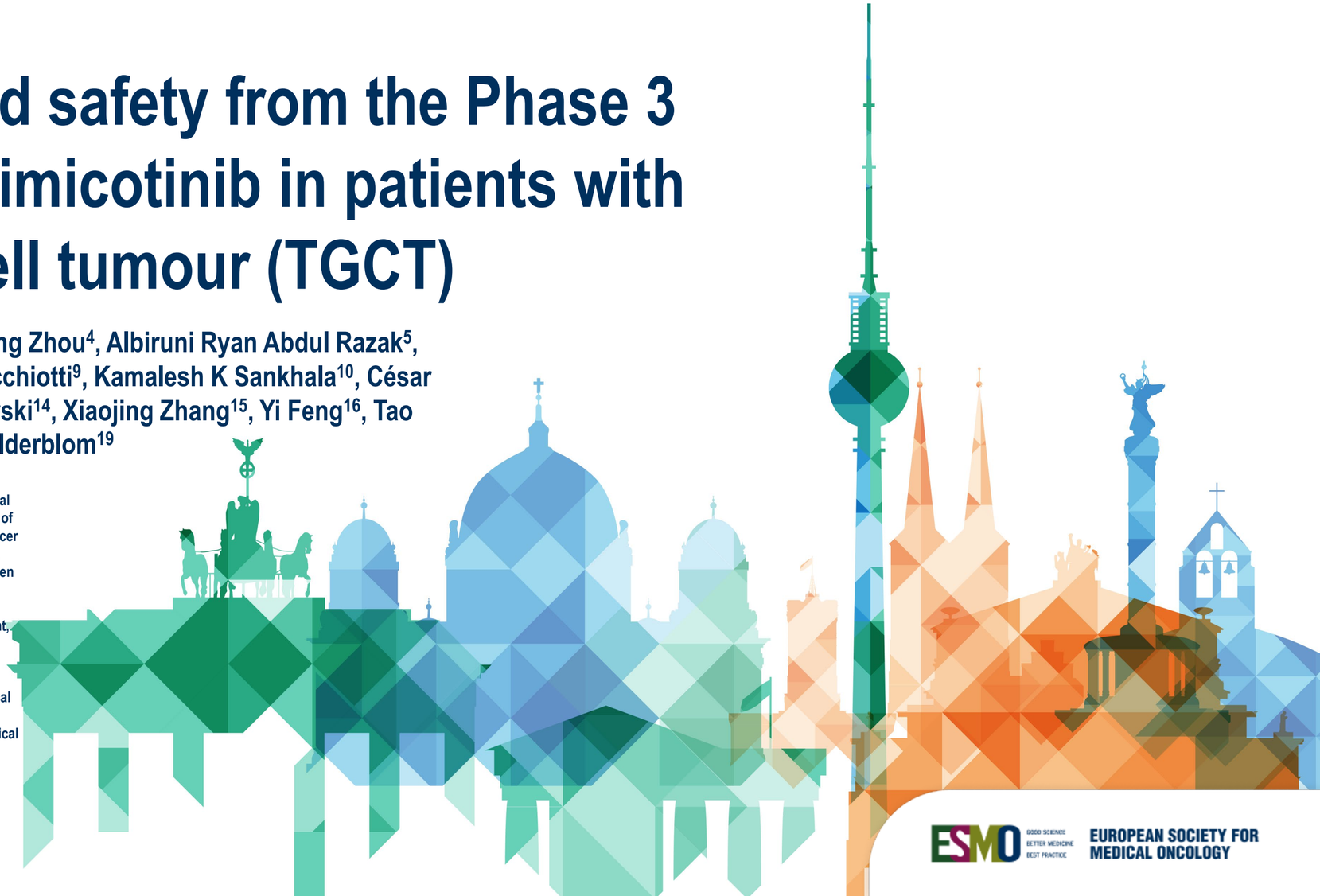

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DECLARATION OF INTERESTS

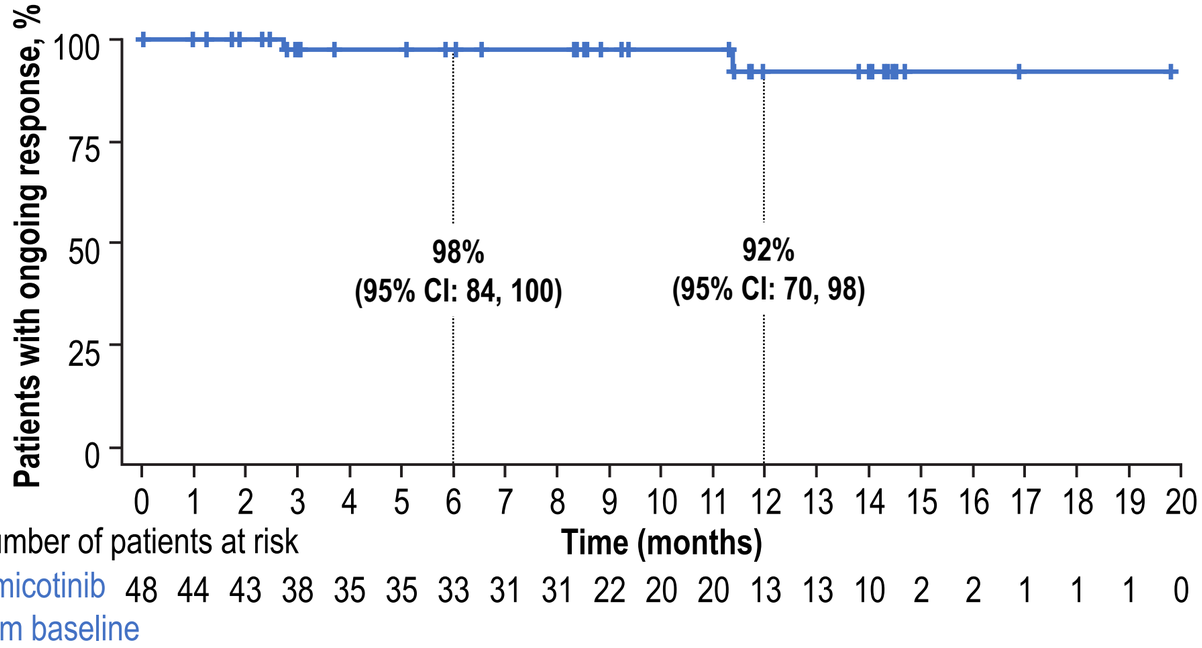
No conflicts of interest to declare

Pimicotinib demonstrated robust and durable antitumour activity at longer-term follow-up[a]

Median follow up in patients randomised to pimicotinib at baseline: 435 (range 78–686) days (14.3 months)

	Pimicotinib from baseline (n=63)
BOR per RECIST v1.1[b], n (%)	
CR	4 (6.3)
PR	44 (69.8)
SD	12 (19.0)
PD	0
NE	3 (4.8)
ORR BIRC RECIST v1.1, % (95% CI)	**76.2** (63.8, 86.0)
ORR BIRC TVS, % (95% CI)	**74.6** (62.1, 84.7)

DOR by BIRC per RECIST v1.1



Patients randomised to placebo at baseline (n=31) also derived benefit when switching to pimicotinib. With a median follow-up of 260 days (range 85–505) (~8.5 months) after switching to pimicotinib, ORR was 64.5% by BIRC per RECIST v1.1 and per TVS

[a]Data cutoff date 12 Mar 2025 (last patient Week 49 visit; follow-up for the majority of patients was ~1 year). [b]Patients who do not have a valid post-baseline tumour assessment are assigned "NE" as BOR.
BIRC, blinded independent review committee; BOR, best overall response; CI, confidence interval; CR, complete response; DOR, duration of response; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; SD, stable disease; TVS, tumour volume score.

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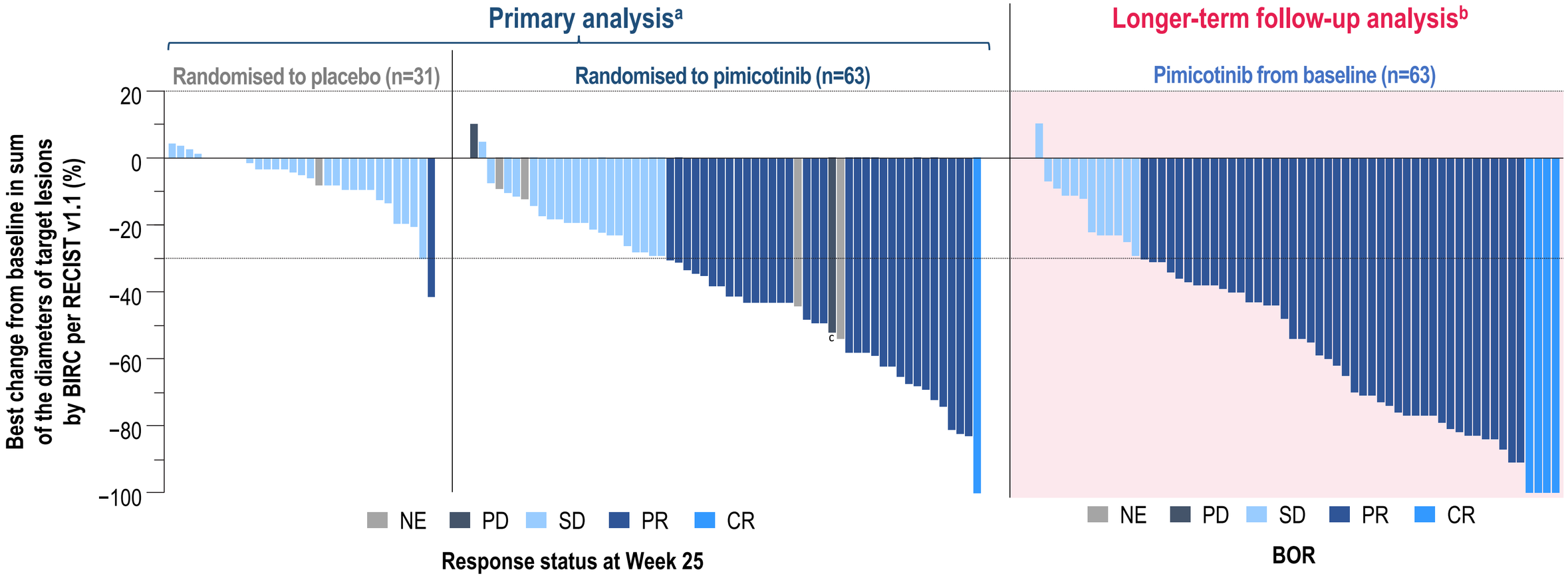
Pimicotinib demonstrated deepened tumour response with longer-term treatment[a]



93.7% of pimicotinib-treated patients experienced a reduction in tumour size by BIRC per RECIST v1.1 at longer-term follow up

[a]Data cutoff date 23 Sept 2024; [b]Data cutoff date 12 Mar 2025 (last patient Week 49 visit; follow-up for the majority of patients was ~1 year); Median duration of treatment: pimicotinib from baseline, 432 (range 56–684) days; [c]This patient initially experienced a decrease in tumour size of 52% (PR) by Week 13 and then a subsequent increase of 38% (PD) at Week 25; however, by Week 37 the tumour size had reduced by 62% (PR), and patient was still on treatment.
BIRC, blinded independent review committee; BOR, best overall response; CR, complete response; NE, not evaluable; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; SD, stable disease.

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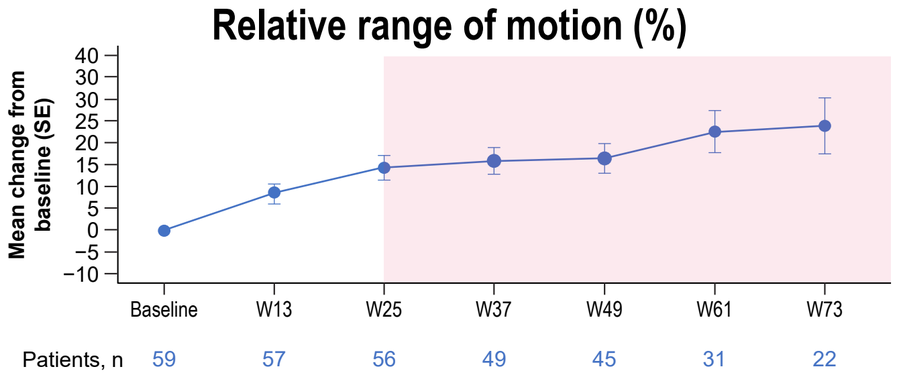
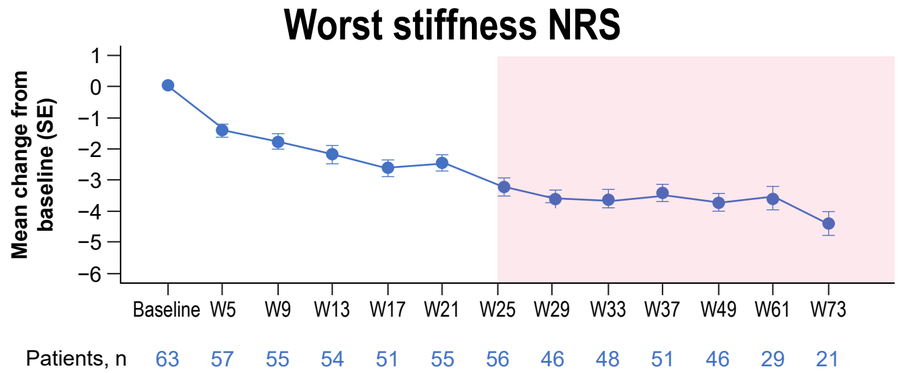
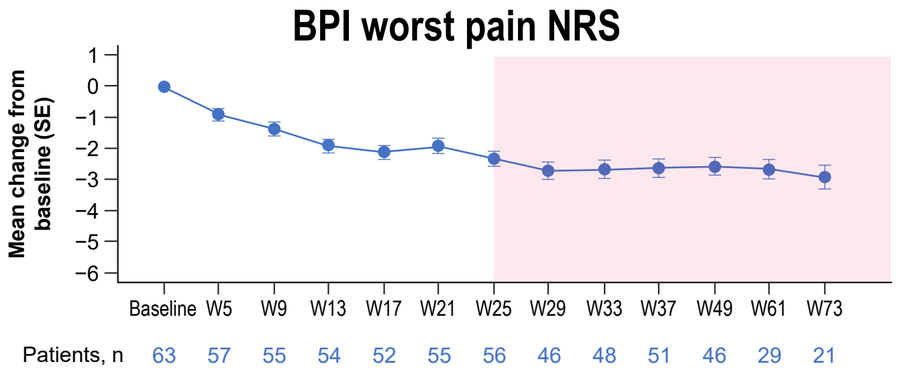
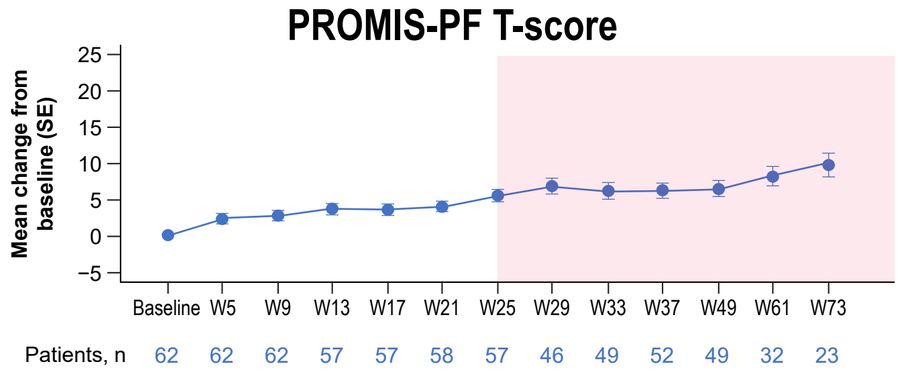
Pimicotinib continued to demonstrate clinically meaningful improvements in all clinical outcome assessments at longer-term follow-up[a]









Pimicotinib continued to demonstrate durable improvements in clinical outcome assessments beyond 1 year

[a]Data cutoff date 12 Mar 2025 (last patient Week 49 visit; follow-up for the majority of patients was ~1 year).
BPI, Brief Pain Inventory; NRS, numeric rating scale; PROMIS-PF, Patient-Reported Outcomes Measurement Information System–Physical Function; SE, standard error; W, week.

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The safety profile of pimicotinib after more than 1 year of treatment remained tolerable, manageable and did not reveal any new safety signals

Most common TEAEs (≥20%), n (%)	Primary analysis[a]		Longer-term follow-up analysis[b]	
	Pimicotinib from baseline (n=63)		Pimicotinib from baseline (n=63)	
Preferred term	**All grades**	**Grade 3 or 4**	**All grades**	**Grade 3 or 4**
Clinical AEs				
Pruritus	33 (52.4)	2 (3.2)	38 (60.3)	2 (3.2)
Facial oedema	30 (47.6)	0	31 (49.2)	0
Rash	22 (34.9)	2 (3.2)	24 (38.1)	4 (6.3)
Periorbital oedema	20 (31.7)	0	23 (36.5)	0
Fatigue	18 (28.6)	0	18 (28.6)	0
Nausea	17 (27.0)	0	18 (28.6)	0
Headache	13 (20.6)	0	16 (25.4)	0
Laboratory AEs				
Blood CPK increased	45 (71.4)	8 (12.7)	45 (71.4)	10 (15.9)
Blood LDH increased	36 (57.1)	0	36 (57.1)	0
AST increased	34 (54.0)	0	35 (55.6)	0
Amylase increased	22 (34.9)	0	24 (38.1)	0
Alpha-HBDH increased	16 (25.4)	0	16 (25.4)	0
Lipase increased	15 (23.8)	2 (3.2)	17 (27.0)	2 (3.2)
Blood CKMB increased	12 (19.0)	0	13 (20.6)	0
ALT increased	11 (17.5)	0	14 (22.2)	0

- **Pimicotinib was well tolerated at longer-term follow-up; no new safety signals were observed**
- No new treatment-related SAEs emerged with longer-term treatment
- There was no evidence of cholestatic hepatotoxicity or drug-induced liver injury
- The rates of dose reductions (25.4%) and discontinuations (6.3%) due to TEAEs were acceptable
- Median dose intensity[c] remained high (88.2%)

[a]Data cutoff date 23 Sept 2024; [b]Data cutoff date 12 Mar 2025; median follow-up in patients randomised to pimicotinib at baseline: 435 (range 78–686) days (14.3 months). [c]Percentage intended dose.
AE, adverse event; alpha-HBDH, alpha-hydroxybutyrate dehydrogenase; ALT, alanine aminotransferase; AST, aspartate transaminase; CKMB, creatine phosphokinase-MB; CPK, creatine phosphokinase; LDH, lactose dehydrogenase; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

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Longer-term pimicotinib leads to robust and durable tumour response and continuous improvement in clinical outcomes of patients with TGCT[a]

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- In this longer-term analysis of the global MANEUVER trial, with median follow-up of 14.3 months, **ORR by BIRC per RECIST v1.1** was **76.2%** (95% CI, 63.8, 86.0) in patients who had received pimicotinib from baseline (n=63)
  - Median DOR per RECIST v1.1 was not reached
  - ORR by BIRC per TVS was 74.6% (95% CI, 62.1, 84.7)
- Clinically meaningful improvements continued to be observed across clinical outcome assessments (relative range of motion, worst stiffness, worst pain and PROMIS-PF)
- Pimicotinib continued to be well tolerated with few discontinuations due to TEAEs, and no evidence of cholestatic hepatotoxicity or drug-induced liver injury

Pimicotinib may offer an effective, convenient and tolerable systemic treatment option for patients with TGCT, providing early and durable tumour response with sustained relief from pain and functional impairments

[a]Data cutoff date 12 Mar 2025 (last patient Week 49 visit; follow-up for the majority of patients was ~1 year).
BIRC, blinded independent review committee; CI, confidence interval; DOR, duration of response; ORR, overall response rate; PROMIS-PF, Patient-Reported Outcomes Measurement Information System–Physical Function; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; TEAE, treatment-emergent adverse event; TGCT, tenosynovial giant cell tumour; TVS, tumour volume score.

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