Patient-reported outcomes following treatment with vimseltinib for tenosynovial giant cell tumor in a phase 2 expansion study

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Conflict of interest

- Brooke Harrow is an employee of Deciphera Pharmaceuticals, LLC (Waltham, MA, USA)

Tenosynovial giant cell tumor and the importance of patient-reported outcome assessments

- Tenosynovial giant cell tumor (TGCT) is a rare, locally aggressive neoplasm caused by upregulation of the colony-stimulating factor 1 (CSF1) gene[1]
- These tumors can grow and cause damage to surrounding tissues and structures causing pain, joint stiffness, restricted mobility, and reduced quality of life[2]
- Surgery is the standard of care for most patients; some patients are not amenable to surgery[2]
- TGCT is a debilitating, but not life-threatening condition; treatments should aim to reduce symptoms and maximize long-term quality of life[3]

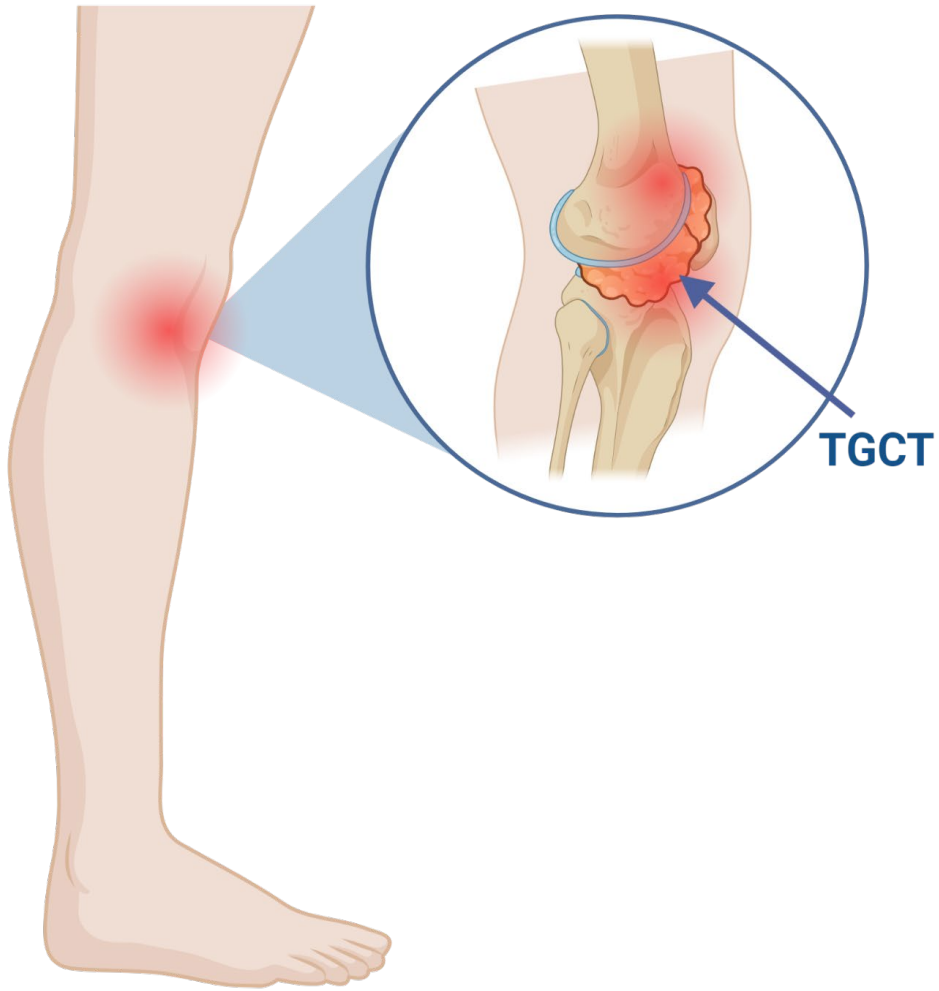


Figure created with biorender.com.

1) Smith BD, et al. *Mol Cancer Ther*. 2021;20:2098–109. 2) Mastboom MJ, et al. *Interact Med Res*. 2018;7:e4. 3) Gelhorn HL, et al. *Clin Ther*. 2016;38:778–93.

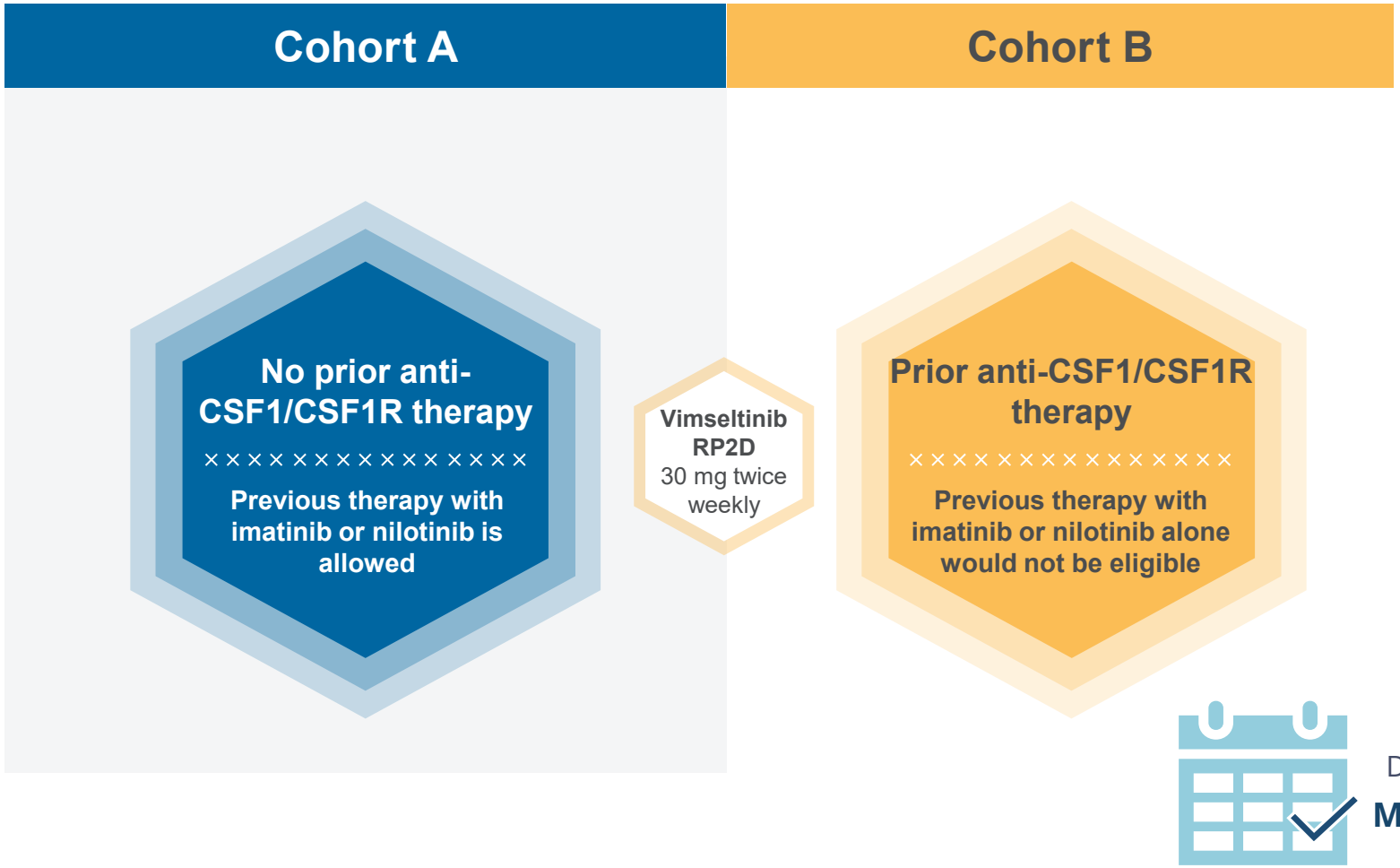
Vimseltinib

- There is only one systemic agent approved by the US FDA for the treatment of patients with TGCT not amenable to surgery, and no approved therapies in Europe[1]
  - Unmet need: Additional CSF1R-targeted therapies
- Vimseltinib is an investigational oral switch-control tyrosine kinase inhibitor specifically designed to selectively and potently inhibit CSF1R[2]
  - Well tolerated with a manageable safety profile in patients with TGCT not amenable to surgery at the recommended phase 2 dose (RP2D) of 30 mg twice weekly in a phase 1/2 study (NCT03069469)[3]

Objective:
To evaluate and present patient-reported outcome (PRO) measures from the phase 1/2 study

1) Pexidartinib (TURALIO®) prescribing information. Basking Ridge, NJ: Daiichi Sankyo, Inc. 2020. 2) Smith BD, et al. *Mol Cancer Ther*. 2021;20:2098–109. 3) Blay J-Y, et al. ESMO 2022. FPN 1509P.
CSF1R, colony-stimulating factor 1 receptor; FDA, Food and Drug Administration; TGCT, tenosynovial giant cell tumor.

Study design and enrollment



- At data cutoff, 58 patients with TGCT were enrolled
  - Cohort A: 46 patients; enrollment complete
  - Cohort B: 12 patients; enrollment ongoing

Data cutoff
May 6, 2022

CSF1, colony-stimulating factor 1; CSF1R, CSF1 receptor; RP2D, recommended phase 2 dose; TGCT, tenosynovial giant cell tumor.

PRO measures

PRO assessment	Assessment details
Brief pain inventory (BPI; short form)	• Self-administered 9-item questionnaire; only worst pain and average pain questions (in the last 24 hours) were evaluated in this study • Numeric scale from 0 (no pain) to 10 (pain as bad as you can imagine) • **BPI responder:** A person who experienced a ≥30% decrease in the mean BPI pain item without experiencing a ≥30% increase in narcotic analgesic use[a]
Numeric rating scale (NRS)	• Symptom-specific self-administered questionnaire developed for use in patients with TGCT[1] • Assesses swelling and stiffness in the last 24 hours • Numeric scale from 0 (none) to 10 (as bad as you can imagine)

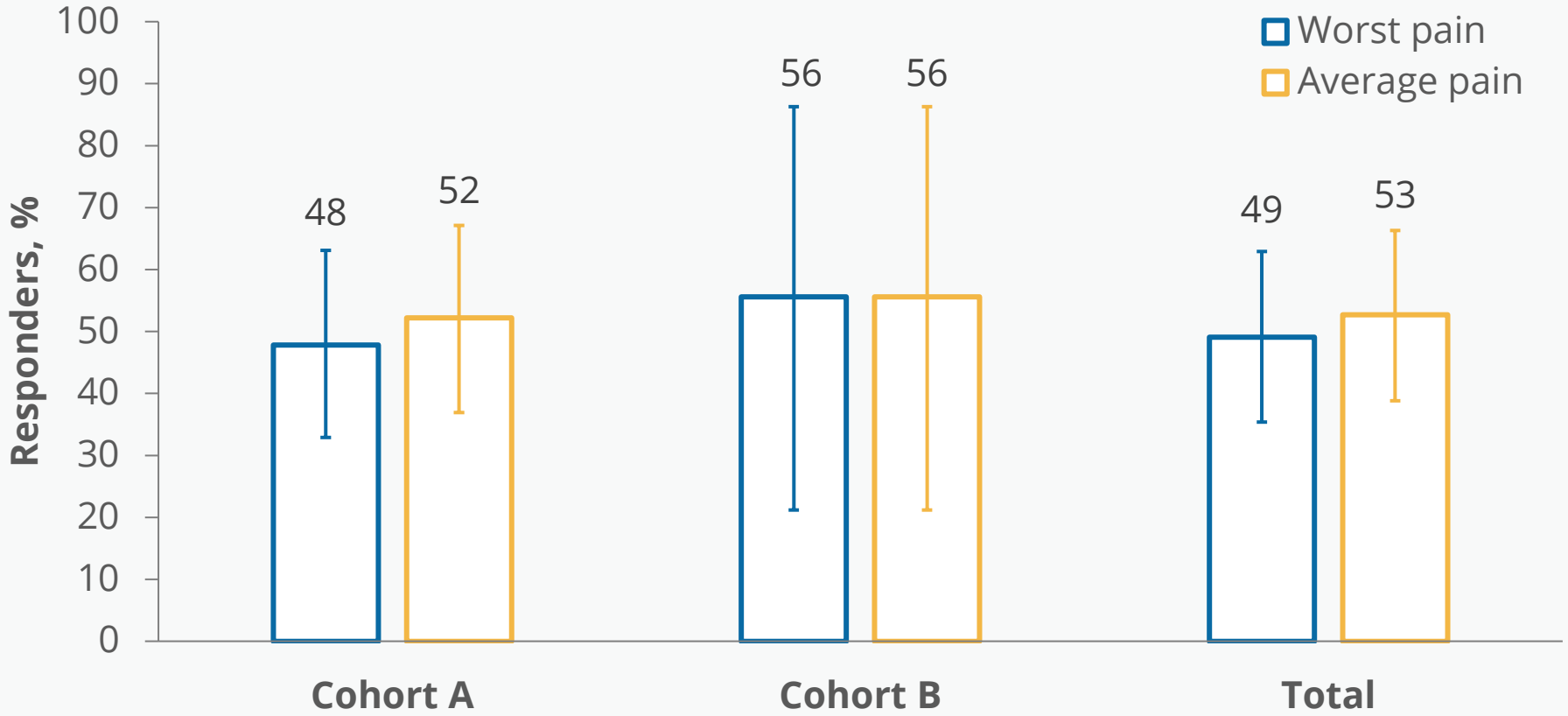
- PRO questionnaires were completed using an electronic device
- Patients were encouraged to complete PRO questionnaires for 14 consecutive days during screening to ensure robust baseline data collection
  - Patients must complete at least 4 baseline assessments of BPI worst pain and NRS worst stiffness
- During treatment cycles 1–6, BPI was collected roughly every day and the NRS was collected every other day; from cycle 7 onward, PROs were collected on day 1 and during the end of treatment visit

[a]The use of narcotic analgesics were collected beginning at screening for at least 1 year (through cycle 12) or until end of treatment, whichever comes first. Examples of narcotic analgesics are acetaminophen with codeine, codeine, fentanyl, hydrocodone-acetaminophen, hydromorphone, morphine sulfate, oxycodone, oxycodone with acetaminophen, and tramadol.

1) Speck RM, et al. *J Patient-Rep Outcomes*. 2020;4:61.

PRO, patient-reported outcome; TGCT, tenosynovial giant cell tumor.

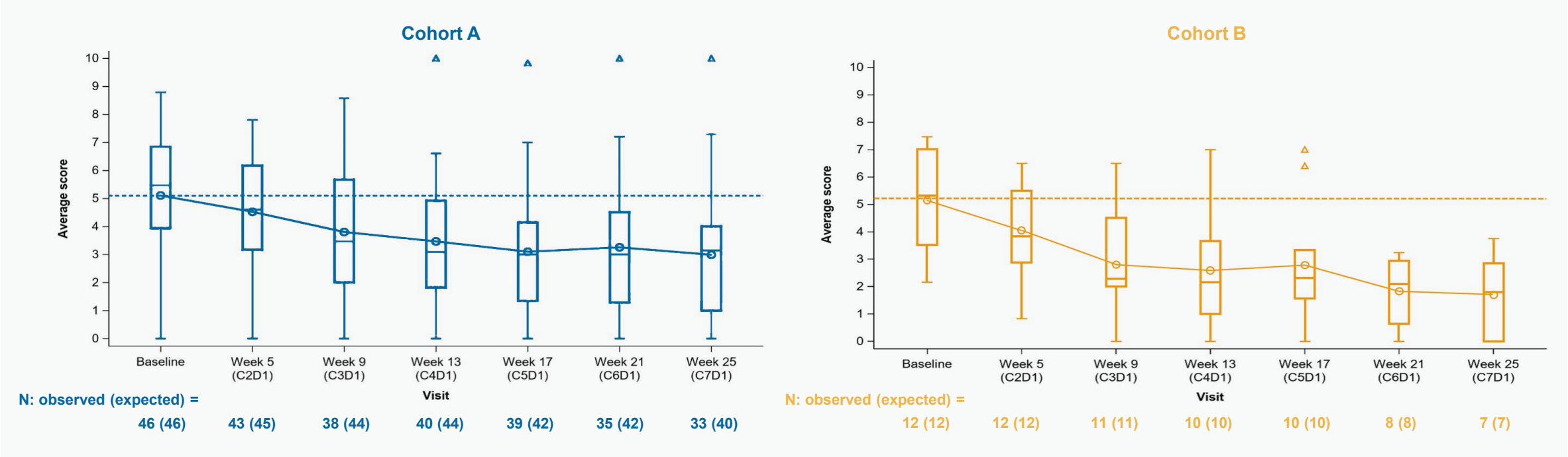
BPI response from baseline to week 25 in patients with TGCT receiving vimseltinib



	Cohort A		Cohort B		Total	
Responders	22	24	5	5	27	29
Total patients	46	46	9	9	55	55

Error bars represent the 95% confidence interval.
BPI, brief pain inventory; TGCT, tenosynovial giant cell tumor.

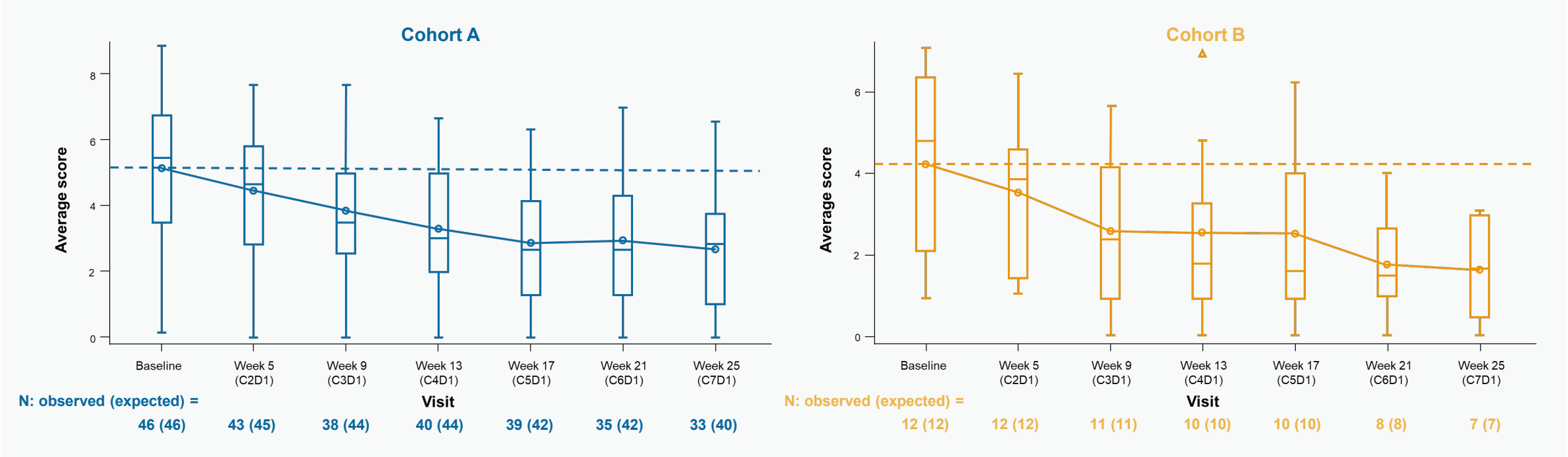
Worst stiffness NRS in patients with TGCT receiving vimseltinib



- Between baseline and week 25, clinically meaningful improvements in stiffness were observed (mean change from baseline: Cohort A, −2.0 points; Cohort B, −2.7 points)

Worst stiffness NRS average score at the site of the tumor in the last 24 hours. Dashed line represents the mean at baseline. The box represents the range from the 1st (bottom) to the 3rd (top) quartile. The circle in the box represents the mean and the horizontal line in the box represents the median. The endpoint of the upper whisker represents the highest observation contained within 1.5 × IQR from the 3rd quartile. The end point of the lower whisker represents the lowest observation contained within 1.5 × IQR from the 1st quartile. The triangles represent any observation outside of the interval defined above as 1.5 × IQR from the 3rd quartile or 1.5 × IQR from the 1st quartile, referred to as outliers.
C, cycle; D, day; IQR, interquartile range; NRS, numeric rating scale; TGCT, tenosynovial giant cell tumor.

Worst swelling NRS in patients with TGCT receiving vimseltinib



- Between baseline and week 25, clinically meaningful improvements in swelling were observed (mean change from baseline: Cohort A, −2.5 points; Cohort B, −2.4 points)

Worst swelling NRS average score at the site of the tumor in the last 24 hours. Dashed line represents the mean at baseline. The box represents the range from the 1st (bottom) to the 3rd (top) quartile. The circle in the box represents the mean and the horizontal line in the box represents the median. The endpoint of the upper whisker represents the highest observation contained within 1.5 × IQR from the 3rd quartile. The end point of the lower whisker represents the lowest observation contained within 1.5 × IQR from the 1st quartile. The triangles represent any observation outside of the interval defined above as 1.5 × IQR from the 3rd quartile or 1.5 × IQR from the 1st quartile, referred to as outliers.
C, cycle; D, day; IQR, interquartile range; NRS, numeric rating scale; TGCT, tenosynovial giant cell tumor.

Conclusions

- In this phase 1/2 study, patients with TGCT not amenable to surgery treated with vimseltinib reported:
  - Improvement in BPI worst and average pain from baseline to week 25
  - Clinically meaningful improvement in joint swelling and stiffness from baseline to week 25
- These results highlight the importance of considering PROs when making treatment decisions, particularly for nonlethal tumors
- Results support continued evaluation of vimseltinib in the actively enrolling phase 3 MOTION trial (NCT05059262)

BPI, brief pain inventory; PRO, patient-reported outcome; TGCT, tenosynovial giant cell tumor.

Acknowledgments

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- Some of this data was presented in part at ESMO 2022 (Blay et al. FPN: 1509P)
- Medical writing support was provided by Lauren Hanlon, PhD, of AlphaBioCom, LLC (King of Prussia, PA, USA), and was funded by Deciphera Pharmaceuticals, LLC (Waltham, MA, USA)

- Presenter contact information: brooke.harrow@deciphera.com

Baseline demographics and clinical characteristics of patients with TGCT receiving vimseltinib

	Cohort A (n = 46)	Cohort B (n = 12)	Total (N = 58)
Age, median (min, max), years	44 (21, 71)	47 (26, 65)	45 (21, 71)
Sex			
Female	31 (67)	7 (58)	38 (66)
Male	15 (33)	5 (42)	20 (35)
Race			
White	36 (78)	9 (75)	45 (78)
Asian	2 (4)	0	2 (3)
Black or African American	0	1 (8)	1 (2)
Pacific Islander	0	1 (8)	1 (2)
Not reported or missing	8 (17)	1 (8)	9 (16)
Disease location			
Knee	26 (57)	7 (58)	33 (57)
Ankle	9 (20)	1 (8)	10 (17)
Foot	6 (13)	0	6 (10)
Hand	0	1 (8)	1 (2)
Other[a]	5 (11)	3 (25)	8 (14)
Tumor type			
Diffuse TGCT	23 (50)	9 (75)	32 (55)
Localized TGCT	23 (50)	3 (25)	26 (45)
Patients with ≥1 prior surgery	31 (67)	10 (83)	41 (71)
2–3 prior surgeries	11 (24)	7 (58)	18 (31)
≥4 prior surgeries	1 (2)	1 (8)	2 (3)
Patients with ≥1 prior systemic therapy	3 (7)	12 (100)	15 (26)
Imatinib	3 (7)	0	3 (5)
Pexidartinib	NA	7 (58)	7 (12)
Imatinib and pexidartinib	NA	2 (17)	2 (3)
Cabiralizumab and pexidartinib	NA	1 (8)	1 (2)
Cabiralizumab	NA	1 (8)	1 (2)
Vimseltinib	NA	1 (8)	1 (2)

Data shown as n (%) unless otherwise noted. Percentages are rounded. [a]Other includes jaw, hip, shoulder, and thigh.
Max, maximum; min, minimum; NA, not applicable; TGCT, tenosynovial giant cell tumor.

TEAEs in ≥15% of patients with TGCT receiving vimseltinib

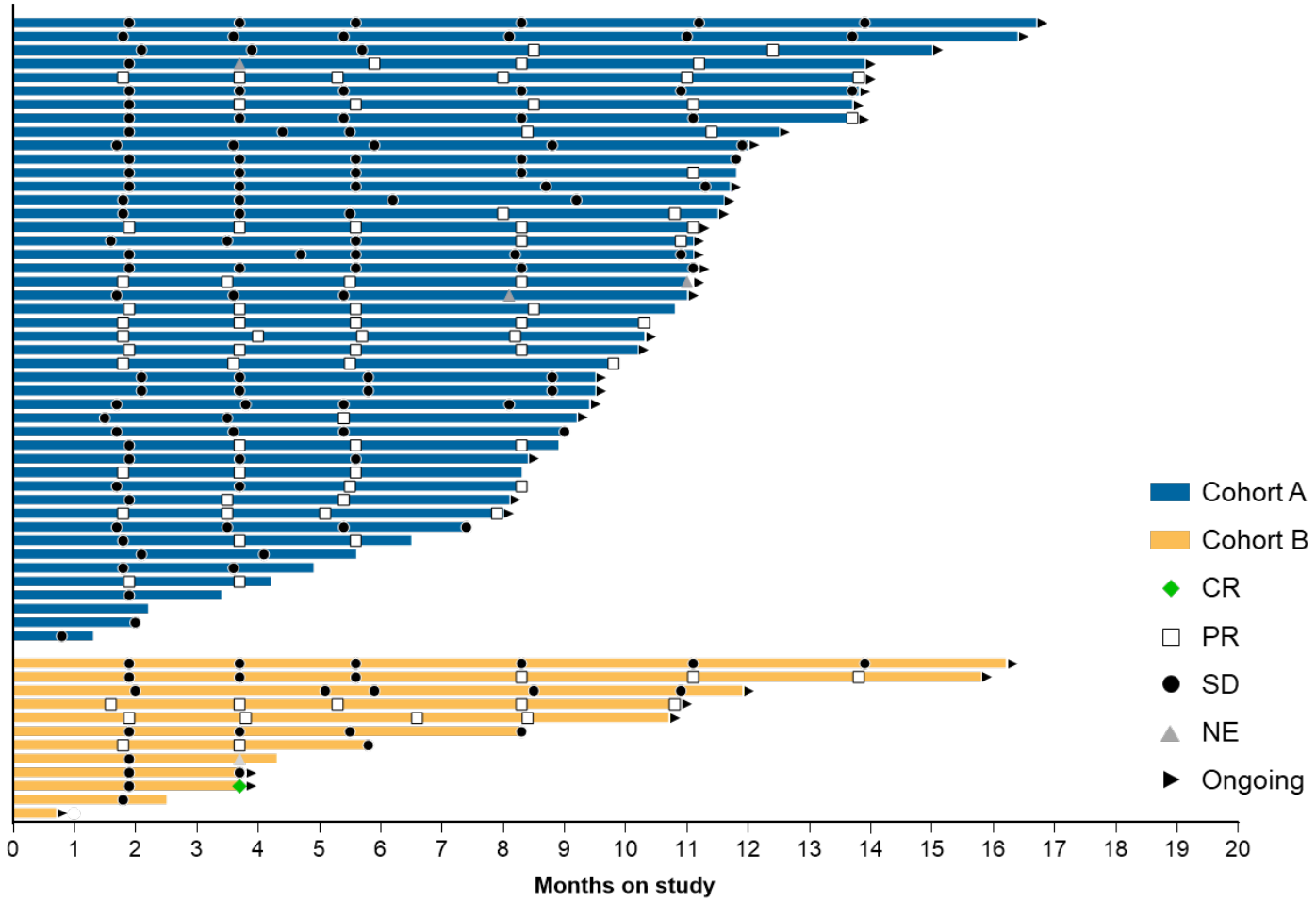
	Cohort A (n = 46)		Cohort B (n = 12)		Total (N = 58)	
Preferred term, n (%)	All grades	Grade 3/4	All grades	Grade 3/4	All grades	Grade 3/4
Blood CPK increased	30 (65)	20 (44)	4 (33)	2 (17)	34 (59)	22 (38)
Headache	19 (41)	0	8 (67)	0	27 (47)	0
Periorbital edema	16 (35)	0	6 (50)	0	22 (38)	0
Nausea	14 (30)	0	5 (42)	0	19 (33)	0
Fatigue	9 (20)	0	7 (58)	0	16 (28)	0
Asthenia	14 (30)	1 (2)	1 (8)	0	15 (26)	1 (2)
Myalgia	13 (28)	0	2 (17)	0	15 (26)	0
Arthralgia	10 (22)	0	3 (25)	1 (8)	13 (22)	1 (2)
Rash maculopapular	10 (22)	1 (2)	3 (25)	0	13 (22)	1 (2)
AST increased	8 (17)	0	2 (17)	0	10 (17)	0
Face edema	8 (17)	0	2 (17)	0	10 (17)	0
Diarrhea	6 (13)	0	3 (25)	0	9 (16)	0
Edema peripheral	7 (15)	0	2 (17)	0	9 (16)	0

- Most non-laboratory TEAEs were low grade
- The only Grade 3/4 TEAE observed in >5% of patients was blood CPK increase; most treatment-related TEAEs were Grade 1/2
- At the RP2D of 30 mg twice weekly, vimseltinib was well tolerated, with a manageable safety profile in patients with TGCT not amenable to surgery

AST, aspartate aminotransferase; CPK, creatine phosphokinase; RP2D, recommended phase 2 dose; TEAE, treatment-emergent adverse event; TGCT, tenosynovial giant cell tumor.

Duration of treatment and response in patients with TGCT receiving vimseltinib

- Vimseltinib demonstrated promising antitumor activity in patients with and without prior anti-CSF1/CSF1R therapy, with no disease progression observed in any patient by IRR
  - ORR, Cohort A: 53%
  - ORR, Cohort B: 46%



CR, complete response; CSF1, colony-stimulating factor 1; CSF1R, CSF1 receptor; IRR, independent radiological review; NE, not estimable; ORR, objective response rate; PR, partial response; SD, stable disease; TGCT, tenosynovial giant cell tumor.