SAFETY, EFFICACY, AND PATIENT-REPORTED OUTCOMES WITH VIMSELTINIB IN PATIENTS WITH TENOSYNOVIAL GIANT CELL TUMOR WHO RECEIVED NO PRIOR ANTI–COLONY-STIMULATING FACTOR 1 THERAPY: ONGOING PHASE 2 UDPATE

Abstract: 1545226

Jean-Yves Blay[1], Piotr Rutkowski[2], Hans Gelderblom[3], Silvia Stacchiotti[4], Alejandro Falcon Gonzalez[5], Jayesh Desai[6], Axel Le Cesne[7], César Serrano[8], Virginia Ferraresi[9], Emanuela Palmerini[10], Breelyn A Wilky[11], Andrew J Wagner[12], Nicholas Bernthal[13], Michiel van de Sande[3], Supraja Narasimhan[14], Brooke Harrow[14], Maitreyi G Sharma[14], Rodrigo Ruiz-Soto[14], Matthew L Sherman[14], William D Tap[15]

[1]Centre Leon Berard, Lyon, France; [2]Maria Sklodowska-Curie National Research Institute of Oncology, Warszawa, Poland; [3]Leiden University Medical Center, Leiden, Netherlands; [4]Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [5]Hospital Universitario Virgen del Rocío Sevilla and Instituto de BioMedicina de Sevilla, Seville, Spain; [6]Peter MacCallum Cancer Centre, Melbourne, Australia; [7]Gustave Roussy, Villejuif, France; [8]Vall d'Hebron Institute of Oncology, Barcelona, Spain; [9]IRCCS Istituto Nazionale Tumori Regina Elena, Rome, Italy; [10]IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy; [11]University of Colorado Cancer Center, Aurora, CO, USA; [12]Dana-Farber Cancer Institute, Boston, MA, USA; [13]University of California Los Angeles, Los Angeles, CA, USA; [14]Deciphera Pharmaceuticals, LLC, Waltham, MA, USA; [15]Memorial Sloan Kettering Cancer Center, New York, NY, USA

Introduction

- Tenosynovial giant cell tumor (TGCT) is a rare, locally aggressive neoplasm caused by aberrant expression of the *colony-stimulating factor 1* (*CSF1*) gene[1]
- There is only 1 systemic agent approved by the US Food and Drug Administration for the treatment of patients with TGCT not amenable to surgery, and none by the European Commission or other regulatory agencies, leaving an unmet need for an effective, CSF1 receptor (CSF1R)–targeted therapy with a favorable safety profile[2]
- Vimseltinib is an investigational, oral switch-control tyrosine kinase inhibitor specifically designed to selectively and potently inhibit CSF1R[1]
- Here, we report updated safety, efficacy, range of motion (ROM), and patient-reported outcome (PRO) data from the phase 2 part (expansion) of an ongoing phase 1/2 study of vimseltinib for patients with TGCT (Cohort A; NCT03069469)

Methods

- This multicenter, open-label, phase 2 trial is designed to evaluate the safety, tolerability, and efficacy of vimseltinib at the recommended phase 2 dose (30 mg twice weekly) in patients with TGCT not amenable to surgery who did not receive prior specific anti-CSF1/CSF1R agents (cohort A; previous therapy with imatinib or nilotinib is allowed)
- Vimseltinib antitumor activity was evaluated by independent radiological review (IRR) using Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) and tumor volume score (TVS) via magnetic resonance imaging[3]
- Total active ROM (in degrees) of the affected joint was normalized to a reference standard value provided by the American Medical Association to compute active ROM
- Pain was assessed by 2 items from the brief pain inventory (BPI; worst pain and average pain), with BPI response defined as ≥30% reduction in pain without a ≥30% increase in narcotic analgesic use
- PRO questionnaires were completed electronically and included 15 questions from Patient-Reported Outcomes Measurement Information System Physical Function (PROMIS-PF) and stiffness from the numeric rating scale (NRS)
  - Clinically meaningful response for these PROs was defined as a ≥3 point increase or ≥1 point decrease from baseline for PROMIS-PF or NRS stiffness, respectively[4]

Results

- As of June 27, 2023, 46 patients were enrolled in cohort A (enrollment complete); median age was 44 years (**Table 1**)
- The most common disease location was the knee and most patients had ≥1 prior surgery

Table 1. Baseline demographics and clinical characteristics

	Cohort A (n = 46)
Age, median (min, max), years	44 (21, 71)
Sex	
Female	31 (67)
Male	15 (33)
Race	
White	36 (78)
Asian	2 (4)
Not reported	5 (11)
Missing	3 (7)
Disease location	
Knee	26 (57)
Ankle	9 (20)
Foot	6 (13)
Hip	3 (7)
Shoulder	1 (2)
Jaw	1 (2)
Tumor type	
Diffuse TGCT	23 (50)
Localized TGCT	23 (50)
Patients with ≥1 prior surgery	31 (67)
1 surgery	18 (39)
2–3 surgeries	11 (24)
≥4 surgeries	2 (4)
Patients with ≥1 prior systemic therapy	3 (7)
Imatinib	3 (7)

Data cutoff: June 27, 2023. Data shown as n (%) unless otherwise noted.
max, maximum; min, minimum; TGCT, tenosynovial giant cell tumor.

Safety

- The majority of non-laboratory treatment-emergent adverse events (TEAEs) were low grade; observed aminotransferase elevations were also low grade (**Table 2**)
- Grade 3/4 TEAEs (>5% of patients) were elevated creatine phosphokinase and hypertension
- Enzyme elevations were consistent with the known mechanism of action of CSF1R inhibitors
- There were no treatment-related serious adverse events and no evidence of cholestatic hepatotoxicity

Table 2. TEAEs in ≥15% of patients

Preferred term, n (%)	Cohort A (n = 46) All grades	Grade 1	Grade 2	Grade 3/4
Blood CPK increased	31 (67)	2 (4)	7 (15)	22 (48)
Headache[a]	19 (41)	15 (33)	4 (9)	0
Periorbital edema[a]	18 (39)	16 (35)	2 (4)	0
Nausea[a]	16 (35)	12 (26)	4 (9)	0
Asthenia[a]	16 (35)	8 (17)	7 (15)	1 (2)
Myalgia[a]	14 (30)	11 (24)	2 (4)	1 (2)
Arthralgia[a]	12 (26)	8 (17)	4 (9)	0
Rash maculopapular[a]	11 (24)	7 (15)	3 (7)	1 (2)
Fatigue[a]	10 (22)	5 (11)	4 (9)	1 (2)
Edema peripheral[a]	10 (22)	8 (17)	2 (4)	0
Face edema[a]	9 (20)	6 (13)	3 (7)	0
AST increased	8 (17)	7 (15)	1 (2)	0
Eyelid edema[a]	8 (17)	5 (11)	3 (7)	0
Rash[a]	8 (17)	7 (15)	1 (2)	0
Blood LDH increased	8 (17)	3 (7)	5 (11)	0
Vomiting	8 (17)	5 (11)	3 (7)	0
Lipase increased	7 (15)	2 (4)	4 (9)	1 (2)
Generalized edema[a]	7 (15)	3 (7)	4 (9)	0
Pruritus[a]	7 (15)	5 (11)	2 (4)	0
COVID-19	7 (15)	4 (9)	3 (7)	0

Data cutoff: June 27, 2023. Safety population includes patients who received ≥1 dose of study drug. Severity was assessed by the investigator according to the toxicity grade described in the National Cancer Institute CTCAE v4.03 (grade 1 [mild] to grade 5 [death]). Grade 3/4 hypertension was observed in 7% (3/46) of patients; 2 of 3 patients had prior history of hypertension.
[a]Denotes events without a grade 4 severity category in the CTCAE v4.03.
AST, aspartate aminotransferase; CPK, creatine phosphokinase; CTCAE v4.03, Common Terminology Criteria for Adverse Events version 4.03; LDH, lactate dehydrogenase; TEAE, treatment-emergent adverse event.

- Median treatment duration was 21.0 months (range, 0.2–30.3; mean 16.2 months) with 48% (22/46) of patients on treatment at data cutoff
  - Treatment discontinuation reasons included adverse events (n = 4), physician decision (n = 5), and withdrawal by patient (n = 15)
- TEAEs led to treatment discontinuation in 9% of patients (**Table 3**)

Table 3. Dose modification due to any TEAEs

	Cohort A (n = 46)
Patients with TEAEs leading to dose modification, n (%)	34 (74)
Dose interruption	32 (70)
Dose reduction	24 (52)
Treatment discontinuation	4 (9)[a]

Data cutoff: June 27, 2023.
[a]G1 rash maculopapular and G1 periorbital edema; G1 dermatitis acneiform; G2 eczema; G2 eyelid edema and G2 asthenia.
G, grade; TEAE, treatment-emergent adverse event.

Efficacy

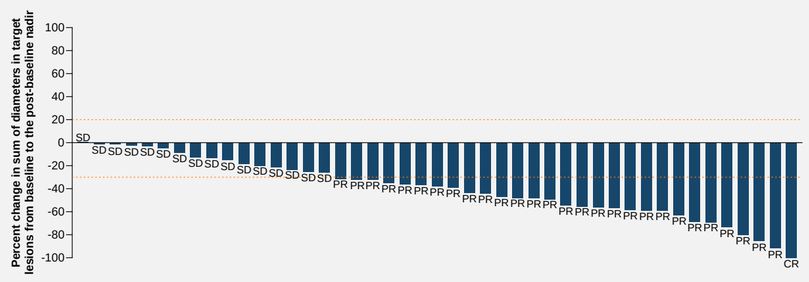
- Best overall response by RECIST v1.1 (64%) and TVS (62%) were comparable; the week 25 objective response rate by RECIST v1.1 was 38% (**Table 4, Figure 1**)
  - The majority of responses (62%, 18/29) were achieved within 6 months of treatment, with a median time to first response of 3.7 months (range, 1.8–24.9; **Figure 2**)
  - Responses also occurred beyond 6 months, with 1 complete response by RECIST v1.1 achieved after >2 years on treatment (**Figure 2**)
- As of data cutoff, no patients progressed as assessed by IRR
- Most patients experienced an increase in active ROM (**Figure 3, Table 5**)

Table 4. Response assessed by IRR using RECIST v1.1 and TVS

	RECIST v1.1 BOR (n = 45)	RECIST v1.1 Week 25 (n = 45)[a]	TVS BOR (n = 45)	TVS Week 25 (n = 45)[a]
ORR, n (%)	29 (64)	17 (38)[b]	28 (62)	23 (51)
Complete response	1 (2)	0	0	0
Partial response	28 (62)	17 (38)	28 (62)	23 (51)
Stable disease	16 (36)	22 (49)	17 (38)	16 (36)
Duration of response, median[c] (min, max), months	NR (0.03+, 25.4+)			

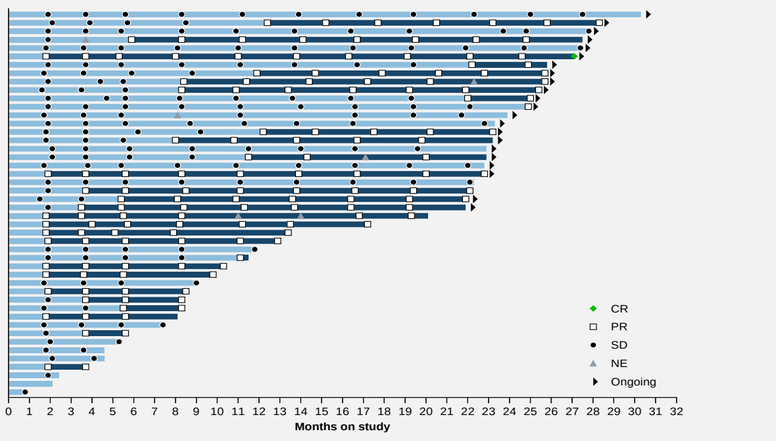
Data cutoff: June 27, 2023; 45/46 patients had at least 1 post-baseline imaging assessment as of the data cutoff (efficacy evaluable population); + indicates that response was ongoing at last assessment.
[a]Patients that either reached week 25 or discontinued treatment or study prior to week 25 were included.
[b]One of the 18 responders had a response prior to week 25 but discontinued the study before the week 25 scan and was considered a nonresponder at week 25.
[c]Based on Kaplan-Meier estimate. Duration of response is defined as time from first imaging result showing response to progressive disease.
BOR, best overall response; IRR, independent radiological review; max, maximum; min, minimum; NR, not reached; ORR, objective response rate; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TVS, tumor volume score.

Figure 1. Best percent change in target lesions



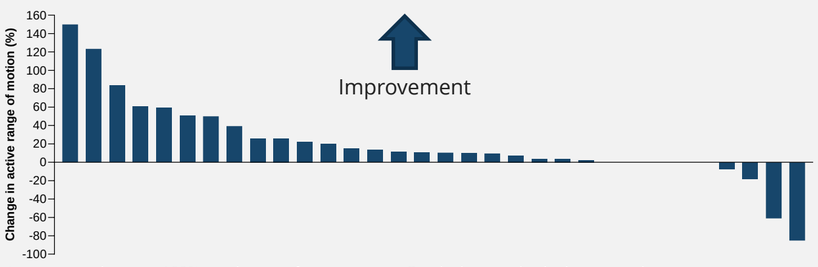
Data cutoff: June 27, 2023. Using RECIST v1.1 by IRR, includes all available follow-up visits. Dotted line at 20% represents threshold for PD; dotted line at −30% represents threshold for PR. Graph shows individual patient values.
CR, complete response; IRR, independent radiological review; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

Figure 2. Duration of treatment and response



Data cutoff: June 27, 2023. Using RECIST v1.1 by IRR; includes all available follow-up visits. Dark blue shading represents duration of response.
CR, complete response; IRR, independent radiological review; NE, not evaluable; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

Figure 3. Change in active ROM



Associations that are >100% are due to reference ranges. Graph shows individual patient values.
Increase from baseline: n = 23; no change: n = 5; decrease: n = 4.
ROM, range of motion.

Table 5. Active ROM change from baseline to week 25

	Cohort A (n = 32)
Active ROM of the affected joint, mean (SD), %	
Baseline	57.8 (32.9)
Week 25	77.6 (39.6)
Change from baseline to week 25, mean (SD), % points	19.8 (44.2)

Data cutoff: June 27, 2023. Analysis only includes patients with active ROM assessments at baseline and week 25.
ROM, range of motion; SD, standard deviation.

Patient-reported outcomes

- At week 25, 50% (23/46) and 54% (25/46) of patients experienced clinically meaningful reductions in their worst and average pain, respectively
- Most patients (59%) who had an objective response by RECIST v1.1 at week 25 were also BPI responders (**Table 6**)
  - Over half of patients (55%) with stable disease at week 25 were also BPI responders
- At week 25, 49% and 66% of patients had clinically meaningful improvements in PROMIS-PF and NRS stiffness, respectively (**Table 7**)

Table 6. Examination of the relationship between RECIST response and BPI worst pain response at week 25

	RECIST v1.1 at week 25 by IRR[a]: Complete or partial response (n = 17)	Stable disease (n = 22)
Worst pain responder, n (%)	10 (59)	12 (55)

Data cutoff: June 27, 2023
[a]Includes patients with both BPI and efficacy data available at week 25 (n = 39); percentages represent proportion of patients with partial response or stable disease with ≥30% pain reduction.
BPI, brief pain inventory; IRR, independent radiological review; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Table 7. PROMIS-PF and NRS stiffness at week 25

	PROMIS-PF (n = 35) Baseline	PROMIS-PF (n = 35) Week 25	NRS stiffness (n = 32) Baseline	NRS stiffness (n = 32) Week 25
Mean (SD)	40.0 (8.2)	43.9 (9.1)	4.9 (2.1)	3.1 (2.2)
Change from baseline, mean (SD)	3.9 (7.8)		−1.8 (2.7)	
Response, n (%)	17 (49)		21 (66)	

Data cutoff: June 27, 2023
NRS, numeric rating scale; PROMIS-PF, Patient-Reported Outcomes Measurement Information System Physical Function; SD, standard deviation.

CONCLUSIONS

- Vimseltinib demonstrated promising antitumor activity with best overall responses of 64% with RECIST v1.1 and 62% with TVS without disease progression observed in any patient by IRR
- Longer follow-up demonstrated that vimseltinib continued to be well tolerated with a manageable safety profile in patients with TGCT not amenable to surgery who received no prior anti-CSF1/CSF1R therapy
  - The median treatment duration increased to 21 months, with 48% of patients remaining on treatment at data cutoff
- Patients experienced clinically meaningful improvements in pain, physical function, and stiffness
  - At week 25, most patients had clinically meaningful reductions in pain regardless of objective response; patients with stable disease also experienced clinically meaningful reductions in pain
  - Between baseline and week 25, nearly half of patients experienced clinically meaningful improvements in physical function, and the majority experienced clinically meaningful improvements in stiffness
- These results support continued evaluation of vimseltinib in the phase 3 MOTION trial (NCT05059262)

PRESENTED AT THE 2023 CTOS ANNUAL MEETING, NOVEMBER 1–4, DUBLIN, IRELAND

STUDY SPONSOR

This study is sponsored by Deciphera Pharmaceuticals, LLC, Waltham, MA, USA.

CORRESPONDING AUTHOR

John-Yves Blay, jean-yves.blay@lyon.unicancer.fr

ACKNOWLEDGEMENTS

We thank the patients and their families and caregivers, the investigators, and the investigational site staff for the study. Medical writing and editorial support were provided by Steven Walker, PhD, of AlphaBioCom, a Red Nucleus company, and were funded by Deciphera Pharmaceuticals, LLC.

REFERENCES

1) Smith BD, et al. *Mol Cancer Ther.* 2021;20:2098-109. **2)** Pexidartinib (TURALIO®) prescribing information. Basking Ridge, NJ: Daiichi Sankyo, Inc. 2022. **3)** Tap W, et al. *N Engl J Med.* 2015;373:428-37. **4)** Tap W, et al. *J Clin Oncol.* 2019;37:15_suppl, e18236.