Abstract: 2111879

Effect of a high-fat meal on the pharmacokinetics of vimseltinib, an oral inhibitor of the colony-stimulating factor 1 receptor, in healthy participants

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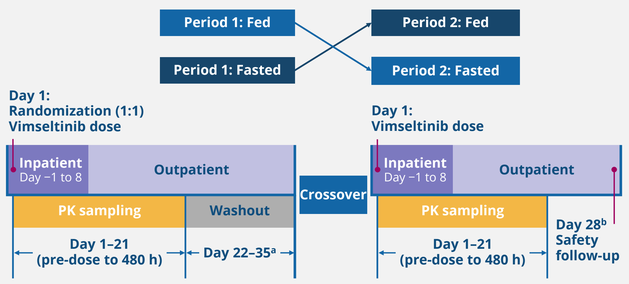
Introduction

- Tenosynovial giant cell tumor (TGCT) is a locally aggressive neoplasm caused by the dysregulation of the colony-stimulating factor 1 (*CSF1*) gene leading to overproduction of CSF1[1]
- Vimseltinib is an oral, switch-control tyrosine kinase inhibitor designed to selectively and potently inhibit the CSF1 receptor[2]
  - Vimseltinib was approved in February 2025 by the US Food and Drug Administration for the treatment of adult patients with symptomatic TGCT for which surgical resection will potentially cause worsening functional limitation or severe morbidity[3]
  - In September 2025, vimseltinib was also approved by the European Commission for the treatment of TGCT in a similar patient population[4]
- Per the US Prescribing Information and European Medicines Agency Summary of Product Characteristics vimseltinib 30 mg can be administered with or without food[3,4]
- Here, we report the results of a randomized, phase 1, crossover study that investigated the effect of a high-fat meal on the pharmacokinetics (PK) of vimseltinib in healthy adults

Methods

- Eligible participants were adults aged 18–60 years with a body mass index ≥18.5 and ≤30.4 kg/m^2
- Key exclusion criteria included history of clinically significant medical or psychiatric conditions that may interfere with the study, use of certain prescribed or over-the-counter medications, and high daily consumption of caffeine or alcohol
- Participants received a single 30-mg dose of vimseltinib in a fed or fasted state in period 1, followed by a 2-week washout period, and then a crossover between states for period 2 (**Figure 1**)
  - Participants in the fed condition received vimseltinib 30 minutes after the start of a high-fat meal (800–1000 kcal, 50% fat), which occurred following a 10-hour overnight fast
  - Participants in the fasted condition received vimseltinib following a 10-hour overnight fast and were fed a standard meal ≥4 hours after vimseltinib administration
- Plasma PK samples were collected pre-dose on day 1 and then at various time points post-dose on days 1–8 and days 10, 12, 14, and 21 in each period
- Plasma concentrations of vimseltinib and the minor metabolite DP-7005 were determined using a validated liquid chromatography tandem mass spectrometry method, and PK parameters were obtained using noncompartmental analysis
- Log-transformed PK parameters (maximum concentration [C_{max}], area under the curve [AUC] from first dose to last quantifiable concentration [$AUC_{0\text{-}tlast}$], and AUC extrapolated to infinity [$AUC_{0\text{-}inf}$]) for fed (test) vs fasted (reference) states were analyzed using an analysis of variance model with period and food as fixed effects
  - Geometric mean ratios along with their corresponding 90% confidence intervals (CIs), were constructed to determine the effect of a high-fat meal on vimseltinib and DP-7005 PK
- Safety was monitored throughout the study

Figure 1. Study design



[a]In period 1, participants had a 10- to 14-day washout period after the last in-clinic visit before crossover to period 2. The washout period was extended for up to 7 additional days for scheduling or if the participant did not meet continuation criteria as determined by the sponsor's medical monitor and the investigator. [b]In period 2, participants had a safety follow-up approximately 7 days (+3) after the last in-clinic visit.
PK, pharmacokinetic.

Results

- A total of 18 healthy adult participants were enrolled in the study
- Participant characteristics are described in **Table 1**

Table 1. Participant characteristics

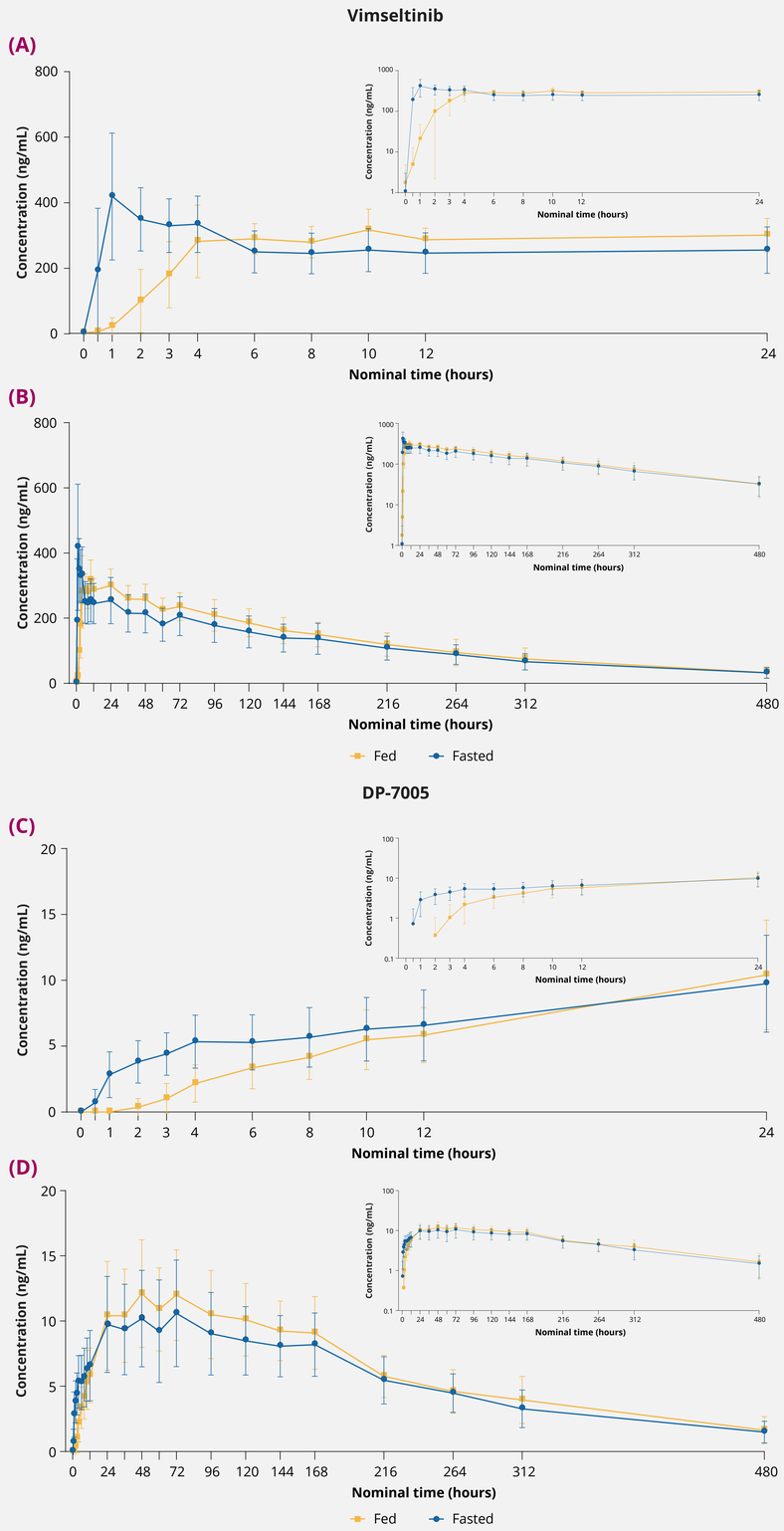
	Fed state during period 1 n = 9	Fasted state during period 1 n = 9
Age, years, median (range)	28 (20–56)	26 (20–56)
Sex, n (%)		
Female	6 (67)	5 (56)
Male	3 (33)	4 (44)
Race, n (%)		
White	8 (89)	6 (67)
Asian	1 (11)	2 (22)
Black or African American	0	1 (11)
Ethnicity, n (%)		
Not Hispanic or Latino	9 (100)	7 (78)
Hispanic or Latino	0	1 (11)
Not Reported	0	1 (11)
Weight, kg, median (range)	68.7 (53.3–84.5)	77.9 (62.5–91.8)
BMI, kg/m^2, median (range)	24.0 (20.8–28.2)	27.7 (23.2–30.1)

BMI, body mass index.

Pharmacokinetics

- Plasma concentration-time profiles for vimseltinib and the metabolite DP-7005 under fed and fasted dosing conditions are presented in **Figure 2**
- PK parameters for vimseltinib and DP-7005 following administration of vimseltinib with and without a high-fat meal are described in **Table 2** and **Figure 3**
- Median time to C_{max} (T_{max}) following vimseltinib administration was 6 hours in the fed state and 1 hour in the fasted state, and mean C_{max} was 351 ng/mL and 433 ng/mL, respectively
- The 90% CIs for the geometric mean ratios of vimseltinib $AUC_{0\text{-}tlast}$ and $AUC_{0\text{-}inf}$ were contained within the equivalence limits of 80% to 125% (**Table 3**)

Figure 2. Mean plasma concentration-time profiles of vimseltinib (A,B) and DP-7005 (C,D) over 24 hours (A,C) and 480 hours (B,D) following administration of 30 mg vimseltinib under fed and fasted conditions on linear and semi-log scales (insets)



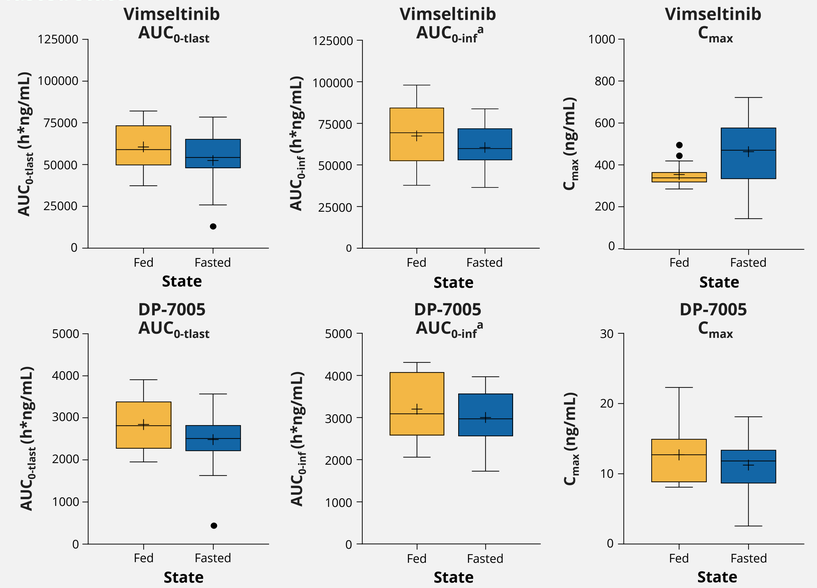
Plasma samples were analyzed using a bioanalytical method with a validated range of 1.00 to 1000 ng/mL; concentrations below the limit of quantification were set to zero (0.00 ng/mL) in the data summarization. Three participants in fasted condition discontinued after period 1 (fed condition). One participant was excluded from the fed condition as their predose concentration was >5% of C_{max} in period 2.
C_{max}, maximum concentration.

Table 2. Plasma PK parameters for vimseltinib and DP-7005 after administration of 30 mg vimseltinib under fed and fasted conditions

	Vimseltinib				DP-7005			
Parameter	**n[a]**	**Fed**	**n[a]**	**Fasted**	**n[a]**	**Fed**	**n[a]**	**Fasted**
T_{max}, h, median (range)	15	6.00 (3.00–25.4)	15	1.00 (0.500–4.00)	16	60.0 (24.0–168)	15	48.1 (24.0–144)
C_{max}, ng/mL, mean (CV%)	15	351 (15)	15	433 (43)	16	12 (31)	15	10 (50)
$AUC_{0\text{-}last}$, h*ng/mL, mean (CV%)	15	58,900 (26)	15	48,500 (49)	16	2780 (23)	15	2290 (53)
$AUC_{0\text{-}inf}$, h*ng/mL, mean (CV%)	15	65,000 (29.8)	11[b]	59,100 (23)	14[b]	3110 (25)	12[b]	2930 (23)
$t_{1/2}$, h, mean (CV%)	15	135 (28)	15	137 (32)	16	130 (48)	14	137 (34)

Relevant values are presented as geometric mean (geometric CV%).
[a]Three participants completed only the fed period; 2 participants completed only the fasted period. The predose concentration for 1 participant (fasted-fed condition) was >5% of C_{max} in period 2. [b]AUC_{Extrap} acceptance criteria was not met for reporting parameter (AUC_{Extrap}>20%) for 4 participants and they were excluded from summary statistics and subsequent calculations or analysis.
$AUC_{0\text{-}inf}$, area under the concentration time-curve from time 0 extrapolated to infinity; $AUC_{0\text{-}tlast}$, area under the concentration-time curve from time 0 to the last quantifiable dose; AUC_{Extrap}, extrapolated area under the concentration time-curve; C_{max}, maximum concentration; CV, coefficient of variation; $t_{1/2}$, terminal elimination half-life; T_{max}, time to reach maximum concentration.

Figure 3. $AUC_{0\text{-}tlast}$, $AUC_{0\text{-}inf}$, and C_{max} for vimseltinib and DP-7005 by fed or fasted state



Solid line (—) represents the median; plus sign (+) represents the mean; box represents the upper (Q3) and lower (Q1) quartiles; whiskers represent 1.5 times the IQR; circles represent outliers. Three participants completed only the fed period; 2 participants completed only the fasted period. The predose concentration for 1 participant (fasted-fed condition) was >5% of C_{max} in period 2.
[a]$AUC_{0\text{-}inf}$ acceptance criteria was not met for reporting parameter (AUC_{Extrap}>20%) for 4 participants and they were excluded from summary statistics and subsequent calculations or analysis.
$AUC_{0\text{-}inf}$, area under the concentration time-curve from time 0 extrapolated to infinity; $AUC_{0\text{-}tlast}$, area under the concentration-time curve from time 0 to the last quantifiable dose; AUC_{Extrap}, extrapolated area under the concentration time-curve; C_{max}, maximum concentration; IQR, interquartile range; Q1, quartile 1; Q3, quartile 3.

Table 3. Statistical comparison of PK parameters for vimseltinib and DP-7005

PK parameter	n[a] Fed state (Test)	n[a] Fasted state (Reference)	Geometric mean[b] Fed state (Test)	Geometric mean[b] Fasted state (Reference)	Ratio, % (90% CI) Test/reference
Vimseltinib, fed vs fasted state					
C_{max}	12	12	318	455	69.9 (62.9–77.6)
$AUC_{0\text{-}tlast}$	12	12	54,300	51,300	105.9 (99.0–113.2)
$AUC_{0\text{-}inf}$[c]	10	10	65,000	62,800	103.5 (98.2–109.1)
DP-7005, fed vs fasted state					
C_{max}	13	13	10.9	11.0	99.7 (93.2–106.7)
$AUC_{0\text{-}tlast}$	13	13	2470	2420	102.3 (96.6–108.3)
$AUC_{0\text{-}inf}$[c]	10	10	2990	3020	98.8 (95.3–102.5)

*Three participants completed only the fed period; 2 participants completed only the fasted period. The predose concentration for 1 participant (fasted-fed condition) was >5% of C_{max} in period 2 (fed).
[b]Geometric mean based on least squares mean. [c]$AUC_{0\text{-}inf}$ could not be estimated or acceptance criteria was not met for 4 participants under fasted conditions.
$AUC_{0\text{-}tlast}$, area under the concentration-time curve from time 0 to the last quantifiable dose; $AUC_{0\text{-}inf}$, area under the concentration time-curve from time 0 extrapolated to infinity; CI, confidence interval; C_{max}, maximum concentration; n, number evaluable; PK, pharmacokinetic.

Safety

- Treatment-emergent adverse events (TEAEs) occurred in 10 (63%) participants in the fed condition and 9 (60%) participants in the fasted condition (**Table 4**)
- Treatment-related TEAEs occurred in 7 (44% and 47%, respectively) participants each in the fed and fasted conditions
- All TEAEs were grades 1 or 2, except for 1 serious TEAE of grade 3 increased blood creatine phosphokinase, which occurred 47 days after dosing in the fed state
  - This TEAE was considered possibly related to vimseltinib by the investigator and resolved after 24 days
- Pruritus was the most common TEAE in either condition and the only event that occurred in >2 participants (4 [25%] and 6 [40%] in the fed and fasted conditions, respectively; **Table 4**)

Table 4. Summary of adverse events

Category	Fed state (n = 16)	Fasted state (n = 15)
Any grade TEAE, n (%)	10 (63)	9 (60)
Any grade treatment-related TEAE	7 (44)	7 (47)
Grade ≥3 TEAE, n (%)	1 (6)[a]	0
Grade ≥3 treatment-related TEAE	1 (6)[a]	0
Serious TEAE, n (%)	1 (6)[a]	0
Serious treatment-related TEAE	1 (6)[a]	0
TEAE leading to treatment discontinuation, n (%)	1 (6)[a]	0
TEAEs in ≥2 participants, n (%)		
Pruritus	4 (25)	6 (40)
Vessel puncture site hemorrhage	2 (13)	2 (13)
Lipase increased	2 (13)	2 (13)
Amylase increased	2 (13)	0
Arthralgia	2 (13)	0
Abdominal pain	0	2 (13)

The safety population included participants who received ≥1 dose of vimseltinib. Three participants completed only the fed period; 2 participants completed only the fasted period. AEs were considered treatment related if they were evaluated as "related" or "possibly related" by the investigator. Severity was assessed by the investigator according to the toxicity grade described in the NCI CTCAE v5.0.
[a]Represents the same serious TEAE of grade 3 increased creatine phosphokinase.
AE, adverse event; NCI CTCAE v5.0, National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0; TEAE, treatment-emergent AE.

CONCLUSIONS

- Administration of vimseltinib with a high-fat meal did not affect the exposures of vimseltinib or the metabolite DP-7005
- Vimseltinib demonstrated a manageable safety profile that was consistent with prior studies
- These data provide the basis for the approved dosing recommendations that vimseltinib can be administered with or without food

PRESENTED AT THE 2025 CTOS ANNUAL MEETING; BOCA RATON, FL, USA; NOVEMBER 12–15, 2025

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ACKNOWLEDGMENTS

We thank the participants, the investigators, and the investigational site staff for the study. This study was sponsored by Deciphera Pharmaceuticals, LLC, a member of ONO Pharma. Medical writing and editorial support was provided by Genevieve R Curtis, PhD, of Red Nucleus, and was funded by Deciphera Pharmaceuticals, LLC.

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