Administration of tirabrutinib suspension in a patient with primary central nervous system lymphoma: A case report

TAKEO YASU[1,2], HIROAKI OHTA[1], YOSHITO GANDO[1,2] and MASAYUKI KOBAYASHI[2,3]

[1]Department of Medicinal Therapy Research, Education and Research Unit for Comprehensive Clinical Pharmacy, Meiji Pharmaceutical University, Tokyo 204-8588, Japan; [2]Bokutoh Hospital-Meiji Pharmaceutical University Joint Research Center, Tokyo 130-8575, Japan; [3]Department of Hematology, Tokyo Metropolitan Bokutoh Hospital, Tokyo 130-8575, Japan

Received August 8, 2025; Accepted January 27, 2026

DOI: 10.3892/ol.2026.15531

Abstract. Tirabrutinib, a selective inhibitor of Bruton's tyrosine kinase, is approved in Japan for the treatment of relapsed or refractory primary central nervous system lymphoma (PCNSL). Dysphagia complicates oral tablet administration in patients with PCNSL. In the present case report, the safety, efficacy and plasma concentration of tirabrutinib administered as a suspension via a nasogastric tube is evaluated, providing insights into alternative administration methods and reviewing the relevant literature. In the present case, a 68-year-old man with PCNSL achieved two complete responses following methotrexate-based therapies but subsequently relapsed. Owing to severe dysphagia, tirabrutinib was initially administered as a suspension via a nasogastric tube and orally, and later transitioned to oral tablets. Plasma tirabrutinib concentrations were comparable following administration via nasogastric tube, oral suspension and oral tablets. After initiating tirabrutinib treatment, the patient remained clinically stable, with no recurrence of lymphoma for 1 year and no adverse events observed. A literature review identified 17 studies describing 19 patients who received a tyrosine kinase inhibitor (TKI) as a suspension. Tirabrutinib remains a crucial treatment option for refractory PCNSL; however, alternative administration routes are required for patients with dysphagia. The present case demonstrated the feasibility and safety of tirabrutinib suspension administration, with plasma concentrations comparable to those achieved with tablet administration. Further pharmacokinetic studies are warranted to evaluate the administration of TKI suspensions in a broader patient population.

Correspondence to: Dr Takeo Yasu, Department of Medicinal Therapy Research, Education and Research Unit for Comprehensive Clinical Pharmacy, Meiji Pharmaceutical University, 2-522-1 Noshio, Kiyose, Tokyo 204-8588, Japan
E-mail: yasutakeo-tky@umin.ac.jp

Abbreviations: PCNSL, primary central nervous system lymphoma; BTK, Bruton's tyrosine kinase; MTX, methotrexate; TKI, tyrosine kinase inhibitor; CR, complete response, C_2, plasma concentration of tirabrutinib at 2 h after administration of tirabrutinib; C_{max}, maximum plasma concentration; HPLC, high-performance liquid chromatography; UV, ultraviolet; AUC, area under the curve; MRI, magnetic resonance imaging

Key words: tirabrutinib, PCNSL, plasma concentration, suspension administration, TKI

Introduction

Tirabrutinib, an orally selective and irreversible Bruton's tyrosine kinase (BTK) inhibitor, covalently binds to BTK (1). Primary central nervous system lymphomas (PCNSLs) are rare and aggressive extranodal lymphomas, with a rising incidence particularly in the elderly population (2). While the majority of lymphoma cases are diffuse large B-cell lymphomas, PCNSL exhibits significant clinicopathological and radiological diversity, and the diagnosis remains challenging, often requiring invasive biopsies (3). Furthermore, the non-germinal center B-cell immunohistochemical subtype is more common in PCNSL than the germinal center B-cell subtype, and is associated with unfavorable prognostic factors, such as advanced age (>60 years), a high Ki-67 labeling index and a shorter overall survival time (4). PCNSLs are commonly treated with high-dose methotrexate (MTX)-based regimens or induction therapy comprising whole-brain radiation therapy, followed by high-dose systemic chemotherapy (5). Although highly responsive to first-line chemotherapy and radiotherapy, ~50% of patients with PCNSL experience relapse or refractory disease within 1 year (6). Tirabrutinib, a second-generation BTK inhibitor, was first approved in Japan for the treatment of relapsed or refractory PCNSL. Tirabrutinib targets key signaling pathways, such as the nuclear factor-κB pathway, which are critical for tumor cell survival (7). Patients with PCNSL often present with neurological deficits, and the clinical impact of dysphagia is particularly important in this population. Tablets with a total dimension >21 mm (length, width and thickness combined) have been reported to affect adherence in patients with swallowing disorders (8). The tirabrutinib tablet has a combined dimension of 21.5 mm. Therefore, administering tirabrutinib in patients with PCNSL can be difficult in cases where oral administration is not feasible. If tirabrutinib therapy is critical, administration of

tirabrutinib as a suspension may be necessary. However, the manufacturer does not provide pharmacokinetic or safety data for tirabrutinib administered as a suspension or in crushed form. Two previous reports have described the administration of tirabrutinib suspension via a nasogastric tube in patients with PCNSL (9,10), but none have reported plasma concentrations. In the present case report, the safety, efficacy and plasma concentration of tirabrutinib administered as a suspension is evaluated in a patient with an inability to swallow tablets. Additionally, the relevant literature on the suspension administration of other tyrosine kinase inhibitors (TKIs), similar to that described in the present case, is reviewed.

Case report

A 68-year-old man first presented in February 2023 to Tokyo Metropolitan Bokutoh Hospital (Tokyo, Japan) with weakness in the right leg and diplopia in the right eye. The diagnosis of primary central nervous system lymphoma (PCNSL) was established based on cerebrospinal fluid (CSF) cytology, immunocytochemical analysis and flow cytometric immunophenotyping, in conjunction with characteristic radiological findings. CSF cytology revealed clusters of atypical large lymphoid cells with irregular nuclei and prominent nucleoli. Immunocytochemical staining demonstrated strong membranous CD20 expression in the majority of atypical cells, and Ki-67 staining showed a high proliferative index. Flow cytometry confirmed a dominant B-cell population expressing CD19 and CD20. Given the typical MRI findings (Fig. 1A) and the clinical context, a diagnosis of PCNSL was made. A stereotactic brain biopsy was not performed due to the deep midbrain location of the lesion and the associated procedural risk. After diagnosis, the patient received intrathecal chemotherapy consisting of 40 mg/body prednisolone, 15 mg/body methotrexate and 40 mg/body cytarabine per administration. In parallel, the patient underwent methotrexate-based systemic chemotherapy combined with rituximab for four cycles. Rituximab was administered at 375 mg/m^2 on day 1 of each 21-day cycle, and high-dose methotrexate was administered at 3,500 mg/m^2 on day 3. Brain magnetic resonance imaging (Fig. 1B) demonstrated disappearance of the intracranial lesions, and the patient was judged to have achieved a complete response (CR). However, 3 months later, the patient relapsed and was treated again with four cycles of intrathecal MTX, cytarabine and steroids using the same dosing as previously applied. This was followed by whole-brain radiotherapy delivered at a total dose of 36 Gy in 20 fractions, which resulted in another CR. At 1-month post-CR, the patient presented with facial paralysis (inability to close the right eye), dysphagia and gait instability. Brain magnetic resonance imaging (MRI) confirmed a second relapse (Fig. 1C). Intrathecal MTX, cytarabine and steroids were reintroduced at the same dosage as previously applied, and tirabrutinib was initiated. Tirabrutinib was administered at a dose of 480 mg once daily on an empty stomach, which is the approved dose in Japan for the treatment of relapsed/refractory PCNSL. Owing to severe dysphagia caused by facial paralysis, a nasogastric tube was inserted and tirabrutinib was administered as a suspension through this once daily. Following a protocol similar to that reported by Yoshioka *et al* (9), six tablets of tirabrutinib (80 mg) were placed in a container, 20 ml of warm water at 55˚C was added and the mixture was left for 10 min to dissolve. After confirming complete dissolution of the tirabrutinib tablets in the container, the resulting suspension was drawn into a syringe and administered via the nasogastric tube. To ensure complete administration of the suspension and prevent tube obstruction, the nasogastric tube was flushed with 20 ml of water after administering the suspension. Upon admission in November 2023, the patient received nutritional support via a nasogastric tube, and the facial paralysis gradually improved. Notably, the patient's dysphagia showed marked clinical improvement within 10 days of tirabrutinib initiation, allowing the patient to transition to an oral suspension (480 mg once daily) by day 11. By day 22, the patient was able to swallow food and tirabrutinib tablets. The patient was discharged on day 23, and oral tablets (480 mg once daily) were continued thereafter. No adverse events were observed during the suspension administration period.

Blood samples were collected on day 5 of tirabrutinib treatment with the patient's consent. Plasma tirabrutinib concentration (C_2) was evaluated 2 h after tirabrutinib administration. This was based on the assumption that C_2 would be close to maximum plasma concentration (C_{max}), given that the mean time to C_{max} was 2.87 h (11). C_2 samples (50 μl plasma) were evaluated using high-performance liquid chromatography (HPLC) coupled with ultraviolet (UV) spectroscopy. The HPLC system included pumps (PU-4180), a UV detector (UV-4075) and an autosampler (AS-4550) (Jasco Corporation). The mobile phase comprised 0.5% potassium dihydrogen phosphate (KH_2PO_4, pH 4.5) and acetonitrile (58:42, v/v), pumped at a flow rate of 1.2 ml/m at 22˚C. Tirabrutinib and ibrutinib (internal standard) were detected at 215 nm using Capcell Pak C18 MG II reversed-phase columns 250x4.6 mm (length x inner diameter) (Osaka Soda Co., Ltd.). The accuracy, precision, pretreatment recovery rate and sample stability of this tirabrutinib detection method were validated according to the U.S. Food and Drug Administration (12).

Hepatic function, which influences tirabrutinib metabolism, was judged to be normal in the patient since blood tests showed that hepatobiliary enzyme levels (aspartate aminotransferase, alanine aminotransferase and total bilirubin) were within the reference ranges. Concomitant previously prescribed medications included 10 mg/day epinastine, 990 mg/day magnesium oxide, 20 mg/day famotidine, 1 mg/day eszopiclone and 900 mg/day acetaminophen, none of which interacted with tirabrutinib. C_2 values on days 5, 6, 8, 22 and 112 were 1,057, 1,064, 1,002, 1,085 and 1,042 ng/ml, respectively. Suspension was administered via the nasogastric tube on days 5, 6 and 8, whereas oral suspension was administered on day 22 (Fig. 2). Additionally, serum soluble interleukin-2 receptor (siL-2R) levels (normal reference range, 157-474 U/ml) decreased from 795 U/ml at relapse to 607 U/ml on day 8 and to 532 U/ml on day 147 after the initiation of tirabrutinib. Oral tirabrutinib tablets were administered on day 112 during the outpatient visit. Follow-up visits were conducted approximately every 2 months, and brain magnetic resonance imaging was performed approximately every 6 months. At the 1-year follow-up in November 2024, the patient remained clinically stable, with no

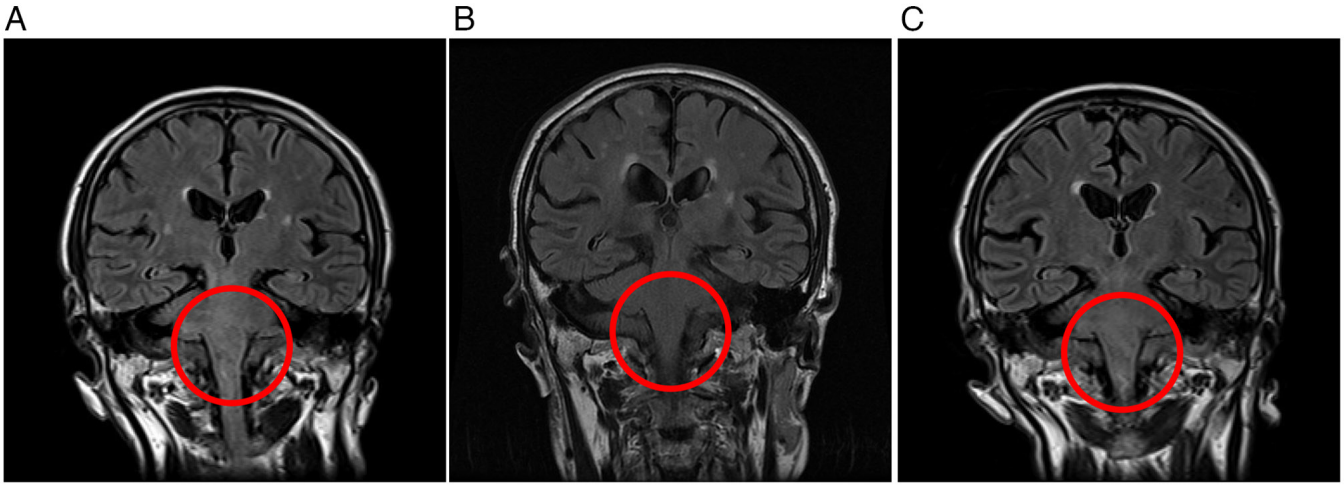

Figure 1. Serial brain coronal fluid-attenuated inversion recovery images of the brain. (A) At initial presentation, hyperintense lesions were observed in the brainstem region. (B) After chemotherapy, complete radiographic resolution of the lesions was confirmed. (C) At second relapse, recurrent hyperintense lesions were detected in the same anatomical region. The red circles indicate the area of interest.

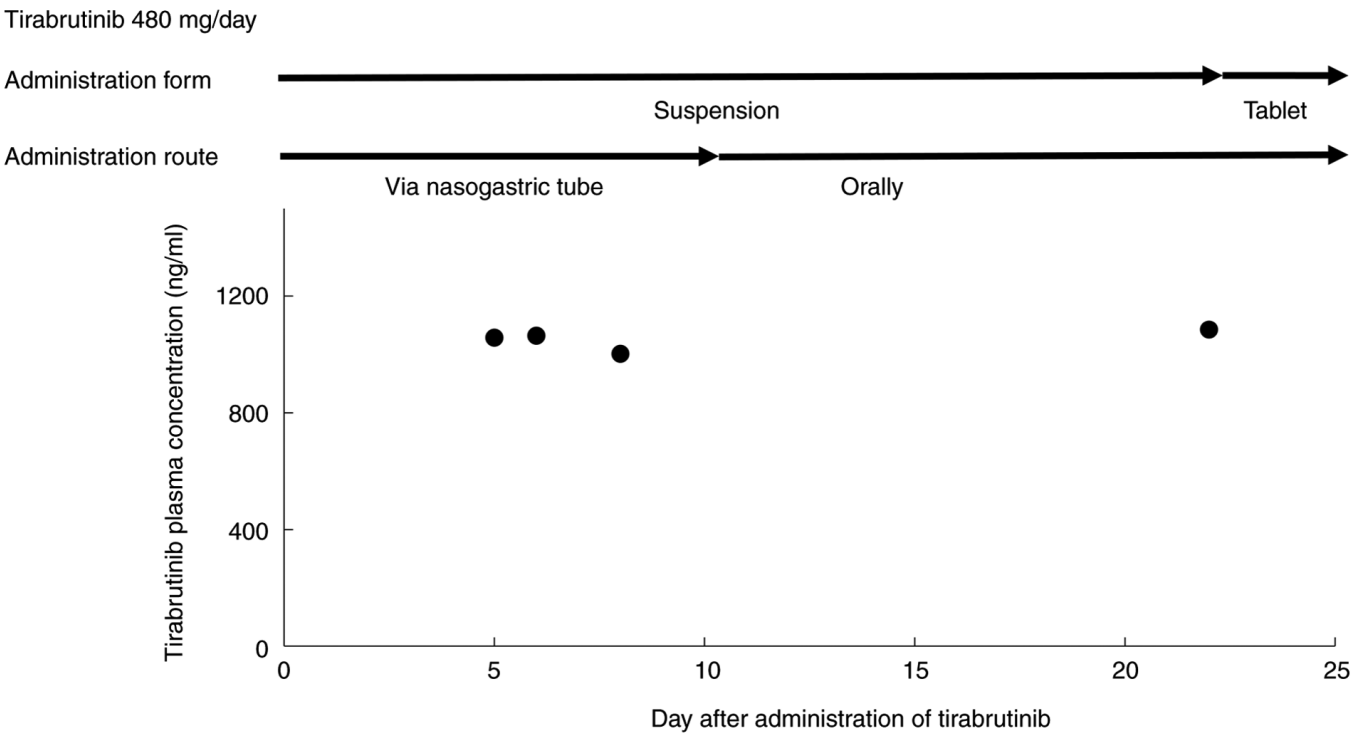

Figure 2. Course of tirabrutinib administration and plasma concentrations. Circles indicate maximum plasma concentrations of tirabrutinib (ng/ml). The patient received 480 mg tirabrutinib once daily on an empty stomach. Tirabrutinib suspension was administered via a nasogastric tube for the first 10 days and then orally from days 11 to 22.

evidence of intracranial or intraorbital lymphoma recurrence on brain MRI. Tirabrutinib treatment has been continuously maintained, and complete remission has been sustained as of December 2025.

Literature review

Using PubMed (https://pubmed.ncbi.nlm.nih.gov/), 17 studies describing 19 patients who were administered TKI suspension were identified (9,10,13-27). These cases are summarized in Table I. The duration of suspension administration ranged from 2 days to 14 months. As in the present case, tirabrutinib was the most frequently used TKI (4 patients), followed by alectinib (3 patients). Lung cancer was the most common malignancy (10 patients). Pharmacokinetics study and blood levels of TKIs were not evaluated in any of the 17 articles.

Discussion

Treatment options for refractory PCNSL are limited, and tirabrutinib remains a crucial therapeutic choice. For patients with dysphagia, alternative administration routes such as

Table I. Cases of administration of tyrosine kinase inhibitor suspension.

First author, year	Tyrosine kinase inhibitor	Malignancy	Age, years	Sex	Administration route and daily dosage (duration)	(Refs.)
Yoshioka *et al*, 2021	Tirabrutinib	PCNSL	76	Female	Nasogastric tube, 480 mg (14 days)	(9)
Yoshioka *et al*, 2022	Tirabrutinib	PCNSL	77/77/70	Female/ female/female	Nasogastric tube, 480 mg (data not shown)	(10)
Okahashi *et al*, 2020	Ibrutinib	Mantle cell lymphoma	70	Male	Nasogastric tube, 560 mg (90 days)	(13)
Alsuliman *et al*, 2018	Ibrutinib	Mantle cell lymphoma	69	Male	Nasogastric tube, 560 mg (2 days)	(14)
Molinaro *et al*, 2019	Lenvatinib	Thyroid cancer	62	Female	Nasogastric tube, 20 mg (1 month); 10 mg (1 month)	(15)
Kawano *et al*, 2020	Lenvatinib	Thyroid cancer	54	Female	Nasogastric tube, 10 mg (10 days)	(16)
Tani *et al*, 2022	Osimertinib	Lung cancer	78	Female	Nasogastric tube, 80 mg (20 days)	(17)
Takeda *et al*, 2017	Osimertinib	Lung cancer	73	Female	Nasogastric tube, 80 mg (20 days)	(18)
Suzumura *et al*, 2014	Gefitinib	Lung cancer	72	Female	Nasogastric tube, 250 mg (9 months)	(19)
Bejarano Varas *et al*, 2019	Alectinib	Lung cancer	66	Female	Nasogastric tube and percutaneous endoscopic gastrostomy tube, 1,200 mg (30 days)	(20)
Kanai *et al*, 2017	Alectinib	Lung cancer	76	Female	Nasogastric tube, 600 mg (14 months)	(21)
Thomas *et al*, 2021	Alectinib	Lung cancer	90	Male	Nasogastric tube and percutaneous endoscopic gastrostomy tube, 1,200 mg (6 months)	(22)
Bosch-Barrera *et al*, 2014	Erlotinib	Lung cancer	60	Female	Nasogastric tube, 150 mg (5 days)	(23)
Sasaki *et al*, 2021	Lorlatinib	Lung cancer	71	Male	Nasogastric tube, 100 mg (4 weeks)	(24)
Wang *et al*, 2023	Lorlatinib	Lung cancer	49	Male	Nasogastric tube, 100 mg (18 days)	(25)
Jang *et al*, 2024	Trametinib, dabrafenib	Lung cancer	44	Female	Nasogastric tube, 300 mg (33 days); Nasogastric tube, 2 mg (33 days)	(26)
Muta *et al*, 2010	Imatinib	Chronic myeloid leukemia	64	Female	Nasogastric tube, 400 mg (3 days); 600 mg (5 days)	(27)

PCNSL, primary central nervous system lymphoma.

nasogastric or gastrostomy tubes may be essential. To the best of our knowledge, this is the first report to evaluate plasma tirabrutinib concentrations following suspension administration via a nasogastric tube or oral administration in a patient with PCNSL.

The C_2 values obtained in the present case during nasogastric and oral administration of tirabrutinib suspension (from days 5 to 22) were comparable to the C_{max} (1,220 ng/ml) reported in a previous study (28) involving a dose of 480 mg/day under fasting conditions. Additionally, the C_2 value on day 112 was consistent with that reported in the previous study (28). However, it must be noted that the reliance on C_2 (a single-point measurement) provides only a limited snapshot of the drug's bioavailability. Without area under the curve (AUC) data,

bioequivalence cannot be definitively confirmed. Future pharmacokinetic evaluations should consider the 24-h AUC rather than C_2 alone. In the present case, dysphagia markedly improved in the patient within 10 days of initiating tirabrutinib suspension. This clinical improvement is consistent with previous reports (9,10), which showed that tirabrutinib suspension can induce a partial response within 2-4 weeks. In the present case, this clinical recovery was accompanied by a rapid decrease in serum sIL-2R levels. This reduction in the tumor marker is consistent with effective drug absorption and an early antineoplastic effect, which likely contributed to the resolution of neurological symptoms. While the clinical improvement with regard to dysphagia may not be solely attributed to tirabrutinib, as the effects of intrathecal MTX, cytarabine and steroids must be considered, the administration of suspension was nonetheless the essential facilitator for treatment initiation. No adverse events were observed during either nasogastric or oral administration of the suspension. Although, to the best of our knowledge, only 5 cases of PCNSL treated with tirabrutinib suspension have been published to date (9,10), including the present case, the administration of tirabrutinib suspension appears to be a viable treatment option for patients with relapsed or refractory PCNSL who are unable to swallow tablets. However, it cannot be definitively concluded that the tirabrutinib suspension and tablet formulations are bioequivalent based on this single-point measurement. This suspension administration method has off-label use, but it was performed with informed consent to save the patient's life. Therefore, suspension administration requires careful handling. Future prospective studies with serial blood sampling are warranted to evaluate the full pharmacokinetic profile and long-term efficacy of tirabrutinib suspension in this patient population.

An aging population likely results in an increased number of elderly patients with dysphagia and poor adherence to TKI therapy. Feeding tube placement has not been associated with improved survival or post-discharge outcomes in older hospitalized adults with dementia (29). Alectinib suspension has been reported to be safe and effective in patients with anaplastic lymphoma kinase-positive non-small cell lung cancer and poor performance status after failure of 14-month crizotinib therapy with continuous treatment via a feeding tube (21). In several case reports, alternative administration of TKI suspensions to patients with transient dysphagia associated with cancer progression and inability to be treated orally improved the dysphagia and other tumor-related symptoms (such as dyspnea and impaired consciousness), allowing the initiation of oral therapy (9,10,13-17,20,23-26). The patient in the present report also showed improvement in swallowing function after 10 days of administration of tirabrutinib suspension. However, the administration of TKIs in suspension form is not officially approved or recommended by pharmaceutical companies, making it an off-label use in clinical practice. Consequently, in routine clinical practice, TKI suspensions may have to be administered via nasogastric tubes. Pharmacokinetic studies on the administration of TKI suspensions have been conducted for gefitinib (30), alectinib (31), dacomitinib (32), dasatinib (33) and pazopanib (34). For gefitinib and alectinib administered to healthy volunteers, the AUC and C_{max} were generally similar for suspensions, tablets and capsules (30,31). For dacomitinib, C_{max} and AUC were significantly decreased when administered via percutaneous feeding gastrostomy tubes compared with oral administration of tablets, in patients with locally advanced head and neck squamous cell carcinoma (32). Compared with oral tablet administration, greater mean drug exposure, decreased half-life and higher C_{max} were observed in patients receiving dasatinib via percutaneous endoscopic gastrostomy tubes (33). In a phase I study evaluating pharmacokinetics, the administration of a single dose of pazopanib suspension increased AUC and C_{max} and decreased time to C_{max} in patients with advanced cancer, indicating an increased rate and extent of oral absorption compared with administration of the whole tablet (34). Pharmacokinetic changes in suspension vary by TKI; for instance, dacomitinib shows decreased exposure via tubes, while pazopanib shows increased absorption (32,34). Such variability necessitates caution when extrapolating results. Therefore, further studies are warranted to evaluate the pharmacokinetics, safety and clinical outcomes of tirabrutinib and other TKIs in suspension form across a broader patient population. Furthermore, as tirabrutinib and other TKIs are antineoplastic agents, healthcare staff must follow hazardous drug handling guidelines, such as using closed systems or personal protective equipment during preparation of suspensions to prevent occupational exposure.

In conclusion, the present case demonstrates the potential feasibility and efficacy of tirabrutinib suspension for patients with PCNSL and severe dysphagia. While C_2 levels were comparable across different administration routes, the lack of comprehensive AUC data and the small sample size remain significant limitations. In the relevant literature, 19 cases of administration of TKI suspension have been reported; however, pharmacokinetic studies were not evaluated in these cases.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

TY contributed to the conception and design of the study, analyzed the data and drafted the manuscript. TY and YG were responsible for measuring plasma tirabrutinib concentrations and analyzing the pharmacokinetic data. MK performed the clinical diagnosis and examinations, interpreted the radiological findings, and was responsible for collecting and analyzing the patient's clinical data. HO contributed to the literature review, collected comparative data and analyzed the patient's clinical data. TY and YG confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for publication.

Competing interests

The authors declare that they have no competing interests.

References

1. Liclican A, Serafini L, Xing W, Czerwieniec G, Steiner B, Wang T, Brendza KM, Lutz JD, Keegan KS, Ray AS, *et al*: Biochemical characterization of tirabrutinib and other irreversible inhibitors of Bruton's tyrosine kinase reveals differences in on- and off-target inhibition. Biochim Biophys Acta Gen Subj 1864: 129531, 2020.
2. Korfel A, Schlegel U, Johnson DR, Kaufmann TJ, Giannini C and Hirose T: Case-based review: Primary central nervous system lymphoma. Neurooncol Pract 4: 46-59, 2017.
3. Fiorentino V, Pizzimenti C, Pierconti F, Lentini M, Ieni A, Caffo M, Angileri F, Tuccari G, Fadda G, Martini M and Larocca LM: Unusual localization and clinical presentation of primary central nervous system extranodal marginal zone B-cell lymphoma: A case report. Oncol Lett 26: 408, 2023.
4. Rizzuto I, Pizzimenti C, Fiorentino V, Scarcella SC, Martini M, Granata F, Germanò A, Ieni A and Tuccari G: Morphological, immunophenotypic and neuroradiological characteristics of primitive B-large cell diffuse lymphoma of the central nervous system: A retrospective cohort analysis. Oncol Lett 30: 433, 2025.
5. Horbinski C, Nabors LB, Portnow J, Baehring J, Bhatia A, Bloch O, Brem S, Butowski N, Cannon DM, Chao S, *et al*: NCCN guidelines® insights: Central nervous system cancers, version 2.2022. J Natl Compr Canc Netw 21: 12-20, 2023.
6. Schaff L, Nayak L and Grommes C: Bruton's tyrosine kinase (BTK) inhibitors for the treatment of primary central nervous system lymphoma (PCNSL): Current progress and latest advances. Leuk Lymphoma 65: 882-894, 2024.
7. Ferreri AJM, Calimeri T, Cwynarski K, Dietrich J, Grommes C, Hoang-Xuan K, Hu LS, Illerhaus G, Nayak L, Ponzoni M and Batchelor TT: Primary central nervous system lymphoma. Nat Rev Dis Primers 9: 29, 2023.
8. Kabeya K, Satoh H, Hori S, Miura Y and Sawada Y: Threshold size of medical tablets and capsules: Based on information collected by Japanese medical wholesaler. Patient Prefer Adherence 14: 1251-1258, 2020.
9. Yoshioka H, Okuda T, Nakao T, Fujita M and Takahashi JC: Experience with nasogastric tube administration of tirabrutinib in the treatment of an elderly patient with primary central nervous system lymphoma. Int Cancer Conf J 10: 290-293, 2021.
10. Yoshioka H, Okuda T, Nakao T, Fujita M and Takahashi JC: Experience with tirabrutinib in the treatment of primary central nervous system lymphoma that is difficult to treat with standard treatment. Anticancer Res 42: 4173-4178, 2022.
11. Narita Y, Nagane M, Mishima K, Terui Y, Arakawa Y, Yonezawa H, Asai K, Fukuhara N, Sugiyama K, Shinojima N *et al*: Phase I/II study of tirabrutinib, a second-generation Bruton's tyrosine kinase inhibitor, in relapsed/refractory primary central nervous system lymphoma. Neuro Oncol 23: 122-133, 2021.
12. National Library of Medicine: Guidance for Industry: Bioanalytical Method Validation. Center for Drug Evaluation and Research, Rockville, MD, 2018. Available: http://resource.nlm.nih.gov/101734209.
13. Okahashi N, Uchihara M and Hoshino E: Mantle cell lymphoma with central nervous system relapse successfully treated with nasogastric-tube administration of ibrutinib. Rinsho Ketsueki 61: 1508-1510, 2020 (In Japanese).
14. Alsuliman T, Belghoul M and Choufi B: Ibrutinib treatment through nasogastric tube in a comatose patient with central nervous system localization of mantle cell lymphoma. Case Rep Hematol 2018: 5761627, 2018.
15. Molinaro E, Viola D, Viola N, Falcetta P, Orsolini F, Torregrossa L, Vagli P, Ribechini A, Materazzi G, Vitti P and Elisei R: Lenvatinib administered via nasogastric tube in poorly differentiated thyroid cancer. Case Rep Endocrinol 2019: 6831237, 2019.
16. Kawano F, Yonekawa T, Yamaguchi H, Shibata N, Tashiro K, Ikenoue M, Munakata S, Higuchi K, Tanaka H, Sato Y, *et al*: Nasogastric administration of lenvatinib solution in a mechanically ventilated patient with rapidly growing anaplastic thyroid cancer. Endocrinol Diabetes Metab Case Rep 2020: 20-0064, 2020.
17. Tani N, Takatsuka S, Kataoka N, Kunimatsu Y, Tsutsumi R, Sato I, Tanimura M, Nakano T, Tanimura K, Kato D and Takeda T: Nasogastric administration of osimertinib suspension for an epidermal growth factor receptor-mutated lung cancer causing an esophageal stricture: Case report. Ann Palliat Med 11: 1542-1545, 2022.
18. Takeda T, Itano H, Takeuchi M, Nishimi Y, Saitoh M and Takeda S: Osimertinib administration via nasogastric tube in an EGFR-T790M-positive patient with leptomeningeal metastases. Respirol Case Rep 5: e00241, 2017.
19. Suzumura T, Yonesaka K, Tsukuda H and Fukuoka M: Successful gefitinib treatment administration via gastrostomy tube in a patient with non-small cell lung cancer with dysphagia. BMJ Case Rep 2014: bcr2013202705, 2014.
20. Bejarano Varas MT, Gould S and Charlot M: Response to alectinib oil-based suspension in anaplastic lymphoma kinase-positive non-small cell lung cancer in a patient unable to swallow: A case report. J Oncol Pharm Pract 25: 1722-1725, 2019.
21. Kanai O, Kim YH, Nakatani K, Fujita K and Mio T: Nasogastric tube-administered alectinib achieved long-term survival in a crizotinib-refractory nonsmall cell lung cancer patient with a poor performance status. Clin Case Rep 5: 927-930, 2017.
22. Thomas QD, Pautas M, Guilhaume MN, Fiteni F, Ge T and Girard N: Enteral administration of alectinib for ALK-positive non-small cell lung cancer in an elderly patient: A case report. Medicine (Baltimore) 100: e27611, 2021.
23. Bosch-Barrera J, Sais E, Lorencio C, Porta R, Izquierdo A, Menéndez JA, Brunet J, Sirvent JM and Rosell R: Successful empirical erlotinib treatment of a mechanically ventilated patient newly diagnosed with metastatic lung adenocarcinoma. Lung Cancer 86: 102-104, 2014.
24. Sasaki K, Yokota Y, Isojima T, Fujii M, Hasui K, Chen Y, Saito K, Takahata T, Kindaichi S and Sato A: Enteral lorlatinib after alectinib as a treatment option in anaplastic lymphoma kinase-positive non-small cell lung cancer with triple problems: Carcinomatous meningitis, poor performance status, and dysphagia-a case report. Respirol Case Rep 9: e00796, 2021.
25. Wang H, Wu Z, Shi G, Zhou J and Xiao Z: Enteral lorlatinib after immune hyperprogression as a treatment option for anaplastic lymphoma kinase-positive non-small cell lung cancer: A case report. Oncol Lett 26: 526, 2023.
26. Jang C, Lau SC and Velcheti V: To crush or not to crush: Administering dabrafenib and trametinib through a nasogastric tube in a critically ill patient with nonsmall cell lung cancer-a case report and review of literature of targeted therapies given through enteral feeding tubes. Clin Lung Cancer 25: e124-e128, 2024.
27. Muta T, Sawada Y, Moriyama Y, Seike Y, Tokuyama T, Ueda Y and Fujisaki T: Chronic myeloid leukemia complicated with cerebellar hemorrhage and acute hydrocephalus successfully treated with imatinib and intensive supportive care. Rinsho Ketsueki 51: 1769-1774, 2010 (In Japanese).
28. Munakata W, Ando K, Hatake K, Fukuhara N, Kinoshita T, Fukuhara S, Shirasugi Y, Yokoyama M, Ichikawa S, Ohmachi K, *et al*: Phase I study of tirabrutinib (ONO-4059/GS-4059) in patients with relapsed or refractory B-cell malignancies in Japan. Cancer Sci 110: 1686-1694, 2019.
29. Hartford AM, Li W, Qureshi D, Talarico R, Fung SG, Bush SH, Casey G, Isenberg SR, Webber C and Tanuseputro P: Use of feeding tubes among hospitalized older adults with dementia. JAMA Netw Open 8: e2460780, 2025.
30. Cantarini MV, McFarquhar T, Smith RP, Bailey C and Marshall AL: Relative bioavailability and safety profile of gefitinib administered as a tablet or as a dispersion preparation via drink or nasogastric tube: Results of a randomized, open-label, three-period crossover study in healthy volunteers. Clin Ther 26: 1630-1636, 2004.

31. Liu SN, Agarwal P, Heinig K, Datye A, Sturm-Pellanda C, Crugnola A, Arca M and Miles D: Relative bioavailability and food effect study of an oral suspension of alectinib in healthy volunteers using venipuncture and capillary microsampling. Clin Transl Sci 16: 1085-1096, 2023.
32. Chiu JW, Chan K, Chen EX, Siu LL and Abdul Razak AR: Pharmacokinetic assessment of dacomitinib (pan-HER tyrosine kinase inhibitor) in patients with locally advanced head and neck squamous cell carcinoma (LA SCCHN) following administration through a gastrostomy feeding tube (GT). Invest New Drugs 33: 895-900, 2015.
33. Brooks HD, Glisson BS, Bekele BN, Johnson FM, Ginsberg LE, El-Naggar A, Culotta KS, Takebe N, Wright J, Tran HT and Papadimitrakopoulou VA: Phase 2 study of dasatinib in the treatment of head and neck squamous cell carcinoma. Cancer 117: 2112-2119, 2011.
34. Heath EI, Forman K, Malburg L, Gainer S, Suttle AB, Adams L, Ball H and LoRusso P: A phase I pharmacokinetic and safety evaluation of oral pazopanib dosing administered as crushed tablet or oral suspension in patients with advanced solid tumors. Invest New Drugs 30: 1566-1574, 2012.