CINC280AJP01 Synopsis

Title	Specified use-results survey of Tabrecta Tablets (*MET* exon 14 skipping mutation-positive unresectable advanced/recurrent non-small cell lung cancer, CINC280AJP01)
Date	June 20, 2025
Type of NIS	NIS with Primary Data Collection; Novartis Drug NIS
Key words	Japan, Tabrecta, capmatinib, non-small cell lung cancer, *MET* exon 14 skipping, non-interventional study, post-marketing surveillance
Rationale and background	Tabrecta Tablets (hereafter called Tabrecta) (generic name: capmatinib) is a potent selective oral MET inhibitor. A study of capmatinib to evaluate its *in vitro* MET inhibition activities and selectivity showed adenosine triphosphate-competitive and reversible inhibition of both wild-type and mutant MET activities with a very high selectivity towards MET. A phase II study of capmatinib alone (400 mg per dosing, BID, daily) (CINC280A2201) was conducted in patients with *MET*-amplified or *MET* exon 14 skipping mutation-positive unresectable advanced/recurrent NSCLC. The Study A2201 results showed prompt, high and long-lasting antitumor responses following administration of capmatinib at 400 mg twice-daily in *MET* mutation-positive NSCLC patients. In Japan, Tabrecta Tablets was approved on June 29, 2020 for an indication of "*MET* exon 14 skipping mutation-positive unresectable advanced/recurrent NSCLC". However, since the number of Japanese patients enrolled in clinical studies was limited, this special drug use-results surveillance was conducted as an additional pharmacovigilance activity as required in the approval condition, in all patients treated with Tabrecta until post-marketing data are collected from a specified number of patients to collect data on the safety and effectiveness of Tabrecta as early as possible so that necessary measures for proper use of Tabrecta can be taken.
Research objectives	To evaluate the safety and effectiveness of Tabrecta in clinical use in patients with *MET* exon 14 skipping mutation-positive unresectable advanced/recurrent non-small cell lung cancer. As part of the safety evaluations, the occurrence of the events specified as safety specifications, which are described below, will be investigated in particular. [Safety specifications] Hepatotoxicity, interstitial lung disease, renal impairment, fluid retention, acute pancreatitis, photosensitivity
Study design	This study is an uncontrolled, primary data collection-based observational study to be conducted as a central registration system,

	multicenter specified use-results survey. As an all-case study, this study collected all patients treated with Tabrecta in a specified post-marketing period. The observation period of each patient was up to 1 year (52 weeks).
Study requirements	Not applicable
Population	All patients receiving Tabrecta for *MET* exon 14 skipping mutation-positive unresectable advanced/recurrent NSCLC during a specified post-marketing period. By allowing patients who started Tabrecta administration before the conclusion of a contract for this study to be included in the study population after the contract, all patients treated with Tabrecta were enrolled in this study.
Variables	Patient characteristics, administration data, adverse events, antitumor response etc.
Result	This study was started on August 26, 2020 in patients who started Tabrecta administration before September 30, 2023. By the end of study (February 28, 2025), 109 patients were registered as patients in the scope of CRF completion and all CRF data were locked. [Study overview] The safety analysis set consisted of 102 patients while the effectiveness analysis set consisted of 82 patients. Of the safety analysis set, accounted for 50.00% (51/102 patients). The mean age (standard deviation) was 72.6 (9.15) years, with those aged ≥ 15 and < 65 years accounting for 17.65% (18/102 patients) and those aged ≥ 65 years accounting for 80.39% (82/102 patients). As for the staging of lung cancer, many patients were at Stage IVA (27.45% [28/102 patients]) or Stage IVB (50.98% [52/102 patients]). The median (range) duration of treatment with Tabrecta (including treatment interruptions) was 98.0 (1-364) days and the actual duration of dosing (except treatment interruptions) was 89.5 (1-364) days. The daily mean dose of Tabrecta was ≥ 200 mg/day and < 400 mg/day in 8.82% (9/102 patients), ≥ 400 mg/day and < 600 mg/day in 23.53% (24/102 patients), ≥ 600 mg/day and < 800 mg/day in 18.63% (19/102 patients), and 800 mg/day in 49.02% (50/102 patients). All patients were treated at doses within the approved range. [Safety] The incidence of adverse reactions was 75.49% (77/102 patients). The common adverse reactions (in ≥ 5 patients) were oedema peripheral in 15.69% (16/102 patients), renal impairment in 14.71% (15/102 patients), nausea and blood creatinine increased in 13.73% (14/102 patients) each, oedema in 12.75% (13/102 patients), decreased appetite in 6.86% (7/102 patients), and fluid retention, interstitial lung disease, and hepatic function abnormal in 4.90% (5/102 patients) each. Adverse reactions corresponding to the safety specifications were hepatotoxicity in 10.78% (11/102 patients), interstitial lung disease in 8.82% (9/102 patients), renal impairment in 28.43% (29/102 patients), fluid retention in 23.53% (24/102 patients), and acute

	pancreatitis in 0.98% (1/102 patients). No adverse reaction corresponding to photosensitivity was reported. The incidences of common adverse reactions (in ≥ 3 patients) of Grade ≥ 3 corresponding to the safety specifications were 5.88% (6/102 patients) for hepatotoxicity (PT: hepatic function abnormal, alanine aminotransferase increased, aspartate aminotransferase increased, liver disorder) and 2.94% (3/102 patients) each for interstitial lung disease (PT: interstitial lung disease, pulmonary toxicity) and fluid retention (PT: fluid retention, oedema peripheral, pleural effusion). During the observation period, 24 patients experienced adverse events resulting in death. Among these patients, the causal relationship between adverse events and Tabrecta was ruled out in 23 patients. However, death due to aspiration in 1 patient was assessed as related to Tabrecta. In the safety analysis by patient characteristics, there was no factor for which 95% CI of odds ratio did not include 1, and no factor was thought to affect the incidence of adverse reactions. In the safety analysis by patient characteristics for each safety specification, adverse reactions related to interstitial lung disease for which the 95% CI of the odds ratio did not include 1 were “complication: respiratory system disease” and“ smoking history.” Furthermore, the 95% CI of the adjusted odds ratio using the logistic regression model did not include 1, suggesting the possible impact on the onset of interstitial lung disease. The safety in populations with specific background such as the elderly, patients with renal impairment or hepatic impairment, showed no findings of special mention. There was no report on administration to pediatrics or pregnant female. [Effectiveness] In the effectiveness analysis set (82 patients), the response (CR + PR) rate based on the best overall response assessed by the investigator per RECIST version 1.1 was 30.49% (25/82 patients) while the disease control (CR + PR + SD + Non-CR/Non-PD) rate was 71.95% (59/82 patients). By line of therapy, the response rate in 8 patients on "1st line therapy" was 50.00% (4/8 patients), and the disease control rate was 87.50% (7/8 patients). The response rate in 73 patients on "2nd or later line therapy" was 27.40% (20/73 patients), and the disease control rate was 69.86% (51/73 patients). The overall survival rate (95% CI) was 90.4% (80.8, 95.3) at Day 180, 85.0% (72.0, 92.3) at Day 270, and 85.0% (72.0, 92.3) at Day 360. By line of therapy, the overall survival rate (95% CI) for "1st line therapy" (8 patients) was 100% (100, 100) up to Day 360 and that for “2nd or later line therapy” (73 patients) was 89.2% (78.6, 94.8) at Day 180, and 82.9% (68.4, 91.2) at Day 270, and 82.9% (68.4, 91.2) at Day 360. Since the survival rate had not reached ≤ 50% either in the overall population or by any line of therapy, the median overall survival was not calculated. The PFS rate (95% CI) was 47.8% (36.4, 58.4) at Day 180, 31.3% (21.0, 42.2) at Day 270, and 26.6% (16.9, 37.3) at Day 360. The median PFS (95% CI) was 156.0 days (107.0, 235.0). The PFS rate

	(95% CI) by line of therapy in patients on “1st line therapy” (8 patients) was 72.9% (27.6, 92.5) at Day 180, 72.9% (27.6, 92.5) at Day 270, and 48.6% (7.7, 81.6) at Day 360. The median PFS (95% CI) was 292.0 days (52.0, not estimable). In patients on "2nd or later line therapy" (73 patients), it was 44.9% (33.0, 56.0) at Day 180, 26.6% (16.6, 37.8) at Day 270, and 23.3% (13.8, 34.2) at Day 360. The median PFS (95% CI) was 148.0 days (97.0, 221.0). As a result of the effectiveness analysis on the response rate by patient characteristics, the factor for which 95% CI of the odd ratio did not include 1 was “prior therapy: kinase inhibitors,” suggesting a potential influence on the effectiveness. The response rate with "prior therapy: kinase inhibitors" was 47.06% (16/34 patients) for "absent" and 19.15% (9/47 patients) for "present" (odds ratio: 0.27, 95% CI: 0.10, 0.72). In addition, as for the “line of therapy”, 95% CI of the odds ratio included but the response rate was 50.00% (4/8 patients) in patients on “1st line therapy” and 27.40% (20/73 patients) in those on “2nd or later line therapy”, demonstrating a numerical difference (odds ratio: 0.38, 95% CI: 0.09, 1.66). The effectiveness in populations with specific background such as the elderly, patients with renal impairment or hepatic impairment showed no findings of special mention. There was no report on administration to pediatrics or pregnant female.
Conclusion	There was no notable finding in the safety results of this study. In addition, a certain level of effectiveness was demonstrated for Tabrecta. Based on the above, it was considered unnecessary to take additional measures based on the results of this study.

List of abbreviations

Abbreviations	Full forms (English)
CI	Confidence Interval
CR	Complete Response
MET	Mesenchymal-Epithelial Transition factor
NIS	Non-Interventional Study
NSCLC	Non-Small-Cell Lung Cancer
PD	Progressive Disease
PFS	Progression Free Survival
PR	Partial Response
PT	Preferred Term
RECIST	Response Evaluation Criteria in Solid Tumors
SD	Stable Disease