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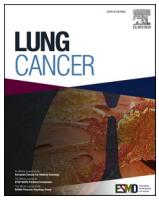

Research Paper

Intracranial activity of sotorasib vs docetaxel in pretreated *KRAS* G12C-mutated advanced non-small cell lung cancer from a global, phase 3, randomized controlled trial

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ABSTRACT

Objectives: To assess the efficacy and safety of sotorasib in patients with brain metastases using data from the phase 3 CodeBreaK 200 study, which evaluated sotorasib in adults with pretreated advanced or metastatic *KRAS* G12C-mutated non-small cell lung cancer (NSCLC).

Materials and methods: Patients with *KRAS* G12C-mutated NSCLC who progressed after platinum-based chemotherapy and checkpoint inhibitor therapy were randomized 1:1 to sotorasib or docetaxel. An exploratory post-hoc analysis evaluated central nervous system (CNS) progression-free survival (PFS) and time to CNS progression in patients with treated and stable brain metastases at baseline. Measures were assessed by blinded independent central review per study-modified Response Assessment in Neuro-Oncology Brain Metastases (RANO-BM) criteria.

Results: Of the patients randomly assigned to receive sotorasib (n=171) or docetaxel (n=174), baseline CNS metastases were present in 40 (23%) and 29 (17%) patients, respectively. With a median follow-up of 20.0 months for this patient subgroup, median CNS PFS was longer with sotorasib compared with docetaxel (9.6 vs 4.5 months; hazard ratio, 0.43 [95% CI, 0.20–0.92]; P=0.02). Among patients with baseline treated CNS lesions of ≥10 mm, the percentage of patients who achieved CNS tumor shrinkage of ≥30% was two-fold higher with

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sotorasib than docetaxel (33.3% vs 15.4%). Treatment-related adverse events among patients with CNS lesions at baseline were consistent with those of the overall study population.
Conclusions: These results suggest intracranial activity with sotorasib complements the overall PFS benefit observed with sotorasib vs docetaxel, with safety outcomes similar to those in the general CodeBreaK 200 population.
Clinical trials registration number: NCT04303780.

1. Introduction

Sotorasib, taken orally once daily, is a selective and irreversible $KRAS^{G12C}$ inhibitor indicated for the treatment of adults with *KRAS* G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC) who received at least one prior systemic therapy [1–3]. In the phase 3 CodeBreaK 200 study of patients with *KRAS* G12C-mutated advanced NSCLC, sotorasib showed a statistically significant improvement in progression-free survival (PFS) compared with intravenous docetaxel (median PFS [95% CI], 5.6 months [4.3–7.8] vs 4.5 months [3.0–5.7]; hazard ratio, 0.66 [0.51–0.86]; P=0.0017). An increased overall response rate (28.1% vs 13.2%), a longer duration of response (median, 8.6 vs 6.8 months), and a faster time to response (median, 1.4 vs 2.8 months) were also observed. Sotorasib was well tolerated, with fewer serious treatment-related adverse events compared with docetaxel and was associated with clinically meaningful improvements in patient-reported outcomes [4].

Brain metastases, identified in up to 40% of patients with advanced NSCLC, are associated with a poor prognosis [5–7]. The overall rate of patients with advanced *KRAS* G12C-mutated NSCLC has been reported at 10.5%, with slightly more patients having brain metastasis with the *KRAS* G12C mutation compared with those with *KRAS* wild-type disease [8]. Most patients with brain metastases receive stereotactic radiosurgery or radiotherapy as well as systemic therapy [3,9], although high-level evidence and the efficacy of conventional chemotherapy and immunotherapy to treat brain metastases remain limited [10,11].

To evaluate the central nervous system (CNS) effects of sotorasib, we examined its efficacy and safety in a post-hoc analysis of patients with NSCLC treated and stable brain metastases at baseline from the phase 3 CodeBreaK 200 study.

2. Methods

2.1. Data source and participants

In this open-label, phase 3 CodeBreaK 200 study, patients at least 18 years of age with *KRAS* G12C-mutated advanced NSCLC, who had disease progression after at least one prior systemic therapy that included prior platinum-based chemotherapy and programmed cell death protein 1 (PD-1) or programmed death ligand 1 (PD–L1) inhibitor therapy, were randomly assigned 1:1 to receive sotorasib 960 mg orally once daily or docetaxel 75 mg/m^2 intravenously every 3 weeks (ClinicalTrials.gov identifier: NCT04303780). Patients with treated and controlled or stable brain metastases were eligible if they had brain metastases resected or received whole-brain radiotherapy at least 4 weeks (or stereotactic radiosurgery ending at least 2 weeks) before study day 1. Details of the study design, inclusion and exclusion criteria, and primary outcome analyses have been previously reported [4].

The trial was conducted in accordance with the International Council for Harmonisation Good Clinical Practice guidelines and the principles of the Declaration of Helsinki. The protocol and amendments were approved by the institutional review board at each participating site and regulatory authorities of participating countries. All patients provided written informed consent. A data monitoring committee provided independent oversight of safety and efficacy throughout the trial [4].

2.2. Procedures

Tumor assessment was performed by contrast-enhanced magnetic resonance imaging (MRI) or computed tomography (CT) scan of the brain, chest, abdomen, and pelvis at screening and every 5–7 weeks from the first day of treatment until week 49, and then every 8–10 weeks until study discontinuation or death. Brain imaging only was mandated at every assessment if screening brain imaging showed disease.

2.3. Endpoints

CNS activity was assessed in patients with brain metastases at baseline by blinded independent central review (BICR) per specific study-modified response criteria in the context of systematically irradiated lesions only at baseline, modified from Response Assessment in Neuro-Oncology Brain Metastases (RANO-BM) [12] with the following study-defined modifications: (1) corticosteroid data and clinical status were not incorporated into the imaging reads and response criteria; (2) diffusion weighted imaging MRI sequences were not required, but could be presented to the independent reviewer if received. CNS time to progression was defined as time from randomization to progression of CNS disease. CNS PFS was defined as the time from randomization until date of CNS progression or death resulting from any cause, whichever occurs first, for patients with brain imaging on study. Patients with extracranial PFS without CNS PFS were not censored.

2.4. Analyses

Demographic and baseline disease characteristics were summarized using descriptive statistics. CNS-related efficacy analyses were similar to those in the CodeBreaK 200 primary analysis [4]. Contrast-enhanced MRI was obtained for all patients at screening. For those with known brain metastases, follow-up brain MRIs were conducted at each subsequent imaging assessment. In patients without baseline CNS involvement, imaging was done at the investigator's discretion in response to neurological symptoms. Progression of radiologic disease was verified centrally prior to cessation of investigational product, local intervention, initiation of new anti-cancer therapy, treatment beyond progression, or crossover. Some patients were followed for subsequent progressive disease events, including scans for CNS assessment after extracranial progressive disease. The CNS full analysis set included all randomized patients with CNS metastases at baseline. The CNS evaluable-for-response set included all randomized patients with at least one CNS lesion $\geq$10 mm in diameter at baseline. CNS evaluable-for-response lesions situated in a previously irradiated area were considered measurable using specific, study-modified response criteria. Efficacy analyses were performed based on the CNS full analysis set except for CNS tumor shrinkage of $\geq$30%, which was based on the CNS evaluable-for-response set. The patient incidence of adverse events was summarized for all treatment-emergent adverse events and treatment-related adverse events for the CNS safety analysis set. The CNS safety analysis set included all patients in the CNS full analysis set who received at least one dose of investigational product.

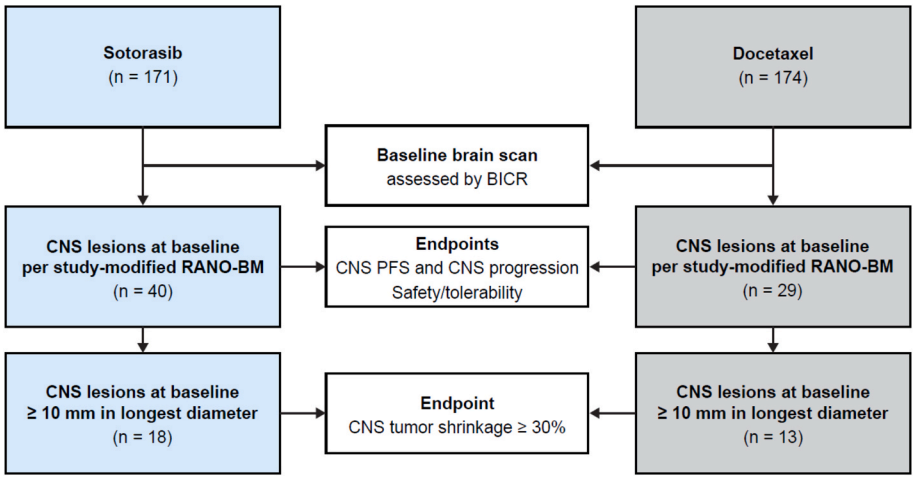

Fig. 1. Patient disposition for CNS endpoint analyses. Patients randomly assigned to sotorasib or docetaxel with treated baseline CNS lesions assessed by BICR per specific study-modified RANO-BM criteria were included in the CNS full analysis set. The CNS evaluable-for-response set include all randomized patients with at least one CNS lesion ≥10 mm in diameter at baseline assessed by BICR per specific study-modified RANO-BM criteria. The data cutoff date was February 16, 2023. BICR = blinded independent central review; CNS = central nervous system; RANO-BM = Response Assessment in Neuro-Oncology Brain Metastases.

3. Results

The post hoc CNS analyses were based on the snapshot data cutoff of February 16, 2023. CNS lesions at baseline were identified in 40 (23%) and 29 (17%) of patients in the sotorasib and docetaxel groups, respectively (Fig. 1). Median study follow-up time for the subset of patients with CNS disease was 20.0 months. Baseline characteristics among patients with CNS lesions and the subset of those with CNS lesions ≥10 mm in diameter were consistent with those of the overall study patient population and population subgroups (Table 1) [4]. The median time of radiotherapy to randomization was 2.8 months (IQR, 1.2–5.5) and 2.5 months (IQR, 1.1–5.7) for the sotorasib and docetaxel groups, respectively (Fig. 2).

In the CNS full analysis set of patients with CNS lesions at baseline, median CNS PFS was longer with sotorasib compared with docetaxel (9.6 vs 4.5 months; hazard ratio, 0.43 [95% CI, 0.20–0.92]; $P = 0.02$) (Fig. 3A) and median time to CNS progression was delayed (11.6 vs 6.0 months; hazard ratio, 0.63 [95% CI, 0.25–1.62]) (Fig. 3B; Supplement Table S1). Median overall survival was comparable between groups (11.7 vs 11.9 months; hazard ratio, 1.41 [95% CI, 0.71–2.81]).

In the CNS evaluable-for-response set of patients, with at least one CNS lesion ≥10 mm in diameter at baseline, as per specific study-modified response criteria, CNS tumor shrinkage ≥30% was two-fold higher with sotorasib compared with docetaxel (33.3% vs 15.4%) (Table 2), per specific study-modified RANO-BM criteria. There was concordance between systemic and CNS disease control based on response assessment (88% in the sotorasib arm and 54% in the docetaxel arm) in the CNS evaluable-for-response set of patients.

The efficacy of sotorasib in two patients with CNS lesions is further illustrated in Supplement Fig. S1. In the first patient, who had a lesion in the right thalamus and prior gamma knife, a 27.7% reduction in the lesion diameter (20.6 mm to 14.9 mm) was observed 1.5 months after the initiation of sotorasib. In the second patient, who had a lesion in the left cerebellar hemisphere and prior stereotactic radiation, an 11.2% decrease (49 mm to 43.5 mm) was observed 1.8 months after the initiation of docetaxel, with no further reduction after 3.5 months. The lesion was reduced by another 12% (to 37.6 mm) after crossover to sotorasib. Lesion reduction for all patients is summarized in a waterfall plot of change in lesion diameter from baseline (Fig. 4).

Patients receiving sotorasib stayed on treatment longer than those receiving docetaxel (median duration of treatment, 6.8 vs 3.0 months), including those with measurable lesions (Fig. 2). Treatment-related adverse events among patients with CNS lesions at baseline were generally consistent with those of the overall study population (Supplement Table S2) [4]. Grade ≥ 3 treatment-related adverse events were comparable between sotorasib and docetaxel groups (n = 12 [30%] vs n = 8 [28%]). The most common grade ≥3 treatment-related adverse events were diarrhea (n = 4 [10%]) and increased alanine aminotransferase (n=3 [7.5%]) with sotorasib and neutropenia (n = 3 [10%]) and fatigue (n = 2 [6.9%]) with docetaxel. Treatment-related adverse events led to the discontinuation of one patient receiving sotorasib; no patients discontinued due to adverse events related to docetaxel. There was one death related to docetaxel (due to ileus).

4. Discussion

This exploratory post-hoc analysis of data from the phase 3 CodeBreaK 200 supports the efficacy and safety of sotorasib compared with docetaxel in patients with *KRAS* G12C-mutated NSCLC and treated/stable brain lesions at baseline. Patient data from the phase 3 CodeBreaK 200 study demonstrate a consistent improvement across measures of CNS PFS, time to CNS progression, CNS complete responses, and CNS tumor shrinkage rates as per specific study-modified response criteria with sotorasib compared with docetaxel. No new brain metastases were detected in patients in either treatment group after the start CodeBreaK 200 study, which included patients who crossed over from docetaxel to sotorasib. However, because routine CNS imaging was not performed in all patients throughout the study, the true incidence of new brain metastases may be underestimated, as asymptomatic cases could have gone undetected. Together, these findings provide compelling evidence of the intracranial activity of sotorasib in this patient population.

The safety profile of sotorasib in this patient subgroup was generally similar to that reported in the general CodeBreaK 200 study population [4]. Diarrhea, while common with both sotorasib and docetaxel, was more severe in the sotorasib group. However, with only one discontinuation and no deaths attributed to sotorasib adverse events, sotorasib was well tolerated in this patient population.

Evidence suggests that currently available KRAS inhibitors share variable degrees of blood–brain barrier penetration as well as CNS activity [13–15]. In the phase 1/2 CodeBreaK 100 study of sotorasib in patients with pretreated *KRAS* G12C-mutated NSCLC, 14 of 16 patients with evaluable brain metastases had intracranial disease control [15]. Similarly, here we report intracranial disease control with sotorasib in 15 of 18 patients with evaluable, pretreated brain metastases. Additionally, encouraging cases from clinical practice are beginning to emerge documenting the effectiveness of sotorasib in patients with

untreated brain lesions [16–20].

The findings of this prespecified post-hoc analysis must be considered within the context of the study design requiring treated and stable CNS lesions at baseline, the lack of mandatory CNS imaging postbaseline to identify asymptomatic brain metastases, and the exploratory nature of the analysis. The non-applicability of RANO-BM or RECIST v1.1 criteria in the context of treated brain lesions and the subsequent use of specific study-modified response criteria limit interpretation, although concordance in outcomes regardless of prior radiation has been reported with these measures [21]. Excluding corticosteroid use and clinical status from CNS imaging reads and response criteria may introduce limitations in interpreting outcomes. However, the blinded independent readers—who were neuroradiology-trained—were aware that patients had received prior CNS treatment. Although radiation necrosis and brain metastases can appear similar on imaging, advanced imaging techniques were used to aid differentiation, helping to mitigate interpretive challenges [22]. Efficacy findings may be confounded by the unbalanced treatment groups and small sample sizes. Although this analysis represents the largest number of patients with CNS lesions treated with sotorasib to date, the relatively small subgroup sample size warrants additional conformational studies, including prospective studies in patients without prior radiotherapy.

In conclusion, sotorasib improved CNS PFS and time to CNS progression vs docetaxel in patients with stable and treated CNS lesions

Table 1
Baseline characteristics.

	CNS lesions		CNS lesions ≥10 mm in diameter	
	Sotorasib (n = 40)	Docetaxel (n = 29)	Sotorasib (n = 18)	Docetaxel (n = 13)
Median (range) age, years	62.0 (32, 88)	59.0 (36, 76)	59.0 (32, 77)	59.0 (36, 76)
Sex, male, n (%)	25 (62.5)	18 (62.1)	10 (55.6)	11 (84.6)
Ethnicity, n (%)				
Hispanic or Latino	0 (0.0)	2 (6.9)	0 (0.0)	1 (7.7)
Not Hispanic or Latino	40 (100.0)	26 (89.7)	18 (100.0)	12 (92.3)
Unknown	0 (0.0)	1 (3.4)	0 (0.0)	0 (0.0)
Race, n (%)				
Asian	8 (20.0)	5 (17.2)	3 (16.7)	3 (23.1)
Black or African American	1 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
White	28 (70.0)	21 (72.4)	14 (77.8)	8 (61.5)
Other	2 (5.0)	3 (10.3)	1 (5.6)	2 (15.4)
Unknown	1 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
Region, n (%)				
North America	4 (10.0)	3 (10.3)	2 (11.1)	2 (15.4)
Europe	28 (70.0)	22 (75.9)	13 (72.2)	9 (69.2)
Rest of world	8 (20.0)	4 (13.8)	3 (16.7)	2 (15.4)
Smoking history, n (%)				
Never	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Current	7 (17.5)	9 (31.0)	3 (16.7)	5 (38.5)
Former	33 (82.5)	20 (69.0)	15 (83.3)	8 (61.5)
ECOG performance status at screening, n (%)				
0	15 (37.5)	12 (41.4)	7 (38.9)	3 (23.1)
1	25 (62.5)	17 (58.6)	11 (61.1)	10 (76.9)
Prior lines of therapy for advanced disease, n (%)				
1	17 (42.5)	12 (41.4)	8 (44.4)	5 (38.5)
2	16 (40.0)	12 (41.4)	7 (38.9)	7 (53.8)
>2	7 (17.5)	5 (17.2)	3 (16.7)	1 (7.7)
CNS lesions, n (%)				
1	NA	NA	13 (72.2)	11 (84.6)
2	NA	NA	1 (5.6)	1 (7.7)
>2	NA	NA	4 (22.2)	1 (7.7)
Mean sum of CNS targeted lesions, mm	NA	NA	26.8	23.2
Prior therapy for brain metastases, n (%)				
WBRT	15 (37.5)	9 (31.0)	6 (33.3)	5 (38.5)
SRT	12 (30.0)	5 (17.2)	6 (33.3)	3 (23.1)
WBRT + SRT	3 (7.5)	1 (3.4)	2 (11.1)	0 (0.0)
Surgery + SRT	1 (2.5)	2 (6.9)	0 (0.0)	2 (15.4)
Surgery + WBRT	1 (2.5)	0 (0.0)	1 (5.6)	0 (0.0)
Median (range) time from prior radiotherapy in brain to randomization, months	3.8 (0.6, 28.3)	3.1 (0.5, 34.4)	2.8 (0.6, 20.4)	2.5 (0.5, 25.2)
Comutations, n (%)				
TP53	21 (52.5)	18 (62.1)	12 (66.7)	7 (53.8)
KEAP1	13 (32.5)	9 (31.0)	8 (44.4)	4 (30.8)
STK11	13 (32.5)	13 (44.8)	10 (55.6)	5 (38.5)
PD-L1 protein expression, n (%)				
<1%	9 (22.5)	9 (31.0)	4 (22.2)	3 (23.1)
≥1% to <50%	7 (17.5)	7 (24.1)	3 (16.7)	3 (23.1)
≥50%	5 (12.5)	3 (10.3)	3 (16.7)	1 (7.7)

[a]Baseline brain imaging by contrast-enhanced MRI was obtained for all patients at screening except for one patient who was imaged by CT. For patients with known brain metastases, brain MRI was obtained at every subsequent imaging assessment, except for one patient who was imaged with CT and MRI. CNS = central nervous system; CT = computerized tomography; ECOG = Eastern Cooperative Oncology Group; MRI = magnetic resonance imaging; NA = not applicable; PD-L1 = programmed death ligand 1; SRT = stereotactic radiotherapy; WBRT = whole-brain radiotherapy.

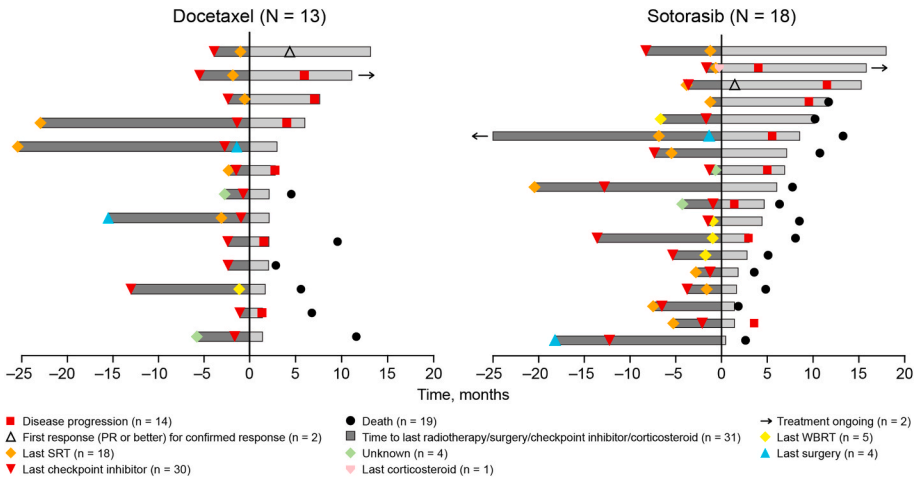

Fig. 2. Duration of treatment in patients with measurable CNS lesions The analysis was conducted in patients with treated and stable CNS lesions at baseline, in which measurable lesions were defined as CNS lesions ≥10 mm in diameter by BICR per specific study-modified response criteria in the context of irradiated lesions, based on RANO-BM. BICR = blinded independent central review; CNS = central nervous system; PR = partial response; RANO-BM = Response Assessment in Neuro-Oncology Brain Metastases; SRT = stereotactic radiosurgery; WBRT = whole-brain radiotherapy.

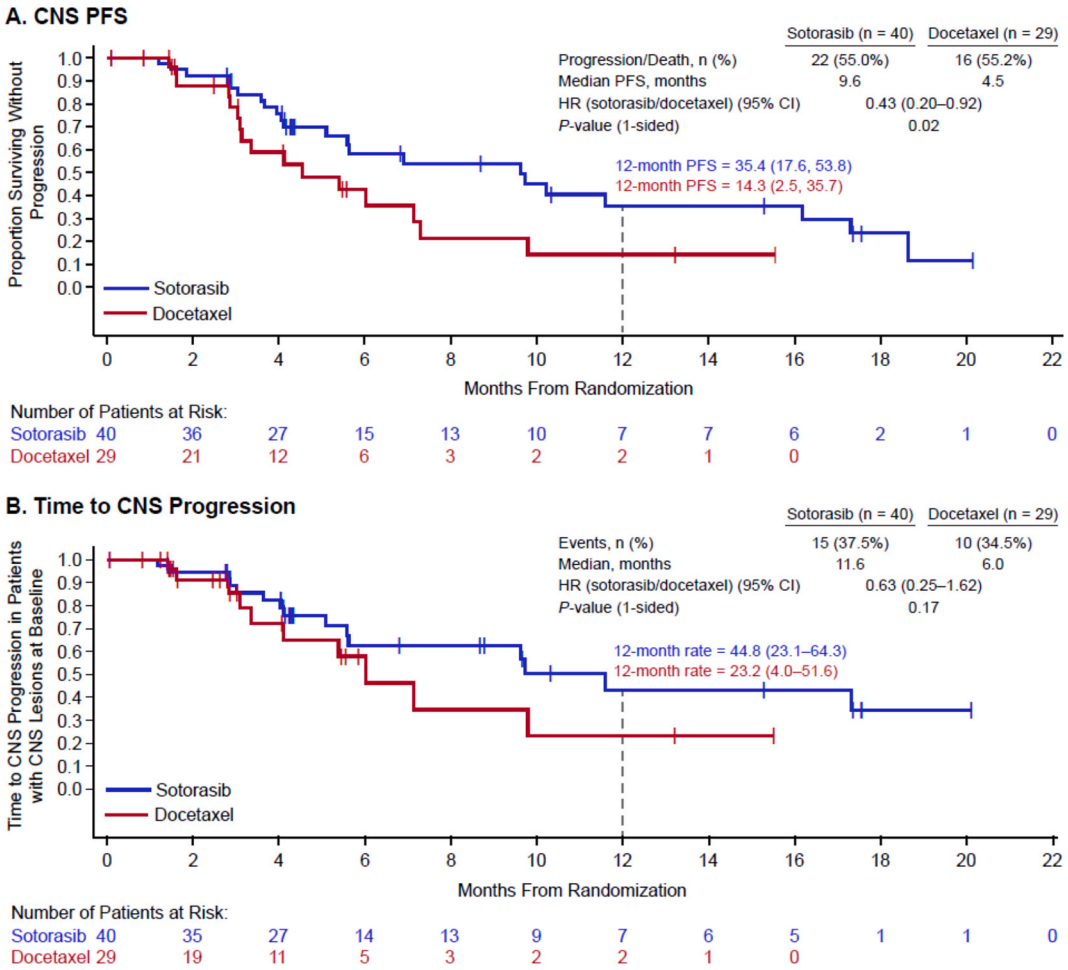

Fig. 3. Time to CNS progression and CNS PFS in patients with CNS lesions at baseline. Panel A. Time to CNS progression Panel B. CNS PFS in patients with CNS lesions at baseline The survival curves and the median time to CNS progression are derived by Kaplan-Meier method; hazard ratios (95%) are reported from unstratified Cox proportional hazard ratio model; P-values are calculated using log-rank test. Hazard ratio <1.0 indicates a lower average event rate on a longer PFS for sotorasib relative to docetaxel. CI = confidence interval; CNS = central nervous system; HR = hazard ratio; PFS = progression-free survival.

Table 2
Intracranial responses per study-modified RANO-BM criteria in patients with CNS lesions at baseline.

Study-modified RANO-BM classification	Patients with stable/treated CNS lesions at baseline[a]	
	Sotorasib (n = 40)	Docetaxel (n = 29)
Complete response, n (%)	8 (20.0)	2 (6.9)
Non–partial response/non–progressive disease, n (%)	29 (72.5)	24 (82.8)
Progressive disease, n (%)	2 (5.0)	3 (10.3)
Not done,[b] n (%)	1 (2.5)	0 (0)
	Patients with CNS lesions ≥10 mm at baseline	
	Sotorasib (n = 18)	Docetaxel (n = 13)
Confirmed CNS tumor shrinkage ≥ 30%, n (% [95% CI])	6 (33.3 [13.3–59.0])	2 (15.4 [1.9–45.4])
Complete response, n (%)	1 (5.6)	1 (7.7)
Partial response, n (%)	5 (27.8)	1 (7.7)
Stable disease or non–partial response/ non–progressive disease, n (%)	9 (50.0)	9 (69.2)
Progressive disease, n (%)	1 (5.6)	2 (15.4)
Not done/not evaluable,[b,c] n (%)	2 (11.1)	0
Disease control, n (%)	15 (83.3)	11 (84.6)
Unconfirmed and confirmed CNS tumor shrinkage ≥30%, n (%)	9 (50.0)	2 (15.4)

[a] By BICR per study-modified RANO-BM criteria, assessing all lesions as non-target in patients with CNS lesions at baseline. [b]Not done because patient started alternative therapy before first postbaseline brain scan. [c]Not evaluable by BICR based on different postbaseline scan modalities. BICR = blinded independent central review; CI = confidence interval; CNS = central nervous system; RANO-BM = Response Assessment in Neuro-Oncology Brain Metastases.

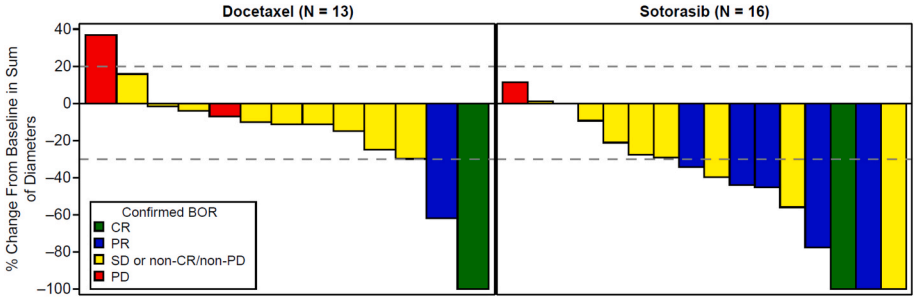

Fig. 4. Change in lesion diameter from baseline. Waterfall plots show the percentage change from baseline in sum of diameters for confirmed CNS best objective response as assessed by BICR per specific study-modified RANO-BM. Patients without baseline target lesions or postbaseline percent changes or those with a BOR of not estimable are not shown. BICR = blinded independent central review; BOR = best observed response; CNS = central nervous system; CR = complete response; PD = progressive disease; PR = partial response; RANO-BM = Response Assessment in Neuro-Oncology Brain Metastases; SD = stable disease.

from the CodeBreaK 200 study. These data support the use of sotorasib in patients with *KRAS* G12C-mutated NSCLC and treated brain metastases.

CRediT authorship contribution statement

Anne-Marie C. Dingemans: Writing – review & editing, Investigation, Data curation. **Konstantinos Syrigos:** Writing – review & editing, Investigation, Data curation. **Lorenzo Livi:** Writing – review & editing, Investigation, Data curation. **Astrid Paulus:** Writing – review & editing, Investigation, Data curation. **Sang-We Kim:** Writing – review & editing, Investigation, Data curation. **Yuanbin Chen:** Writing – review & editing, Investigation, Data curation. **Enriqueta Felip:** Writing – review & editing, Investigation, Data curation. **Frank Griesinger:** Writing – review & editing, Investigation, Data curation. **Kadoaki Ohashi:** Writing – review & editing, Investigation, Data curation. **Gerard Zalcman:** Writing – review & editing, Investigation, Data curation. **Brett G.M. Hughes:** Writing – review & editing, Investigation, Data curation. **Jens Benn Sørensen:** Writing – review & editing, Investigation, Data curation. **Normand Blais:** Writing – review & editing, Investigation, Data curation. **Carlos G.M. Ferreira:** Writing – review & editing, Investigation, Data curation. **Colin R. Lindsay:** Writing – review & editing, Investigation, Data curation. **Rafal Dziadziuszko:** Writing – review & editing, Investigation, Data curation. **Patrick J. Ward:** Writing – review & editing, Investigation, Data curation. **Cynthia Chinedu Obiozor:** Writing – review & editing, Methodology, Conceptualization. **Yang Wang:** Writing – review & editing, Validation, Formal analysis. **Solange Peters:** Writing – review & editing, Investigation, Data curation.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: **Anne-Marie C. Dingemans** reports grants or contracts from Amgen, Dutch Cancer Society, HANART; consulting fees from Amgen, Bayer, Boehringer Ingelheim, Sanofi, Roche, Johnson & Johnson, AstraZeneca, Pfizer, Mirati; payment or honoraria from Janssen, Pfizer, AstraZeneca, Lilly, Amgen; participation on a data safety monitoring board or advisory board for Takeda, Roche, Lilly; and leadership role for EORTIC LCG. **Konstantinos Syrigos** reports consulting fees from Merck Sharp & Dohme, AstraZeneca, Bristol-Myers Squibb, and Amgen. **Yuanbin Chen** reports research grants from Amgen, AstraZeneca, Merck, AbbVie, Daiichi Sankyo, Shanghai Junshi; and speakers bureau for Amgen, AstraZeneca, Pfizer, Jazz, Takeda, Bristol Myers Squibb. **Enriqueta**

Felip reports participating in advisory boards for AbbVie, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Roche, Genmab, Gilead, GlaxoSmithKline, ITeos Therapeutics, Janssen, Johnson & Johnson, Merck Sharp & Dohme, Novartis, Pfizer, Pierre Fabre, Regeneron, Turning Point; speakers' bureau for Amgen, AstraZeneca, Bristol-Myers Squibb, Daiichi Sankyo, Eli Lilly, F. Hoffman-La Roche, Genentech, Gilead, Janssen, Johnson & Johnson, Medical Trends, Medscape, Merck Serono, Merck Sharp & Dohme, Novartis, Peer Voice, Pfizer, Pierre Fabre, Regeneron; travel support from AstraZeneca, Janssen, Roche; and board member for Grifols. **Frank Griesinger** reports scientific support from CRISP; grants from Amgen, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Daiichi Sankyo, Gilead Sciences, GlaxoSmithKline, Janssen-Cilag, Lilly, MSD Sharp & Dohme, Novartis, Pfizer, Regeneron, Roche, Takeda; speaker for ASTRA, Boehringer, Bristol-Myers Squibb, Celgene, Lilly, MSD, Novartis, Pfizer, Roche, Takeda, Ariad, AbbVie, Siemens, Tesaro/GlaxoSmithKline, Amgen, Sanofi, Daiichi-Sankyo, BeiGene, Gilead; and advisory board for ASTRA, Boehringer, Bristol-Myers Squibb, Celgene, Lilly, MSD, Novartis, Pfizer, Roche, Takeda, Ariad, AbbVie, Tesaro/GlaxoSmithKline, Siemens, Tesaro, Amgen, Sanofi, Daiichi-Sankyo, BeiGene, Gilead. **Kadoaki Ohashi** reports consulting fees from Amgen. **Gerard Zalcman** reports funding from Amgen for ESMO meeting 2024, travel and attendance. **Jens Benn Sørensen** reports consulting fees from Bristol-Myers Squibb, Roche, AstraZeneca, Novartis, Pfizer, Takeda, and Janssen. **Normand Blais** reports consulting fees from Amgen. **Carlos G. M. Ferreira** reports grants from Bristol-Myers Squibb, MSD; nonremunerative positions of influence for IASLC, ASCO; speakers bureau for BeiGene; stock from Oncoclinicas; employment at Oncoclinicas. **Colin R. Lindsay** reports financial interests in Amgen; invited speaker for Amgen, Qiagen; advisory board for Amgen; investigator for Apollomics, Mirati Therapeutics, Revolution Medicines, Roche, Boehringer Ingelheim; and travel funding from Amgen. **Rafal Dziadziuszko** reports speaker bureau for Pfizer; consultant for Amgen, AstraZeneca, Bristol Myers Squibb, F. Hoffman-La Roche, Merck, Sharp & Dohme, Pfizer, Takeda; and drug samples from Novartis. Patrick J. Ward reports advisory board for Amgen, Fresenius Kabi, Astra Zeneca, AZ/DSI, Neuvogen, MD Outlook. **Cynthia Chinedu Obiozor** and **Yang Wang** are employees of Amgen and report owning stock in Amgen. **Solange Peters** reports grants, attending advisory board, delivering talks (all fees to institution) for AbbVie, Amgen, Arcus, AstraZeneca, Bayer, BeiGene, BioNTech, BerGenBio, Bicycle Therapeutics, Biocartis, BioInvent, Blueprint Medicines, Boehringer Ingelheim, Bristol-Myers Squibb, Clovis, Daiichi Sankyo, Debiopharm, Eli Lilly, F-Star, Foundation Medicine, Genmab, Genzyme, Gilead, GlaxoSmithKline, Hutchmed, Illumina, Incyte, Ipsen, iTeos, Janssen, Qlucore, Merck Sharp and Dohme, Merck Serono, Merrimack, Mirati, Nuvation Bio, Nykode Therapeutics, Novartis, Novocure, Pharma Mar, Promontory Therapeutics, Pfizer, Regeneron, Roche/Genentech, Sanofi, Seattle Genetics, Takeda, Zymeworks; speaker for AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly, Foundation Medicine, GlaxoSmithKline, Illumina, Ipsen, Merck Sharp and Dohme, Mirati, Novartis, Pfizer, Roche/Genentech, Sanofi, Seattle Genetics, Takeda; and investigator for Amgen, Arcus, AstraZeneca, BeiGene, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, iTeos, Merck Sharp and Dohme, Mirati, Pharma Mar, Pfizer, Promontory Therapeutics, Roche/Genentech, Seattle Genetics. Lorenzo Livi, Astrid Paulus, Sang-We Kim, Brett G. M. Hughes report no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.lungcan.2025.108683.

Data availability

Qualified researchers can request data from Amgen clinical studies. Complete details are available at https://www.amgen.com/science/clinical-trials/clinical-data-transparency-practices/clinical-trial-data-sharing-request

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