European Journal of Cancer 219 (2025) 115301

Contents lists available at ScienceDirect

European Journal of Cancer

journal homepage: www.ejcancer.com

Original research

Real-world effectiveness and tolerability of sotorasib in patients with KRAS G12C-mutated metastatic non-small cell lung cancer: The IFCT-2102 Lung KG12Ci study

M. Wislez [a,b,*], C. Mascaux [c], J. Cadranel [d,e], Q.D. Thomas [f], C. Ricordel [g,h], A. Swalduz [i], E. Pichon [j], R. Veillon [k], V. Gounant [l], G. Rousseau-Bussac [m], A. Madroszyk [n], C. Daniel [o], M. Ravoire [p], A.-C. Metivier [q], P. Fournel [r], P. Missy [s], F. Morin [s], F. Guisier [t], V. Westeel [u]

[a] APHP, Hôpital Cochin, Service de Pneumologie, Unité d'Oncologie Thoracique, Paris, France
[b] Université Paris Cité, Paris, France
[c] CHU de Strasbourg, Nouvel Hôpital Civil, Service de Pneumologie, Pôle de Pathologie Thoracique, Strasbourg, France
[d] APHP, Hôpital Tenon, Service de Pneumologie et Oncologie Thoracique, Paris, France
[e] GRC04, Theranoscan Sorbonne Université, Paris, France
[f] Institut du cancer de Montpellier, Service d'Oncologie Médicale, Montpellier, France
[g] Université de Rennes 1, Unité COSS INSERM U1242 - CEM, Rennes, France
[h] CHU Rennes, Service de Pneumologie, Rennes, France
[i] Centre Léon Bérard, Department of Medical Oncology, Lyon, France
[j] CHU de Tours, Hôpital Bretonneau, Service de Pneumologie, Tours, France
[k] CHU de Bordeaux, Service Des Maladies Respiratoires, Bordeaux, France
[l] APHP, Hôpital Bichat, Service d'Oncologie Thoracique, Paris, France
[m] Centre hospitalier Intercommunal de Créteil, Service de Pneumologie, Créteil, France
[n] Institut Paoli Calmettes, Service d'Oncologie Médicale, Marseille, France
[o] Institut Curie, Département d'Oncologie Médicale, Paris, France
[p] Institut du Cancer Avignon-Provence, Service de Pneumologie, Avignon, France
[q] Hôpital Foch, Service de Pneumologie, Suresnes, France
[r] CHU de Saint-Etienne, Service de Pneumologie et d'oncologie Thoracique, France
[s] IFCT, Unité de Recherche Clinique, Paris, France
[t] Univ Rouen Normandie, LITIS Lab QuantIF team EA4108, CHU Rouen, Inserm CIC-CRB 1404, Department of Pneumology, Thoracic Oncology and Respiratory Intensive Care, Rouen, France
[u] Service de Pneumologie, Hôpital Jean Minjoz, Besançon, France

ARTICLE INFO

Keywords:
Non-small-cell lung cancer
KRAS mutation
Targeted therapy
KRAS inhibitor
Sotorasib
Real-world evidence

ABSTRACT

Introduction: Sotorasib has shown efficacy in a phase 3 trial compared to docetaxel among previously treated non-small cell lung cancer (NSCLC) patients with a KRAS G12C mutation. However, its real-world effectiveness and tolerance, especially post-immunotherapy, remain debated.

Methods: This French retrospective multicentre study analysed NSCLC patients receiving at least one dose of sotorasib as part of early access program The main objective was to assess real-world progression-free survival (rwPFS), and secondary objectives included assessment of overall survival (rwOS) and sotorasib-related hepatotoxicity.

Results: 458 patients from 76 centres were analysed, with a median age 65.8. Among them, 43.4 % were female, 28.3 % had performance status $\geq$ 2, 95.4 % were active/former smokers, and 38.0 % had brain metastases with 55.2 % in progression at sotorasib initiation. PD-L1 expression was $<$ 1 %, $\geq$ 1–49 %, $\geq$ 50 %, and unknown in 35.1 %, 34.1 %, 23.4 %, and 7.4 % of patients, respectively. Most patients had received prior treatments (96.7 %), including immunotherapy (54.9 %). Median (95 % confidence interval [CI]) rwPFS and rwOS were 3.5 (3.1–4.2) and 8.3 (7.5–9.3) months, with a median (95 % CI) follow-up of 15.8 (13.9–17.3) and 16.4 (15.5–17.3) months, respectively. The real-world objective response rate (rwORR) was 33.2 % and disease control rate (rwDCR) was 63.2 %. In patients with brain metastases, cerebral rwORR and rwDCR were 20.1 % and 66.9 %,

* Correspondence to: Unité d'Oncologie Thoracique, Service de Pneumologie, Hopital Cochin, AP-HP, 27 rue du Faubourg Saint-Jacques, Paris 75014, France
E-mail address: marie.wislez@aphp.fr (M. Wislez).

https://doi.org/10.1016/j.ejca.2025.115301
Received 26 November 2024; Received in revised form 3 February 2025; Accepted 8 February 2025
Available online 11 February 2025
0959-8049/© 2025 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

respectively. Grade 3–4 adverse events related to hepatotoxicity occurred in 5.2 % of patients. Sotorasib was discontinued for toxicity in 16.5 % of patients.
Conclusion: This study gave insights into effectiveness and safety of sotorasib in a real-world setting, in advanced or metastatic KRAS G12C-mutated non-squamous NSCLC.

1. Introduction

Non-small cell lung cancer (NSCLC) represents the majority of lung cancers and is a leading cause of cancer-related mortality worldwide [16]. Recent advances in molecular biology have highlighted the importance of specific genetic mutations in the pathogenesis and treatment of NSCLC [2]. *KRAS G12C* mutation occurs in a significant subset of non-squamous NSCLC patients (13 %), mostly in smokers, and has historically been associated with poor prognosis and limited treatment options [8,13,21]. The development of targeted therapies for *KRAS G12C* mutation has provided new hope for this patient population ([18,19]; 2024).

Sotorasib, the first FDA-approved KRAS G12C inhibitor, has emerged as a promising therapeutic agent [6,10,17]. In particular, sotorasib has demonstrated enhanced quality-of-life and safety metrics, alongside prolonged progression-free survival (PFS) and superior management of central nervous system (CNS) metastases compared to docetaxel [1]. The Early Access Program (EAP, called "Autorisation temporaire d'utilisation" at the time of the study) allow access to sotorasib for patients in a therapeutic impasse, or who can neither wait for the conventional availability of the drug nor be included in a clinical trial [4]. This EAP in France has provided an opportunity to evaluate sotorasib in a broader patient population outside controlled clinical trial environments.

This retrospective observational, multicentre, cohort study (NCT05273047) aimed to describe the characteristics and clinical outcomes of a sample of NSCLC patients with a *KRAS G12C* mutation treated with sotorasib under the EAP in France. By analysing this cohort, we aim to determine the real-world applicability of sotorasib, its impact on disease progression, and its safety profile in routine clinical practice.

2. Materials and methods

2.1. Population and data collection

This retrospective observational study involved adult patients with advanced or metastatic *KRAS G12C*-mutated non-squamous NSCLC. A total of 115 centres which have prescribed sotorasib as part of EAP were contacted, 76 of them agreed to take part in this study. All patients' records (556) from these 76 centres were monitored and 461 were included in the database. Patients initiated sotorasib via an EAP between January 2021 and April 2022. The indication of the EAP was "as monotherapy for the treatment of adult patients with advanced NSCLC harbouring the *KRAS G12C* mutation, whose disease has progressed after at least one prior line of systemic therapy. For the present study, the selection criteria included adult patients with Stage IV NSCLC and a confirmed *KRAS G12C* mutation who received at least one dose of sotorasib through the French EAP, while excluding those enrolled in clinical trials, with psychiatric issues affecting consent, under guardianship, or where data collection was not possible.

Data were extracted from medical records by a dedicated and trained IFCT clinical research associate, documented in a standard form, and managed by the French Collaborative Thoracic Intergroup (IFCT) for quality assurance.

2.2. Endpoints

The primary endpoint was real-world PFS (rwPFS), defined as the time from the first sotorasib dose to disease progression assessed by the treating physician or death from any cause. Secondary endpoints included objective response rate (rwORR, percentage of patients with partial or complete response), disease control rate (rwDCR, percentage of patients with objective response or stable disease), best CNS response (response of CNS metastases from treatment start to tumour progression or new treatment), duration of CNS response (first cerebral response to tumour progression or death) assessed by the treating physician, overall survival (rwOS, time from sotorasib initiation to death from any cause), and duration of treatment (DOT, time from initiation to discontinuation or death). Sotorasib hepatic toxicity was also assessed, with adverse events graded by common terminology criteria for adverse events v5.0.

2.3. Statistical analysis

The database was locked on August 30th, 2023, with a cutoff date of March 31st, 2023. Categorical variables were expressed as frequencies and percentages, and quantitative variables as medians (range). When relevant, 95 % confidence intervals (CI) were calculated. The Kaplan-Meier method estimated rwPFS, DOT, and rwOS. Prognostic factors for patient survival were identified using a Cox regression model, testing sex, age, performance status, and brain metastases in a univariate model. A multivariate model with backward stepwise selection included all univariate variables. Statistical analyses were performed using SAS 9.4 software.

3. Results

3.1. Patient characteristics at baseline

Out of 461 patients included in the sotorasib EAP database, 458 met the inclusion criteria (data couldn't be updated for 3 patients) and 58 were still treated with sotorasib at database lock (Figure S1). At sotorasib initiation, 43.4 % of patients were female, median age was 65.8 years, and 95.4 % were current or former smokers (Table 1). A performance status ≥ 2 was seen in 28.3 % of patients. Brain metastases were present in 38.0 % of patients, with 55.2 % showing progression at sotorasib initiation. PD-L1 expression levels were ≤ 1 %, $\geq$ 1–49 %, ≥ 50 %, and unknown in 35.1 %, 34.1 %, 23.4 %, and 7.4 % of patients, respectively. The median number of previous lines of systemic treatment was 1.5 (0–10; Table 1). Most patients had received one (47.2 %) or two (25.1 %) previous lines of treatment (Table 1), and received an initial dose of sotorasib of 960 mg/day (98.7 %). Except KRAS, patients did not have any driver mutations; TP53, STK11, and KEAP1 were expressed in 13.5 %, 11.1 %, and 1.7 % of tested patients (Table S1).

3.2. Sotorasib effectiveness on clinical outcomes

The median (95 % CI) duration of sotorasib treatment was 4.0 (3.5–4.4) months. Median (95 % CI) rwPFS and rwOS were 3.5 months (3.1–4.2; Table 2 & Fig. 1A) and 8.3 months (7.5–9.3; Table 2 & Fig. 1B), respectively, with a median (95 % CI) follow-up duration of 15.8 months (13.9–17.3) for the rwPFS and 16.4 months (15.5–17.3) for the rwOS. At 6 and 12 months, rwPFS was 32.8 % and 12.5 %, and rwOS was 59.2 % and 39.6 %, respectively (Table 2). There was no difference in rwPFS and rwOS by line of treatment (data not shown). Among the 458 patients, 454 were assessable for response, with rwORR, rwDCR, and disease progression observed in 35.5 % (31.1–39.9), 63.7 % (59.2–68.1), and 35.7 % (31.3–40.1) of patients, respectively (Table 2). Overall, 389 patients experienced tumour progression, predominantly in the lung (46.8 %) and the brain (25.2 %; Table S2).

Table 1
Patient characteristics at sotorasib initiation.

	N = 458
Sex	
Female, n (%)	199 (43.4)
Male, n (%)	259 (56.6)
Age	
Median (min-max)	65.8 (35.9–89.7)
Smoking status	
Former or current smoker, n (%)	434 (95.4)
Non-smoker, n (%)	21 (4.6)
Packs per year	
Median (Min-Max)	35.0 (1−120)
Histology	
Adenocarcinoma, n (%)	431 (94.1)
Squamous, n (%)	8 (1.7)
Others, n (%)	19 (4.2)
Stage at diagnostic	
I-IIIA, n (%)	81 (17.8)
IIIB-IVB, n (%)	374 (82.2)
Stage at sotorasib initiation	
IIIB-IIIC, n (%)	1 (0.2)
IVA, n (%)	126 (27.5)
IVB, n (%)	331 (72.3)
Performance status at sotorasib initiation	
0–1, n (%)	220 (71.7)
≥ 2, n (%)	87 (28.3)
Brain metastasis at sotorasib initiation	
Yes, n (%)	174 (38.0)
No, n (%)	284 (62.0)
Brain metastasis in progression at sotorasib initiation	
Yes, n (%)	96 (55.2)
No, n (%)	78 (44.8)
Number of previous lines of systemic treatment	
0, n (%)	15 (3.3)
1, n (%)	216 (47.2)
2, n (%)	115 (25.1)
3, n (%)	62 (13.5)
≥ 4, n (%)	50 (10.9)
Median (minimum – maximum)	1.5 (0−10)
PDL1 expression (IHC)*	
< 1 %, n (%)	161 (35.1)
1–49 %, n (%)	156 (34.1)
≥ 50 %, n (%)	107 (23.4)
Unknown, n (%)	34 (7.4)

* Not done and undetermined are not presented

Table 2
Clinical outcomes with sotorasib.

Real-world progression-free survival (rw PFS), N = 458	
Median (95 % CI), months	3.5 (3.1–4.2)
6-month rwPFS, % (95 % CI)	32.8 (28.5–37.2)
12-month rwPFS, % (95 % CI)	12.5 (9.4–16.0)
Median follow-up time, months (95 % CI)	15.8 (13.9–17.3)
Real-world overall survival (rwOS)	
Median (95 % CI), months	8.3 (7.5–9.3)
6-month rwOS, % (95 % CI)	59.2 (54.5–63.5)
12-month rwOS, % (95 % CI)	39.6 (35.0–44.2)
Median follow-up time, months (95 % CI)	16.4 (15.5–17.3)
Duration of treatment (months), N = 458	
Median (95 % CI)	4.0 (3.5–4.4)
Real-world best overall response, N = 458	
Complete response, n (%) [95 % CI]	4 (0.9) [0.0–1.7]
Partial response, n (%) [95 % CI]	157 (34.6) [30.2–39.0]
Objective response, n (%) [95 % CI]	161 (35.5) [31.1–39.9]
Stable disease, n (%) [95 % CI]	128 (28.2) [24.1–32.3]
Disease control, n (%) [95 % CI]	289 (63.7) [59.2–68.1]
Progressive disease, n (%) [95 % CI]	162 (35.7) [31.3–40.1]
Not evaluable, n (%) [95 % CI]	3 (0.7) [0.0–1.4]
Not done/missing, n	4
Real-world best central nervous system metastasis response, N = 174	
Complete response, n (%) [95 % CI]	4 (2.9) [0.1–5.7]
Partial response, n (%) [95 % CI]	24 (17.3) [11.0–23.5]
Objective response, n (%) [95 % CI]	28 (20.1) [13.5–26.8]
Stable disease, n (%) [95 % CI]	65 (46.8) [38.5–55.1]
Disease control, n (%) [95 % CI]	93 (66.9) [59.1–74.7]
Progression disease, n (%) [95 % CI]	44 (31.7) [23.9–39.4]
Not evaluable, n (%) [95 % CI]	2 (1.4) [0.0–3.4]
Not done/missing, n	35
Duration of response (months), N = 127	
Median (95 % CI)	3.8 (3.0–5.0)
Duration of treatment beyond progression (months), N = 389	
Median (95 % CI)	0.5 (0.4–0.7)

CI: confidence interval;

To better interpret the results of this real-world analysis, we evaluated sotorasib effectiveness on clinical outcomes in a population strictly meeting the eligibility criteria of CodeBreaK 200 (performance status <2, prior first-line treatment, and no symptomatic or progressing untreated brain metastases). Eligible patients showed better outcomes in terms of rwOS (9.6 [95 % CI: 8.6–12.5] versus 5.4 [95 % CI: 4.2–6.7] months), rwPFS (4.4 [95 % CI: 3.5–5.2] versus 2.7 [95 % CI: 2–3.2] months), and rwORR (127 (40.6 %) [35.1 % - 46.0 %] versus 34 (24.1 %) [17.1 % - 31.2 %]) compared to non-eligible patients (Table S3).

Among the co-mutations, we evaluated sotorasib effectiveness on clinical outcomes in the biggest subgroups 51 STK11 62 TP53 co-mutated patients, as the other subgroups were too small for statistical assessments. STK11 co-mutated patients had lower outcome (median rwOS 5.1 months [95 % CI: 3.6–6.7], median rwPFS 2.1 months [95 % CI: 1.5–3.2]; Table S4). For TP53 co-mutated patients, the median rwOS and rwPFS were 7.2 [95 % CI: 4.4–11.7] and 3.2 [95 % CI: 2.0–3.9], respectively (Table S4).

3.3. Prognostic factors and impact on brain metastases

To understand prognostic factors for sotorasib treatment, rwOS factors were analysed. Patients with ECOG performance status ≥ 2 had a more than twofold increase in the risk of death compared to those with ECOG < 2 (HR: 2.12 [1.58–2.84]; p < 0.0001; Table 3).

In patients with brain metastases at the start of sotorasib treatment, the best CNS response was rwORR (95 % CI) at 20.1 % (13.5–26.8), and rwDCR (95 % CI) at 66.9 % (59.1–74.7; Table 2). Median (95 % CI) rwPFS and rwOS were shorter in these patients compared to those without brain metastases: 3.1 (2.7–3.5) versus 4.3 (3.3–5.2) months, and 7.2 (5.6–9.1) versus 8.8 (7.8–11) months, respectively (Fig. 2A and B). Prognosis was even worth in patients with untreated brain metastases at sotorasib initiation (Table S5).

3.4. Therapeutic sequence

To explore treatment sequencing, data based on prior therapies (detailed in Table S6) were explored. The median time between the last treatment and starting sotorasib was 1.3 months (0.1–47.4). Patients in their first or second line of treatment had a rwPFS of 3.2 months (95 % CI: 2.8–3.9), while those with more than two prior lines had a rwPFS of 5.3 months (95 % CI: 3.5–6.4; Figure S2).

The median (95 % CI) rwPFS was similar between patients who received immunotherapy (3.8 [2.6–5.7] months) or chemotherapy (4.0 [2.9–5.4] months) alone or in combination (3.0 [2.4–4.0] months) just before sotorasib (Figure S3).

Out of 199 patients receiving treatment after sotorasib, 182 (91.5 %) received systemic therapy (detailed in Table S7), and 51 (25.6 %) had

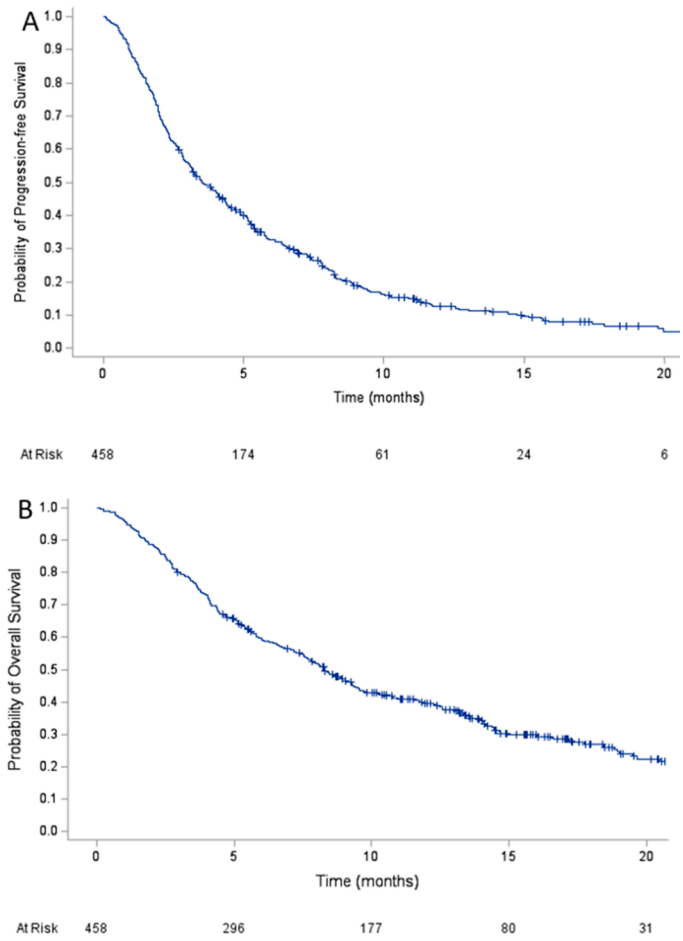

Fig. 1. Real-world progression-free survival and overall survival analysis. 1A. Kaplan-Meier estimate of real-world progression-free survival (rwPFS) after sotorasib initiation. Tick marks on the survival curves indicate censoring of data. CI: confidence interval. 1B. Kaplan-Meier estimate of real-world overall survival (rwOS) after sotorasib initiation. Tick marks on the survival curves indicate censoring of data. CI: confidence interval.

local radiotherapy. Overall, response rates to first subsequent systemic therapy included 16 patients with rwORR (11.7 %, 95 % CI: 6.3–17.1), 43 with rwDCR (31.4 %, 95 % CI: 23.6–39.2), and 91 with disease progression (66.4 %, 95 % CI: 58.5–74.3; Table S7). The median duration of subsequent treatment was 1.4 (0.03–17.6) months.

3.5. Discontinuation, suspension, and dose reduction of sotorasib treatment

Out of 458 patients, 400 discontinued sotorasib treatment, mostly due to disease progression (70 %) and toxicity (16.5 %; Figure S1). During the study, treatment was suspended 152 times for a median duration of 16 days (3−80). A quarter of patients (25.5 %) had at least one suspension, primarily due to toxicity (71.1 %). Among the 119 patients who underwent a dose reduction, 73.1 % decreased their dose from 960 to 480 mg, 25.3 % of them reduced their dose from 480 to 240 mg, while 6.7 % reduced directly from 960 to 240 mg.

3.6. Toxicity and adverse events during sotorasib treatment

Hepatotoxicity and gastrointestinal disorders were the primary reasons for sotorasib discontinuation (54.6 % and 33.3 %, respectively) and suspension (52.8 % and 34.2 %, respectively; Table 4). Grade 3 or 4 treatment-related adverse events occurred in 24 (5.2 %) patients, with elevated gamma-glutamyltransferase (n = 18; 4.0 %) alanine aminotransferase (n = 13; 2.8 %) and aspartate aminotransferase (n = 9; 2.0 %) levels being most frequent (Table 5).

Among patients who received immunotherapy (alone or with chemotherapy) as last treatment before sotorasib, 20 (8.3 %) experienced grade 3 or 4 treatment-related adverse events. Conversely, those who received only chemotherapy before starting sotorasib had a lower incidence of severe adverse events (0.7 %). The toxicity profile was comparable between eligible and ineligible patients in the CodeBreak 200 study (Table S8).

4. Discussion

Sotorasib, the first FDA-approved KRAS *G12C* inhibitor, has shown significant efficacy in clinical trials but lacks extensive real-world data, especially in patients previously treated with immunotherapy. This study provides a comprehensive analysis of the effectiveness and safety of sotorasib in a cohort of 458 patients with NSCLC treated within an EAP in France.

The results of this French real-world study indicated that the rwORR was consistent with previous reports; however, the rwPFS and rwDCR were lower compared to prior sotorasib trials (rwPFS: 3.5 vs. 5.6 months; rwDCR: 62.3 % vs. 82.5 %; [1]). These discrepancies can be attributed to differences in patient characteristics at baseline. Clinical trials typically involve controlled conditions, whereas observational studies provide insights into a drug's effectiveness in broader clinical practice. Notably, clinical trials for sotorasib excluded patients with a performance status higher than 2, those who were heavily pretreated, or those with uncontrolled brain metastases [11,1,10]. This observational study included such patients, offering a more comprehensive view of the

Table 3
Univariate and multivariate analysis of real-world overall survival (Cox model).

		Univariate model			Multivariate model		
Factors	N	HR	95 % CI	p	HR	95 % CI	p
Sex							
Female	199	1.00		-	1.00	-	-
Male	259	1.21	0.96–1.51	0.099	1.21	0.91–1.61	0.19
Age							
< 70	312	1.00		-			
≥ 70	146	0.94	0.74–1.18	0.59			
ECOG performance status							
< 2	220	1.00		-	1.00	-	-
≥ 2	87	2.13	1.59–2.86	< 0.0001	2.12	1.58–2.84	< 0.0001
Brain metastasis							
No	284	1.00		-			
Yes	174	1.19	0.95–1.49	0.14			

ECOG: Eastern Cooperative Oncology Group; For multivariate analysis, the input p-value for stepwise selection is 0.2.

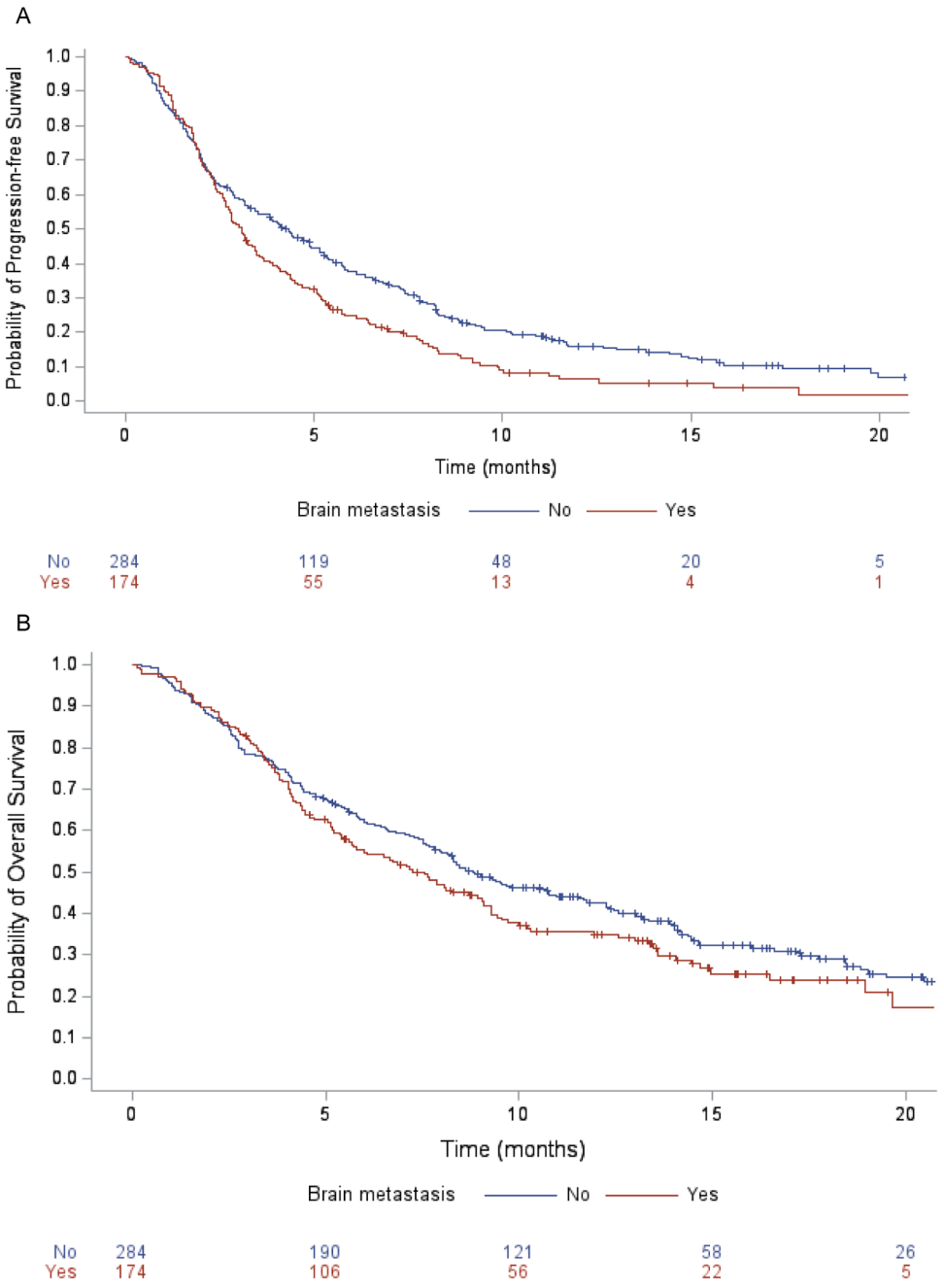

Fig. 2. Real-world progression-free survival and overall survival in relation to brain metastasis. 2A. Kaplan-Meier estimate of real-world progression-free survival (rwPFS) after sotorasib initiation. Tick marks on the survival curves indicate censoring of data. CI: confidence interval. 2B. Kaplan-Meier estimate of real-world overall survival (rwOS) after sotorasib initiation. Tick marks on the survival curves indicate censoring of data. CI: confidence interval.

Table 4
Toxicities leading to sotorasib discontinuation or suspension.

Discontinuation, n (%)	N = 66
Hepatotoxicity, n (%)	36 (54.6)
Gastrointestinal disorders, n (%)	22 (33.3)
Both, n (%)	5 (7.6)
Other, n (%)	3 (4.5)
Suspension, n (%)	N = 108
Hepatotoxicity, n (%)	57 (52.8)
Gastrointestinal disorders, n (%)	37 (34.2)
Both, n (%)	11 (10.2)
Other, n (%)	3 (2.8)

drug's performance in real-world settings. When comparing to previously published real-word studies, the rwORR and rwOS of the French cohort were similar (rwORR: 33.2 % vs. 26–39 %; median rwOS: 8.3 vs. 8.2–12.6 months), French real-word rwPFS and duration of response were lower (median rwPFS: 3.5 vs. 4.8–5.8 months; median duration of response: 3.8 vs. 5.7–7.9 months; Table 6). This difference could be due to the larger sample size in our study. Additionally, the current study included more patients with poor performance status (≥2) compared to previous reports [14,20]. When using in our population eligibility criteria of CodeBreak 200, outcome was better for eligible patients (Table S3). Our inclusion of patients with untreated brain metastases contrasts with the CodeBreak 200 trial, which excluded such patients (de [10]. In this study, 55.2 % of patients had brain metastasis at the time of sotorasib initiation, significantly higher than the typically

Table 5
Adverse events related to hepatotoxicity.

Adverse events, n (%)	N = 458			
	Any grade	Grade 2	Grade 3	Grade 4
Any adverse event	29 (6.3 %)	5 (1.1 %)	18 (3.9 %)	6 (1.3 %)
Gamma-glutamyl transferase elevation	21 (4.6 %)	3 (0.7 %)	14 (3.1 %)	4 (0.9 %)
Alanine aminotransferase elevation	19 (4.1 %)	6 (1.3 %)	12 (2.6 %)	1 (0.2 %)
Aspartate aminotransferase elevation	16 (3.5 %)	7 (1.5 %)	9 (2.0 %)	0 (0.0 %)
Blood alkaline phosphatase elevation	10 (2.2 %)	5 (1.1 %)	5 (1.1 %)	0 (0.0 %)
Blood bilirubin elevation	5 (1.1 %)	3 (0.7 %)	1 (0.2 %)	1 (0.2 %)

reported 30 % in the general NSCLC population ([9,12]). This discrepancy can be attributed to the advanced disease stage in our cohort, as sotorasib is generally used in patients who have progressed after prior treatments. Patients with brain metastases had poorer outcomes (median rwPFS: 3.1 vs. 4.3 months; median rwOS: 7.2 vs. 8.8 months) compared to those without and even more those with untreated brain metastases (Table S5). Despite these challenges, sotorasib showed some intracranial activity (rwORR: 20.1 %, rwDCR: 66.9 %), indicating its potential in managing CNS involvement in lung cancer. Performance status emerged as a significant determinant of OS, with poorer outcomes for patients with a status of 2 or higher. This finding is consistent with existing literature [15,23] and highlights the importance of maintaining a good performance status to achieve better outcomes in cancer treatment.

Around 50 % of our patients had received two or more lines of treatment before sotorasib, compared to those in the CodeBreak 200 study who were treated with sotorasib after previous platinum-based chemotherapy and a PD-1 or PD-L1 inhibitor (de [10]). Interestingly, in the present study, patients with more than two prior lines of treatment had a longer rwPFS (5.3 months) than those with fewer lines (3.2 months), suggesting that these patients had favourable prognostic criteria. In the future, it would be interesting to identify these criteria in order to improve NSCLC management. After sotorasib, most patients (91.5 %) received further systemic therapy, but the response rates to these treatments were low (rwORR: 11.7 %), reflecting the advanced disease stage and limited treatment options. This underscores the need for new therapeutic strategies.

Disease progression (70.0 %) and toxicity (16.5 %) were the main reasons for treatment discontinuation, highlighting the aggressive nature of the disease in this patient population. Treatment suspensions occurred in 25.5 % of patients, primarily due to toxicity, with a median suspension duration of 16 days. Sotorasib treatment is known to be associated with hepatic and gastrointestinal toxicities [7]. These were the main reasons for treatment discontinuation and suspension in our real-world study. Sotorasib-related hepatotoxicity was lower than in the CodeBreak 200 trial, possibly due to the less rigorous monitoring and reporting protocols in observational studies. Indeed, in our study, the detection might be limited to significant cases, aligning with real-world requirements where only notable hepatotoxicity is of clinical concern. Furthermore, in observational studies, both patients and investigators may prioritize managing the primary disease over documenting all side effects, especially mild or expected ones, unlike interventional studies where strict protocols mandate tracking and reporting every adverse event.

Severe (grade 3 or 4) treatment-related adverse events were reported in 5.2 % of patients, mostly hepatotoxicity, which was lower than previously reported (33 %) (de [10]). Patients previously treated with immunotherapy experienced higher rates of severe adverse events (8.3 %) compared to those treated only with chemotherapy (0.7 %). This suggests a potential interaction or heightened sensitivity following immunotherapy. In addition, to minimize the risk of hepatotoxicity, studies have shown that the timing between immunotherapy and sotorasib initiation may be important to consider [3,5]. These results underscore the need for careful monitoring and management of hepatotoxicity in patients undergoing sotorasib treatment, particularly in

Table 6
Real-world data of sotorasib in KRAS *G12C*–mutated advanced non–small-cell lung cancer.

Study design	Baseline characteristics	Efficacy outcomes	Safety outcomes	Reference
- Italian EAP (2020–2022) - 196 patients analysed - 30 centres - 960 mg of sotorasib, orally, once daily - Second (45 %) or third (32 %) line	- Median age was 69 years (range 33–86). - Females: 39 % - Former (49 %) or current smokers (43 %), - Adenocarcinoma subtype (90 %) - Brain metastases: 33 % - Performance status ≥ 2: 8 %	- ORR: 26 % - Median duration of response: 5.7 months (95 % CI: 4.4 – 7.0) - Median rwPFS: 5.8 months (95 % CI: 5 – 6.5) - Median OS: 8.2 months (95 % CI: 6.3 – 9.9)	- Grade 3–4 TRAEs: in 16.5 % of patients - Grade ≥ 3 liver enzyme increase in 12 % of cases - TRAEs-related discontinuation in 4.6 % of patients	Passiglia [14]
- German compassionate use program (2020–2022) - 163 patients analysed - 58 centres - 960 mg of sotorasib, orally, once daily - Median of 2 treatment lines (range, 0 – 7)	- Median age of 64 years (range 41 – 82) - Females: 47 % - Former (53 %) or current smokers (40 %) - Adenocarcinomas (89 %) - All patients had metastatic disease - Brain metastases: 38 % - Performance status ≥ 2: 23 %	- ORR: 39 % - Median duration of response: 7.9 months (95 % CI: 4.9 – 10.8) - Median rwPFS: 4.8 months (95 % CI, 3.9 – 5.9) - Median OS: 9.8 months (95 % CI, 6.5 – not reached)	- Grade ≥ 3 TRAEs in 17 % of patients - TRAEs-related dose reductions in 22 % of patients - TRAEs-related discontinuation in 4 % of patients	Stratmann [20]
- Multicentre retrospective study in the USA - 105 patients analysed - 3 centres - 960 mg of sotorasib, orally, once daily (97 %) - Median of 1 (range 0 – 5)	- Median age of 70 years (range 51 – 90) - Females: 59 % - Former (88 %) or current smokers (10 %) - Adenocarcinomas (89 %) - Untreated brain metastases: 7 % - Treated brain metastases: 27 % - Performance status ≥ 2: 21 %	- ORR: 28 % (95 % CI: 20 – 37) - Median duration of response: 7.2 months (95 % CI: 4.6 – 10.4) - Median rwPFS: 5.3 months (95 % CI: 3.6 – 6.6), - Median OS: 12.6 months	- Grade 3 TRAEs in 15 % of patients - Grade 4 TRAEs in 1 % of patients - TRAEs-related dose reductions in 15 % patients - TRAEs-related discontinuation in 13 % of patients	Thummalapalli et al., [22]

those with a history of immunotherapy.

At the end of the study, 58 patients were still under sotorasib treatment. The 6- and 12-month rwPFS rates were 32.8 % and 12.5 %, respectively, while the rwOS rates were 59.2 % and 39.6 %. Despite challenges due to adverse events, the continued benefit for a considerable proportion of patients highlights sotorasib's potential role in the therapeutic landscape. Further research is needed to identify which patient subgroups are most likely to benefit from sotorasib. More studies are necessary to confirm the pejorative impact of STK11 co-mutations and the role of other co-mutations, on the efficacy of sotorasib.

5. Conclusions

Sotorasib shows promise in treating NSCLC in a real-world setting, despite lower rwPFS and rwDCR compared to clinical trials, largely due to the inclusion of a broader patient population. Notably, hepatotoxicity was lower than previously reported. Its continued benefit underscores its potential, but further research is needed to identify which subgroups benefit most and optimize adverse event management.

Ethics statement

The study has been made in accordance with Declaration of Helsinki, Good Clinical Practice guidelines, and compliance commitment to reference method MR-004 submitted to the CNIL (French National Commission for the protection of private data and rights). It was registered in the Health Data Hub (HDH) public directory (https://www.health-data-hub.fr/projets) and in clinicaltrials.gov database under the ID NCT05273047. An information letter drafted in accordance with article 14 of the European GDPR regulations was given to living patients to obtain their nonobjection to collection of their medical data and to inform them of their rights. Patients were able to exercise their rights at any time with their doctors or the DPO of the IFCT. Information pertaining to deceased patients may be subject to data processing, except if the concerned patient voiced refusal while still alive.

Funding

This work was supported by an unrestricted grant from Amgen. The funding source had no role in the study design, data collection, data analysis, data interpretation, or preparation of this manuscript.

Declaration of Competing Interest

M. Wislez: Amgen, Roche, BMS, MSD, Astra-Zeneca, Sanofi, Novartis, Lilly, Takeda, Kephren, Amgen, Janssen. C. Mascaux: Amgen, AstraZeneca, BMS, MSD, Lilly, Novartis, Pfizer, Roche, Sanofi, Takeda, Kephren, Janssen. J. Cadranel: AbbVie, Amgen, AstraZeneca, Boehringer Ingelheim, BMS, Daiichi Sankyo, MSD, Lilly, Novartis, Pfizer, F. Hoffmann-La Roche Ltd, Sanofi, Takeda. Q. D. Thomas: Amgen, AstraZeneca, Sanofi. A. Swalduz: AstraZeneca, Janssen, Roche, Amgen, BMS, Pfizer, Lilly. E. Pichon: BMS, AstraZeneca, Takeda, Janssen, BeiGene. R. Veillon: Janssen, BMS, Takeda, Amgen, Sanofi, Roche, AstraZeneca, Abbvie, GSK, Novartis, Merck KGaA, Pfizer. V. Gounant: BMS, AstraZeneca, Takeda, Sanofi, Pfizer. G. Rousseau-Bussac: AstraZeneca, Takeda, BMS, Boehringer, Sanofi, Lilly, Pfizer. A. Madroszyk: AstraZeneca, Roche, Pfizer. C. Daniel: AstraZeneca, MSD, Amgen, Sanofi. P. Fournel: Amgen, AstraZeneca, BMS, Janssen, MSD, Sanofi, Takeda, Ipsen. F. Guisier: Amgen, AstraZeneca, BMS, Janssen, MSD, Pfizer, Roche, Sanofi, Takeda. V. Westeel: Amgen, AstraZeneca, BMS, MSD, Roche, Sanofi, Pfizer, Janssen, Ipsen. All the other authors declare that they have no conflicts of interest.

Acknowledgements

We thank the IFCT-2102 LungKG12Ci collaborators listed below who contributed to this project and provided data for at least 1 patient (not included in the list of authors). We also acknowledge Marina Schverer, PhD, and Solenn Le Clanche, PhD, for medical writing assistance in the development and editing of this manuscript.

The IFCT-2102 LungKG12Ci contributors, listed here, collaborated in this project and provided data for 1 patient or more (not included in the list of authors):

- Amale AIT-ADDI, Service d'Oncologie, Centre Hospitalier, DAX, France
- Pascal ASSOULINE, Service Oncologie - Hématologie, Centre Hospitalier de Bligny, BRIIS-SOUS-FORGES, France
- Clarisse AUDIGIER-VALETTE, Service de Pneumologie, CHITS Toulon Sainte Musse, TOULON, France
- Laurent BASSON, Pneumologie, Centre Pierre Curie, BEUVRY, France
- Christelle CLEMENT-DUCHENE, Oncologie Médicale, Centre Alexis Vautrin, Institut de cancérologie de Lorraine, VANDOEUVRE-LES-NANCY, France
- Nicolas CLOAREC, Service d'Oncologie, Centre Hospitalier, AVIGNON, France
- Charles DAYEN, Service de Pneumologie, Centre Hospitalier, SAINT-QUENTIN, France
- Gonzague DE CHABOT, Service d'Oncologie de jour, Centre Hospitalier Bretagne Atlantique, VANNES, France
- Didier DEBIEUVRE, Service de Pneumologie, Groupe Hospitalier Région Mulhouse et Sud-Alsace, MULHOUSE, France
- Clotilde DELDYCKE, Service de Pneumologie, CHU de Poitiers, POITIERS, France
- Maxime DEWOLF, Service de pneumologie, CHU, Hôpital Maison Blanche, REIMS, France
- Pierre DIAZ, Service de Pneumologie, Centre Hospitalier William Morey, CHALON-SUR-SAONE, France
- Adrien DIXMIER, Service de Pneumologie, Centre Hospitalier Universitaire, Hôpital de la Source, ORLEANS, France
- Thomas EGENOD, Unité d'Oncologie Thoracique et Cutanée, CHU Dupuytren, LIMOGES, France
- Élizabeth FABRE, Service de Chirurgie Thoracique, Hôpital Européen George Pompidou, PARIS, France
- Cléa FRAISSE, Oncologie médicale, Centre Georges-François Leclerc, DIJON, France
- Hugues FRANCOIS, Service de Pneumologie, Centre Hospitalier de la Polynésie Française, PIRAE, France
- Georges GARNIER, Hôpital de Jour, Centre Hospitalier Princesse Grace, MONACO, France
- Laurène GAVOILLE, Service de Pneumologie, Polyclinique de Gentilly, NANCY, France
- Elisabeth GAYE, Département Oncologie Générale, Centre Oscar Lambret, LILLE, France
- Benoît GODBERT, Service de Pneumologie, Hôpital Robert Schuman, VANTOUX, France
- Daiddin HAMDAN, Pôle Oncologie / Oncogériatrie, Hôpital la Porte Verte, VERSAILLE, France
- Pierre-Alexandre HAUSS, Service Pneumologie, Centre Hospitalier Intercommunal, ELBEUF, France
- Carole HELISSEY, Oncologie Médicale, HIA Begin, SAINT-MANDE, France
- Chloé HERREMAN, Service de Pneumologie, Centre Hospitalier, CHAMBERY, France
- Eric HUCHOT, Service de Pneumologie, CHU de La Réunion-Site Sud, SAINT-PIERRE, France
- Benjamin HURET, Service de Pneumologie, Hôpital Privé de la Louvière, LILLE, France
- Henri JANICOT, Service d'oncologie thoracique, Hôpital de jour, Hôpital Gabriel Montpied, CLERMONT-FERRAND, France

- Virginie JOUBERT, Service Oncologie - Radiothérapie, Centre Hospitalier Robert Boulin, LIBOURNE, France
- Sylvestre LE MOULEC, Groupe de Radiothérapie et d'Oncologie des Pyrénées, PAU, France • Jacques LE TREUT, Service d'Oncologie Thoracique, Hôpital Européen, MARSEILLE, France
- Olivier LELEU, Service de Pneumologie, Centre Hospitalier, ABBEVILLE, France
- Ulrike LEROLLE, Service de Pneumologie, Clinique Saint-Joseph, TRELAZE, France
- Vincent LEROY, Service de pneumologie, Clinique Médico-chirurgicale Teissier Groupe A.H.N.A.C, VALENCIENNES France
- Bénédicte LETERRE, Service de Pneumologie, Centre Hospitalier, NEVERS, France
- Chrystèle LOCHER, Service de pneumologie, Centre Hospitalier, MEAUX, France
- Jeannick MADELAINE, Service de Pneumologie, CHU Côte de Nacre, CAEN, France
- Stéphanie MARTINEZ, Service de Pneumologie, Centre Hospitalier, SALON DE PROVENCE, France
- Philippe MASSON, Service de Pneumologie, Centre Hospitalier, CHOLET, France
- Karine MICHAUX, Service de Pneumologie Unité R2, Centre Hospitalier les Chanaux, MACON, France
- Diane MOREAU, Service des Maladies Respiratoires, Centre Hospitalier Départemental F. Guyon, SAINT-DENIS, France
- Yann MOTTAZ, Oncologie Médicale, Polyclinique de Blois, France • Assaad NAKAD, Service de Pneumologie, Service de Pneumologie, Bar-le-Duc, France
- Luc ODIER, Service de Pneumologie, Centre Hospitalier de Villefranche-sur-Saône, VILLEFRANCHE-SUR-SAONE, France
- Nicolas PALEIRON, Service de Pneumologie, HIA Sainte-Anne, TOULON, France
- Davy PICARD, Service de Pneumologie, Centre Hospitalier, CHALONS-EN-CHAMPAGNE, France
- Elvire PONS-TOSTIVINT, Service de Pneumologie, CHU de Nantes, Hôpital Laennec, NANTES, France
- Claire POULET, Service de Pneumologie, CHU Amiens, Groupe Hospitalier Sud, AMIENS, France
- Aldo RENAULT, Service de Pneumologie, Centre Hospitalier Général, PAU, France
- Philippe ROMAND, Service de Pneumologie, Centre Hospitalier Alpes Léman, CONTAMINE SUR ARVE, France
- Stanislas ROPERT, Oncologie Médicale, Hôpital privé d'Antony, ANTONY, France
- Antonio ROZZI, Service de pneumologie, CHG Compiègne, COMPIEGNE, France
- Antoine SERRE, Service d'Oncologie - Radiothérapie, Clinique Valdegour, NIMES, France
- Dorine TEMPLEMENT, Service de pneumologie, Centre Hospitalier de la Région d'Annecy, PRINGY, France
- Safae TERRISSE, Service d'Oncologie Médicale, Hôpital Saint-Louis, PARIS, France
- Fanny THEPAULT, Fédération de Pneumologie, Centre Hospitalier Broussais, SAINT-MALO, France
- Thierry URBAN, Service de Pneumologie, CHU d'Angers, ANGERS, France
- Ayoube ZOUAK, Service de Pneumologie, CHU Hôpital du Bocage, DIJON, France

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ejca.2025.115301.

References

[1] Alharbi Malak, Awidi Muhammad, et, Dy Grace K. CodeBreak 200: study limitations, and future directions. Transl Cancer Res 2024;13(1):15–21. https://doi.org/10.21037/tcr-23-1477.

[2] Araghi Mahmood, Mannani Reza, Heidarnejad maleki Ali, Hamidi Adel, Rostami Samaneh, Safa Salar Hozhabri, Faramarzi Fatemeh, et al. Recent advances in non-small cell lung cancer targeted therapy; an update review. Cancer Cell Int 2023;23(1):162. https://doi.org/10.1186/s12935-023-02990-y.

[3] Chour Ali, Denis Julie, Mascaux Céline, Zysman Maeva, Bigay-Game Laurence, Swalduz Aurélie, Gounant Valérie, et al. Brief Report: Severe Sotorasib-Related Hepatotoxicity and Non-Liver Adverse Events Associated With Sequential Anti-Programmed Cell Death (Ligand)1 and Sotorasib Therapy in KRASG12C-Mutant Lung Cancer. 5 *J Thorac Oncol: Publ Int Assoc Study Lung Cancer*, mai 2023;S1556-0864(23):00572. https://doi.org/10.1016/j.jtho.2023.05.013.

[4] « Demande d'autorisation d'accès précoce ». s. d. ANSM. Consulté le 13 septembre 2024. https://ansm.sante.fr/vos-demarches/industriel/demande-dautorisation-dacces-precoce.

[5] Desai Aakash, Rakshit Sagar, Bansal Radhika, Ashara Yash, Potter Ashley, Manochakian Rami, Lou Yanyan, et al. Time from immune checkpoint inhibitor to sotorasib use correlates with risk of hepatotoxicity in non-small cell lung cancer: a brief report. Cancer Treat Res Commun 2023;36:100743. https://doi.org/10.1016/j.ctarc.2023.100743.

[6] Dy Grace K, Govindan Ramaswamy, Velcheti Vamsidhar, Falchook Gerald S, Italiano Antoine, Wolf Jürgen, Sacher Adrian G, et al. Long-term outcomes and molecular correlates of sotorasib efficacy in patients with pretreated KRAS G12C-mutated non-small-cell lung cancer: 2-year analysis of CodeBreaK 100. J Clin Oncol: J Am Soc Clin Oncol 2023;41(18):3311–7. https://doi.org/10.1200/JCO.22.02524.

[7] Ernst Sophie M, Hofman Maaike M, van der Horst Tessa E, Paats Marthe S, Heijboer Frank WJ, Aerts Joachim GJV, Dumoulin Daphne W, et al. Hepatotoxicity in patients with non-small cell lung cancer treated with sotorasib after prior immunotherapy: a comprehensive clinical and pharmacokinetic analysis. EBioMedicine 2024;102(mars):105074. https://doi.org/10.1016/j.ebiom.2024.105074.

[8] Fatima Sheereen, Pansuriya Nirav, Lakhani Alisha, Madhuri Sai, Ajmal Reshma, Clementina Ruchira, Lakdawala Zahabiya, et al. KRAS as a prognostic and predictive marker in metastatic non-small cell lung carcinoma: a systematic review. Cureus 2024;16(5):e60061. https://doi.org/10.7759/cureus.60061.

[9] Kelly Karen, et, Bunn Paul A. Is it time to reevaluate our approach to the treatment of brain metastases in patients with non-small cell lung cancer? Lung Cancer 1998;20(2):85–91. https://doi.org/10.1016/S0169-5002(98)00020-8.

[10] Langen Adrianus Johannes de, Johnson Melissa L, Mazieres Julien, Dingemans Anne-Marie C, Mountzios Giannis, Pless Miklos, Wolf Jürgen, et al. Sotorasib versus docetaxel for previously treated non-small-cell lung cancer with KRASG12C mutation: a randomised, open-label, phase 3 trial. Lancet (Lond, Engl) 2023;401(10378):733–46. https://doi.org/10.1016/S0140-6736(23)00221-0.

[11] Li BT, Falchook GS, Durm GA, Burns TF, Skoulidis F, Ramalingam SS, Spira A, et al. OA03.06 CodeBreaK 100/101: First Report of Safety/Efficacy of Sotorasib in Combination with Pembrolizumab or Atezolizumab in Advanced KRAS p.G12C NSCLC. *J Thorac Oncol*, Abstr 2022 World Conf Lung Cancer 2022;17(9, ement):S10–1. https://doi.org/10.1016/j.jtho.2022.07.025.

[12] Lombardi Giuseppe, Di Stefano Anna Luisa, Farina Patrizia, Zagonel Vittorina, et, Tabouret Emeline. Systemic treatments for brain metastases from breast cancer, non-small cell lung cancer, melanoma and renal cell carcinoma: an overview of the literature. Cancer Treat Rev 2014;40(8):951–9. https://doi.org/10.1016/j.ctrv.2014.05.007.

[13] Ostrem Jonathan ML, et, Shokat Kevan M. Direct small-molecule inhibitors of KRAS: from structural insights to mechanism-based design. Nat Rev Drug Discov 2016;15(11):771–85. https://doi.org/10.1038/nrd.2016.139.

[14] Passiglia Francesco. Sotorasib in KRASp.G12C mutated advanced NSCLC: real-world data from the italian expanded access program. Lung Cancer 2024.

[15] Sehgal Kartik, Gill Ritu R, Widick Page, Bindal Poorva, McDonald Danielle C, Shea Meghan, Rangachari Deepa, et, Costa Daniel B. Association of performance status with survival in patients with advanced non–small cell lung cancer treated with pembrolizumab monotherapy. JAMA Netw Open 2021;4(2). https://doi.org/10.1001/jamanetworkopen.2020.37120.

[16] Siegel Rebecca L, Miller Kimberly D, Wagle Nikita Sandeep, et, Jemal Ahmedin. Cancer Statistics, 2023. CA: A Cancer J Clin 2023;73(1):17–48. https://doi.org/10.3322/caac.21763.

[17] Skoulidis Ferdinandos, Li Bob T, Dy Grace K, Price Timothy J, Falchook Gerald S, Wolf Jürgen, Italiano Antoine, et al. Sotorasib for lung cancers with KRAS p.G12C mutation. N Engl J Med 2021;384(25):2371–81. https://doi.org/10.1056/NEJMoa2103695.

[18] Staff. 2021. « Further Analyses Expand Upon Duration of Benefit With Sotorasib in KRAS G12C+ NSCLC », Targeted Therapies in Oncology, 10 (octobre). https://www.targetedonc.com/view/further-analyses-expand-upon-duration-of-benefit-with-sotorasib-in-kras-g12c-nsclc.

[19] ———. 2024. « Experts Examine the Need for Targeted Therapy Options for KRAS G12C–Mutated NSCLC » , Oncology, 38 (février):15-17.

[20] Stratmann Jan A. Sotorasib in KRAS G12C -mutated non-small cell lung cancer: a multicenter real-world experience from the compassionate use program in Germany. Eur J Cancer 2024.

[21] Thomas QD, Quantin X, Lemercier P, Chouaid C, Schneider S, Filleron T, Remon-Masip J, et al. Clinical Characteristic and Survival Outcomes of Patients with Advanced NSCLC According to KRAS Mutational Status in the French Real-Life

ESME Cohort. ESMO Open 2024;9(6):103473. https://doi.org/10.1016/j.esmoop.2024.103473.

[22] Thummalapalli Rohit, Bernstein Ezra, Herzberg Benjamin, Li Bob T, Iqbal Afsheen, Preeshagul Isabel, Santini Fernando C, et al. Clinical and genomic features of response and toxicity to sotorasib in a real-world cohort of patients with advanced KRAS G12C-mutant non-small cell lung cancer. JCO Precis Oncol 2023;7(juin): e2300030. https://doi.org/10.1200/PO.23.00030.

[23] Ying X, You G, et Shao. The analysis of the efficacy and safety of stereotactic body radiotherapy with sequential immune checkpoint inhibitors in the management of oligoprogressive advanced non-small cell lung cancer. Transl Cancer Res 2024;13 (5). https://doi.org/10.21037/tcr-23-2232.