Overall survival (OS) with sotorasib plus carboplatin and pemetrexed in *KRAS* G12C-mutated advanced non-small cell lung cancer (NSCLC) from the global phase 1b CodeBreaK 101 study

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Background

- Sotorasib monotherapy confers meaningful clinical benefit in patients with previously treated *KRAS* G12C-mutated advanced NSCLC[1]
- Rational combination strategies are needed to achieve deeper and more durable control, particularly in the 1L setting[2,3]
- In the ongoing, global, phase 1b CodeBreaK 101 study, treatment with sotorasib plus carboplatin and pemetrexed (platinum doublet chemotherapy) has shown encouraging outcomes in the 1L and 2L+ settings[4]

We report OS data along with additional efficacy and safety outcomes for sotorasib plus platinum doublet chemotherapy in patients with *KRAS* G12C-mutated advanced NSCLC

Study Design

CodeBreaK 101 phase 1b, multicenter, open-label study (subprotocol F)*

Key eligibility criteria

- *KRAS* G12C-mutated advanced NSCLC, identified through molecular testing
- Patients were treatment-naïve or previously treated*
- Measurable disease per RECIST v1.1
- ECOG PS ≤ 2
- No active brain metastases

Up to 4 cycles†

Sotorasib 960 mg PO daily + Carboplatin AUC 5 IV Q3W + Pemetrexed 500 mg/m^2 IV Q3W

Maintenance†

Sotorasib 960 mg PO daily + Pemetrexed 500 mg/m^2 IV Q3W

Data were pooled from dose exploration and expansion cohorts and analyzed by exposure to prior therapy in the locally advanced/metastatic setting: **1L (n = 44) and 2L+ (n = 23)‡**

Primary endpoints: Safety and tolerability (including DLT)
Secondary endpoints: ORR, DCR, DOR, TTR, OS, PFS, duration of SD, and PK

Data cutoff: June 13, 2025.
*NCT04185883. Patient enrollment cohorts were Part 1 Cohort A (prior anti–PD-[L]1 immunotherapy and / or platinum-based combination chemotherapy or refused standard therapy), Part 2 Cohort A1 (no prior anti–PD-[L]1 immunotherapy or platinum-based combination chemotherapy), and Part 2 Cohort A2 (prior anti–PD-1 monotherapy, platinum-based chemotherapy, or neoadjuvant / adjuvant chemotherapy).
†Treatment until evidence of disease progression, intolerance to study medication, withdrawal of consent, or end of study.
‡Of 23 patients in the 2L+ setting, 21 (91%) received 1 prior line of therapy, 1 (4%) received 2 prior lines of therapy, and 1 (4%) did not receive any prior line of therapy.

Baseline Characteristics

- *TP53*, *STK11*, and *KEAP1* were the most prevalent co-alterations in the overall population, consistent with previous reports[5] (supplementary slides)

Characteristic	Sotorasib + Carboplatin + Pemetrexed 1L (n = 44)	Sotorasib + Carboplatin + Pemetrexed 2L+ (n = 23)
Median age, years (range)	65 (46-82)	67 (44-76)
Male	18 (41)	12 (52)
White / Black or African American / Other	41 (93) / 2 (5) / 1 (2)	18 (78) / 3 (13) / 2 (9)
Never / Current / former smoker	1 (2) / 7 (16) / 36 (82)	2 (9) / 5 (22) / 16 (70)
ECOG PS 0 / 1	15 (34) / 29 (66)	7 (30) / 16 (70)
Stage III / IV at screening	1 (2) / 43 (98)	2 (9) / 21 (91)
History of brain metastasis	6 (14)	5 (22)
History of liver metastasis	4 (9)	4 (17)
Prior neoadjuvant / adjuvant chemotherapy	2 (5)	2 (9)
Prior anti–PD-(L)1	0	20 (87)
High tumor burden at screening (SOD ≥ 100 mm)	10 (23)	7 (30)
PD-L1 protein expression*		
< 1%	26 (59)	5 (22)
1% – 49%	11 (25)	5 (22)
≥ 50%	7 (16)	13 (57)

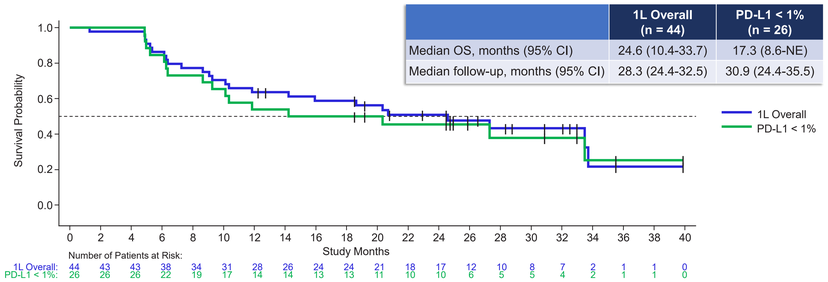
Data reported as n (%) unless otherwise specified.
*PD-L1 status was assessed on locally available assays without central confirmation.

Key Findings

Sotorasib 960 mg plus platinum doublet chemotherapy in *KRAS* G12C-mutated advanced NSCLC showed encouraging OS benefit in the 1L setting, including patients with PD-L1 < 1%, supporting further investigation in the CodeBreaK 202 study

OS in 1L Setting (Overall & PD-L1 < 1%)

	1L Overall (n = 44)	PD-L1 < 1% (n = 26)
Median OS, months (95% CI)	24.6 (10.4-33.7)	17.3 (8.6-NE)
Median follow-up, months (95% CI)	28.3 (24.4-32.5)	30.9 (24.4-35.5)



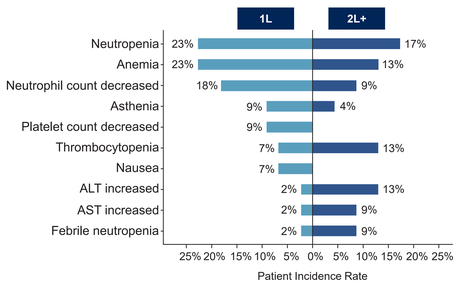
- PD-L1 status was assessed on locally available assays without central confirmation
- Of 33 patients eligible to receive subsequent therapy, 18 (55%) received immunotherapy
- In the 2L+ setting, median OS was 19.6 months (supplementary slides)

Safety

TRAE, n (%)	Sotorasib + Carboplatin + Pemetrexed 1L (n = 44)	Sotorasib + Carboplatin + Pemetrexed 2L+ (n = 23)
Any grade	43 (98)	23 (100)
Grade ≥ 3	28 (64)	17 (74)
Leading to dose reduction / interruption of any treatment	35 (80)	19 (83)
Sotorasib	26 (59)	15 (65)
Carboplatin	15 (34)	10 (44)
Pemetrexed	28 (64)	13 (57)
Leading to discontinuation of any treatment	13 (30)	10 (44)
Sotorasib	3 (7)	4 (17)
Carboplatin	1 (2)	0
Pemetrexed	13 (30)	7 (30)
Fatal*	0	1 (4)

*Fatal TRAE was febrile neutropenia, attributed to carboplatin and pemetrexed.

Most Common Grade ≥ 3 TRAEs (≥ 5% of patients)

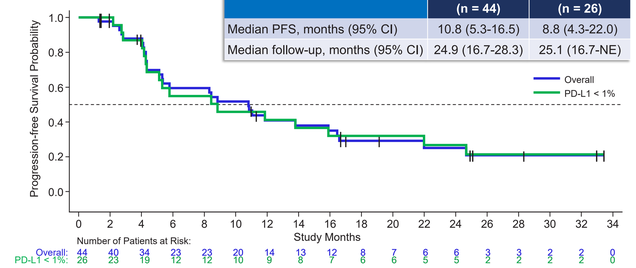


- Adverse events were consistent with the known safety profiles of sotorasib and platinum doublet chemotherapy

Progression-free Survival

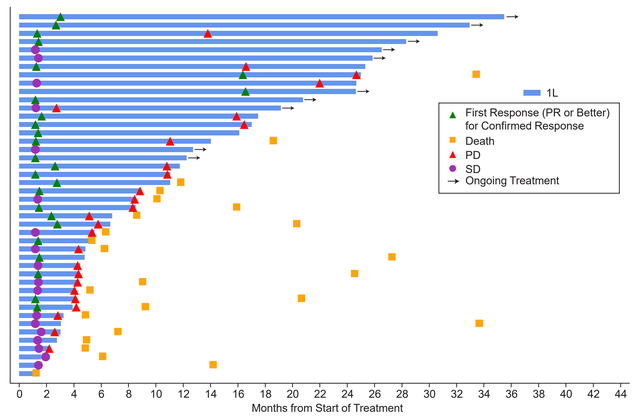
- Median PFS in the 1L analysis set overall and in PD-L1 < 1% was 10.8 months and 8.8 months, respectively
- In the 2L+ analysis set, median PFS was 10.3 months (supplementary slides)

	1L Overall (n = 44)	PD-L1 < 1% (n = 26)
Median PFS, months (95% CI)	10.8 (5.3-16.5)	8.8 (4.3-22.0)
Median follow-up, months (95% CI)	24.9 (16.7-28.3)	25.1 (16.7-NE)



Durability of Clinical Benefit

- Median DOR in the 1L setting was 9.7 months
- In the 2L+ setting, the median DOR was 9.1 months (supplementary slides)



Subsequent Anticancer Therapies

- Of 33 patients eligible to receive subsequent therapy, 18 (55%) received immunotherapy
- Median PFS2 with subsequent therapy in the 1L cohort overall was 19.9 months

	Sotorasib + Carboplatin + Pemetrexed 1L (n = 44)
Patients eligible for subsequent therapy, n (%)	33 (75)
Any therapy*	25 (76)
Radiotherapy	12 (36)
Palliative†	11 (33)
Unknown	2 (6)
Surgery	1 (3)
Curative‡	1 (3)
Unknown	0
Any systemic therapy	23 (70)
Immunotherapy	18 (55)
Checkpoint Inhibitor	18 (55)
Chemotherapy	13 (39)
Targeted small molecule therapy	6 (18)
Other anti-cancer therapy	5 (15)

*Percentages are calculated out of patients eligible to receive subsequent therapy. †Abdominal cavity, adrenal, bone, brain, chest, hypogastric subcutaneous nodule, left chondrocostal lesion, liver, lumbar region, lung, lymph node, pelvis and spine. ‡Lymph node.

Scan for:
- Poster
- Supplementary slides
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Abbreviations:
1L, first-line; 2L+, second-line or higher; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; DCR, disease control rate; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; KRAS, Kirsten rat sarcoma viral oncogene homolog; NE, not estimable; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PD, progression of disease; PD-(L)1, programmed cell death protein (ligand) 1; PFS, progression-free survival; PO, per oral; PR, partial response; Q3W, once every 3 weeks; RECIST, response evaluation criteria in solid tumors; SD, stable disease; TRAE, treatment-related adverse event.

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