Single-Agent Divarasib in Patients With *KRAS G12C*–Positive Non–Small Cell Lung Cancer: Long-Term Follow-Up of a Phase I Study

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ABSTRACT

Divarasib (GDC-6036), an oral, highly potent and selective next-generation KRAS G12C inhibitor, has demonstrated a manageable safety profile and promising antitumor activity in patients with advanced *KRAS G12C*–positive non–small cell lung cancer (NSCLC). Here, we report long-term (≥1 year) follow-up of single-agent divarasib from the ongoing, open-label, and multicenter phase I study (ClinicalTrials.gov identifier: NCT04449874). The primary objective was safety, and the other objectives included preliminary antitumor activity. Overall, 65 patients with advanced *KRAS G12C*–positive NSCLC received single-agent oral divarasib 50-400 mg once daily and 31 patients (48%) were treated beyond 1 year. Divarasib continued to be well tolerated, and the safety profile beyond 1 year was consistent with the overall safety profile. In patients with measurable disease at baseline across all dose levels (n = 63), the confirmed objective response rate was 55.6% (95% CI, 42.5 to 68.1), and the median duration of response was 18.0 months (95% CI, 11.1 to 24.9). The median progression-free survival was 13.8 months (95% CI, 9.8 to 25.4) in the overall population (N = 65) and 15.3 months (95% CI, 12.3 to 26.1) among patients assigned to the 400-mg dose level (n = 44). With extended follow-up, divarasib demonstrated long-term safety and antitumor activity in patients with advanced *KRAS G12C*–positive NSCLC.

ACCOMPANYING CONTENT

Appendix

Protocol

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INTRODUCTION

The Kirsten rat sarcoma viral oncogene homolog (*KRAS*) *G12C* mutation is one of the most prevalent *KRAS* mutations in cancer and present in approximately 12%-14% of patients with non–small cell lung cancer (NSCLC).[1,2] Although current approved KRAS G12C inhibitors, sotorasib and adagrasib, have shown antitumor activity in patients with *KRAS G12C*–positive NSCLC, there remains a need for therapies with an improved clinical benefit and safety profile.[3-7]

Divarasib (GDC-6036) is an oral, highly potent and selective next-generation KRAS G12C inhibitor that locks the protein in its inactive state. Compared with sotorasib and adagrasib, divarasib has been shown to be 5-20 times as potent and up to 50 times as selective in vitro.[8] In the initial report of the phase I study of patients with *KRAS G12C*–positive NSCLC, single-agent divarasib 400 mg once daily demonstrated a confirmed objective response rate (ORR) of 56.4% (95% CI, 39.6 to 72.2), a median duration of response (DOR) of 11.9 months (95% CI, 6.9 to could not be estimated), and a median progression-free survival (PFS) of 13.7 months (95% CI, 8.1 to could not be estimated) while maintaining a tolerable safety profile.[9] Here, we report the long-term (≥1 year) follow-up of single-agent divarasib in patients with NSCLC.

METHODS

Study Design and Patients

We report an update from the previously described ongoing, open-label, dose-escalation, dose-expansion, and multicenter phase I study (ClinicalTrials.gov identifier: NCT04449874).[9] Patients 18 years or older with advanced *KRAS G12C*–positive NSCLC were enrolled and received single-agent oral divarasib 50-400 mg once daily until

TABLE 1. Patient Demographics and Disease Characteristics

Characteristic	NSCLC (N = 65)
Age, years, median (range)	66 (43-82)
Sex, female, No. (%)	37 (57)
Race, No. (%)	
White	57 (88)
Asian	4 (6)
Unknown	3 (5)
Black or African American	1 (2)
ECOG, No. (%)	
0	24 (37)
1	41 (63)
PD-L1 TPS score (n = 53), No. (%)	
<1%	18 (34)
1%-49%	13 (24.5)
≥50%	21 (40)
Not available	1 (2)
No. of previous lines of systemic therapy, No. (%)	
0	1 (2)
1	25 (39)
2	20 (31)
3+	19 (29)
Previous platinum chemotherapy, No. (%)	57 (88)
Previous PD-1/PD-L1 inhibitor, No. (%)	57 (88)
Time on divarasib treatment, months, median (range)	11 (0-40)

Abbreviations: ECOG, Eastern Cooperative Oncology Group; NSCLC, non–small cell lung cancer; TPS, tumor proportion score.

disease progression or intolerability. The protocol was approved by local institutional review boards and regulatory authorities before study start, and all patients provided written informed consent before enrollment.

Objectives and Assessments

The primary objective of the study was safety, as assessed by the incidence and severity of adverse events (National Cancer Institute—Common Terminology Criteria for Adverse Events v5), changes in laboratory test results, and changes in vital signs and electrocardiograms. New-onset (occurring after 1 year of treatment) treatment-related adverse events (TRAEs) were assessed as an exploratory analysis. Other objectives include preliminary antitumor activity (ORR, DOR, and PFS) per RECIST v1.1. Additional details about objectives, assessments, and statistical methods are included in Appendix 1 (online-only).

RESULTS

Patient Disposition

As of the clinical cutoff date (April 01, 2024), 65 patients with NSCLC were enrolled (400 mg, n = 44; 200 mg, n = 10; 100 mg, n = 5; 50 mg, n = 6) and 17 patients (26%) remained on treatment. Thirty-one patients (48%) were treated beyond 1 year and the median time on treatment was 11 months (range, 0-40). Patient demographics and disease characteristics are summarized in Table 1.

Safety

Overall, 61 patients (94%) experienced at least one TRAE, with 11 patients (17%) experiencing a grade 3 to 4 TRAE; there were no grade 5 TRAEs (Table 2). No dose-limiting toxicities were reported. The most common TRAEs were nausea, vomiting, and diarrhea. The majority of TRAEs (95.4%) were grade 1 or 2. TRAEs led to dose modifications (interruption/reduction/discontinuation) in 25 patients (38.5%), including dose reductions in 15 patients (23.1%) and discontinuation in three patients (4.6%; grade 4 anaphylactic reaction, grade 2 diarrhea, and grade 2 upper abdominal pain; Appendix Table A1, online only).

Among the 31 patients who continued single-agent divarasib beyond 1 year, 17 (54.8%) experienced a new-onset TRAE, with no patients experiencing a new-onset grade 3 to 5 TRAE (Table 2). The most common new-onset TRAEs were amylase increase (n = 4), diarrhea

TABLE 2. TRAE Summary

TRAE	Any Grade TRAEs	Grade 3 to 5 TRAEs
TRAEs occurring in ≥10% of all patients (N = 65)		
Patients with at least one TRAE, No. (%)	61 (93.8)	11 (16.9)
Nausea	51 (78.5)	1 (1.5)
Vomiting	43 (66.2)	0
Diarrhea	40 (61.5)	2 (3.1)
Fatigue	16 (24.6)	1 (1.5)
Decreased appetite	15 (23.1)	0
Amylase increased	11 (16.9)	0
ALT increased	10 (15.4)	4 (6.2)
Lipase increased	10 (15.4)	2 (3.1)
AST increased	9 (13.8)	3 (4.6)
New-onset[a] TRAEs occurring in ≥5% of patients who continued single-agent divarasib beyond 1 year (n = 31)		
Patients with at least one TRAE, No. (%)	17 (54.8)	0
Amylase increased	4 (12.9)	0
Diarrhea	3 (9.7)	0
Lipase increased	3 (9.7)	0
Anemia	2 (6.5)	0
Nausea	2 (6.5)	0
Neutropenia	2 (6.5)	0
Vomiting	2 (6.5)	0

Abbreviation: TRAEs, treatment-related adverse events.
[a]TRAEs occurring after 1 year of treatment.

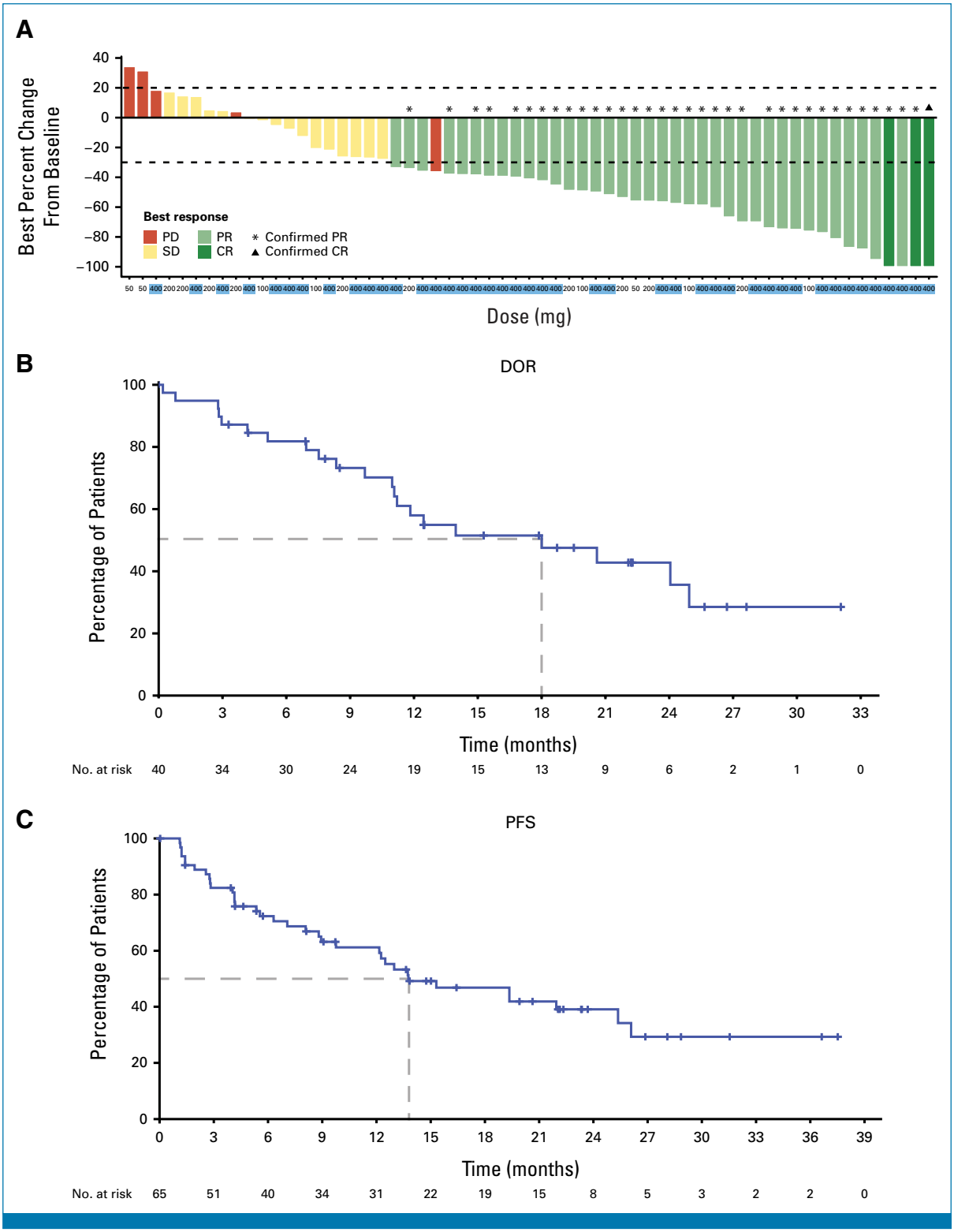

FIG 1. Preliminary antitumor activity in patients with NSCLC. (A) Waterfall plot of the best percentage change from baseline in the tumor burden (defined as the sum of the longest diameters of all target lesions) in the 63 patients with NSCLC who had measurable disease at baseline and available postbaseline tumor-assessment data. Of the patients with a best response of CR (dark green), one had a confirmed best response of CR and two had a confirmed best response of PR. Patients receiving divarasib 400 mg are highlighted in blue. (B) Kaplan-Meier plot for DOR in the 40 patients with NSCLC who had a CR or PR. (C) Kaplan-Meier plot for PFS among all 65 patients with NSCLC. PFS was defined as the time from first treatment to the first occurrence of disease progression or death from any cause during the study (whichever occurred first). CR, complete response; DOR, duration of response; NSCLC, non–small cell lung cancer; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.

(n = 3), and lipase increase (n = 3). No new-onset TRAEs led to dose reductions or divarasib discontinuation (Appendix Table A2).

Preliminary Antitumor Activity

Across all evaluated dose levels, the confirmed ORR was 55.6% (95% CI, 42.5 to 68.1) among patients with measurable disease at baseline (n = 63). One patient (1.6%) had a complete response, 34 (54.0%) had a partial response, 21 (33.3%) had stable disease, and five (7.9%) had progressive disease as their best response (Fig 1A). The median time to response was 1.3 months (range, 1.2-28.8) and the median DOR (Fig 1B) was 18.0 months (95% CI, 11.1 to 24.9). The median PFS (Fig 1C) was 13.8 months (95% CI, 9.8 to 25.4) in the overall population (N = 65). Exploratory analysis of activity by PD-L1 status is shown in Appendix Table A3.

Among the patients with measurable disease at baseline assigned to divarasib 400 mg (n = 44), the confirmed ORR was 59.1% (95% CI, 43.3 to 73.7) and the median DOR was 14.0 months (95% CI, 11.1 to 24.9). The median PFS was 15.3 months (95% CI, 12.3 to 26.1).

DISCUSSION

With additional follow-up, single-agent divarasib continued to demonstrate encouraging radiographic response rates and durable clinical activity while maintaining an acceptable safety profile with no new safety signals.

Overall, there was a low rate of grade ≥3 TRAEs with divarasib in this study, including an approximately 5% rate of hepatic events (ALT or AST increased), and the safety profile for patients treated beyond 1 year was consistent with the overall safety profile.

In this study, divarasib 400 mg once daily demonstrated a confirmed ORR of 59.1% and a median PFS of 15.3 months, which are numerically higher than those reported for sotorasib and adagrasib in their respective early-phase studies. Sotorasib (960 mg once daily) reported an ORR of 41% and a median PFS of 6.3 months in a pooled 2-year analysis of the phase I/II CodeBreaK 100 study.[10] Adagrasib (600 mg twice a day) reported an ORR of 43% and a median PFS of 6.9 months in a pooled 2-year analysis of the phase I/II KRYSTAL-1 study.[11] Given the promising ORR and median PFS of divarasib, the phase III randomized Krascendo 1 study (ClinicalTrials.gov identifier: NCT06497556) is currently evaluating the efficacy and safety of divarasib versus sotorasib and adagrasib in previously treated advanced or metastatic *KRAS G12C*–positive NSCLC.

The tolerability and potent activity of divarasib presented here render it an attractive partner for PD-L1/PD-1 inhibitors,[12] in which combinations with other KRAS G12C inhibitors have been challenged by toxicity.[13,14] Additionally, initial safety results from the divarasib and atezolizumab (PD-L1 inhibitor) combination arm of this study have yielded a manageable safety profile of divarasib in combination with a PD-L1 inhibitor.[15] Divarasib is also being investigated in combination with pembrolizumab (PD-1 inhibitor) with or without chemotherapy in patients with previously untreated advanced or metastatic *KRAS G12C*–positive NSCLC in the phase Ib/II Krascendo 170 study (ClinicalTrials.gov identifier: NCT05789082).

In conclusion, divarasib demonstrated long-term safety and antitumor activity in patients with advanced *KRAS G12C*–positive NSCLC, with promising characteristics for combination therapy to overcome mechanisms of resistance.

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DATA SHARING STATEMENT

For eligible studies qualified researchers may request access to individual patient level clinical data through a data request platform. At the time of writing this request platform is Vivli: https://vivli.org/ourmember/roche/. For up to date details on Roche's Global Policy on the Sharing of Clinical Information and how to request access to related clinical study documents, see here: https://www.roche.com/innovation/process/clinical-trials/data-sharing. Anonymized records for individual patients across more than one data source external to Roche can not, and should not, be linked due to a potential increase in risk of patient re-identification.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Research Funding: Genentech, Revolution Medicines, Novartis, Kronos Bio, Amgen, Black Diamond Therapeutics
Patents, Royalties, Other Intellectual Property: A patent filed by Memorial Sloan Kettering Cancer Center related to multimodal features to predict response to immunotherapy (PCT/US2023/021178) (Inst)
Travel, Accommodations, Expenses: Genentech/Roche

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Travel, Accommodations, Expenses: AstraZeneca, Janssen Oncology

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Research Funding: Roche (Inst), GlaxoSmithKline (Inst), Novartis (Inst), BeiGene (Inst), Bristol Myers Squibb (Inst), AstraZeneca/MedImmune (Inst), Amgen (Inst), Genentech (Inst)

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Uncompensated Relationships: Roche, Janssen, MSD, PharmaMar, Lilly, Novartis, Genmab, AbbVie, Array BioPharma, Sanofi, Salubris Biotherapeutics, Seagen, SERVIER, HiFiBiO Therapeutics

Sanjeev Deva
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Alejandro Falcon
Consulting or Advisory Role: AstraZeneca, Pfizer, Steve, Roche/Genentech, Menarini Group, MSD
Speakers' Bureau: AstraZeneca, Pfizer, Seagen, Novartis, Lilly, Roche/Genentech, Eisai, Daiichi Sankyo/Astra Zeneca, Grunenthal, Gilead Sciences, Dr Reddy's Laboratories

Guzman Alonso
Consulting or Advisory Role: Boehringer Ingelheim, Ellipses Pharma

João Daniel Guedes
Honoraria: Merck, AstraZeneca, Daiichi Sankyo, Pint Pharma
Research Funding: Amgen, AstraZeneca, Bayer, BMS, Daiichi-Sankyo, Eurofarma, Genetech, HuyaBio, Incyte, Lilly, MSD, Pfizer, PTC, Roche, Sanofi, Takeda
Travel, Accommodations, Expenses: Gilead, Pfizer, AstraZeneca

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Consulting or Advisory Role: Takeda, Pfizer

Matthew G. Krebs
Honoraria: Roche
Consulting or Advisory Role: Roche, Achilles Therapeutics, Janssen, Seagen, OM Pharma, Bayer, Guardant Health, Zai Lab
Speakers' Bureau: Roche, Janssen, BMS, Guardant Health, Eisai
Research Funding: Roche (Inst), Novartis (Inst)
Travel, Accommodations, Expenses: AstraZeneca, BerGenBio, Immutep, Janssen, Roche, Zai Lab, BMS

Scott A. Laurie
Research Funding: Bristol Myers Squibb (Inst), AstraZeneca (Inst), Novartis (Inst), 23andMe (Inst)
Patents, Royalties, Other Intellectual Property: UpToDate

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Honoraria: AstraZeneca, Physicians' Education Resource
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Travel, Accommodations, Expenses: Physicians' Education Resource, Johnson & Johnson/Janssen

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Stock and Other Ownership Interests: Genentech, Veracyte, BeiGene (I)

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Stock and Other Ownership Interests: Genentech/Roche

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Mark T. Lin
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Stephanie Royer-Joo
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Stock and Other Ownership Interests: Genentech/Roche

Julie Chang
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Stock and Other Ownership Interests: Roche
Travel, Accommodations, Expenses: Genentech

Tomi Jun
Employment: Genentech
Stock and Other Ownership Interests: Roche
Open Payments Link: https://openpaymentsdata.cms.gov/physician/7228039

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Stock and Other Ownership Interests: Roche
Patents, Royalties, Other Intellectual Property: Patent applications related to employment at Genentech/Roche

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Patricia Lorusso
Honoraria: Five Prime Therapeutics
Consulting or Advisory Role: Takeda, Sotio, Agenus, Pfizer, GlaxoSmithKline, EMD Serono, Kyowa Kirin International, Kineta, I-Mab, MEKanistic Therapeutics, Actuate Therapeutics, Atreca, Amgen, Cullinan Oncology, DAAN Biotherapeutics, Quanta Therapeutics, Schrodinger, Boehringer Ingelheim, Prelude Therapeutics, Wells Therapeutics, Zai Lab
Research Funding: Genentech (Inst)
Travel, Accommodations, Expenses: Genentech

No other potential conflicts of interest were reported.

APPENDIX 1. SUPPLEMENTARY METHODS

Study Drug Action Taken

For each adverse event that resulted in a dose modification, only one action taken with regard to the study drug was selected for data analysis, according to the following hierarchy: discontinuation, reduction, or interruption.

Tumor Assessments

Confirmed response in patients with measurable disease was defined as complete response or partial response on two consecutive tumor assessments at least 4 weeks apart, whereas best response did not require a confirmatory assessment.

Statistical Analysis

This analysis included all patients who received at least one dose of divarasib. Confirmed response was reported for patients with measurable disease at baseline and summarized with 95% CIs calculated with the use of the Clopper-Pearson method. The time-to-event end points, including the duration of the response and progression-free survival (PFS), were reported descriptively and were summarized with the use of the Kaplan-Meier method; the median estimates were reported with 95% CIs. Progression-free survival was defined as the time from first treatment to the first occurrence of disease progression or death from any cause during the study (whichever occurred first).

TABLE A1. Study Treatment Action Taken Due to Treatment-Related Adverse Events

Study Treatment Action	NSCLC (N = 65), No. (%)
Divarasib modification (interruption/reduction/withdrawal)	25 (39)
Divarasib reduction	15 (23)
Divarasib withdrawal	3 (5)

NOTE. For each adverse event that resulted in a dose modification, only one action taken with regard to the study drug was selected for data analysis, according to the following hierarchy: discontinuation, reduction, or interruption.
Abbreviations: AEs, adverse events; NSCLC, non–small cell lung cancer.

TABLE A2. Study Treatment Action Taken Due to New-Onset Treatment-Related Adverse Events in Patients Who Continued Single-Agent Divarasib Beyond 1 Year

Study Treatment Action	NSCLC (n = 31), No. (%)
Divarasib modification (interruption/reduction/withdrawal)	3 (9.7)
Divarasib reduction	0
Divarasib withdrawal	0

NOTE. For each adverse event that resulted in a dose modification, only one action taken with regard to the study drug was selected for data analysis, according to the following hierarchy: discontinuation, reduction, or interruption.
Abbreviations: AEs, adverse events; NSCLC, non–small cell lung cancer.

TABLE A3. Exploratory Analysis of PD-L1 Status

PD-L1 TPS	No.	CR/PR	Confirmed ORR, %	95% CI
TPS ≥1%	34	17	50	32.4 to 67.6
TPS <1%	18	10	55.6	30.8 to 78.5

NOTE. PD-L1 Status was based on local testing and only available for a subset of patients.
Abbreviations: CR, complete response; ORR, objective response rate; PR, partial response; TPS, tumor proportion score.

TABLE A4. GO42144 Investigators and Study Group

Country	Investigator	Site
Australia	Samantha Bowyer	Linear Clinical Research Limited
Australia	Rasha Cosman	St Vincent's Hospital Sydney
Australia	Jayesh Desai	Peter MacCallum Cancer Center
Australia	Ben Markman	Alfred Health
Belgium	Pierre Freres	CHU de Liège
Belgium	Marc Lambrechts	AZ Sint-Maarten
Belgium	Hans Prenen	UZ Antwerpen
Brazil	Carlos Barrios	Hospital Sao Lucas Da Pontificia Universidade Catolica Do Rio Grande Do Sul (PUCRS)
Brazil	Joao Daniel Cardoso Guedes	Fundacao Faculdade Regional de Medicina de Sao Jose Do Rio Preto Hospital de Base
Brazil	Sergio De Azevedo	Hospital de Clinicas de Porto Alegre (HCPA)
Brazil	Rita De Cassia Costamilan	Universidade de Caxias do Sul
Brazil	Carolina Gomes Jacobina Silva	Santa Casa de Misericórdia de Belo Horizonte
Brazil	Tabatha Nakakogue Dallagnol	Hospital Erasto Gaertner
Canada	Scott Laurie	Ottawa Hospital
Canada	Wilson Miller	Jewish General Hospital
Canada	Adrian Sacher	Princess Margaret Cancer Center
Hungary	István Láng	Clinexpert Kft.—Gyöngyös
Hungary	István Takács	Semmelweis Egyetem
Israel	Ravit Geva	Tel Aviv Sourasky Medical Center
Israel	Ruth Perets	Rambam Medical Center
Israel	Einat Shacham-Shmueli	Sheba Medical Center
Italy	Chiara Cremolini	Azienda Ospedaliero Universitaria Pisana
Italy	Gianluca Del Conte	Ospedale San Raffaele S.r.l.
Italy	Angelo Delmonte	Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori"
Italy	Armando Santoro	Istituto Clinico Humanitas
Italy	Salvatore Siena	ASST Grande Ospedale Metropolitano Niguarda - Presidio Ospedaliero Ospedale Niguarda
Kenya	Mansoor Saleh	Aga Khan University Hospital
Korea, Republic of	Myung-Ju Ahn	Samsung Medical Center
Korea, Republic of	Sae-Won Han	Seoul National University Hospital
Korea, Republic of	Tae Won Kim	Asan Medical Center
Korea, Republic of	Jong-Seok Lee	Seoul National University Bundang Hospital
Netherlands	Hans Gelderblom	Leids Universitair Medisch Centrum
Netherlands	Eelke Gort	Universitair Medisch Centrum Utrecht Cancer Center
Netherlands	Loes Latten-Jansen	Maastricht University Medical Center
Netherlands	Marloes Van Dongen	Het Nederlands Kanker Instituut Antoni Van Leeuwenhoek Ziekenhuis
New Zealand	Sanjeev Deva	Auckland City Hospital
New Zealand	Rajiv Kumar[a]	New Zealand Clinical Research - Christchurch
Norway	Øystein Fløtten	Haukeland University Hospital
Norway	Tormod Guren	Oslo University Hospital Radiumhospitalet
Poland	Rafal Dziadziuszko	Uniwersyteckie Centrum Kliniczne, Osrodek Badan Klinicznych Wczesnych Faz
Poland	Jacek Mackiewicz	Szpital Kliniczny im. Heliodora Swiecickiego w Poznaniu
Poland	Rafal Stec	Biokinetica, Przychodnia Jozefow
Russian Federation	Rustem Safin	Republican Clinical Oncology Dispensary of Ministry of Healthcare of Tatarstan Republic
Spain	Andres Cervantes Ruizperez	Hospital Clinico Universitario de Valencia
Spain	Maria De Miguel Luken	START Madrid Hospital Universitario HM Sanchinarro

(continued on following page)

TABLE A4. GO42144 Investigators and Study Group (continued)

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Spain	Elena Garralda Cabanas	Hospital Universitario Vall d'Hebron
Spain	Laura Medina	Hospital Universitario Virgen de la Victoria
Spain	Victor Moreno	START Madrid Hospital Universitario Fundacion Jimenez Diaz
Spain	Luis Paz-Ares Rodriguez	Hospital Universitario 12 de Octubre
Switzerland	Christian Britschgi	Universitätsspital Zürich
Switzerland	Eugenio Fernandez	Hôpitaux Universitaires de Genève
Switzerland	Simon Häfliger	Universitätsspital Bern - Inselspital
Switzerland	Sacha Rothschild	Universitätsspital Basel
United Kingdom	Martin Forster	University College London Hospitals
United Kingdom	Robert Jones	Velindre Cancer Center
United Kingdom	Matthew Krebs	The Christie NHS Foundation Trust
United States	Raid Aljumaily	University of Oklahoma Peggy and Charles Stephenson Cancer Center
United States	Kathryn Arbor	Memorial Sloan Kettering Cancer Center - David H. Koch Center for Cancer Care
United States	Lyudmila Bazhenova	UC San Diego Moores Cancer Center
United States	Timothy Burns	UPMC Hillman Cancer Center
United States	Michael Cheng[b]	Dana Farber Cancer Institute
United States	Thomas Karasic	Abramson Cancer Center of The University of Pennsylvania
United States	Patricia LoRusso	Yale University
United States	Erminia Massarelli	City of Hope—Comprehensive Cancer Center (CCC)
United States	Pamela Munster	University of California San Francisco
United States	Sai-Hong Ou	UCI Health Chao Family Comprehensive Cancer Center
United States	Manish Patel	Florida Cancer Specialists
GO42144 Study Group		
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[a]Rajiv Kumar was at New Zealand Clinical Research—Christchurch during the time of work associated with this manuscript and is currently at the St George's Cancer Care, Christchurch, New Zealand.

[b]Michael Cheng was at Dana-Farber Cancer Institute during the time of the work associated with this manuscript and is currently at the Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, CA.