CONTACT-01: A Randomized Phase III Trial of Atezolizumab + Cabozantinib Versus Docetaxel for Metastatic Non–Small Cell Lung Cancer After a Checkpoint Inhibitor and Chemotherapy

Joel Neal, MD, PhD[1]; Nick Pavlakis, MMed, PhD, MBBS, FRACP[2]; Sang-We Kim, MD, PhD[3]; Yasushi Goto, MD[4]; Sun Min Lim, MD, PhD[5]; Giannis Mountzios, MD, PhD, MSc[6]; Elena Fountzilas, MD[7]; Anastasia Mochalova, MD[8]; Daniel C. Christoph, MD, PhD[9]; Alessandra Bearz, MD[10]; Xavier Quantin, MD, PhD[11]; Ramon Palmero, MD[12]; Vladan Antic, MD, PhD[13]; Elaine Chun, PharmD[14]; Tirupathi Rao Edubilli, MSc[15]; Ya-Chen Lin, PhD[14]; Mahrukh Huseni, MS[14]; Marcus Ballinger, PhD[14]; Vilma Graupner, PhD[13]; Dominic Curran, MBChB[16]; Piet Vervaet, MD[16]; and Thomas Newsom-Davis, PhD, MBBS, FRCP[17]

DOI https://doi.org/10.1200/JCO.23.02166

ABSTRACT

PURPOSE Although checkpoint inhibitors have improved first-line treatment for non–small cell lung cancer (NSCLC), a therapeutic need remains for patients whose disease does not respond or who experience disease progression after anti–PD-L1/PD-1 immunotherapy. CONTACT-01 (ClinicalTrials.gov identifier: NCT04471428) evaluated atezolizumab plus cabozantinib versus docetaxel in patients with metastatic NSCLC who developed disease progression after concurrent or sequential treatment with anti–PD-L1/PD-1 and platinum-containing chemotherapy.

METHODS This multicenter, open-label, phase III trial randomly assigned patients 1:1 to atezolizumab 1,200 mg intravenously once every 3 weeks (q3w) plus cabozantinib 40 mg orally once daily or docetaxel 75 mg/m² intravenously once every 3 weeks. The primary end point was overall survival (OS).

RESULTS One hundred eighty-six patients were assigned atezolizumab plus cabozantinib, and 180 docetaxel. Minimum OS follow-up was 10.9 months. Median OS was 10.7 months (95% CI, 8.8 to 12.3) with atezolizumab plus cabozantinib and 10.5 months (95% CI, 8.6 to 13.0) with docetaxel (stratified hazard ratio [HR], 0.88 [95% CI, 0.68 to 1.16]; $P = .3668$). Median progression-free survival was 4.6 months (95% CI, 4.1 to 5.6) and 4.0 months (95% CI, 3.1 to 4.4), respectively (stratified HR, 0.74 [95% CI, 0.59 to 0.92]). Serious adverse events (AEs) occurred in 71 (38.4%) patients receiving atezolizumab plus cabozantinib and 58 (34.7%) receiving docetaxel. Grade 3/4 treatment-related AEs occurred in 73 (39.5%) patients receiving atezolizumab plus cabozantinib and 58 (34.7%) receiving docetaxel. Grade 5 AEs occurred in 14 (7.6%) and 10 (6.0%) patients in the atezolizumab plus cabozantinib and docetaxel arms, respectively (treatment-related in four [2.2%] and one [0.6%], respectively).

CONCLUSION Atezolizumab plus cabozantinib after disease progression following anti–PD-L1/PD-1 immunotherapy and platinum-containing chemotherapy for metastatic NSCLC did not improve OS compared with docetaxel. Safety was consistent with known profiles of these agents.

ACCOMPANYING CONTENT

Editorial, p. 2367
Appendix
Data Supplement
Protocol

Accepted February 1, 2024
Published March 29, 2024

J Clin Oncol 42:2393-2403

View Online Article

INTRODUCTION

Most patients with non–small cell lung cancer (NSCLC) are initially diagnosed with metastatic disease.[1] For metastatic NSCLC without molecular alterations[2,3] platinum-containing regimens are standard first-line (1L) treatment approaches. The introduction of cancer immunotherapies has improved survival outcomes, with several approved as 1L treatment for metastatic NSCLC.[4-12]

For patients whose disease progresses on anti–PD-L1/PD-1 (PD(L)1) and platinum-containing therapy, subsequent options include single-agent chemotherapy, or combination treatment with docetaxel plus ramucirumab or

CONTEXT

Key Objective

To evaluate the efficacy and safety of atezolizumab plus cabozantinib versus docetaxel in patients with metastatic non–small cell lung cancer (NSCLC) after disease progression following anti–PD-L1/PD-1 immunotherapy and chemotherapy.

Knowledge Generated

Overall survival was not improved with atezolizumab plus cabozantinib compared with docetaxel. Secondary end points of progression-free survival and duration of response showed numerical improvements favoring atezolizumab plus cabozantinib. No new safety findings were reported for atezolizumab or cabozantinib. Overall, results do not support the combined use of atezolizumab plus cabozantinib after progression on previous checkpoint inhibitor (CPI) and platinum-based chemotherapy in metastatic NSCLC.

Relevance *(T.E. Stinchcombe)*

This study did not demonstrate activity of a multi-targeted tyrosine kinase inhibitor in combination with immune CPI in unselected patients with progressive disease after immunotherapy.*

*Relevance section written by *JCO* Associate Editor Thomas E. Stinchcombe, MD.

nintedanib.[2,13,14] As disease progression during or after initial treatment remains common, effective and tolerable 2L+ options are needed, particularly for those previously treated with immunotherapy.

Cabozantinib is a potent inhibitor of multiple receptor tyrosine kinases, including VEGFR2, MET, and RET, and TAM family kinases TYRO3, AXL, and MER, which play important roles in tumor cell proliferation and neovascularization, and are implicated in antitumor immune response suppression.[15,16] In the United States, Europe, and other countries, cabozantinib is approved to treat advanced renal cell carcinoma (RCC) as monotherapy or in combination with nivolumab, and as monotherapy in hepatocellular carcinoma and differentiated thyroid cancer.[17-20] In preclinical models, cabozantinib promotes an immune-permissive environment, suggesting potential synergistic effects when combined with checkpoint inhibitors (CPIs).[21] In advanced NSCLC, cabozantinib demonstrated encouraging preliminary clinical activity when used in combination with atezolizumab in patients with previous CPI exposure.[22] CONTACT-01 is a phase III multicenter, randomized, open-label study of atezolizumab plus cabozantinib versus docetaxel for metastatic NSCLC previously treated with anti–PD-(L)1 therapy and platinum-based chemotherapy. Here, we report the final overall survival (OS) analysis.

METHODS

Study Design and Participants

CONTACT-01 (ClinicalTrials.gov identifier: NCT04471428) evaluated atezolizumab and cabozantinib versus docetaxel in patients age 18 years and older with metastatic NSCLC, measurable disease per RECIST 1.1, and an Eastern Cooperative Oncology Group performance status of 0 or 1. Patients with asymptomatic, treated CNS metastases were eligible. Patients must have had radiologic progression after treatment with platinum-containing chemotherapy and anti–PD-(L)1 immunotherapy, administered concurrently or sequentially for metastatic NSCLC. Additional eligibility criteria are provided in the Data Supplement (online only).

The final protocol (Data Supplement), amendments, and patients' informed consent documents were reviewed and approved by the institutional review boards and independent ethics committees at each site. This study was conducted in compliance with the Declaration of Helsinki and the International Conference on Harmonisation Guideline for Good Clinical Practice.

Randomization and Masking

Patients were centrally randomly assigned 1:1 to receive open-label atezolizumab plus cabozantinib or docetaxel using a parallel-group design. Randomization was stratified by histology (nonsquamous *v* squamous) and previous NSCLC treatment regimen(s): (1) concurrent platinum-containing chemotherapy and anti–PD-(L)1 antibody; (2) platinum-containing chemotherapy first, occurrence of disease progression, followed by anti–PD-(L)1 antibody; (3) anti–PD-(L)1 antibody monotherapy first, occurrence of disease progression, followed by platinum-containing chemotherapy; and (4) anti–PD-(L)1 antibody monotherapy first, occurrence of disease progression, followed by continued anti–PD-(L)1 antibody plus platinum-containing chemotherapy.

Procedures

During each 21-day cycle, patients received atezolizumab 1,200 mg intravenously on day 1 with cabozantinib 40 mg

(two 20-mg tablets) orally once daily or docetaxel 75 mg/m² intravenously on day 1. Patients continued atezolizumab with cabozantinib until RECIST 1.1 disease progression, unacceptable toxicity, or loss of clinical benefit per the investigator (Data Supplement). Patients receiving docetaxel continued treatment until unacceptable toxicity or RECIST 1.1 disease progression.

Outcomes

The primary efficacy end point was OS. Secondary efficacy end points were progression-free survival (PFS), confirmed objective response rate (ORR), and duration of response (DOR), all investigator-assessed per RECIST 1.1, 6-month and 1-year PFS rates, and 1-year and 2-year OS rates. Safety was evaluated using National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5.0.

Statistical Analysis

Sample size determination was based on the estimated number of OS events required to demonstrate superiority with regards to OS, using the following assumptions: 1:1 random assignment; two-sided significance level of 0.05; 90% power to detect a hazard ratio (HR) of 0.64 in OS; one planned interim OS analysis; and a dropout rate of 5% per 24 months for each arm. A sample size of approximately 350 patients was targeted and the final OS analysis was planned when approximately 220 OS events had occurred. The number of final OS events corresponds to a minimum detectable difference in the HR of 0.757. Crossing boundaries determining statistical significance for OS were based on the Hwang-Shih-DeCani alpha spending function with the gamma parameter of −2.5.[23] The prespecified interim OS analysis was conducted by the independent Data Coordinator Center and reviewed by the independent Data Monitoring Committee (iDMC) after 180 OS events had occurred. The iDMC recommended continuation of the trial until its prespecified final OS analysis. A stratified log-rank test was used to compare the primary end point of OS between arms. OS was defined as the time from random assignment to death from any cause. Patients who were not reported as having died at the time of analysis were censored at the date they were last known to be alive. Patients without postbaseline information were censored at the randomization date. HRs and associated 95% CIs were estimated using a stratified Cox regression model. Unstratified OS analyses were also performed. The log-rank test and Cox model used the same stratification factors as those used for random assignment. Kaplan-Meier methodology was used for estimation of OS medians and survival curves. Brookmeyer-Crowley methodology was used to construct the 95% CI for median OS.[24] For details on efficacy end points, see the Data Supplement.

The safety-evaluable population was defined as randomly assigned patients who received any amount of study drug. Patients were grouped according to treatment received. SAS version 9.4 (SAS Institute, Cary, NC) was used for statistical analyses.

RESULTS

From October 2020 to November 2021, 366 patients at 97 study sites in 15 countries (Appendix Table A1, online only) were enrolled, comprising the intention-to-treat (ITT) population, with 186 patients assigned to atezolizumab plus cabozantinib and 180 to docetaxel (Fig 1). At the clinical cutoff date (CCOD: September 28, 2022), minimum follow-up was 10.9 months. Baseline characteristics were generally well balanced between arms (Table 1). PD-L1 expression status was available for 334 patients (91.3%), predominantly based on archival, CPI-naïve tumors; 248 (74.3%) samples were tested locally using one of several approved PD-L1 assays, and 86 (25.7%) were tested centrally using SP263 (Table 1). The most common previous regimen for metastatic NSCLC was concurrent platinum and anti–PD-(L)1 therapy, in 107 patients (57.5%) and 106 (58.9%) in the atezolizumab plus cabozantinib and docetaxel arms, respectively.

Median OS in the ITT population was 10.7 months (95% CI, 8.8 to 12.3) in the atezolizumab plus cabozantinib arm and 10.5 months (95% CI, 8.6 to 13.0) in the docetaxel arm (stratified HR, 0.88 [95% CI, 0.68 to 1.16]; $P = .3668$; Fig 2A). At CCOD, 114 patients (61.3%) in the atezolizumab plus cabozantinib arm and 106 (58.9%) in the docetaxel arm had died. The 1-year OS rate was 43.3% (95% CI, 36.0 to 50.6) in the atezolizumab plus cabozantinib arm and 44.1% (95% CI, 36.2 to 52.1) in the docetaxel arm; 2-year OS rates were not estimable.

Exploratory OS analyses showed that the treatment effect among most subgroups was consistent with the ITT population (Fig 2B). Some subgroups appeared to favor docetaxel, albeit with overlapping CIs, including women, patients with current tobacco use, patients who received anti–PD-(L)1 followed by platinum as previous NSCLC treatment, and patients with PD-L1 ≥50%. Median OS for women was 9.8 months in the atezolizumab plus cabozantinib arm and not reached in the docetaxel arm (unstratified HR, 1.70 [95% CI, 0.98 to 2.96]); for men, the respective median OS durations were 10.8 and 9.5 months (unstratified HR, 0.72 [95% CI, 0.53 to 0.98]; Fig 2B and Data Supplement, Fig S1). Baseline characteristics by sex were generally well balanced between arms, except for histology (squamous: male, 31.4%; female, 9.5%; nonsquamous: male, 68.6%; female, 90.5%) and tobacco use history (never: male, 8.4%; female, 25.7%; former: male, 71.3%; female, 57.1%; Data Supplement, Table S2). Higher PD-L1 expression did not appear to favor atezolizumab plus cabozantinib over docetaxel. Median OS for the PD-L1 ≥50% subgroup was 11.9 months in the atezolizumab plus cabozantinib arm versus 13.4 months in the docetaxel arm (unstratified HR, 1.25; 95% CI, 0.73-2.15). In the PD-L1 1%-49% subgroup, median OS was 11.6 and 11.0 months, respectively (unstratified HR, 0.66 [95% CI, 0.40 to 1.11]; Fig 2B).

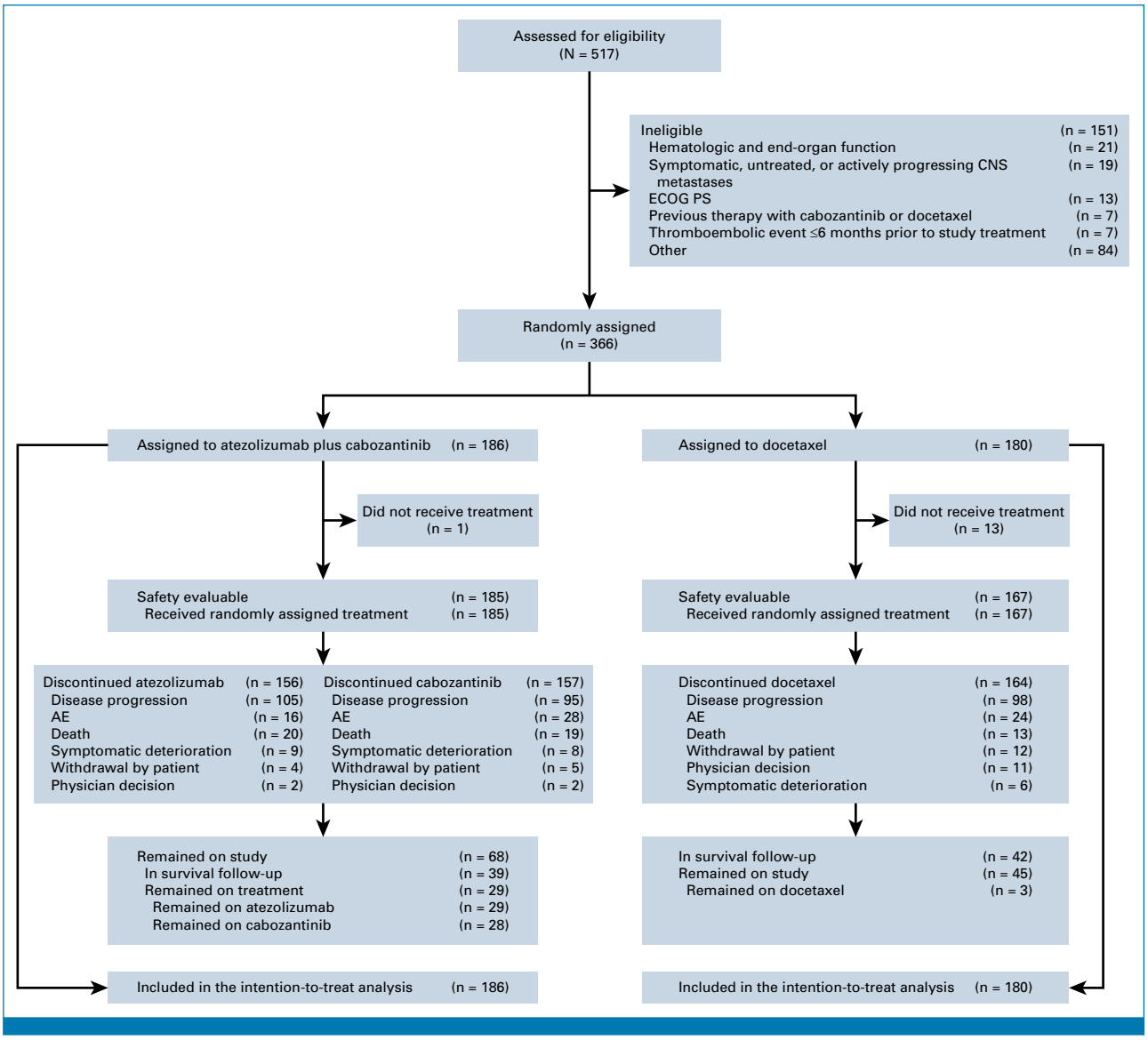

FIG 1. CONSORT diagram. Screened, randomly assigned, and treated patients, as well as analysis populations, are shown. AE, adverse event; ECOG PS, Eastern Cooperative Oncology Group performance status.

PFS events occurred in 162 patients (87.1%) in the atezolizumab plus cabozantinib arm and 150 (83.3%) in the docetaxel arm (Fig 3). Median PFS was 4.6 months (95% CI, 4.1 to 5.6) with atezolizumab plus cabozantinib and 4.0 months (95% CI, 3.1 to 4.4) with docetaxel (HR, 0.74 [95% CI, 0.59 to 0.92]). The 6-month PFS rates were 39.5% (95% CI, 32.4 to 46.6) and 23.7% (95% CI, 17.0 to 30.3), respectively, and 1-year PFS rates were 14.7% (95% CI, 9.4 to 20.0) and 8.4% (95% CI, 4.0 to 12.8), respectively. ORR was 11.8% (n = 22; 95% CI, 7.6-17.4) in the atezolizumab plus cabozantinib arm and 13.3% (n = 24; 95% CI, 8.7 to 19.2) in the docetaxel arm. Median DOR was 5.6 months (95% CI, 3.1 to 10.3) with atezolizumab plus cabozantinib and 4.3 months (95% CI, 3.3 to 5.6) with docetaxel (Table 2).

In the atezolizumab plus cabozantinib and docetaxel arms, 64 (34.4%) and 68 (37.8%) patients, respectively, received subsequent nonprotocol anticancer therapy (Data Supplement, Table S3). In the atezolizumab plus cabozantinib arm, 58 patients (31.2%) received chemotherapy, 19 (10.2%) received targeted therapy, and 1 (0.5%) received cancer immunotherapy. In the docetaxel arm, 55 patients (30.6%) received chemotherapy, 14 (7.8%) received targeted therapy, and 11 (6.1%) received cancer immunotherapy.

Overall, 185 patients in the atezolizumab plus cabozantinib arm and 167 in the docetaxel arm received ≥1 dose of study treatment and were included in the safety-evaluable population. Median treatment duration was 4.2 months (range, 0-20 months) for atezolizumab, 3.9 months (range, 0-21 months) for cabozantinib, and 2.1 months (range, 0-19 months) for docetaxel. Any-cause adverse events (AEs) occurred in 98.4% of patients in the atezolizumab plus cabozantinib arm and 94.0% in the docetaxel arm (grade 3/4

TABLE 1. Baseline Characteristics

Characteristic	Atezolizumab + Cabozantinib (n = 186)	Docetaxel (n = 180)
Age, years, median (range)	64 (33-84)	66 (26-91)
Sex, No. (%)		
Male	134 (72.0)	127 (70.6)
Female	52 (28.0)	53 (29.4)
Race, No. (%)[a]		
White	130 (69.9)	111 (61.7)
Asian	41 (22.0)	53 (29.4)
Black or African American	2 (1.1)	1 (0.6)
Ethnicity, No. (%)[b]		
Not Hispanic or Latino	164 (88.2)	158 (87.8)
Hispanic or Latino	4 (2.2)	7 (3.9)
ECOG PS, No. (%)		
0	73 (39.2)	52 (28.9)
1	113 (60.8)	128 (71.1)
Histology, No. (%)[c]		
Squamous	48 (25.8)	44 (24.4)
Nonsquamous	138 (74.2)	136 (75.6)
Tobacco use history, No. (%)		
Never	26 (14.0)	23 (12.8)
Former	127 (68.3)	119 (66.1)
Current	33 (17.7)	38 (21.1)
Previous NSCLC treatment, No. (%)[c]		
Concurrent platinum + anti–PD-(L)1	107 (57.5)	106 (58.9)
Platinum-based chemotherapy, then anti–PD-(L)1	53 (28.5)	51 (28.3)
Anti–PD-(L)1 monotherapy, then platinum	24 (12.9)	23 (12.8)
Anti–PD-(L)1 monotherapy, then platinum added at progression	2 (1.1)	0
Duration of previous CPI treatment to PD, No. (%)[d]		
<6 months	76 (41.1)	67 (37.6)
≥6 months	109 (58.9)	111 (62.4)
PD-L1 status, No. (%)[e]		
<1%	68 (36.6)	70 (38.9)
≥1%	100 (53.8)	103 (57.2)
1%-49%	49 (26.3)	49 (27.2)
≥50%	47 (25.3)	51 (28.3)

NOTE. Data are based on the intention-to-treat population. PD-L1 data were collected from 93% of patients. Archival pre–anti-PD-(L)1 treatment tumors were tested centrally (25%, VENTANA SP263 assay) or locally (75%, multiple assays).
Abbreviations: CPI, checkpoint inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; IHC, immunohistochemistry; NSCLC, non–small cell lung cancer; TPS, tumor proportion score.
[a]Race was unknown in 13 (atezolizumab + cabozantinib arm) and 15 (docetaxel arm) patients.
[b]Ethnicity was unknown or not reported in 18 (atezolizumab + cabozantinib arm) and 15 (docetaxel arm) patients.
[c]Per electronic case report form.
[d]On the basis of available data for 185 (atezolizumab + cabozantinib arm) and 178 (docetaxel arm) patients.
[e]PD-L1 status was unknown in 22 (atezolizumab + cabozantinib arm) and 10 (docetaxel arm) patients. Seven patients in the PD-L1 ≥1% category were excluded from evaluation in the PD-L1 1%-49% or ≥50% subsets as the reported PD-L1 data from these patients did not enable these categorizations. PD-L1 ≥1% was defined as ≥1% TPS for 22C3, ≥1% PD-L1 for 28-8, ≥1% TC for SP263, ≥1% IC/1% TC for SP142, or ≥1% TPS for QR1 IHC assays. PD-L1 1%-49% was defined as 1%-49% TPS for 22C3, 1%-49% PD-L1 for 28-8, 1%-49% TC for SP263, or 1%-49% TPS for QR1 IHC assays. PD-L1 ≥50% was defined as ≥50% TPS for 22C3, ≥10% PD-L1 for 28-8, ≥50% TC for SP263, ≥10% IC/50% TC for SP142, or ≥50% TPS for QR1 IHC assays.

AEs in 89 [48.1%] and 76 [45.5%], respectively; Data Supplement, Table S4). In the atezolizumab plus cabozantinib and docetaxel arms, 177 (95.7%) and 135 (80.8%) patients, respectively, had AEs related to any study treatment (Table 3). In the atezolizumab plus cabozantinib arm, treatment-related AEs that occurred in ≥20% of patients

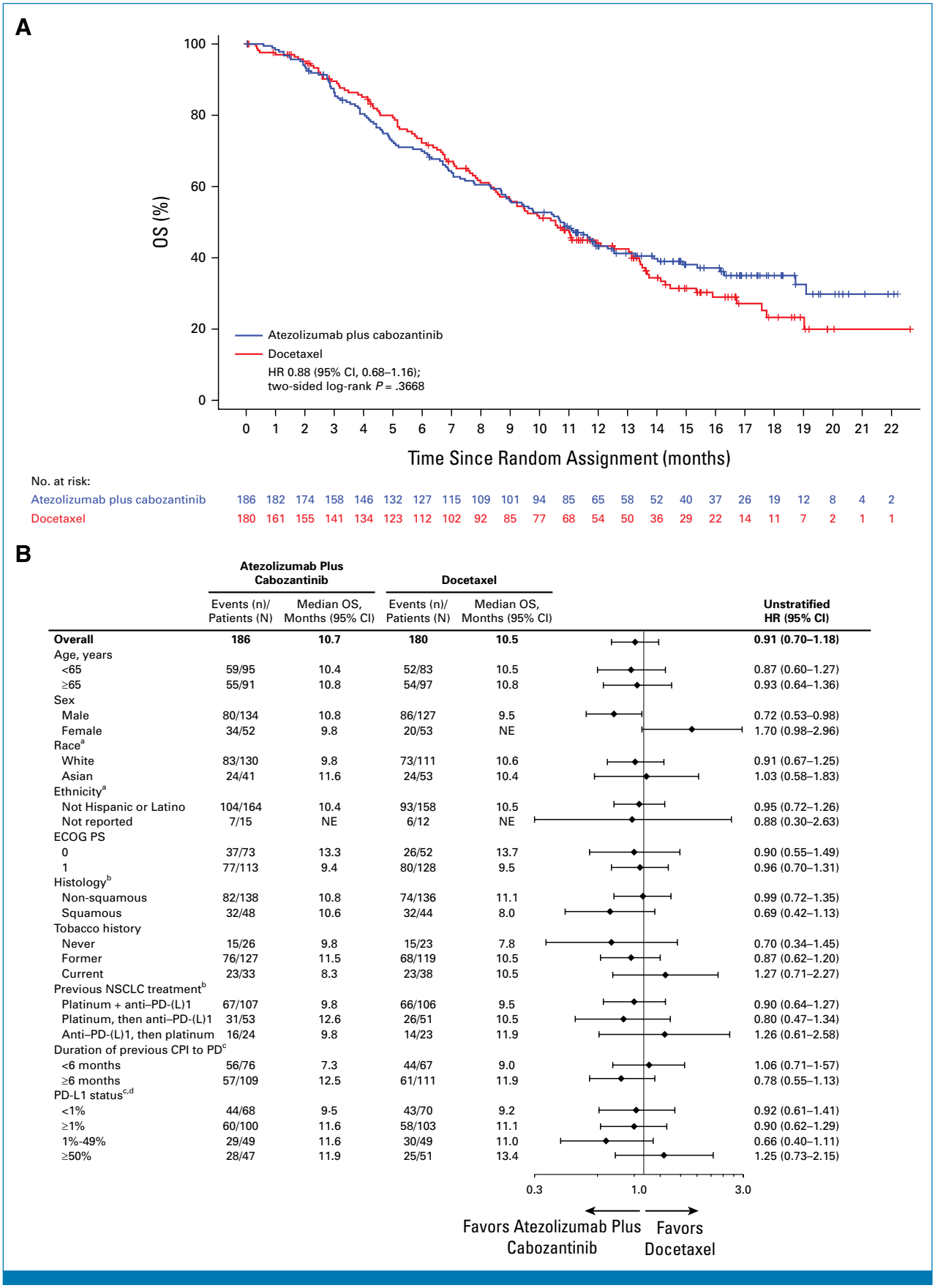

FIG 2. OS. (A) Kaplan-Meier analysis of OS with atezolizumab plus cabozantinib versus docetaxel monotherapy in the intention-to-treat population. Stratified HR is reported. (B) Forest plot of OS by treatment arms in subgroups defined by (continued on following page)

FIG 2. (Continued). patient baseline characteristics in the intention-to-treat population. Unstratified HRs are reported. [a]Not plotted because of small patient numbers: Black or African American (n = 3); Hispanic or Latino (n = 11); anti–PD-(L)1 monotherapy, then platinum added at PD (n = 2). [b]Per electronic case report form. [c]Only includes patients with available or evaluable data. [d]Seven patients in the PD-L1 ≥1% category were excluded from evaluation in the PD-L1 1%-49% or ≥50% subsets, as the reported PD-L1 data from these patients did not enable these categorizations. CPI, checkpoint inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; NE, not estimable; NSCLC, non–small cell lung cancer; OS, overall survival; PD, progressive disease.

were diarrhea (40.5%), decreased appetite (24.9%), and palmar-plantar erythrodysesthesia syndrome (21.6%). In the docetaxel arm, treatment-related AEs that occurred in ≥20% of patients were alopecia (22.2%) and asthenia (21.6%).

Grade 5 AEs occurred in 14 patients (7.6%) in the atezolizumab plus cabozantinib arm and 10 (6.0%) in the docetaxel arm; these were deemed related to study treatment by the investigator in 4 (2.2%) and 1 (0.6%) patients, respectively (Data Supplement, Table S4). In the atezolizumab plus cabozantinib arm, two patients (1.1%) had grade 5 pneumonitis (related to atezolizumab), one patient (0.5%) had a grade 5 pulmonary hemorrhage (related to cabozantinib), and one patient (0.5%) had grade 5 pneumopericardium (related to atezolizumab and cabozantinib). In the docetaxel arm, one patient (0.6%) had grade 5 treatment-related sepsis. In the atezolizumab plus cabozantinib and docetaxel arms, 71 (38.4%) and 58 (34.7%) patients, respectively, had serious AEs (SAEs; Data Supplement, Table S4). In the atezolizumab plus cabozantinib arm, SAEs that occurred in ≥2% of patients were pneumonia (5.4%), pyrexia (2.7%), and vascular device infection (2.2%). In the docetaxel arm, SAEs that occurred in ≥2% of patients were pneumonia (6.0%), febrile neutropenia (4.8%), pneumonitis (3.0%), and respiratory failure (2.4%). In the atezolizumab plus cabozantinib and docetaxel arms, 32 patients (17.3%) and 24 (14.4%), respectively, had AEs leading to study drug discontinuation. In the atezolizumab plus cabozantinib arm, 138 patients (74.6%) had AEs leading to dose interruption or reduction versus 77 (46.1%) in the docetaxel arm.

AEs of special interest (AESIs) corresponding to the immune-mediated mechanism of action of atezolizumab (Data Supplement, Table S5) were observed in 123 patients (66.5%) in the atezolizumab plus cabozantinib arm and 46 (27.5%) in the docetaxel arm. Atezolizumab AESIs that occurred in ≥20% of patients in the atezolizumab plus cabozantinib arm were rash (37.8%), hepatitis—diagnosis and laboratory abnormalities (31.4%), and hepatitis—laboratory abnormalities (27.6%); these AEs are known to occur with both drugs. Cabozantinib AESIs, corresponding to events associated with its mechanism of action, were reported in 104 patients (56.2%) in the atezolizumab plus cabozantinib arm and 35 (21.0%) in the docetaxel arm (Data Supplement, Table S6). Palmar-plantar erythrodysesthesia

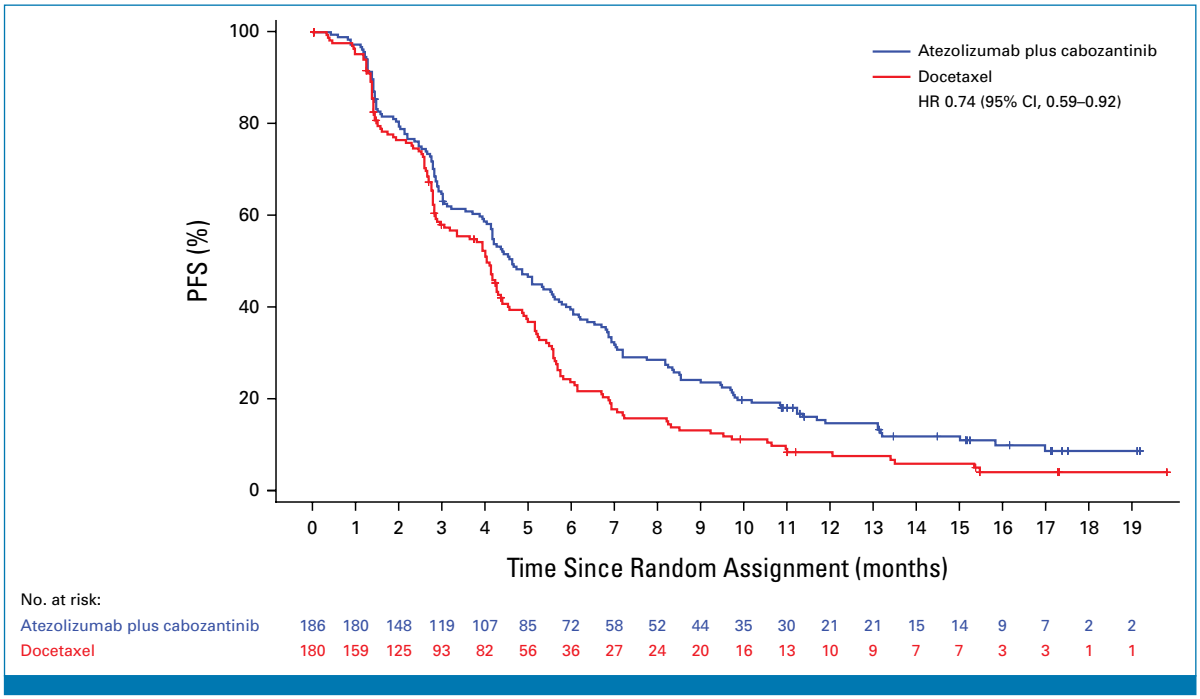

FIG 3. PFS. Kaplan-Meier analysis of PFS with atezolizumab plus cabozantinib versus docetaxel monotherapy in the intention-to-treat population. Stratified HR is reported. HR, hazard ratio; PFS, progression-free survival.

TABLE 2. Tumor Response and Duration

Response	Atezolizumab + Cabozantinib (n = 186)	Docetaxel (n = 180)
ORR, No. (%) [95% CI]	22 (11.8) [7.6 to 17.4]	24 (13.3) [8.7 to 19.2]
CR, No. (%)	0	0
PR, No. (%)	22 (11.8)	24 (13.3)
SD, No. (%)	122 (65.6)	99 (55.0)
PD, No. (%)	29 (15.6)	33 (18.3)
Unevaluable, No. (%)	0	2 (1.1)
Missing, No. (%)	13 (7.0)	22 (12.2)
Duration of response, months, median (95% CI)	5.6 (3.1 to 10.3)	4.3 (3.3 to 5.6)

NOTE. Response was investigator assessed per RECIST 1.1 in patients with measurable disease at baseline. Confirmed objective response was defined as a CR or PR on two consecutive occasions at least 4 weeks apart. Patients were classified as missing or unevaluable if no postbaseline response assessments were available or all postbaseline response assessments were unevaluable.
Abbreviations: CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

TABLE 3. Treatment-Related AEs in ≥10% of Patients

AE[a]	Atezolizumab + Cabozantinib (n = 185)	Docetaxel (n = 167)
Any-grade treatment-related AE	177 (95.7)	135 (80.8)
Diarrhea	75 (40.5)	32 (19.2)
Decreased appetite	46 (24.9)	20 (12.0)
Palmar-plantar erythrodysesthesia syndrome	40 (21.6)	2 (1.2)
Nausea	35 (18.9)	27 (16.2)
Fatigue	32 (17.3)	33 (19.8)
ALT increased	32 (17.3)	5 (3.0)
Asthenia	30 (16.2)	36 (21.6)
Stomatitis	26 (14.1)	12 (7.2)
Hypothyroidism	25 (13.5)	0
AST increased	23 (12.4)	3 (1.8)
Vomiting	20 (10.8)	8 (4.8)
Dysgeusia	19 (10.3)	10 (6.0)
Rash	19 (10.3)	9 (5.4)
Anemia	12 (6.5)	31 (18.6)
Alopecia	2 (1.1)	37 (22.2)

NOTE. Data are indicated as No. (%).
Abbreviation: AE, adverse event.
[a]Includes AEs related to any study treatment.

syndrome (21.6%) was the only cabozantinib AESI that occurred in ≥20% of patients in the atezolizumab plus cabozantinib arm.

DISCUSSION

The phase III CONTACT-01 study in CPI-experienced metastatic NSCLC investigated whether a tyrosine kinase inhibitor (TKI) could reinvigorate immune response with a cancer immunotherapy after previous treatment failure. This study did not meet its primary end point of OS. Numerical improvements favoring atezolizumab plus cabozantinib over docetaxel were observed for secondary end points of PFS and DOR. Overall, the safety profile for atezolizumab plus cabozantinib was consistent with previously established safety profiles of each agent.

With the expanding use of PD-(L)1 inhibitors in earlier lines of therapy for advanced or metastatic NSCLC, an unmet need remains for patients whose disease progresses on or after anti–PD-(L)1 and platinum-containing therapies. Real-world evidence showed that nearly 30% of patients with advanced NSCLC received subsequent CPI rechallenge.[25] However, prospective data of CPI sequencing in NSCLC are sparse, although some phase III trials are ongoing. The phase Ib COSMIC-021 study (ClinicalTrials.gov identifier: NCT03170960) demonstrated clinical activity with cabozantinib, with or without atezolizumab, in patients with advanced NSCLC previously exposed to CPI.[22] However, these results were not reproduced in CONTACT-01. A phase II single-arm study (ClinicalTrials.gov identifier: NCT02954991) of TKI sitravatinib plus nivolumab in patients with non-squamous NSCLC previously treated with an anti–PD-(L)1 regimen and/or platinum-doublet chemotherapy showed improved OS versus historic controls.[26] However, SAPPHIRE (ClinicalTrials.gov identifier: NCT03906071; phase III), which further evaluated this combination versus docetaxel, did not meet its primary OS end point at the final analysis.[27] TROPION-Lung01 (ClinicalTrials.gov identifier: NCT04656652; phase III), which evaluated datopotamab deruxtecan versus docetaxel in patients with locally advanced or metastatic NSCLC previously treated with an anti–PD-(L)1 therapy and platinum-based chemotherapy, met its dual primary end point of PFS at an interim analysis, with immature OS.[28] A phase II study (ClinicalTrials.gov identifier: NCT02501096) of pembrolizumab plus lenvatinib demonstrated promising antitumor activity in patients with advanced NSCLC.[29] However, LEAP-008 (ClinicalTrials.gov identifier: NCT03976375; phase III), assessing lenvatinib with or without pembrolizumab in patients with metastatic NSCLC who were refractory to anti–PD-(L)1 therapy and platinum-based chemotherapy, did not meet its OS and PFS primary end points.[30] Lung-MAP S1800A (ClinicalTrials.gov identifier: NCT03971474; randomized phase II), testing pembrolizumab plus VEGFR2 antagonist ramucirumab versus standard of care in patients with advanced NSCLC previously treated with CPI, demonstrated improved OS[31] with this combination being further investigated in Pragmatica-Lung (ClinicalTrials.gov identifier: NCT05633602; phase III).

An important consideration in CPI rechallenge is determining which patients may benefit from treatment. In CONTACT-01, PD-L1 expression did not appear to be predictive for OS benefit, although it should be noted that PD-L1 expression

was tested predominantly on archival tumor samples acquired before their first cancer immunotherapy exposure. The predictive effect of PD-L1 on archival samples may be restricted to the setting of initial immunotherapy challenge.

It is expected that the CONTACT-01 study population combined patients with primary and acquired resistance to CPI therapy. The study protocol did not stipulate a minimum time to treatment failure on previous CPI, and patients were not stratified by this characteristic. An exploratory subgroup analysis of OS in patients with <6-month versus ≥6-month duration from start of previous CPI to disease progression suggested that patients with more durable response to the first challenge with CPI showed better outcomes with CPI rechallenge than those with a shorter duration of initial response to CPI (unstratified OS HR of 0.78 *v* 1.06). However, limitations of this analysis are that CONTACT-01 was not powered for this comparison and that information on prestudy therapy may have been collected from nonstudy centers that may not have assessed responses using RECIST criteria. Biomarker analyses may provide further insight into underlying resistance mechanisms.

In CONTACT-01, patients with squamous NSCLC appeared to derive treatment benefit with atezolizumab plus cabozantinib more so than patients with nonsquamous NSCLC, similar to findings from the Lung-MAP S1800A phase II study with pembrolizumab plus ramucirumab.[31] In addition, notable differences in OS outcomes between men and women were observed in CONTACT-01, with women appearing to have improved survival with docetaxel versus women in the experimental arm and men in either arm. Imbalances of prognostic factors may have contributed to this effect: 69% of men and 90% of women presented with nonsquamous histology, and 92% of men versus 74% of women were previous or current smokers. Data from previous studies warrant caution when interpreting these CONTACT-01 results by sex. In several studies resulting in approval of PD-(L)1 inhibitors in NSCLC, women appeared to have similar or better outcomes versus men.[6,7,32,33] However, in a more recent phase III trial studying cemiplimab plus chemotherapy versus chemotherapy alone in patients with advanced NSCLC without previous exposure to cancer immunotherapy, OS favored the experimental arm in most subgroups, with women being among the few outliers (OS HR, 2.11).[10] Notably, the study was not powered for subgroup analyses, and the OS HR for women improved with a subsequent update.[34] Furthermore, in clinical trials leading to cabozantinib approval for use in RCC and hepatocellular carcinoma,[17-19] treatment benefitted patients of both sexes.

The safety profile of atezolizumab plus cabozantinib was generally consistent with the established safety profiles of each drug, and no new safety signals were observed. A higher incidence of treatment-related AEs was noted in the atezolizumab plus cabozantinib versus the docetaxel arm, mainly driven by grade 1 and 2 events. Overall incidences of grade 3-5 AEs, SAEs (including treatment-related SAEs), and AEs leading to discontinuation of any study treatment were comparable between arms. However, in the atezolizumab plus cabozantinib arm, the incidence of treatment-related grade 5 AEs was higher than in the docetaxel arm, and more patients receiving atezolizumab and cabozantinib experienced AEs requiring dose modifications or treatment interruptions versus the docetaxel arm.

The study had several limitations. The relative contribution of atezolizumab versus cabozantinib to the treatment effect was difficult to estimate, given the study design. Also, in CONTACT-01, PD-L1 had limited significance as a biomarker because of potential status change during treatment and predominant assessment of PD-L1 status in archival tissue obtained before the first CPI exposure. Moreover, PD-L1 status was not a stratification factor and was mostly assessed locally using different PD-L1 assays. Although other treatment options were available, docetaxel was chosen as the comparator given its approval for both histologies and its frequent use as single-agent chemotherapy in the 2L/3L disease setting after platinum therapy failure globally.

In conclusion, CONTACT-01 does not support the combination of atezolizumab plus cabozantinib after progression on previous CPI and platinum-based chemotherapy in metastatic NSCLC. We await results of ongoing trials in CPI-refractory NSCLC.

AFFILIATIONS

[1]Stanford Cancer Institute, Stanford University, Palo Alto, CA
[2]Royal North Shore Hospital, University of Sydney, St Leonards, Australia
[3]Asan Medical Centre, University of Ulsan College of Medicine, Seoul, South Korea
[4]National Cancer Center, Tokyo, Japan
[5]Yonsei University College of Medicine, Seoul, Republic of Korea
[6]Henry Dunant Hospital Center, Athens, Greece
[7]Euromedica General Clinic of Thessaloniki, Thessaloniki, Greece
[8]MEDSI Clinic, Moscow, Russia
[9]Evang, Kliniken Essen-Mitte, Essen, Germany
[10]CRO Aviano, National Cancer Institute, IRCCS, Aviano, Italy
[11]Montpellier Cancer Institute, Inserm U1194, University of Montpellier, Montpellier, France
[12]Catalan Institute of Oncology, Barcelona, Spain
[13]F. Hoffmann-La Roche Ltd, Basel, Switzerland
[14]Genentech Inc, South San Francisco, CA
[15]Roche Products Limited, Welwyn, United Kingdom
[16]Exelixis, Alameda, CA
[17]Chelsea and Westminster Hospital, London, United Kingdom

CORRESPONDING AUTHOR

Joel Neal, MD, PhD; e-mail: jwneal@stanford.edu.

PRIOR PRESENTATION

Presented in part at the European Lung Cancer Congress 2023, Copenhagen, Denmark, March 29-April 1, 2023.

SUPPORT

Sponsored by F. Hoffmann-La Roche Ltd.

CLINICAL TRIAL INFORMATION

NCT04471428 (CONTACT-01).

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI https://doi.org/10.1200/JCO.23.02166.

DATA SHARING STATEMENT

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 https://go.roche.com/data_sharing. Anonymized records for individual patients across more than one data source external to Roche cannot, and should not, be linked because of a potential increase in risk of patient reidentification.

AUTHOR CONTRIBUTIONS

Conception and design: Joel Neal, Nick Pavlakis, Sang-We Kim, Yasushi Goto, Thomas Newsom-Davis
Provision of study materials or patients: Joel Neal, Nick Pavlakis, Sang-We Kim, Yasushi Goto, Sun Min Lim, Giannis Mountzios, Elena Fountzilas, Anastasia Mochalova, Daniel C. Christoph, Alessandra Bearz, Xavier Quantin, Ramon Palmero, Thomas Newsom-Davis
Collection and assembly of data: Joel Neal, Nick Pavlakis, Sang-We Kim, Yasushi Goto, Sun Min Lim, Giannis Mountzios, Elena Fountzilas, Anastasia Mochalova, Daniel C. Christoph, Alessandra Bearz, Xavier Quantin, Thomas Newsom-Davis, Ramon Palmero
Data analysis and interpretation: Joel Neal, Nick Pavlakis, Sang-We Kim, Daniel C. Christoph, Vladan Antic, Elaine Chun, Tirupathi Rao Edubilli, Ya-Chen Lin, Mahrukh Huseni, Marcus Ballinger, Vilma Graupner, Dominic Curran, Piet Vervaet
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

ACKNOWLEDGMENT

Exelixis provided cabozantinib and cofunded the study.
The authors thank the patients and their families for their participation in the study, as well as all investigational sites. The authors thank Andrea Liptrot (Roche), Ida Enquist (Genentech), Shradha Bhagani (Roche), Sammi Tam (Genentech), and Tomohiro Tanaka (Chugai) for reviewing the data. Medical writing assistance for this manuscript was provided by Michael J. Williams, PhD, and Ashley J. Pratt, PhD, CMPP, of Nucleus Global, an Inizio Company, and funded by F. Hoffmann-La Roche Ltd.

REFERENCES

1. Herbst RS, Morgensztern D, Boshoff C: The biology and management of non-small cell lung cancer. Nature 553:446-454, 2018
2. Hendriks LE, Kerr KM, Menis J, et al: Non-oncogene-addicted metastatic non-small-cell lung cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. Ann Oncol 34:358-376, 2023
3. Hong DS, Fakih MG, Strickler JH, et al: KRAS(G12C) inhibition with sotorasib in advanced solid tumors. N Engl J Med 383:1207-1217, 2020
4. Johnson ML, Cho BC, Luft A, et al: Durvalumab with or without tremelimumab in combination with chemotherapy as first-line therapy for metastatic non-small-cell lung cancer: The phase III POSEIDON study. J Clin Oncol 41:1213-1227, 2023
5. Reck M, Rodriguez-Abreu D, Robinson AG, et al: Pembrolizumab versus chemotherapy for PD-L1-positive non-small-cell lung cancer. N Engl J Med 375:1823-1833, 2016
6. Gandhi L, Rodriguez-Abreu D, Gadgeel S, et al: Pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer. N Engl J Med 378:2078-2092, 2018
7. Paz-Ares L, Luft A, Vicente D, et al: Pembrolizumab plus chemotherapy for squamous non-small-cell lung cancer. N Engl J Med 379:2040-2051, 2018
8. Socinski MA, Jotte RM, Cappuzzo F, et al: Atezolizumab for first-line treatment of metastatic nonsquamous NSCLC. N Engl J Med 378:2288-2301, 2018
9. Hellmann MD, Paz-Ares L, Bernabe Caro R, et al: Nivolumab plus ipilimumab in advanced non-small-cell lung cancer. N Engl J Med 381:2020-2031, 2019
10. Gogishvili M, Melkadze T, Makharadze T, et al: Cemiplimab plus chemotherapy versus chemotherapy alone in non-small cell lung cancer: A randomized, controlled, double-blind phase 3 trial. Nat Med 28:2374-2380, 2022
11. Herbst RS, Giaccone G, de Marinis F, et al: Atezolizumab for first-line treatment of PD-L1-selected patients with NSCLC. N Engl J Med 383:1328-1339, 2020
12. Sezer A, Kilickap S, Gumus M, et al: Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: A multicentre, open-label, global, phase 3, randomised, controlled trial. Lancet 397:592-604, 2021
13. Popat S, Mellemgaard A, Fahrbach K, et al: Nintedanib plus docetaxel as second-line therapy in patients with non-small-cell lung cancer: A network meta-analysis. Future Oncol 11:409-420, 2015
14. Singh N, Temin S, Baker S Jr., et al: Therapy for stage IV non-small-cell lung cancer without driver alterations: ASCO living guideline. J Clin Oncol 40:3323-3343, 2022
15. Yakes FM, Chen J, Tan J, et al: Cabozantinib (XL184), a novel MET and VEGFR2 inhibitor, simultaneously suppresses metastasis, angiogenesis, and tumor growth. Mol Cancer Ther 10:2298-2308, 2011
16. Exelixis: Cabometyx (Cabozantinib) tablets for oral use [prescribing information]. https://www.cabometyxhcp.com/sites/default/files/2021-03/prescribing-information.pdf
17. Choueiri TK, Powles T, Burotto M, et al: Nivolumab plus cabozantinib versus sunitinib for advanced renal-cell carcinoma. N Engl J Med 384:829-841, 2021
18. Abou-Alfa GK, Meyer T, Cheng AL, et al: Cabozantinib in patients with advanced and progressing hepatocellular carcinoma. N Engl J Med 379:54-63, 2018
19. Choueiri TK, Escudier B, Powles T, et al: Cabozantinib versus everolimus in advanced renal cell carcinoma (METEOR): Final results from a randomised, open-label, phase 3 trial. Lancet Oncol 17: 917-927, 2016
20. Brose MS, Robinson B, Sherman SI, et al: Cabozantinib for radioiodine-refractory differentiated thyroid cancer (COSMIC-311): A randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol 22:1126-1138, 2021
21. Kwilas AR, Ardiani A, Donahue RN, et al: Dual effects of a targeted small-molecule inhibitor (cabozantinib) on immune-mediated killing of tumor cells and immune tumor microenvironment permissiveness when combined with a cancer vaccine. J Transl Med 12:294, 2014
22. Neal JW, Santoro A, Viteri S, et al: Cabozantinib (C) plus atezolizumab (A) or C alone in patients (pts) with advanced non–small cell lung cancer (aNSCLC) previously treated with an immune checkpoint inhibitor (ICI): Results from Cohorts 7 and 20 of the COSMIC-021 study. J Clin Oncol 40, 2022 (suppl 16; abstr 9005)
23. Hwang IK, Shih WJ, De Cani JS: Group sequential designs using a family of type I error probability spending functions. Stat Med 9:1439-1445, 1990
24. Brookmeyer R, Crowley J: A confidence interval for the median survival time. Biometrics 38:29-41, 1982
25. Giaj Levra M, Cotte FE, Corre R, et al: Immunotherapy rechallenge after nivolumab treatment in advanced non-small cell lung cancer in the real-world setting: A national data base analysis. Lung Cancer 140:99-106, 2020
26. Leal TA, Berz D, Rybkin I, et al: 43P MRTX-500: Phase II trial of sitravatinib (sitra) + nivolumab (nivo) in patients (pts) with non-squamous (NSQ) non-small cell lung cancer (NSCLC) progressing on or after prior checkpoint inhibitor (CPI) therapy. Ann Oncol 33:S19-S20, 2022

27. Borghaei H, de Marinis F, Dumoulin D, et al: SAPPHIRE: Phase III study of sitravatinib plus nivolumab versus docetaxel in advanced nonsquamous non-small-cell lung cancer. Ann Oncol 35:66-76, 2024
28. Ahn M-JL, Lisberg A, Paz-Ares L, et al: LBA12 Datopotamab deruxtecan (Dato-DXd) vs docetaxel in previously treated advanced/metastatic (adv/met) non-small cell lung cancer (NSCLC): Results of the randomized phase III study TROPION-Lung01. Ann Oncol 34:S1305-S1306, 2023
29. Taylor MH, Lee CH, Makker V, et al: Phase IB/II trial of lenvatinib plus pembrolizumab in patients with advanced renal cell carcinoma, endometrial cancer, and other selected advanced solid tumors. J Clin Oncol 38:1154-1163, 2020
30. Leighl NB, Hui R, Rodríguez-Abreu D, et al: Pembrolizumab plus lenvatinib vs docetaxel in patients with previously treated metastatic non-small-cell lung cancer (NSCLC) and PD after platinum-doublet chemotherapy and immunotherapy: Phase 3, randomized, open-label LEAP-008 trial. Cancer Res 80, 2020 (suppl 16; abstr CT289)
31. Reckamp KL, Redman MW, Dragnev KH, et al: Phase II randomized study of ramucirumab and pembrolizumab versus standard of care in advanced non-small-cell lung cancer previously treated with immunotherapy-lung-MAP S1800A. J Clin Oncol 40:2295-2306, 2022
32. Rittmeyer A, Barlesi F, Waterkamp D, et al: Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): A phase 3, open-label, multicentre randomised controlled trial. Lancet 389:255-265, 2017
33. Borghaei H, Paz-Ares L, Horn L, et al: Nivolumab versus docetaxel in advanced nonsquamous non-small-cell lung cancer. N Engl J Med 373:1627-1639, 2015
34. Makharadze T, Gogishvili M, Melkadze T, et al: Cemiplimab plus chemotherapy versus chemotherapy alone in advanced NSCLC: 2-year follow-up from the phase 3 EMPOWER-Lung 3 Part 2 trial. J Thorac Oncol 18:755-768, 2023

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

CONTACT-01: A Randomized Phase III Trial of Atezolizumab + Cabozantinib Versus Docetaxel for Metastatic Non–Small Cell Lung Cancer After a Checkpoint Inhibitor and Chemotherapy

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

Joel Neal
Honoraria: CME Matters, Clinical Care Options, Research to Practice, Medscape, Biomedical Learning Institute, Peerview, Prime Oncology, Projects in Knowledge, Rockpointe CME, MJH Life Sciences, Medical Educator Consortium, HMP Education
Consulting or Advisory Role: AstraZeneca, Genentech/Roche, Exelixis, Takeda, Lilly, Amgen, Iovance Biotherapeutics, Blueprint Medicines, Regeneron, Natera, Sanofi/Regeneron, D2G Oncology, Surface Oncology, Turning Point Therapeutics, Mirati Therapeutics, Gilead Sciences, AbbVie, Summit Therapeutics, Novartis, Novocure
Research Funding: Genentech/Roche (Inst), Merck (Inst), Novartis (Inst), Boehringer Ingelheim (Inst), Exelixis (Inst), Nektar (Inst), Takeda (Inst), Adaptimmune (Inst), GlaxoSmithKline (Inst), Janssen (Inst), AbbVie (Inst), Novocure (Inst)
Patents, Royalties, Other Intellectual Property: UpToDate—Royalties

Nick Pavlakis
Honoraria: BeiGene, Bayer, BeiGene, Takeda, Pierre Fabre
Consulting or Advisory Role: Roche, Boehringer Ingelheim, AstraZeneca, Merck KGaA, Merck Serono, Amgen, Merck Sharp & Dohme, Novartis, Pfizer, Takeda, Bristol Myers Squibb, BeiGene, Gilead Sciences, Janssen Oncology
Research Funding: Bayer (Inst), Pfizer (Inst), Roche (Inst)

Yasushi Goto
Honoraria: AstraZeneca, Boehringer Ingelheim, Lilly Japan, Chugai Pharma, Taiho Pharmaceutical, Ono Pharmaceutical, MSD, Pfizer, Bristol Myers Squibb Japan, Novartis, Thermo Fisher Scientific, Merck, Guardant Health AMEA, Takeda, Daiichi Sankyo/AstraZeneca, Daiichi Sankyo/UCB Japan, Amgen, Janssen, Sandoz, Nichi-Iko, Daiichi Sankyo/AstraZeneca
Consulting or Advisory Role: Lilly, Boehringer Ingelheim, Taiho Pharmaceutical, Pfizer, Novartis, AstraZeneca, Chugai Pharma, Guardant Health AMEA, Daiichi Sankyo/UCB Japan, Janssen, Ono Pharmaceutical
Research Funding: AbbVie (Inst), Lilly Japan (Inst), Pfizer (Inst), Ono Pharmaceutical (Inst), Daiichi Sankyo (Inst), Bristol Myers Squibb Japan (Inst), Chugai Pharma (Inst), Taiho Pharmaceutical (Inst), MSD (Inst), AstraZeneca (Inst), Novartis (Inst), Merck Serono (Inst), Genomic Health (Inst), CMIC (Inst), Takeda (Inst), EPS Holdings (Inst), IQVIA (Inst), Daiichi Sankyo/UCB Japan (Inst), Janssen (Inst), Amgen (Inst), EP Croit Co (Inst), Amgen Astellas BioPharma (Inst), Bayer (Inst), Preferred Network (Inst), Medpace (Inst), Sysmex (Inst)
Uncompensated Relationships: Cancer Net Japan, JAMT

Sun Min Lim
Honoraria: Takeda, Boehringer Ingelheim, Yuhan
Research Funding: Janssen Research & Development

Giannis Mountzios
Honoraria: Roche, Boehringer Ingelheim, AstraZeneca, MSD, BMS GmbH & Co KG, Novartis, Amgen, Takeda
Consulting or Advisory Role: Roche, AstraZeneca/Greece, MSD, Amgen, Novartis, BMS GmbH & Co KG, Takeda
Speakers' Bureau: AstraZeneca
Travel, Accommodations, Expenses: AstraZeneca, Ipsen, MSD, Roche, Novartis, BMS GmbH & Co KG, Demo Pharmaceutical

Elena Fountzilas
Stock and Other Ownership Interests: Deciphera, Genprex
Honoraria: AstraZeneca, Roche, Amgen, Roche/Genentech, Pfizer, AstraZeneca
Consulting or Advisory Role: Pfizer, Sanofi, Roche, Amgen
Travel, Accommodations, Expenses: Genesis Pharmaceuticals, AstraZeneca, Pfizer

Daniel C. Christoph
Honoraria: AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Chugai Pharma, Ipsen, Janssen, MSD Sharp & Dohme, Novartis, Novocure, Pfizer, Pierre Fabre, Roche, Sanofi, Takeda
Consulting or Advisory Role: AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Chugai Pharma, Ipsen, Janssen, Merck Sharp & Dohme, Novartis, Novocure, Pfizer, Pierre Fabre, Roche, Sanofi, Takeda
Speakers' Bureau: AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Chugai Pharma, Ipsen, Janssen, MSD Sharp & Dohme, Novartis, Novocure, Pfizer, Pierre Fabre, Roche, Sanofi, Takeda
Expert Testimony: AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Chugai Pharma, Ipsen, Janssen, MSD Sharp & Dohme, Novartis, Novocure, Pfizer, Pierre Fabre, Roche, Sanofi, Takeda
Travel, Accommodations, Expenses: AstraZeneca, Bristol Myers Squibb, Janssen, MSD Sharp & Dohme, Pfizer, Roche, Sanofi

Alessandra Bearz
Consulting or Advisory Role: Takeda, Pfizer, Boehringer Ingelheim, Regeneron, Novartis
Speakers' Bureau: Roche/Genentech, Pfizer, Lilly
Research Funding: Janssen Oncology

Xavier Quantin
Honoraria: BMS France (Inst), AstraZeneca (Inst), AstraZeneca, Amgen, Lilly, AstraZeneca (Inst), BMS (Inst), Daiichi, Sanofi (Inst), AstraZeneca (Inst)
Consulting or Advisory Role: Ipsen
Travel, Accommodations, Expenses: MSD Oncology, Janssen Oncology, Daiichi, Pfizer, Sanofi, Daiichi Sankyo/AstraZeneca

Ramon Palmero
Consulting or Advisory Role: Boehringer Ingelheim, Roche, AstraZeneca Spain
Speakers' Bureau: Boehringer Ingelheim, Roche, Bristol Myers Squibb, Lilly, Guardant Health, Pfizer, AstraZeneca Spain
Travel, Accommodations, Expenses: Roche, MSD Oncology

Vladan Antic
Employment: Roche
Stock and Other Ownership Interests: Roche

Elaine Chun
Employment: Genentech
Stock and Other Ownership Interests: Genentech
Travel, Accommodations, Expenses: Genentech

Tirupathi Rao Edubilli
Employment: Roche

Ya-Chen Lin
Employment: Genentech/Roche
Stock and Other Ownership Interests: Roche

Mahrukh Huseni
Employment: Roche/Genentech
Stock and Other Ownership Interests: Roche/Genentech
Patents, Royalties, Other Intellectual Property: Holds patents as an employee of Roche/Genentech
Travel, Accommodations, Expenses: Roche/Genentech

Marcus Ballinger
Employment: Genentech
Stock and Other Ownership Interests: Roche
Patents, Royalties, Other Intellectual Property: coinventor of an unpublished patent application (Inst)
Travel, Accommodations, Expenses: Genentech/Roche

Vilma Graupner
Employment: Roche
Stock and Other Ownership Interests: Roche

Dominic Curran
Employment: Exelixis, Quanta Therapeutics
Stock and Other Ownership Interests: Exelixis
Travel, Accommodations, Expenses: Exelixis

Piet Vervaet
Employment: Exelixis
Stock and Other Ownership Interests: Exelixis

Thomas Newsom-Davis
Honoraria: Amgen, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, MSD, Novartis, Roche, Takeda, Merck Serono, Janssen, AbbVie, Daiichi Sankyo/Lilly, Gilead Sciences, GlaxoSmithKline, Chugai Pharma, Lilly, Sanofi, Novocure, EQRx
Consulting or Advisory Role: Amgen, AstraZeneca, Bristol Myers Squibb, MSD, Novartis, Roche, Takeda, Boehringer Ingelheim, AbbVie, Lilly, GlaxoSmithKline, Gilead Sciences, Janssen, Sanofi, Novocure, EQRx
Speakers' Bureau: AstraZeneca, Roche, Takeda, Amgen, GlaxoSmithKline
Travel, Accommodations, Expenses: Boehringer Ingelheim, MSD, Roche, Takeda, AbbVie, Lilly

No other potential conflicts of interest were reported.

APPENDIX

TABLE A1. CONTACT-01 Study Sites and Investigators

Country	Study Site	Name
Australia	Flinders Medical Centre	Christos Karapetis
Australia	Royal North Shore Hospital; Oncology	Nick Pavlakis
Australia	Townsville Hospital	Abhishek Joshi
Australia	Austin Hospital Olivia Newton John Cancer Centre	Sagun Parakh
Australia	Affinity Oncology	Adnan Khattak
Austria	Lkh-Univ. Klinikum Graz; Klinische Abteilung Für Onkologie	Gudrun Absenger
Austria	Lhk Feldkirch; Interne Medizin Abt.	Thomas Winder
Austria	Medizinische Universität Wien; Univ.Klinik Für Innere Medizin I—Abt. Für Onkologie	Barbara Kiesewetter-Wiederkehr
Austria	Lkh Salzburg—Univ. Klinikum Salzburg; III. Medizinische Abt.	Richard Greil
Austria	Ordensklinikum Linz Elisabethinen	Michael Schumacher
Belgium	Uz Gent	Veerle Surmont
Belgium	Clinique Ste-Elisabeth	Jean-Charles Goeminne
Belgium	Institut Jules Bordet	Thierry Berghmans
Belgium	Cliniques Universitaires St-Luc	Thierry Pieters
France	Hopital Tenon; Pneumologie	Jacques Cadranel
France	Centre Regional de Lutte contre le Cancer Val d Aurelle—Paul Lamarque; Service d Oncologie	Xavier Quantin
France	Hopital Dupuytren; Pneumologie	Thomas Egenod
France	Clinique de l'Europe	Charles Dayen
France	CHU Angers, Service de Pneumologie	Thierry Urban
France	Hôpital Saint Joseph; Oncologie Medicale	Cyril Foa
France	CHU de Grenoble	Denis Moro-Sibilot
Germany	KRH Klinikum Siloah-Oststadt-Heidehaus	Monika Heilmann
Germany	Universitaetsklinikum Giessen und Marburg	Thomas Wündisch
Germany	Zentralklinik Bad Berka GmbH; Pneumologie	Ekkehard Eigendorff
Germany	Klinikum Koeln-Merheim; Lungenklinik	Eva-Lotte Buchmeier
Germany	Kliniken Essen Mitte Evang. Huyssens Stiftung/Knappschaft GmbH	Daniel Christoph
Germany	Brüderkrankenhaus St Josef Paderborn	Harald Müller-Huesmann
Germany	Universitaetsklinikum Giessen und Marburg GmbH; Medizinische Klinik IV und V	Bastian Eul
Greece	Henri Dunant Hospital; Oncology Department	Giannis Mountzios
Greece	Univ General Hosp Heraklion; Medical Oncology	Dimitris Mavroudis
Greece	Euromedical General Clinic of Thessaloniki; Oncology Department	George Fountzilas
Greece	Uoa Sotiria Hospital; Oncology	Konstantinos Syrigos
Italy	IRCCS Centro Di Riferimento Oncologico	Alessandra Bearz
Italy	Instituto Europeo di Oncologia	Filippo De Marinis
Italy	IRCCS AOU San Martino—IST	Carlo Genova
Italy	Azienda Ospedaliera San Camillo Forlanini	Maria Rita Migliorino
Italy	Ospedale Vito Fazzi	Gianpiero Romano
Italy	Istituto Clinico Humanitas	Armando Santoro
Italy	Azienda Ospedaliero Universitaria di Parma	Marcello Tiseo
Italy	Policlinico Umberto I, Oncologia B	Alain Gelibter
Italy	ASST Spedali Civili di Brescia	Salvatore Grisanti
Italy	A.O.U. Careggi	Lorenzo Antonuzzo
Italy	AORN Ospedali dei Colli Ospedale Monaldi; UOC Pneumologia ad indirizzo Oncologico	Fabiana Vitiello
Italy	Ospedale Provinciale Santa Maria Delle Croci; Oncologia Medica	Manolo D'arcangelo

(continued on following page)

TABLE A1. CONTACT-01 Study Sites and Investigators (continued)

Country	Study Site	Name
Italy	Azienda Ospedaliero-Universitaria S.Orsola-Malpighi; Unità Operativa Oncologia Medica	Andrea Ardizzoni
Japan	National Cancer Center Hospital	Yasushi Goto
Japan	The Cancer Institute Hospital of JFCR	Noriko Yanagitani
Japan	Sendai Kousei Hospital	Shunichi Sugawara
Japan	Osaka International Cancer Institute	Motohiro Tamiya
Japan	Hyogo Cancer Center	Yoshihiro Hattori
Republic of Korea	Asan Medical Center	Sang-We Kim
Republic of Korea	Severance Hospital, Yonsei University Health System	Sun Min Lim
Republic of Korea	National Cancer Center	Ji-Youn Han
Republic of Korea	Seoul National University Bundang Hospital	Yu Jung Kim
Republic of Korea	Seoul St Mary's Hospital	Jin-Hyoung Kang
Republic of Korea	Chungbuk National University Hospital	Ki Hyeong Lee
Republic of Korea	Gachon University Gil Medical Center	Hee Kyung Ahn
Republic of Korea	St Vincent's Hospital	Byoung Yong Shim
Republic of Korea	Ajou University Medical Center	Yong Won Choi
Republic of Korea	Ulsan University Hospital	Young Joo Min
Republic of Korea	Samsung Changwon Hospital	Sungmin Kim
Republic of Korea	Korea University Anam Hospital	Yoon Ji Choi
Poland	Centrum Onkologii im. Prof. Franciszka Łukaszczyka; Ambulatorium Chemioterapii	Bogdan Zurawski
Poland	SP ZOZ Wojewódzki Szpital Specjalistyczny nr 4; Oddzial Onkologii Klinicznej	Ewa nowakowska-Zajdel
Poland	Szpital Wojewódzki im. Mikołaja Kopernika; Oddział Dzienny Chemioterapii	Mariusz Kwiatkowski
Poland	Mazowieckie Centrum Leczenia Chorob Pluc I Gruzlicy; Oddzial III	Aleksandra Szczesna
Poland	Narodowy Inst.Onkol.im.Sklodowskiej-Curie Panstw.Inst.Bad Gliwice; III Klin. Radioter. i Chemioter.	Adam Idasiak
Portugal	IPO do Porto; Servico de Oncologia Medica	Cristina Oliveira
Portugal	CHVNG/E_Unidade 1; Servico de Pneumologia	Ana Barroso
Portugal	Hospital Pulido Valente; Servico de Pneumologia	Direnda Hasmucrai
Portugal	Centro Hospitalar do Porto—Hospital de Santo António; Oncologia	Antonio Araujo
Portugal	Hospital CUF Porto; Servico Pneumologia	Barbara Parente
Portugal	Hospital Pedro Hispano; Servico de Oncologia	Fernanda Estevinho
Russian Federation	MEDSI Clinical Hospital on Pyatnitsky Highway; Department of Antitumor Drug Therapy	Anastasia Mochalova
Russian Federation	Regional Clinical Oncology Hospital	Nikolay Kislov
Russian Federation	GBUZ Leningradskaya State Clinical Hospital	Maria Smagina
Russian Federation	S-Pb Clinical Scientific Practical Center of Specialized Kinds of Medical Care (Oncological)	Vladimir Moiseenko
Spain	Hospital Arnau de Vilanova (Valencia) Servicio de Oncologia	Javier Garde Noguera
Spain	Institut Catala d Oncologia Hospital Duran i Reynals	Ramon Palmero Sanchez
Spain	Hospital Universitari i Politecnic La Fe; Oncologia	Oscar Juan Vidal
Spain	Complejo Hospitalario Universitario A Coruña (CHUAC); Servicio de Oncologia	M. Rosario Garcia Campelo
Spain	Hospital Univ. Nuestra Señora de Valme; Servicio de Oncologia	Jose Fuentes Pradera
Spain	Vall d'Hebron Institute of Oncology (VHIO), Barcelona	Enriqueta Felip
Spain	Hospital Universitario La Paz; Servicio de Oncologia	Javier De Castro Carpeno
United Kingdom	Chelsea & Westminster Hospital	Thomas Newsom-Davis
United Kingdom	Beatson West of Scotland Cancer Centre	Nicola Steele
United Kingdom	Barts & London School of Medicine; Medical Oncology	Farah Lim
United Kingdom	Addenbrookes Hospital	Huiqi Yang

(continued on following page)

TABLE A1. CONTACT-01 Study Sites and Investigators (continued)

Country	Study Site	Name
United Kingdom	University College London Hospital	Dionysios Papadatos-Pastos
United States	Northwest Georgia Oncology Centers P.C.—Marietta	Steven L. McCune
United States	San Juan Oncology Associates	Jeffrey Neidhart
United States	Stanford University	Joel Neal
United States	Regional Cancer Care Associates	Ralph Boccia
United States	Oncology and Hematology Associates of Southwest Virginia, Inc, Blacksburg	Jerome Goldschmidt-Jr
United States	Cancer Care Centers of Brevard	Pavan Kancharla
United States	Arizona Oncology	Richard Rosenberg
United States	Rocky Mountain Cancer Centers	Hossein Maymani
United States	Hartford Healthcare	Wylie Hosmer
United States	Sansum Clinic	Eric Bank
United States	Consultants in Medical Oncology and Hematology	Stephen A. Shore
United States	Texas Oncology—Baylor Charles A. Sammons Cancer Center	Kartik Konduri
United States	Charleston Oncology, P.A.	Brian Lingerfelt
United States	Minnesota Oncology Hematology	Timothy Larson
United States	Virginia Cancer Specialists (Fairfax)—USOR	Timothy McCarthy
United States	Oncology Associates of Oregon, P.C.	James Butrynski
United States	Kaiser Permanente—San Diego	Eric McGary
United States	Huntsman Cancer Institute at The University of Utah	Sonam Puri

NOTE. Includes sites that screened or enrolled ≥1 patient.