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ORIGINAL RESEARCH

Real-world outcomes with durvalumab after chemoradiotherapy in patients with unresectable stage III NSCLC: interim analysis of overall survival from PACIFIC-R

A. R. Filippi[1*†], J. Bar[2,3], C. Chouaid[4], D. C. Christoph[5], J. K. Field[6], R. Fietkau[7], M. C. Garassino[8], P. Garrido[9], V. D. Haakensen[10], S. Kao[11], B. Markman[12], F. McDonald[13], F. Mornex[14], M. Moskovitz[15‡], S. Peters[16], A. Sibille[17], S. Siva[18], M. van den Heuvel[19], P. Vercauter[20], S. Anand[21], P. Chander[21], M. Licour[22], A. R. de Lima[21], Y. Qiao[21] & N. Girard[23,24]

[1]Radiation Oncology Department, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico Policlinico San Matteo and University of Pavia, Pavia, Italy; [2]Institute of Oncology, Sheba Medical Centre, Ramat Gan; [3]Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [4]Service de Pneumologie, Centre Hospitalier Intercommunal de Créteil, Créteil, France; [5]Department of Medical Oncology, Evang. Kliniken Essen-Mitte, Evang. Huyssens-Stiftung Essen-Huttrop, Essen, Germany; [6]Roy Castle Lung Cancer Research Programme, Department of Molecular and Clinical Cancer Medicine, University of Liverpool, Liverpool, UK; [7]Department of Radiation Oncology, Universitätsklinikum Erlangen, Erlangen, Germany; [8]Department of Hematology/Oncology, The University of Chicago, Chicago, USA; [9]Medical Oncology Department, Hospital Ramón y Cajal, Universidad de Alcalá, Madrid, Spain; [10]Department of Oncology and Institute for Cancer Research, Oslo University Hospital, Oslo, Norway; [11]Chris O'Brien Lifehouse, Sydney; [12]Cabrini Hospital and Monash University, Melbourne, Australia; [13]Lung Unit, The Royal Marsden NHS Foundation Trust, London, UK; [14]Department of Radiation Oncology, Centre Hospitalier Universitaire de Lyon, Lyon, France; [15]Rambam Health Care Campus, Haifa, Israel; [16]Department of Oncology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; [17]Department of Pneumology, Centre Hospitalier Universitaire de Liège, Liège, Belgium; [18]Peter MacCallum Cancer Centre and The University of Melbourne, Melbourne, Australia; [19]Department of Pulmonary Diseases, Radboud University Medical Center, Nijmegen, The Netherlands; [20]Department of Pneumology, OLV Hospital Aalst, Aalst, Belgium; [21]AstraZeneca, Gaithersburg, USA; [22]AstraZeneca, Courbevoie, France; [23]Institut du Thorax Curie Montsouris, Institut Curie, Paris; [24]UVSQ, Paris Saclay, Versailles, France

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Background: Based on the findings of the PACIFIC trial, consolidation durvalumab following platinum-based chemoradiotherapy (CRT) is a global standard of care for patients with unresectable, stage III non-small-cell lung cancer (NSCLC). An earlier analysis from the ongoing PACIFIC-R study (NCT03798535) demonstrated the effectiveness of this regimen in terms of progression-free survival (PFS). Here, we report the first planned overall survival (OS) analysis.

Patients and methods: PACIFIC-R is an observational/non-interventional, retrospective study of patients with unresectable, stage III NSCLC who started durvalumab (10 mg/kg intravenously every 2 weeks) within an AstraZeneca-initiated early access program between September 2017 and December 2018. Primary endpoints are OS and investigator-assessed PFS, estimated using the Kaplan—Meier method.

Results: By 30 November 2021, the full analysis set included 1154 participants from 10 countries (median follow-up in censored patients: 38.7 months). Median OS was not reached, and the 3-year OS rate was 63.2% (95% confidence interval 60.3% to 65.9%). Three-year OS rates were numerically higher among patients with programmed death-ligand 1 (PD-L1) expression on $\geq$1% versus $<$1% of tumor cells (TCs; 67.0% versus 54.4%) and patients who received concurrent CRT (cCRT) versus sequential CRT (sCRT) (64.8% versus 57.9%).

Conclusions: PACIFIC-R data continue to provide evidence for the effectiveness of consolidation durvalumab after CRT in a large, diverse, real-world population. Better outcomes were observed among patients with PD-L1 TCs $\geq$1% and patients who received cCRT. Nevertheless, encouraging outcomes were still observed among patients with TCs $<$1% and patients who received sCRT, supporting use of consolidation durvalumab in a broad population of patients with unresectable, stage III NSCLC.

Key words: durvalumab, immunotherapy, PD-L1, real-world evidence, locally advanced NSCLC

INTRODUCTION

Approximately 20%-35% of patients with non-small-cell lung cancer (NSCLC) are diagnosed with stage III disease,[1-3] and median survival for stage III NSCLC is reported to range from 9 to 34 months.[1] Therefore, there has been a focus on developing treatments to improve outcomes in these patients. The results of the placebo-controlled, phase III PACIFIC trial (NCT02125461) established consolidation immunotherapy with durvalumab for up to 12 months

*Correspondence to: Prof. Andrea R. Filippi, Istituto Nazionale Tumori, via Venezian 1, 20133 Milan, Italy. Tel: +39-349-4694526
E-mail: andrearicardo.filippi@istitutotumori.mi.it (A. R. Filippi).

†Present address: Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori and Department of Oncology, University of Milan, Milan, Italy.

‡Present address: Davidoff Cancer Center, Rabin Medical Center, Petah Tikva, Israel.

following platinum-based chemoradiotherapy (CRT) (the 'PACIFIC regimen') as a global standard of care for patients with unresectable, stage III NSCLC.[4-8] The primary analyses demonstrated significant improvements in overall survival (OS) and progression-free survival (PFS) with durvalumab in patients whose disease had not progressed following platinum-based, concurrent CRT (cCRT).[4,5] Furthermore, durvalumab was associated with a manageable safety profile and did not detrimentally impact patient-reported quality of life.[4,5,9] Following publication of the primary results, subsequent updates from PACIFIC demonstrated that the benefit of durvalumab is sustained over time.[8,10] At the most recent update, median OS was 47.5 months [95% confidence interval (CI) 38.1-52.9 months] with durvalumab versus 29.1 months (95% CI 22.1-35.1 months) with placebo [hazard ratio (HR) 0.72, 95% CI 0.59-0.89]; 3-year OS rates were 56.7% versus 43.6% with durvalumab versus placebo, and 5-year OS rates were 42.9% versus 33.4%, respectively.[8] At the same update, median PFS was 16.9 months (95% CI 13.0-23.9 months) with durvalumab versus 5.6 months (95% CI 4.8-7.7 months) with placebo (HR 0.55, 95% CI 0.45-0.68); 3-year PFS rates were 39.7% versus 20.8% with durvalumab versus placebo, and 5-year PFS rates were 33.1% versus 19.0%, respectively.

Real-world evidence is required to confirm if the benefit seen with durvalumab in the clinical trial setting is achieved in everyday clinical practice. The observational, retrospective PACIFIC-R study (NCT03798535) was initiated with the aim of providing the first, longitudinal, real-world data on patients with unresectable, stage III NSCLC who received durvalumab after CRT. Participants were recruited from the global PACIFIC early access program (EAP), which opened before durvalumab received regulatory approvals (to provide ethical access to durvalumab following the initial data readout from PACIFIC). In addition to patients who qualified because their clinical characteristics reflected those of the primary target population for PACIFIC [e.g. receipt of cCRT and initiation of durvalumab $\leq$42 days after finishing radiotherapy (RT)], patients who received sequential CRT (sCRT) and patients who started durvalumab $>$42 days after finishing RT were also enrolled into PACIFIC-R. Furthermore, PACIFIC-R included patients with programmed death-ligand 1 (PD-L1) expression on $<$1% of tumor cells (TCs), a population enrolled in PACIFIC that was included in the United States Food and Drug Administration (FDA)-approved label for durvalumab but was excluded from the European Medicines Agency (EMA)-approved label based on a *post hoc* analysis.[7,11-13] Inclusion of a wider range of patients in PACIFIC-R reflects the real-world variability in multidisciplinary treatment approaches for unresectable, stage III NSCLC.

PACIFIC-R comprises a series of retrospective chart extractions spread over a 5-year period. A previous publication reported analyses from the second chart extraction, with ~2 years of follow-up, including the first planned analysis of investigator-assessed PFS and an unplanned, preliminary analysis of OS[14]; the 2-year PFS and OS rates were 48.2% and 71.2%, respectively. Here, we report analyses from the third chart extraction, with ~3 years of follow-up, including the first planned analysis of OS and an updated analysis of PFS.

PATIENTS AND METHODS

Study design

PACIFIC-R is an ongoing, international, observational/non-interventional, retrospective study of a cohort of adult patients with a histologically/cytologically documented diagnosis of stage III, unresectable NSCLC (according to the seventh or eighth editions of the American Joint Committee on Cancer staging manual, as per local practice) who started durvalumab (10 mg/kg intravenously every 2 weeks) within an AstraZeneca-initiated EAP between September 2017 and December 2018. Comprehensive details regarding the EAP and the design of PACIFIC-R are published elsewhere.[14] Briefly, the EAP provided ethical access to durvalumab for patients who had completed CRT for unresectable, stage III NSCLC and who, in their treating physician's opinion, had an unmet clinical need that could not be treated with approved and commercially available therapies. PACIFIC-R comprises a retrospective review of established medical records, with several planned chart extractions sequenced over a 5-year period starting from the date of the first durvalumab infusion within the EAP (the index date) (Supplementary Figure S1, available at https://doi.org/10.1016/j.esmoop.2024.103464).

Eligible patients had no evidence of disease progression following platinum-based cCRT or sCRT and had provided informed consent as per local regulations (if applicable) for data to be retrieved from their medical records. In compliance with local regulations, patients were eligible to enter PACIFIC-R once the EAP enrollment had closed in their country; patients who died during or after the EAP but before the study enrollment for PACIFIC-R opened were eligible where local regulations allowed for a consent waiver or next-of-kin consent.

Objectives

The primary objective of PACIFIC-R was to evaluate the effectiveness of durvalumab in terms of OS and investigator-assessed PFS in the full analysis set. Secondary objectives reported in this article include OS and PFS for subgroups of interest and time to death or distant metastasis (TTDM), time to death or local recurrence (TDLR), and time to death or first subsequent treatment after durvalumab (TFST) in the full analysis set. Multivariable analyses of prognostic factors for OS and PFS are also reported.

Statistical analysis

Analyses were based on the full analysis set, which included all screened patients who met key inclusion criteria and had provided written informed consent as required by local regulations (if applicable). In a previous report from PACIFIC-R, which presented analyses based on the second planned chart extraction,[14] data for Spanish

patients were integrated into the full analysis set; the data sourced were from an externally sponsored, locally initiated study with the same design and study materials as PACIFIC-R (NCT04285866). Additional data from this external study were not available for integration into the current analyses, based on the third planned chart extraction, as regulatory restrictions in Spain only allowed one chart extraction.

The main analyses were descriptive in nature with summary statistics for continuous variables or numbers and frequency for calculation of categorical variables. Missing values were not imputed. Medians and landmark rates for time-to-event endpoints were estimated using the Kaplan–Meier method; time-to-event endpoints were measured from the date that durvalumab was initiated within the EAP (i.e. the PACIFIC-R index date). All analyses in this article were based on the third planned chart extraction (end date: 30 November 2021), which was timed for maturity of the survival data to provide an accurate estimate of the 3-year OS rate. The last date of data entry for the analyses reported in this article was 30 November 2021; data cleaning was carried out up to a database cut-off date of 7 February 2022.

Sensitivity analyses were carried out to assess the robustness of the main OS and PFS results. PACIFIC-R is subject to selection bias as local regulations in the UK and Germany did not allow for informed consent to be waived, so EAP participants who died before PACIFIC-R enrollment opened in these two countries were not taken into consideration for data collection. Therefore, outcomes could be overestimated for these two countries as patients with the worst prognoses (namely, those who died before consent could be given) were not included in PACIFIC-R. We carried out two sensitivity analyses to explore the impact of this selection bias on OS and PFS. The first analysis excluded UK and German data from the full analysis set (and is referred to as the 'informed consent sensitivity analysis'), and the second analysis used an immortal bias adjustment method (which is described in the Supplementary Methods, available at https://doi.org/10.1016/j.esmoop.2024.103464). An additional sensitivity analysis of PFS was also conducted to explore the impact of excluding patients with unknown progression status (as recorded in the electronic case report form; patients with unknown progression status were censored at the most recent date they were known not to have progressed in the main analysis).

To assess the prognostic association of patient characteristics with outcomes, Cox regression models were built for both OS and PFS using a backward selection model with variable selection based on Akaike information criterion. The variables considered for the backward selection model were: age (as a continuous predictor), sex, country, medical condition and/or history of another cancer, smoking status, disease stage (at stage III diagnosis), type of histology at stage III diagnosis, PD-L1 expression status, initiation of durvalumab relative to end of RT, previous RT total dose, previous type of CRT, platinum used for CRT, secondary chemotherapy agent, and induction chemotherapy. Adjusted HRs were calculated by fitting a multivariable Cox regression model that included the selected variables.

RESULTS

Patients and treatment

As of 30 November 2021 (the end date of the third chart extraction), the full analysis set included 1154 participants from 10 different countries, including France (342 patients), Australia (165), the Netherlands (154), Belgium (118), Italy (116), Israel (92), Germany (62), the UK (54), Norway (36), and Switzerland (15). The median duration of follow-up among patients who were censored at the end of the third chart extraction was 38.7 months (range 13.6-49.0 months).

Patients in the full analysis set had a median age of 65 years (range 26-88 years), and 102 of 1154 patients (8.8%) were aged $\geq$75 years (Table 1). Most were male [748/1154 (64.8%)] and current or former smokers [1051/1154 (91.1%)]. Among patients with available data, nearly all had a performance status of 0 or 1 [744/756 (98.4%)], most had non-squamous tumor histology [752/1153 (65.2%)], and over half of them had stage IIIB or IIIC disease [585/1091 (53.6%)]. Overall, 790 patients had available data regarding PD-L1 expression and most of these patients had PD-L1 expression on $\geq$1% of TCs [573/790 (72.5%)]. While the antibody used to assess PD-L1 expression was unknown or missing for most patients [447/790 (56.6%)], the most common among those with available data was DACO 22C3 [228/343 (66.5%)]. Most patients received cCRT [900/1063 (84.7%)] and started durvalumab $>$42 days [732/1130 (64.8%)] following the end of RT.

OS and updated PFS

In total, 446 of 1154 patients (38.6%) in the full analysis set had died at the time of the database cut-off; median OS was not reached (95% CI 46.3 months-not estimable) and the 2-and 3-year OS rates were 72.3% (95% CI 69.7% to 74.8%) and 63.2% (95% CI 60.3% to 65.9%), respectively (Figure 1A). Overall, 666 of 1154 patients (57.7%) in the full analysis set had either experienced progression ($n = 595$) or had died in the absence of progression ($n = 71$); median PFS was 24.1 months (95% CI 20.2-27.8 months) and the 2-and 3-year PFS rates were 50.1% (95% CI 47.2% to 53.0%) and 42.2% (95% CI 39.2% to 45.1%), respectively (Figure 1B).

Three-year OS rates were numerically higher among patients with PD-L1 expression on $\geq$1% versus $<$1% of TCs [67.0% (95% CI 63.0% to 70.8%) versus 54.4% (95% CI 45.7% to 62.4%), respectively]; patients who received cCRT versus sCRT [64.8% (95% CI 61.5% to 67.9%) versus 57.9% (95% CI 49.8% to 65.2%), respectively]; patients who started durvalumab $\leq$42 days versus $>$42 days following the end of RT [66.0% (95% CI 61.1% to 70.5%) versus 61.8% (95% CI 58.1% to 65.2%), respectively]; and patients with non-squamous versus squamous tumor histology [68.0% (95% CI 64.5% to 71.2%) versus 53.2% (95% CI 48.0% to 58.1%), respectively] (Figure 2). Meanwhile, 3-year OS rates were numerically similar between patients with stage IIIA and

Table 1. Patient demographics, disease characteristics, and treatment characteristics

Characteristics[a]	*n* (%)
Age category at EAP inclusion ($N = 1154$)[b]	
<70 years	806 (69.8)
70-75 years	246 (21.3)
>75 years	102 (8.8)
Sex ($N = 1154$)	
Male	748 (64.8)
Female	406 (35.2)
Smoking status at EAP inclusion ($N = 1154$)[b]	
Never	64 (5.5)
Current	300 (26.0)
Former	751 (65.1)
ECOG PS ($N = 756$)[b]	
0 or 1	744 (98.4)
≥2	12 (1.6)
Disease stage ($N = 1091$)[b,c]	
IIIA	506 (46.4)
IIIB or IIIC	585 (53.6)
Tumor histology ($N = 1153$)[b]	
Squamous	386 (33.5)
Non-squamous	752 (65.2)
Unknown	15 (1.3)
PD-L1 expression level ($N = 790$)[b]	
TC ≥1%	573 (72.5)
TC <1%	138 (17.5)
Unknown	79 (10.0)
EGFR status ($N = 483$)[b]	
Mutated	44 (9.1)
Non-mutated	422 (87.4)
Unknown	17 (3.5)
Prior CRT type ($N = 1063$)[b]	
Concurrent	900 (84.7)
Sequential	163 (15.3)
Total prior RT dose ($N = 1120$)	
≤60 Gy	485 (43.3)
>60 Gy	635 (56.7)
Time elapsed between the end of RT and the start of durvalumab ($N = 1130$)[b]	
≤42 days	398 (35.2)
>42 days	732 (64.8)

CRT, chemoradiotherapy; EAP, early access program; ECOG, Eastern Cooperation Oncology Group; Gy, units of gray; PD-L1, programmed death-ligand 1; PS, performance status; RT, radiotherapy; TC, tumor cell.
[a]All characteristics are summarized based on the full analysis set for the third chart extraction from PACIFIC-R (end date: 30 November 2021).
[b]Summaries are based on patients with available information for each characteristic (i.e. patients with missing responses are not included).
[c]Disease stage could be determined according to the seventh or eighth editions of the American Joint Committee on Cancer staging manual.

stage IIIB/IIIC disease [62.3% (95% CI 57.8% to 66.4%) versus 63.7% (95% CI 59.6% to 67.5%), respectively]. Similar trends were observed across these subgroups for PFS (Figure 3).

Sensitivity analyses of OS and PFS

Results from the informed consent sensitivity analysis, which was carried out to assess the impact of selection bias brought about by the local regulations in the UK and Germany not allowing consent to be waived for deceased patients, are reported in Supplementary Table S1, available at https://doi.org/10.1016/j.esmoop.2024.103464; among patients not from the UK and Germany ($n = 1038$), median OS was not reached (44.6 months-not estimable), the 3-year OS rate was 60.8% (95% CI 57.7% to 63.7%), median PFS was 21.7 months (95% CI 18.7-25.6 months), and 3-year PFS rate was 40.4% (95% CI 37.2% to 43.5%). Similar results were obtained when utilizing an immortal bias adjustment method; median OS was not reached (95% CI not estimable-not estimable), the 3-year OS rate was 60.4% (95% CI 60.4% to 60.4%), median PFS was 21.3 months (95% CI 20.8-21.4 months), and the 3-year PFS rate was 40.3% (95% CI 40.3% to 40.4%). In an additional sensitivity analysis of PFS that excluded patients with unknown progression status, median PFS was 24.3 months (95% CI 20.5-28.2 months), and the 3-year PFS rate was 42.4% (95% CI 39.4% to 45.4%) among the patients with known progression status ($n = 1145$).

Identification of factors associated with OS and PFS

Multivariable analyses demonstrated that non-squamous tumor histology is a favorable prognostic factor for OS compared with squamous histology and that the use of carboplatin during CRT is an unfavorable prognostic factor for OS compared with the use of cisplatin (i.e. the adjusted HR 95% CI did not cross 1 for these comparisons) (Supplementary Table S2, available at https://doi.org/10.1016/j.esmoop.2024.103464). These analyses also demonstrated that non-squamous tumor histology is a favorable prognostic factor for PFS compared with squamous tumor histology and that current or former smoking status is a favorable prognostic factor for PFS compared with never having smoked (Supplementary Table S3, available at https://doi.org/10.1016/j.esmoop.2024.103464).

TTDM, TDLR, and TFST in the full analysis set

Median TTDM was 35.5 months (95% CI 32.2-38.0 months), with 49.5% (95% CI 46.4% to 52.6%) of the patients estimated to be alive and without any distant metastases at 3 years (Figure 4A). Median TDLR was not reached (95% CI 42.3 months-not estimable), with 65.6% (95% CI 62.2% to 68.8%) of the patients estimated to be alive and without local recurrence (i.e. recurrence within the thoracic RT field) at 3 years (Figure 4B). Median TFST was 35.9 months (95% CI 31.3-42.9 months), with 49.9% (95% CI 47.0% to 52.8%) of the patients estimated to be alive and without subsequent treatment (post-durvalumab) at 3 years (Figure 4C).

DISCUSSION

With ∼3 years of follow-up, median OS was not reached in the current analysis from PACIFIC-R. Over 60% of all patients were estimated to remain alive 3 years after starting durvalumab, and >40% of all patients remained both alive and without disease progression at this time point. The findings of PACIFIC-R are broadly consistent with outcomes from the PACIFIC trial,[4,5,8] as well as observational studies of patients receiving the PACIFIC regimen,[15,16] and support the real-world effectiveness of consolidation durvalumab after CRT.

We observed favorable OS and PFS outcomes with durvalumab across different subgroups. The updated PFS results from the current chart extraction are consistent with the earlier PFS findings from PACIFIC-R.[14] Moreover, aligned

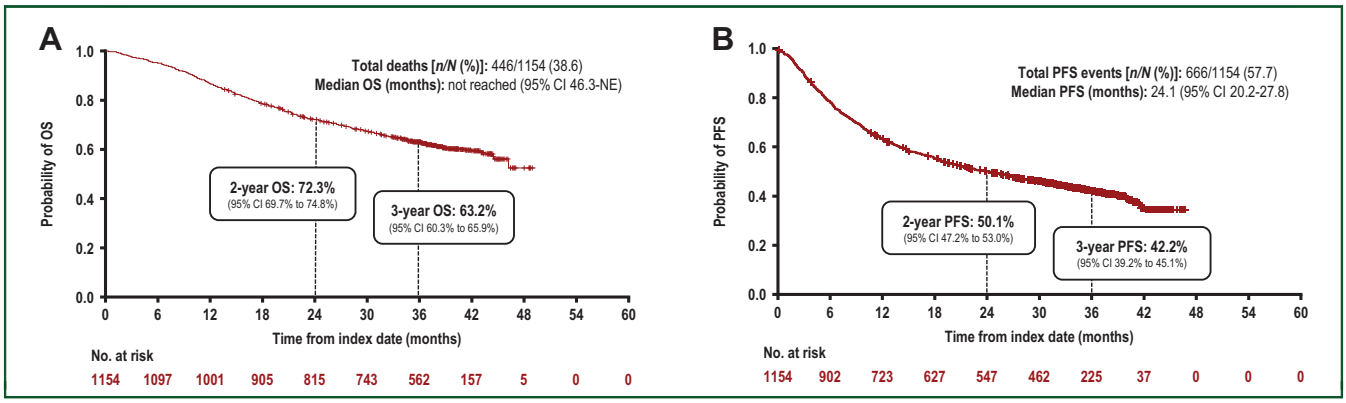

Figure 1. OS and investigator-assessed PFS in the full analysis set. Shown are Kaplan—Meier distributions of (A) OS and (B) investigator-assessed PFS. The tick marks on each trendline represent censored observations, and the dashed lines arising from the *x*-axes represent 2- and 3-year landmark analyses. OS was defined as the time from the index date to the date of death from any cause, or the last recorded date the patient was known to be alive for censored patients. PFS was defined as the time from the index date to the date of investigator-determined disease progression, or death from any cause (in the absence of progression), whichever occurred first; if no progression or death occurred, patients were censored at the time of the last available tumor assessment. Note: given the real-world nature of PACIFIC-R, progression could be determined by either investigator's assessment or according to the Response Evaluation Criteria in Solid Tumors version 1.1, depending on local practice. The median duration of follow-up in patients censored at the time of database cut-off was 38.7 months (range 13.6-49.0 months).
CI, confidence interval; NE, not estimable; OS, overall survival; PFS, progression-free survival.

with results from the PACIFIC trial, survival outcomes were better among patients with PD-L1 expression on ≥1% of TCs, patients who started durvalumab closer to the end of RT, and patients with non-squamous tumor histology.[8,12,17] Sensitivity analyses exploring potential biases yielded similar findings to the main analyses of OS and PFS, confirming the robustness of the PACIFIC-R results and further supporting the real-world effectiveness of consolidation durvalumab.

Results from the multivariable Cox analyses identified non-squamous tumor histology as a favorable prognostic factor for OS compared with squamous tumor histology, while the use of carboplatin during CRT was an unfavorable prognostic factor compared with the use of cisplatin. In addition, non-squamous tumor histology (versus squamous histology) and a history of smoking (versus never having smoked) were identified as favorable prognostic factors for PFS. Aligned with findings from PACIFIC-R, non-squamous tumor histology was also identified as a favorable prognostic factor for OS and PFS in PACIFIC.[8] The other prognostic factors identified in PACIFIC-R (i.e. smoking status and the platinum agent used during CRT) were also identified in external studies of patients with stage III NSCLC.[8,18] The association of smoking status with PFS seen in PACIFIC-R aligns with findings from other studies, which suggest that patients with a history of smoking benefit more from immunotherapy compared with patients who have never smoked.[19] This phenomenon could be attributed to higher neoantigen load among smokers or the presence of unobserved driver mutations among patients who have never smoked. While the optimal chemotherapeutic agent(s) in the context of the PACIFIC regimen is not yet known, *post hoc* analysis of data from PACIFIC found a PFS and OS benefit with durvalumab versus placebo regardless of the prior chemotherapeutic agents received.[17] The worse OS prognosis associated with carboplatin use in PACIFIC-R could, at least partially, be linked to factors that influence the physician's choice of platinum agent; indeed, findings from other real-world studies suggest that the choice is influenced by baseline patient and disease characteristics, with cisplatin typically being reserved for fitter patients.[20,21]

The better outcomes observed among patients with PD-L1-expressing tumors in PACIFIC-R aligned with our expectations. Higher PD-L1 expression is, to a certain extent, considered a predictive biomarker for response to immune checkpoint inhibitors in patients with advanced NSCLC. However, expression of PD-L1 is a labile parameter that can be influenced by external factors, making it a useful, but sub-optimal, biomarker for response to immunotherapy.[22,23] For example, PD-L1 expression can vary according to anatomical sites and the immunohistochemistry assays used to determine expression.[22] Moreover, RT can induce up-regulation of tumoral PD-L1 expression,[24,25] which is relevant in the context of the PACIFIC regimen as tumoral PD-L1 expression is typically determined from tumor samples obtained before receiving CRT. The label approved for durvalumab by the EMA excludes patients with PD-L1 expression on <1% of TCs based on a *post hoc* analysis,[7,12] while similar restrictions are not applied by other regulatory bodies, including the United States FDA.[13] Nevertheless, encouraging outcomes were still observed among patients with PD-L1 expression on <1% of TCs in the present study, with over 50% of these patients estimated to remain alive at 3 years.

Historically, use of sCRT alone was associated with inferior survival compared with cCRT alone in several studies, including a meta-analysis of several randomized trials.[26] Therefore, as recommended by international treatment guidelines, physicians should provide cCRT when possible, reserving sCRT for frailer patients who may be unable to tolerate cCRT.[6,27,28] We observed encouraging outcomes with durvalumab among patients who received sCRT, with nearly 60% of these patients estimated to remain alive at 3 years in PACIFIC-R. Reflecting the clinical characteristics that

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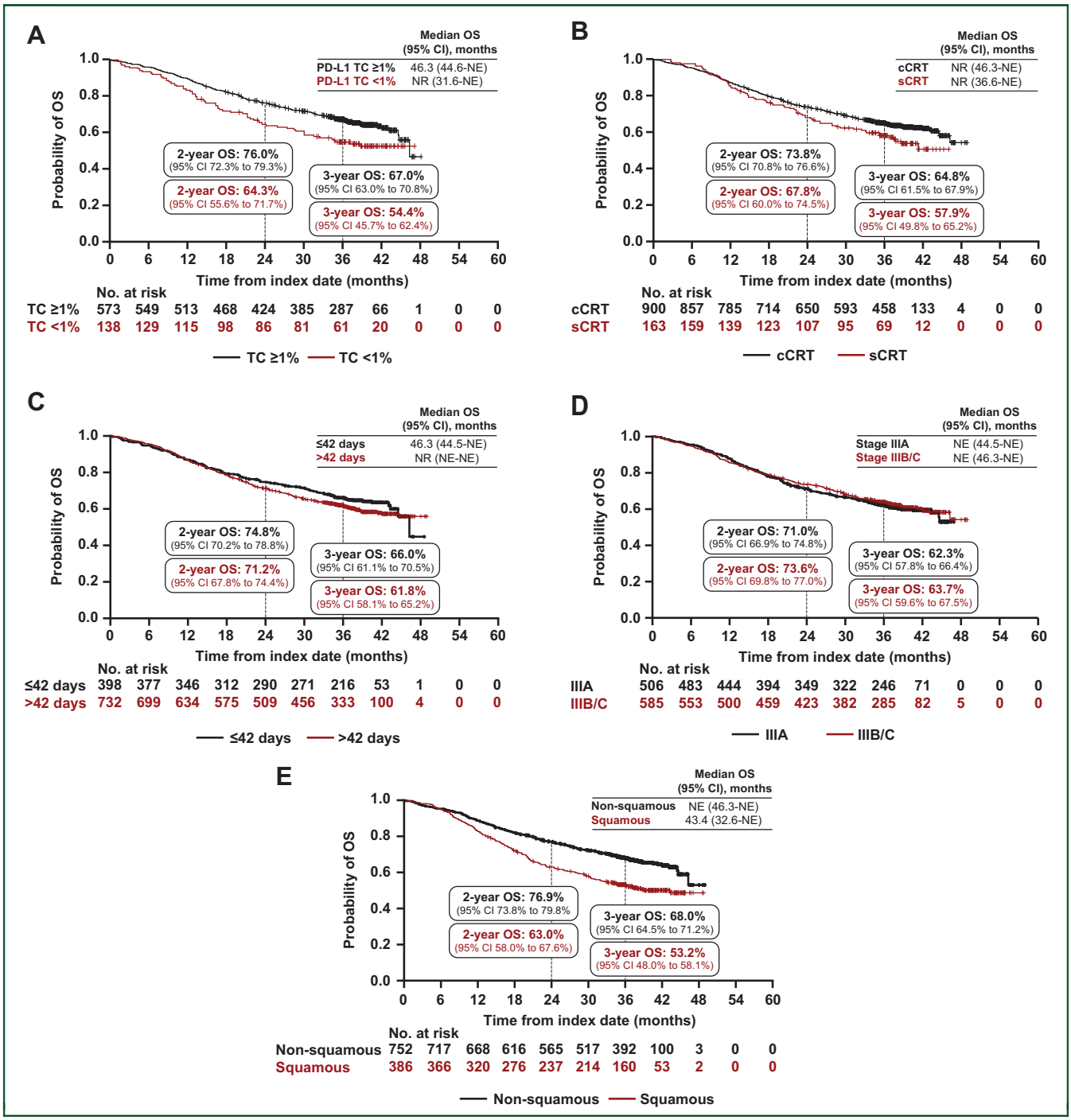

Figure 2. OS for subgroups of interest. Shown are Kaplan–Meier distributions of OS according to (A) PD-L1 expression level; (B) prior CRT type; (C) time elapsed between the end of RT and the start of durvalumab; (D) disease stage; and (E) tumor histologic type. The tick marks on each trendline represent censored observations, and the dashed lines arising from the *x*-axes represent 2- and 3-year landmark analyses.
CI, confidence interval; cCRT, concurrent chemoradiotherapy; NE, not estimable; NR, not reached; OS, overall survival; PD-L1, programmed death-ligand 1; RT, radiotherapy; sCRT, sequential chemoradiotherapy; TC, tumor cell.

we would expect to correlate with sCRT use, patients in PACIFIC-R who received sCRT were typically older and had more advanced disease (i.e. stage IIIB/IIIC disease) versus those who received cCRT.[14] Although PACIFIC trial enrollment was restricted to patients who received cCRT,[5,8] the findings from PACIFIC-R provide support for the effectiveness of durvalumab after sCRT and are complemented by the promising efficacy observed with this treatment approach in the phase II, single-arm, PACIFIC-6 trial (NCT03693300).[29]

Utilizing the large sample size available in PACIFIC-R, which enrolled >1000 patients across all participating countries, the present article reports analyses based on the global study cohort to allow generalizability of the findings to a broad population. A limitation of this approach is that it does not account for the substantial heterogeneity in

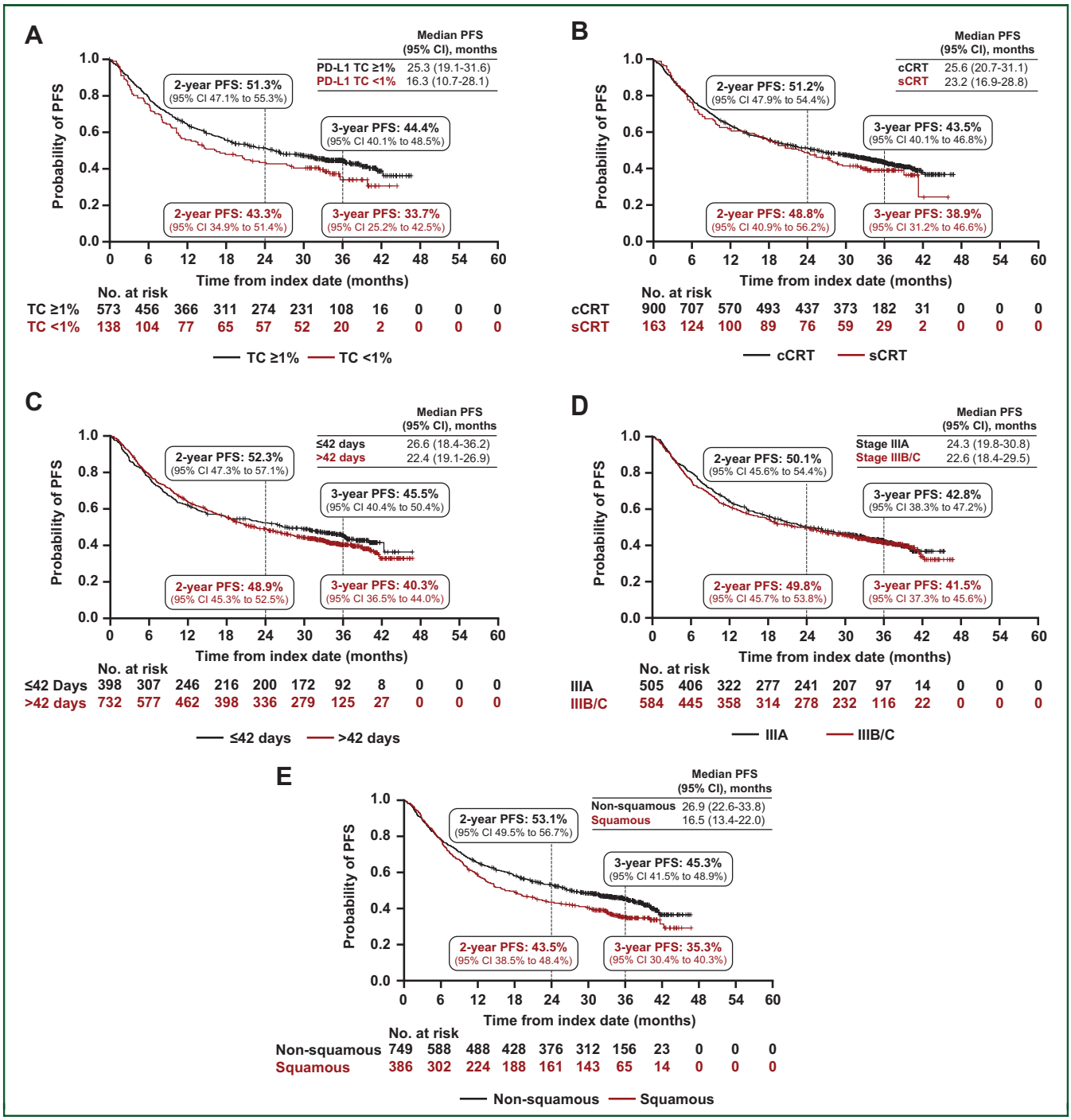

Figure 3. Investigator-assessed PFS for subgroups of interest. Shown are Kaplan—Meier distributions of investigator-assessed PFS according to (A) PD-L1 expression level; (B) prior CRT type; (C) time elapsed between the end of RT and the start of durvalumab; (D) disease stage; and (E) tumor histologic type. The tick marks on each trendline represent censored observations, and the dashed lines arising from the *x*-axes represent 2- and 3-year landmark analyses. Note: given the real-world nature of PACIFIC-R, progression could be determined by either investigator's assessment or according to the Response Evaluation Criteria in Solid Tumors version 1.1, depending on local practice. CI, confidence interval; cCRT, concurrent chemoradiotherapy; NE, not estimable; NR, not reached; PFS, progression-free survival; PD-L1, programmed death-ligand 1; RT, radiotherapy; sCRT, sequential chemoradiotherapy; TC, tumor cell.

clinical characteristics and investigations across different countries and hospital sites. For example, the outcomes reported for PD-L1 subgroups may be biased by real-world differences in the uptake of PD-L1 testing, the approach used for tissue sampling, and the choice of assay for determining tumoral PD-L1 expression (as lower concordance has been observed between certain assays).[30] Country- or region-specific analyses from PACIFIC-R may provide further insights. Additionally, PACIFIC-R enrolled a predominantly European population, so the findings cannot necessarily be extrapolated to patients of all ethnic or racial backgrounds. Recently published findings from PACIFIC-KR ($N = 157$), an observational study of patients who received durvalumab through the EAP in South Korea, were aligned with the findings from PACIFIC-R (with 3-year OS and PFS rates of 69.2% and 43.5%, respectively),[31]

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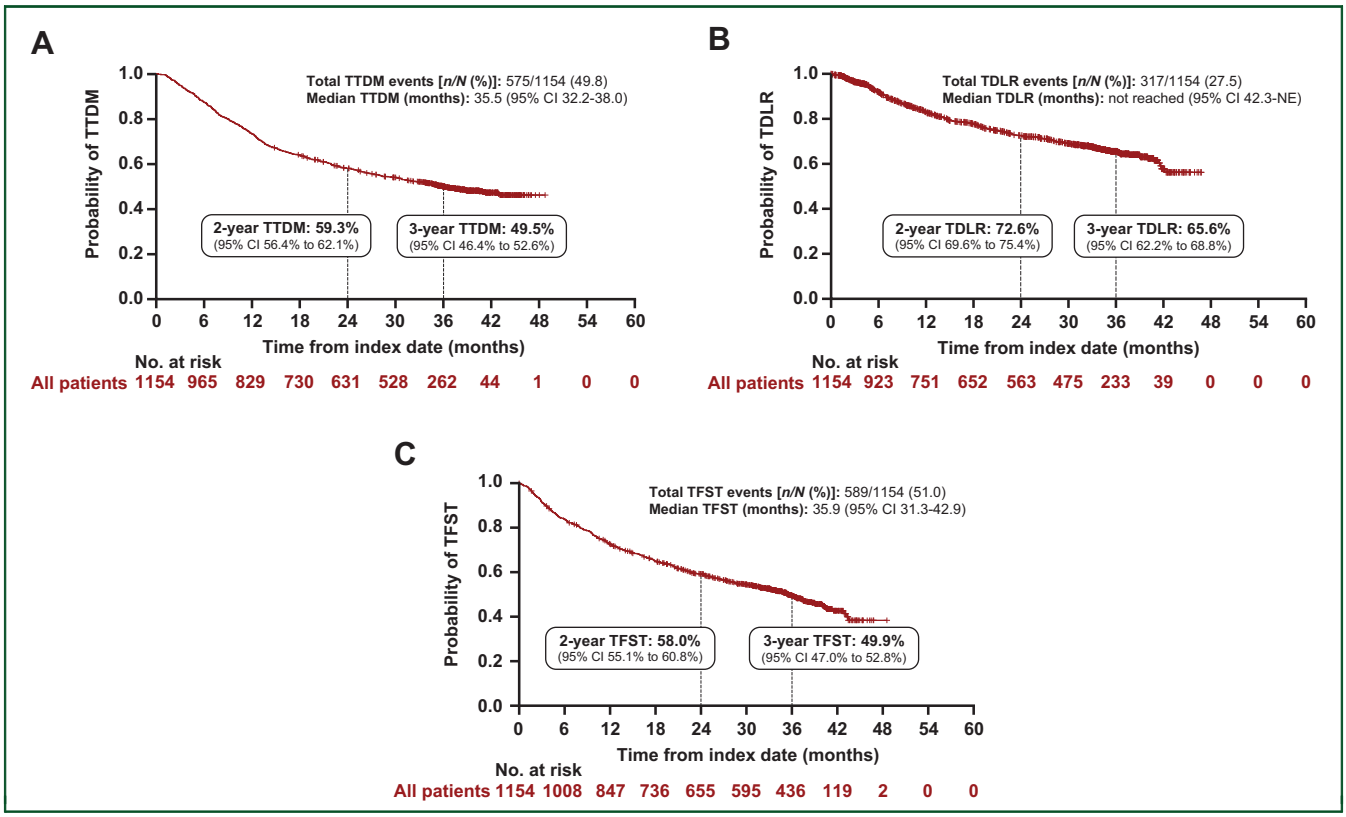

Figure 4. TTDM, TDLR, and TFST in the full analysis set. Shown are Kaplan—Meier distributions of (A) TTDM, (B) TDLR, and (C) TFST. The tick marks on each trendline represent censored observations, and the dashed lines arising from the *x*-axes represent 2- and 3-year landmark analyses. TTDM was defined as the time from the index date to the date of first distant metastasis, as determined by the investigator, or death in the absence of distant metastasis; patients who had not developed a distant metastasis, and who had not died at the time of the analysis, were censored for TTDM at the time of their last available tumor assessment. TDLR was defined as time from the index date until the date of first documentation of local recurrence (i.e. recurrence within the thoracic radiation field), as determined by the investigator; local recurrence was only applicable when there was no distant relapse at the same time or before the local recurrence (in the latter case, it was considered distant relapse and the censoring date was the date of diagnosis in the metastatic setting). Patients who did not experience a local recurrence, or experienced local recurrence and distant metastasis at the same time, or experienced distant metastasis only, were censored; death in the absence of both local recurrence and distant metastasis was considered an event. TFST was defined as time from the index date until the start date of the first subsequent treatment after durvalumab discontinuation or death from any cause, whichever occurred first.
CI, confidence interval; NE, not estimable; TDLR, time to death or local recurrence; TFST, time to death or first subsequent treatment after durvalumab; TTDM, time to death or distant metastasis.

suggesting that similar outcomes can be achieved among non-European populations.

In conclusion, durvalumab has been demonstrated to provide improvements in OS and PFS following cCRT in unresectable, stage III NSCLC,[4,5] with PFS benefits being seen across a range of PD-L1 expression levels.[12] Moreover, durvalumab shows promising signs of efficacy after sCRT in unresectable, stage III NSCLC.[29] The PACIFIC-R data continue to provide evidence for the effectiveness of consolidation durvalumab after CRT in a large, diverse, real-world population. Consistent with PFS findings from a previous analysis of this ongoing study,[14] better OS and PFS outcomes were observed among patients with PD-L1 expression on $\geq$1% of TCs and patients who received cCRT in the current analysis. Nevertheless, encouraging outcomes were still observed among patients with PD-L1 expression on $<$1% of TCs and patients who received sCRT, supporting the use of consolidation durvalumab in a broad population of patients with unresectable, stage III NSCLC.

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DATA SHARING

Data underlying the findings described in this manuscript may be obtained in accordance with AstraZeneca's data sharing policy described at: https://astrazenecagrouptrials.pharmacm.com/ST/Submission/Disclosure. Data for studies directly listed on Vivli can be requested through Vivli at: www.vivli.org. Data for studies not listed on Vivli could be requested through Vivli at: https://vivli.org/members/enquiries-about-studies-not-listed-on-the-vivli-platform/. The AstraZeneca Vivli member page is also available outlining further details: https://vivli.org/ourmember/astrazeneca/.

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