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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors. **This online publication has been corrected. The corrected version first appeared at thelancet.com on February 2, 2017**.

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Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Inclusion criteria

Patients must meet all of the following criteria to be eligible for study entry:

- Signed informed consent form
- Ability to comply with protocol
- Aged 18 years or older
- Histologically or cytologically documented non-small-cell lung cancer (NSCLC) that is currently locally advanced or metastatic (ie, stage IIIB not eligible for definitive chemoradiotherapy, stage IV or recurrent) NSCLC (per the UICC/AJCC staging system, 7th edition); pathological characterisation may be from tumour specimens collected at a time when the NSCLC was at an earlier stage but must be sufficient to define patients as having either squamous or non-squamous histology
- Representative formalin-fixed paraffin-embedded (FFPE) tumour specimens in paraffin blocks (preferred) or at least 15 unstained slides, with an associated pathology report, for central testing and determined to be evaluable for tumour programmed death-ligand 1 (PD-L1) expression prior to study enrolment; patients with fewer than 15 unstained slides available at baseline (but no fewer than ten) may be eligible following discussion with the Medical Monitor
    - Tumour tissue should be of good quality based on total and viable tumour content. Fine-needle aspiration, brushing, cell pellet from pleural effusion, and lavage samples are not acceptable. For core needle biopsy specimens, at least three cores should be submitted for evaluation
    - Patients who do not have tissue specimens meeting eligibility requirements may undergo a biopsy during the screening period. Acceptable samples include core needle biopsies for deep tumour tissue (minimum three cores) or excisional, incisional, punch or forceps biopsies for cutaneous, subcutaneous or mucosal lesions
    - Tumour tissue from bone metastases is not evaluable for tumour PD-L1 expression; therefore, it is not acceptable
    - Patients having additional tissue samples from procedures performed at different times during the course of their NSCLC will be requested (but not required) to also submit these samples for central testing. Tissue samples obtained at multiple times for individual patients will greatly contribute to an improved understanding of the dynamics of PD-L1 expression and relationship with intervening anti-cancer therapy
- Disease progression during or following treatment with a prior platinum-containing regimen for locally advanced, unresectable/inoperable or metastatic NSCLC or disease recurrence within 6 months of treatment with a platinum-based adjuvant/neoadjuvant regimen or combined modality (eg, chemoradiation) regimen with curative intent
    - Adjuvant/neoadjuvant chemotherapy or chemoradiation counts as a prior chemotherapy regimen if < 6 months have elapsed between the last dose and the date of recurrence. Combined treatment with chemotherapy and radiation constitutes a single regimen; surgery is not considered a regimen
    - Patients may have received one additional cytotoxic chemotherapy regimen (maximum of two prior cytotoxic chemotherapy regimens)
    - Chemotherapy regimens will be counted based on interval disease progression and not the number of agents or switches in agents (eg, a first-line therapy that consists of several cycles of a platinum doublet and subsequent maintenance therapy that introduces or switches to a new chemotherapy agent without interval disease progression will all be considered one chemotherapy regimen)
    - Patients with advanced lung cancer and a sensitising *EGFR* mutation will additionally be required to have experienced disease progression (during or after treatment) with an EGFR tyrosine kinase inhibitor (TKI; erlotinib, gefitinib, etc)
    - Patients with unknown *EGFR* mutational status not previously treated with an EGFR TKI but whose tumour may harbour a sensitizing *EGFR* mutation (ie, non-squamous histology, *KRAS* status wild-type or unknown, *ALK* fusion oncogene negative or unknown) will be tested by a central laboratory prior to enrolment
    - Patients with a previously detected *ALK* fusion oncogene must additionally have experienced disease progression (during or after treatment) with crizotinib or another ALK inhibitor
    - The last dose of prior systemic anti-cancer therapy must have been administered ≥ 21 days prior to randomisation, with the exception being TKIs approved for treatment of NSCLC have to be discontinued ≥ 7 days prior to Cycle 1, Day 1

    - The baseline scan must be obtained after discontinuation of prior TKIs (washout not required prior to obtaining the scan)
    - The last dose of treatment with any investigational agent or participation in another interventional study must have ended ≥ 28 days prior to randomisation
    - Anti-cancer agents used for pleurodesis are not counted as a line of therapy
    - Prior radiation therapy is allowed provided the patient has recovered from any toxic effects thereof
- Measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST; version 1.1)
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Life expectancy ≥ 12 weeks
- Adequate hematologic and end-organ function, defined by the following laboratory results obtained within 14 days prior to the first study treatment:
    - ANC ≥ 1500 cells/μL (without granulocyte colony-stimulating factor support within 2 weeks of laboratory test used to determine eligibility)
    - White blood cell counts > 2500/μL
    - Lymphocyte count ≥ 500/μL
    - Serum albumin ≥ 2.5 g/dL
    - Platelet count ≥ 100,000/μL (without transfusion within 2 weeks of laboratory test used to determine eligibility)
    - Haemoglobin ≥ 9.0 g/dL
    - Patients may be transfused or receive erythropoietic treatment to meet this criterion
    - Liver function tests meeting one of the following criteria:
        - Aspartate aminotransferase (AST) and alanine transaminase (ALT) ≤ 2.5 times the upper limit of normal (ULN), with alkaline phosphatase ≤ 2.5×ULN or
        - AST and ALT ≤ 1.5×ULN, with alkaline phosphatase > 2.5×ULN
    - Serum bilirubin ≤ 1.0×ULN
    - Patients with known Gilbert's disease who have serum bilirubin level ≤ 3×ULN may be enrolled
    - International normalised ratio and activated partial thromboplastin time ≤ 1.5×ULN
    - This applies only to patients who are not receiving therapeutic anticoagulation; patients receiving therapeutic anticoagulation should be on a stable dose for at least 1 week prior to randomisation
    - Creatinine clearance ≥30 mL/min
        - Cockcroft-Gault, Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), or Modification of Diet in Renal Disease (MDRD) formulas may be used for creatinine clearance calculation. Note that 24-hour urine collection is not required but is allowed
- For female patients of childbearing potential and male patients with partners of childbearing potential, agreement (by patient and/or partner) to use highly effective form(s) of contraception (ie, one that results in a low failure rate [< 1% per year] when used consistently and correctly) and to continue its use for 6 months after the last dose of atezolizumab
- Patients must have recovered (ie, improvement to Grade 1 or better) from all acute toxicities from previous therapy, excluding alopecia

Exclusion criteria

Patients who meet any of the following criteria will be excluded from study entry:

Cancer-specific exclusions

- Active or untreated central nervous system (CNS) metastases as determined by computerised tomography (CT) or magnetic resonance imaging evaluation during screening and prior radiographic assessments
    - Patients with a history of ***treated asymptomatic*** supratentorial CNS metastases are eligible, provided they meet all of the following criteria:
        - Measurable disease outside the CNS
        - Only supratentorial metastases allowed (ie, no metastases to midbrain, pons, cerebellum, medulla or spinal cord)
        - No history of intracranial haemorrhage
        - No ongoing requirement for corticosteroids as therapy for CNS disease; anticonvulsants at a stable dose allowed
        - No stereotactic radiation within 7 days or whole-brain radiation within 14 days prior to Cycle 1, Day 1
        - No evidence of interim progression between the completion of CNS-directed therapy and the screening radiographic study
        - Note: Patients with new asymptomatic CNS metastases detected at the screening scan must receive radiation therapy and/or surgery for CNS metastases. Following treatment, these patients may then be eligible without the need for an additional brain scan prior to enrolment, if all other criteria are met
- Spinal cord compression not definitively treated with surgery and/or radiation or previously diagnosed and treated spinal cord compression without evidence that disease has been clinically stable for ≥ 2 weeks prior to randomisation
- Leptomeningeal disease
- Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures
- Uncontrolled tumour-related pain
    - Patients requiring pain medication must be on a stable regimen at study entry
    - Symptomatic lesions amenable to palliative radiotherapy (eg, bone metastases or metastases causing nerve impingement) should be treated prior to enrolment
    - Asymptomatic metastatic lesions whose further growth would likely cause functional deficits or intractable pain (eg, epidural metastasis that is not presently associated with spinal cord compression) should be considered for loco-regional therapy if appropriate prior to enrolment
- Uncontrolled hypercalcemia (> 1.5 mmol/L ionised calcium or calcium > 12 mg/dL or corrected serum calcium > ULN) or symptomatic hypercalcemia requiring continued use of bisphosphonate therapy or denosumab
    - Patients who are receiving bisphosphonate therapy or denosumab specifically to prevent skeletal events and who do not have a history of clinically significant hypercalcaemia are eligible
    - Patients who are receiving denosumab prior to enrolment must be willing and eligible to discontinue its use and replace it with a bisphosphonate instead while in the study
- Malignancies other than NSCLC within 5 years prior to randomisation, with the exception of those with a negligible risk of metastasis or death and treated with expected curative outcome (such as adequately treated carcinoma in situ of the cervix, basal or squamous cell skin cancer, localised prostate cancer treated with curative intent or ductal carcinoma in situ treated surgically with curative intent)

General medical exclusions

- Pregnant and lactating women
- Evidence of significant uncontrolled concomitant disease that could affect compliance with the protocol or interpretation of results, including significant liver disease (such as cirrhosis, uncontrolled major seizure disorder or superior vena cava syndrome)
- Significant cardiovascular disease, such as New York Heart Association cardiac disease (Class II or greater), myocardial infarction within 3 months prior to randomisation, unstable arrhythmias or unstable angina

    - Patients with a known left ventricular ejection fraction (LVEF) < 40% will be excluded
    - Patients with known coronary artery disease, congestive heart failure not meeting the above criteria, or LVEF < 50% must be on a stable medical regimen that is optimised in the opinion of the treating physician, in consultation with a cardiologist if appropriate
- Severe infections within 4 weeks prior to randomisation including but not limited to hospitalisation for complications of infection, bacteraemia or severe pneumonia
- Received therapeutic oral or intravenous antibiotics within 2 weeks prior to randomisation
    - Patients receiving prophylactic antibiotics (eg, for prevention of a urinary tract infection or chronic obstructive pulmonary disease) are eligible
- Major surgical procedure within 4 weeks prior to randomisation or anticipation of need for a major surgical procedure during the course of the study other than for diagnosis
- Inability to understand the local language(s) for which the EORTC QLQ-C30 and QLQ-LC13 questionnaires are available

Exclusion criteria related to docetaxel

- Prior treatment with docetaxel
- History of severe hypersensitivity to docetaxel or to other drugs formulated with polysorbate 80
- Grade ≥ 2 peripheral neuropathy as defined by NCI CTCAE v4.0 criteria
- Inability to discontinue use of strong cytochrome P450 (CYP)3A4 inhibitors including but not limited to ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin or voriconazole

Exclusion criteria related to atezolizumab

- History of severe allergic, anaphylactic or other hypersensitivity reactions to chimeric or humanised antibodies or fusion proteins
- Known hypersensitivity or allergy to biopharmaceuticals produced in Chinese hamster ovary cell products or any component of the atezolizumab formulation
- History of autoimmune disease including but not limited to myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, vascular thrombosis associated with antiphospholipid syndrome, Wegener's granulomatosis, Sjögren's syndrome, Guillain-Barré syndrome, multiple sclerosis, vasculitis or glomerulonephritis
    - Patients with a history of autoimmune-related hypothyroidism on a stable dose of thyroid replacement hormone may be eligible for this study
    - Patients with controlled Type 1 diabetes mellitus on a stable insulin regimen may be eligible for this study
- Patients with prior allogeneic bone marrow transplantation or prior solid organ transplantation
- Known tumour PD-L1 expression status from other clinical trials (eg, patients whose PD-L1 expression status was determined during screening for entry into a trial with anti-PD-1 or anti-PD-L1 antibodies but were not eligible are excluded)
- History of idiopathic pulmonary fibrosis (including pneumonitis), drug-induced pneumonitis, organizing pneumonia (ie, bronchiolitis obliterans, cryptogenic organising pneumonia) or evidence of active pneumonitis on screening chest CT scan. History of radiation pneumonitis in the radiation field (fibrosis) is permitted
- Positive test for human immunodeficiency virus
- Patients with active hepatitis B (defined as having a positive hepatitis B surface antigen [HBsAg] test at screening) or hepatitis C
    - Patients with past hepatitis B virus (HBV) infection or resolved HBV infection (defined as having a negative HBsAg test and a positive antibody to hepatitis B core antigen [anti-HBc] antibody test) are eligible
    - Patients positive for hepatitis C virus (HCV) antibody are eligible only if polymerase chain reaction (PCR) is negative for HCV RNA
- Active tuberculosis
- Administration of a live, attenuated vaccine within 4 weeks prior to randomization or anticipation that such a live attenuated vaccine will be required during the study
- Patients with prior treatment with CD137 agonists, anti-CTLA-4, or therapies targeting the PD-L1 and PD-1 pathway are excluded
- Treatment with systemic immunostimulatory agents (including but not limited to interferons or interleukin-2) within 4 weeks or five half-lives of the drug, whichever is shorter, prior to randomisation

- Treatment with systemic corticosteroids or other systemic immunosuppressive medications (including but not limited to prednisone, dexamethasone, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumour necrosis factor agents) within 2 weeks prior to randomisation, or anticipated requirement for systemic immunosuppressive medications during the trial
    - Patients who have received acute, low-dose, systemic immunosuppressant medications (eg, a one-time dose of dexamethasone for nausea) may be enrolled in the study after discussion with and approval by the Medical Monitor
    - The use of inhaled corticosteroids and mineralocorticoids (eg, fludrocortisone) is allowed. Low-dose supplemental corticosteroids for adrenocortical insufficiency are allowed

Supplementary Table S1. PD-L1 scoring criteria on TC and IC using the SP142 assay

PD-L1 tumour cell scoring		PD-L1 tumour-infiltrating immune cell scoring	
Score	**Percentage of PD-L1-expressing cells**	**Score**	**Percentage of PD-L1-expressing cells**
TC3	≥50%	IC3	≥10%
TC2	≥5% and <50%	IC2	≥5% and <10%
TC1	≥1% and <5%	IC1	≥1% and <5%
TC0	<1%	IC0	<1%

TC scored as percentage of tumour cells and IC scored as percentage of tumour area.
IC=tumour-infiltrating immune cell. PD-L1=programmed death-ligand 1. TC=tumour cell.

Supplementary Table S2. Baseline characteristics of the TC3 or IC3 population

Characteristic	Atezolizumab (n=72)	Docetaxel (n=65)	Overall (N=137)
Age (years)			
Median	62·0	67·0	64·0
Range	39–82	45–85	39–85
Age ≥65 years	28 (38·9)	40 (61·5)	68 (49·6)
Sex			
Male	50 (69·4)	38 (58·5)	88 (64·2)
Female	22 (30·6)	27 (41·5)	49 (35·8)
Race			
White	57 (79·2)	49 (75·4)	106 (77·4)
Asian	11 (15·3)	10 (15·4)	21 (15·3)
Black	1 (1·4)	1 (1·5)	2 (1·5)
Other*	1 (1·4)	3 (4·6)	4 (2·9)
Unknown	2 (2·8)	2 (3·1)	4 (2·9)
ECOG performance status			
0	27 (37·5)	21 (32·3)	48 (35·0)
1	45 (62·5)	44 (67·7)	89 (65·0)
Tobacco use history			
Never	10 (13·9)	11 (16·9)	21 (15·3)
Current	15 (20·8)	12 (18·5)	27 (19·7)
Previous	47 (65·3)	42 (64·6)	89 (65·0)
EGFR mutation			
Positive	6 (8·3)	3 (4·6)	9 (6·6)
Negative	54 (75·0)	47 (72·3)	101 (73·7)
Unknown	12 (16·7)	15 (23·1)	27 (19·7)
EMLA-ALK translocation			
Positive	0	0	0
Negative	39 (54·2)	32 (49·2)	71 (51·8)
Unknown	33 (45·8)	33 (50·8)	66 (48·2)
KRAS mutation			
Positive	3 (4·2)	6 (9·2)	9 (6·6)
Negative	23 (31·9)	11 (16·9)	34 (24·8)
Unknown	46 (63·9)	48 (73·8)	94 (68·6)
Histology			
Nonsquamous	49 (68·1)	47 (72·3)	96 (70·1)
Squamous	23 (31·9)	18 (27·7)	41 (29·9)
Number of prior therapies in the locally advanced or metastatic setting			
1	53 (73·6)	52 (80·0)	105 (76·6)

2	19 (26·4)	13 (20·0)	32 (23·4)

Data are n (%), unless otherwise indicated. ECOG=Eastern Cooperative Oncology Group. EGFR=the gene encoding epidermal growth factor receptor. EMLA-ALK=the EMLA-anaplastic lymphoma kinase fusion gene. IC=tumour-infiltrating immune cell. KRAS=KRAS proto-oncogene. PD-L1=programmed death-ligand 1. TC=tumour cell. *Other includes American Indian, Alaska Native, Hawaiian native, other Pacific Islander and other.

Supplementary Table S3. Lung cancer treatments received after discontinuation of study treatment (intention-to-treat population)

Treatment	Atezolizumab n=425	Docetaxel n=425
Total patients with at least one treatment	206 (48·5)	192 (45·2)
Chemotherapy	176 (41·4)	131 (30·8)
Docetaxel	110 (25·9)	10 (2·4)
Carboplatin	35 (8·2)	29 (6·8)
Gemcitabine	24 (5·6)	38 (8·9)
Vinorelbine	18 (4·2)	22 (5·2)
Gemcitabine hydrochloride	17 (4·0)	20 (4·7)
Pemetrexed	15 (3·5)	22 (5·2)
Vinorelbine tartrate	15 (3·5)	22 (5·2)
Paclitaxel	20 (4·7)	12 (2·8)
Cisplatin	7 (1·6)	11 (2·6)
Pemetrexed disodium	7 (1·6)	8 (1·9)
Paclitaxel albumin	7 (1·6)	6 (1·4)
Gimeracil/oteracil potassium/tegafur	7 (1·6)	5 (1·2)
Irinotecan	6 (1·4)	6 (1·4)
Etoposide	3 (0·7)	2 (0·5)
Amrubicin	1 (0·2)	2 (0·5)
Irinotecan hydrochloride	2 (0·5)	1 (0·2)
Methotrexate	0	2 (0·5)
Mitomycin	0	2 (0·5)
Amrubicin hydrochloride	1 (0·2)	0
Cytarabine	0	1 (0·2)
Oxaliplatin	0	1 (0·2)
Targeted therapy	63 (14·8)	66 (15·5)
Erlotinib hydrochloride	14 (3·3)	27 (6·4)
Erlotinib	18 (4·2)	20 (4·7)
Bevacizumab	9 (2·1)	9 (2·1)
Afatinib	5 (1·2)	6 (1·4)
Ramucirumab	6 (1·4)	1 (0·2)
Osimertinib mesylate	1 (0·2)	5 (1·2)
Gefitinib	3 (0·7)	2 (0·5)
Crizotinib	2 (0·5)	2 (0·5)
Abemaciclib	2 (0·5)	1 (0·2)
Osimertinib	2 (0·5)	1 (0·2)
AUY922 (HSP90 inhibitor)	0	2 (0·5)
Blinded patritumab	1 (0·2)	1 (0·2)
Ceritinib	2 (0·5)	0
Trastuzumab emtansine	2 (0·5)	0
Aflibercept	1 (0·2)	0
BBI608 (cancer stem cell inhibitor)	1 (0·2)	0
BVD-523 (ERK inhibitor)	1 (0·2)	0
Cabozantinib	1 (0·2)	0
Cetuximab	0	1 (0·2)
Lurbinectedin	1 (0·2)	0
Ranibizumab	1 (0·2)	0
Vemurafenib	1 (0·2)	0
Vorinostat	1 (0·2)	0
Immunotherapy	19 (4·5)	73 (17·2)
Nivolumab	16 (3·8)	58 (13·6)
MEDI4736 (anti-PD-L1 monoclonal antibody)	0	7 (1·6)
L-DOS47 (anti-CEACAM6 AFAIKL2 immunoconjugate)	2 (0·5)	3 (0·7)
Lambrolizumab	0	4 (0·9)
Ipilimumab	0	2 (0·5)
Durvalumab	0	1 (0·2)
RO6958688 (T-cell bispecific monoclonal antibody)	1 (0·2)	0
Tremelimumab	0	1 (0·2)

Data are n (%), unless otherwise indicated. Patients were only counted once if they received more than one nonprotocol therapy of the same type. Patients were counted more than once if they received more than one type of the nonprotocol therapy. CEACAM6=carcinoembryonic antigen related cell adhesion molecule 6. ERK=extracellular signal–regulated kinase. HSP90=heat shock protein 90. PD-L1=programmed death-ligand 1.

Supplementary Table S4. Objective response rate, and duration of response by PD-L1 status

	Atezolizumab	Docetaxel
Objective response rate, n (%)		
TC3 or IC3	22/72 (30·6)	7/65 (10·8)
TC2/3 or IC2/3	29/129 (22·5)	17/136 (12·5)
TC1/2/3 or IC1/2/3	43/241 (17·8)	36/222 (16·2)
TC0 and IC0	14/180 (7·8)	21/199 (10·6)
Duration of response		
TC3 or IC3	**n=22**	**n=7**
Median (months)	12·5	6·3
HR* (95% CI) p value	0·62 (0·23–1·64) 0·3296	
TC2/3 or IC2/3	**n=29**	**n=17**
Median (months)	14·7	9·2
HR* (95% CI) p value	0·48 (0·23–1·00) 0·0452	
TC1/2/3 or IC1/2/3	**n=43**	**n=36**
Median (months)	16·0	6·2
HR* (95% CI) p value	0·38 (0·22–0·65) 0·0003	
TC0 and IC0	**n=14**	**n=21**
Median (months)	NE	6·2
HR* (95% CI) p value	0·2 (0·07–0·63) 0·0026	

CI=confidence interval. HR=hazard ratio. IC=tumour-infiltrating immune cell. NE=not evaluable. PD-L1=programmed death-ligand 1. TC=tumour cell. * Unstratified.

Supplementary Table S5. Adverse events in at least 10% of patients in any arm

Adverse event	Atezolizumab n=609		Docetaxel n=578	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
Fatigue	163 (26·8)	17 (2·8)	205 (35·5)	23 (4·0)
Decreased appetite	143 (23·5)	2 (0·3)	136 (23·5)	9 (1·6)
Cough	141 (23·2)	2 (0·3)	105 (18·2)	1 (0·2)
Nausea	108 (17·7)	4 (0·7)	131 (22·7)	2 (0·3)
Diarrhoea	94 (15·4)	4 (0·7)	141 (24·4)	11 (1·9)
Asthenia	116 (19·0)	8 (1·3)	114 (19·7)	13 (2·2)
Dyspnoea	118 (19·4)	15 (2·5)	112 (19·4)	14 (2·4)
Anaemia	70 (11·5)	14 (2·3)	136 (23·5)	33 (5·7)
Alopecia	3 (0·5)	0	202 (34·9)	1 (0·2)
Constipation	107 (17·6)	2 (0·3)	82 (14·2)	1 (0·2)
Pyrexia	108 (17·7)	1 (0·2)	76 (13·1)	1 (0·2)
Peripheral oedema	54 (8·9)	1 (0·2)	82 (14·2)	3 (0·5)
Vomiting	74 (12·2)	2 (0·3)	62 (10·7)	4 (0·7)
Arthralgia	73 (12·0)	3 (0·5)	58 (10·0)	1 (0·2)
Myalgia	39 (6·4)	1 (0·2)	91 (15·7)	4 (0·7)
Back pain	67 (11·0)	7 (1·1)	42 (7·3)	4 (0·7)
Neutropenia	10 (1·6)	3 (0·5)	90 (15·6)	75 (13·0)
Peripheral neuropathy	24 (3·9)	0	65 (11·2)	7 (1·2)
Musculoskeletal pain	64 (10·5)	4 (0·7)	25 (4·3)	1 (0·2)
Stomatitis	19 (3·1)	1 (0·2)	63 (10·9)	11 (1·9)
Dysgeusia	18 (3·0)	0	58 (10·0)	0
Febrile neutropenia	1 (0·2)	1 (0·2)	62 (10·7)	62 (10·7)

Data are n (%), unless otherwise indicated.

Supplementary Table S6. Predictive relationship of PD-L1 expression level for atezolizumab efficacy

Endpoint: Overall survival*	**Mutually exclusive PD-L1 expression levels**
Treatment by PD-L1 expression interaction p-value*	**0.0086**

***From Cox proportional hazard model with treatment, PD-L1 expression and treatment by PD-L1 expression interaction.**

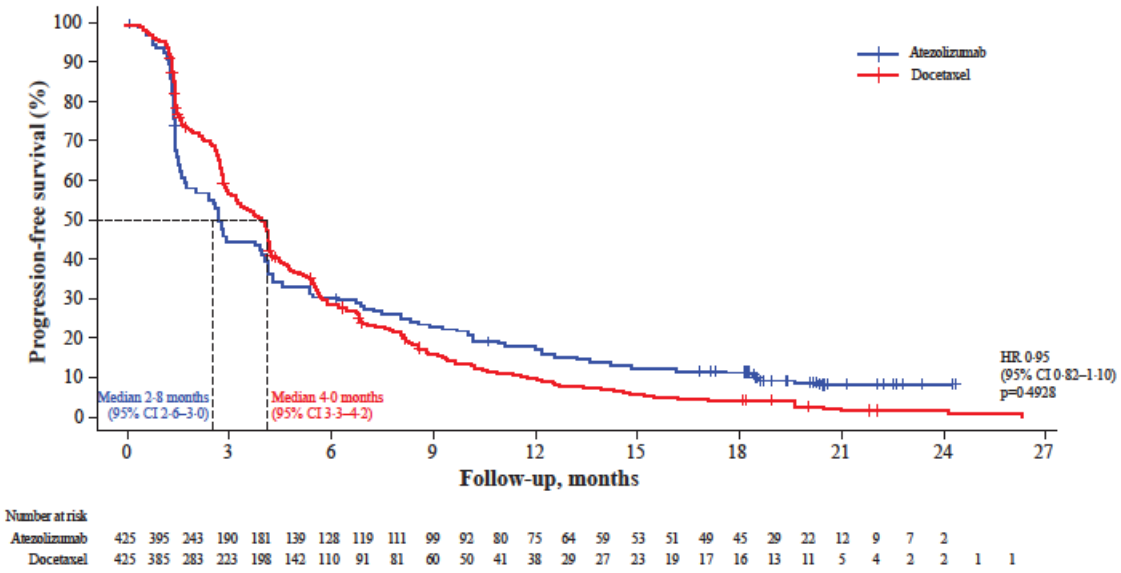
The mutually exclusive PD-L1 expression levels include TC3 or IC3 (i.e., ≥50% on TC or ≥10% on IC), TC2 or IC2 (i.e., ≥5%-<50% on TC or ≥5%-<10% IC), TC1 or IC1 (i.e., ≥1%-<5% on TC or IC), TC0 and IC0 (i.e., <1% on TC and IC).

IC=tumour-infiltrating immune cellPD-L1=programmed death-ligand 1. TC=tumour cell.

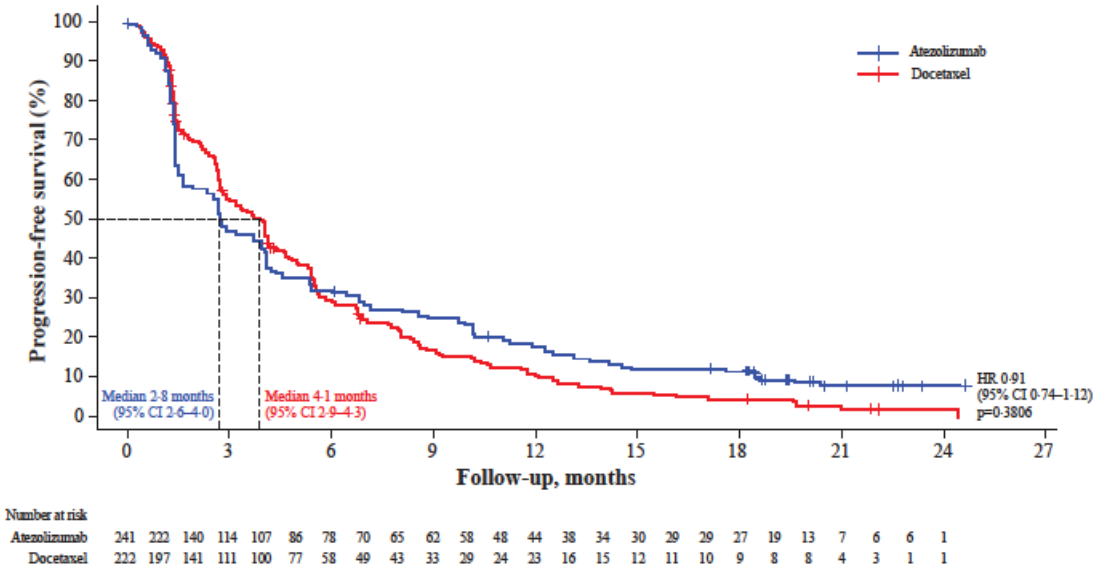
Supplementary Figure S1. Progression-free survival in the ITT and PD-L1 subgroups

Kaplan-Meier estimates in the ITT primary population, stratified according to PD-L1 expression on IC (IC0, IC1, IC2, and IC3), the number of prior chemotherapy regimens (1 *vs* 2), and histology (nonsquamous *vs* squamous) (A). Kaplan-Meier estimates in the TC1/2/3 or IC1/2/3 group using the same strata (B). Kaplan-Meier estimates in the TC2/3 or IC2/3 group (unstratified) (C). Kaplan-Meier estimates in the TC3 or IC3 group (unstratified) (D). Kaplan-Meier estimates in the TC0 and IC0 group (unstratified) (E).
Patients not reported as having progressed or died at the time of analysis were censored at the date of the last tumour assessment. Patients without post-baseline information were censored at the randomisation date plus 1 day.
CI, confidence interval. HR=hazard ratio. IC=tumour-infiltrating immune cell. ITT=intention-to-treat. PD-L1=programmed death-ligand 1. TC=tumour cell.

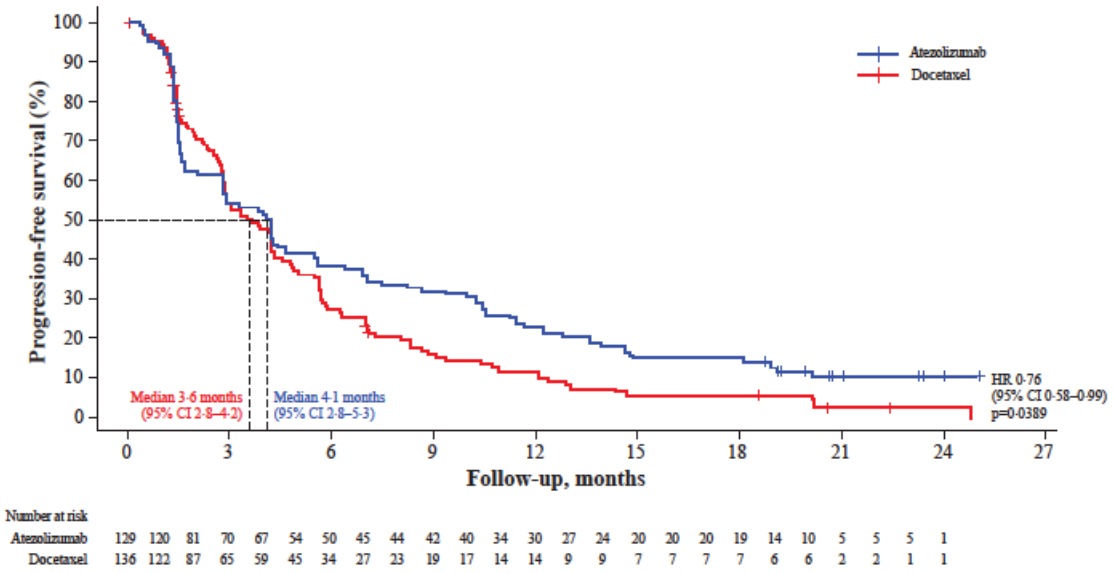
A
ITT



B
TC1/2/3 or IC1/2/3



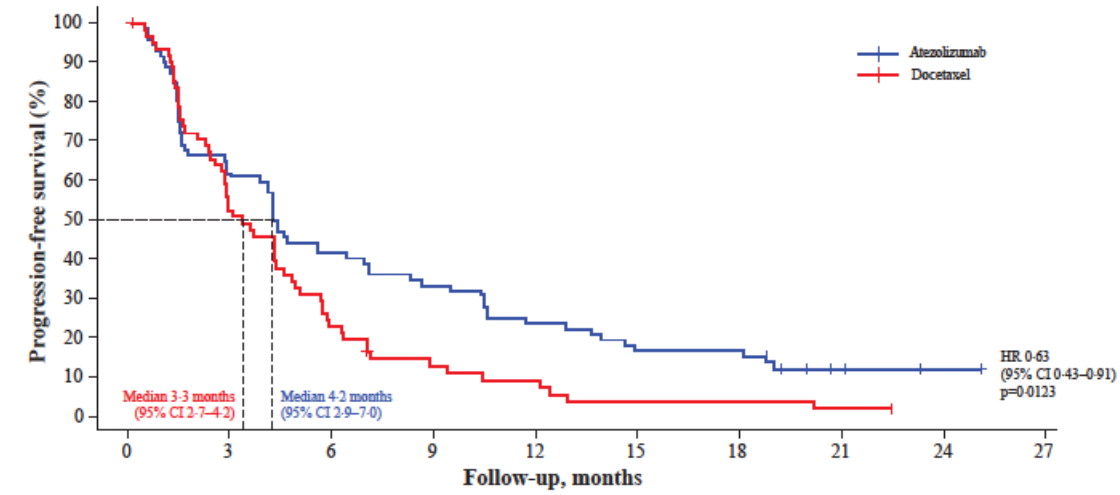
C
TC2/3 or IC2/3



Number at risk

Atezolizumab	129	120	81	70	67	54	50	45	44	42	40	34	30	27	24	20	20	20	19	14	10	5	5	5	1
Docetaxel	136	122	87	65	59	45	34	27	23	19	17	14	14	9	9	7	7	7	7	6	6	2	2	1	1

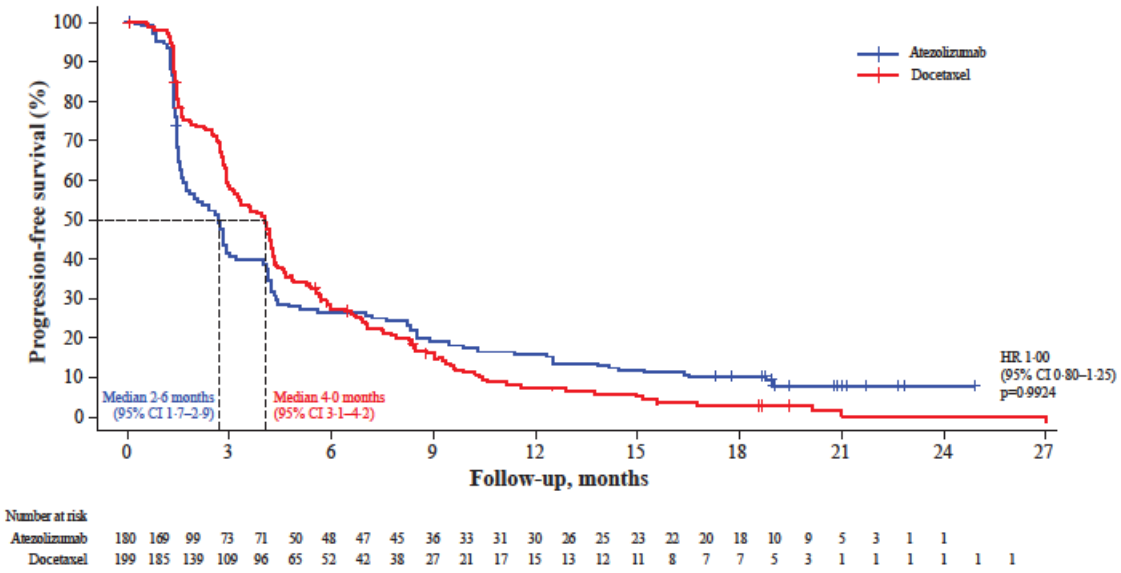
D
TC3 or IC3



Number at risk

Atezolizumab	72	65	48	44	43	32	30	26	26	24	23	18	17	16	14	12	12	12	11	7	5	2	2	2	1
Docetaxel	65	57	43	31	28	19	14	9	8	7	6	5	5	2	2	2	2	2	2	2	2	1	1		

E
TC0 and IC0


Progression-free survival (%)
100
90
80
70
60
50
40
30
20
10
0
Atezolizumab
Docetaxel
HR 1·00
(95% CI 0·80–1·25)
p=0·9924
Median 2·6 months
(95% CI 1·7–2·9)
Median 4·0 months
(95% CI 3·1–4·2)
0
3
6
9
12
15
18
21
24
27
Follow-up, months
Number at risk
Atezolizumab 180 169 99 73 71 50 48 47 45 36 33 31 30 26 25 23 22 20 18 10 9 5 3 1 1
Docetaxel 199 185 139 109 96 65 52 42 38 27 21 17 15 13 12 11 8 7 7 5 3 1 1 1 1 1 1

Supplementary Figure 2. Overall survival by *PD-L1* gene expression

Median overall survival was estimated using the Kaplan-Meier method, unstratified for subgroups.
HRs and 95% CIs for overall survival in subgroups defined by gene expression
CI, confidence interval. HR=hazard ratioITT=intention-to-treat. PD-L1=programmed death-ligand 1.

	n (%)	HR	95% CI	Median overall survival (months)	
				Atezolizumab	Docetaxel
PD-L1 gene expression ≥ median	356 (50)	0·68	0·52–0·89	16·3	11·3
PD-L1 gene expression < median	355 (50)	0·74	0·58–0·96	12·7	8·7
Biomarker evaluable population	711 (100)	0·69	0·57–0·83	14·2	9·5