Supplementary Appendix A

Supplementary Methods

Criteria for continuing atezolizumab treatment after radiographic progression

Patients could continue atezolizumab after radiographic progression per Response Evaluation Criteria in Solid Tumors (RECIST 1.1) if they meet all of the following criteria:

- Evidence of clinical benefit (defined as the stabilization or improvement of disease-related symptoms) as assessed by the investigator
- Absence of symptoms and signs (including worsening of laboratory values [eg, new or worsening hypercalcemia]) indicating unequivocal progression of disease
- No decline in Eastern Cooperative Oncology Group (ECOG) performance status that could be attributed to disease progression
- Absence of tumor progression at critical anatomical sites (eg, leptomeningeal disease) that could not be readily managed and stabilized by protocol-allowed medical interventions prior to repeat dosing

Patient Eligibility for TAIL

Eligible patients who had progressed following up to 2 chemotherapy regimens—including if given in combination with anti–programmed death 1 (PD-1) therapy, after anti–PD-1 monotherapy, or after tyrosine kinase inhibitors for patients with sensitizing epidermal growth factor receptor *EGFR* mutations or *ALK* gene arrangements—were included.

OAK-Like Patients

The OAK-like population contained all atezolizumab-treated patients who matched as closely as possible the eligibility criteria of the OAK phase III study.[1]

Therefore, patients with the following characteristics are excluded from the OAK-like population:

- ECOG performance status 2
- Previous anti–PD-1, anti–programmed death-ligand 1 (PD-L1), or anti–cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) therapy
- Presence of untreated central nervous system metastases at baseline
- Severe renal impairment (creatine clearance < 30 mL/min [Cockcroft-Gault])
- Liver impairment
- Concomitant denosumab treatment at baseline
- HIV positive status
- Active hepatitis B/C virus serology

Reference:

1. 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*. 2017;389:255-265.

Supplementary Table A1: PD-L1 immunohistochemistry assays used in laboratory testing

PD-L1 assay and laboratory, n (%)	**Atezolizumab (N = 615)**	**OAK-like population (n = 406)**
Central laboratory	**106 (17.2)**	**73 (18.0)**
SP263 (Ventana)	106 (17.2)	73 (18.0)
Local laboratory	**275 (44.7)**	**174 (42.9)**
22C3 (Agilent)	163 (26.5)	108 (26.6)
28-2 (Agilent)	15 (2.4)	6 (1.5)
SP263 (Ventana)	67 (10.9)	43 (10.6)
Other/unknown	30 (4.9)	17 (4.2)
No Result	**234 (38.0)**	**159 (39.2)**

Supplementary Table A2. Most common AEs (any grade in ≥ 5% of patients, grade ≥ 3 or grade ≥ 3 treatment-related AEs in ≥ 1% patients)

Number of patients with AE (%)	Safety population (n = 615)				
	Any grade	Grade 3	Grade 4	Grade 5	Treatment-related AE, grade ≥ 3
Any AE	558 (90.7)	162 (26.3)	22 (3.6)	35 (5.7)	63 (10.2)
Decreased appetite	101 (16.4)	2 (0.3)	0	0	1 (0.2)
Cough	97 (15.8)	1 (0.2)	0	0	0
Asthenia	90 (14.6)	8 (1.3)	0	0	3 (0.5)
Fatigue	89 (14.5)	9 (1.5)	1 (0.2)	0	4 (0.7)
Dyspnea	82 (13.3)	9 (1.5)	1 (0.2)	0	0
Anemia	74 (12.0)	11 (1.8)	1 (0.2)	0	4 (0.7)
Pyrexia	71 (11.5)	1 (0.2)	0	0	1 (0.2)
Diarrhea	66 (10.7)	4 (0.7)	1 (0.2)	0	3 (0.5)
Nausea	63 (10.2)	3 (0.5)	0	0	1 (0.2)
Arthralgia	57 (9.3)	2 (0.3)	0	0	0
Hypothyroidism	56 (9.1)	1 (0.2)	0	0	1 (0.2)

Back pain	55 (8.9)	2 (0.3)	0	0	0
Constipation	49 (8.0)	0	0	0	0
Vomiting	42 (6.8)	3 (0.5)	0	0	1 (0.2)
Pruritus	41 (6.7)	1 (0.2)	0	0	1 (0.2)
Headache	37 (6.0)	0	0	0	0
Urinary tract infection	37 (6.0)	2 (0.3)	1 (0.2)	0	0
Hyperthyroidism	36 (5.9)	0	0	0	0
Pain in extremity	35 (5.7)	0	0	0	0
Upper respiratory tract infection	35 (5.7)	4 (0.7)	0	0	0
Musculoskeletal chest pain	34 (5.5)	4 (0.7)	0	0	NR
Nasopharyngitis	32 (5.2)	0	0	0	0
Pneumonia	29 (4.7)	14 (2.3)	1 (0.2)	4 (0.7)	1 (0.2)
Pneumonitis	22 (3.6)	5 (0.8)	1 (0.2)	1 (0.2)	7 (1.1)
Increased hyponatremia	20 (3.3)	8 (1.3)	3 (0.5)	0	3 (0.5)
Increased hypertension	17 (2.8)	7 (1.1)	0	0	1 (0.2)

Lung infection	12 (2.0)	8 (1.3)	0	0	NR
Pulmonary embolism	10 (1.6)	8 (1.3)	0	2 (0.3)	2 (0.3)

AE, adverse event; NR, not reported.

Supplementary Table A3. Efficacy by tumor PD-L1 expression[a]

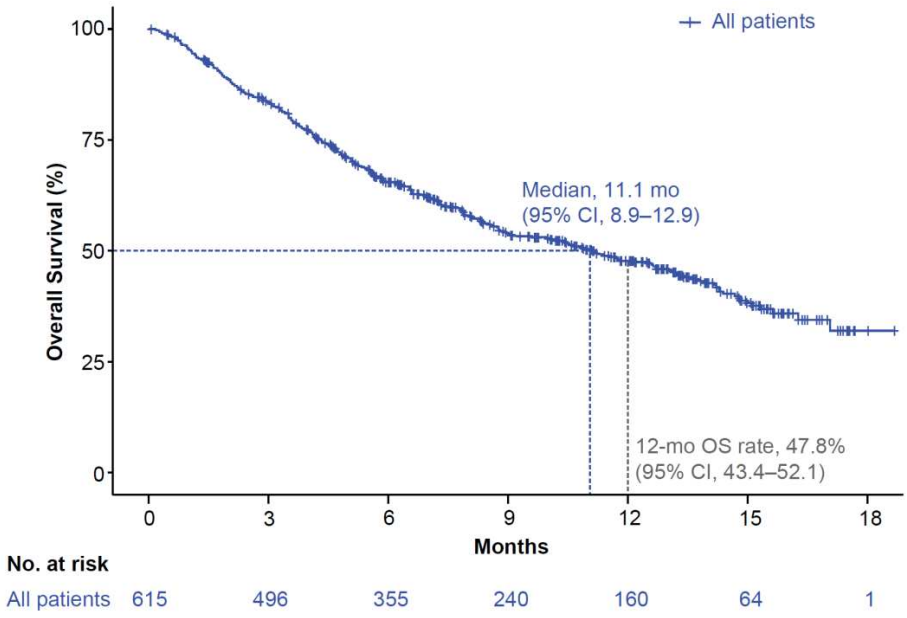
	Overall study population (N = 615)			**OAK-like population (n = 406)**		
	n (%)	**Median OS mo (95% CI)**	**ORR % (95% CI)**	**n (%)**	**Median OS mo (95% CI)**	**ORR % (95% CI)**
All patients	615 (100)	11.1 (8.9–12.9)	11.1 (8.7–13.8)	406 (100)	13.7 (11.6–15.5)	13.5 (10.4–17.3)
PD-L1–positive (TC or TPS ≥ 1%)	213 (34.6)	12.6 (8.7–15.5)	11.7 (7.7–16.8)	142 (35.0)	15.5 (11.7–NE)	15.5 (10.0–22.5)
PD-L1–negative (TC or TPS < 1%)	168 (27.3)	8.7 (6.5–11.7)	8.3 (4.6–13.6)	105 (25.9)	11.7 (8.0–13.7)	7.6 (3.3–14.5)
PD-L1 unknown	234 (38.0)	12.5 (8.6–15.0)	12.4 (8.5–17.3)	159 (39.1)	13.8 (9.0–NE)	15.7 (10.4–22.3)

NE, not estimable; ORR, objective response rate; OS, overall survival; PD-L1; programmed death-ligand 1; TC, tumor cells; TPS, tumor proportion score.

[a] PD-L1 expression on TC and TPS results from central and local testing were pooled.

Supplementary Figure A1. Kaplan-Meier curves of overall survival (OS) in (A) overall population and (B) OAK-like population.

A



B