
Supplementary information

Atezolizumab versus chemotherapy in advanced or metastatic NSCLC with high blood-based tumor mutational burden: primary analysis of BFAST cohort C randomized phase 3 trial

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Supplementary tables

Supplementary Table 1. Follow-up cancer therapies

Patients receiving follow up therapy, n (%)	bTMB ≥ 10		bTMB ≥ 16	
	Atezo (n=234)	Chemo (n=237)	Atezo (n=145)	Chemo (n=146)
≥ 1 therapy	94 (40.2)	124 (52.3)	51 (35.2)	73 (50.0)
Chemotherapy	93 (39.7)	58 (24.5)	50 (34.5)	37 (25.3)
Immunotherapy	8 (3.4)	100 (42.2)	5 (3.4)	54 (37.0)
Targeted Therapy	13 (5.6)	10 (4.2)	8 (5.5)	6 (4.1)

Atezo, atezolizumab; bTMB, blood-based tumor mutational burden; Chemo, chemotherapy.

Supplementary Table 2. Treatment exposure

	Atezo (n=234)	Chemo (n=221)			
		Pem	Gem	Carbo	Cis
Median treatment duration, months	3.5	3.5	2.6	2.1	2.1
Number of doses, median (range)	6 (1–45)	6 (1–31)	7 (1–12)	4 (1–6)	4 (1–7)

Atezo, atezolizumab; Carbo, carboplatin; Chemo, chemotherapy; Cis, cisplatin; Gem, gemcitabine; Pem, pemetrexed.

Supplementary Table 3. Adverse events of special interest

Medical concept	Atezo (n=234)		Chemo (n=221)	
	All grade	Grade 3/4	All grade	Grade 3/4
Rash	33 (14)	1 (<1)	21 (10)	4 (2)
Hypothyroidism	20 (9)	1 (<1)	4 (2)	0
Pneumonitis	14 (6)	8 (3)	3 (1)	1 (<1)
Hepatitis diagnosis	8 (3)	5 (2)	1 (<1)	0
Hyperthyroidism	5 (2)	0	3 (1)	0
Infusion-related reactions	5 (2)	1 (<1)	1 (<1)	0
Colitis	2 (<1)	0	1 (<1)	0
Diabetes mellitus	2 (<1)	0	2 (<1)	1 (<1)
Adrenal insufficiency	2 (<1)	1 (<1)	0	0
Severe cutaneous adverse reaction	1 (<1)	0	0	0
Myocarditis	1 (<1)	1 (<1)	0	0
Vasculitis	1 (<1)	0	1 (<1)	0
Meningoencephalitis	3 (1)	2 (<1)	1 (<1)	0
Pancreatitis	2 (<1)	1 (<1)	1 (<1)	0
Guillain-Barré syndrome	1 (<1)	0	0	0
Hypophysitis	0	0	1 (<1)	0
Myositis	1 (<1)	1 (<1)	0	0

Atezo, atezolizumab; Chemo, chemotherapy.

Supplementary Table 4. Clinical and biomarker variables associated with progression within 4 months

Clinical variable	Atezo bTMB ≥16 (n=145)				Chemo bTMB ≥16 (n=146)			
	Early (≤4 mo) (n=61), n (%)	Late (>4 mo) (n=84), n (%)	Odds ratio (95% CI)	P	Early (≤4 mo) (n=52), n (%)	Late (>4 mo) (n=94), n (%)	Odds ratio (95% CI)	P
Liver metastasis	19 (31)	11 (13)	0.34 (0.13, 0.83)	0.012 ^b	15 (29)	11 (12)	0.33 (0.12, 0.85)	0.013 ^b
Bone metastasis	20 (33)	14 (17)	0.41 (0.17, 0.96)	0.029 ^b	13 (25)	17 (18)	0.66 (0.27, 1.7)	0.393
Squamous histology	18 (30)	14 (17)	0.48 (0.2, 1.1)	0.072 ^a	6 (12)	28 (30)	3.2 (1.2, 10)	0.014 ^b
SLD ≥86 mm	46 (75)	51 (61)	0.51 (0.23, 1.1)	0.075 ^a	41 (79)	59 (63)	0.45 (0.19, 1)	0.062 ^a
Adrenal gland metastasis	16 (26)	20 (24)	0.88 (0.39, 2.0)	0.846	25 (48)	19 (20)	0.28 (0.12, 0.61)	0.001 ^c
Brain metastasis	11 (18)	10 (12)	0.62 (0.22, 1.7)	0.344	17 (33)	11 (12)	0.28 (0.1, 0.7)	0.004 ^b
≥3 Metastatic sites	47 (77)	53 (63)	0.51 (0.22, 1.1)	0.101	41 (79)	55 (59)	0.38 (0.16, 0.87)	0.018 ^b
Baseline SLD by INV, mm, mean (SD)	n=51 125 (59)	n=71 104 (49)	NA	0.034 ^b	n=45 131 (45)	n=79 104 (55)	NA	0.004 ^b
<i>KEAP1</i>	9 (15)	5 (6)	0.37 (0.092, 1.3)	0.092 ^a	3 (6)	7 (7)	1.3 (0.28, 8.2)	1.000
<i>SMARCA</i>	7 (11)	11 (13)	1.2 (0.38, 3.8)	0.805	12 (23)	7 (7)	0.27 (0.084, 0.81)	0.01 ^b
<i>ASXL1</i>	8 (13)	11 (13)	1 (0.34, 3.1)	1.000	3 (6)	20 (21)	4.4 (1.2, 24)	0.017 ^b
<i>CDKN2A</i>	8 (13)	9 (11)	0.8 (0.25, 2.5)	0.795	10 (19)	6 (6)	0.29 (0.081, 0.95)	0.026 ^b
<i>STK11</i>	9 (15)	10 (12)	0.78 (0.26, 2.3)	0.627	9 (17)	7 (7)	0.39 (0.11, 1.3)	0.096 ^a

AE, adverse event; Atezo, atezolizumab; bTMB, blood-based tumor mutational burden; Chemo, chemotherapy; INV, investigator assessment; NA, not analyzed; SAE, serious adverse event; SLD, sum of longest diameters.

^a P<0.1 and ≥0.05

^b P<0.05 and ≥0.001

Supplementary Table 5. Comparison of bTMB assessed by CTA vs F1L CDx

F1L CDx	bTMB CTA		
	bTMB ≥ 16	bTMB < 16	Total
bTMB ≥ 13.6 mut/Mb	203	24	227
bTMB < 13.6 mut/Mb	42	258	300
Non-evaluable	3	3	6
Total	248	285	533

bTMB, blood-based tumor mutational burden, CTA, clinical trial assay; F1L CDx, FoundationOne Liquid Companion Diagnostic assay.

Supplementary Table 6. Agreement between the F1L CDx assay and bTMB CTA assay

	Calculation	Agreement, % (95% CI)
bTMB CTA (bTMB≥ 16)	PPA	82.9 (77.6, 87.1)
bTMB CTA (bTMB< 16)	NPA	91.5 (87.7, 94.2)
F1L CDx+ (bTMB≥ 13.6 mut/Mb)	PPV	89.4 (84.8, 92.8)
F1L CDx- (bTMB< 13.6 mut/Mb)	NPV	86.0 (81.6, 89.5)
F1L CDx	OPA	87.5 (84.4, 90.0)

bTMB, blood-based tumor mutational burden, CTA, clinical trial assay; F1L CDx, FoundationOne Liquid Companion Diagnostic assay; NPA, negative percentage agreement; NPV, negative predictive value; OPA, overall percentage agreement; PPA, positive percentage agreement; PPV, positive predictive value.

Supplementary Table 7. Investigators who participated in the Phase 3 BFAST study

Country	Investigators
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