Supplementary material

Supplementary Patients and Methods

All participating lung cancer centers were certified by the German Cancer Society (DKG). Patient enrollment by participating hospital was: Thoarxklinik Heidelberg (n=37); Charité Berlin (n=12); Robert-Bosch-Krankenhaus (RBK) Stuttgart (n=3); Universitätsklinikum Augsburg (n=2); Klinikum Esslingen (n=1); Evangelische Lungenklinik Berlin (n=11); SLK-Fachklinik Löwenstein (n=6); LungenClinic Grosshansdorf (n=8); Helios Klinikum Emil von Behring Berlin (n=11); LMU Klinikum München (n=19). Response to treatment and time of disease progression were assessed through retrospective review of radiologic images, i.e. CT of the chest/abdomen and MRI of the brain every 6-12 weeks, based on the RECIST v1.1 criteria. The PD-L1 tumor proportion score (TPS) was determined locally using certified immunohistochemistry assays with validated clones (Ventana SP263, Cell Signaling E1L3N, Thermo Fisher ZR3, Abcam CAL10, Dako 73-10) and dichotomized at the level of 50%.

Supplementary Table 1. Genetic results for study patients with known *TP53* status

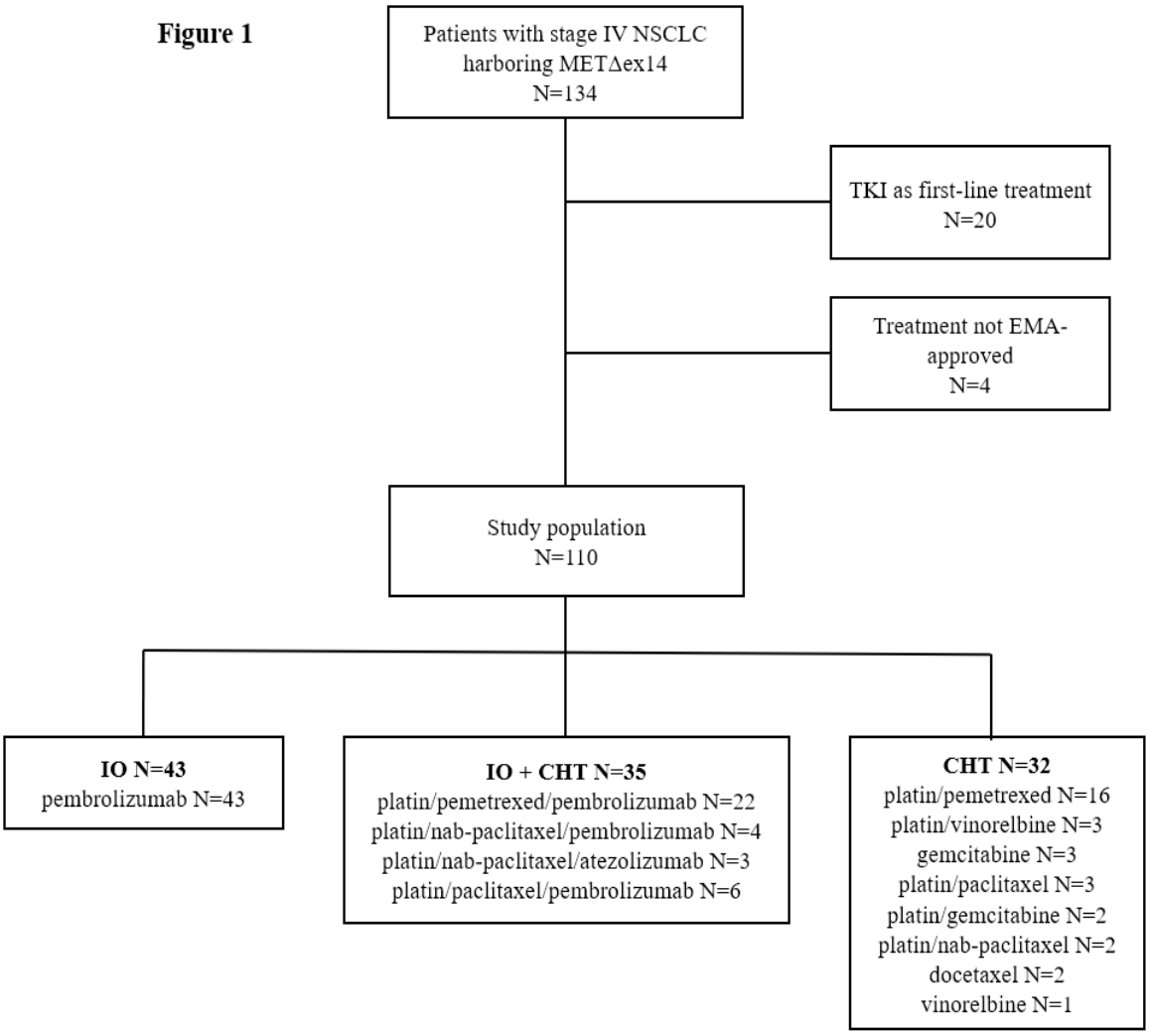
#	***MET* mutation**	**Comment**	***TP53* mutation**	***TP53* exon**	**Tested *TP53* exons**
2	c.3028G>C (p.D963_D1010del)		WT		4-10
3	c.3028G>T(p.D963_D1010del)		WT		4-10
4	MET(13)-MET(15)		WT		4-8
5	p.Ala1005_Glu1009delAlaThrPheProGlu		p.spl? (c.783-1G>A)	9	4-8
6	p.Asp1010Asn		WT		-
7	c.3028+2T>C (p.spl?)		WT		4-8
8	c.3023_3028del		p.P278S	7	4-8
9	c.3028G>A (p.D963_D1010del)		p.V173L	4	4-8
10	c.3018_3028del (p.Phe1007fs*4)		p.L194A	6	4-8
11	p.spl? (c.3082+1G>-)		p.R248W	7	4-8
12	p.D963_D1010del (c.3028+1G>A)		WT		4-8
13	MET(13)-MET(15)	RNA NGS	WT		4-8
14	MET(13)-MET(15)	RNA NGS	p.E285K	8	-
15	p.A1010T (c.3028G>T)		p.C135P	5	4-8
16	p.Asp1028His (c.3082G>C)		WT		-
17	p.Asp1010Asn (c.3028G>A)		WT		4-8
18	p.Asp1010Tyr (c.3028G>T)		p.G331*	9	4-8
19	MET(13)-MET(15)	RNA NGS	p.Q331*	6	-
20	p.Pro1008fs (c.3022_3028del)		WT		4-8
21	MET(13)-MET(15)	RNA NGS	p.P278S	7	4-8
22	p.spl? (c.3028+1G>T)		p.W91*	4	4-8
23	p.spl? (c.3028+3A>G)		p.spl? (c.673-2A>T)	intron 8	-
24	p.spl? (c.2888-15_2888-4del)		WT		4-8
25	MET(13)-MET(15)	RNA NGS	WT		4-8
26	p.spl? (c.3028+2T>C)		p.P177H	5	4-8
27	p.Arg1004fs*22 (c.3009_3018del)		WT		4-8
28	c.3077_3082+9del		p.G262Vfs*83	8	-
29	MET(13)-MET(15)	RNA NGS	p.R158H	4	4-8
30	MET(13)-MET(15)	RNA NGS	WT		-
31	p.D1028N (c.3082G>A)		WT		4-8
32	c.2942-18_2942-17ins		p.H179R	5	-

33	p.D1028H (c.3023G>C)		p.E258K	6	4-10
34	c.2941+70G>A		WT		4-10
35	c.2942_18_2942-4del		p.Y234C	6	4-10
36	c.2942-20_2942-4del		p.R65*	3	4-10
37	c.2942-21_2942-20insAGA		WT		4-10
38	c.3082+1G>A		p.V157F	4	4-10
39	3028+1G>T		p.R249M	6	4-10
40	p.D1028H		WT		4-10
41	c.3082+3A>G		WT		4-10
44	c.3082+1G>A		WT		4-10
45	c.3082G>C (p.D1028H)		p.R280K	8	-
46	c.3082+3A>G		P301Qfs*50	8	4-8
47	c.3082+2T>C		WT		4-10
48	c.3082G>C (p.D1028Y)		WT		4-10
49	c.2942-28_2942-16del		WT		4-10
50	c.2942-9_2967del		p.C135Y	5	4-10
51	c.3066_3081delA		p.A161T	5	4-8
52	c.3028+2T>C		WT		4-8
53	c.3007T>C		WT		4-8
54	c.3007T>A		p.M237I	6	4-10
55	c.2962C>T		P.S106_G112del	4	4-10
56	c.2962C>T		WT		4-10
57	c.3029C>T		WT		4-8
58	c.3029C>T		P.R175L + E285*	5-8	4-8
60	c.3028+1G>A		WT		4-8
61	MET(13)-MET(15)	RNA NGS only	p.E298*	8	4-8
62	MET(13)-MET(15)	RNA NGS only	WT		4-8
63	MET(13)-MET(15)	RNA NGS only	WT		4-8
64	MET(13)-MET(15)	RNA NGS only	p.S241T	7	4-10
65	MET(13)-MET(15)	RNA NGS only	p.R249fs*96	7	4-8
66	MET(13)-MET(15)	RNA NGS only	WT		4-8
67	MET(13)-MET(15)		WT		4-8
68	MET(13)-MET(15)		WT		4-8
69	MET(13)-MET(15)		WT		4-10
71	MET(13)-MET(15)		p.C242F	6	4-10

80	c.3028+2T>A		WT		4-8
81	c.3028+1G>C		p.S127P	4	4-8
82	c.3028+3G>A		WT		4-8
83	c.3028G>C		WT		4-8
84	MET(13)-MET(15)	RNA NGS only	WT		4-8
85	c.3005_3028+3		WT		4-8
86	c.3028+1G>C		WT		4-8
87	c.3005_3028+13delinsCTC		WT		4-8
88	c.3028+3A>G		WT		4-10
89	c.3028G>A		WT		4-8
90	MET(13)-MET(15)	RNA NGS	WT		4-8
91	MET(13)-MET(15)	RNA NGS	p.I195T	5	4-8
92	c.3082G>C		WT		4-8
93	MET(13)-MET (15)	RNA NGS	N131Y	5	4-8
94	c3082G>A		WT		-
95	c.3082+2T>C		p.L206Wfs*41	6	-
96	c.2942-18_2942-2del		WT		-
97	c.2942-29_2942-2del		WT		-
98	MET(13)-MET (15)	RNA NGS	WT		-
99	c.3014_3028del		WT		-
100	c.3028G>T		WT		-
101	c.2888-27_2888-16del12		WT		-
102	c.3028G>C		WT		-
103	c.2888-18_2888-3del		WT		-
104	MET(13)-MET (15)	RNA NGS	WT		-
105	MET(13)-MET (15)	RNA NGS	p.R175H	5	-

WT: wild-type.

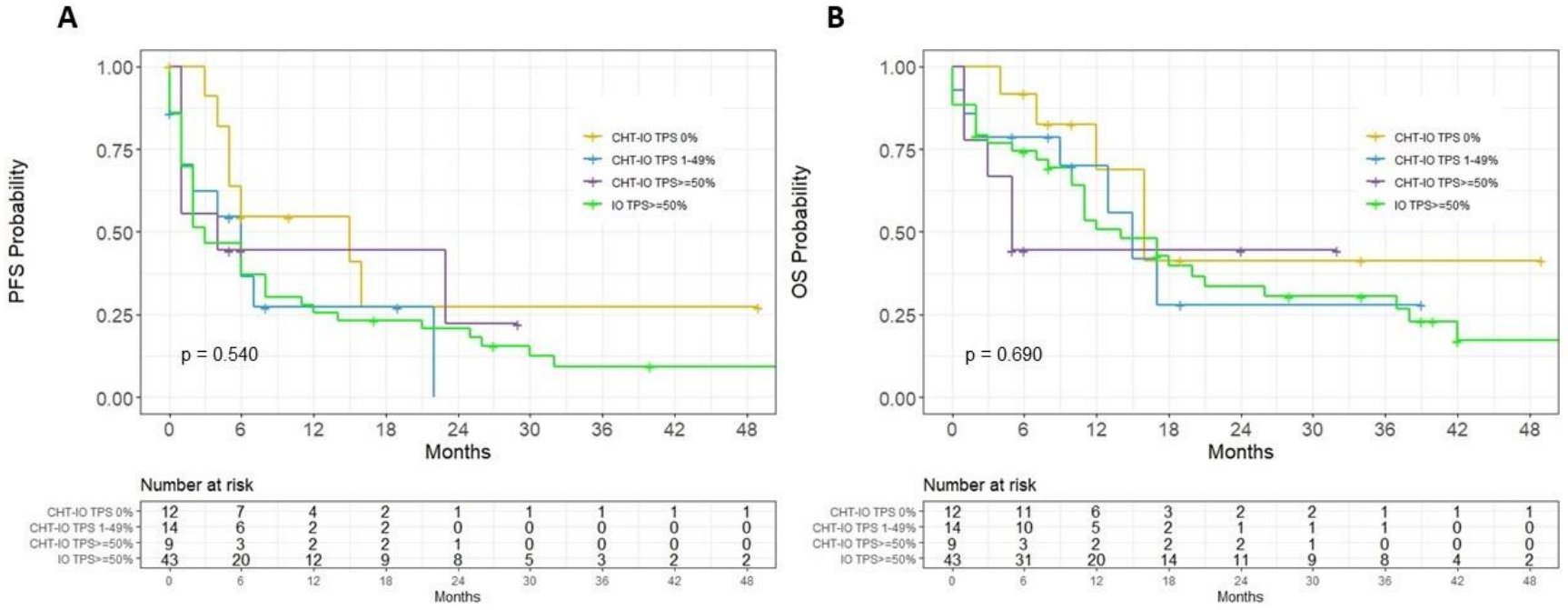
Supplementary Figure 1. Flowchart of patient cohort selection. Non-EMA approved treatments (n=4) excluded from this analysis were carboplatin/paclitaxel/durvalumab (n=1), nivolumab/ipilimumab (n=1), pembrolizumab first-line monotherapy in a tumor with PD-L1 TPS 5% (n=1), and carboplatin/pemetrexed/nivolumab/ipilimumab (n=1, study patient at the time of treatment).



Supplementary Figure 2. Survival of lung cancer patients with METΔex14 under immunotherapy according to PD-L1 expression

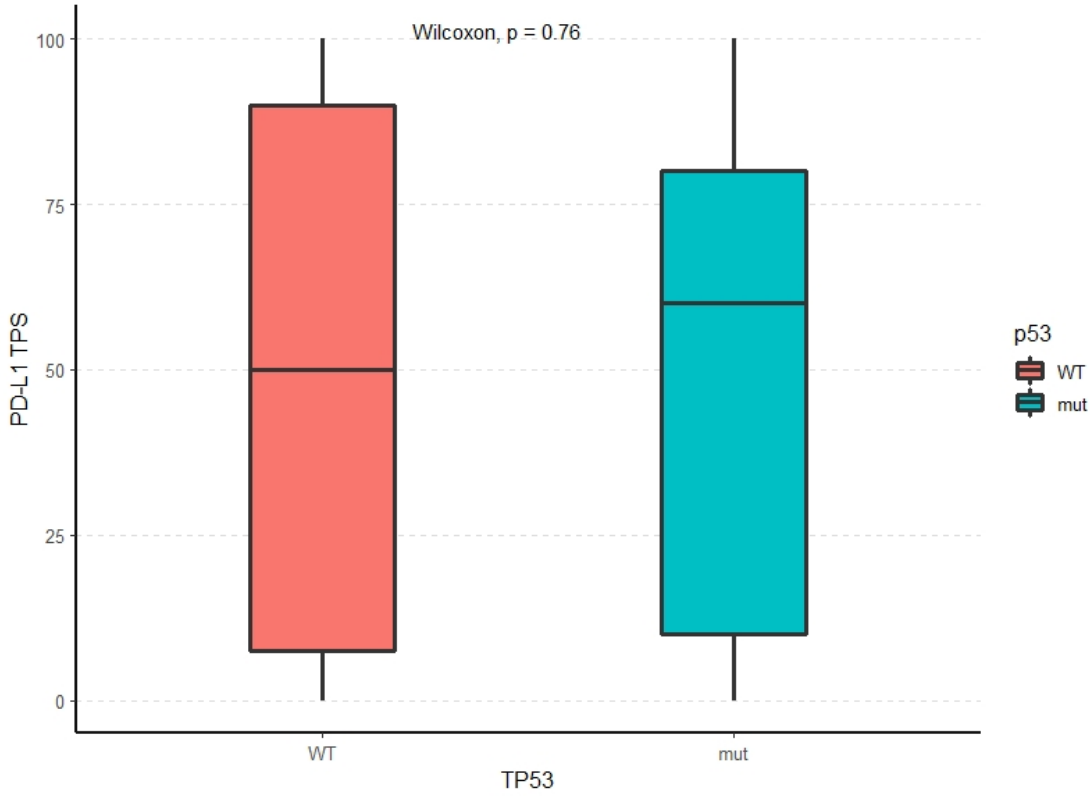
(A) Median progression-free survival (PFS) was 3 months (95% CI 2-8) for patients with PD-L1≥50% under immunotherapy (IO) alone as monotherapy *vs.* 4 months (95% CI 1-NR) for patients with PD-L1≥50% under chemoimmunotherapy (CHT-IO) *vs.* 6 months (95% CI 1-NR) for patients with PD-L1 1-49% *vs.* 15 months (95% CI 5-NR) for patients with PD-L1 0% (logrank p= 0.540). All patients treated with first-line PD-(L)1 inhibitors (n=78) were included in this analysis.

(B) Median overall survival (OS) was 14 months (95% CI 11-26) for patients with PD-L1≥50% under IO monotherapy *vs.* 5 months (95% CI 3-NR) for patients with PD-L1≥50% under CHT-IO *vs.* 15 months (95% CI 9-NR) for patients with PD-L1 1-49% *vs.* 16 months (95% CI 12-NR) for patients with PD-L1 0% (logrank p= 0.690). All patients treated with first-line PD-(L)1 inhibitors (n=78) were included in this analysis.



Supplementary Figure 3. Association between PD-L1 expression and *TP53* status in lung cancer patients with METΔex14.

Statistical comparison was performed with a Wilcoxon test.



Supplementary Figure 4. Progression-free and overall survival of patients with non-small-cell lung cancer harboring METΔex14 by second-line TKI agent. (A) Median progression-free survival (PFS) was 10 months (95% confidence interval [95% CI] 7-NR) for tepotinib or capmatinib vs. 3 months (95% CI 2-NR) for crizotinib (logrank p= 0.013). Patients who received second-line TKIs (n=13) were included in this analysis. (B) Median overall survival (OS) was 16 months (95% CI 15-NR) for tepotinib or capmatinib vs. 13 months (95% CI 5-NR) for crizotinib (logrank p= 0.270). Patients who received second-line TKIs (n=13) were included in this analysis.