Appendix 1

Study population

In the SWIPE trial (SWItch maintenance Pembrolizumab trial/NCT02705820), 48 aNSCLC patients who did not progress after first-line platinum-doublet chemotherapy, received maintenance pembrolizumab immunotherapy. Whole blood samples were obtained before pembrolizumab initiation (baseline, t0) and during treatment at the Bank of Cyprus Oncology Centre, Nicosia, Cyprus, between 2016 and 2019. Of the 48 patients, two were excluded: one had plasma collected only at t0, and another had no follow-up data beyond 6-weeks, as the individual died from septic shock, unrelated to the study medication. Of the remaining 46 patients, all of them had plasma collected at t0, 45 at 3-weeks (t1), 35 at 6-weeks (t2) and 41 at 9-weeks (t3) post-treatment.

Follow-up data included progression-free-survival (PFS), defined as the time between the initiation of treatment and the first documented disease progression (PD) or death, and OS, defined as the time between the initiation of treatment and date of death from any cause. The treatment response was initially evaluated using RECIST v1.1 (19). Patients were also classified as having durable clinical benefit (DCB) if they presented with PFS ≥6 months or non-durable benefit (NDB) if they presented with PFS <6 months.

Isolation and characterization of CTCs

A total volume of 20 mL of whole blood was obtained from each patient at each timepoint. To avoid contamination by skin epithelial cells, the first 5 mL of the blood sample was discarded. Plasma was isolated by centrifugation of 10 mL whole blood at 500 ×g for 15 min. The supernatant was transferred to sterile tubes and centrifuged twice at 2,000 ×g for 15 min, aliquoted, and stored at −80 ℃. Peripheral blood mononuclear cells (PBMCs) were isolated from 10 mL of whole blood in the presence of Ficoll-Hypaque density gradient (d=1,077 g/mol) and centrifuged at 670 g for 30 min. PBMCs were washed thrice with PBS and centrifuged at 530 ×g for 10min. Aliquots of 106 cells were centrifuged at 700 ×g for 2 min on glass slides. The cytospins were dried and stored at −80 ℃. A total of 6×10^6 PBMCs per patient were analysed and the results were expressed as CTCs/6×10^6 PBMCs (Table S2). A triple immunofluorescence staining assay was used for CTC detection and phenotypic characterization based on cytokeratin, PD-L1, and Ki67 markers, as previously described (20).

Immunostaining experiments

PBMCs' cytospins for each patient were triple stained with pancytokeratin, PD-L1 and Ki67. Briefly, cytospin fixation and permeabilization was performed with ice-cold acetone/methanol, 9/1 (V/V) for 20 minutes at RT, followed by incubation with blocking buffer (PBS/10% normal goat serum) for 60 minutes. Detection of cytokeratin (CK)-positive cells was performed using the pancytokeratin mouse antibody, (AE1/AE3+5D3, Abcam, Cambridge, UK), 1:100 dilution overnight at 4 ℃. This was followed by incubation with the FITC antibody, diluted 1:400 (Invitrogen, Thermo Fisher Scientific, Waltham, USA) for 50 min. The cytomorphological criteria (i.e., high nuclear to cytoplasmic ratio and larger than white blood cells in size) were used to characterize a CK-positive cell as a CTC. To evaluate PD-L1 expression, cells were stained with the PD-L1 rabbit antibody (E1L3N, Cell Signaling Technology Inc., Danvers, USA) diluted 1:100 for 1 h, followed by the secondary Alexa555 antibody (Invitrogen, Thermo Fisher Scientific, Waltham, USA) diluted 1:500 for 50 min. To identify Ki67 expression, cells were labelled with the rabbit Ki67-conjugated with Alexa 647 antibody (Abcam, Cambridge, UK) diluted 1:150 for 1 h. Finally, 4',6-diamidino-2-phenylindole (DAPI) reagent (Invitrogen, Thermo Fisher Scientific, Waltham, USA) was added to each sample for nuclear staining.

To evaluate the specificity of the antibodies, cytospins of cell lines spiked into healthy volunteers' PBMCs were used as positive and negative controls. Negative controls were prepared by omitting the corresponding primary antibody and adding the secondary IgG isotype antibody. Moreover, cytospins consisting of H1975 cells spiked in PBMCs were stained along with patients' samples in order to standardize the staining protocol, the background from PD-L1positive PBMCs, microscope settings, different antibodies' batch, during the whole period of the study. Cytospins were evaluated with a Leica microscope and the Leica LASX software.

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Furthermore, in patients presenting high CTC numbers, PBMCs' cytospins were double stained with pancytokeratin and the common leukocyte antigen CD45. For double staining experiments, PBMC cytospins were incubated with the pancytokeratin mouse antibody diluted 1:100, overnight at 4 ℃ followed by the corresponding secondary FITC antibody for 50 min and the Alexafluor 647 anti-human CD45 (HI30, BioLegend, CA, USA) diluted 1:300 for 1h. DAPI was added to each sample for nuclear staining.

The Oncomine Lung Cancer Assay Technology

The panel consisted of a single pool of primers used to perform multiplex PCR to sequence 35 amplicons covering >150 hotspots across 11 lung cancer-related genes: *ALK*, *BRAF*, *EGFR*, *ERBB2*, *KRAS*, *MAP2K1*, *MET*, *NRAS*, *PIK3CA*, *ROS1*, *TP53*. Library construction involved a two-cycle PCR reaction, where target regions were amplified and each cfDNA template molecule was tagged with a unique molecular tag (UMT) to allow for the detection of somatic mutations down to a 0.1% limit of detection (LOD). The UMT technology that is implemented in the Oncomine Lung Cancer Assay can distinguish the true hotspot variants from workflow errors, by counting the frequency of the variants in families that have the same UMI. Three or more families of sequenced amplicons with the same UMT were used to define a mutation as true, according to the company's recommendations. The resulting tagged amplicons of around 100–140 bp length were then cleaned up using Agencourt AMPure XP (Beckman Coulter, Brea, USA) at a bead to sample ratio of 1.5× and purified products were eluted in low TE buffer. A second round of PCR (18 cycles) was performed to amplify the purified amplicons and introduce Ion Torrent™ Tag-Sequencing adapters containing sample-specific barcodes. The resulting library of target DNA fragments was purified by performing a two-step cleanup using Agencourt AMPure XP (Beckman Coulter) at a bead to sample ratio of 1.15× and 1.0×, respectively. Detailed NGS results are showed in table available at https://cdn.amegroups.cn/static/public/tlcr-2024-1095-3.xlsx.

Performance of the Oncomine Lung Cancer Assay

The performance of the Oncomine Lung Cancer Assay was initially evaluated using the Multiplex I cfDNA Reference Standard Set (Horizon Discovery, Waterbeach, UK) loaded at 20 ng and 3 ng. The Standards cover 8 somatic mutations at 5%, 1% and 0.1% allelic frequencies. We chose to evaluate the performance of the assay at two cfDNA input amounts: (I) at 20 ng, which is the suggested amount to be used in Oncomine Lung cfDNA assay to succeed the 0.1% LOD; and (II) 3 ng which is closer to the total cfDNA amount that was isolated from our samples and would therefore enable us to determine possible reduction in assay sensitivity. The assessment resulted in the detection of 8/8 somatic mutations with a calculated sensitivity of 100% with 20 ng input cfDNA and 6/8 somatic mutations, with a calculated sensitivity of 75% with 3 ng input cfDNA.

Limitations of our study include the small study size and the fact that no NGS was undertaken on tissue, as at the time of the conduct of the study between 2016 and 2019, targeted molecular testing for *EGFR* and *BRAF* was done which was PCR-based, and ALK was tested by fluorescence in situ hybridization (FISH) (Table S5). Due to the small size biopsies often provided for patients with NSCLC, no further tissue was available to allow testing with NGS, and therefore time-matched tissue-biopsy samples were unavailable for validation of the cfDNA NGS results. Whilst the study protocol specified voluntary re-biopsy of patients prior to initiation of pembrolizumab, patients were reluctant to agree to further biopsies. When we looked at PCR-based targeted testing on tissue, this revealed deletions in *EGFR* exons 19 in two patients, but this testing may have failed to detect rarer EGFR mutations, such as p.E709K. In one case, ctDNA-NGS identified an ALK mutation in patient 18 that was not detected through tissue-genotyping. Neither method identified any BRAF mutations.

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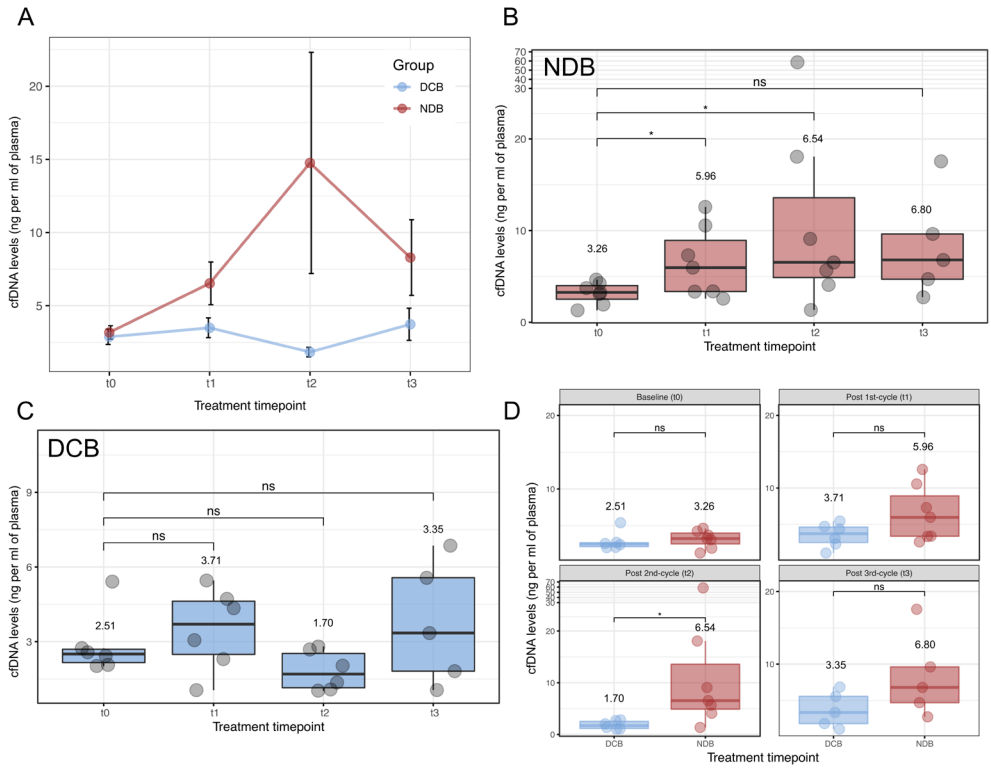

Figure S1 Preliminary assessment of the dynamics of cfDNA levels at baseline and at early treatment timepoints. (A) The levels of cfDNA of the DCB (n=6) and NDB (n=7) patients at each timepoint: baseline (t0), post 1[st]-cycle (t1), post 2[nd]-cycle (t2) and post 3[rd]-cycle (t3). DCB patients show similar levels of cfDNA at all timepoints, with a decreasing trend at t2. NDB patients show an overall increase in cfDNA at t1 and t2 and a decrease at t3. (B) Comparison of the cfDNA levels between DCB (n=6) and NDB (n=7) at each timepoint showed significantly higher levels in NDB patients at t2 only. (C,D) Comparison of the levels of cfDNA for each group of patients DCB (n=6) and NDB (n=7) across time showed a significant increase in cfDNA levels at t2 compared to t0 in NDB patients. cfDNA, cell-free DNA; NDB, non-durable benefit; DCB, durable clinical benefit.

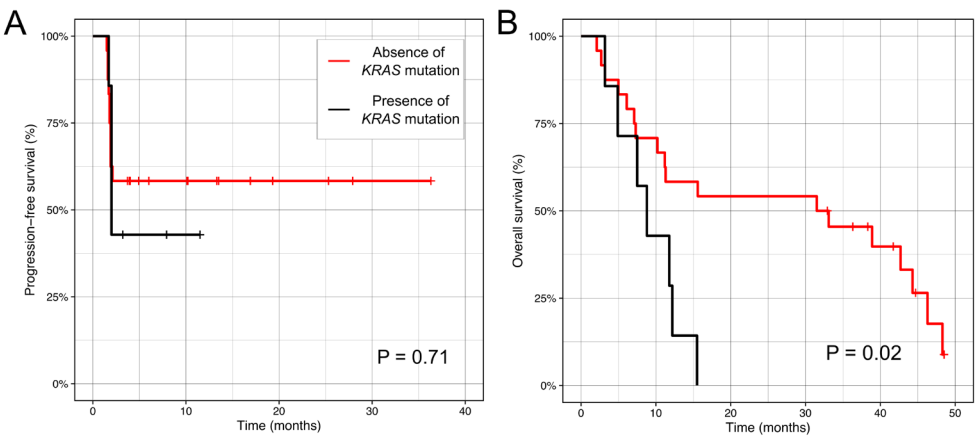

Figure S2 Survival analysis by *KRAS* mutation status at post 2[nd]-cycle of pembrolizumab. (A,B) Kaplan-Meier plots showed that patients carrying *KRAS* mutations at post 2[nd]-cycle (t2) had significantly lower OS compared to patients with no *KRAS* mutations (8.7 *vs.* 32.2 months, P=0.02). OS, overall survival.

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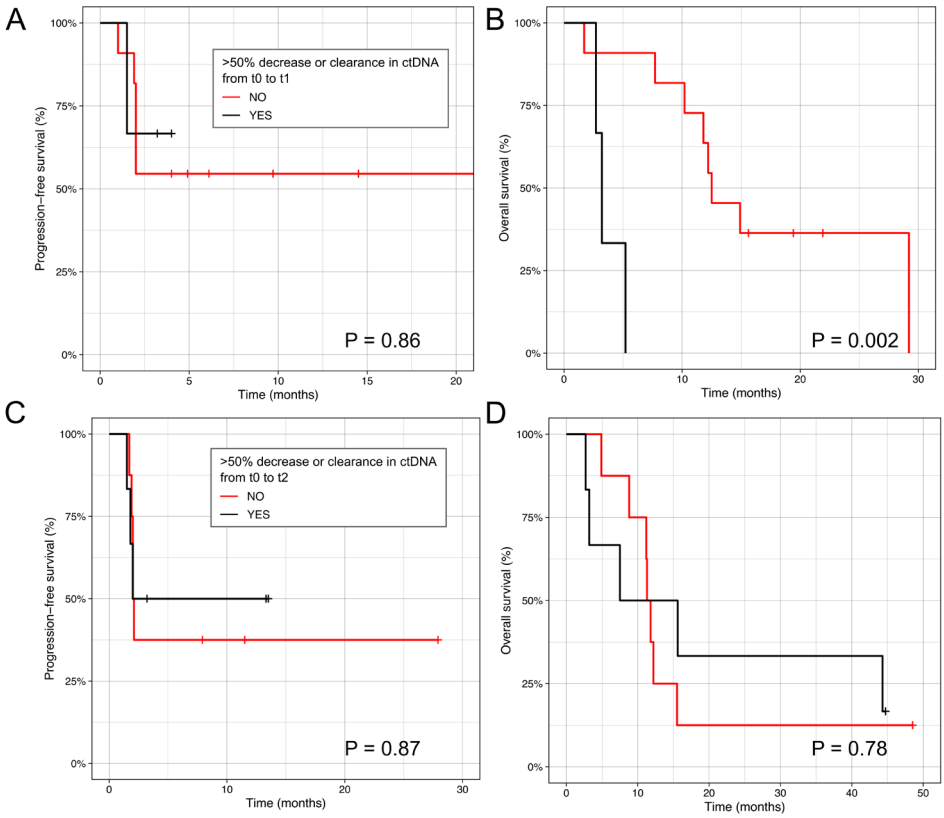

Figure S3 Kaplan-Meier plots show the difference in PFS and OS between patients presenting >50% decrease or clearance in ctDNA. (A,B) from baseline (t0) to post 1st-cycle (t1), or (C,D) from baseline (t0) to post 2nd-cycle (t2), compared to those who do not. Significance was only observed for OS between patients presenting >50% decrease or clearance in ctDNA from t0 to t1 and those who do not. However, due to the limited sample size (n=14), patients showing >50% decrease or clearance in ctDNA had a shorter OS than those showing <50% decrease or increase in ctDNA (3.2 *vs.* 12.5 months). Consequently, this result is considered non-valid and has been excluded. PFS, progression-free survival; OS, overall survival; ctDNA, circulating tumour DNA.

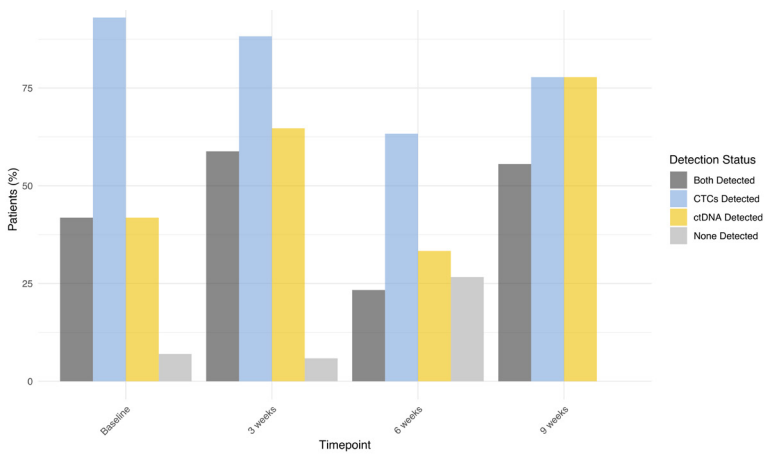

Figure S4 Distribution of biomarker detection status across treatment timepoints. The percentage of patients with detectable CTCs, ctDNA, both biomarkers, or neither biomarker is shown at baseline, 3-week, 6-week, and 9-week after treatment initiation. CTCs, circulating tumour cells; ctDNA, circulating tumour DNA.

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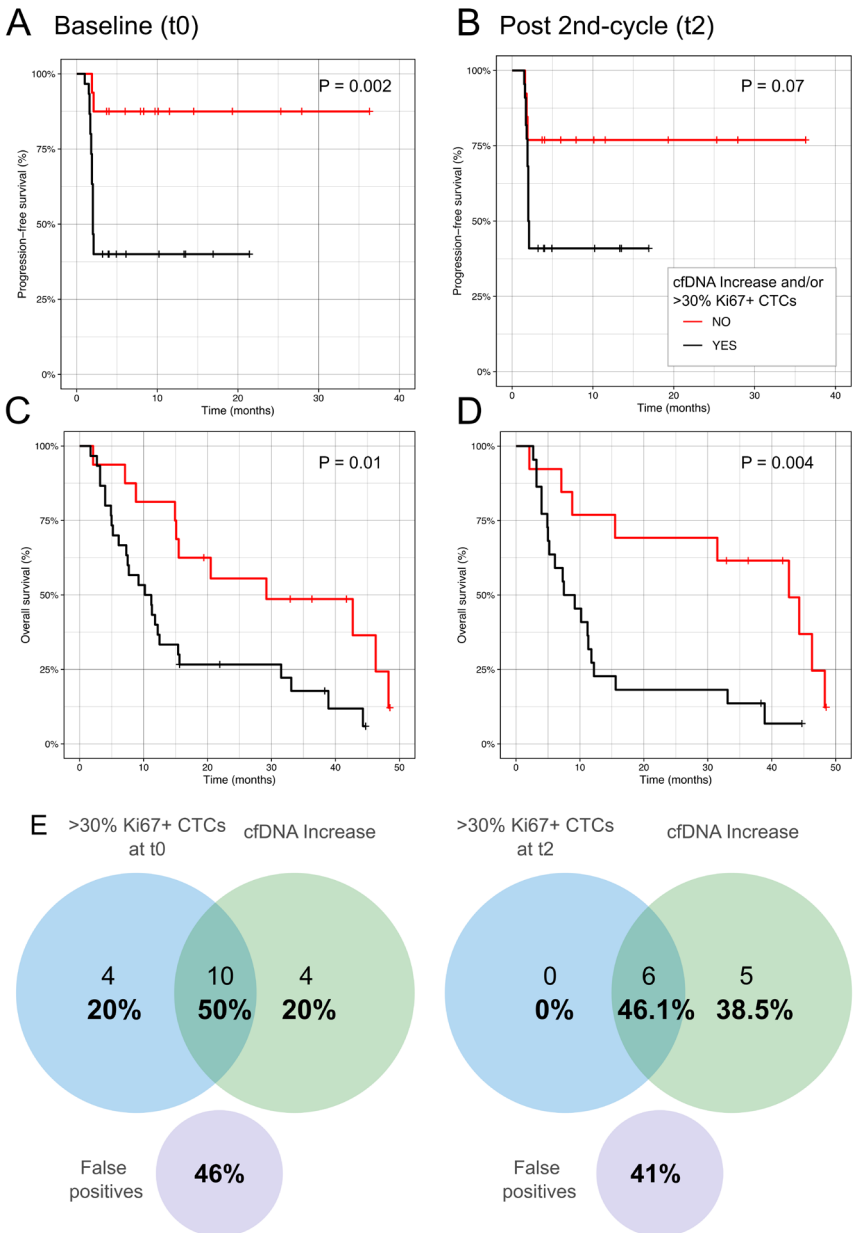

Figure S5 Predictive value of the combined assessment of cfDNA dynamics and Ki67-index of CTCs. (A-D) Kaplan-Meier plots of the combined effect of cfDNA dynamics (cfDNA increase or decrease) and >30% Ki67-positive (Ki67+) CTCs detected before treatment (t0) and after 2nd-cycle (t2) on PFS and OS. The plots show a significant difference in PFS and OS of patients presenting either or both markers compared to patients not presenting these markers (PFS: 2 *vs.* 9 months, P=0.002 for t0, 2.05 *vs.* 7.9 months, P=0.07 for t2, OS: 10.7 *vs.* 24.8 months, P=0.01 for t0, 8.35 *vs.* 36.3 months, P=0.004 for t2). (E) Venn diagrams showing the number and percentage of PD patients detected by either >30% Ki67+ CTCs or increase in cfDNA or both for each timepoints: before treatment (t0) and after the 2nd-cycle (t2). The purple circle indicates the number and percentage of SD/PR patients who had either >30% Ki67+ CTCs or increase in cfDNA or both and were therefore detected as PD (false positives). Although the combined sensitivity of these analyses increased to 90% for t0 and 84.6% for t2, the rate of false positives (i.e., true SD/PR patients classified as PD) was calculated at 46% for t0 and 41% for t2. Further evaluation is needed in a larger cohort of patients and at additional sequential timepoints to confirm this result. CTCs, circulating tumour cells; cfDNA, cell-free DNA; PFS, progression-free survival; OS, overall survival; PD, progression disease; SD, stable disease; PR, partial response.

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Table S1 List of somatic mutations covered in Horizon discoveries multiplex I cfDNA reference standard set

Gene	Variant	Coding sequence mutation	Expected allelic frequency (%)
EGFR	L858R	c.2573T>G	0.1
EGFR	ΔE746-A750	c.2235_2249del	0.1
EGFR	T790M	c.2369C>T	0.1
EGFR	V769-D770insASV	c.2300_2308dup	0.1
KRAS	G12D	c.35G>A	0.1
NRAS	Q61K	c.181C>A	0.1
NRAS	A59T	c.175G>A	0.1
PIK3CA	E545K	c.1633G>A	0.1

Table S2 Clinicopathological characteristics of our cohort of patients with non-small cell lung cancer

Variable	Number of patients (%)
RECIST v1.1 classification	
Partial response (PR)	2 (4.3)
Stable disease (SD)	24 (52.2)
Progression disease (PD)	20 (43.5)
Gender	
Male	38 (82.6)
Female	8 (17.4)
Smoking history	
Former	34 (73.9)
Current	7 (15.2)
Never	5 (10.9)
Histological subtype	
Adenocarcinoma	33 (71.7)
Squamous cell carcinoma	13 (28.3)
Performance status	
0	18 (39.1)
1	23 (50.0)
2	5 (10.9)

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Table S3 The amount of isolated cfDNA from each sample at baseline (t0), post-1st cycle (t1), post-2nd cycle (t2) and post-3rd cycle (t3) of treatment

Sample ID	Classification based on PFS	RECIST v.1.1	Timepoint	cfDNA (ng/mL of plasma)
1	NDB	PD	0	3.73
1	NDB	PD	1	3.34
1	NDB	PD	2	6.54
1	NDB	PD	3	2.75
2	NDB	PD	0	1.29
2	NDB	PD	1	2.58
2	NDB	PD	2	1.35
2	NDB	PD	3	4.7
3	DCB	SD	0	5.41
3	DCB	SD	1	5.46
3	DCB	SD	2	2.81
3	DCB	SD	3	6.86
4	NDB	SD	0	1.53
4	NDB	SD	2	1.02
5	DCB	SD	0	2.74
5	DCB	SD	2	2
5	DCB	SD	3	5.57
6	NDB	SD	0	2.46
6	NDB	SD	1	7.91
6	NDB	SD	2	0.69
7	NDB	PD	0	3.5
7	NDB	PD	2	2.3
8	NDB	SD	0	3.26
8	NDB	SD	1	7.3
8	NDB	SD	2	9.08
10	DCB	PR	0	2.58
10	DCB	PR	1	4.72
10	DCB	PR	2	2.04
10	DCB	PR	3	1.39
11	NDB	PD	0	5.59
11	NDB	PD	1	7.15
11	NDB	PD	2	11.15
12	NDB	PD	0	4.02
12	NDB	PD	1	2.83
12	NDB	PD	2	10.37
13	NDB	PD	0	2.88
13	NDB	PD	1	5.28
13	NDB	PD	2	11.53
14	NDB	PD	0	3.22
14	NDB	PD	2	3.65
15	NDB	PD	0	2.5
15	NDB	PD	2	2.92
16	DCB	SD	0	2
16	DCB	SD	2	2.02
17	NDB	PD	0	4.26
17	NDB	PD	1	10.55
17	NDB	PD	2	18.07
17	NDB	PD	3	17.56
18	NDB	PD	0	14.02
18	NDB	PD	2	15.98
18	NDB	PD	3	3.44
19	DCB	SD	0	1.85
19	DCB	SD	2	2.48
20	NDB	PD	0	4.13
20	NDB	PD	2	12.02
22	DCB	SD	0	1.68
22	DCB	SD	2	1.97
23	DCB	SD	0	2.43
23	DCB	SD	1	4.35
23	DCB	SD	2	1.08
23	DCB	SD	3	1.06
24	NDB	SD	0	3.1
24	NDB	SD	1	5.96
24	NDB	SD	2	5.67
24	NDB	SD	3	9.63
25	DCB	SD	0	2.68
25	DCB	SD	2	1.4
25	DCB	SD	3	0.77
26	NDB	PD	0	10.6
26	NDB	PD	1	11.53
27	NDB	PD	0	2.875
27	NDB	PD	2	1.85
28	DCB	SD	0	2.07
28	DCB	SD	1	3.06
28	DCB	SD	2	2.69
28	DCB	SD	3	3.35
29	DCB	SD	0	6.38
29	DCB	SD	2	5.21
29	DCB	SD	3	2.38
30	NDB	SD	0	3.67
30	NDB	SD	2	4.12
31	DCB	PR	0	2.03
31	DCB	PR	1	1.05
31	DCB	PR	2	1.36
32	NDB	SD	0	3.66
32	NDB	SD	2	2.98
33	NDB	PD	0	0.98
33	NDB	PD	2	2.5
34	NDB	SD	0	3.3
34	NDB	SD	1	4.5
34	NDB	SD	2	8.16
35	DCB	SD	0	3.37
35	DCB	SD	2	2.59
36	NDB	PD	0	3.42
36	NDB	PD	1	3.13
37	NDB	PD	0	4.65
37	NDB	PD	1	12.57
37	NDB	PD	2	58.5
37	NDB	PD	3	6.8
38	DCB	SD	0	3.78
38	DCB	SD	1	1.14
38	DCB	SD	3	8.875
39	DCB	SD	0	3.45
39	DCB	SD	1	7.92
39	DCB	SD	3	6.67
40	NDB	PD	0	1.94
40	NDB	PD	1	3.38
40	NDB	PD	2	4.09
41	DCB	SD	0	2.94
41	DCB	SD	3	0.91
42	NDB	PD	0	1.71
42	NDB	PD	1	1.58
42	NDB	PD	2	6.59
43	DCB	SD	0	3.59
43	DCB	SD	1	2.7
43	DCB	SD	3	4.76
44	NDB	PD	0	2.9
44	NDB	PD	1	2.62
45	DCB	SD	0	3.82
45	DCB	SD	1	2.73
46	NDB	SD	0	2.39
46	NDB	SD	1	2.21
47	DCB	SD	0	3.11
47	DCB	SD	1	1.29
47	DCB	SD	3	3.69
48	NDB	PD	0	4.26
48	NDB	PD	1	1.13

The classification of patients according to RESICT v1.1 criteria is designated, as well as based on their PFS. PR, partial response; SD, stable disease; PD, progression disease; PFS, progression-free survival.

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Table S4 The results of molecular analysis of tissue and liquid biopsies

Sample ID	Molecular analysis blood	Molecular analysis tissue		
	Oncomine lung cfDNA assay findings	EGFR (pos/neg)	ALK (pos/neg)	BRAF (pos/neg)
1	Not done	Neg	Neg	Neg
2	KRAS p.G12R, KRAS p.G12A	Neg	N/A	N/A
3		Neg	N/A	N/A
4		Neg	Neg	Neg
5		N/A	N/A	Neg
6	EGFR:p.E709K	N/A	N/A	N/A
7	EGFR p.L747_A750delinsP	Pos exon19	N/A	N/A
8	KRAS p.G12C,TP53 p.R282W	Neg	Neg	N/A
10	TP53 p.G245S	N/A	N/A	N/A
11	KRAS:p.G12C	Neg	Neg	Neg
12		Neg	Neg	N/A
13	EGFR:p.E709K	Neg	Neg	N/A
14		N/A	N/A	N/A
15	TP53 p.R273H	N/A	N/A	N/A
16	EGFR p.E709K	Neg in tissue, Pos exon 21 blood	Neg	Neg
17		Neg	Neg	N/A
18	EGFR p.E709K,EGFR p.L747_P753delinsS, TP53 p.R248Q, ALK p.I1171TfsTer15	Pos exon19	N/A	N/A
19	EGFR p.E709K	N/A	N/A	N/A
20	PIK3CA:p.E542K, KRAS:p.G13C	Neg	Neg	Neg
22		Neg	Neg	N/A
23		N/A	N/A	N/A
24	Not done	Neg	Neg	N/A
25	KRAS p.Q61L, TP53 p.Y220C, TP53 p.G245D	Neg	Neg	Neg
26	TP53:p.H179R,TP53:p.R158L,TP53:p.V157F	N/A	N/A	N/A
27		Neg	Neg	Neg
28		Neg	Neg	N/A
29	KRAS:p.Q61H, TP53:p.G154V, EGFR p.K745N	Neg	Neg	N/A
30		Neg	borderline pos (inconclusive)	N/A
31		Neg	Neg	N/A
32		N/A	N/A	N/A
33	Not done	N/A	N/A	N/A
34	MAP2K1:p.P124L	Neg	Neg	Neg
35		Neg	Neg	N/A
36		N/A	N/A	N/A
37		N/A	N/A	N/A
38	TP53 p.R282W, EGFR:p.E709K, TP53 p.T125=C>T	Neg	Neg	Neg
39	KRAS:p.G13C	Neg	Neg	N/A
40	KRAS p.G12R	Neg	Neg	N/A
41	EGFR:p.E709K	Neg	N/A	Neg
42		Neg	Neg	Neg
43	TP53:p.R248Q, TP53:p.R248W, TP53:p.R175H, TP53:p.R248Q, TP53:p.H179R	Neg	Neg	Neg
44		N/A	N/A	N/A
45		N/A	N/A	N/A
46	EGFR:p.E709K,TP53:p.M237I,TP53:p.Y220C, TP53:p.Y205C	N/A	N/A	N/A
47	TP53:p.R273H	Neg	Neg	Neg
48	EGFR:p.E709K	Neg	Neg	Neg

In tissue biopsies, PCR-based targeted molecular testing was performed for the detection of EGFR and BRAF mutations, and FISH for the detection of ALK rearrangements.

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Table S5 Multivariate Cox proportional hazard models were constructed to evaluate the effect of each variable measured at post 1st-cycle (t1) on either PFS or OS

Variable	PFS				OS			
	HR	Lower 95% CIs	Upper 95% CIs	P value	HR	Lower 95% CIs	Upper 95% CIs	P value
Age (years)	1.014	0.9503	1.081	0.681	1.028	0.9755	1.084	0.301
Gender (male)	1.511	0.3191	7.154	0.603	1.556	0.5056	4.786	0.441
cfDNA (ng/mL)	1.165	0.9488	1.43	0.145	1.192	1.0118	1.404	0.036
CTCs								
Presence	0.2276	0.03023	1.714	0.151	1.32	0.2154	8.088	0.764
Number of CTCs	1.001	0.9989	1.003	0.345	1.001	0.999	1.003	0.286
PDL1+ CTCs	1.001	0.9987	1.003	0.4	1.001	0.9989	1.003	0.323
Percentage PD-L1+ CTCs	0.9828	0.9637	1.002	0.0823	0.9828	0.9659	1	0.05
PDL1- CTCs	1.026	0.9958	1.056	0.0931	1.016	0.9888	1.043	0.257
Percentage PD-L1– CTCs	1.005	0.9867	1.024	0.58	1.021	1.0042	1.039	0.0149
Ki67+ CTCs	1.002	0.998	1.005	0.394	1.002	0.9985	1.005	0.271
Percentage Ki67+ CTCs	0.9967	0.9808	1.013	0.684	0.9828	0.9659	1	0.05
Ki67– CTCs	1.003	0.9974	1.009	0.285	1.003	0.997	1.009	0.335
Percentage Ki67– CTCs	0.9971	0.984	1.01	0.662	1.021	1.0042	1.039	0.0149
>30% Ki67+ CTCs	0.8258	0.2459	2.773	0.757	1.959	0.7068	5.43	0.196
ctDNA								
Mutation identified	0.4077	0.09081	1.83	0.242	0.7716	0.2355	2.528	0.668
Number of mutations	0.6576	0.282	1.533	0.332	0.8888	0.5024	1.573	0.686
Allele molecular frequency (%)	1.084	0.8502	1.381	0.516	1.158	0.9378	1.429	0.173
Presence of KRAS	0.9051	0.1793	4.568	0.904	1.9307	0.4351	8.567	0.387
Number of KRAS	0.9051	0.1793	4.568	0.904	1.9307	0.4351	8.567	0.387
KRAS G12_G13	0.9051	0.1793	4.568	0.904	1.9307	0.4351	8.567	0.387
Presence of EGFR	0.7761	0.09089	6.628	0.817	0.404	0.07311	2.233	0.299
Number of EGFR	0.7761	0.09089	6.628	0.817	0.404	0.07311	2.233	0.299
Presence of TP53	0.5478	0.1131	2.653	0.455	0.4816	0.1411	1.644	0.243
Number of TP53	0.8208	0.3896	1.729	0.604	0.8916	0.4856	1.637	0.711
Combined markers (<50%-decrease/increase in ctDNA and/or >30% Ki67+ CTCs)	3.1255	0.3662	26.676	0.298	0.9826	0.2888	3.343	0.978

The variable and unit are indicated for each analysis. The HR along with the 95% confidence intervals and P value are designated. Red bold: P value <0.05 and HR >1, Black bold: P value <0.05 but HR ~1. PFS, progression-free survival; OS, overall survival; HR, hazard ratio.

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