Document downloaded from http://www.elsevier.es, day 10/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Supplementary Table 1. Assays used in the KRAS mutation analysis in plasma.

***KRAS* Mutation**	**Assay**
p.G12C c.34C>T	AH0JEUD-KRAS_516
p.G12V c.35G>T	AHX1IHY-KRAS_520
p.G12A c.35G>C	AHPAVDP-KRAS_522
p.G12R c.34G>C	AHMSYXY-KRAS_518
p.G12D c.35G>A	AH6R5PI-KRAS_521
p.G13C C.37G>T	AHRSRP5-KRAS_527
p.G13D c.38G>A	AHD2BW0-KRAS_532
p.G12F and p.G12E	Custom assays using Custom TaqMan® Assay Design Tool (Thermo Fisher Scientific)

Document downloaded from http://www.elsevier.es, day 10/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Supplementary Table 2. Plasma/tumor biopsy group.

	Plasma/Tumor biopsy group (51 biopsies /49 patients)
Age, median (range)*	60 (45-82)
Sex, n (%)*	
Male	34 (69%)
Female	15 (31%)
Smoking status, n (%)*	
Never	4 (8%)
Former	13 (27%)
Active	32 (65%)
Number of biopsies per patient, n (%)	
1 biopsy	47 (96%)
2 biopsies	2 (4%)
Disease extension, n (%)**	
Limited to thorax	14 (27%)
Extrathoracic	37 (73%)
Number of metastatic locations, n (%)**	
0	5 (10%)
1	17 (33%)
2	12 (23%)
3	6 (12%)
4	5 (10%)
5	4 (8%)
6	1 (2%)
8	1 (2%)
Liver metastases, n (%)**	
No	41 (80%)
Yes	10 (20%)
Type of biopsy and *KRAS* mutation in tissue, n (%)	
Codon 12	49 (96%)
Gly12Cys	22 (43%)
Gly12Val	9 (17%)
Gly12Ala	7 (14%)
Gly12Asp	6 (12%)
Gly12Phe	2 (4%)
Gly12Arg	2 (4%)
Gly12Glu	1 (2%)
Codon 13	2 (4%)
Gly13Cys	2 (4%)
Days between biopsy-plasma, median (range)	19 (-53 – 94)

*n=2 (patients with more than one biopsy were counted only 1 time.

**At the moment of tumor biopsy

Document downloaded from http://www.elsevier.es, day 10/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Supplementary Table 3. Treatment monitoring group.

	Treatment monitoring group (52 treatment lines /32 patients)
Age, median (range)*	59 (51-82)
Sex, n (%)*	
Male	23 (72%)
Female	9 (28%)
Smoking status, n (%)*	
Never	2 (6%)
Former	9 (28%)
Active	21 (66%)
Number of treatment lines per patient, n (%) *	
1	19 (60%)
2	8 (25%)
3	3 (9%)
4	2 (6%)
Treatment line, n (%)	
No treatment	5 (10%)
1	24 (46%)
2	13 (25%)
3	7 (13%)
4	2 (4%)
5	1 (2%)
Treatment type, n (%)	
No treatment	5 (10%)
Carboplatin – Pemetrexed	12 (22%)
Cisplatin – Pemetrexed	9 (16%)
Docetaxel	5 (10%)
Nivolumab	4 (8%)
Vinorelbine	3 (6%)
Abemaciclib**	3 (6%)
Carboplatin - Gemcitabine	2 (4%)
Carboplatin - Vinorelbine	1 (2%)
Pemetrexed	1 (2%)
Erlotinib	1 (2%)
Paclitaxel	1 (2%)
Docetaxel – Custirsen**	1 (2%)
Carboplatin – Paclitaxel – Atezolizumab**	1 (2%)
Carboplatin – Paclitaxel - RT	1 (2%)
Cisplatin – Vinorelbine - RT	1 (2%)
RT	1 (2%)
Disease stage, n (%)***	
III	3 (6%)
IVa	10 (19%)
IVb	1 (1%)
IVc	38 (74%)

Document downloaded from http://www.elsevier.es, day 10/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Number of metastatic locations, n (%)**	
0	3 (6%)
1	14 (27%)
2	14 (27%)
3	11 (21%)
4	5 (9%)
5	3 (6%)
6	1 (2%)
7	1 (2%)
Liver metastases, n (%)**	
No	46 (89%)
Yes	6 (11%)
RECIST radiological response, n (%)	
Disease progression	26 (50%)
Stable disease	15 (29%)
Partial response	11 (21%)

* n=20 (patients with more than one analyzed treatment line were counted only 1 time)
** Clinical trial
*** At the beginning of the studied treatment line
RT: Radiotherapy; RECIST: Radiological Evaluation Criteria In Solid Tumors

Document downloaded from http://www.elsevier.es, day 10/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Supplementary Table 4. Details on analyzed treatment lines of cases in the treatment monitoring group.

Line of treatment	Therapy	Days between plasma predicting RESP and CT	Days between plasma correlating RESP and CT	Days between plasma predicting PROG and CT	Days between plasma correlating PROG and CT	PFS (months)
Patient #1 / Analyzed treatment lines: 1 / Follow-up: 3.25 months						
2nd line	Docetaxel	No RESP	No RESP	No plasma	26	1.87
Patient #3 / Analyzed treatment lines: 1 / Follow-up: 8.31 months						
2nd line	Docetaxel	54	11	No plasma	20	6.24
Patient #5 / Analyzed treatment lines: 2 / Follow-up: 18.43 months						
1st line	BSC	No RESP	No RESP	No plasma	16	8.19
2nd line	VRL	No RESP	No RESP	No plasma	16	2.46
Patient #9 / Analyzed treatment lines: 4 / Follow-up: 30.29 months						
1st line	CBDCA - Pem	No RESP	No RESP	120	13	12.81
2nd line	BSC	No RESP	No RESP	No plasma	4	1.47
3rd line	Abemaciclib*	No RESP	No RESP	No plasma	10	3.22
4th line	VRL	No RESP	No RESP	No prediction of PROG	9	1.77
Patient #12 / Analyzed treatment lines: 2 / Follow-up: 14.78 months						
2nd line	CBDCA -Pem	42	7	No plasma	14	5.03
3rd line	Abemaciclib*	No RESP	No RESP	No prediction of PROG	11	1.25
Patient #13 / Analyzed treatment lines: 2 / Follow-up: 17.12 monts						
2nd line	BSC	No RESP	No RESP	No plasma	7	5.5
3rd line	CBDCA - Gem	59	3	65	23	9.03
Patient #15 / Analyzed treatment lines: 4 / Follow-up: 11.93 monts						
1st line	CBDCA - VRL	No plasma	No RESP	No plasma	16	4.14
2nd line	Pem	No RESP	No RESP	No PROG prediction	3	1.77
3rd line	CBDCA - Gem	No RESP	No RESP	13	8	1.81
4th line	Erlotinib*	No RESP	No RESP	No plasma	7	1.12
Patient #17 / Analyzed treatment lines: 1 / Follow-up: 1.61						
1st line	CBDCA - Pem	No RESP	No RESP	No plasma	4	1.02
Patient #19 / Analyzed treatment lines: 1 / Follow-up: 14.39 months						
1st line	CBDCA – VRL + RT	No plasma	No plasma	No plasma	18	5.85
Patient #22 / Analyzed treatment lines: 3 / Follow-up: 53.39 months						
1st line	Cis - Pem	No plasma	16	No plasma	9	6.87
2nd line	RT	No plasma	6	No plasma	15	18.92
3rd line	Paclitaxel	67	3	No plasma	No plasma	19.06
Patient #24 / Analyzed treatment lines: 1 / Follow-up: 3.48 months						
1st line	CBDCA - Pem	No RESP	No RESP	No plasma	2	2
Patient #25 / Analyzed treatment lines: 1 / Follow-up: 13.08 months						
5th line	Nivolumab	54	2	No plasma	No plasma	8.08
Patient #26 / Analyzed treatment lines: 2 / Follow-up: 4.34 months						
1st line	Cis - Pem	No RESP	No RESP	No plasma	7	1.61
2nd line	Docetaxel	No RESP	No RESP	No plasma	5	1.05
Patient #27 / Analyzed treatment lines: 1 / Follow-up: 8.94 months						
1st line	Cis - Pem	No RESP	No RESP	No plasma	10	4.24

Document downloaded from http://www.elsevier.es, day 10/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Patient #28 / Analyzed treatment lines: 3 / Follow-up: 19.29						
1st line	CBDCA - Pem	No RESP	No RESP	No PROG prediction	10	4.96
2nd line	BSC	No RESP	No RESP	54	27	7.5
3rd line	Nivolumab	No RESP	No RESP	No PROG prediction	6	2.5
Patient #29 / Analyzed treatment lines: 1 / Follow-up: 3.58 months						
1st line	CBDCA - Pem	No RESP	No RESP	No plasma	No concordance with PROG	1.74
Patient #30 / Analyzed treatment lines: 1 / Follow-up: 1.58 months						
1st line	CBDCA - Pem	No RESP	No RESP	No plasma	0	1.51
Patient #34 / Analyzed treatment lines: 1 / Follow-up: 11.86 months						
1st line	CBDCA - Pem	No plasma	No plasma	No plasma	8	9.17
Patient #35 / Analyzed treatment lines: 1 / Follow-up: 17.71 months						
1st line	CBDCA - Pem	No respuesta	No respuesta	No plasma	2	12.35
Patient #36 / Analyzed treatment lines: 1 / Follow-up: 40.41 months						
1st line	Cis - VRL + RT	66	3	No PROG	No PROG	40.21
Patient #37 / Analyzed treatment lines: 1 / Follow-up: 5.29 months						
1st line	CBDCA - Pem	No plasma	8	19	5	4.40
Patient #39 / Analyzed treatment lines: 3 / Follow-up: 14.72 months						
1st line	Cis - Pem	14	7	60	32	7.72
2nd line	Docetaxel	No RESP	No RESP	47	13	1.51
3rd line	VRL	No RESP	No RESP	17	4	1.97
Patient #47 / Analyzed treatment lines: 1 / Follow-up: 6.01 months						
1st line	BSC	No RESP	No RESP	No plasma	14	2.29
Patient #49 / Analyzed treatment lines: 2 / Follow-up: 27.8 months						
1st line	CBDCA - Pem	No plasma	No plasma	No PROG prediction	15	11.47
2nd line	Nivolumab	No RESP	No RESP	90	41	3.42
Patient #50 / Analyzed treatment lines: 2 / Follow-up: 20.14 months						
1st line	Cis – Pem	No RESP	No RESP	No PROG prediction	11	1.91
2nd line	Nivolumab	No RESP prediction	No concordance with RESP	70	No plasma	16.13
Patient #51 / Analyzed treatment lines: 2 / Follow-up: 11.24 months						
2nd line	Docetaxel – Custirsen*	No RESP	No RESP	No plasma	1	3.02
3rd line	Abemaciclib*	19	9	21	23	4.86
Patient #52 / Analyzed treatment lines: 2 / Follow-up: 22.77						
1st line	Cis - Pem	28	3	40	23	6.18
2nd line	Docetaxel	31	10	No plasma	No plasma	6.64
Patient #60 / Analyzed treatment lines: 1 / Follow-up: 17.28 months						
1st line	CBDCA – paclitaxel – atezolizumab*	17	4	No PROG	No PROG	13.31
Patient #61 / Analyzed treatment lines: 1 / Follow-up: 8.05 months						
1st line	CBDCA - Pem	20	4	No PROG	No PROG	7.24
Patient #62 / Analyzed treatment lines: 1 / Follow-up: 9.89 months						
1st line	Cis - Pem	57	15	No plasma	No plasma	4.83
Patient #63 / Analyzed treatment lines: 1 / Follow-up: 12 months						
1st line	Cis - Pem	33	No plasma	No PROG	No PROG	11.30

Document downloaded from http://www.elsevier.es, day 10/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

RESP, response; PROG, progression; CT, computed tomography; BSC, Best supportive care; CBDCA, carboplatin; Cis, cisplatin; Pem, pemetrexed; VRL, vinorelbine; Gem, gemcitabine; RT, radiotherapy.

* Clinical trial

Document downloaded from http://www.elsevier.es, day 10/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Supplementary Table 5. Bivariate analysis between *KRAS* mutational load dynamics and radiological response and progression prediction.

	% Response predicion	OR (CI 95%)	% Progression predicion	OR (CI 95%)
Liver metastases: yes vs no	100 vs 92.9	0.93 (0.8-1.1)	75 vs 60	2 (0.2-24.1)
Disease limited to thorax: yes vs no	100 vs 90.9	1.1 (0.9-1.3)	50 vs 64.7	1.83 (0.9-34.8)
Metastatic locations: ≤1 vs >1	6.7 vs 100	0.66 (0.3-1.4)	50 vs 69.2	2.25 (0.3-16.4)
GE: 1st vs 2nd and 3rd tertiles	75 vs 100	0.75 (0.4-1.3)	100 vs 50	2 (1.1-3.5)

OR, odds ratio; CI, confidence interval; GE, genomic equivalents.