

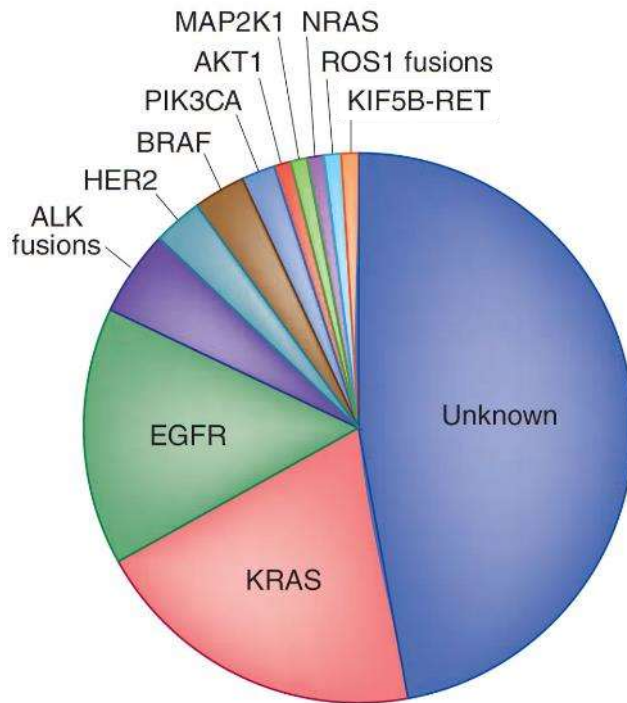
Detection of somatic mutations in plasma allows for non-invasive real time therapy response monitoring of lung cancer patients

José Carlos Machado

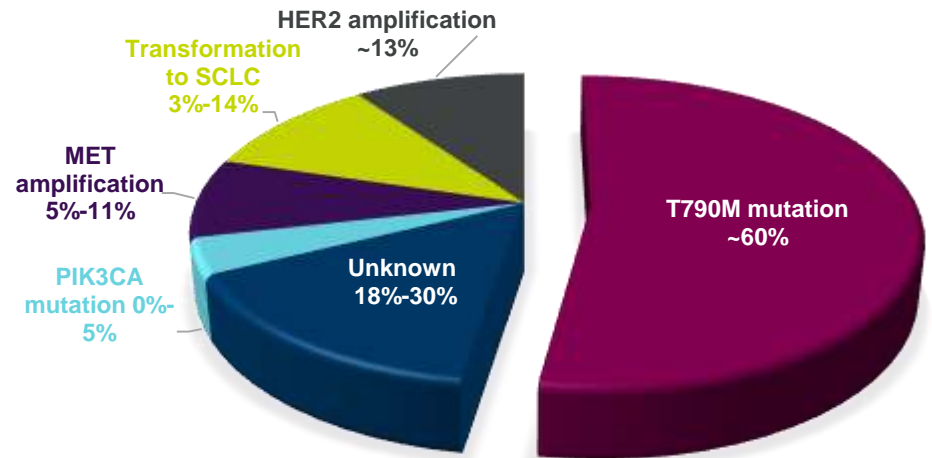


Screening lung cancer clinically relevant alterations

Diagnosis



Progression



EGFR T790M mutation testing should be performed in patients with NSCLC who have progressed on 1st/2nd generation EGFR TKIs

Patient diagnosed with
EGFR–sensitising mutation positive NSCLC

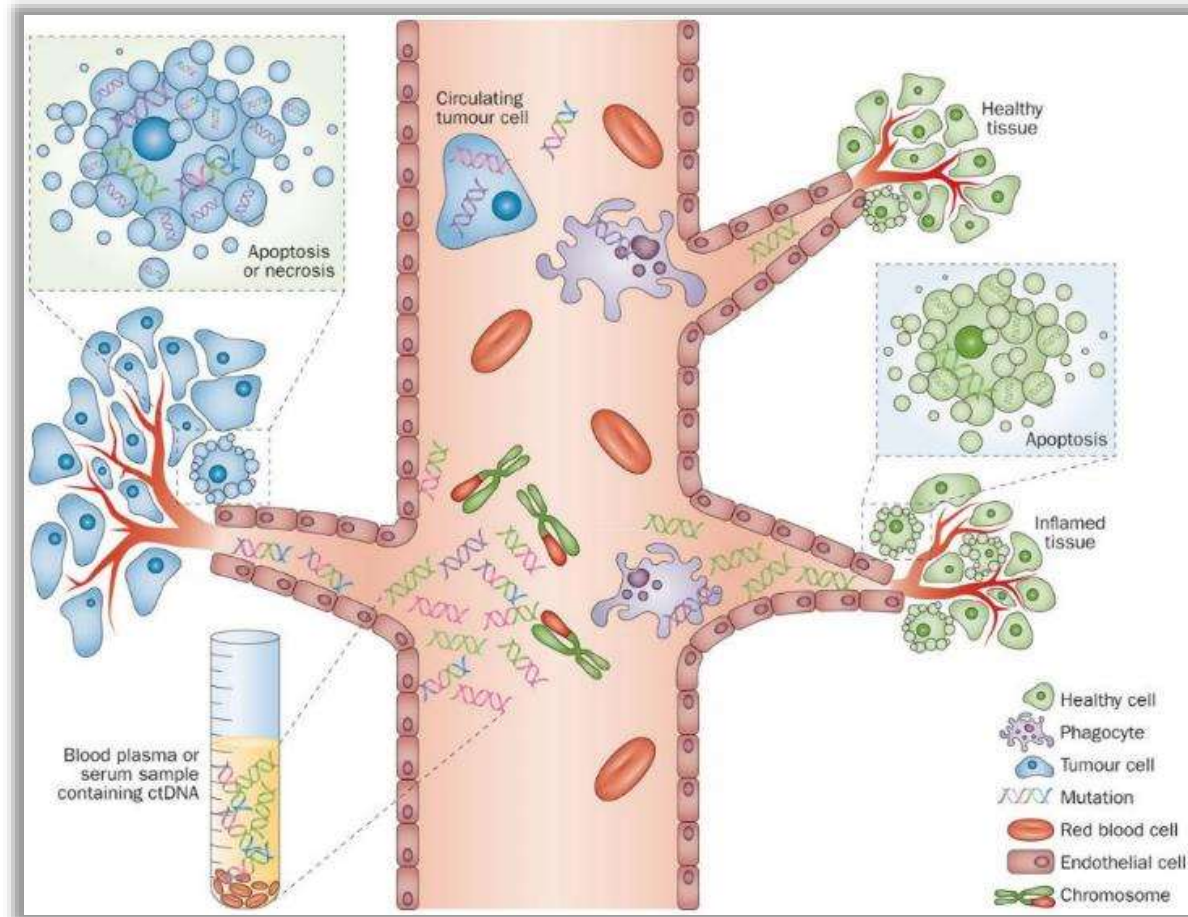


1st/2nd generation EGFR TKI



EGFR T790M mutation testing should be performed in EGFR mutant advanced NSCLC patients that have progressed on treatment with 1st / 2nd generation EGFR TKIs

Liquid biopsy - concept

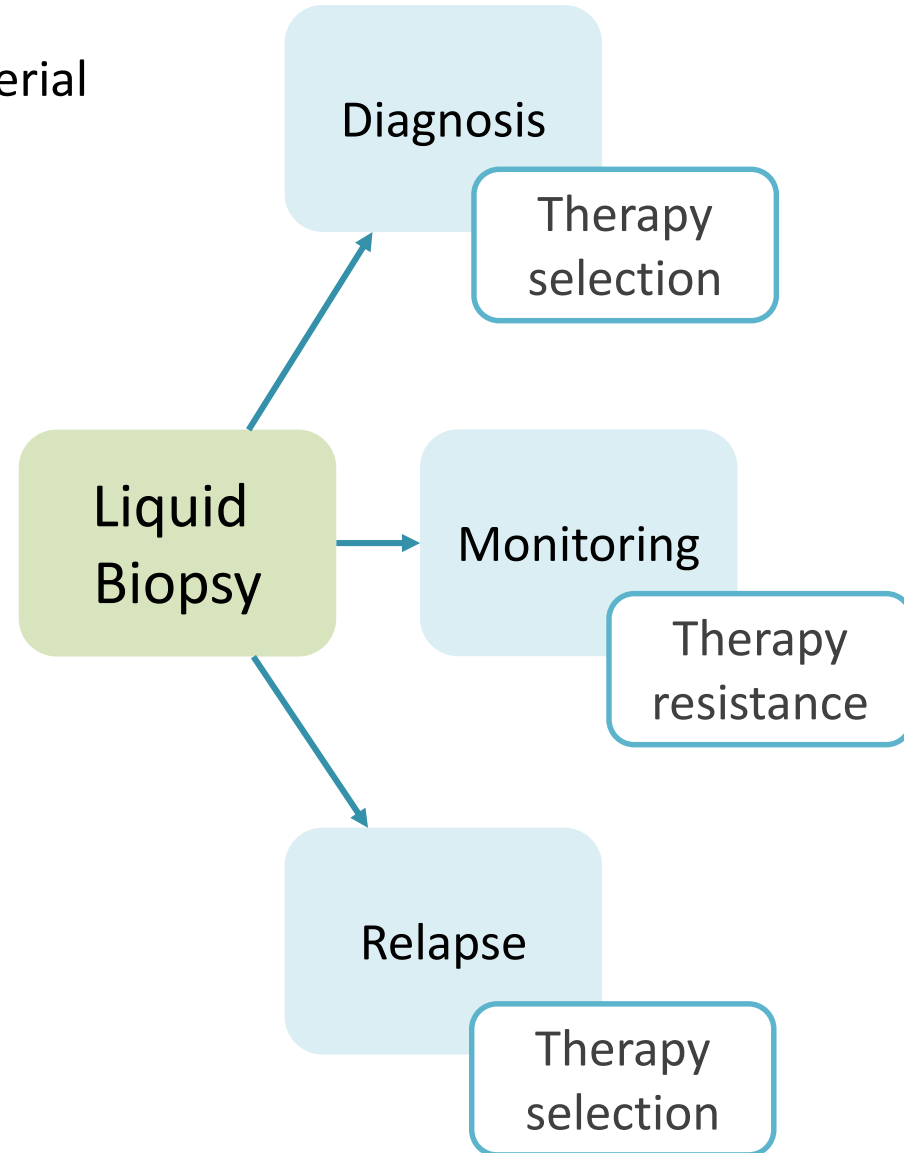
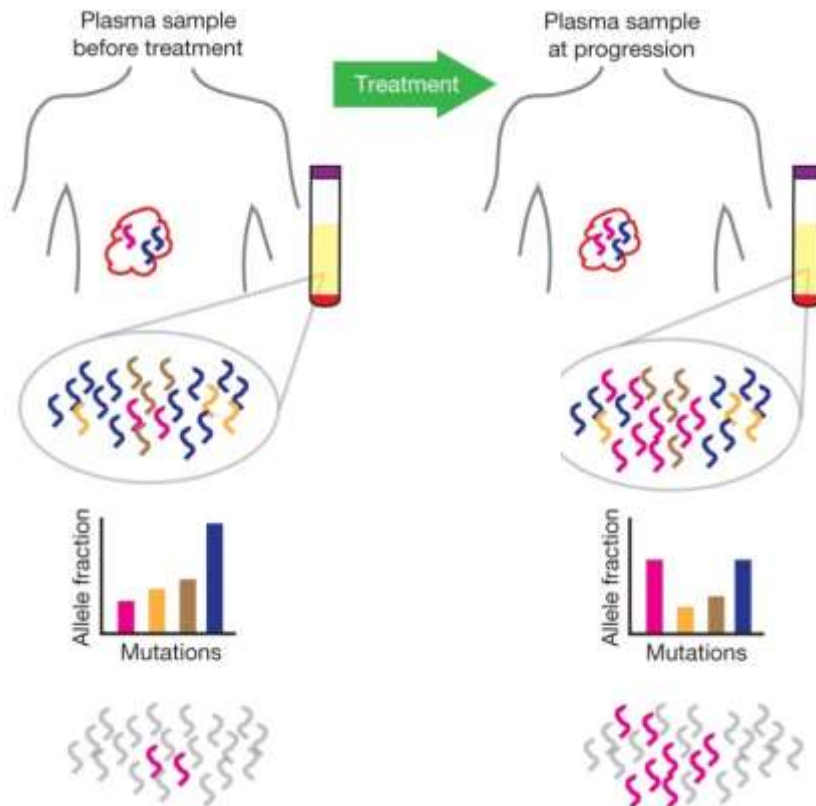


Liquid biopsies

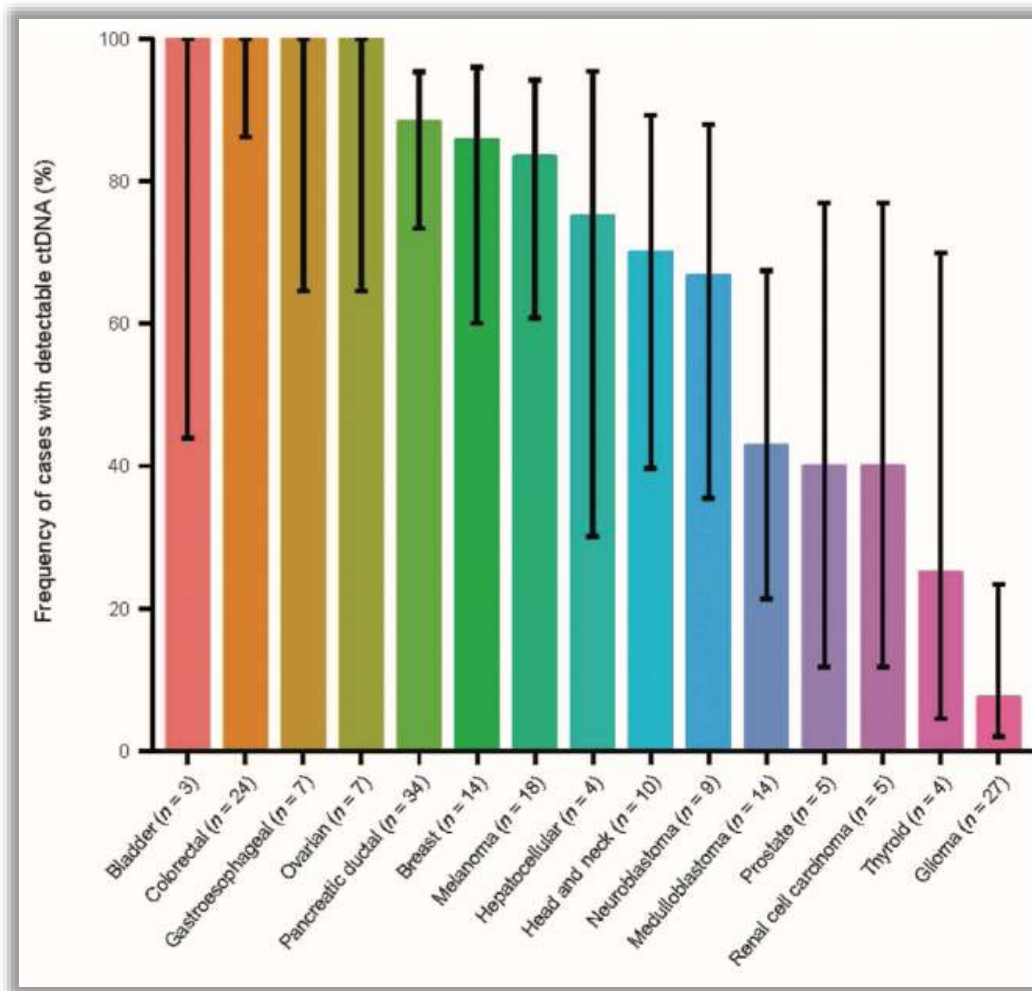
Potential advantages

Overcomes low availability of tumour material

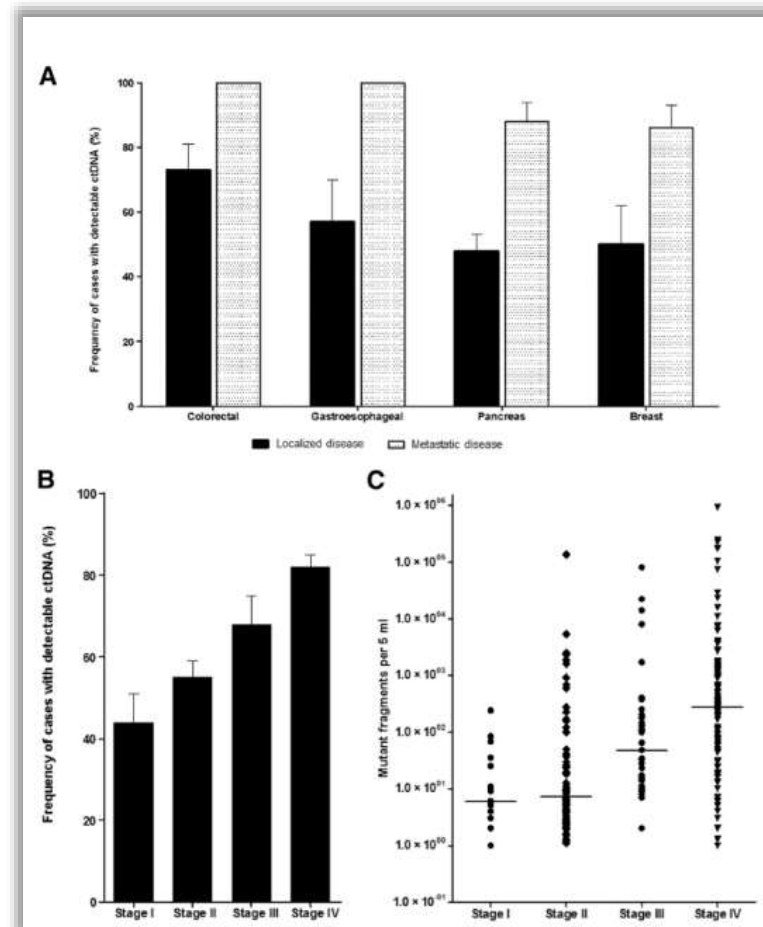
Representative of tumour heterogeneity



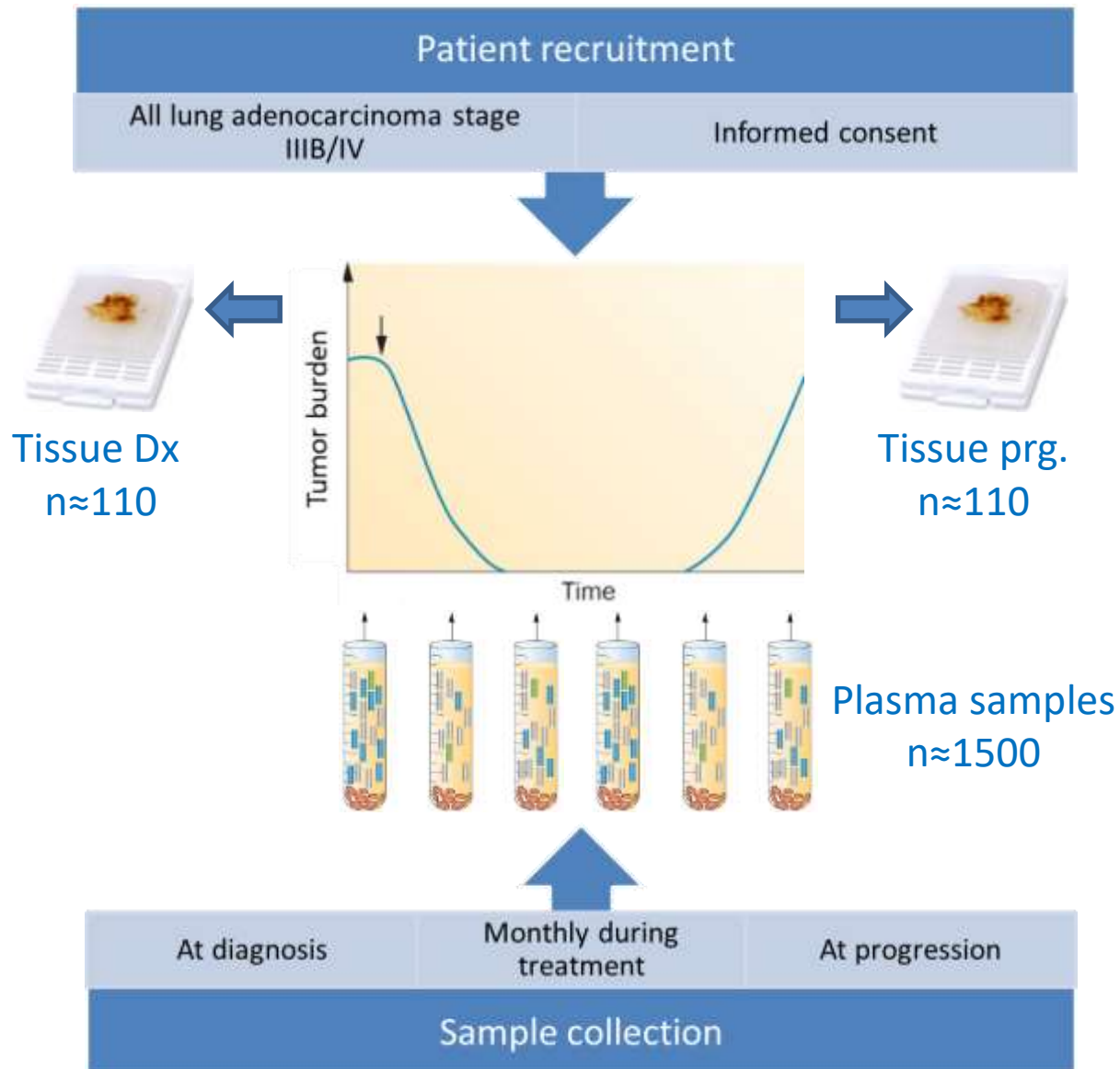
ctDNA in different cancers



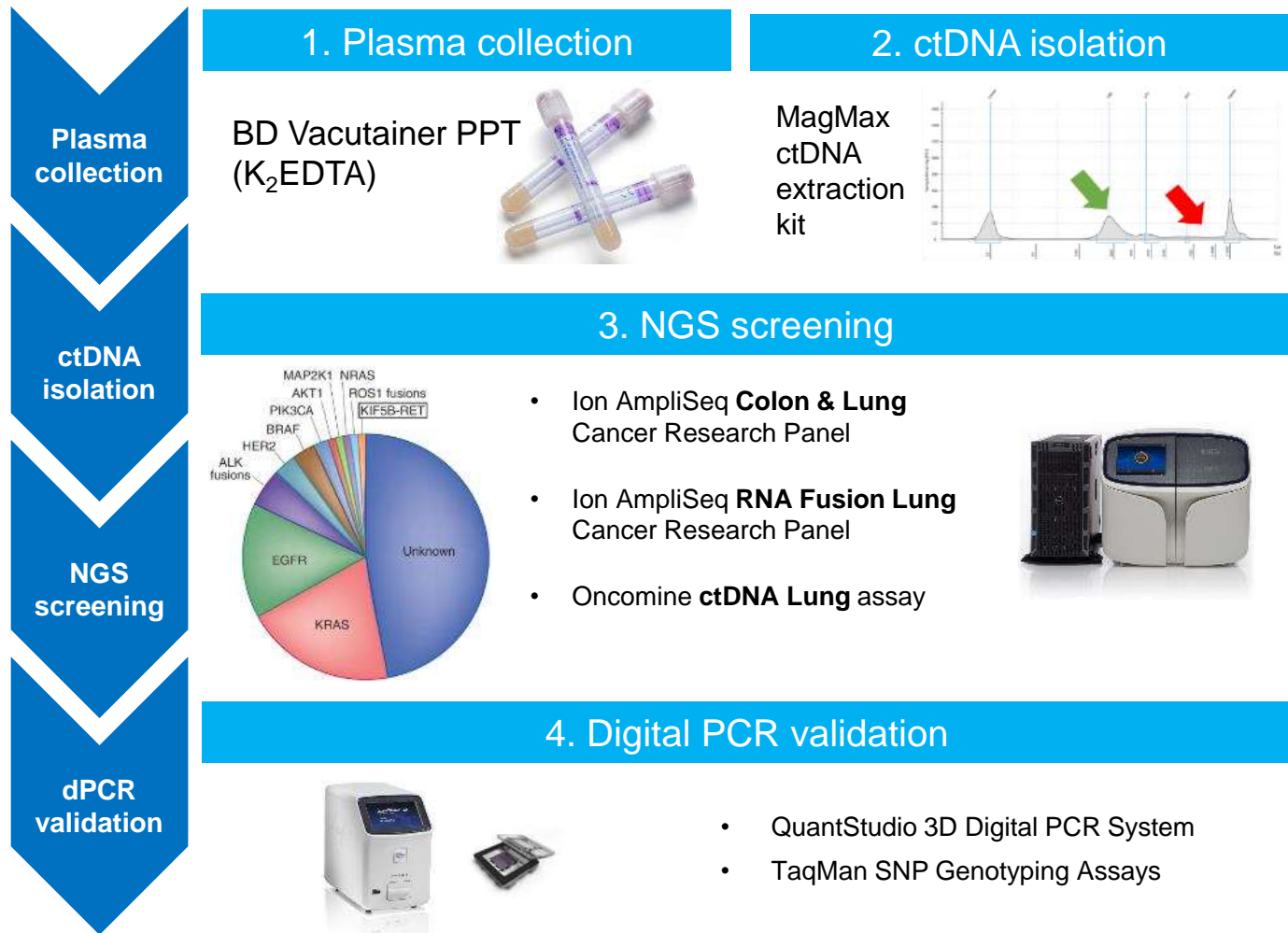
Irrespective of cancer type, ctDNA correlates with disease stage



Prospective study



Validated workflow



Confident detection variants at 0,1% AF

NGS

Digital PCR

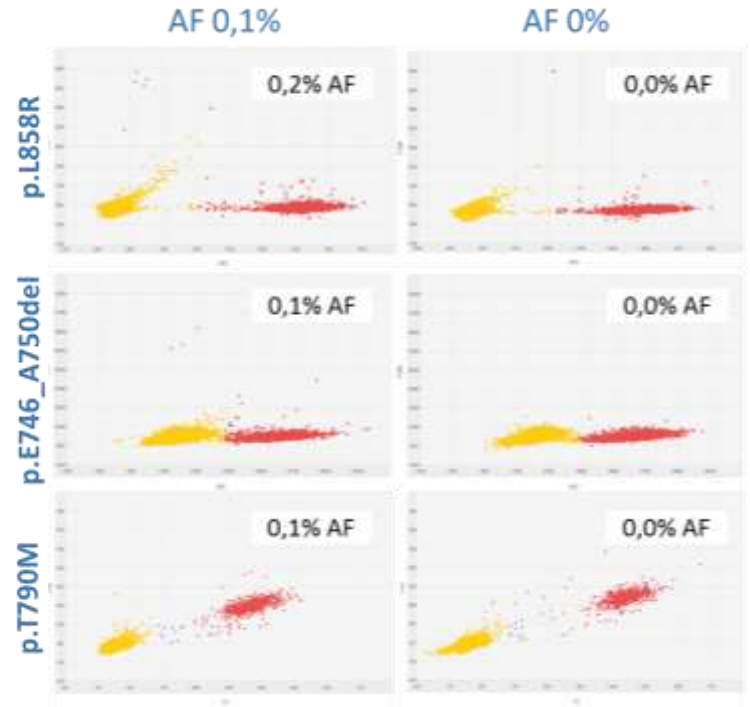
Sensitivity Specificity

- Oncomine cfDNA assay 97,2 100

AF (%)	Variant	AF (%)
0,1	EGFR p.L858R	0,071
	EGFR ΔE746 - A750	0,144
	EGFR p.T790M	0,144
	EGFR p. V769 - D770insASV	0,164
	KRAS p.G12D	0,130
	PIK3CA p. E545K	0,109
0	EGFR p.L858R	0,000
	EGFR ΔE746 - A750	0,000
	EGFR p.T790M	0,000
	EGFR p. V769 - D770insASV	0,000
	KRAS p.G12D	0,000
	PIK3CA p. E545K	0,000

Pearson Correlation

Oncomine cfDNA 0,95



Pearson Correlation

dPCR 0,99

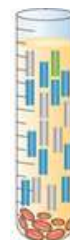
cfDNA can be used in the absence of FFPE

Case	Gene	Variants		Tissue (AF %)	Plasma (AF %)	Observations
		Genomic	Protein	Colon & Lung	Oncomine cfDNA	
107	EGFR	c.2240_2257del18	p.Leu747_Pro753delinsSer	67,2	5,5	-
	EGFR	c.2369C>T	p.Thr790Met	ND	1,25	dPCR tissue 0,6% AF
93	EGFR	c.2573T>G	p.Leu858Arg	31,3	0,18	-
	EGFR	c.2235_2249del15	p.Glu746_Ala750del	ND	0,11	dPCR tissue 0% AF
106	EGFR	c.2248_2276del29ins5	p.Ala750_Ile759delinsSerLys	84,5	ND	cfDNA highly degraded
74	EGFR	c.2236_2250del15	p.Glu746_Ala750del	11,1	0,27	-
	KRAS	c.182A>G	p.Gln61Arg	0,38	0,07	-
104	KRAS	c.35G>C	p.Gly12Ala	50,6	ND	dPCR confirmed both
15	KRAS	c.182A>G	p.Gln61Arg	8,8	0,43	-
	TP53	c.461G>T	p.Gly154Val	24,7	0,71	-
	STK11	c.597G>T	p.Glu199Asp	12,8	0,53	-
80	BRAF	c.1799T>A	p.Val600Glu	50,4	9,9	-
	TP53	c.476C>G	p.Ala159Gly	39,2	4,9	-
8	WT	-	-	-	-	-
9	WT	-	-	-	-	-
10	WT	-	-	-	-	-



Sensitivity 90%
(95% CI 80%-96%)

Specificity 100%



Sensitivity 85%
(95% CI 74%-93%)

Specificity 100%

Follow up results – Case 74

Male, 59y, ex-smoker

Jun 2015: Left hemiparesis, progressive dyspnea, weight loss

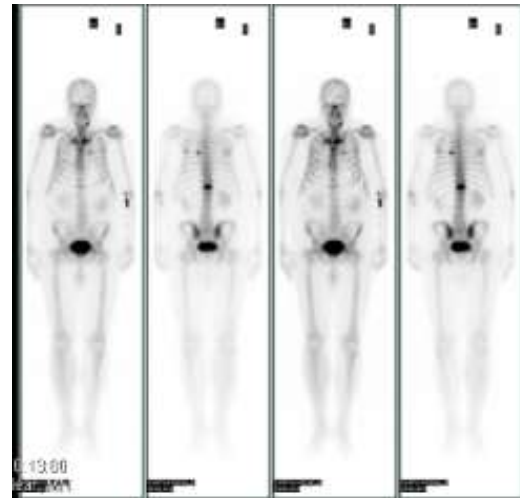
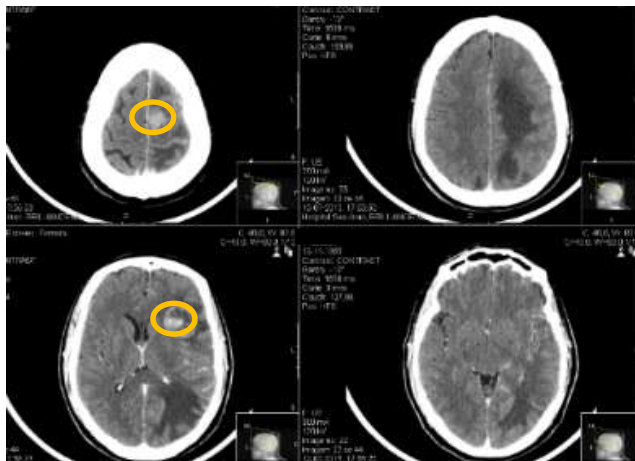
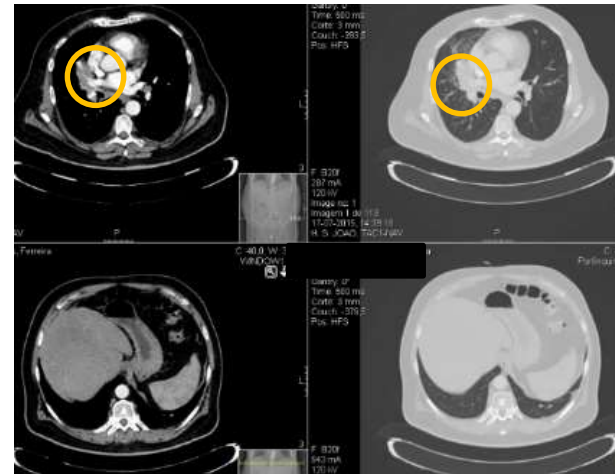
Brain CT: brain metastasis

Chest CT: right middle lobe mass, lung nodules, 4r and subcarinal LN; bilateral PE

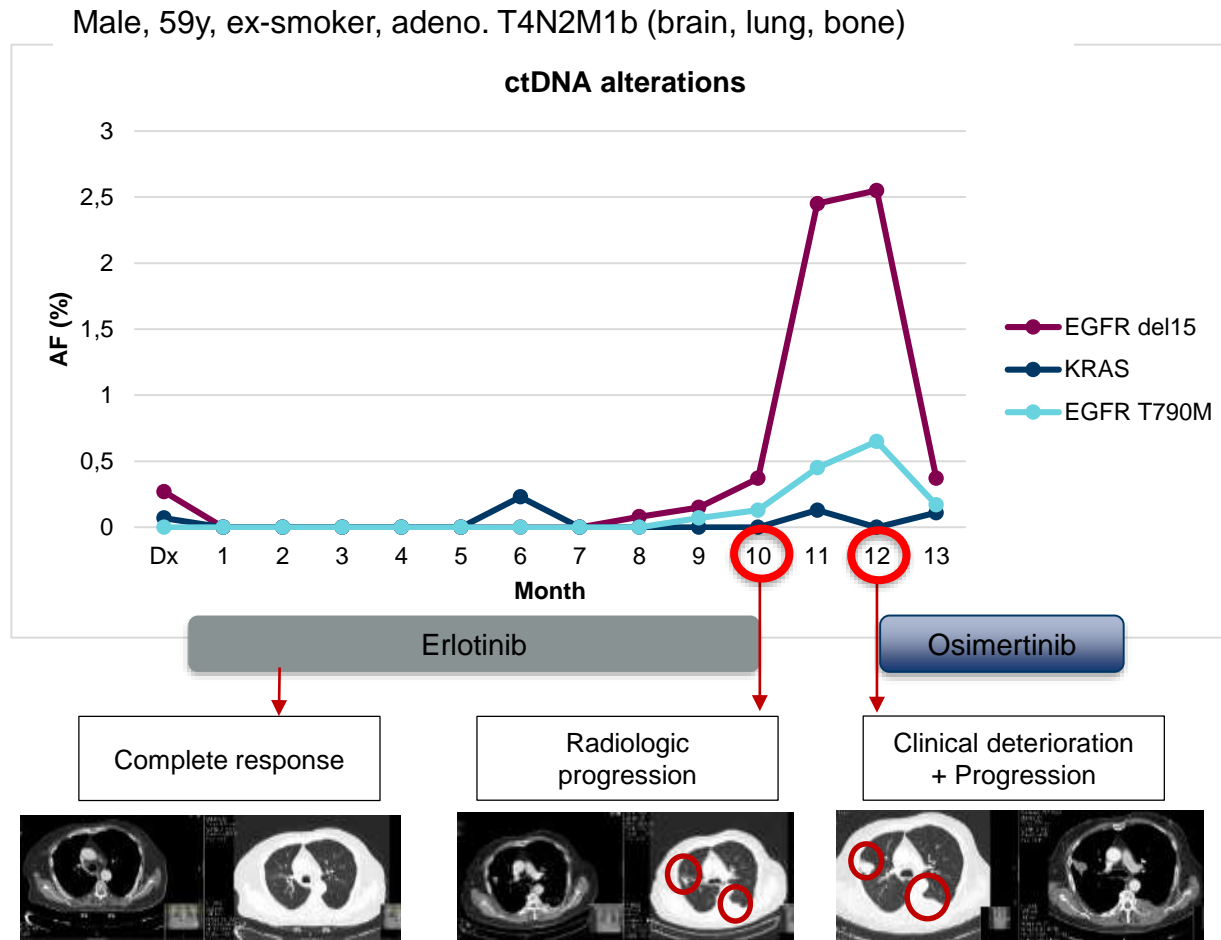
Bone scintigraphy: Bone metastasis

Bronchial biopsy: **Adenocarcinoma TTF1+, p63-, EGFR del19**

Clinical Stage: T4N2M1b



Follow up results – Case 74



Follow up results – Case 80

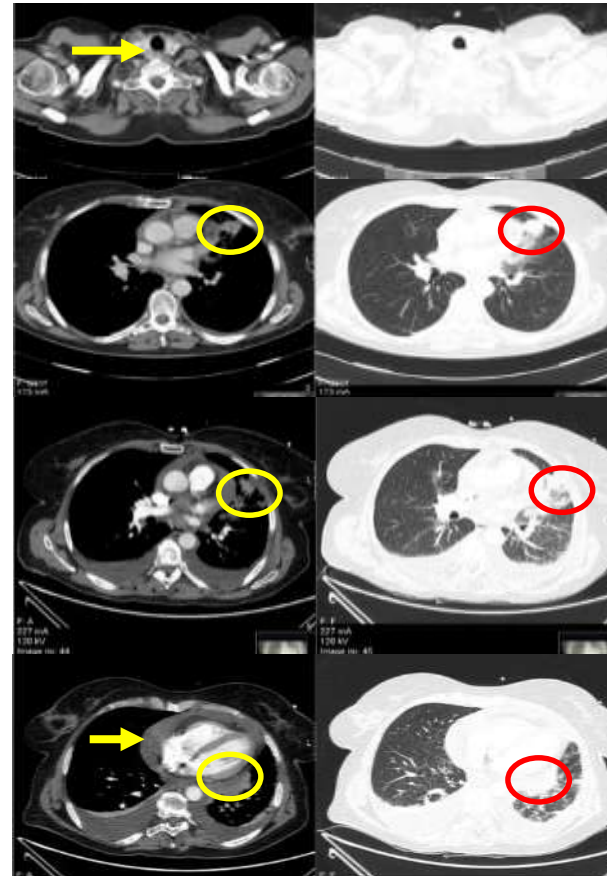
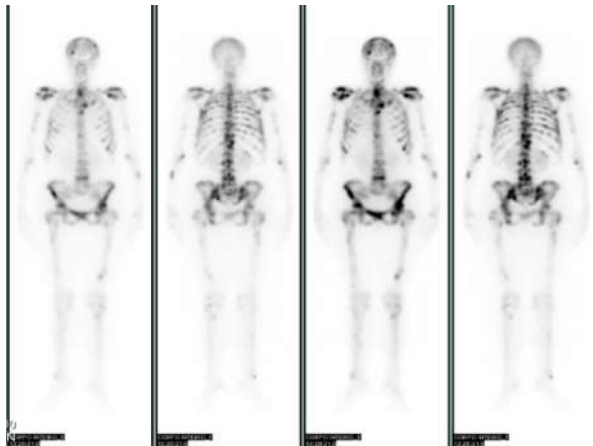
Female, 55y, non smoker

Jul 2015: Dyspnea, bone pain, headache,
nausea

Cardiac effusion
Diffuse bone metastasis
Thyroid metastasis
Brain CT and MRI negative

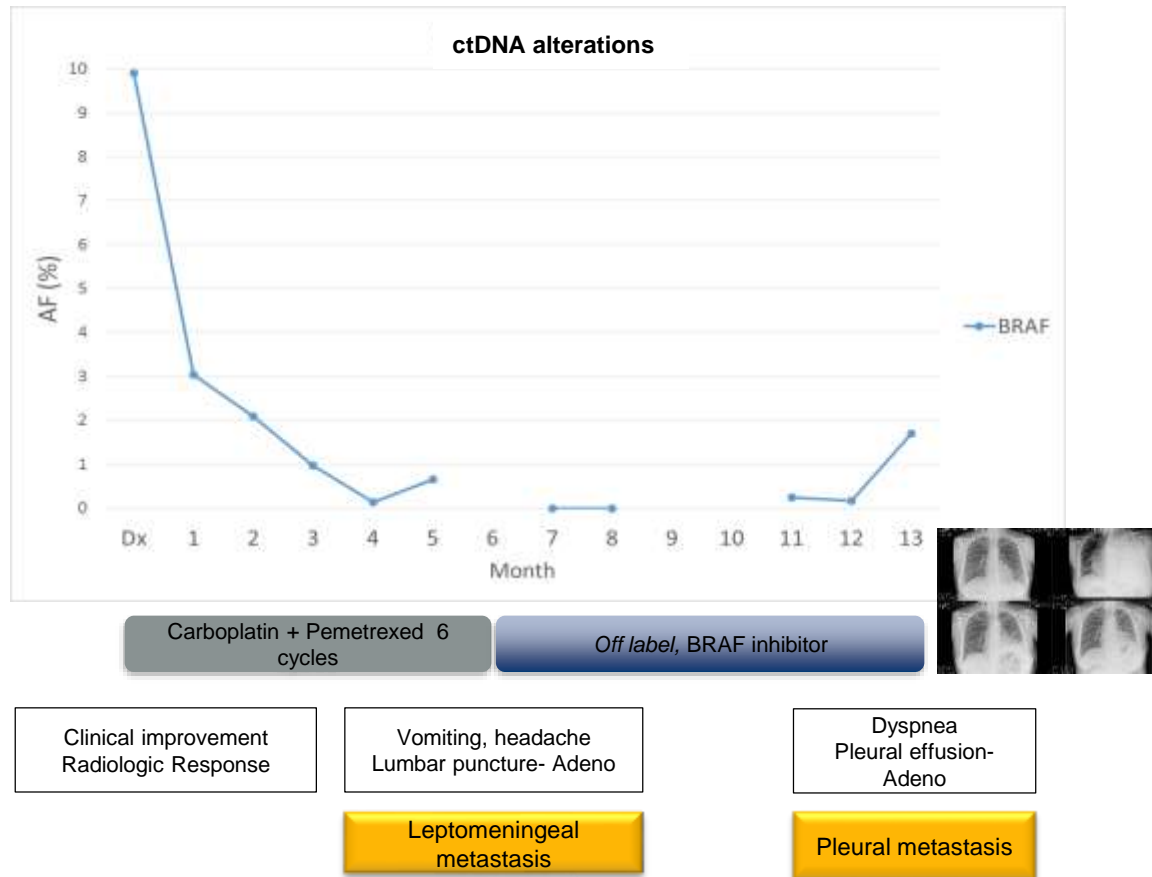
Pericardial effusion analysis: **Adenocarcinoma TTF1+,
EGFR -, ALK -; NGS BRAF V600E**

Clinical Stage: T4N2M1b



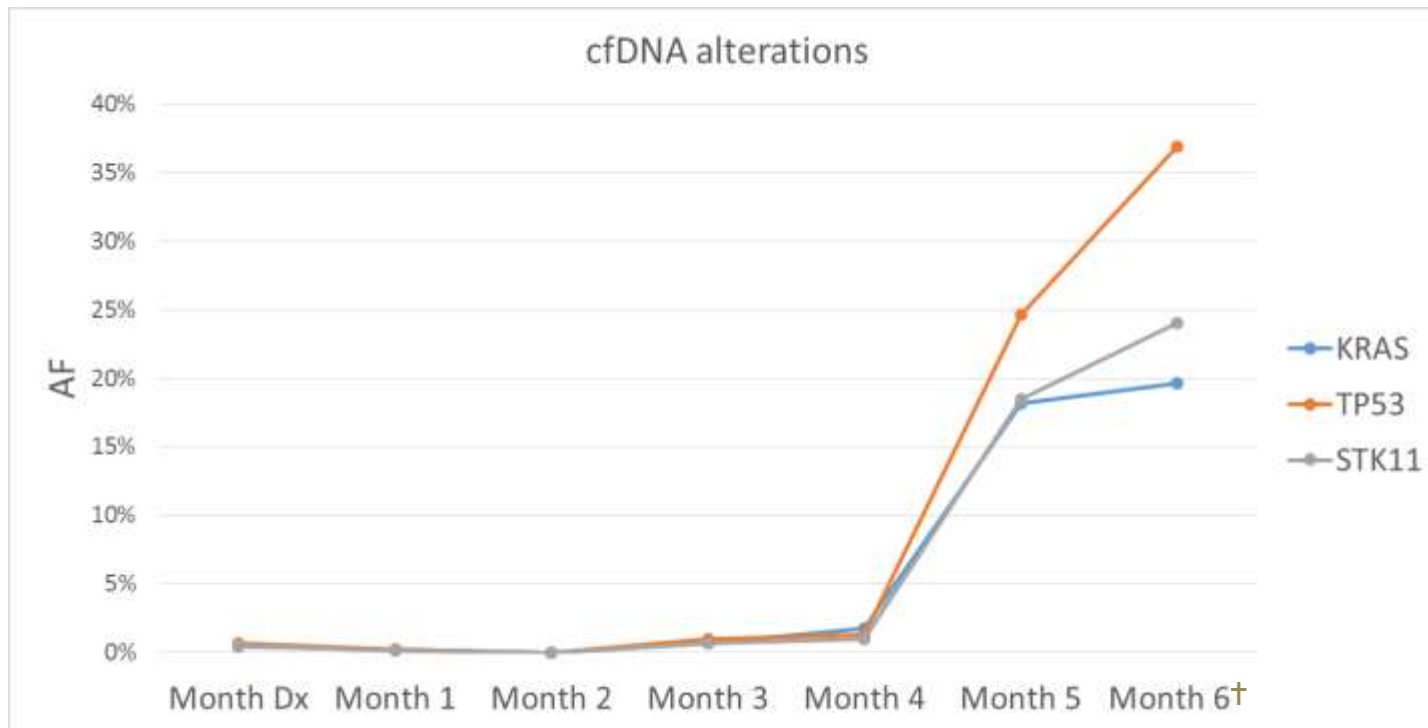
Follow up results – Case 80

Female, 55y, non smoker, adeno. T4N2M1b (bone, thyroid, cardiac effusion)



Follow up results – Case 15

Male, 60 years old, ex-smoker, adeno. T4N2M1 (lung + bones)



Carboplatin/Pemetrexed

Erlotinib



Progression



Conclusions

- Cancer-associated mutations can be detected in ctDNA in plasma
- The mutation frequency correlates with tumor burden and stage
- Therapy resistance mutations can be detected using this approach
- Liquid biopsies can be used to follow-up disease and to inform therapy decision making