Circulating tumor DNA (ctDNA) analysis for genomic testing in non-small cell lung cancer (NSCLC) patients with isolated central nervous system progression (iCNS)

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BACKGROUND

In oncogene-addicted NSCLC patients (pts) with progression (PD) limited to CNS, tissue biopsy is difficult and the feasibility of plasma ctDNA is unknown.

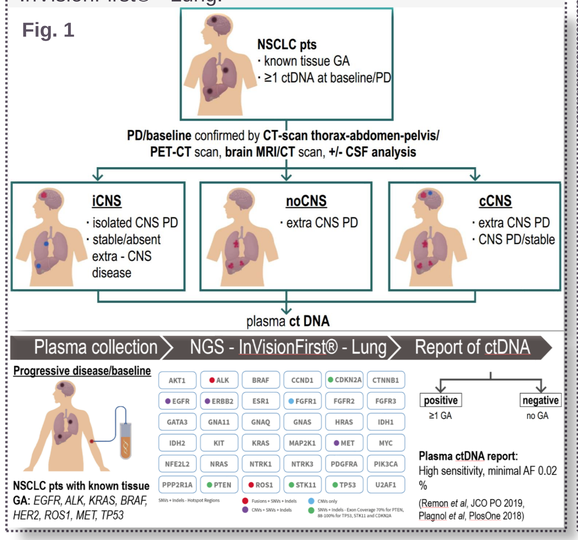
Aim: to determine the feasibility of ctDNA in iCNS.

METHODS

Retrospective study, including: stage IV NSCLC pts with known tissue genomic alterations (GA) and ≥ 1 ctDNA at baseline or PD;

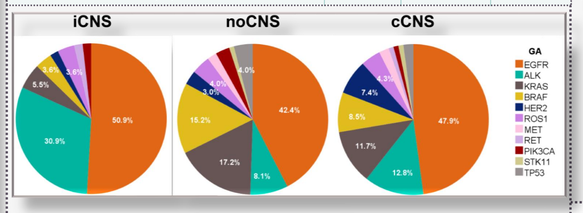
Pts stratified in 3 groups: **iCNS**, **noCNS**, **cCNS** (CNS and extra-CNS PD) (Fig. 1); ctDNA analyzed by NGS InVisionFirst® - Lung.

Fig. 1



RESULTS

Pts – baseline characteristics	iCNS N = 55	noCNS N = 99	cCNS n = 94
Median age, years	59	65	59
Female gender (%)	73	60	55
Adenocarcinoma (%)	98	90	94
Never smoker (%)	67	47	47
Median number of metastatic sites at diagnosis [range]	1 [1-5]	2 [1-6]	2 [1-6]
CNS metastases at diagnosis (%)	71	NA	70
Samples	**N=65**	**N=128**	**N=110**
Median number of metastatic sites at collection [range]	2 [1-5]	3 [1-6]	3 [1-7]
Median number of failure sites	1	1	2
Median number of prior treatments	1	1	1
Previous brain radiotherapy (%)	59	NA	45
Under tyrosine kinase inhibitors (TKI) (%)	66	34	41
1st & 2nd generation TKI (%)	63	30	29
3rd generation TKI (%)	3	4	12



iCNS vs noCNS/cCNS

- higher frequency of ALK fusion at tissue baseline (P<0.01)

iCNS vs cCNS

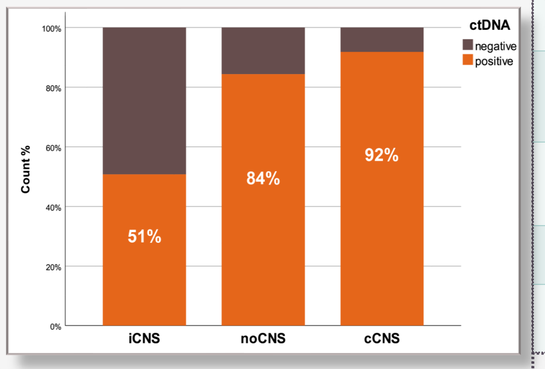
- higher frequency of leptomeningeal involvement (P<0.0001)

Higher tumor load in noCNS/cCNS

More metastatic and failure sites (P<0.001)

Positive ctDNA samples

51% iCNS vs **84%** noCNS and **92%** cCNS (P < 0.0001)



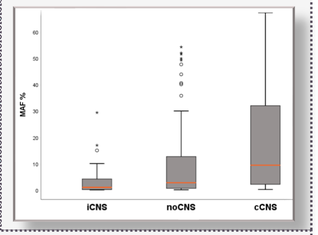
Number of metastatic sites (>2) at ctDNA collection independently associated with a positive ctDNA (OR=3.44, 95%CI 1.65-7.18, P=0.001).

Detection of drivers and resistance mutations in iCNS vs noCNS/cCNS

Type of GA	iCNS	noCNS	cCNS	P value
Actionable drivers (*EGFR, ALK, BRAF, HER2, ROS1, MET, RET*)	36% (22/61)	77% (79/102)	73% (68/93)	<0.001
Targetable resistance	6% (3/50)	46% (18/39)	44% (22/50)	0.009
EGFR T790M in the *EGFR* subgroup	7% (2/30)	48% (16/33)	50% (20/40)	0.0002
Other	31% (20/65)	65% (83/128)	67% (74/110)	<0.001

Median allele frequency MAF% [25%, 75%]

iCNS 0.95 [0.12, 4.19]
noCNS 2.74 [0.59, 12.77]
cCNS 9.38 [1.98, 32.51]
P < 0.0001



Serial ctDNA in iCNS
(N = 18 pts)

In 39% of cases, a **negative** ctDNA at time of iCNS shifted to **positive** when pts progressed systemically.

Paired CSF – plasma ctDNA
(N = 12 pts)

In the iCNS group, positive ctDNA in 6 (50%) plasma vs 10 (83%) CSF, P=0.193

CONCLUSIONS

Clinical utility of plasma ctDNA in NSCLC pts with isolated CNS progression is limited.
Alternative liquid biopsies, such as CSF ctDNA, may be more sensitive when approaching iCNS and should be considered in the future for this population.

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