1213P: Clinical Utility of Liquid Biopsy for the Early Diagnosis of EGFR Mutant Advanced Lung Cancer in a Real-life Setting (CLEAR)

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1- Background

- Liquid biopsies have been shown to be reliable as a complementary tool to identify tumor related mutations. High procedure cost and sub-optimal sensitivity have been hurdles to public funding of this technique in Canadian centers.
- The CLEAR trial was designed to evaluate the clinical and economic impact of early diagnosis with circulating free DNA (cfDNA) EGFR testing for suspected lung cancer patients.
- The objectives are to demonstrate clinically relevant improved time to detection of an EGFR mutation, evaluate the impact of cfDNA diagnosis on patient investigation and time to initiate specific EGFR inhibitor therapy.

- Herein, we present results of the first 100 patients recruited of the 500 patients planned.

2- Methods

- After obtaining their consent, blood samples were obtained from patients undergoing investigation for a radiological suspicion of stage III/IV advanced lung cancer.
- CfDNA were extracted from plasma and analyzed for EGFR mutation using Cobas® EGFR Mutation Test v2.

3- Results

Characteristics	Number	%
Age range	34-95	--
Mean Age	65	--
Female	52	52%
Male	48	48%
Pathology		
SCLC	5	5%
ADK	67	67%
Squamous	6	6%
Non small cell-NOS	9	9%
Other*	13	13%

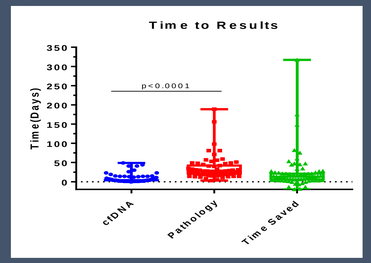
Table-1: Some characteristics of patients recruited. SCLC: Small cell lung Cancer; ADK: Adenocarcinoma; FU: follow-up for patients with multiple lesions but did not undergo tissue biopsy.*Include a patient with colon cancer, patients who didn't undergo tissue biopsy for lung nodules or those with no results available.

3- Results

Figure-1: Stage Distribution of patients recruited

IIB	IIIA	IIIB	IIIC	IV
• 1 (1%) • operated	• 10(10%) • All patients had a PET scan.	• 8 (8%) • 7 patients had PET scan	• 1 (1%)	• 75 (75%) • 66,67% had a PET scan.

Figure-2: Time to obtain EGFR mutation results.



EGFR Result by Tissue Biopsy	Median time to results: 27 Days
	9% of cases had no results due to sub-optimal specimen
	10% of patients had the results after a second biopsy
	11% of patients found to have EGFR mutation

EGFR Result by cfDNA	Median time to results: 4 Days
	9% of cases had an EGFR mutation detected
	Sensitivity: 84.6%
	Concordance: 83% Cohen's Kappa ratio: 0.37

Median time saved= Median of (Time to results by biopsy – time to results by cf DNA)= 13 days

Patient	Age (year)	Sex	Stage	Smoker	Pathology	Type of Mutation	Brain Mets	Whole Brain Radiotherapy
1	34	M	IV	<15 PY	ADK poorly diff	Ex19 Del	Yes	No
2	45	F	IV	No	ADK (acinar)	Ex 20Ins	Yes	Yes
3	46	F	IV	No	ADK	Ex 20Ins	No	NA
4	48	M	IV	No	x	Ex 19Del	x	x
5	56	M	IV	< 15 PY	ADK	Ex 19Del	Yes	No
6	62	F	IV	No	ADK	Ex 21 L858R	No	NA
7	63	M	IV	Stopped	ADK	Ex 19Del	No	NA
8	70	F	IV	No	ADK (micropapillary)	Ex 21 L858R	Yes	No
9	77	M	IV	No	ADK (acinar)	Ex 18 et 20	No	NA

Table-2: Characteristics of patients with EGFR mutation detected by cf DNA.
Patients who were omitted whole brain radiotherapy according to cf DNA results are labelled in orange.
F: Female; M: Male; ADK: Adenocarcinoma; NA: Not applicable

Figure-3: Time line of some patients showing the importance of early detection of EGFR mutation

Patient 1 Ex19Del

Time saved: 17 days Theoretical: 27 days Patient had ECOG=2

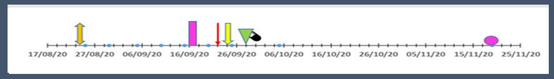
Patient 5 Ex19Del

Time saved: 27 days Theoretical: **45** days

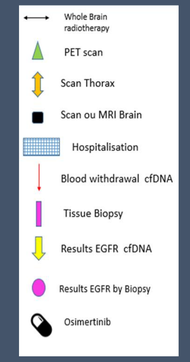
Patient 6 L858R

Time saved: 7 days Theoretical: **63** days

Patient 7 Ex19Del



Time saved: 24 days Theoretical: **56** days Patient had ECOG=2



Theoretical time saved = Date of EGFR results by pathology – date of scan (assuming that blood withdrawal can be made at the same day)

4- Conclusions

- EGFR mutation detection by cf DNA and tissue biopsy are complementary. Early detection by cf DNA can improve time to diagnosis and accelerate appropriate therapy. Our preliminary evaluation suggests that even earlier use of cf DNA may further improve time to treatment.

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