Abstract #532

The Impact of Liquid Next-Generation Testing Timing on Treatment-naïve Advanced Non-small Cell Lung Cancer: A Prospective Observational Study

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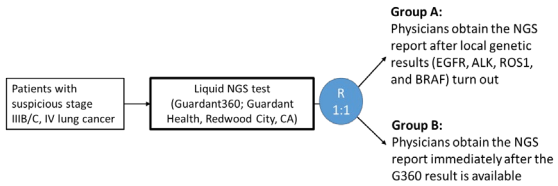
BACKGROUND

- More than 60% of East Asian non-small cell lung cancer (NSCLC) harbor druggable driver mutations which can be effectively treated with molecular targeted therapy, making genetic testing a standard approach for NSCLC.
- Liquid next-generation sequencing (NGS) of plasma cell-free DNA (cfDNA) has become a promising tool for the identification of driver mutations in NSCLC because of several advantages including a short turnaround time, a broad spectrum of detection, a relatively high sensitivity, and the absence of tissue biopsy-related complications.
- Liquid NGS is well known to supplement tissue NGS in the initial work up of NSCLC. Whether liquid NGS performed immediately at the start of tumor workup could further enhance NSCLC patient survival is unclear.

METHODS

- Patients with suspicious advanced NSCLC who meeting the followed criteria were enrolled in this trial during the period from 2019/11 to 2022/1.
  Inclusion criteria:
  Age ≥20
  Suspected clinically stage IIIB, IIIC, and IV lung cancer
  Did not receive tissue diagnosis
  ECOG 0-2
  Patients agree with and can tolerate systemic treatment
  Exclusion criteria:
  Pregnancy
  Diagnosed as advanced stage cancer before enrollment
  History of other cancer
  Ever received anti-cancer treatment
- The study algorithm and primary/secondary endpoints are as follows:

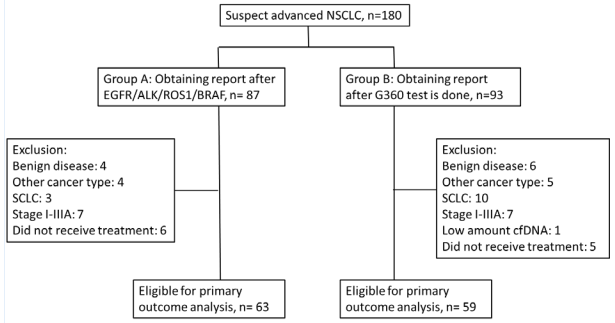


Primary endpoint: Time-to-treatment of NSCLC
Secondary endpoint: the proportion of confirmed advanced NSCLC diagnosis, objective response rate (ORR), progression-free survival (PFS), and overall survival (OS).

- A value of 10 days will be added in the time to treatment of group A to represent the time consumed for liquid NGS.

RESULTS

- The study consortium diagram is as follows:



- A total of 180 patients were enrolled, with 87 in group A and 93 in group B. Demographic data were listed the table 1, without significant difference between two groups.
- 63 in group A and 59 in group B entered final analysis

Table 1. Demographic data of the study

	Group A n=63	Group B n=59	p-value
Age, median (range)	64 (39~88)	64 (38~83)	p= 0.599
Male gender, n (%)	36 (57.1%)	33 (55.9%)	p= 0.893
Stage IIIBC/IV	4/59	5/54	p= 0.654
Smoking, n(%)	27 (42.9%)	29 (49.2%)	p= 0.486
ECOG 0-1/2-4	58/5	57/2	p= 0.281
Histology			
Adenocarcinoma	49	47	
Squamous Cell Carcinoma	8	6	
Adenosquamous cell carcinoma	1	0	
Poorly differentiated carcinoma	2	2	
LEC	1	2	p= 0.909
Pleomorphic carcinoma	2	2	
Driver Mutation detected by G360 or local test			
EGFR	36 (1 in SqCC)	34 (1 in SqCC)	
ALK	2	0	
ROS1	1	0	
BRAF	0	2	
MET exon14 skipping	0	1*	
RET	0	0	
KRAS	2	1	p= 0.333
HER2	2	5	
Others	0	1**	

- The median time to treatment of group A vs B was 33 vs 20 days, with a p-value <0.0001. The result was similar in patients receiving targeted therapy or chemo/immunotherapies.

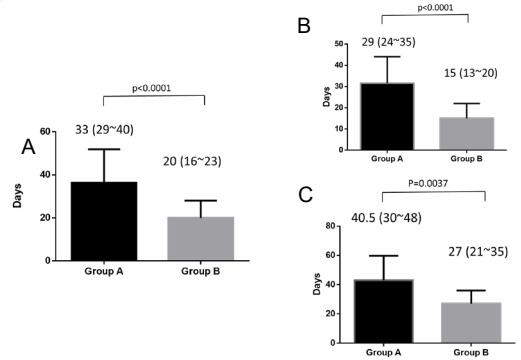


Figure 1. Median time to treatment (days) in group A and B. A. All patients (n=122); B Patients received target therapy (n=73); C. Patients received chemotherapy or immunotherapy (n=44)

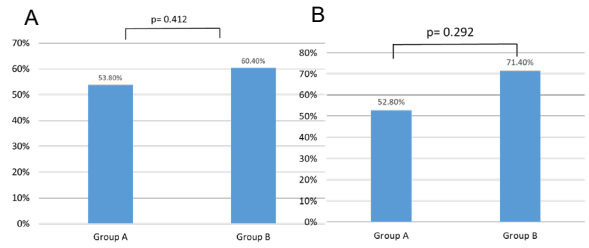


Figure 2. Objective response rates. A. All patients (n=122); B. Patients received target therapy (n=73)

- Regarding PFS, patients who treated with targeted therapy had no difference in group A and B.
- Patients treated with immunotherapy with or without chemotherapy, group B patients seemed to have a longer PFS (A vs B, 4.5 vs NE months, p=0.010), though the data was premature.
- OS is not analyzed at this time because of the short follow-up duration

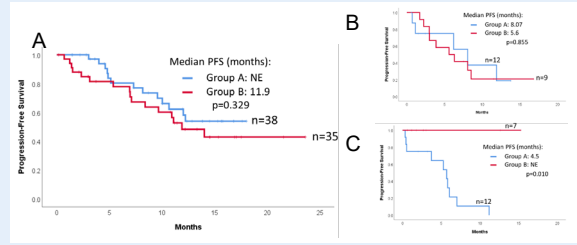


Figure 3. Progression-free survival. A. Patients treated with targeted therapy (n=73); B Patients received chemotherapy (n=21); C. Patients received immunotherapy with or without chemotherapy (n=19)

- In patients confirmed to be advanced non-squamous NSCLC (n=114), most of the typical driver mutations were found by liquid NGS, including EGFR (n= 62), ERBB2 (n=8), BRAF (n=3, 1 with V600E), KRAS (n=4), MET (n=2, both are exon 14 skipping) and ALK (n=1).
- Among the liquid NGS-positive patients, 3 of 62 EGFR, and all the ERBB2, BRAF, KRAS, and MET mutant cases were not detected as driver-positive by local genetic testing. Most of them received relevant targeted therapy.
- TP53 is the most frequent genetic mutations identified.

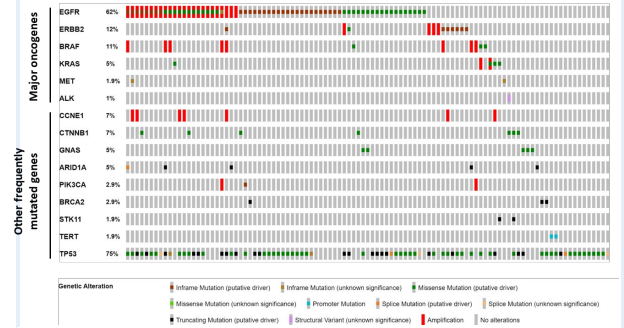


Figure 4. Genetic landscape of our cohort (n=114)

Conclusion

- Performing liquid NGS as an initial approach of advanced NSCLC tumor workup can shorten the interval between diagnosis to anti-cancer treatment and perhaps may improve survival in selected patients

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