Genomic profiling of circulating tumour DNA in East Asian head and neck squamous cell carcinoma

Ning Jia[1], Shanshan Zhang[2], Yonglei Shi[2], Xiaohua Shi[3], Chunmei Bai[1]

[1]Department of Medical Oncology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China, [2]Geneplus-Beijing, Beijing, China, [3]Department of Pathology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China.

Introduction

- Novel effective therapy is limited in head and neck squamous cell carcinoma (HNSCC).
- Next generation sequencing (NGS) with sophisticated bioinformatics allows the distinct identification of tumour-specific DNA mutations in circulating tumor DNA (ctDNA).
- CtDNA may represent the real-time genomic profile and biology of cancers to be treated. Identification of molecular characterization of ctDNA may potentially provide a way to precisely treat the patients with novel options.

Methods

Study design

- A retrospective analysis at Peking Union Medical College Hospital.

Patient eligibility

- Patients had pathologically confirmed squamous cell carcinoma of the oropharynx, oral cavity, hypopharynx, or larynx.

Sample collection

- Peripheral blood samples were collected in tubes from Streck and stored for up to 5 days at room temperature before plasma preparation and DNA extraction.

Circulating tumor DNA analysis

- Target-capture deep sequencing with a panel covering 1021 genes was performed to detected somatic mutations in ctDNA.

Methods *(continued)*

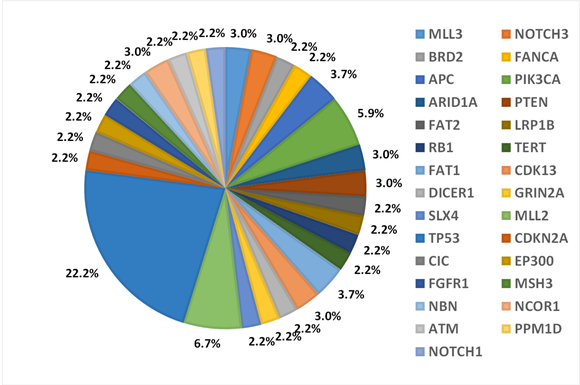
- Tumour mutation burden (TMB) analysis interrogated SNVs and small indels with the variant allele frequency (VAF) ≥ 0.5%.
- TMB-U (unknown) is defined as the maximum VAF < 0.5%. TMB-H was defined as the top quartile of all TMB values.

Statistical analysis

- SPSS Statistics and GraphPad Prism were used for statistical analysis.
- *P* values of <0.05 were considered significant.

Results

Frequencies of genomic mutations in ctDNA observed more than 5% in the overall samples (N=51)

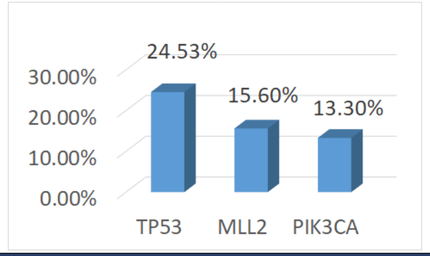


Results *(continued)*

Patient characteristics

Characteristic	N (%)	bTMB (mutations/Mb) Median (IQR)	P Value
All patients	45	3.00(2.00-9.00)	
Age (years), median	61(36-92)		
Age group			
<65	26(57.8)	3.00(1.75-7.20)	-
65+	13(28.9)	4.00(2.00-14.20)	0.35
UNK	6(13.3)		
Gender			
Female	9(20.0)	3.00(2.00- 11.50)	-
Male	36(80.0)	3.42(1.25-8.91)	0.86
Primary tumor site			
Oral cavity	15(33.3)	2.88(1.00-5.00)	-
Oropharynx	10(22.2)	4.32(1.75-14.10)	-
Larynx	11(24.4)	6.00(3.00-14.00)	-
Hypopharynx	9(20)	3.84(2.44-8.50)	0.50

The three most common altered genes identified by ctDNA analysis



Results *(continued)*

Patients with bTMB-H had been identified genetic alteration in either MLL3, NOTCH3, BRD2, or FANCA genes.

Conclusions

- **Analysis of ctDNA may provide novel and clinically relevant insights into precise therapeutic decisions in HNSCC.**
- **Some genetic mutation might associate with high bTMB status.**
- **The potential utility and validity of large-scale ctDNA genomic profiling approaches should be explored in future studies.**

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Contact: jianing@pumch.cn

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