

## EDITORIAL

# Targeted Next-Generation Sequencing of Tissue Obtained by Endoscopic Ultrasound-Guided Fine Needle Biopsy for Pancreatic Cancer: A New Paradigm for Management

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## INTRODUCTION

Pancreatic ductal Adenocarcinoma (PDAC) is the one of the lethal pancreatobiliary malignancy with extremely poor prognosis. The only curative treatment is surgical resection; unfortunately, less than 20% of patients are resectable at diagnosis as most of them either having locally advanced or metastatic disease at the time of diagnosis [1]. Endoscopic Ultrasonography (EUS) guided pancreatic biopsy is the method of choice for obtaining pancreatic tissue, with diagnostic accuracy ranging from 80% to 95% [2].

Next Generation Sequencing (NGS) has been applied to EUS guided biopsies and may classify patients based on specific molecular pattern. One possible reason for the poor prognosis is the lack of specific targeted genetic biomarkers for therapeutic stratification, unlike the situation as EGFR in lung cancer and BRCA1/2 in ovarian cancer. Genomic biomarkers for potential therapeutic target in pancreatic cancer are still lacking, however, NGS may reveal potential predictive molecular target for treatment response.

In few recent available studies, genomic analyses of pancreatic cancer have revealed a large number of mutations with the 4 most common oncogenic wellknown cancer genes in various proportions which includes K-ras, TP53, CDKN2A and SMAD4 and many other mutated genes at low prevalence [3]. In addition, Next-Generation Sequencing (NGS) has also ability to classify patients into

potential therapeutic responsive subgroups based on their different molecular profiles [3].

The pre-requisite is acquisition of good quantity and quality of tissue for a meaningful NGS analysis. With the introduction of newer target specific biologics, it will open a new window of opportunity for more personalized therapies for PDAC patients. Recently, with availability of different types of EUS-FNB needles (Franssen and Endcutting) of various diameters, EUS guided large amount tissue acquisition has become easier, this is further supplemented with the advancement of molecular biology techniques, the analysis of specific molecular biomarkers either on DNA, RNA, or microRNA [2]. However, application of this new technique is challenging. The quantity of cells obtained from EUS-guided tissue acquisition is important for successful NGS.

The different needles can give different results in terms of adequacy of the material and inconclusive results may be obtained due to inherent desmoplastic reaction, inflammatory components, or necrotic content in the specimens. Again, it is not clear about adequacy of sample size, needed for NGS study. Lastly, its applicability in resource constraint countries is limited, which can be solved by performing a targeted resequencing of a limited number of commonly known mutated genes in pancreatic cancer, which will be cost effective and time saving. Based on next generation sequencing report recently, targeted immunotherapy Pembrolizumab showed both efficacy and safety in different tumour types with microsatellite instability-high (MSI-H), and was approved for the treatment of refractory pancreatic cancer with MSI-H [4].

Similarly, another phase II trial underway, which will evaluate the efficacy of Pembrolizumab in treating patients with metastatic pancreatic cancer with germline BRCA1 or BRCA2 mutations. Apart from early detection, a major impetus for wide-spread adoption of NGS technologies is for solid tumour genotyping. Combining NGS and pathological evaluation of pancreatic EUS guided specimen would increase the detection rate of malignancy and identified specific mutation may stratify patients for specific anticancer therapies for this lethal malignancy.

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