Circulating tumour DNA-based minimal residual disease detection for biliary tract cancer

Z. Li¹, P. Yan¹, Q. Hao², L. Guo², F. Pang², X. Jiang¹, Y. Yu¹

¹ Department of Biliary Surgery, Third Affiliated Hospital of Naval Military Medical University, Shanghai, China
² Medical Department, Shanghai OrigiMed Co., Ltd, Shanghai, China

Background

Although circulating tumor DNA-based minimal residual disease (MRD) is useful for prediction of prognosis, but clinical value of MRD for BTCs are remain clear.

Methods

The OriMIRACLE ST™ MRD assay (OrigiMed, Shanghai, China) uses whole exome sequencing (WES) for detecting patient-specific somatic alterations from tumor tissues and for blood a personalized panel designed to target up to 45 variants.

Results

A total of 26 biliary tract cancer (BTC) patients including 13 gallbladder carcinoma and 13 extrahepatic cholangiocarcinoma patients were enrolled. Among the patients, 53.85% (14/26) were male and 46.15% (12/26) were female, and the median age was 61 years, ranging from 49 to 73 years old. Fifteen patients underwent radical surgery, 4 patients underwent local tumor resection and 7 patients could not undergo radical surgery. Based on WES, we found that 58.33% (4005/6866) of the mutated genes were unique to each patient and 100% (26/26) of patients successfully constructed MRD panels, suggesting that tumor-informed MRD is superior to panel-based MRD in BTC. For each patient, we selected up to 45 clonal somatic mutations for a personalized ctDNA assay design. MRD detection was performed on 26 cases and revealed a positive rate of 42.31% (11/26). Among the 11 patients with positive MRD at postoperative or, 71% (5/7) of patients who could not undergo radical surgery, 100% (4/4) of the patients underwent local tumor resection and 13.3% (2/15) of patients underwent radical surgery. MRD detection was performed 4 times on one female GBC patient with stage IV throughout the treatment course. we found that MRD at baseline was positively detected by tumor-informed assay with a higher variant allele fraction (VAF), and decreased after neoadjuvant therapy. CT image also showed local control of the tumor, but CA199 and CEA levels were elevated in patients with obstruction, suggesting the limits of tumor markers in BTC patients with obstruction.

Conclusions

Up to 58% of mutated genes of BTC are unique individually, and 100% of patients successfully constructed MRD panels, which may be more suitable for monitoring with tumor-informed MRD panel. The VAF of ctDNA could be used to predict the efficacy of neoadjuvant therapy and tumor progression in BTC patients.

Legal entity responsible for the study

The authors.

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Disclosure

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