Perioperative ctDNA-Based MRD Detection in NSCLC—Letter

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We read with great interest the article by Xia and colleagues reporting circulating tumor DNA (ctDNA) as biomarker for early detection of molecular residual disease (MRD) and predictor for relapse after surgery in patients with non–small cell lung cancer in a prospective multicenter cohort named LUNGCA-1 (1).

LUNGCA-1 was designed to predict prognosis by perioperative ctDNA detection, including preoperative, 3 days postoperative and 1 month postoperative ctDNA. The number of patients in prognosis analysis is 330 (Fig. 1), whereas Supplementary Table S5 shows only 329 patients with at least one postoperative ctDNA sample. In LUNGCA-1, some patients tested postoperative ctDNA before or without adjuvant therapies, while others tested postoperative ctDNA after adjuvant therapies. We questioned the trial design because the authors mixed different aims: MRD detection at a specific postoperative timepoint for recurrence prediction; MRD detection at both preadjuvant/postadjuvant therapies timepoints for evaluation of the outcome of adjuvant therapies. The authors could separate different aims into different trials or do statistics separately in preadjuvant/postadjuvant groups.

The authors defined "MRD positive" for patients with detectable ctDNA at 3 days and/or 1 month postoperatively. We noticed that 5 of 26 patients with MRD positive (19.2%) had ctDNA positive only in the detection at postoperative 3 days and their ctDNA detection was negative before and 1 month after surgery. Therefore, we consider the issue of timepoint setting for postoperative blood collection. Diehl and colleagues reported that ctDNA increased after surgery, most likely due to release of ctDNA from damaged tissue (2). Thus, it may be more reasonable to collect blood at a later timepoint after surgery from 10 days to 16 weeks (3). As reported by Chaudhuri and colleagues (4) and Moding and colleagues (5), blood sample should be collected within 4 months for ctDNA detection after surgery or completing radiation and chemotherapy. In this article, the cell-free DNA concentration at 3 days after surgery is also significantly higher than before and 1 month after surgery (Supplementary Table S1), suggesting a more reasonable manner to collect blood for a longer period after surgery. Also, whether the 5 patients with ctDNA positive for only 3 days after surgery relapsed or not was not mentioned.

Chaudhuri and colleagues (4) reported that concentration of ctDNA should be correlated with stage and tumor volume, which the authors did not mention. Furthermore, how to determine ctDNA status is positive or negative needs to be clarified. In addition, the criteria for judging the patient's disease relapse were not mentioned in the text or Supplementary Materials and Methods.

Authors' Disclosures

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