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Multimodality Management of Borderline Resectable Pancreatic Cancer

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ABSTRACT

Study 1: Creation of evidence for new preoperative treatment for pancreatic cancer.

Introduction: Along with the development of chemotherapy for unresectable pancreatic cancer, attempts have been made to apply to surgeon-led preoperative treatment.

Methods: We demonstrate the role of surgery in creating stronger evidence for meta-analyses and multicenter collaborative phase II trials from clinical trials of new preoperative anticancer drug treatments led by surgeons.

Results: We conducted a pilot trial of preoperative FOLFILINOX therapy for BR pancreatic cancer and reported the safety and efficacy of the treatment. This study provides an international collaborative study of meta-analysis in the form of data providing 283 patients with BR pancreatic cancer who received preoperative FOLFIRINOX therapy with a median overall survival of 22.2 months, an ablation rate of 68% and 84%. We report a high R0 resection rate and good results as stronger evidence (JNCI2019). It became clear that it should be verified in the randomized controlled trial as the next task. In addition, we report phase I clinical trial results of preoperative GEM+nab-Paclitaxel treatment for BR pancreatic cancer at the center and are currently verifying the same treatment in multi-center joint phase II trial.

Study 2: Diffusion-weighted MRI predicts the histologic response for neoadjuvant therapy in patients with pancreatic cancer; a prospective phase II studies (DIFFERENT trial).

Background: Preoperative prediction of histological response to neoadjuvant therapy aids decisions regarding surgical management of borderline resectable pancreatic cancer (BRPC). We elucidate correlation between pre/post-treatment whole tumor apparent diffusion coefficient (ADC) value and rate of tumor cell destruction. We verify whether post-treatment ADC value on site of vascular contact predicts negative surgical margin (NSM) of BRPC.

Methods: We prospectively reviewed 28 patients with BRPC who underwent diffusion-weighted magnetic resonance imaging before neoadjuvant chemotherapy and surgery. Correlation between percentage of tumor cell destruction and various parameters was analyzed. Strong parameters were assessed for their ability to predict therapeutic histological response and NSM.

Results: Pre/post-treatment whole tumor ADC value correlated with tumor cell destruction rate by all parameters (R=0.630/0.714, P<0.001/<0.0001). The post-treatment cut-off value of ADC on site of vascular contact for discriminating between grade <IIb and ≥ grade IIb was determined as 1.42×10^{-3} mm^2/s and it predicts NSM with 88% sensitivity, 50% specificity and 61% accuracy. For histological response, the post-treatment whole tumor ADC cut-off value for discriminating between grade <IIb and ≥ grade IIb was determined as 1.40×10^{-3} mm^2/s with 100% sensitivity, 81% specificity and 89% accuracy.

Conclusion: Post-treatment whole tumor or ADC value on site of vascular contact may be a predictor of NSM in patients with BRPC. There was significant correlation between pre/post-treatment whole tumor ADC values and rates of tumor cell destruction after neoadjuvant therapy.

Trial registration: This trial is registered at UMIN Clinical Trials Registry, UMIN000022010, 000028030 and at ClinicalTrials.gov, NCT02777463.

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