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Switching Chemotherapy In Neoadjuvant Treatment For Resectable/borderline Resectable Pancreatic Cancer - New Treatment Strategy In The Era Of Biological Borderline Resectable-

Daisuke HASHIMOTO*, Sohei SATOI, Tomohisa YAMAMOTO, So YAMAKI, Hidetaka MIYAZAKI, Yuki MATSUI, Yuki TSYBULSKYI, Mitsugu SEKIMOTO

Department Of Surgery, Kansai Medical University, JAPAN

Background : The best timing of surgery after neoadjuvant therapy (NAT) for resectable (R)/ borderline resectable (BR)- pancreatic ductal adenocarcinoma (PDAC) has been still controversial. Recently, the idea of biological BR based on CA19-9 as a population with poor prognosis among radiological R has been proposed. We are introducing switching chemotherapy targeting CA19-9 in NAT. This does not limit the duration of NAT, but rather continues NAT until CA19-9 declines, after which surgery is performed. The objective of this study was to investigate the effect of switching chemotherapy in NAT for R/BR-PDAC, regarding biological BR.

Methods : In this single center retrospective study, 226 patients with R/BR-PDAC underwent NAT from 2010 to 2021 were included. Anatomical R-PDAC with CA19-9 greater than 150 IU/ml was defined as biological BR in this study.

Results : Anatomically, 143 patients (63%) were R-PDAC, 49 (22%) were BR-A, and 34 (15%) were BR-PV. The first-line of NAT was gemcitabine (GEM) + S-1 in 164 patients (73%), GEM+ nab-Paclitaxel in 29 (13%), S-1(+ radiation therapy) in 26 (12%), and FOLFIRINOX in 7 (3%). Pancreatic resection was performed in 206 patients (91%), whereas 20 (9%) did not receive it. Median survival time (MST) was 38.3 months in the total cohort, and 41.9 months in the resected group and 18.4 months in the un-resected group, respectively ($p<0.001$). Of the anatomical R, 71 patients (31%) were Biological BR. When Biological BR is considered, MST in the new BR group (n=154, Biological BR, BR-A, and BR-PV) was shorter than that in the R group (n=72), although there was no significant difference (46.9 months vs 36.4 months, $p=0.225$). In the new BR group, 26 patients (17%) received switching chemotherapy to achieve a CA19-9 of less than 150 IU/ml. The patients who were able to achieve a CA19-9 of less than 150 IU/ml after switching chemotherapy (n=18, MST 63.8 months) showed similar MST as those who were able to achieve a CA19-9 of less than 150 IU/ml without switching chemotherapy (n=72, MST 83.8 months, $p=0.546$), and significantly better MST in those who did not archive a CA19-9 of less than 150 IU/ml without switching chemotherapy (n=56, MST 25.7 months, $p=0.033$). Disease free survival analysis similarly showed the benefit of switching chemotherapy.

Conclusions : Although it needs to be verified in the future studies including more patients, implementation of the switching chemotherapy targeting CA19-9 regarding Biological BR may improve prognosis in NAT for R/BR-PDAC.

Corresponding Author : **Daisuke HASHIMOTO** (daisukeh007@gmail.com)