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The current status of adjuvant chemotherapy for colorectal cancer in Japan: A paradigm shift from oral fluoropyridine single therapy to the oxaliplatin regimen

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Above the study

This paper describes the paradigm shift in adjuvant chemotherapy for CRC (Colorectal Cancer), namely the shift in standard treatment from oral fluoropyrimidine monotherapy to oxaliplatin-based regimens [1]. Previously, there was a long debate about the applicability of L-OHP combination therapy in Japan, partly due to the favorable prognosis of CRC surgery patients. However, in recent years, the ACHIEVE trial (a large-scale clinical trial conducted in Japan), part of the results of the IDEA collaboration), has clarified the situation, and the standard consensus in Japan establishes Capecitabine Plus Oxaliplatin (CAPOX or FOLFOX) for a duration of 3 months as the adjuvant treatment for CRC [2,3]. Even in the previously common oral monotherapy for CRC adjuvant chemotherapy in Japan, the effectiveness of different drugs has been investigated. In the JCOG0205 study, equivalence was shown between Uracil-Tegafur plus Leucovorin (UFT/LV) and 5-Fluorouracil (5-FU) intravenous administration, and in the Adjuvant Chemotherapy Trial of S-1 for Colon Cancer (ACTS-CC) study, equivalence was shown between UFT/LV and S-1 [4,5]. However, in the JCOG0910 study, equivalence of S-1 to Capecitabine was not shown [6]. Furthermore, in the Xeloda in Adjuvant Colon Cancer Trial (X-ACT) study, although there was no statistically significant difference, Capecitabine outperformed intravenous FU monotherapy [7]. Considering these factors, the efficacy of FU monotherapy in adjuvant chemotherapy is considered to be Capecitabine>UFT+LV=S-1=intravenous 5-FU.

The superiority of Capecitabine over other drugs in FU monotherapy is a result that has been extrapolated to oxaliplatin combination therapy. It had already been shown that CAPOX is superior to fluoropyridine single therapy in adjuvant chemotherapy for CRC (XELOXA study) [8]. The CAPOX group showed a 6.3%increase in 5-year DFS compared to the bolus 5-FU group (Mayo or RPMI regimen) (median follow-up period=57 months; HR=0.80), and a 7% increase in 7-year DFS (56% *vs* 63%, P=0.004). As concerns the long-term survival observations of XELOXA, the differences in Disease-Free Survival (DFS) and Overall Survival (OS)in the CAPOX group became larger over time compared to the group treated with FU alone. This suggests that oxaliplatin (L-OHP) provides a definite effect in postoperative adjuvant chemotherapy for Stage III CRC. A comparative study was conducted in Japan between high-risk Stage III patients treated for 6 months with either SOX therapy or UFT+LV therapy; however, the superiority of SOX therapy was not demonstrated [9]. The reasons for this result may be related to the fact S-1 is not proven to be equivalent to capecitabine in CRC adjuvant chemotherapy, and the amount of oxaliplatin in SOX therapy was low, at 100 mg/m2. While SOX therapy and CAPOX therapy have been reported to have equivalent therapeutic effects for advanced CRC. Grothy A, et al. stated that 'SOX therapy is not widely used in Asia, has strong adverse events, and lacks evidence for its combination with antibody therapy, so it will not become widespread worldwide [10,11]. Furthermore, in adjuvant therapy, CAPOX therapy is considered to have superior therapeutic effects compared to SOX therapy.

Therefore, we considered the therapeutic effects of adjuvant therapy for Stage III colorectal cancer cases in Japan as shown in the Figure, and presented our findings at the 13th International Conference of the Federation of Asian Clinical Oncology [12].

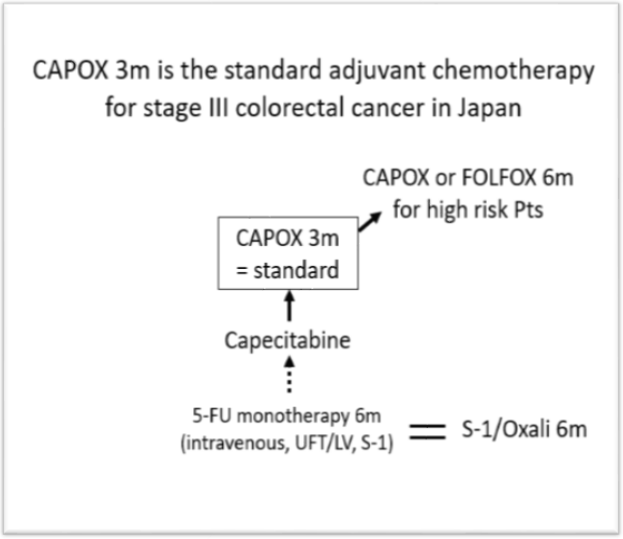

Figure 1. CAPOX 3m is the standard adjuvant chemotherapy for stage III colorectal cancer in Japan.

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