Feasibility study of sequential adjuvant chemotherapy with three months oxaliplatin-based regimen (modified FOLFOX6 or CAPOX) followed by three months capcitabine in patients with stage III and high risk stage II colorectal cancer: (JSWOG C2)

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Background

- Six months oxaliplatin (OX)-based chemotherapy (modified FOLFOX6 or CAPOX) is the standard adjuvant chemotherapy for completely resected stage III colorectal cancer (CRC) in Japan.
- However, neurotoxicity is the most frequent toxicity of these chemotherapy regimens and often decline their QOL.
- OX-induced neurotoxicity is well known to be appeared by dose-dependently and progresses to irreversible in some cases.
- Six months OX regimen has been reported to leave neurotoxicity after treatment in patients with completely resected stage III CRC.

Objectives

- To investigate the feasibility of sequential approach with three months OX-based regimen followed by three months capcitabine in Japanese patients with stage III CRC, in addition to high-risk stage II CRC. (UMIN000004934)
- Primary endpoint: Frequency and Grade of peripheral sensory and motor neuropathy (PSN/PMN) (CTCAE v4 and PNQ)
- Secondary endpoints: Proportion of completion in oxaliplatin base therapy
- Proportion of completion in adjuvant chemotherapy
- Proportion of treatment selection
- Adverse event
- Compare FOLFOX to CAPOX in efficacy or adverse event

Methods

- Patients enrolled in 11 institutes (between 2011 and 2014)
- Participants were randomized into 2 arms:
  - Arm A: mFOLFOX6 (6 cycles) and capcitabine (4 cycles)
  - Arm B: CAPOX (56 cycles) followed by three months OX treatment

Consort flow diagram

Patients enrolled (n=91)

- Not fulfill the eligibility (n=2)
- Reject treatment (n=5)
- Eligible patients (n=86)

Characteristics of the patients

All patients (n=86)

- Age median (range): 65 (36–81)
- Sex: Male/Female: 49/37
- Tumor site (rectal/non-rectal): 32/54
- Histologic appearance (well/mod/or/other): 14/65/5/2
- Disease stage (II/III/IIb): 15/47/24

Results

- Proportion of completion and Dose of OX
  - Number: 86
  - mFOLFOX6: 30
  - CAPOX: 56
  - P value: 0.544
- Median dose of OX (range) mg/m2
  - All: 479 (82-531)
  - All treatments: 467 (82-512)
  - CAPOX: 490 (120-531)
  - P value: 0.123

- Frequency of severity (PSN, PMN)

PNQ-PSN

PNQ grade C≤
CTCAE grade ≤

PNQ-PMN

Cranial-CTCAE grade C≤

PSN during treatment and after 6 M follow-up

Conclusion

- The proportion of grade 3 PSN (3.3%) and PMN (1.2%) during treatment was lower than 6 months OX-based adjuvant treatment previously reported.
- At 6 months after the end of treatment, there was no grade 3 PSN patient.
- Sequential approach with three months OX-based regimen followed by 3 months capcitabine is a safe adjuvant treatment for CRC.
- PNQ appears to detect OX induced neurotoxicity earlier than CTCAE.

Acknowledgement

- This study was supported by Japan Southwest Oncology Research Support Organization (JSWOG/ORG).
- We would like to thank all participating patients and investigators participated in this study.

Statistical Design

- Main inclusion criteria
  - Histopathologically confirmed colorectal cancer.
  - Stage II (or high risk stage II) and R0 resection.
  - After resection, it is possible to begin the adjuvant chemotherapy within 8 weeks
  - Age: ≥ 20 years
  - ECOG PS: 0–1
- Main exclusion criteria
  - more than grade 1 (CTCAE v4.0) PN

Adverse Events

<table>
<thead>
<tr>
<th>All Patients</th>
<th>mFOLFOX6(n=32)</th>
<th>CAPOX(n=56)</th>
<th>P value</th>
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<tbody>
<tr>
<td>%</td>
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<td>G3</td>
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<tr>
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<tr>
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<tbody>
<tr>
<td>%</td>
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</table>

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