

COST-EFFECTIVENESS OF ADJUVANT FOLFOX THERAPY FOR STAGE III COLON CANCER IN JAPAN

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Objective

The FOLFOX regimen for adjuvant colon cancer consists of oxaliplatin, a platinum-based anticancer drug, combined with FU/LV. RCTs have demonstrated that the FOLFOX regimen prolongs disease-free survival (DFS) and overall survival (OS) compared with FU/LV for colon cancer patients.

The Multicenter International Study of Oxaliplatin, 5-Fluorouracil, and Leucovorin in the Adjuvant Treatment of Colon Cancer (MOSAIC) trial reported that the 3-year disease-free survival (DFS) rate was 78.2% for patients receiving FOLFOX and 72.9% for those receiving FU/LV (hazard ratio for recurrence, 0.77; P=0.002). At 5 years, in patients with stage III cancer, the 6-year OS was 72.9% in the FOLFOX group and 68.7% in the FU/LV group, (hazard ratio, 0.80; P=0.023).

In Japan adjuvant FOLFOX therapy was approved in 2009. We performed the cost-effectiveness of adjuvant FOLFOX therapy for patients with stage III colorectal cancer compared with standard FU/LV therapy.

Method

We retrospectively analyzed patient-level data from the multinational randomized controlled MOSAIC trial. We used the date of patient characteristics, DFS, and OS at 3 years, as well as dose of oxaliplatin.

FU/LV: LV (200 mg/m² IV infusion) on days 1 and 2, and 5-FU (400 mg/m² bolus IV injection followed by 600 mg/m² continuous infusion for 22 hours) on days 1 and 2, repeating 12 cycles every 2 week.

FOLFOX: 12 cycles of oxaliplatin (85 mg/m² intravenous [IV] infusion) on day 1 of the 2-week cycle and the FU/LV.

This cost-effectiveness analysis was performed from the perspective of the healthcare payer, and included only direct medical costs, not indirect costs (e.g., productivity costs). Using a time horizon of 30 years, both cost and effectiveness were discounted by 3% per year.

Utility scores were 0.8 (DFS), 0.6 (metastatic recurrence), and 0 (death) based on a Japanese study that measured general population utility scores of colorectal cancer using time trade-off and standard gamble methods.

As costs of metastasis, we used JPY 2.0 million per year for our base-case analysis. This cost was subject to sensitivity analysis. Adverse event (AE) costs were not included in the base-case analysis, because costs were unclear and the difference in costs was not expected to be large. AE costs were also subject to sensitivity analysis.

Results

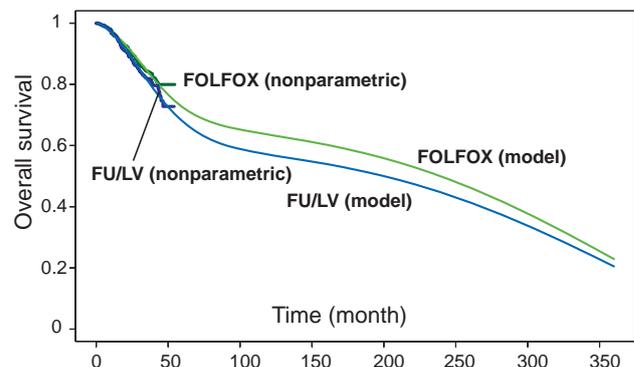
The Results of base-case cost-effectiveness analysis are shown in the below table. The ICER with FOLFOX was JPY 1.5 million (USD 17,000) per QALY compared with FU/LV.

	C (JPY 10,000)	IC	E (QALY)	IE (QALY)
FU/LV	194	-	9.07	-
FOLFOX	307	113	9.83	0.76
95% CI		34–174		-0.08–1.62

C: cost, IC: incremental cost, E: effectiveness, IE: incremental effectiveness

ICER (JPY 10,000/QALY)
149

Estimated OS curves are shown in the below figure.



ICER increased with shorter time horizons and lower costs of metastasis.

Cost of metastasis (JPY 10,000/year)	Time horizon (years)			
	10	15	20	30
100	444	278	216	174
150	409	257	201	161
200	375	236	184	149
250	341	216	169	137

With an additive mean AE cost of JPY 50,000 per patient, the ICER was JPY 1.7 million (USD 19,000), but at an additive mean AE cost of JPY 200,000 per person, ICER increased to JPY 1.9 million (USD 21,000) per QALY.

Conclusion

The National Institute for Health and Clinical Excellence in the UK uses a threshold range of £20,000 to £30,000 (approximately JPY 2.5 million to JPY 4.5 million), and in the US, USD 50,000 to USD 100,000 (JPY 4.5 million to JPY 9.0 million) is often used. A Japanese study on willingness to pay for an additional one QALY suggests JPY 5.0 million to JPY 6.0 million is an appropriate threshold.

Considering these criteria, FOLFOX is a cost-effective treatment for stage III colon cancer in Japan. Even when parameters were changed to reflect smaller improvements with FOLFOX, the conclusion is the same.