

# Cost-Minimization Analysis of Sequence Changes Between FOLFIRI and FOLFOX6 Therapy for Advanced Colorectal Cancer in Japan

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## ABSTRACT

**Background:** Randomized, controlled trials (RCTs) in 220 patients with advanced colorectal cancer reported no significant differences in survival periods between folinic acid/5-fluorouracil/irinotecan (FOLFIRI) and folinic acid/5-fluorouracil/oxaliplatin (FOLFOX6) therapies, irrespective of the treatment sequence. Based on a literature search, an economic assessment of both treatments given in 1 of 2 sequences (FOLFIRI and FOLFOX6, or FOLFOX6 and FOLFIRI) has not been conducted in Japan.

**Objective:** The present cost-minimization analysis used a mathematical Markov model to assess health care costs of these 2 treatment sequences from the perspective of National Health Insurance (NHI) in Japan.

**Methods:** The analysis simulated the expected costs resulting from the influence of treatment sequence in a hypothetical cohort of 10,000 patients with nonresectable advanced colorectal cancer over a period of 100 months using a hypothetical Markov model. Clinical parameters were obtained from the RCTs. Cost parameters included those for physical examination, medication, and personnel. Medication and physical examination costs were based on 2008 NHI drug prices and medical service fees, respectively. Costs were discounted at a monthly rate of 0.4575% (equivalent to an annual rate of 3%). The influence of each parameter (clinical and cost parameters) was assessed using a probabilistic sensitivity analysis by the 10,000-time Monte Carlo simulation.

**Results:** When FOLFIRI was used as the initial treatment in this analysis, costs to the NHI were reduced. On analysis of the influence of each parameter,

the expected reduction in costs, compared with FOLFOX administered as the initial treatment, was significant (¥7,787,828 [95% CI, ¥6,098,517–¥9,499,952]).

**Conclusions:** The findings of this cost-minimization analysis suggest that using FOLFIRI followed by FOLFOX versus the reverse strategy produced cost savings from the perspective of the NHI in Japan. However, differences in adverse-events profiles may warrant treatment adjustments in individual patients. (*Clin Ther.* 2009;31[Theme Issue]:2433–2441) © 2009 Excerpta Medica Inc.

**Key words:** cost-effectiveness, FOLFIRI, FOLFOX6, advanced colorectal cancer.

## INTRODUCTION

Colorectal cancer is the third most common type of cancer in both men and women in Japan,<sup>1</sup> with 37.9 advanced cases per 100,000 population (~210,000 cases total<sup>2</sup>) reported in 2008.<sup>3</sup> According to the Cancer Statistics in Japan, the estimated rate of cancer-related deaths was 17.3 per 100,000 population; 5-year relative survival, 68.9% for colonic cancer and 65.2% for rectal cancer.<sup>4</sup>

There have been remarkable advances in the surgical and medical treatment of inoperable advanced colorectal cancer. The chemotherapeutic regimens folinic acid/5-fluorouracil/irinotecan (FOLFIRI) and folinic acid/5-fluorouracil/oxaliplatin (FOLFOX6) have

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been associated with prolonged survival (improvement in median survival, 3.5 months [95% CI, 1.27–5.73;  $P = 0.008$ ]),<sup>5</sup> with good efficacy in terms of 3-year disease-free survival (improvement, 5.3%;  $P = 0.002$ ) and tolerability (patients who experienced National Cancer Institute Common Toxicity Criteria grade 3/4 toxicity, 30%).<sup>6,7</sup> These 2 regimens have been modified (FOLFIRI2 and 3, and FOLFOX2–7) since their development in the 1990s.<sup>8–10</sup> In randomized, controlled trials in 220 patients with advanced colorectal cancer, Tournigand et al<sup>11</sup> and Colucci et al<sup>12</sup> reported no significant differences in efficacy between these 2 regimens when used as first-line treatment.

Because chemotherapy for colorectal cancer is expensive (estimated 12-month medical costs in Japan in 2007, ¥300 billion<sup>13</sup>) and can be an inestimable financial burden for individual patients, the allocation of medical resources and the economic burden on patients must be considered. Based on the 2008 drug price list in Japan, medical costs of FOLFOX6

were ~2-fold those of FOLFIRI (¥357,344/mo vs ¥180,596/mo, respectively).<sup>14</sup> A literature search revealed no economic assessments of both treatments given in 1 of 2 sequences (FOLFIRI and FOLFOX6, or FOLFOX6 and FOLFIRI). Data on permitting the selection of appropriate chemotherapy in each patient were lacking. The aim of the present economic analysis was to determine the cost differences between these 2 sequences from the perspective of National Health Insurance (NHI) in Japan, using a mathematical Markov method.

**MATERIALS AND METHODS**

**Model Description**

A Markov model was developed using TreeAge Pro Healthcare 2008 (TreeAge Software Inc., Williamstown, Massachusetts).<sup>15</sup> Changes over time in 3 probabilistic health states (Figure 1) were used to estimate the expected costs of the 2 administration sequences in patients with nonresectable advanced

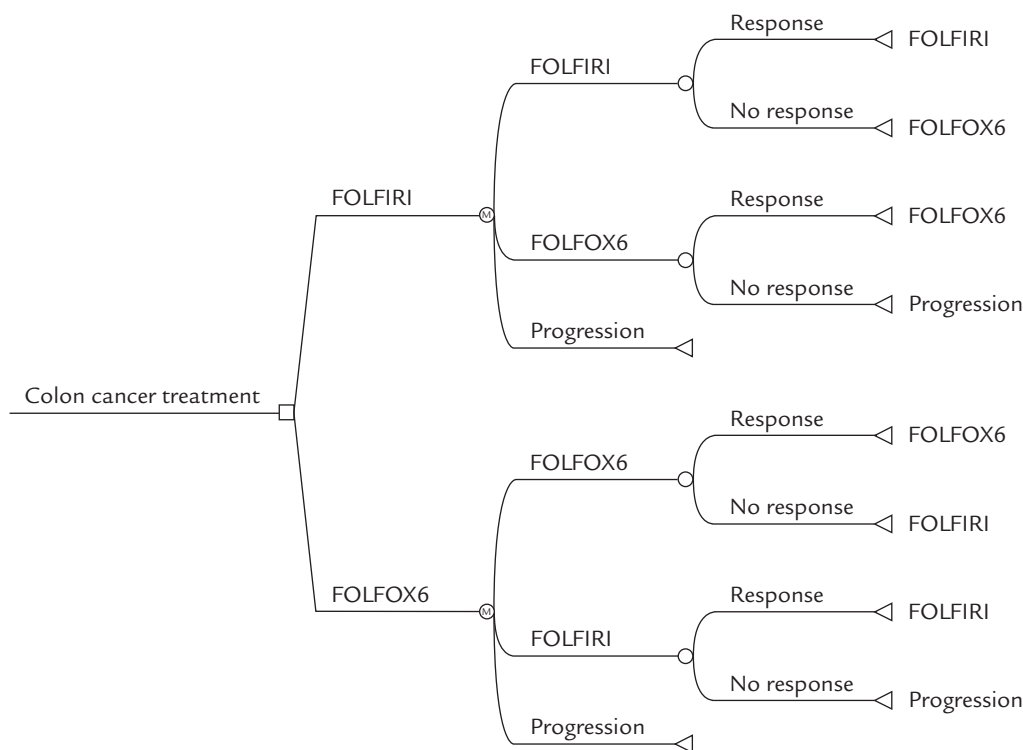


Figure 1. Cost minimization of sequence changes between folinic acid/5-fluorouracil/irinotecan (FOLFIRI) and folinic acid/5-fluorouracil/oxaliplatin (FOLFOX6) chemotherapy regimens for advanced colorectal cancer in Japan (hypothetical Markov model).

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