Discussion: This model shows that the difference in TWS, TWiST and the Q-TWiST proxy are significant. It further suggests that the benefits of a TWiST or Q-TWiST approach in advanced ovarian cancer can transparently highlight serious adverse events (toxicity) in the outcome as well as the costs to a decision-maker. Showing both TWS, TWiST and Q-TWiST outcomes may give the decision-maker greater scope for evaluating treatments. These outcomes are further relevant to oncology where serious adverse events play a critical role in patient well-being. Q-TWiST values are being derived to truly reflect patient preferences for different health states.

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OP4. Cost-effectiveness of Irinotecan (CPT-11) and best estimated chemotherapy regimen in patients with metastatic colorectal cancer after failure of 5fluorouracil (5FU) containing regimen: Results based on a phase III trial

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Background: Increased survival due to aggressive chemotherapy in metastatic colorectal cancer may be considered as a major breakthrough as long as patients' Quality of Life is not unduly jeopardized by toxicity. The issue of whether response or stabilization bring benefit in terms of Quality of Life (QOL) despite toxicity effects is still controversial. In addition, given the high acquisition cost of new chemotherapies, it is becoming more common to conduct economic evaluations comparing these new chemotherapies to older alternatives, that is to compare simultaneously their impact on costs (acquisition, administration, management of toxicities, complications) and on consequences (survival, other clinical benefit, QOL).
Methods: A randomised multi-center phase III trial has been conducted comparing CPT-11 as single agent to best estimated 5FU based chemotherapy regimen (single agent or combinations) in patients with metastatic colorectal cancer who have previously failed a 5FU containing regimen. Primary endpoint was survival. Median time to progression, response rates and symptom assessment were evaluated as secondary endpoints. QOL was assessed using the EORTC QLQ-C30. Use of hospital and ambulatory resources were also recorded.
Results: 267 patients have been enrolled with a median follow-up of 11 months. Final clinical results are currently being compiled, as well as QOL and resources usage, and will be presented. This will be one of the first economic evaluations in medical oncology based on prospectively collected data as part of a phase III clinical trial.
Discussion: Results of the economic evaluation based on this phase III trial will be compared to those obtained from modelling, and to results found in the literature.

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OP5. Economic evaluation of chemotherapy with Mitoxantrone plus Prednisone for symptomatic hormone resistant prostate cancer based on a Canadian randomised trial with palliative endpoints

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Background: A recently published Canadian randomised trial with palliative endpoints in patients with symptomatic hormone-resistant prostate cancer found reduction in pain and improvement of health related quality of life. The economic attractiveness of this strategy was uncertain.
Methods: A descriptive costing study and cost-utility analysis was performed from the perspective of the Canadian health care system. The trial randomised 161 patients to initial treatment with mitoxantrone and prednisone (M+P) or to prednisone alone (P), and showed better palliation with mitoxantrone and prednisone. There was no significant difference in survival. Detailed retrospective chart review was undertaken of resources used from randomisation to death of 114/161 patients enrolled at the three largest centres; these included hospital admissions, outpatient visits, investigations, therapies (including all chemotherapy and radiation) and hospice care. Hospital costs were calculated using the hotel approximation method and case costing from the Ontario Case Costing Project. Cost- utility analysis was performed by transforming the EORTC QLQ-C30 global quality of life item measured every 3 weeks on trial to an estimate of utility, and extending the last known value through to death.
Results: The mean total cost until death by intention to treat analysis was: prednisone alone CDN $29,000, mitoxantrone and prednisone CDN $27,300; a cost saving in favour of M+P of CDN $1,700. The largest single component of cost was hospital admission (M+P 65.8% vs. P 53%). Confidence intervals at 95% range from a saving of CDN $9,200 for M+P to an increased cost of CDN $5,800 for M+P. Best estimates of resource utilisation indicated that the strategy of using initial mitoxantrone and prednisone was consistently cheaper whichever time period was used to compare costs. A simple conservative estimate of the upper margin of the cost-utility ratio was obtained by applying the mean incremental utility to the upper limit of 95% CI for costs gives a value of $22,400 per QALY. The data set comprises individual patient costs and individual patient utilities. To additionally explore how to integrate two measures of variation (cost and utility) into one confidence interval, Fieller's Theorem was used to calculate confidence intervals for the ratio of differences in observed costs and effectiveness, i.e. the incremental cost-effectiveness ratio.
Discussion: Considering cost alone, a consistent but nonsignificant trend was found for initial use of M +P to be less costly than prednisone alone. This is due to a reduction in inpatient costs. A treatment that reduces symptoms and improves quality of life has the potential to reduce costs in other areas. Incorporating utilities results in a dominant strategy in favour of mitoxantrone and prednisone.

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OP6. Costs of care in a randomised trial of early hospital discharge after surgery for breast cancer

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Background: Inpatient hospital care is the major cost determinator of surgical treatment and totals up to 60 % of total health care costs for cancers. Shortening of hospitalisation is expected to reduce health care costs. However, a shifting of care to outpatient care and home care may counteract the savings achieved by shortening hospitalisation. We designed a study to determine the effect of reduction of length of hospital stay after breast cancer surgery on the rate of care consumption in and outside the hospital and on the costs of care.
Methods: 125 patients were randomised for a short or long postoperative hospital stay after surgery for breast cancer. Data on care consumption inside and outside the hospital were collected for a period of 4 months in diaries administered by the patients, and socioeconomic status was evaluated by questionnaires. Complications were also recorded. A cost-

minimisation analysis using the "societal" perspective was performed. Relevant resources were tabulated in appropriate units and the use was measured. After valuation of the resources the volumina were multiplied by the prices. Savings were compared with the savings of hospital charges.
Results: The cost of hospital care was reduced with US $ 1320 by introducing the short stay program. There was no difference in the incidence of complications. The use of professional home care was higher for the short stay group during the first month. The number of outpatient consultations, the intensity of informal home care and patient's costs were not increased after early discharge. Total costs of care were US $ 3062 for the short stay and US $ 4382 for the long stay group (p=0.0007). The savings of hospital charges by introduction of the short stay program was $ 2680.
Discussion: Early discharge after breast cancer surgery results in a substitution of hospital care for professional home care, but not medical care, during the first month postoperatively. The overall costs of home care are not different between the short stay and the long stay group. The shifting of care results in a potential cost saving, but this is substantially lower than the savings of hospital charges.

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OP7. Country-specific adaptations of a cost-utility decision model comparing chemotherapy in recurrent metastatic breast cancer

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Background: Analytic models of new medical therapies provide information for health care payers and providers who frequently must make decisions before long term outcome data become available. The international focus of pharmaceutical companies necessitates that models be developed for multiple countries. To facilitate multi-country analyses, we describe a process for developing a flexible basic model to be modified for specific settings using published data, physician opinion and nurse utility scores.
Methods: A decision analytic model for recurrent metastatic breast cancer was developed for a representative patient who has failed first-line chemotherapy containing an anthracycline. The model simulates the course of treatment for the representative patient and compares outcomes, costs and utilities of docetaxel, paclitaxel and country-specific usual other chemotherapy. An expert panel of oncologists in the UK and U.S. aided in designing the basic model. Data from published and unpublished clinical trials were used to estimate the proportion of patients having complete and partial response, stable disease or progressive disease and the proportion of patients having intercurrent or cumulative toxicities. The model assumes that there is no extension of survival for any of the treatments. Resources used in the management of metastatic breast cancer patients were obtained from oncologists in the UK, U.S., Germany, Italy, the Netherlands, and Spain. Each country panel identified a most commonly used chemotherapy to compare with the two new taxoid regimens. Health economists from each country provided costing data for the resources. Between 25 and 30 oncology nurses in each country completed a standard gamble to obtain health utility scores. The health state descriptions were translated and back-translated to assure compatibility between countries. Cost-utility analyses were conducted from the perspective of the country's health care system.
Results: A generalised model for managing recurrent breast cancer was sufficiently flexible to permit country-specific adaptation to reflect local management patterns, costs and utilities. Utility scores were comparable across countries. Costs for model disease states (i.e., terminal disease, administration of chemotherapy) varied across countries and the cost utility ratios ranged between £37,000 and £120,000 per QALY.
Discussion: By carefully defining the patient population a flexible analytic model was constructed for adaptation to multiple countries. Variation in the costs for disease states may reflect actual or methodological differences. Precise definitions of disease states and costing methods are essential for obtaining results that can be compared across countries.

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OP8. Economic implications of hepatic arterial infusion chemotherapy in the treatment of nonresectable colorectal liver metastases

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Background: Approximately 20% of patients with colorectal cancer die from metastases confined to the liver. A meta-analysis recently performed by our group confirmed that in these patients, hepatic arterial infusion of 5-fluoro-2-deoxyuridine improved tumor response compared to intravenous chemotherapy with fluoropyrimidines or supportive care (including palliation when necessary).
Purpose: Because of the high cost of hepatic arterial infusion we undertook a cost-effectiveness analysis which related the cost of such therapy to its medical efficacy. Methods: The patient population was drawn from the seven randomized clinical trials included in the meta-analysis, and included individual data from 654 patients. Of these seven trials, five compared hepatic arterial infusion and intravenous chemotherapy, and two compared hepatic arterial infusion and an ad libitum control group in which some patients could be left untreated. Patients allocated to hepatic arterial infusion were the hepatic arterial infusion group, and the others the control group. The measures of efficacy were survival and tumor response. Healthcare costs (in 1995 U.S. dollars) were computed over the duration of patient follow-up, derived from actual costs in two centers, one at Hopital Henri Mondor (Paris France) and the other at Stanford University Medical Center (Palo Alto, California). The total cost of treatment included the initial procedure, chemotherapy cycles and main complications.
Results: The total gain in life expectancy in the hepatic arterial infusion compared with the control group was 3.2 months (standard error : 0.7 month). For patients treated by hepatic arterial infusion in Paris, the hepatic arterial infusion pump, initial hospitalization and the entire process (including follow-up and complications) cost on average $8,400, $15,172, and $29,562 respectively; in Palo Alto these costs were $4,700, $13,784 and $25,208 respectively. For patients in the control groups in Paris and Palo Alto the total treatment costs were on average $9,926 and $5,928. The additional costs of hepatic arterial infusion over control treatment were $19,636 in Paris and $19,280 in Palo Alto. The additional costs of hepatic arterial infusion over control were $19,636 and $19,280 respectively. The cost-effectiveness (i.e. the additional cost divided by the additional benefit) with respect to survival of hepatic arterial infusion group patients compared with control group patients was $73,635 per life-year in Paris, and $72,300 per life-year in Palo Alto.
Discussion: The cost-effectiveness of localized chemotherapy for colorectal liver metastases is within the range of accepted treatments for serious medical conditions, although it might be considered borderline by policy-makers in some countries. Prospective clinical trials should be conducted to more definitively answer this question.

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