

### OP19. Quality of life assessments of patients with pancreatic cancer receiving MTA (LY231514, a multi-targeted antifolate)

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**Background:** Prognosis for late stage pancreatic cancer has typically been poor. Chemotherapy has offered some improvement, but with the risk of toxicity. Quality of life (QoL) instruments may be used to assess a patient's perception of the safety and efficacy of chemotherapy.

**Methods:** QoL was assessed in a multicenter phase II trial of chemonaive patients with unresectable pancreatic cancer receiving MTA (600 mg/m<sup>2</sup> every 21 days). QoL was assessed using the FACT-G at baseline and at the end of each cycle.

**Results:** Thirty-three patients completed 133 questionnaires over the first 6 cycles of therapy (median=4). For all patients, no significant changes ( $p < 0.05$ ) from baseline mean scores were seen in the physical, social/family, and functional well-being subscales. Statistically significant improvements were noted in the relationship to doctor and emotional well-being subscales. When comparing patients with progressive disease (PD) to those without PD, changes from baseline were significantly different in the social/family well-being subscale, where patients with PD worsened and those without PD improved.

**Discussion:** Statistical analyses were limited by the small number of patients and by the interpatient variability of scores. Although only 2 patients responded to MTA, 13 patients had stable disease for at least 6 months. The most commonly reported toxicities associated with MTA were myelosuppression, rash, stomatitis, nausea/vomiting, and diarrhea. Despite these toxicities, QoL was maintained during treatment with MTA for pancreatic cancer. Symptom-related data could be obtained with a pancreatic cancer-specific instrument, such as the FACT-PA, which was not available at the time this protocol was initiated.

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### OP20. Discordance between physicians' estimations and breast cancer patients' self-assessment of side-effects of chemotherapy : An issue for measuring the impact of anticancer treatments

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**Background:** Because side-effects of chemotherapy may be more diverse and reactions of patients more variable and individualistic than tends to be assessed by clinicians, we have carried out a study among no metastatic breast cancer patients in order to compare their own self-assessment of physical symptoms with the parallel estimations done by clinicians during adjuvant chemotherapy.

**Methods :** The study was carried out in three outpatient clinics of Marseilles (South-Eastern France) between May 1995 and June 1996. All breast cancer patients receiving an adjuvant NC polychemotherapy comprised of Mitoxantrone (12 mg/m<sup>2</sup>) and Cyclophosphamide (600 mg/m<sup>2</sup>) I.V. administered in 4 cycles of 21 days and concomitant radiotherapy were included in the study. The self-administered questionnaire evaluated the prevalence, duration/severity and distress level of 19 physical symptoms. It was proposed to patients at each cycle of chemotherapy. In parallel, the physicians completed a standardized sheet about toxicity of treatment, containing the same list of symptoms than in patients' questionnaire.

**Results:** 52 patients were asked to participate to the study. All the patients agreed to participate and overall patients' compliance rate to questionnaires was 89%. Symptom prevalence, self-reported by patients in 185 cycles, was high. By example, nausea was reported in 92% of cycles, tiredness in 88% and alopecia in 73%. In addition, some symptoms, which do not usually focus clinicians' attention, are frequently self-reported by patients (54% to 44% of cycles). Some of these latter as hot flushes, stomach pain, muscular pain and headache lasted, when present, one week or more and were very distressing for patients. The values of Cohen's Kappa coefficients, computed in 178 cycles, for measuring the concordance between patient's and physicians' assessments are less than 0.70 for all symptoms. They are between 0.53 and 0.40 for diarrhoea, weight loss, taste change, cystitis, hot flush and fever and less than 0.40 for some important symptoms as nausea, vomiting, alopecia, mucitis.

**Discussion :** These results demonstrate that physicians underestimate the symptoms experienced by their patients during chemotherapy and raises the problem of the evaluation of the impact of treatments in oncologic clinical research. In the current context of most health care systems, where resource allocation constraints tend to impose more and more "tragic choices" to clinicians, it is worth better knowing what matters most for oncology patients in terms of their subjective daily experience of their illness and their care.

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### OP21. Macro-financing mechanisms, micro-innovation incentives and resources (re-) allocation in anticancer treatments : experience from a French cancer institute

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**Background:** French public and private but non-profit hospitals have been experiencing for two years a major change in the financing mechanisms. Because of skyrocketing health expenditures, average costs calculated from inpatients and outpatients stays over a sample of 3 regional and 18 general public hospitals, 11 private non-profit hospitals and 3 cancer institutes (for the year 1995) constitute the backbone tariffs of the prospective payment-like system given by the regulator on the basis of the casemix of the hospitals.

**Methods:** The paper uses the framework of industrial economics in analysing the micro-(dis-)incentives involved by financing macro-mechanisms. It takes the case of a French cancer institute which has to make a tradeoff between health and financial interests in the managing of medical change and technological innovations.

**Results:** The new prospective payment-like system moves the purpose of innovation from health improving to cost saving. Technological innovation was clearly aimed at improving (quality of) life whatever the cost may be under retrospective payment-like system whereas it is from now biased towards cost cutting without too important loss in health quality. This is due to the gulf between the timing of medical innovations and the financial one. Hospitals must most often bear significant expenditures before the new technology has been adopted and agreed by the health care regulator which reschedules the costs associated to Diagnosis Related Groups (DRG) using it. Then, the hospital copes with sunk costs. This delay is about 2 years and a half for new chemotherapy drugs in the French DRG classification. Because of this inertia, hospitals may develop pareto-optimal procedures by carrying out internal resources reallocation. Experience from a French cancer institute points out standardization of treatment of breast cancers with good prognosis and treatment of relapses in acute leukaemia. This strategy intends to monitor and reduce costs in the previously said parts of treatments *ceteris paribus*, and to enlarge the financial support for

treatment of breast cancers with bad prognosis and of primitive treatment of acute leukaemia.

**Discussion:** There is a puzzling dilemma for hospitals in general and more especially for cancer institutes between profit-based and health output-based strategies. Public health interest only goes hand in hand with financial interest in implementing new techniques or methods when they cut treatment costs. When they are both life saving and cost improving they may be not adopted even if they are most cost-effective. The prospective payment-like system obviously offers very slight incentives to innovate, which may be detrimental to medical activities such as anticancer ones where medical progresses still remain to be done.

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## OP22. Economic evaluation of Amifostine in the treatment of small cell lung cancer (SCLC)

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An economic evaluation is being conducted as part of a randomised multicentre study assessing the role of the cytoprotective agent, amifostine, in the treatment of small cell lung cancer. This study - the DART study (Does Amifostine Reduce Toxicity?) - was developed following a phase II pilot study to assess response rate in 30 previously untreated patients with favourable prognosis SCLC. Treatment was given with ICE (ifosfamide, carboplatin and etoposide) chemotherapy. A high objective response rate was reported (83% (95% CI (70%, 97%))), but myelotoxicity was severe. 86% of patients had WHO grade 3/4 neutropenia (95% CI (73%, 99%)) and 63% had WHO grade 3/4 thrombocytopenia (95% CI (46%, 81%)). One third of patients spent time in hospital for treatment-related complications. The length of stay is shown in the table:

Cycle number	No. of patients receiving cycle	No. of patients spending time in hospital	Median days in hospital	Range
1	30	7	9	1-16
2	29	4	10.5	2-13
3	27	6	2	1-11
4	25	6	2	1-11
5	24	8	2	1-10
6	17	2	2.5	23

It has been suggested that cytoprotection of the normal tissues might allow the preservation of tumour cytotoxic dose intensity with fewer and less severe side effects. If amifostine were found to be effective in reducing myelosuppression, there might be advantages in patient outcome and in resource costs relating to management of chemotherapy-related toxicities.

This study aims to investigate whether the administration of amifostine before each cycle of ICE chemotherapy will attenuate toxicity. Eighty-four previously untreated patients with favourable prognosis SCLC will be randomised to receive either amifostine followed by chemotherapy or chemotherapy alone, for a maximum of 6 cycles.

Resource use will be examined using data about hospital visits, investigational procedures undertaken, and treatments administered. In-patient admissions and length of hospital stays for all reasons, the number of out-patient visits and day patient admissions will be recorded. All medication with associated costs and details of any other procedures will be recorded. Patient outcome will be assessed using the EuroQoL questionnaire, completed immediately prior to each cycle of treatment and then at three monthly intervals for 18 months or until death.

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## OP23. Elicitation of preferences and patients participation in the decision making process

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**Background:** The purpose of this study was to give patients the choice between two ways of adjuvant treatment for breast cancer: a *short* during 9 weeks chemotherapy and radiotherapy concomitant - and a long during 16 weeks chemotherapy followed by radiotherapy - with the intention to determine the explicative factors of this choice, to elicit patients' preferences and the need to choose for the patients.

**Methods:** As we faced an uncertainty decision problem the referenced economic model is the expected utility theory. We then have developed the questionnaire in order to elicit: patients' behaviour towards risk, present preference and risk perception. Patients enrolled were menopausal or non menopausal. Non menopausal patients had 1 to 3 involved axillary lymph nodes or none with at least 1 of the prognostic factors as SBRIII, HR-, PVTE+. The chemotherapy associated 4 cycles of 12mg/m<sup>2</sup> mitoxantrone and 600mg/m<sup>2</sup> cyclophosphamide, every 21 days. At the first consultation, the physician explained to patients what was the choice and gave them an information letter explaining the advantages and disadvantages of each way of treatment and some probabilistic information about side effects. Then (s)he filled out a questionnaire to let us know if patients were influenced by him(her). The day of the first cycle, patients gave their responses and filled out the first questionnaire which had to elicit the three main indicators above in accordance with the economic theory. They received a second one at the end of the treatment so as to know their choice *a posteriori*, the satisfaction to be able to choose the treatment and the degree of desire for participation in the therapeutic decision making process.

**Results:** At the present time, choice was proposed to 57 patients: 39 (67%) of them chose the *short*. 49 patients had already filled out the first questionnaire. The univariate analysis showed that 7 variables had a statistical significant explicative part for the choices fear of adverse effects, length of treatment, value of gains associated to the chosen treatment, trade off in number of weeks making patients changed their choice: fear of fatigue and fear of amassing adverse effects both linked to the *short* treatment, behaviour toward risk. Among the 34 patients (26 in the short) who had filled out the second questionnaire, only 2 (long) thought that they will "recommend" the other treatment. About satisfaction with the possibility to choose treatment, 88% answered "quite" and 76% said that it wasn't or it was a little difficult to make it. About the degree of participation, 73% wanted to take the decision.

**Discussion:** At first, because the choice being not statistically associated with patients' social demographics characteristics, we could say that patients' choice could be effectively considered as a trade off between side effects (the risk) and time. Secondly, results demonstrate how important it is to let patients having a more active participation in the decision making process and then to work about elicitation of preferences. Finally, the expected utility theory seems here to be adapted for modelize the decision making process in oncology.

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## OP24. Costs and quality of life in metastatic breast cancer

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**Background:** With an annual incidence of 26,000 cases in France, breast cancer is the most common malignancy in French women, accounting