Correspondence and Short Communications

Comments on published articles, short communications of a preliminary nature, case reports, technical notes and the like are accepted under this heading. The articles should be short and concise and contain a minimum of figures, tables and references.

QUALITY OF LIFE IN NON-SMALL CELL LUNG CANCER PATIENTS

Dear Sir,

We have read with interest the excellent report by Fernández et al. on the quality of life (QL) in advanced non-small cell lung cancer (NSCLC) (1). However, there are a number of comments which we would like to make. Some doubt still remains as to whether the toxicity is outweighed by the benefit of chemotherapy in advanced NSCLC. In addition, it is unclear whether chemotherapy has any major influence on survival when compared to symptomatic treatment alone (2).

There is improvement of symptoms, and thereby of QL, in most patients with NSCLC after chemotherapy. Furthermore nausea and vomiting are no longer major problems, thanks to efficient antiemetic treatment.

The Karnofsky performance status (KPS) scale is a system for measuring patient independence with moderately high reliability, and it has considerable value as a global indicator of the functional status of cancer patients, but this index conveys no information about quality of survival (3).

The study by Fernández et al. (1) unfortunately includes only 31 patients and larger studies are obviously needed in order to further elucidate this important issue. It must be emphasized that subjective evaluation plays an important role in these studies. Surely this is a field where intercenter collaboration based on properly designed protocols is necessary in order to answer specific questions.

It is not clear whether the report commented on includes hospitalized patients or outpatients, although the first possibility seems more likely. This factor should be taken into consideration for QL evaluation. We have had some experience of the assessment of a visual analogue scale (in the measurement of the pain in cancer patients, a key component of QL) and we think that the patients must be directly evaluated by the oncologist and not by the nurse, as was done in the trial by Fernández et al.

It is also of interest to evaluate anticipatory and delayed emesis. In a recent trial of our group (not yet published) on antiemesis therapy, we found 39 episodes of anticipatory vomiting after 282 chemotherapy courses (13.8%). We feel that this is a significant percentage.

It seems reasonable to record by the questionnaire the onset and the duration of symptomatic improvement since chemotherapy initially often induces a worsening of QL, a fact which might be important (4, 5).

Finally, some general considerations:

1. For 15 years now, we have been using the ECOG scale for performance status (6) which is quite an easy system to use and as useful as KPS. In our chemotherapy trials, stratification of patients into two subgroups (≤ 2 and >2, on ECOG scale) has been found to yield important prognostic information.

2. Accurate definition of QL is difficult, due to its composition of physical, emotional and social elements. While performance status may be an index of functional status, it does not reflect QL, and QL measurement should regularly contain an assessment of satisfaction with life (7). Therefore, a number of different parameters is needed in order to assess QL of cancer patients. Conclusions about this issue must be viewed with caution.

In summary, there are still many questions to be answered within this field and clinical trials evaluating QL are ongoing and will continue to be pursued.

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Dear Sir,

We appreciate the interest of Ordóñez et al. in regard to our study of quality of life (QL) assessment in patients with non-small cell lung cancer (NSCLC) while receiving chemotherapy (1).

Ordóñez et al. appropriately point out that the putative benefit of chemotherapy could be outweighed by toxicity. However, they also mention that chemotherapy may ameliorate the severity of symptoms to some degree. We can also agree with the statement that Karnofsky performance status (PS) does not measure survival quailty.

Ordóñez et al. point out that our sample was a small one, and they draw attention to the subjectivity bias of such studies. As indicated in our paper, the study was not planned as a broad QL assessment. However, we did measure issues relevant to some facets of QL, namely subjective response, improvement or worsening of lung related symptoms, anorexia, weakness, weight loss, level of physical activity and gastrointestinal toxicity. The term QL has been used with regard to many aspects of the physical and mental condition, including functional ability, symptoms, perception of health and psychological relation between patients and oncological physicians. Some patients can have the quality of their

lives enriched by trained nurses with a knowledge of symptom management (2). Feasibility, internal consistency, test–retest variation and validity of using 100 mm-visual analogue scales (VAS) have been extensively evaluated in our institution in a prior study (3). More important, however, is the opinion by Ordóñez et al. that nurses are the right persons to help patients in answering the VAS questionnaire and scoring by way of categorical scales (e.g. number of emetic episodes, severity of emesis). In our opinion trained nurses have proved to be more able than physicians to observe and register patients' complaints.

We have not had the opportunity to read the unpublished work on antiemesis evaluation by Ordóñez et al. in which they found 13% anticipatory emesis. Measuring anticipatory and delayed emesis was beyond the scope of our study and these issues are not really related to QL. With regard to anticipatory vomiting, their figure seems to be high, suggesting that an inadequate antiemesis regimen was used. In our experience 4% anticipatory vomiting was observed in 145 patients receiving high-dose cisplatin. Furthermore we have measured the incidence and severity of delayed emesis and conducted a trial with a delayed antiemesis regimen (4). Strategies to prevent delayed onset of nausea and vomiting should start with patient information. The nurse should explain to the patient that this phenomenon can occur and should assess the chemotherapy tolerance at home by telephone follow-up and on readmission. The nurse is in the key position of helping patients and to enhance their QL by dealing with side-effects such as nausea and vomiting (5). Finally Ordóñez et al. suggest that 'we have been using the ECOG scale for performance status (6) which is quite an easy system to use and as useful as KPS . . .'. We endorse this statement, but not without reservation; Karnofsky PS has in fact turned out to be a very accurate tool. In one study Karnofsky scale was rescaled, showing that the prognostic information increased significantly with the use of a recoded scale (e.g. defiing an 85 value between 80 and 90) (6).

Clearly, additional research is needed in order to further clarify the degree of suffering associated with lung cancer; further studies should be carried out to determine which items are linked with high and low suffering; duplicate trials need to be conducted with larger sample sizes to allow comparisons of groups by ethnicity, socioeconomical status and educational levels (7).

No practical purpose can be served by fallacious comments with no real support.

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ACLARUBICIN IN THE TREATMENT OF ADVANCED GASTROINTESTINAL ADENOCARCINOMA

Anthracyclines have been widely used in the treatment of gastrointestinal cancer as single agent and in combination chemotherapy (1–3). However, the treatment results have been relatively discouraging.

Aclarubicin is a novel anthracycline differing in many aspects from daunorubicin and doxorubicin; it has been reported to be active also orally (4). It has a greater inhibitory effect on RNA synthesis, especially on ribosome RNA synthesis, and thus designated as a class II anthracycline while daunorubicin and doxorubicin belong to class I (5). Aclarubicin has a more rapid cellular uptake than daunorubicin and doxorubicin.

Since the late 1970s aclarubicin has been investigated mostly in leukemia but also in limited series of solid tumors (6–10). The efficacy of aclarubicin seems to be about the same as for daunorubicin and probably somewhat lower than for doxorubicin. The drug has much less pronounced side effects, especially cardiotoxicity, than doxorubicin and produces no or minimal alopecia (6–10). Extravasation necrosis has been uncommon (7). The aim of this study was to evaluate the efficacy and tolerability of aclarubicin as a single agent in metastatic or inoperable gastrointestinal adenocarcinoma.

Patients. Fifty patients entered into the study. Only patients with a performance status of Karnofsky $\geqslant 70\%$ were included. Patient characteristics and primary therapy are presented in the Table. Out of these 50 patients 11 received only one cycle; nine of them died early due to disease progression and in the other two the therapy was interrupted for other reasons (submyocardial infarction and hemiplegic attack respectively.) In the remaining 39 patients the response could be evaluated. Aclarubicin was given intravenously at a dose of 100 to 120 mg/m^2 and the infusion was repeated every fourth week. The median number of courses was three (range 2–9) and the mean dose per cycle 177 mg (range 120–230 mg).

Results. Complete response was obtained in one patient (colon cancer) who is still alive. Two patients (gastric cancer) obtained partial response, and the total response rate was thus 8%. No change was observed in 11 and progressive disease in 25 patients. Forty percent of the patients survived one year and 10% two years. Side effects were mostly mild (WHO grades 1 and 2): nausea and vomiting in 64%, diarrhea in 20%, thrombocytopenia in 28% and leukopenia in only 4%. One patient has mucositis (grade 1), and alopecia (grade 1) appeared in two cases. One patient with a history of coronary disease developed submyocardial infarction after the first cycle and a concomitant blood transfusion. No other episodes of cardiac adverse reaction were recorded.

Discussion. In this trial aclarubicin showed modest activity with good tolerability. There are few studies available concerning aclarubicin in gastrointestinal carcinoma. Response rates of 15% have been presented in gastric cancer, 12% in pancreatic and 7% in colorectal cancer (1, 3, 9, 11–13). Similar response rates have been reported with epirubicin (1, 11, 14). Thus the low response rate is not unexpected.