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Letter to the Editor

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Professor F. Labrie offers the following reply to the preceding letter.

IN RESPONSE to the comments of Professor Newling, we are pleased to see that the criteria of response of the EORTC are becoming closer to those of the NPCP, since the use of different sets of criteria creates unnecessary confusion and has been the subject of too much debate. When Professor Newling refers to 12-year-old criteria, it should be mentioned that we have used the latest available EORTC criteria published in 1986 [1] and have stated: 'The EORTC criteria of response are to a very large extent identical to those developed by the NPCP' [2]. It should be indicated, however, that significant differences still remain which, in our opinion, should be resolved. Some problems are also caused by the lack of sufficient precision of the EORTC criteria, a concern which is further illustrated in Professor Newling's letter.

As indicated in the more recently published criteria of response of the EORTC in 1988 [3], there are still differences in the definition of complete response since the EORTC only requires 'no evidence of progression of osteolytic lesions if any present' [3] while, according to NPCP criteria, 'osteoblastic lesions, if present, disappeared with a negative bone scan' [4].

Concerning the partial response criteria, Professor Newling indicates: 'There should be normalization of bone scan and recalcification of lytic lesions on X-ray.' How does this requirement differ from a complete response? These are simply marked differences in the EORTC criteria published in 1986 [1], 1988 [3] and those indicated in the letter of Professor Newling. Moreover, one should also indicate if the EORTC criteria of partial response include all five as described in Professor Newling's letter or if any of the five or a combination of some is sufficient.

Moreover, we feel, as indicated in our paper (*Eur J Cancer Clin Oncol* 1988, **24**, 1869–1878), that a 50% decrease in local disease should not, by itself, be sufficient for partial response. In fact, if the combination therapy is used in previously untreated patients, at least a 50% reduction in prostatic tumor size will be seen in almost all patients.

It is thus quite clear that more uniformity and precision is needed concerning the EORTC criteria. We would suggest that the NPCP criteria of response as described and enumerated in reference [2] can monitor with precision and relative ease the evolution of advanced prostate cancer and take into account the new technology for assessment of local and regional disease (especially ultrasonography and MRI).

We are a little concerned over Professor Newling's remarks about bone scintigraphy. It is well understood that bone scintigraphy measures reactive bone. This is why bone scintigraphy remains positive some time after disappearance of an active invading tumor. However, after a certain delay necessary for bone repair, the finding of a negative bone scan is the most reliable index of control of cancer progression in the bones [4, 5].

Concerning the category of stable disease, this aspect is discussed in detail in our paper and, with proper controls, we suggest that it is an important category of response which has a significant prognostic value. The best argument for the use of stable response is that the patients having stable disease as best response have a prognosis almost superimposable to that of patients having partial response as best response (see Figs. 2 and 3 in reference [2]).

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Concerning the complete responses, our study performed in a large series of 199 previously untreated stage D_2 patients has shown a rate of 26.3%. The results obtained are the best arguments and certainly supersede any experimental animal model where various hormonal manipulations have been performed and could well be responsible for the change in hormone sensitivity of the cancer [6, 7].

Concerning the other questions mentioned in Professor Newling's letter, it should be mentioned that when relapse occurs, it usually takes place at the site of previous metastases. We strongly feel that there is no indication for a second biopsy of the primary after the response has been measured. Concerning the time for CR, an appropriate comment is that complete disappearance of clinical signs of cancer takes longer than stabilization or partial response. The important point is that CR patients live longer and have a better quality of life. The median time to stable disease is a function of the timing of the visits. Obviously, the true median time of a stable response is likely to be shorter but its precise timing would require more frequent evaluations which were not judged useful for proper follow-up of the patients.

Concerning toxicity, it is well recognized in our studies and in many other recent studies that combination therapy with castration (surgical or medical) and Flutamide has minimal side-effects, thus prolonging life with a good quality of life.

It is untrue to indicate that the results of combination therapy are equivocal and Professor Newling should be well aware of such data. In fact, in all studies where a pure antiandrogen and castration were used in a sufficiently large number of patients for a sufficiently long period of time, life was prolonged with a good quality of life [8, 9]. Please do not refer to studies using steroidal antiandrogens and studies at a too early stage where a significant difference has not yet been reached due to a lack of sufficient evaluable numbers. With the experience of recent studies where premature disclosure of the data led to erroneous suggestions which have all been corrected at a later date, one should restrain from disclosing data which are too immature and unable to yield to significant conclusions.

Combination therapy is the first and only treatment of prostate cancer which has been shown in randomized studies to prolong life. With the available data [8–11], we suggest that the combination therapy (using pure antiandrogens) is the treatment of choice for all patients with advanced prostatic cancer. Efforts should now, in our opinion, be focused on early detection and early treatment of the disease. This is where new progress is likely to be made with the collaboration of research groups like that of the EORTC GU Group.

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