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Chairman's Summary

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THE MAIN point made by E. Cvitkovic in proposing for the motion is that every patient must be seen almost as an experiment in themself; thus, the outcome measures used should be tailored to the individual situation. Seconding for the motion, K. Redmond argued that patients' well-being and economic cost are the most important endpoints missing from most anticancer drug trials at the moment.

In opposing the motion, W. ten Bokkel Huinink suggested that response rate is the only value of real importance that may be drawn from phase II studies, although he acknowledged the need to look at other endpoints in the subsequent further evaluation of an agent. Seconding against the motion, K. MacRae considered that the methods available to the oncologist were superb, but that they were not being used to their best advantage. He pleaded for better randomisation and more rigorous statistical analysis.

SUMMARY: PROPOSER FOR THE MOTION (E. CVITKOVIC)

Are the current methods and rules for evaluating the efficacy of anticancer treatments good? In my view, the current methods of evaluation are good, but they are not yet good enough. Flexibility is essential.

In recurrent glioma, for example, I would need evidence of stabilisation of the condition for at least 3 years, together with a clear histology, to convince me that treatment had been effective. If such a tumour was histologically malignant grade IV before surgery and the computer-assisted tomography scan remained unchanged for 3 or 4 years, I would be satisfied that the treatment has been worthwhile. In the specific situation of a rapidly growing testicular cancer or lymphoma, which may double almost before your eyes, I would accept evidence of tumour shrinkage over as little as a week as enough to convince me that the treatment was useful. In my view, therefore, the only rules regarding efficacy determination should be those that are most valid for that situation at that time.

At the same time, the statisticians' arguments that rigorous, randomised, controlled trials are essential if the benefits of a given treatment (in terms of improved survival and quality of life) are to be fully evaluated for our patients are certainly acceptable. Even so, it remains important that the numbers of patients involved in controlled trials are minimised. This both avoids the unnecessary exposure of large numbers of patients to useless compounds and accelerates the overall pace of drug development.

For all these reasons, I suggest that the focus of drug development research is shifted such that promising new agents are evaluated in small trials in those extreme situations where the treatment effect is most likely to be rapidly apparent. On the basis of favourable results obtained in such trials, an accelerated progression to registration may be possible. The drugs' true merits may, therefore, be evaluated more quickly during the post-registration period of combination, schedule experimentation and explorations that follows.

SUMMARY: PROPOSER AGAINST THE MOTION (W. TEN BOKKEL HUININK)

I cannot emphasise strongly enough that most phase II studies yield negative results and I therefore share the view of E. Cvitkovic that such trials should be carried out as quickly as possible in as few patients as possible. I agree with him that response must be measured in the most appropriate way, but I stress that it must be defined precisely. Generally, I believe that outcomes, such as minimum response or no change, should be abandoned, but acknowledge that exceptions to this must apply in special situations.

I also agree with K. Redmond that aspects such as economics and nursing time are important over the years in drug evaluation. Nonetheless, I think that these are outcomes for consideration during the later phases of drug evaluation. Within the context of phase II studies, response rate should remain the primary endpoint.

Current methods of drug evaluation have provided the framework for the major breakthroughs of the past, such as the development of cisplatin, etoposide and carboplatin. A revitalisation of oncology is now taking place with the promise of new agents. This is also the result of the methodology currently used, and re-affirms the ability of this methodology to continue to yield progress.