Letters to the Editor

Survival in renal cell carcinoma: a randomized evaluation of tamoxifen vs interleukin-2, α-interferon (leucocyte) and tamoxifen

Sir

The paper by Henriksson and colleagues has methodologic variabilities leading to important drawbacks and therefore is of limited value in answering the question of whether immunotherapy improves survival.

The authors state that they compare ‘one of the present (and presumed best) treatments, interleukin-2, α-interferon and tamoxifen, with a control arm of tamoxifen only’ and that they use ‘a schedule reported previously by Atzpodien and colleagues’ (Atzpodien et al, 1990). There is a dramatic and probably important difference in the doses of interleukin-2 (IL-2) and α-interferon (IFN-α) between the two protocols. For example, Atzpodien and colleagues gave a total of 36 million IU IL-2/day for 2 days to start their protocol, whereas the Swedish study protocol called for 9 million IU IL-2/day. In general, doses used in the Swedish protocol are 50% of the cited schedule or less. In addition, the authors state that only 40 patients of the 65 patients in the treatment arm received 75% or more of the intended dose; 25 of the patients received less than 75% of the intended dose and five of them less than 25% of the intended dose. No data are available how many patients received the intended dose or at least 90% of it.

It cannot be expected that cytokine effects are completely dose-independent as it seems to be assumed by the authors. The treatment schedule of this protocol constitutes a very different schedule from the one they cite, and substantial dose reduction might decrease therapeutic effects substantially. This treatment variant could be inefficient in improving survival. However, it has to be questioned even whether this is answered by the study. Relevant patient information is missing. No information is available whether only patients with proven progressive disease were included in the study. Generally accepted and well-known risk factors on survival have not been shown to substitute for Elson’s risk factors (Elson et al, 1988), are not used to stratify the study population of the seven institutions involved in treating the patients. Instead the authors use laboratory data and an evaluation of specific time frames. However, the laboratory data (haemoglobin, platelets, white-cell count, creatinine and albumin) and the time frame analysis have not been shown to substitute for Elson’s risk factors in determining survival as assumed by the authors.

Important methodological issues, such as significant dose reduction, are not stated in the Abstract or Methods section and are not discussed. Treatment protocol is given as a legend only and recognition of these important dose modifications in the Abstract is not possible and in the paper needs detailed search. The paper contains little information on the effect of IL-2, IFN-α treatment on survival in progressive metastatic renal cell cancer. A major concern of the authors was toxicity of treatment. In fact, they state that ‘immunological manipulation is associated with toxicity, at least during the treatment period’. This is true only for systemic applications. Local applications of cytokines can have immunomodulatory effects and no toxicity at all, as we have shown previously (Huland and Huland, 1989). Inhaled, local IL-2 has also been used with only moderate toxicity by our group (Huland et al 1992, 1997) resulting in stable quality of life during mean 13, 4 months of treatment (Heinzer et al, 1999). Survival data in patients treated with inhalation of IL-2 are promising, compared to risk factors on survival, published by Elson. Local treatment schedules without toxicity might allow efficient therapies to be found without the limitations of dose-dependent systemic toxicity.

E Huland and H Heinzer
Department of Urology, University Hospital Eppendorf, Martinistr. 52, 22046 Hamburg, Germany

REFERENCES

Atzpodien J, Körfer A, Franks CR, Poliwoda H and Kirchner H (1990) Home therapy with recombinant interleukin-2 and interferon-2β in advanced human malignancies. Lancet 335: 1509–1512
Elson PJ, Witt RS and Trump DL (1988) Diagnostic factors for survival in patients with recurrence of metastatic renal cell carcinoma. J Cancer Res 48: 7310–7313
Heinzer H, Mir TS, Huland E, Huland H (1999) Subjective and objective prospective long-term analysis of quality of life during inhaled interleukin-2 immunotherapy. J Clin Oncol (in press)
Huland E and Huland H (1989) Local continuous high-dose interleukin-2: a new therapeutic model for the treatment of advanced bladder carcinoma. Cancer Res 49: 5469–5474
Huland E, Huland H and Heinzer H (1992) Interleukin-2 by inhalation. Local therapy for metastatic renal cell carcinoma. J Urol 147: 344–348
Huland E, Heinzer H, Mir T and Huland H (1997) Inhaled interleukin-2 therapy in pulmonary metastatic renal cell carcinoma: six years of experience. Cancer J Sci Am 3: 98–105

Survival in renal cell carcinoma: a randomized evaluation of tamoxifen vs interleukin-2, α-interferon (leucocytic) and tamoxifen – reply

Sir

Although the comments by Drs Huland and Heinzer regarding our study comparing tamoxifen versus interleukin-2, α-interferon (leucocyte) and tamoxifen in general terms are acknowledged, it is obvious that there is a need for clarification.

We are well aware that our study could be questioned for
Hereditary factors in basal cell carcinoma of the skin: a population-based cohort study in twins

Sir,

Milan et al (Br J Cancer 1998 78: 1516–1520) reported on a large twin study investigating the contribution of hereditary factors in basal cell carcinoma (BCC) in Finland. This twin study based on 12 941 adult twin pairs with 43 years follow-up data concluded that genetic factors are not necessary to explain the distribution of BCC in twins. These findings are of major importance; however, a number of points need to be addressed in the analysis before these conclusions can be accepted.

© 2000 Cancer Research Campaign