Treatment of Metastatic Renal Cell Carcinoma: How Reliable are Small Non-Randomised Clinical Trials?

Concerning Mross et al.: Phase II Study with Interferon alpha-2a and 13-cis-Retinoic Acid in Patients with Metastatic Renal Cell Carcinoma. A Trial of the Phase II Study Group of the Association for Medical Oncology of the German Cancer Society. Onkologie 1999;22:412–415.

This paper contains a 'confirmatory' phase II study of interferon alpha and cis-retinoic acid in metastatic renal cell carcinoma. The investigation had been instigated by a strongly enthusiastic report from MRSCC (ref. 7) published in 1995. Similar to the results of a later randomised phase III trial from MRSCC (ref. 16) and the interim analysis of an ongoing phase II/III randomised trial from EORTC (30951) [1], this study found predominantly toxicity arising from the combination. Efficacy definitely lacked behind the expectations with 2/24 evaluable patients (2/29 enrolled patients) exhibiting a PR. The question arises whether a protocol alteration contri-

buted to the low efficacy. In the present protocol, treatment was strictly limited to 12 weeks even in patients not being progressive or suffering from significant toxicity. In the large MRSCC series as well as in EORTC 30951 the protocol featured one year targeted treatment duration, with a majority of patients receiving therapy between 5 and 8 months. Given these differences, both protocols are not amenable for direct comparison. However, because of a similar response rate in the present study and the large MRSCC series, the authors may glean some justification for their treatment protocol. Overall, this negative study laudably sets things straight, and may serve as a timely warning against overly enthusiastic reports derived from small numbers of patients. Clearly, new therapies for metastatic renal cell carcinoma should be sought for and the way to go, as stated by the authors, is to participate in controlled clinical trials.

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Reference

Fossa SD, Mickisch GHJ, Mulder PM, Goran D, van Glabbeke M: Interferon α -2a with or without 13 cis-retinoic acid in metastatic renal cell carcinoma: Toxicity analysis of a randomized EORTC phase II study. Proc ASCO 1998;17:331a(abstr 1276).