

Letters

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**Comments on Role of
Recombinant Interferon-gamma
Maintenance in Responding
Patients with Small Cell Lung
Cancer. A Randomised Phase III
Study of the EORTC Lung Cancer
Cooperative Group,
van Zandwijk et al., *Eur J Cancer*
1997, 33, 1759–1766**

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IN A recent issue of the *European Journal of Cancer*, van Zandwijk and colleagues reported a randomised study on gamma-interferon maintenance in small cell lung cancer (SCLC) [1]. In their discussion, they summarised a number of similar studies in none of which a significant improvement of median survival could be demonstrated in the interferon arm.

We would like to draw attention to a randomised study on alpha-interferon in SCLC published in the *European Respiratory Journal* shortly before the acceptance of van Zandwijk's article [2]. The protocol included the application of alpha-interferon both in the induction and in the maintenance phase. The results show that patients in the interferon arm achieved significantly higher response rates after induction (complete response plus partial response, 72% versus 44%; $P < 0.05$) and median survival (11.0 versus 9.0 months; $P < 0.02$).

The role of interferons in the treatment of advanced lung cancer remains to be defined. There is a lack of consensus on which patient populations to treat and which type and dose of interferon to use. There is some evidence that SCLC cell lines are more susceptible to alpha-interferon while non-SCLC cell lines are more effectively suppressed by gamma-interferon [3]. This might explain in part the treatment failures of gamma-interferon in SCLC [1,4]. Furthermore, van Zandwijk and colleagues point out that the lack of effect in previous studies may also be due to the limited cumulative dose of interferon, which was given as maintenance only. The more favourable results of our study [2] may be explained by the use of alpha- rather than gamma-interferon, and its

application over a prolonged period of time (starting 1 week before induction chemotherapy).

1. Zandwijk H van, Groen HJM, Postmus PE, et al. Role of recombinant interferon-gamma maintenance in responding patients with small cell lung cancer. A randomised phase III study of the EORTC Lung Cancer Cooperative Group. *Eur J Cancer* 1997, 33, 1759–1766.
2. Prior C, Oroszy S, Oberaigner W, et al. Adjunctive interferon-alpha-2c in stage IIIB/IV small-cell lung cancer: a phase III trial. *Eur Resp J* 1997, 10, 392–396.
3. Jabbar SAB, Twentyman PR. The use of clonogenic assays in assessing the response of human lung cancer cell lines to alpha and gamma interferons alone or in combination with adriamycin. *Int J Cancer* 1990, 46, 546–551.
4. Jett JR, Maksymiuk AW, Su JQ, et al. Phase III trial of recombinant interferon gamma in complete responders with small cell lung cancer. *J Clin Oncol* 1994, 12, 2321–2326.

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Response from N. van Zandwijk

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IN A reaction to the Discussion of our publication [1] Drs Prior, Thaler and Huber mention their favourable experience with alpha-interferon when given to small cell lung cancer patients from the beginning of treatment onwards. We indeed theorised that the lack of effect of the interferons observed in our and other studies might be caused by the limited exposure to this agent. However, we consider that the additional data provided by Prior and colleagues may be too optimistic. Their study, which was prematurely stopped due to poor accrual, included a patient percentage of more than 10% that did not receive treatment as planned, another 5% of patients were not evaluable for survival. In the remaining limited group of patients, subtle differences in performance status might have had an impact on treatment results and we think we must wait for studies with an adequate number of patients to express firm conclusions on the efficacy of alpha-interferon.

1. Zandwijk N van. Role of recombinant interferon-gamma maintenance in responding patients with small cell lung cancer, a randomised phase III study of the EORTC Lung Cancer Cooperative Group. *Eur J Cancer* 1997, 33(11), 1759–1766.