Re: “A Threefold Dose Intensity Treatment With Ifosfamide, Carboplatin, and Etoposide for Patients With Small-Cell Lung Cancer: A Randomized Trial”

Leyvraz et al. (1) have recently reported on a multicenter phase 3 study of conventional dose ifosfamide, carboplatin, etoposide (ICE) vs high-dose chemotherapy (HDC) with stem cell support in patients with limited or extensive small-cell lung cancer (SCLC). The trial did not demonstrate any advantage of HDC on survival. As a result, the authors conclude that the HDC strategy should be abandoned in SCLC, and research should focus on other treatment approaches.

The authors have to be commended for their continued efforts though fading interest in intensification for the treatment of solid tumors over the years. Results of this study are, however, disappointing, because experimental data and early clinical reports suggested that dose intensification, with or without stem cell support, may be beneficial in SCLC (2).

Some limitations of the study may have accounted for the lack of favorable results. The study had a much lower than expected accrual rate (145 instead of the 360 originally planned patients were enrolled over a 8-year period), and the initial trial design had to be altered to include interim analyses. The trial allowed inclusion of a heterogeneous study population—patients with limited and extensive disease were enrolled. Because of the low number of patients, subgroup analyses (performed as “exploratory”) clearly could not provide additional information.

Eight percent of patients in the HDC arm, including two patients in course of stem cell mobilization, died of therapy-related toxicity, a rate that is hardly acceptable today. Thirty of 74 (40%) patients in the HDC arm either never started or completed protocol treatment, making the assumption that “the present trial succeeded in raising the dose, total dose, and dose intensity of ICE by threefold” questionable.

Because of the reasons noted above, we believe that the role of dose intensification with stem cell support, including less toxic chemotherapy regimens, deserves further evaluation in patients with SCLC. In fact, we have to take into consideration the very poor advances obtained in SCLC over the last 20 years and the so far pessimistic scenario of targeted therapy in this disease.

MARCO BREGNI
PAOLO PEDRAZZOLI

References


Notes

Affiliations of authors: European Blood and Marrow Transplantation (EBMT) Solid Tumor Working Party (MB); Gruppo Italiano per il Trapianto di Midollo Osseo (GITMO), Sezione Tumori Solidi (PP), Milan, Italy.

Correspondence to: Paolo Pedrazzoli, MD, Gruppo Italiano per il Trapianto di Midollo Osseo, Oncologia Medica Falck, Ospedale Niguarda Ca’ Granda, 20162 Milano, Italy (e-mail: paolo.pedrazzoli@ospedaleniguarda.it).

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