

Treatment of children and adolescents with Hodgkin's Lymphoma without radiotherapy for patients in complete remission after chemotherapy

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More than sixty years ago Hodgkin's Lymphoma was considered a "systemic" malignancy and universally fatal. More recently less extensive radiation therapy in combination with chemotherapy has resulted in an excellent overall survival and prolonged disease free survival in children and adolescents. Unfortunately, the occurrence of radiotherapy-associated long terms adverse events such cardiovascular complications, infertility, endocrine disfunctions and secondary malignant neoplasia became of great concern. In the attempt to minimize the risk of these late effects, several international pediatric trials were organized to reply to the question: can radiotherapy be omitted with early stage Hodgkin's Lymphoma in patients who achieved complete remission after chemotherapy alone? Current evidence demonstrated that the use of radiotherapy as consolidation of complete remission after chemotherapy do not offer a benefit; therefore, it would seem reasonable to restrict the use of radiotherapy to the few patients in partial remission after first-line therapy (8-10%) and in those with bulk disease (1).

Dörffel and colleagues now report the final results of the GPOH-HD95 trial in which seven European countries entered 925 children and adolescent patients with classical Hodgkin's Lymphoma, registered in the German Society of Pediatric Oncology and Hematology Hodgkin Lymphoma trial 95 (2). The primary questions of this trial were: (I) is it safe to omit radiotherapy in patients achieving complete remission after chemotherapy? (II) is it safe to reduce the standard radiotherapy dose in early and intermediate stages? Three categories of patients entered the trial: patients with early stages (TG-1) who received 2 cycles of chemotherapy and patients with intermediate (TG-2)

or advanced stages (TG-3) who received additional 2 or 4 cycles of chemotherapy, respectively. Those with tumor reduction >75% received 20 Gy of involved field radiotherapy and an additional 10 or 15 Gy boost only for larger residuals (2). The final results can be briefly summarized as follows: the response-adapted treatment strategy with omission of radiotherapy in patients with chemotherapy-induced complete remission proved to be safe for TG-1 patients only; on the contrary, in the TG-2/TG-3 group of patients, a significantly increased relapsed rate was found, mainly in those who did not receive radiotherapy. The conclusion was that radiotherapy can be omitted in early stage Hodgkin's Lymphoma patients in complete remission following chemotherapy.

The omission of radiotherapy has been evaluated in several other international pediatric trials and the results have been encouraging (3-5). In particular, two randomized trials in USA compared chemotherapy alone *vs.* combined modality treatment. In the first trial, the patients received 6 cycles of mechlorethamine, vincristine, procarbazine, and prednisone (MOPP) alternated with adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD) or 4 cycles of the same chemotherapy plus involved field radiotherapy. No significant difference was found between the two groups in terms of overall survival and event-free survival (6). The second trial was stopped after 3 years only since the children in complete remission, who did not receive consolidation radiotherapy, had reduced event-free survival with respect to those receiving also involved-field radiotherapy (7).

In conclusion, the GPOH-HD95 trial for the first time demonstrated that consolidation with radiotherapy can be omitted safely in patients with early stage disease

who have achieved complete remission with conventional chemotherapy; this is extremely important in the treatment of younger patients where the most important goal should be maximizing the cure rate while minimizing late morbidity and mortality.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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