controversy I: do we need radiotherapy in early HL?

004 Controversy I: DO WE NEED RADIOTHERAPY IN EARLY HODGKIN LYMPHOMA? (PROS)

J. Yahalom[1]
[1]*Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, United States*

In order to obtain the most effective and safe outcome in early-stage HL, modern ''mini'' radiotherapy (RT) should follow a brief course of chemotherapy. All adequately designed prospective randomized studies that compared combined-modality to chemotherapy alone showed significantly superior freedom-from-treatment failure when RT was included. With adequate follow-up, one has already demonstrated an improved overall survival. While many patients who fail first-line treatment may still be salvaged with high-dose therapy and stem cell rescue, the aggressive salvage adds significant short and long-term morbidity and is best avoided by selecting a more effective and safe upfront treatment. Radiation is considered to be the most effective single agent for HL. Indeed, more than 40 years ago, prior to the availability of effective and safe chemotherapy, most patients with early-stage HL were cured with ''radical'' RT alone. Yet, in those early days, radiation in relatively high doses was given indiscriminately to extensive areas of the body in order to include all lymphatic organs at risk. Decades later, survivors of this ''radical RT'' showed higher risk for developing second tumors; primarily breast and lung cancers. The increased risk was associated with young age at time of RT and with the volume of breast irradiated with a higher dose. An increase in risk for coronary heart disease was also detected, especially when other coronary risk co-existed. When radiotherapy of HL transformed from a single modality (used in a radical manner) into a consolidating treatment after chemotherapy, the volume of radiation exposure and the dose delivered were dramatically reduced. Large randomized studies showed that this change in strategy is effective and safe. Further, they showed that freedom-from failure above 90-95% could be reached with ''mini'' combined modalities. Importantly, recent data have demonstrated marked reduction in the risk of second tumors with the reduced radiation strategy. We should recognize that the 1960's radical radiotherapy is no longer practiced. ''Involved-field RT'' and even more so the new ''involved lymph node RT'' eliminated most normal organs exposure, reduced the target dose by 50%, and the new technique is sparing most and often all breast tissue. Thus, there is no need to increase the cumulative amount of potentially toxic chemotherapy or accept a higher failure rate in order to avoid radiotherapy. For favorable early-stage only 2 rather that 6 cycles of ABVD can be safely given if mini RT is added. Many hope that interim PET would serve as an oracle for tailoring treatment. Indeed, trials designed with interim PET at a randomization point are in progress. Recently one such randomized study demonstrated that adding radiotherapy is important even in patients that became PET-negative after chemotherapy.

005 Controversy I: DO WE NEED RADIOTHERAPY IN EARLY HODGKIN LYMPHOMA? (COS)

J.M. Connors[1]
[1]*Medical Oncology, British Columbia Cancer Agency, Vancouver, BC, Canada*

Background: Radiotherapy (RT) is effective for limited stage HL but associated with second neoplasms of the skin, head and neck, breast, lung, gastrointestinal and thoracic tissues; cardio-pulmonary dysfunction; dental caries; and hypothyroidism. A very high cure rate following combined modality chemo-RT despite reduction of RT fields from large extended to small involved nodal fields suggests that highly effective chemotherapy may eliminate the need for RT for most patients with limited stage HL. Building on the experience from the ABVD alone arm of the NCIC CTG/ECOG HD6 trial and the predictive value of mid-treatment FDG-PET, we have the evidence and tools needed to rely on chemotherapy alone, without RT, for 90 % of patients while maintaining very high cure rates.

Methods: HD6 included 182 patients with stage IA-IIA, non-bulky (< 10 cm) classical HL in the ABVD alone arm consisting of 2 cycles of ABVD followed by complete re-assessment including CT but not PET. Patients with a complete response (CR) received 2 more cycles of ABVD; those with < CR, 4 more cycles.

Results: Among 182 patients on the ABVD alone arm of HD6, 40 % had a CR (based on CT without PET) after 2 cycles of ABVD, completed treatment with another 2 cycles of ABVD and had a 5y freedom from progression (FFP) of 95 %. 60 % of patients had < CR after 2 cycles of ABVD, completed treatment with 4 more cycles and had a 5y FFP of 80 %. On the standard ABVD + RT arm, regardless of response status after 2 cycles of ABVD, patients had a 5y FFP of ~ 95 %. These data indicate that ~ 90% of patients with limited stage HL can be cured with chemotherapy alone. What is needed is a technique that can identify the 10% who do require RT. Of the first 56 patients assessed at our center with FDG-PET after 2 cycles of ABVD, ~ 10 % had a positive PET scan and received involved nodal RT, with the other 90 % completing treatment with 2 more cycles of ABVD and no RT. 2y FFP is 97 %.

Conclusion: These results indicate that ~ 90 % of patients with limited stage HL can be cured without RT. The ~ 10 % who require radiation can be accurately identified with FDG-PET and its integration into the management of limited stage HL allows almost all patients to be successfully treated with chemotherapy alone.