

Hodgkin lymphoma - Section 2

Risk adapted treatment in early stage Hodgkin lymphoma

Marc André

CHU UCL Namur, Yvoir, Belgium

Combined modality treatment, usually ABVD and radiotherapy (RT), is the standard of care for localized Hodgkin lymphoma but 5-20% of patients will be refractory or ultimately relapse.^{1,2} However, as most of the patients are cured, it appeared that long-term toxicities, *i.e.* second cancers^{3,4} and cardiovascular events,⁵ are of major concern.

Subsequent trials were performed to show that RT could be safely reduced but not omitted.⁶ PET scan has emerged as an interesting tool to predict outcome when performed after two cycles of ABVD.^{7,8} It can be used to early adapt treatment planning according to the chemo sensitivity evaluated by PET. Omission of RT was tested in early PET negative patients in two large randomized trials.^{9,10} Both failed to demonstrate the non-inferiority of the no RT arm in terms of progression free survival (PFS). However, the outcome in the no RT arm was excellent and follow-up is actually too short to know if the increased risk of relapse is balanced by a significant decrease in long-term toxicities when omitting RT. Omission of RT in early PET negative patients remains intensively debated.

Conversely, the H10 study, a phase III intergroup (EORTC, LYSA and FIL) randomized trial, evaluated chemotherapy intensification in patients PET positive after 2 ABVD.¹¹ The patients in the standard arm continued on ABVD and RT while in the experimental arm, patients switched from ABVD to 2 cycles of BEACOPPesc and RT. The 5-year PFS were 77.4% (ABVD arm) and 90.6% (BEACOPPesc arm) with a difference of 13.2% favoring BEACOPPesc ($p=0.002$).

Based on these recent trials, PET adapted strategy is warranted in early stage HL.

References

- *1. Ferme C, Eghbali H, Meerwaldt JH, Rieux C, Bosq J, Berger F, et al. Chemotherapy plus involved-field radiation in early-stage Hodgkin's disease. *N Engl J Med.* 2007;357(19):1916-27.
Confirms that combined modality therapy is superior to radiotherapy alone.
2. Engert A, Franklin J, Eich HT, Brillant C, Sehlen S, Cartoni C, et al. Two cycles of doxorubicin, bleomycin, vinblastine, and dacarbazine plus extended-field radiotherapy is superior to radiotherapy alone in early favorable Hodgkin's lymphoma: final results of the GHSG HD7 trial. *J Clin Oncol.* 2007;25(23):3495-502.
- *3. Schaapveld M, Aleman BM, van Eggermond AM, Janus CP, Krol AD, van der Maazen RW, et al. Second Cancer Risk Up to 40 Years after Treatment for Hodgkin's Lymphoma. *N Engl J Med.* 2015;373(26):2499-511.
Illustrates the late toxicities up to 40 years after treatment.
4. Andre M, Henry-Amar M, Blaise D, Colombat P, Fleury J, Milpied N, et al. Treatment-related deaths and second cancer risk after autologous stem-cell transplantation for Hodgkin's disease. *Blood.* 1998;92(6):1933-40.
5. Hancock SL, Tucker MA, Hoppe RT. Factors affecting late mortality from heart disease after treatment of Hodgkin's disease. *JAMA.* 1993;270(16):1949-55.
- *6. Engert A, Plutschow A, Eich HT, Lohri A, Dorken B, Borchmann P, et al. Reduced treatment intensity in patients with early-stage Hodgkin's lymphoma. *N Engl J Med.* 2010;363(7):640-52.
Determines the dose of radiotherapy in localized HL.
7. Biggi A, Gallamini A, Chauvie S, Hutchings M, Kostakoglu L, Gregianin M, et al. International validation study for interim PET in ABVD-treated, advanced-stage Hodgkin lymphoma: interpretation criteria and concordance rate among reviewers. *J Nucl Med.* 2013;54(5):683-90.
- *8. Rigacci L, Puccini B, Zinzani PL, Biggi A, Castagnoli A, Merli F, et al. The prognostic value of positron emission tomography performed after two courses (INTERIM-PET) of standard therapy on treatment outcome in early stage Hodgkin lymphoma: A multicentric study by the fondazione italiana linfomi (FIL). *Am J Hematol.* 2015;90(6):499-503.
Confirms the prognostic value of early PET in localized HL.
- *9. Radford J, Illidge T, Counsell N, Hancock B, Pettengell R, Johnson P, et al. Results of a trial of PET-directed therapy for early-stage Hodgkin's lymphoma. *N Engl J Med.* 2015;372(17):1598-607.
Evaluates radiotherapy omission in PET negative patients after 3 ABVD.
- *10. Raemaekers JM, Andre MP, Federico M, Girinsky T, Oumedaly R, Brusamolino E, et al. Omitting radiotherapy in early positron emission tomography-negative stage I/II Hodgkin lymphoma is associated with an increased risk of early relapse: Clinical results of the preplanned interim analysis of the randomized EORTC/LYSA/FIL H10 trial. *J Clin Oncol.* 2014;32(12):1188-94.
Evaluates radiotherapy omission in PET negative patients after 2 ABVD.
11. Raemaekers JM et al; Lugano 2015, oral presentation.