Reduced-intensity chemotherapy and PET-guided radiotherapy in patients with advanced stage Hodgkin's lymphoma (HD15 trial): a randomised, open-label, phase 3 non-inferiority trial.


University Hospital of Cologne, Department of Internal Medicine I, Köln, Germany. a.engert@uni-koeln.de


Abstract

BACKGROUND: The intensity of chemotherapy and need for additional radiotherapy in patients with advanced stage Hodgkin's lymphoma has been unclear. We did a prospective randomised clinical trial comparing two reduced-intensity chemotherapy variants with our previous standard regimen. Chemotherapy was followed by PET-guided radiotherapy.

METHODS: In this parallel group, open-label, multicentre, non-inferiority trial (HD15), 2182 patients with newly diagnosed advanced stage Hodgkin's lymphoma aged 18-60 years were randomly assigned to receive either eight cycles of BEACOPP(escalated) (8×B(esc) group), six cycles of BEACOPP(escalated) (6×B(esc) group), or eight cycles of BEACOPP(14) (8×B(14) group). Randomisation (1:1:1) was done centrally by stratified minimisation. Non-inferiority of the primary endpoint, freedom from treatment failure, was assessed using repeated CIs for the hazard ratio (HR) according to the intention-to-treat principle. Patients with a persistent mass after chemotherapy measuring 2.5 cm or larger and positive on PET scan received additional radiotherapy with 30 Gy; the negative predictive value for tumour recurrence of PET at 12 months was an independent endpoint. This trial is registered with Current Controlled Trials, number ISRCTN32443041.

FINDINGS: Of the 2182 patients enrolled in the study, 2126 patients were included in the intention-to-treat analysis set, 705 in the 8×B(esc) group, 711 in the 6×B(esc) group, and 710 in the 8×B(14) group. Freedom from treatment failure was sequentially non-inferior for the 6×B(esc) and 8×B(14) groups as compared with 8×B(esc). 5-year freedom from treatment failure rates were 84.4% (97.5% CI 81.0-87.7) for the 8×B(esc) group, 89.3% (86.5-92.1) for 6×B(esc) group, and 85.4% (82.1-88.7) for the 8×B(14) group (97.5% CI for difference between 6×B(esc) and 8×B(esc) was 0.5-9.3). Overall survival in the three groups was 91.9%, 95.3%, and 94.5% respectively, and was significantly better with 6×B(esc) than with 8×B(esc) (97.5% CI 0.2-6.5). The 8×B(esc) group showed a higher mortality (7.5%) than the 6×B(esc) (4.6%) and 8×B(14) (5.2%) groups, mainly due to differences in treatment-related events (2.1%, 0.8%, and 0.8%, respectively) and secondary malignancies (1.8%, 0.7%, and 1.1%, respectively). The negative predictive value for PET at 12 months was 94.1% (95% CI 92.1-96.1); and 225 (11%) of 2126 patients received additional radiotherapy.
**INTERPRETATION:** Treatment with six cycles of BEACOPP(escalated) followed by PET-guided radiotherapy was more effective in terms of freedom from treatment failure and less toxic than eight cycles of the same chemotherapy regimen. Thus, six cycles of BEACOPP(escalated) should be the treatment of choice for advanced stage Hodgkin's lymphoma. PET done after chemotherapy can guide the need for additional radiotherapy in this setting.

**FUNDING:** Deutsche Krebshilfe and the Swiss Federal Government.

Copyright © 2012 Elsevier Ltd. All rights reserved.

**Comment in**


PMID: 22480758 [PubMed - indexed for MEDLINE]

---
