Eight cycles of escalated-dose BEACOPP compared with four cycles of escalated-dose BEACOPP followed by four cycles of baseline-dose BEACOPP with or without radiotherapy in patients with advanced-stage Hodgkin's lymphoma: final analysis of the HD12 trial of the German Hodgkin Study Group

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PURPOSE
Eight cycles of BEACOPP (escalated) (escalated dose of bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone) followed by radiotherapy (RT) to initial bulk or residual tumor mass is the German Hodgkin Study Group standard of care for advanced-stage Hodgkin's lymphoma (HL). However, treatment-related toxicity is a concern, and the role of RT in this setting is unclear. The HD12 study thus aimed to reduce toxicity while maintaining efficacy.

PATIENTS AND METHODS
In this prospectively randomized multicenter trial, eight cycles of BEACOPP (escalated) was compared with four cycles of BEACOPP (escalated) followed by four cycles of the baseline dose of BEACOPP (BEACOPP (baseline); 4 + 4), and RT with no RT in the case of initial bulk or residual disease. The study was designed to exclude a difference in 5-year freedom from treatment failure (FFTF) rate of 6%.

RESULTS
Between January 1999 and January 2003, 1,670 patients age 16 to 65 years were enrolled onto the HD12 study. At 5 years, FFTF was 86.4% in the BEACOPP (escalated) arm and 84.8% in the 4 + 4 arm (difference, -1.6%; 95% CI, -5.2% to 1.9%), and overall survival was 92% versus 90.3% (difference, -1.7%; 95% CI, -4.6% to 1.1%). Deaths related to acute toxicity of chemotherapy were observed in 2.9% of patients (BEACOPP (escalated), n = 19; 4 + 4, n = 27). FFTF was inferior without RT (90.4% v 87%; difference, -3.4%; 95% CI, -6.6% to -0.1%), particularly in patients who had
residual disease after chemotherapy (difference, -5.8%; 95% CI, -10.7% to -1.0%), but not in patients with bulk in complete response after chemotherapy (difference, -1.1%; 95% CI, -6.2% to 4%).

CONCLUSION
The reduction of BEACOPP to the 4 + 4 regimen did not substantially reduce severe toxicity but might decrease efficacy. Our results do not support the omission of consolidation RT for patients with residual disease. Alternative strategies for improving the risk-to-benefit ratio for patients with advanced HL are needed.