Eight Cycles of BEACOPP Escalated Compared with 4 Cycles of BEACOPP Escalated followed by 4 Cycles of BEACOPP Baseline with or without Radiotherapy in Patients in Advanced-stage Hodgkin Lymphoma (HL): Final Analysis of the Randomized HD12 Trial of the German Hodgkin Study Group (GHSG)

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Purpose/Objective(s): The HD 12 trial of the GHSG was a multicenter four-arm randomized study: arm A was 8 x BEACOPP escalated (BE) plus 30 Gy RT, arm B was 8 x BE, arm C was 4 x BE plus 4 x BEACOPP baseline (BB) plus 30 Gy RT, arm D was 4 x BE plus 4 x BB. This study was designed to test (1) whether the BEACOPP dosage can be reduced to baseline in the last 4 cycles without loss of effectiveness, and (2) whether consolidative RT in the region of initial bulky disease ($5 cm) and of residual disease ($1.5 cm) is necessary following effective chemotherapy. Entry to the trial was restricted to HL patients who were in Stage IIB with one or both of the risk factors: bulky mediastinal mass or extranodal involvement, and all Stage III or IV patients. A multidisciplinary panel reviewed all patients´ imaging and recommended either the continuation of therapy according to randomization, or RT independent of the randomization for patients with poor response to chemotherapy.

Materials/Methods: Between September 9, 1999, and January 1, 2003, a total of 1,670 patients aged 16–65 were randomized. For this final analysis, 99 patients were excluded resulting in 1,571 eligible patients equally distributed between the 4 study arms.

Results: Chemotoxicity was high with 97% of patients receiving at least one toxicity of WHO Grade 3 or 4. Death due to acute toxicity was 3% (sepsis, cardiac, pulmonary, infection), with 20 deaths in the 8 BE arms and 27 in the 4BE+4BB arms. Treatment outcome was complete remission for 92.1% of patients with another 1.7% experiencing early progression. Total progression/relapse rate was 7.8% (n = 52 vs. 71) with a median follow-up of 78 months. Secondary neoplasias were observed in 77 patients (4.9%): 12 vs. 11 AML/MDS, 11 vs. 5 NHL and 20 vs. 18 solid tumors/others. The OS after 5 years was 91%, 5-year FFTF was 85.4%, and 5-year progression free survival (PFS) was 86.2%. Estimates for the difference at 5 years are -1.7% (-4.6%, 1.2%) for OS, -1.6% (95% CI, -5.2%, 1.9%) for FFTF and -2.5% (-6.0%, 1.0%) for PFS. The FFTF was 90% in the ‘RT’ arms A+C and 87% in the ‘no-RT’ arms B+D: Estimates for the difference FFTF at 5 years are -3.2% (-6.5%, 0.0%).

Conclusions: The confidence intervals show that 4BE+4BB are clearly not significantly different from 8 BE in all 3 long-term outcome parameters (p . 0.19, log–rank test). The RT can be reduced substantially after effective chemotherapy. However, due to the irradiation of 11% of patients in the ‘no-RT’ arms due to the panel recommendation, equivalent effectiveness of a no-RT strategy cannot be proven. A substantial limitation of consolidative RT according to expert panel recommendations appears to be possible without reducing effectiveness.

Author Disclosure: H. Eich, None; A. Engert, None; H. Haverkamp, None; S. Staar, None; J. Kriz, None; R. Engenhart-Cabillic, None; P. Lukas, None; N. Willich, None; V. Diehl, None; R. Mueller, None.