Radiotherapy to bulky disease PET-negative after immunochemotherapy in elderly DLBCL patients: Results of a planned interim analysis of the first 187 patients with bulky disease treated in the OPTIMAL>60 study of the DSHNHL.

Michael Pfreundschuh, Konstantinos Christofyllakis, Bettina Altmann, Marita Ziepert, Mathias Haenel, Andreas Viardot, Andreas Neubauer, Gerhard Held, Lorenz Truemper, Christian Schmidt, Lothar Kanz, Michael J. Hallek, Norbert Schmitz, Tobias Heintges, Christian Koelbel, Guenther Schneider, Christian Ruebe, Dirk Hellwig, Viola Poeschel, Niels Murawski

University Saarland Medical School, Homburg Saar, Germany, Saarland University Medical Center, Homburg, Germany, Institute for Medical Informatics, Statistics and Epidemology, Leipzig University, Leipzig, Germany, Klinik für Innere Medizin III, Klinikum Chemnitz, Chemnitz, Germany, Department of Internal Medicine, University Hospital of Ulm, Ulm, Germany, University Clinic Giessen Marburg, Marburg, Germany, Saarland University Medical School, Homburg, Germany, University Medical Center Göttingen, Göttingen, Germany, University Hospital of Munich, Munich, Germany, Medizinische Uniklinik Tuebingen, Tuebingen, Germany, University Hospital Cologne, Cologne, Germany, Asklepios Hospital St. Georg, Hamburg, Germany, Medical Department II, Städtisches Klinikum Neuss Lukaskrankenhaus GmbH, Neuss, Germany, Krankenhaus der Barmherzigen Brueder, Trier, Trier, Germany, Department of Diagnostic and Interventional Radiology, Saarland University Hospital, Homburg, Germany, Universitätsklinikum Regensburg, Regensburg, Germany

Background:RT to bulky sites improves outcome of elderly DLBCL patients [Lancet Oncol 2008; 9: 105-116; J Clin Oncol 2014; 32:112-1118]. Whether RT can be spared in PET-negative pts. after R-CHOP was prospectively addressed in OPTIMAL >60.

Methods:61 to 80 y-old pts. were randomized in a 2x2 factorial design to 6xCHOP-14 or 6xCHLIP-14 (liposomal instead of conventional vincristine) plus 8 x rituximab 375 mg/m^2(R) q 2 wks. or 12xR (days -4,-1,1,4,14,28,42,56,91,126,175, 238). Pts. with bulk (>=7.5 cm) PET-positive after 6 cycles chemotherapy were assigned to RT (39.6 Gy), while PET-negative bulks were observed.

Results:187/505 (37%) had bulky disease and were compared to 117/306 (38%) RICOVER-60 pts. (38%) who had received 6xCHOP-14+8R. OPTIMAL>60 pts. were older (70 vs. 68 years) and had more IPI=3 (33% vs. 29%) and IPI=4,5 (34% vs. 23%) compared to RICOVER-60. PET was performed in 166/187 OPTIMAL>60 bulk pts. (reasons for no PET: early death: 5; excessive toxicity: 3; protocol violation: 1, non-compliance: 4, change of diagnosis: 6, others: 2). 80/166 (48%) bulks remained PET-positive after 6 cycles of chemotherapy and 62/80 (78%) were irradiated (reasons for no RT: progression: 8; medical reasons: 9; negative biopsy: 1), reducing RT from 67/117 (57%) in RICOVER-60 by 42% to 62/187 (33%) in OPTIMAL>60. Despite the unfavorable demographics, outcome of the 187 bulk pts. in OPTIMAL>60 was non-inferior to RICOVER-60, not even in the least intensive of the 4 OPTIMAL>60 treatment arms consisting of 47 pts. who received 6xCHOP-14+8R as in RICOVER-60. 2-year PFS and OS in OPTIMAL>60 was 79% and 88%, respectively, compared to 75% and

78% of the 117 RICOVER-60 pts. In a multivariable analysis adjusting for the IPI risk factors, the hazard ratio of the OPTIMAL>60 compared to the RICOVER-60 bulk pts. was 0.7 (95% CI: 03.; 1.5; p=0.345) for PFS and 0.5 (95% CI: 02.; 1.3; p=0.154) for OS.

Conclusions:RT can be spared in bulky disease PET-negative after chemotherapy. This strategy results in a 42% reduction of RT without compromising the outcome of these patients. Supported by Amgen, Roche, Spectrum. Clinical trial information: NCT01478542