

## **Protocol Synopsis DSHNHL 2004-1**

PROTOCOL TITLE:	<i>2-weekly CHOP chemotherapy with dose-dense rituximab for the treatment of patients aged 61 to 80 years with aggressive CD20-positive B-cell lymphomas : A Phase-II / Pharmacokinetic Study</i>
SHORT TITLE:	<i>DSHNHL-2004-1 (CHOP-R-ESC)</i>
PRINCIPAL INVESTIGATOR:	<i>Prof. Dr. med. M. Pfreundschuh, Med. Klinik I, Saarland University Medical School, D-66421 Homburg/Saar.</i>
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PROTOCOL VERSION:	<i>8.0</i>
SPONSOR:	<i>Deutsche Studiengruppe für Hochmaligne Lymphome (DSHNHL).</i>
PROJECT PHASE:	<i>Phase II and pharmacokinetic study</i>
INDICATION:	<i>untreated aggressive B-cell lymphomas, CD20-positive</i>
OBJECTIVES:	<i><u>Primary:</u> 1. To establish a pharmacokinetic profile for rituximab within an escalated rituximab (12x) + CHOP-14 (6x) regimen; 2. To evaluate the safety and toxicity profile of this regimen <u>Secondary:</u> To determine complete remission rate, rate of primary progression, event-free-survival and overall survival</i>
STUDY DESIGN:	<i>Phase-II and pharmacokinetic, multicentre, open-label trial</i>
PLANNED SAMPLE SIZE:	<i>100 patients, pharmacokinetic study only in first 20 patients</i>
NUMBER OF CENTERS:	<i>3 participating centres After the first 20 patients the study will be open for all participants of the DSHNHL.</i>
PATIENT SELECTION CRITERIA:	<i>Male or female adult patients aged 61 to 80 years with untreated CD20-positive aggressive B-cell non-Hodgkin's lymphoma stages I-IV, HIV-negative</i>
STUDY MEDICATION:	<i>Rituximab vials of 500 mg and 100 mg. The antibody will be given at a dosage of 375 mg/m<sup>2</sup> i.v. infusion, days zero, one, four, eight, fifteen, twenty-two, twenty-nine, forty-three, fifty-seven, seventy-one, eighty-five and ninety-nine of each of 6 cycles of chemotherapy, together with CHOP-14 chemotherapy on day one, fifteen, twenty-nine, forty-three, fifty-seven, and seventy-one.</i>
MAIN PARAMETERS OF EFFICACY:	<i>TTF (time to treatment failure): primary endpoint; secondary endpoints: objective response rates, rates of primary progression, survival after one and two years.</i>
MAIN PARAMETERS OF SAFETY:	<i>Adverse events according to the NCI CTC for hematologic and non-hematologic toxicities</i>
RATIONALE:	<i>Pilot study to establish a safety, toxicity and pharmacokinetic profile of an escalated rituximab + CHOP regimen. In a follow-up trial, this regimen, if found safe and feasible, will be tested in the setting of elderly patients, assuming that this patient group cannot benefit from increased doses of chemotherapy, but may benefit from increased rituximab doses, especially during the first weeks of treatment.</i>
STUDY PROCEDURE:	<i>Patients will receive a total of 12 rituximab standard dose infusions (375mg/m<sup>2</sup>) over approx 3.5 months together with 6 infusions of CHOP every 14 days. Details on the administration on the following chart. Patients with primary bulky disease (diameter ≥7.5 cm) or extranodal involvement receive additional involved-field radiotherapy to these areas with 36 Gy.</i>
STATISTICAL ANALYSIS:	<i>The treatment results will be compared for time to treatment failure (TTF) by log-rank test with the treatment results of matched patients from the RICOVER-60 trial of the DSHNHL, respectively.</i>
DURATION OF THE STUDY	<i>The study will start in February 2004, recruitment will be terminated in June 2006, based on an expected recruitment of 8 patients per month. The minimum follow-up time after the end of the recruitment period will be 2 years, with a total study period of 3 years. Afterwards, beyond clinical investigation, lifelong follow-up will be carried out.</i>