2 STUDY OBJECTIVES

2.1 MAIN GOALS OF THE STUDY

Satisfactory disease control rates (>90%) can be achieved in paediatric Hodgkin's lymphoma with established therapeutic modalities (documented for the GPOH-HD study group since the DAL-HD-82 study).

The remaining challenges for further treatment optimisation are:

- Reduction of acute and long-term toxicity of the chemotherapy and radiotherapy employed.
- Reduction of the amount of treatment in those children who are currently over-treated.

This study aims to eliminate Procarbazine from chemotherapy. Procarbazine is gonadotoxic and may lead to male infertility and premature menopauses. Previous studies (DAL-HD 85 and DAL-HD 87) have shown that Procarbazine is a very effective drug in Hodgkin's Lymphoma and cannot safely be omitted:

- Intensified OEPA using Etoposide instead of Procarbazine replaces OPPA for both boys and girls in the first two cycles.
- COPDAC in which Dacarbazine replaces Procarbazine is compared to standard COPP chemotherapy using a randomised study design.

Both OEPA and COPDAC have been piloted (DAL-HD 90 + GPOH-HD 95 and GPOH-HD 2002 Pilot respectively), are feasible, effective and have an acceptable toxicity profile.

The main question for further therapy optimization is a strategy for treatment adapted to response (STAR), i.e. to tailor the amount of treatment to the individual needs of the patient, safely reduce treatment where not needed, and intensify treatment where indicated.

In the study GPOH-HD 95 the STAR concept was investigated restricting indication for radiotherapy to patients not in complete remission after chemotherapy as assessed by CT/MRI. Radiotherapy is a major cause of secondary malignancies.

The CT/MRI imaging techniques used cannot reliably distinguish between active and fibrotic/necrotic residual masses. Therefore sensitivity (rate of test positive results in true positives) is reasonably high, but the specificity (rate of test-negative results in true negatives) is rather low (in the order of 30%) and a high negative predictive value can only be achieved, if most patients are already cured after chemotherapy.