The GHSG HD18 study for patients with advanced stage Hodgkin Lymphoma

Andreas Engert, MD
Chairman, German Hodgkin Study Group
University Hospital of Cologne
• Early favorable stages: CS I/II without risk factors*

• Early unfavorable stages: CS I/II with risk factors*

• Advanced stages: CS III/IV; selected CS IIB

* a) large mediastinal mass; b) extranodal disease; c) high ERS; d) 3 or more areas
CS IIB-IIIA with RF
CS IIIB; CS IV

Arm A
8 x (COPP/ABVD)
± RT

Arm B
8 x BEACOPP baseline
± RT

Arm C
8 x BEACOPP escalated + G-CSF
± RT

Diehl et al NEJM 2003
GHSG HD9 trial

FFTF by treatment arm

Engert et al; JCO 2009

p <0.001

Years

Percentage

0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

18%

A (64%)

B (70%)

C (82%)

p <0.001

Engert et al; JCO 2009
GHSG HD9 trial
OS by treatment arm

Engert et al; JCO 2009

p <0.001
„Catch it with the first grip, otherwise you lose your chance!“

„Catch the moment“...

2 BEACOPP esc

2-4 ABVD
Ongoing HD18 trial for advanced stages

After chemo: PET; RX to PET+ res nodes >2.5 cm
PET-: Follow up
Inclusion Criteria

- Previously untreated HL
- Histology: cHL and NLPHL
- Stages III/IV; IIB with bulk or extranodal involvement
- 18-60 years
- No composite lymphoma
- No concomittant malignancy or infection
• **Primary:**
  - PFS

• **Secondary:**
  - Acute- and late tox
  - OS
  - QoL
  - Rate of 2nd npl
  - CR rate
  - Rate of HL-specific mortality
  - Prognostic impact of PET2
• Ratio PET+/PET- of 30/70 assumed
• PET+: 8xB.esc+R > 8xB.esc (317 pts needed)
• PET-: Non-inferiority between 8x and 4xB.esc
  1050 pts needed (margin 6%)
• Adaptive design; 80% power; alpha 5%
• Planned interim analyses: 3
GHSG HD18 trial
Recruitment 5/08-3/10
Patient

01MAY08 30OCT08 01MAY09 30OCT09 01MAY10
Recruitment
planned (all)
recruited
N=595
### PET Result in 4 Categories (3/09)

<table>
<thead>
<tr>
<th>Score Description</th>
<th>N</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Score 0: No FDG avid lesions</td>
<td>46</td>
<td>43.4</td>
</tr>
<tr>
<td>Score 1: Not more than background activity of mediastinal blood pool</td>
<td>16</td>
<td>15.1</td>
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<tr>
<td>Score 2: More than background activity of the mediastinal blood pool but not more than liver</td>
<td>23</td>
<td>21.7</td>
</tr>
<tr>
<td>Score 3: More than background activity of the liver</td>
<td>21</td>
<td>19.8</td>
</tr>
<tr>
<td></td>
<td>Randomized</td>
<td>95% confidence interval</td>
</tr>
<tr>
<td>---------------</td>
<td>------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Total</td>
<td>240</td>
<td>100.0%</td>
</tr>
<tr>
<td>Arm C/D (PET neg.)</td>
<td>142</td>
<td>59.2% (53.0% - 65.4%)</td>
</tr>
<tr>
<td>Arm A/B (PET pos.)</td>
<td>98</td>
<td>40.8% (34.6% - 47.1%)</td>
</tr>
</tbody>
</table>

- The rate of PET-2 positive patients is higher than expected.
- The statistical section of the study protocol was amended to ensure that the study objectives for both, PET positive and PET negative patients can still be met.
• PET-adapted design for advanced-stage HL

• 8xB.esc+R vs 8xB.esc in PET+ pts

• 8xB.esc vs 4xB.esc in PET-pts

• Total of 1600 pts to be included

• More PET+ pts due to more conservative approach

• Study recruitment according to plan
CS I/II without RF*

Standard Arm
- 2 x ABVD PET (+/-)
  - 20 Gy IF

Experimental Arms
- 2 x ABVD PET-
- 2 x ABVD PET+
  - Follow up
  - 20 Gy IF

* a) large mediastinal mass; b) extranodal disease; c) high ERS; d) 3 or more areas
<table>
<thead>
<tr>
<th>Role</th>
<th>Members</th>
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</thead>
<tbody>
<tr>
<td>Chairman</td>
<td>A. Engert</td>
</tr>
<tr>
<td>Secretary</td>
<td>P. Borchmann</td>
</tr>
<tr>
<td>Honorary Chairman</td>
<td>V. Diehl</td>
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<tr>
<td>Pathology</td>
<td>H. Stein</td>
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<tr>
<td>Radiotherapy</td>
<td>R.-P. Müller, H. Eich</td>
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<tr>
<td>Nuclear Medicine</td>
<td>M. Dietlein, C. Kobe</td>
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<td>Trial coordinating Center</td>
<td>Head: M. Fuchs</td>
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<tr>
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<td>Trial physicians: B. Gawlik, A. Pfau</td>
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<tr>
<td>Data Management</td>
<td>B. Koch, H. Nisters-Backes, H. Ossadnik, R. Sistermanns, K. Tittmann</td>
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<tr>
<td>Project /Quality Management</td>
<td>J. Jeske, M. Platz, D. Redweik</td>
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<tr>
<td>Database / IT</td>
<td>A. Bellamou, D. Böhmer, T. Schober, P. Zerhusen</td>
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<tr>
<td>Statistics</td>
<td>H. Görgen, H. Haverkamp, H. Müller, A. Plütschow</td>
</tr>
<tr>
<td>Secretary</td>
<td>M. Schumacher</td>
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<tr>
<td>Year Range</td>
<td>HD Range</td>
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<tr>
<td>--------------</td>
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</tr>
<tr>
<td>1978 - 88</td>
<td>HD 1 - 3</td>
</tr>
<tr>
<td>1988 - 94</td>
<td>HD 4 - 6</td>
</tr>
<tr>
<td>1994 - 98</td>
<td>HD 7 - 9</td>
</tr>
<tr>
<td>1998 - 02</td>
<td>HD10-12</td>
</tr>
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<td>2003 - 08</td>
<td>HD13-15</td>
</tr>
<tr>
<td>2008 -</td>
<td>HD16-18</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>Total</strong></td>
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