Aktuelle Studien und Therapiekonzepte Aggressive Lymphome

Michael Pfreundschuh

German High-Grade Non-Hodgkin Lymphoma Study Group (DSHNHL)
Dept. Internal Medicine I, Saarland University Medical School
Homburg (Saar), Germany
IPI in the Rituximab Era?
RICOVER-60 Trial
61-80 years, CD20+ B-cell, with Rituximab (n=610)
by IPI score

IPI 1: 184 (30%); IPI 2: 172 (28%); IPI 3: 155 (26%); IPI 4, 5: 99 (16%)

Ziepert et al., J Clin Oncol 2010
Risk Factors in the Rituximab Era

Conclusion:

- The „R-IPI“ (365 pts.) does not hold scrutiny

- The IPI (4500 pts.) is alive and valid in the rituximab era (1068 pts.)
Risk Factors in the Rituximab Era

**Conclusion:**

- The „R-IPI“ (365 pts.) does not hold scrutiny
- The IPI (4500 pts.) is alive and valid in the rituximab era (1068 pts.)
Conclusion:

- The „R-IPI“ (365 pts.) does not hold scrutiny
- The IPI (4500 pts.) is alive and valid in the rituximab era (1068 pts.)
<table>
<thead>
<tr>
<th><strong>Risk-adapted Approaches for Aggressive Lymphomas</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Germany et al.</strong></td>
</tr>
<tr>
<td>Stage I No bulk</td>
</tr>
<tr>
<td>IPI=0,1</td>
</tr>
<tr>
<td>Elderly</td>
</tr>
<tr>
<td>IPI=2,3</td>
</tr>
<tr>
<td>U S A (CALBG)</td>
</tr>
<tr>
<td><strong>France (GELA)</strong></td>
</tr>
<tr>
<td>IPI=0</td>
</tr>
<tr>
<td>Elderly IPI=0</td>
</tr>
<tr>
<td>IPI=1</td>
</tr>
<tr>
<td>Elderly IPI=1, 2,3</td>
</tr>
<tr>
<td>aalPI=2,3</td>
</tr>
<tr>
<td>U S A (SWOG)</td>
</tr>
<tr>
<td>I,noBulk</td>
</tr>
<tr>
<td>Limited</td>
</tr>
<tr>
<td>Elderly II-IV</td>
</tr>
<tr>
<td>aalPI=2,3</td>
</tr>
<tr>
<td>Japan (JCOG)</td>
</tr>
<tr>
<td>Elderly IPI=1, 2,3</td>
</tr>
<tr>
<td>Elderly IPI=0,1</td>
</tr>
<tr>
<td>Elderly IPI=0</td>
</tr>
<tr>
<td>Limited</td>
</tr>
<tr>
<td>Over 70</td>
</tr>
</tbody>
</table>

---

- U S A (CALBG)
- U K (NCRI)
- Japan (JCOG)

---

**Notes:**
- IPI: International Prognostic Index
- aalPI: Additional prognostic factor
- UNFIT: Not fit for standard treatment
I. Young Good-Prognosis Patients (aa IPI = 0, 1)
CD20⁺ DLBCL
18-60 years
IPI 0,1
Stages II-IV, I with bulk

Random

6 x CHOP-like
+ 30-40 Gy (Bulk, E)

6 x CHOP-like
+ Rituximab
+ 30-40 Gy (Bulk, E)
**MLnT**

**Overall Survival**

- **Probability**
- **Months**

Overall Survival:
- **R-CHEMO (n=413)**: 89.8%
- **CHEMO (n=410)**: 80.0%

Significance: p=0.001

*Pfreundschuh et al. Lancet Oncol 2011*
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hazard Ratio (95%-CI)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment arm</td>
<td>0.49 (0.38;0.63)</td>
<td>&lt; 0.0001*,**</td>
</tr>
<tr>
<td>Bulky disease</td>
<td>1.43 (1.12;1.83)</td>
<td>0.004**</td>
</tr>
<tr>
<td>IPI</td>
<td>1.73 (1.33;2.25)</td>
<td>&lt;0.001*,**</td>
</tr>
</tbody>
</table>

* = also significant for PFS  ** = also significant for OS
Prognostic Groups in the Rituximab Era: Favourable vs. Unfavourable

Favourable: IPI=0 / ∅ bulk

Unfavourable: IPI=1 and / or bulk
Favourable Subgroup (IPI=0 / no Bulk): 6 x R-CHOP-21

Event-free Survival

Overall Survival

Pfreundschuh et al. Lancet Oncol 2011
Current  Risk-adapted Approaches

Young DLBCL:  
Subgrouping  
*before*  MInT
Current Risk-adapted Approaches

Young DLBCL: Subgrouping *before* MInT

- Stage I without bulk
- Stage I Bulk, Stages II-IV IPI=0.1
- aalPI=2,3
Current Risk-adapted Approaches

Young DLBCL: Subgrouping before MInT

- Stage I without bulk
- Stage I Bulk, Stages II-IV IPI=0.1
- aalPI=2,3

Young DLBCL: Subgrouping after MInT
Current Risk-adapted Approaches

Young DLBCL: Subgrouping before MInT

- Stage I without bulk
- Stage I Bulk, Stages II-IV  
  IPI=0.1
- IPI=2,3

Young DLBCL: Subgrouping after MInT

- IPI=0 (Stages I&II) without bulk
- IPI=1 and/ or Bulk
- IPI=2,3

EFS>90%  
OS ≈ 100%
FLYER (6-6/6-4) STUDY DESIGN

Stage I/II
aaIPI=0
no Bulk
18-60 years
FLYER (6-6/6-4):

PLANNED SAFETY ANALYSIS

200 Patients:
- 4 events
  - 1 death (standard arm, swine flu)
  - 3 other events (arm 2?)
200 Patients:
- 4 events
  - 1 death (standard arm, swine flu)
  - 3 other events (arm 2?)

Worst-case scenario:
- 4xR-CHOP+2R: EFS 97%, OS=100%
200 Patients:

4 events

1 death (standard arm, swine flu)
3 other events (arm 2?)

worst-case scenario:

4xR-CHOP+2R: EFS 97%, OS=100%

⇒ study safe, 600 pts. needed
Current Risk-adapted Approaches

- IPI=0 (Stages I&II)
  - No bulk
  - OS ~ 90%
  - EFS ~ 75%

- IPI=1
  - and/or Bulk

- aIPI=2,3
LNH 03-2B Study
DLBCL <60 years, IPI=1

*No radiotherapy in both arms

ClinicalTrials.gov: NCT00140595
Overall Survival

The 3-y OS was 92% (95% CI, 87-95) in the R-ACVBP arm and 84% (95% CI, 77-89) in the R-CHOP arm

Recher et al, Lancet 2012
aalIPI = 1 :

Where do we stand?
LNH 03-2B vs. MInt_{aaIPI=1}

3-Year Results

<table>
<thead>
<tr>
<th></th>
<th>EFS</th>
<th>PFS</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>GELA:</td>
<td>67%</td>
<td>73%</td>
<td>84%</td>
</tr>
<tr>
<td>R-CHOP-21 (n=183)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GELA:</td>
<td>81%</td>
<td>87%</td>
<td>92%</td>
</tr>
<tr>
<td>R-ACVBP (n=196)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MInt:</td>
<td>80%</td>
<td>86%</td>
<td>90%</td>
</tr>
<tr>
<td>R-CHOP-21 (n=118)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MInt:</td>
<td>77%</td>
<td>83%</td>
<td>91%</td>
</tr>
<tr>
<td>R-CHEMO (n=203)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Where do we stand?

\[ \text{aaIPI} = 1 \]

\[ 8 \times \text{R-CHOP-21}_{\text{GELA}} < 6 \times \text{R-CHOP-21}_{\text{MInT}} \]
Where do we stand?

\[ \text{aaIPI} = 1 \]

\[ 8 \times R-\text{CHOP-21}_{\text{GELA}} < 6 \times R-\text{CHOP-21}_{\text{MInT}} \]

\[ R-\text{ACVBP}_{\text{GELA}} = 6 \times R-\text{CHOP-21}_{\text{MInT}} \]
Where do we stand?

$\text{aaIPI} = 1$

$8 \times \text{R-CHOP-21 GelA} < 6 \times \text{R-CHOP-21 MinT}$
Where do we stand?

aaIPI = 1

8 x R-CHOP-21_{GELA}^* < 6 x R-CHOP-21_{MINT}^{MINT}

R-ACVBP_{GELA}^* = 6 x R-CHOP-21_{MINT}^{MINT}

* No Radiotherapy
Where do we stand?

\[ \text{aaIPI} = 1 \]

\[ 8 \times \text{R-CHOP-21}_{\text{GELA}}^* < 6 \times \text{R-CHOP-21}_{\text{MInT}}^{**} \]

\[ \text{R-ACVBP}_{\text{GELA}}^* = 6 \times \text{R-CHOP-21}_{\text{MInT}}^{**} \]

* No Radiotherapy  
** Radiotherapy to bulky disease
Where do we stand?

aaIPI = 1:

Is Radiotherapy back in the Game?
UNFOLDER (21/14) STUDY DESIGN

+/− Radiatio to Bulky Disease

IPI = 1 and/or Bulk

+/− Radiatio to Bulky Disease
UNFOLDER Study

Patients 18-60 years, B-cell (CD20+), aaIPI=0 with bulk or aaIPI=1, ITT (n=443)

EFS – Patients randomised to 4 arms (n=285)

Months

0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80

Proportion

0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1

R-CHOP 21/14 + Rx (n=139)

R-CHOP 21/14 + RX (n=146)

p=0.004

81%

65%
UNFOLDER Study

Patients 18-60 years, B-cell (CD20+), aalPl=0 with bulk or aalPl=1, ITT (n=443)

EFS – Patients randomised to 4 arms (n=285)

- R-CHOP 21/14 + RX (n=146)
- R-CHOP 21/14 + Rx (n=139)

p=0.004

α Spending 0.008

Termination!!!
UNFOLDER (21/14) STUDY DESIGN

 +/- Radiatio to Bulky Disease

 IPI = 1 and/or Bulk

 +/- Radiatio to Bulky Disease
IPI = 1 and/or Bulk

 +/- Radio to Bulky Disease

 +/- Radio to Bulky Disease

 CHOP 21 R

 CHOP 21 R

 CHOP 21 R

 CHOP 21 R

 CHOP 21 R

 CHOP 21 R

 d 1

 d 75

 d 105

 R

 R

 R

 R

 R

 R

 R
Conclusions:

- Radiotherapy to bulky disease indicated
- UNFOLDER to be continued as planned
  - to consolidate Rx effects (PFS, OS)
  - to answer R-CHOP-14 vs. R-CHOP-21
- 142 additional patients needed
II. Young Poor-Prognosis Patients (aa IPI = 2, 3)
DSHNL 2002-1 ("Mega-CHOEP"/):
TRIAL DESIGN (≤60 YRS., AGE-ADJUSTED IPI ≥2)

n=230

mCHOEP I
CYC 1500
ADR 70
VCR 2
ETO 600
PRD 500

mCHOEP II
CYC 4500
ADR 70
VCR 2
ETO 960
PRD 500

mCHOEP III
CYC 4500
ADR 70
VCR 2
ETO 960
PRD 500

mCHOEP IV
CYC 6000
ADR 70
VCR 2
ETO 1480
PRD 500

n=230

CHOEP-14: CYC 750
ADR 50
VCR 2
ETO 300
PRED 500
G-CSF
R-MegaCHOEP Study
OS ACCORDING TO TREATMENT ARM

GERMAN HIGH-GRADE NHL STUDY GROUP (DSHNHL)

www.lymphome.de/en/Groups/DSHNHL

R-CHOEP-14 (n=130)
R-MegaCHOEP (n=132)
p=0.081

Proportion

0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1

0 10 20 30 40 50 60 70 80 90 100

Months

R-CHOEP-14
(n=130)

R-MegaCHOEP
(n=132)
p=0.081
R-MegaCHOEP Study
OS: PATIENTS WITH aaIPI 2 ONLY!

p=0.013

R-CHOEP-14 (n=95)
R-MegaCHOEP (n=97)
R-MegaCHOEP Study

OS: PATIENTS WITH aaIPI 3 ONLY!

![Graph showing survival rates for R-CHOEP-14 and R-MegaCHOEP studies.]

- R-CHOEP-14 (n=35)
- R-MegaCHOEP (n=35)

p=0.753
Young Poor-Prognosis DLBCL (aaIPI= 2, 3)

Conclusions in the Rituximab Era:
Young Poor-Prognosis DLBCL (aaIPI= 2, 3)

Conclusions in the Rituximab Era:

• Best results with R-CHOEP-14
Conclusions in the Rituximab Era:

- Best results with R-CHOEP-14
- 6 cycles enough?
Young Poor-Prognosis DLBCL (aaIPI = 2, 3)

Conclusions in the Rituximab Era:

- Best results with R-CHOEP-14
- 6 cycles enough?
- Role of etoposide?
DSHNHL 2002-1 („Mega-CHOEP“):
TRIAL DESIGN (≤60 YRS., AGE-ADJUSTED IPI ≥2)

n=230

mCHOEP I
CYC 1500
ADR 70
ETO 600
PRD 500

mCHOEP II
CYC 4500
ADR 70
ETO 960
PRD 500

mCHOEP III
CYC 4500
ADR 70
ETO 960
PRD 500

mCHOEP IV
CYC 6000
ADR 70
ETO 1480
PRD 500

CHOEP-14
CYC 750
ADR 50
E 300
G-CSF

= Rituximab

= additional Rituximab

CHOEP-14: CYC 750 ADR 50 PRED 500 VCR 2 ETO 300

TRIAL DESIGN (≤60 YRS., AGE-ADJUSTED IPI ≥2)

R

Rituximab

additional Rituximab
III.

Elderly Patients
RICOVER-60

Study Design

CD20+ DLBCL
Stages I-IV
61 to 80 years

Random 2x2 Factorial Design

- 6 x CHOP-14
  + 30-40 Gy (Bulk, E)

- 8 x CHOP-14
  + 30-40 Gy (Bulk, E)

- 6 x CHOP-14
  + 36 Gy (Bulk, E)
  + 8 x Rituximab

- 8 x CHOP-14
  + 36 Gy (Bulk, E)
  + 8 x Rituximab
RICOVER-60
- Progression-free Survival -

1, 2: p=0.616
1, 3: p<0.001
1, 4: p=0.001
3, 4: p=0.317

3-year rates:
73.4%
68.8%
56.9%
56.9%

Pfreundschuh et al., Lancet Oncol. (2008)
RICOVER-60
Overall Survival

Pfreundschuh et al., Lancet Oncol. (2008)
III. Elderly Patients:

*Do we still need Dose Densification / Interval Reduction?*

[R-CHOP-14 vs. R-CHOP-21]
Primary endpoint: EFS
Expected improvement: 10% at 3 years with R-CHOP 14 (55 to 65%)
600 patients required (over 4 years)
### Relative Dose Cyclophosphamide (median)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 x CHOP-14</td>
<td>99%</td>
</tr>
<tr>
<td>6 x R-CHOP-14</td>
<td>99%</td>
</tr>
<tr>
<td>8 x CHOP-14</td>
<td>96%</td>
</tr>
<tr>
<td>8 x R-CHOP-14</td>
<td>96%</td>
</tr>
<tr>
<td>GELA 8xR-CHOP-14</td>
<td>83%</td>
</tr>
</tbody>
</table>
ESMO GUIDELINES 2012

Recommendation Elderly DLBCL:

- 6 cycles R-CHOP-14
- 8 cycles R-CHOP-21

What about long-term toxicity?
R-CHOP: Reduction of EF
III. Elderly Patients

Can R-CHOP-14 for Elderly be Further improved (fool-proved)?
SMARTE-R-CHOP-14

Simulation for a Maximum Area under the Curve (AUC) with 8 x Rituximab
Rituximab Schedules for DLBCL

**SMARTER-R-CHOP-14**

(8 x R)

-4 -1 15 29 43 57 71 85 99 155 239
Rituximab Schedules for DLBCL

**SMART-E-R-CHOP-14**
(8 x R)

**RICOVER-60 R-CHOP-14**
(8 x R)

Days:
Overall Survival

Overall survival curves for SMARTER (n=189) and RICOVER-60 (n=306) treatments. The median time of observation is 37/34 months. The 3-year survival rates are 84% for SMARTER and 78% for RICOVER-60.
Overall Survival

**SMARTE-R-CHOP-14**

RICOVER-60 (n=306)

SMARTER (n=189)

Proportion

0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0

Month

0 5 10 15 20 25 30 35 40 45 50 55 60

84%

78%

p=0.118

median time of observation: 37/34 months
SMARTE-R-CHOP-14
IPI=1,2

Overall Survival
Overall Survival

SMARTE-R-CHOP-14

IPI=1,2

p=0.489

Proportion

0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0

0 5 10 15 20 25 30 35 40 45 50 55 60

Months

RICOVER-60 (n=183)

SMARTE (n=90)
Overall Survival

SMARTE-R-CHOP

14

IPI=1,2

IPI>2

p=0.489

Proportion

Months

0 5 10 15 20 25 30 35 40 45 50 55 60

SMARER (n=90)

RICOVER-60 (n=183)
Overall Survival

SMARTE-R-CHOP-14

IPI=1,2

IPI>2

p=0.489

SMARTER (n=90)

RICOVER-60 (n=183)

DSHNHL

80%
Overall Survival

SMARTE-R-CHOP-

14

IPI=1,2

IPI>2

RICOVER-60 (n=183)

SMARTER (n=90)

p=0.489

80%

67%

SMARTER (n=99)

RICOVER-60 (n=123)
Overall Survival

SMARTE-R-CHOP-14

IPI=1,2

IPI>2

RICOVER-60 (n=183)

SMARTER (n=90)

p=0.489

80%

p=0.034

67%

(DSHNHL)
RICOVER-60 Trial: Rituximab Clearance

Müller et al., Blood 2012
RICOVER-60 Trial:
Rituximab Serum Elimination Half Life

Müller et al., Blood 2012
SMARTE-R vs. RICOVER
Sex-differential Improvement
SMARTE-R vs. RICOVER
Sex-differential Improvement

OS of Females (IPI=3-5)

- 80% for female SMARTER (n=48)
- 76% for female RICOVER (n=57)
SMARTE-R vs. RICOVER
Sex-differential Improvement

OS of Females (IPI=3-5)

- Female SMARTER (n=48)
- Female RICOVER (n=57)

OS of Males (IPI=3-5)

- Male SMARTER (n=51)
- Male RICOVER (n=66)

80% & 76% improvements for females
80% & 60% improvements for males
SMARTE-R vs. RICOVER
Sex Differences in Outcome

OS RICOVER (IPI=3-5)

76%
60%

female RICOVER
(n=57)
male RICOVER
(n=66)

Months
SMARTE-R vs. RICOVER
Sex Differences in Outcome

OS RICOVER (IPI=3-5) vs. OS SMARTER (IPI=3-5)

- RICOVER (male: n=66, female: n=57)
  - Female: 76%
  - Male: 60%

- SMARTER (male: n=51, female: n=48)
  - Female: 80%
  - Male: 80%
Adherence to Protocol

Relative Dose Cyclophosphamide (median)

- 6 x CHOP-14: 99%
- 6 x R-CHOP-14: 99%
- 8 x CHOP-14: 96%
- 8 x R-CHOP-14: 96%
## RICOVER-60: Vincristine Administration

<table>
<thead>
<tr>
<th>Dosage [mg]</th>
<th>cycle 1</th>
<th>cycle 2</th>
<th>cycle 3</th>
<th>cycle 4</th>
<th>cycle 5</th>
<th>cycle 6</th>
<th>cycle 7</th>
<th>cycle 8</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2.5%</td>
<td>2.4%</td>
<td>5.3%</td>
<td>9.8%</td>
<td>16.4%</td>
<td>22.0%</td>
<td>30.4%</td>
<td>35.5%</td>
<td>11.8%</td>
</tr>
<tr>
<td>0.1 - 1.9</td>
<td>10.9%</td>
<td>12.5%</td>
<td>14.7%</td>
<td>17.0%</td>
<td>17.6%</td>
<td>17.4%</td>
<td>17.3%</td>
<td>15.2%</td>
<td>15.0%</td>
</tr>
<tr>
<td>2</td>
<td>86.5%</td>
<td>84.9%</td>
<td>79.5%</td>
<td>72.6%</td>
<td>65.3%</td>
<td>59.0%</td>
<td>51.0%</td>
<td>47.9%</td>
<td>72.5%</td>
</tr>
<tr>
<td>&gt; 2</td>
<td>-</td>
<td>0.1%</td>
<td>0.2%</td>
<td>-</td>
<td>-</td>
<td>0.2%</td>
<td>-</td>
<td>0.3%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Vinblastine</td>
<td>0.1%</td>
<td>0.2%</td>
<td>0.3%</td>
<td>0.6%</td>
<td>0.8%</td>
<td>1.4%</td>
<td>1.3%</td>
<td>1.1%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Dosage [mg]</td>
<td>cycle 1</td>
<td>cycle 2</td>
<td>cycle 3</td>
<td>cycle 4</td>
<td>cycle 5</td>
<td>cycle 6</td>
<td>cycle 7</td>
<td>cycle 8</td>
<td>total</td>
</tr>
<tr>
<td>------------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>-------</td>
</tr>
<tr>
<td>0</td>
<td>2.5%</td>
<td>2.4%</td>
<td>5.3%</td>
<td>9.8%</td>
<td>16.4%</td>
<td>22.0%</td>
<td>30.4%</td>
<td>35.5%</td>
<td>11.8%</td>
</tr>
<tr>
<td>0.1 - 1.9</td>
<td>10.9%</td>
<td>12.5%</td>
<td>14.7%</td>
<td>17.0%</td>
<td>17.6%</td>
<td>17.4%</td>
<td>17.3%</td>
<td>15.2%</td>
<td>15.0%</td>
</tr>
<tr>
<td>2</td>
<td>86.5%</td>
<td>84.9%</td>
<td>79.5%</td>
<td>72.6%</td>
<td>65.3%</td>
<td>59.0%</td>
<td>51.0%</td>
<td>47.9%</td>
<td>72.5%</td>
</tr>
<tr>
<td>&gt; 2</td>
<td>-</td>
<td>0.1%</td>
<td>0.2%</td>
<td>-</td>
<td>-</td>
<td>0.2%</td>
<td>-</td>
<td>0.3%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Vinblastine</td>
<td>0.1%</td>
<td>0.2%</td>
<td>0.3%</td>
<td>0.6%</td>
<td>0.8%</td>
<td>1.4%</td>
<td>1.3%</td>
<td>1.1%</td>
<td>0.6%</td>
</tr>
</tbody>
</table>
Towards the Cure of DLBCL

Vincristine polyneuropathy: an unmet medical need
CD20⁺ DLBCL
IPI 2-4
IPI 1 Bulk
61 to 80 years

Random 2x2 Factorial Design

R-CHOP-14§
+ 36 Gy BULK-IN-RT*

Opti-R-CHLIP-14&
+ 36 Gy BULK-IN-RT*

R-CHLIP-14&
+ 36 Gy BULK-IN-RT*

Opti-R-CHLIP-14&
+ 36 Gy BULK-IN-RT*

Study Design

OPTIMAL >60

Except PET-neg.

§ conventional vincristine 2 mg (absol.)
& liposomal vincristine 2 mg/m²
Rituximab Schedules for DLBCL

**OPTIMAL**
- **R-CHOP-14**
- **R-CHLIP-14**
  (12 x R)

**2-week**
- **R-CHOP-14**
- **R-CHLIP-14**
  (8 x R)

---

Days:
- **R-CHOP-14**: 1, 15, 29, 43, 57, 71, 85, 99
- **R-CHLIP-14**: 155, 239

---

Supported by DSHNHL
Unresolved Issues in DLBCL

IV.

Very old / frail Patients

DLBCL
>81 Jahre oder 61-80 Jahre mit CIRS>6

BRENSDA Studie

1 22 43 64 85 106 127

T a g e

B E N D A

B E N D A

B E N D A

B E N D A

B E N D A

B E N D A

= Rituximab 375 mg/m² i.v.

= Rituximab 375 mg/m² s.c.
Current Risk-adapted Approaches

- **aalPI=0**
  - No bulk
  - FLYER

- **aalPI=1**
  - And/or bulk
  - UNFOLDER

- **aalPI=2,3**
  - Mega-CHOEP

Age Groups:
- 18 – 60 years
- 61 – 80 years
- >80 years

- **OPTIMAL**
  - >60 years

- **BREnda**
Vielen Dank !