Dose-Dense Chemoimmunotherapy and Early CNS Prophylaxis for High-Risk DLBCL – Interim Results from a Nordic Phase II Study

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OBJECTIVES

Co-primary objectives

- FFS from date of registration (3 yrs)
- CNS relapse rate (1.5 yrs)

Secondary objectives

- Toxicity
- Clinical response rate
- Incidence of CNS relapse (CSF cytology -/ flow cytometry +)
- Incidence of CNS relapse in pts with >1 extranodal site and LDH⇧
- PFS (3 yrs)
- OS (3 yrs)
- Molecular predictors of outcome

METHODS

Inclusion criteria

- Age 18-65 yrs
- Primary DLBCL or grade 3B FL without clinical or radiological signs of CNS disease and cytology- CSF
- aaIPI 2-3

And/or

- Site specific risk factors for CNS recurrence
  - >1 extranodal site
  - Testicular lymphoma, stage IIE and higher
  - Paranasal sinus and orbital lymphoma with destruction of bone
  - Large cell infiltration of the BM
- WHO PS 0-3
- Previously untreated except steroids allowed

Schedule

Dxm + vincristine + R prephase

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HD-MTX+R-CHOP(D)14x2 and R-CHOED-14 with liposomal cytarabine IT cycle 1 and 3

CR, CRu, PR

→ **SD, PD → 2nd line, f-up for OS**

↓

R-CHOEP(D)14x3 + liposomal cytarabine IT on cycle 5 →R-cytarabine 12 g/m²

CR, PR+PET- without viable tumour tissue

→ **SD, PD → 2nd line, f-up for OS**

→ **PR → viable tumour tissue → 2nd line, f-up for OS**

↓

Regular follow-up

RESULTS

Clinicopathological features and treatment background

- A total of 143 pts were recruited (3/2011 - 12/2014)
- From 3/2012 to 11/2013 treatment was given without liposomal cytarabine
- Results from 125 pts are presented:
  - 116 pts (93%) received full treatment
  - Liposomal cytarabine was given to 71 (57%) pts
  - RT was given to 35 pts (28%)
  - Median F-UP is 15 mos (0.5-46 mos)

Characteristic	n=125	%
Age yrs, median (range)	56 (20-64)	
Male Female	80 45	64 36
DLBCL	121	97
PS WHO>1	40	32
Stage III-IV	116	93
B-symptoms	81	65
LDH⇧	113	90
Bulky disease	49	39
>1 extranodal site	88	70
CSF flow +	7	6

*PML, Progressive multifocal leukoencephalopathy

Feasibility

Category	Adverse event	n	%	Death
Infections	Gr 3 Gr 4 Pneumonia Septicaemia	84 13 11 8	67 10 8.8 6.4	 1
Cardio vascular	Pulmonary embolism Thrombosis Atrial fibrillation/bradycardia	3 2 2	2.4 1.6 1.6	
Gastro-intestinal	Gr 3-4 Perforation GI hemorrhage Mucositis Gr 3-4	33 4 1 30	26 3.2 0.8 24	 1
Neurological	Peripheral neuropathy Gr >1 Arachnoiditis Gr>1 PML*	53 3 1	42 4.2 0.8	 1
Renal	MTX excretion delayed Other	7 2	5.6 1.6	
Other	AML	1	0.8	

Efficacy

Response	n	%
CR/CRu	91	76
PR	22	18
PD	4	3.3
Metabolic CR (DS 1-3)	81	76

- 3 primary refractory, 15 relapses; 2 in CNS (both FC-)
- 8 deaths (3 due to toxicity)
- 2-y FFS 72%, PFS 77%, OS 91%

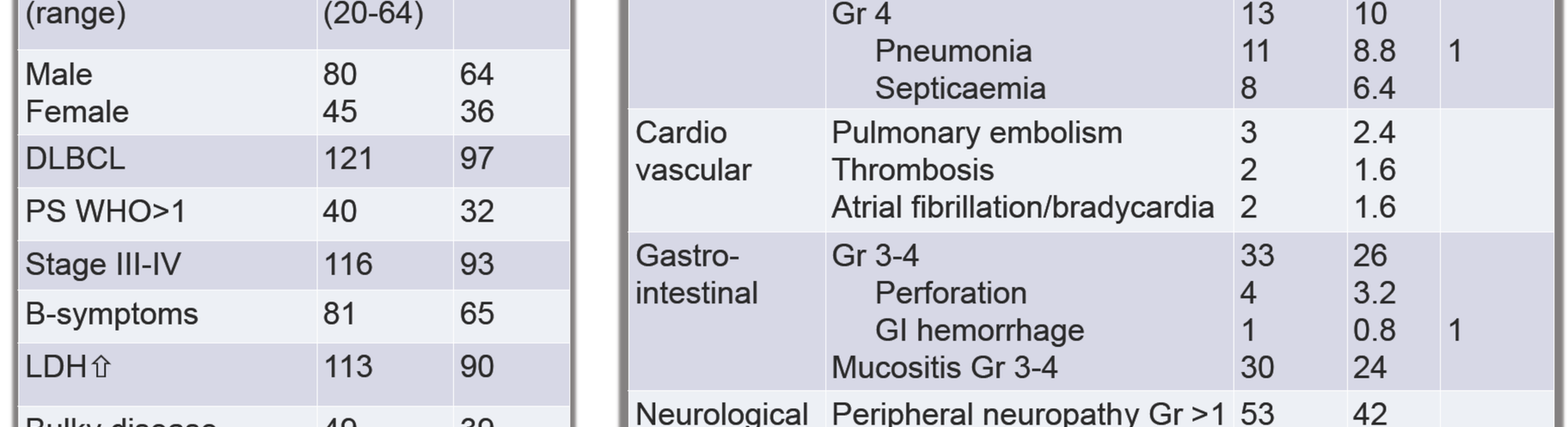

Figure 1. PFS rates according to PET positivity, BCL2 and CD5 expression.

CONCLUSIONS

- High protocol adherence
- Highly satisfactory response rates, FFS and PFS
- Reasonable toxicity

References

Schmitz N et al., Ann Oncol 2012; Björkholm M et al., Ann Oncol, 2007; Holte H et al., Ann Onc 2013

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