



# **Excellent outcome of young patients (18-60 years) with favourable-prognosis diffuse large B cell lymphoma (DLBCL) treated with 4 cycles CHOP plus 6 applications of rituximab: Results of the 592 patients of the FLYER trial of the DSHNHL/GLA.**

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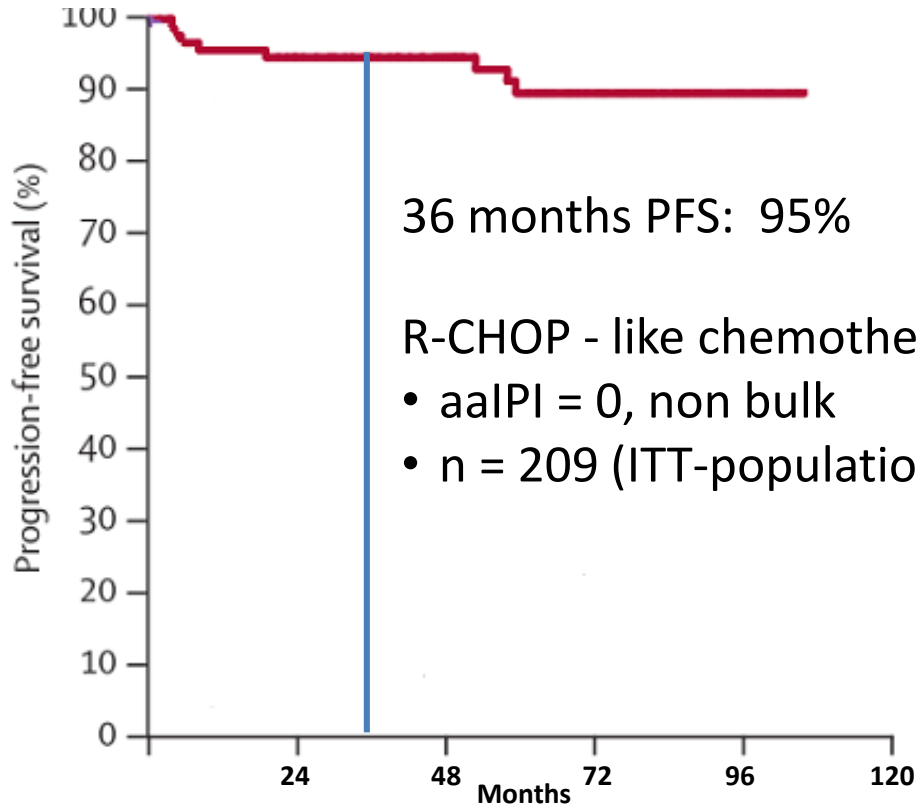
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# Background: MInT Trial



Primary objective of the

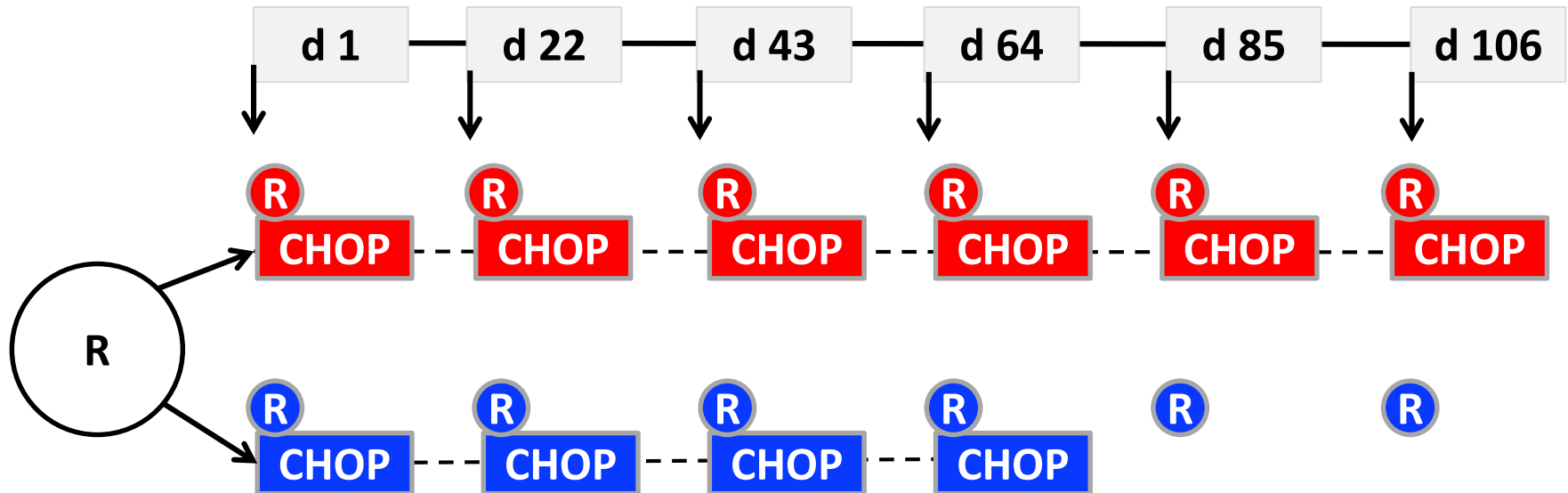
FLYER trial:

- maintaining **efficacy** and
- reducing **toxicity**

by reduction of CHOP cycles

# FLYER: Study Design

- Front-line treatment of aggressive B-cell lymphoma
- 18-60 years, stage I/II, aalPI = 0, no bulk (max. diameter < 7.5 cm)



# Assumptions & Endpoints

**Primary endpoint: 3-year PFS, non-inferiority design**

- **Assumption 3-year PFS:**

- 6 x R-CHOP-21: 93 %

- 4 x R-CHOP-21 + 2 x R: -5.5 % tolerated

- **Power = 80 %,  $\alpha$  = 5 %, one-sided**

- **Planned sample size: 532 + 10% lost -> 592 total**

- **Endpoints: PFS (primary), Response, EFS, OS, toxicity**

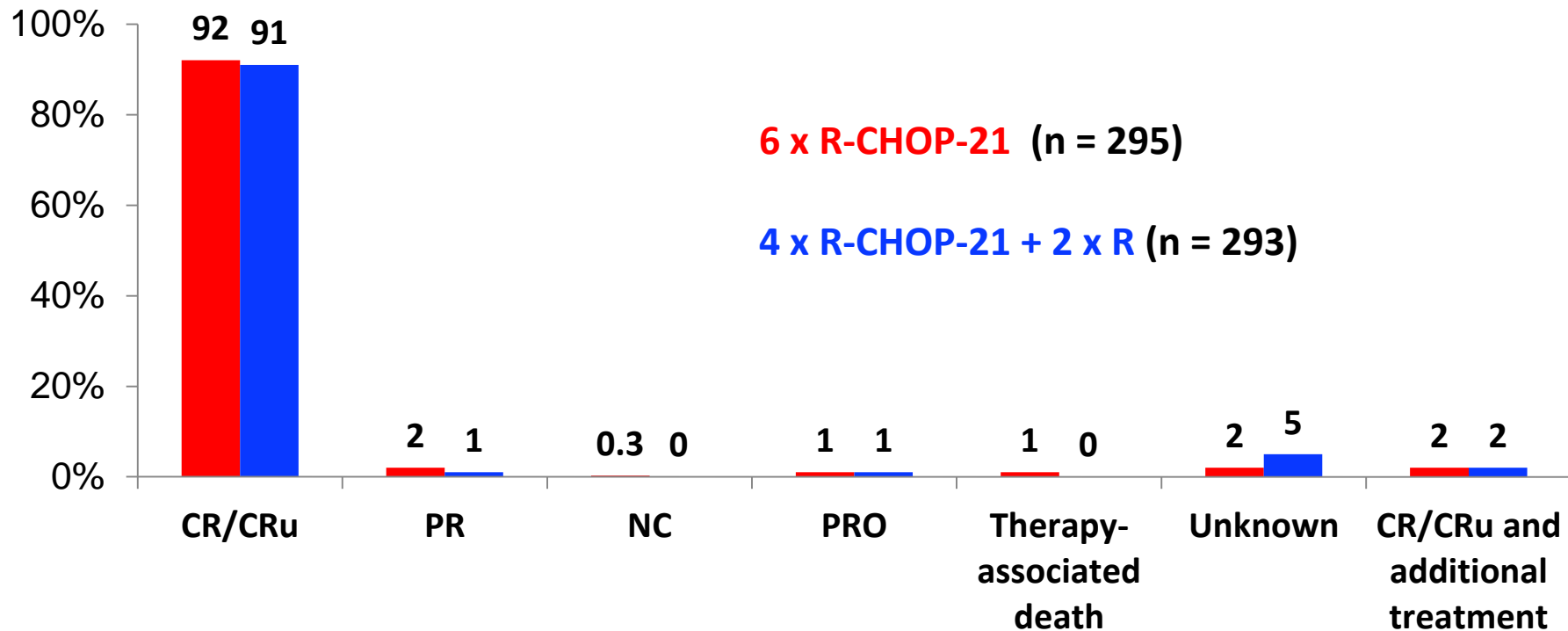
# Demographics

	Total (n = 588)		6 x R-CHOP (n = 295)		4 x R-CHOP (n = 293)		p-value
<b>Female</b>	234	(40 %)	116	(39 %)	118	(40 %)	0.814
<b>Age, median (range)</b>	48	(18, 60)	47	(19, 60)	49	(18, 60)	0.438
<b>LDH &gt; UNV</b>	0	(0 %)	0	(0 %)	0	(0 %)	-
<b>ECOG &gt; 1</b>	0	(0 %)	0	(0 %)	0	(0 %)	-
<b>Stage I</b>	346	(59 %)	172	(58%)	174	(59 %)	0.953
<b>II</b>	236	(40 %)	119	(40 %)	117	(40 %)	
<b>III/IV</b>	6	(1 %)	4	(1 %)	2	(1 %)	
<b>aaIPI 0</b>	582	(99 %)	291	(99 %)	291	(99 %)	0.686
<b>1</b>	6	(1 %)	4	(1 %)	2	(1 %)	
<b>Extralymp. involvement</b>	191	(32 %)	96	(32 %)	95	(32 %)	0.975
<b>Bulky disease</b>	2	(0.3 %)	1	(0.3 %)	1	(0.3 %)	1.000
<b>B-symptoms</b>	36	(6 %)	9	(3 %)	27	(9 %)	0.002

# Histology

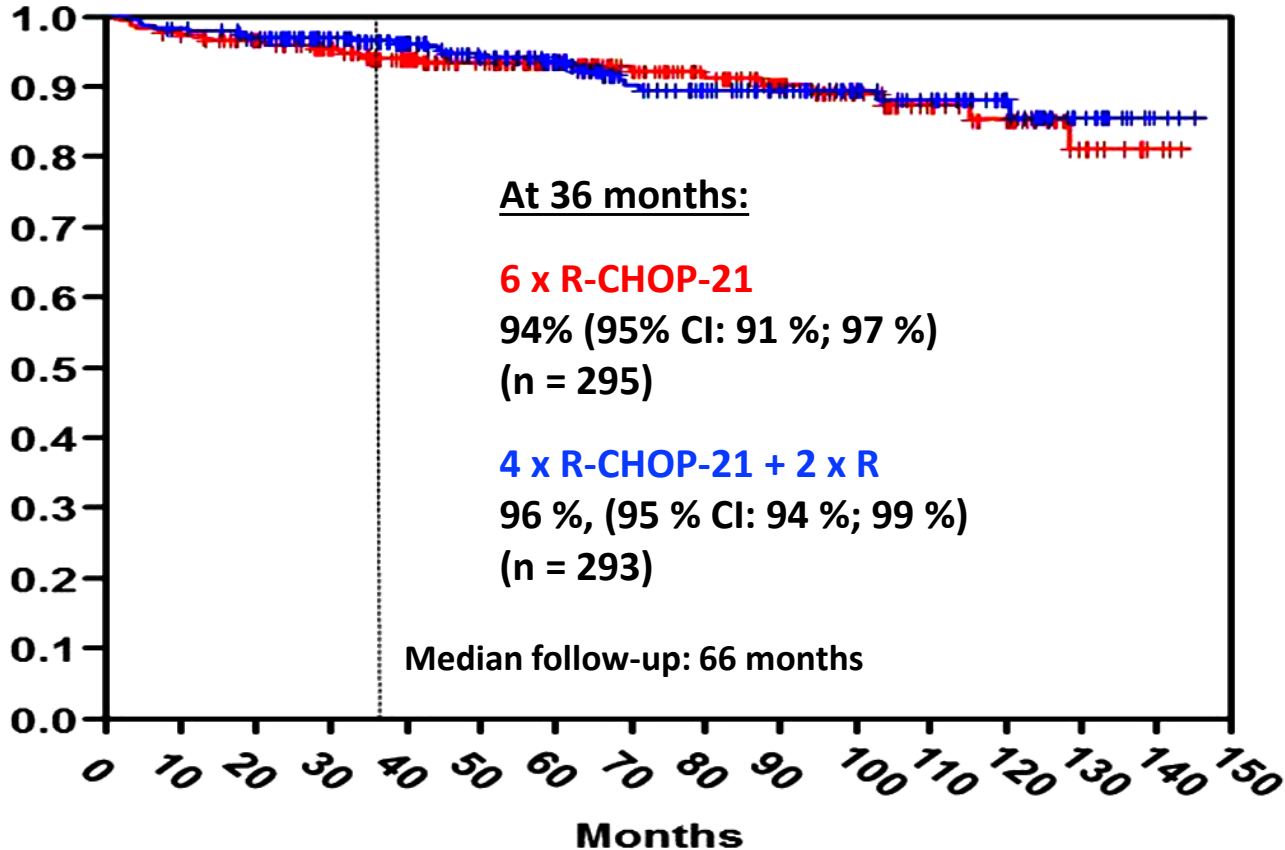
Reference pathology	Total (n = 508)	6 x R-CHOP-21 (n = 251)	4 x R-CHOP-21 + 2 x R (n = 257)
<b>Diffuse large B-cell lymphoma</b>	79 %	80 %	78 %
Centroblastic	42 %	44 %	40 %
Immunoblastic	2 %	2 %	2 %
Plasmoplastic	0.2 %	0 %	0.4 %
Anaplastic large cell (ALC)	1 %	0.4 %	2 %
T-cell-rich B-cell lymphoma	1 %	0.4 %	1 %
NOS	32 %	34 %	32 %
Prim. mediast. B-cell lymphoma	1 %	0.4 %	2 %
<b>Follicular lymphoma IIIB°</b>	4 %	3 %	5 %
<b>Follicular lymphoma III° + DLBCL</b>	9 %	10 %	9 %
<b>Burkitt lymphoma</b>	1 %	1 %	1 %
<b>Mantle cell lymphoma (blastoid)</b>	0.2 %	0.4 %	0 %
<b>Aggressive marginal zone lymphoma</b>	1 %	1 %	0.4 %
<b>NOS</b>	1 %	1 %	2 %
<b>Unclassified (techn. insufficient mat.)</b>	1 %	1 %	1 %

# Response Rates

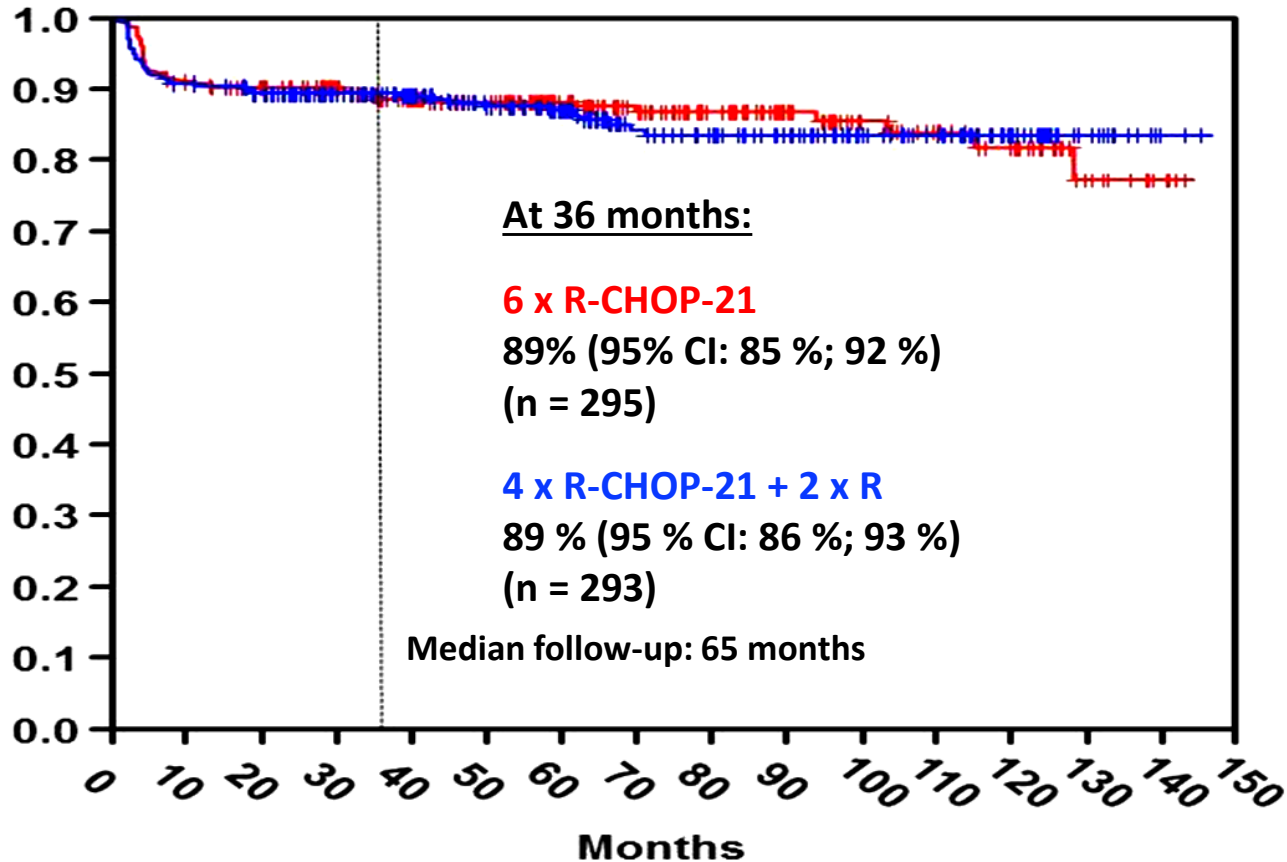




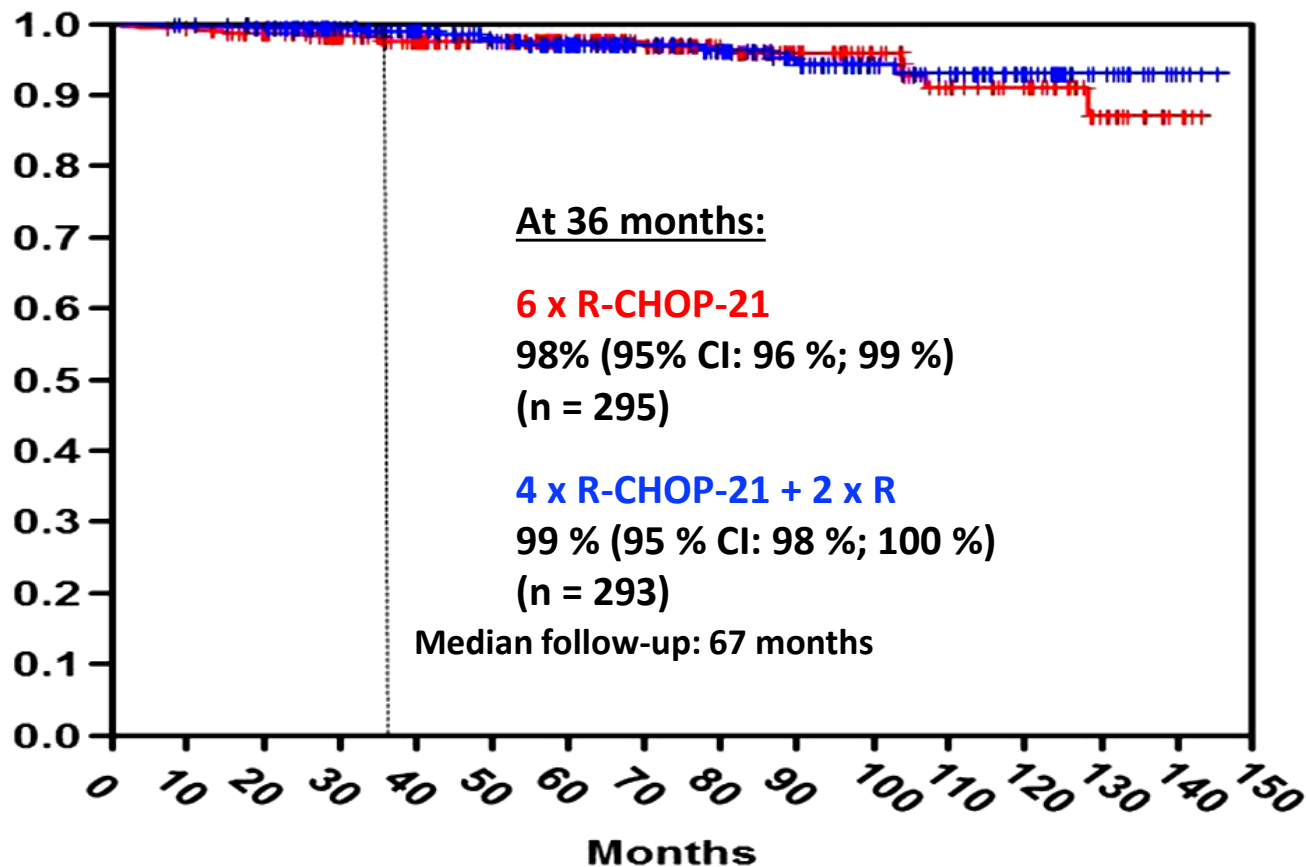
# Primary Endpoint: PFS



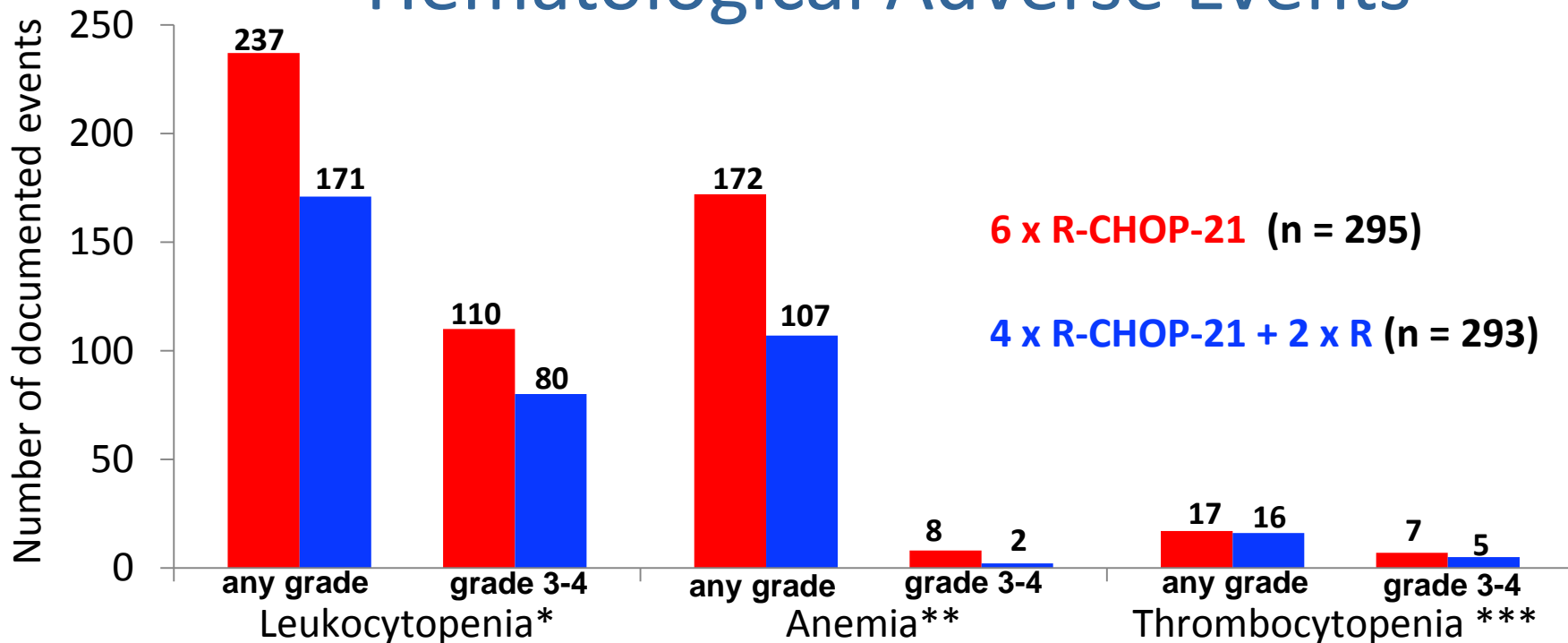
# Event Free survival (EFS)



# Overall Survival (OS)



# Total Number of Hematological Adverse Events



\* - \*\*\* Blood counts in between chemotherapy cycles were only available in 69 % cycles resp. 73% cycles

# Total Number of non-Hematological Adverse Events

	6x R-CHOP-21 (n=295)		4 x R-CHOP-21 + 2 x R (n = 293)	
	any grade	grade 3-4	any grade	grade 3-4
All	1295	70	835	46
Paresthesia	370	14	227	12
Nausea	319	12	195	6
Infection	156	23	98	20
Vomiting	117	7	56	1
Mucositis	105	3	68	1



**Overall reduction of non-hem AEs by approx a third**

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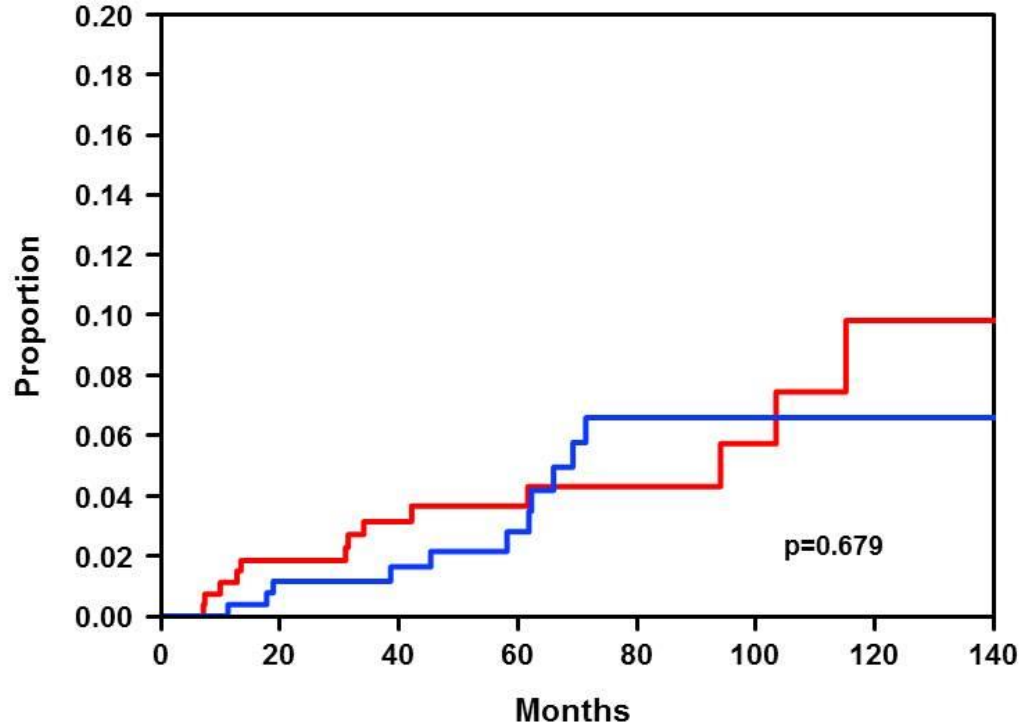
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**Overall reduction of non-hem AEs by approx a third**

# Cumulative Incidence of Relapse



**6 x R-CHOP-21** n = 271

**4 x R-CHOP-21 + 2 x R** n = 267

## Relapse Rates:

— **13 (5%)**, (95%CI: 3%;8%)

— **11 (4%)**, (95%CI: 2%; 7%)

**Total: 24 (4%)**, (95%CI: 3%; 7%)



# Conclusion

- In younger patients with favourable prognosis aggr. B-NHL (aaIPI=0, no bulk) efficacy (PFS, EFS, OS) with 4 cycles of R-CHOP + 2 x R is non-inferior to the previous standard 6 x R-CHOP
- AEs with 4 cycles were reduced by about a third, which means a significant benefit for patients
- Relapse pattern is similar in both arms with longer follow-up

# FLYER Trial Team

## **Coordinating Investigators:**

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**Christian Berdel**

## **Reference Pathology:**

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## **Statistics- Leipzig/Germany:**

**Marita Ziepert, Bettina Altmann, Markus Löffler**

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# Prof. Dr. Michael Pfreunds Schuh

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