

# **Managing Risk in advanced-stage HL**

**Andreas Engert, MD**

**Chairman, German Hodgkin Study Group**  
**University Hospital of Cologne**

# Managing risk in advanced stage HL

## Key issues

- **Background**
- **Advanced Stages**
- **Perspectives**
- **Summary**

# GHSQ Risk Allocation for HL

	<b>Stage (Ann Arbor)</b>			
<b>Risk factors</b>	<b>IA, IB, IIA</b>	<b>IIB</b>	<b>IIIA, IIIB</b>	<b>IVA, IVB</b>
<b>None</b>	<b>Early favorable</b>		<b>Advanced</b>	
<b>≥ 3 LK- Areas</b>	<b>Early unfavorable</b>			
<b>Elevated ESR</b>				
<b>Large Med Mass</b>				
<b>Extranodal disease</b>				

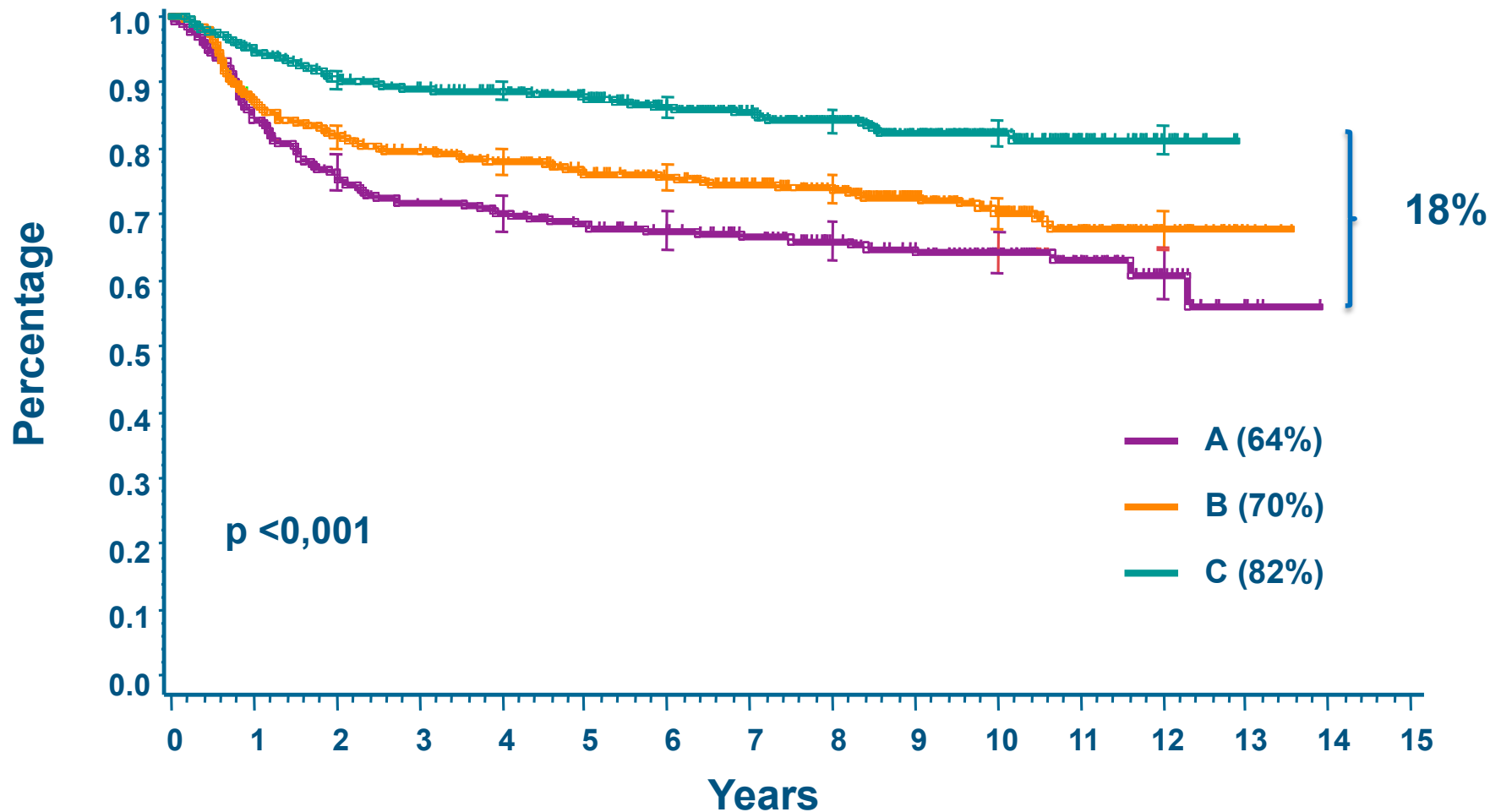
# Hodgkin Lymphoma

## Late side effects after treatment

- **2nd NPL**
  - AML**
  - NHL**
  - Solid tumours**
- **Organ damage**
  - Lung**
  - Heart**
  - Thyroid**
- **Others**
  - Fertility**
  - OPSI**
  - Fatigue**
  - Psycho-social**

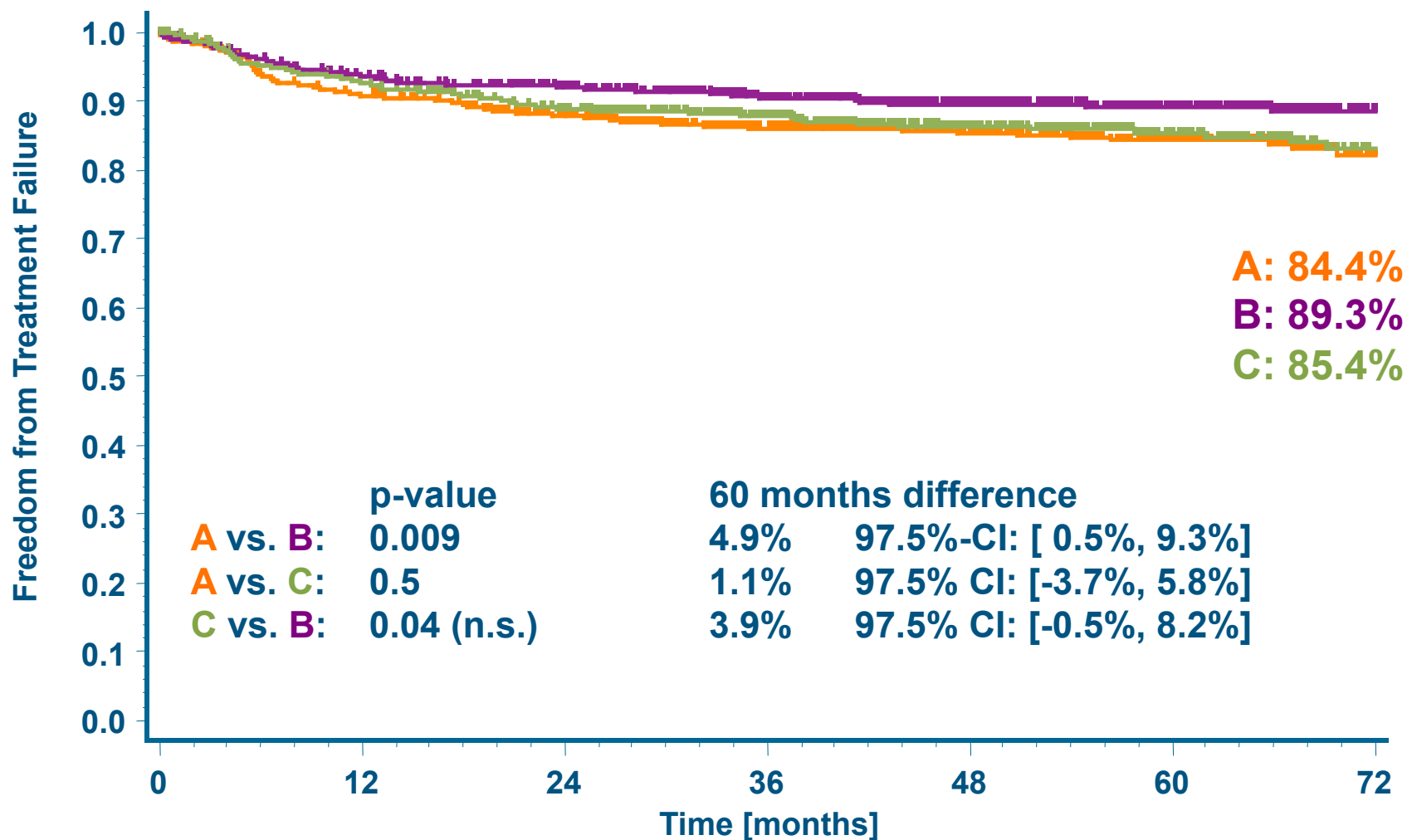
# GHSQ HD9 trial

## FFTF by treatment arm



# HD15 in advanced HL

## Freedom from Treatment Failure (FFTF)



# TRM of BEACOPP escalated\*

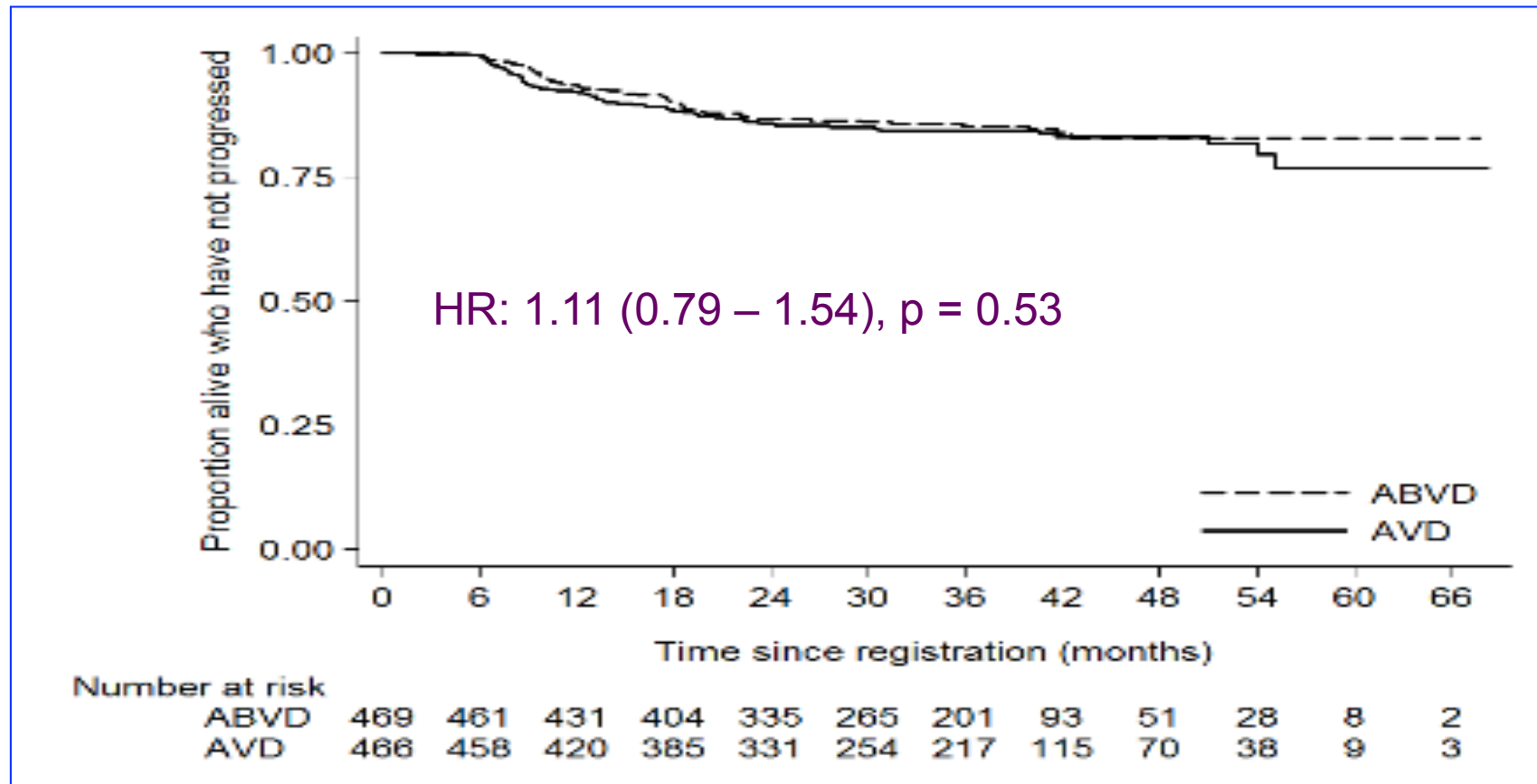
## Multivariate model

Age <sub>≥</sub> 40	Age <sub>≥</sub> 50	ECOG 2 or Karn.<80	Patients	TRM rate
-	-	-	2156	0.7
+	-	-	590	1.7
-	-	+	108	0.9
+	+	-	445	5.6
+	-	+	40	13.3
+	+	+	45	15.0

\*Pts treated in HD9, 12, 15 (64/3565; 1.9%)

Wongso et al, JCO 2013

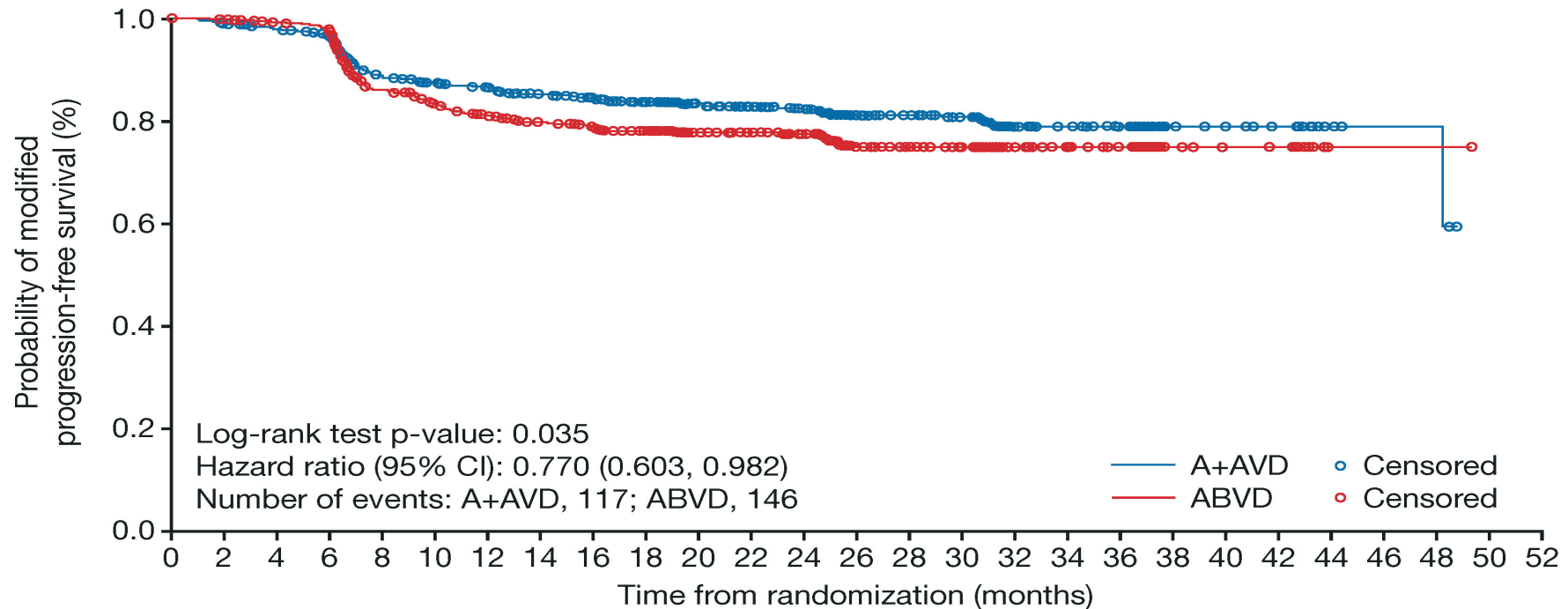
# UK RATHL: Impact of Bleomycin PFS for PET-negative patients (ITT)





# Hodgkin Lymphoma

## ECHELON-1: modified PFS



Number of patients at risk:

A+AVD	664	640	623	606	544	530	516	496	474	447	350	334	311	200	187	174	99	85	77	27	24	21	6	4	4	0	0
ABVD	670	644	626	613	522	496	476	459	439	415	328	308	294	179	168	153	78	68	62	16	13	12	1	1	1	0	0

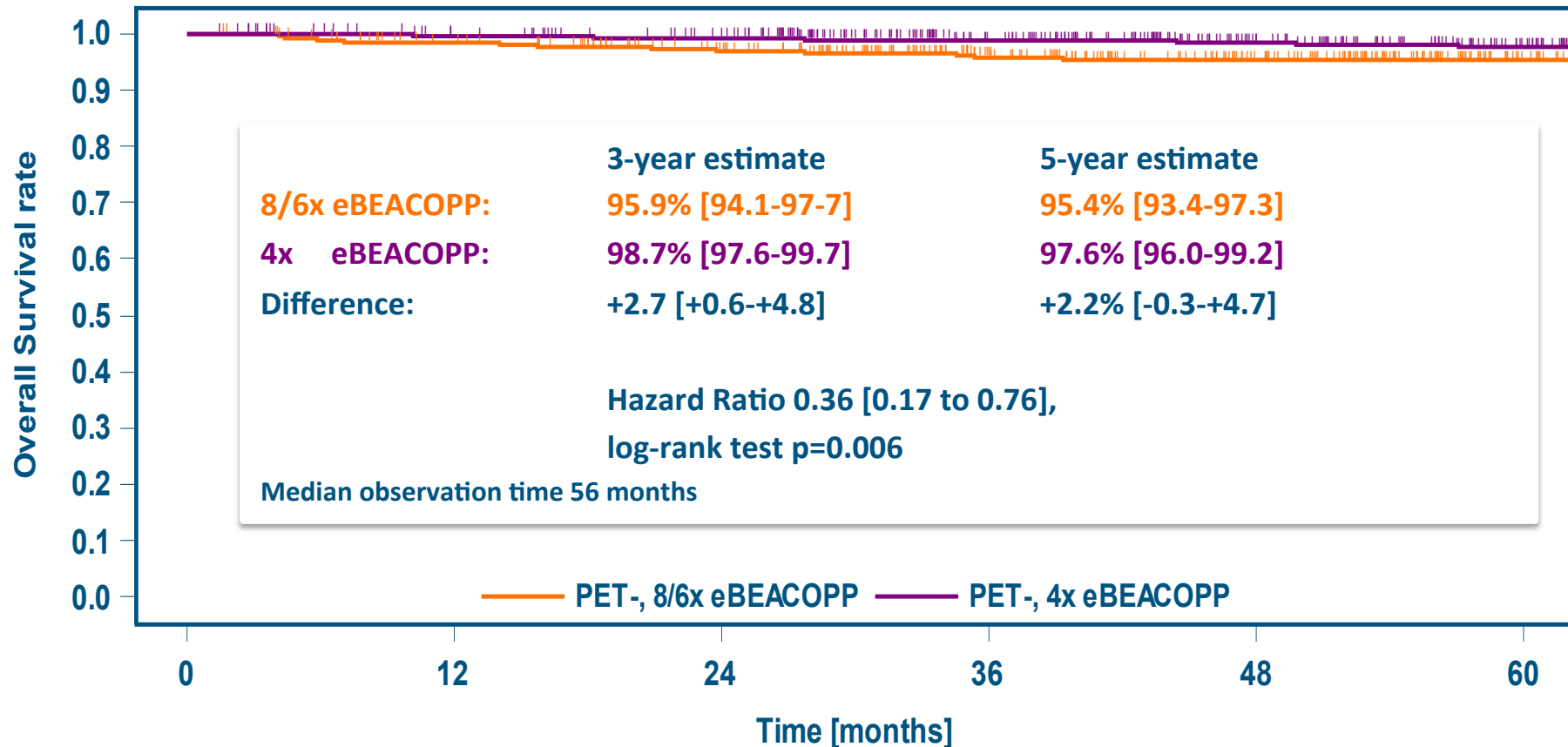
# Hodgkin Lymphoma

## ECHELON-1: Side effects

	<b>A+AVD</b>	<b>ABVD</b>
<b>Neutropenia (%)</b>	<b>58</b>	<b>45</b>
<b>Infection grade <math>\geq 3</math> (%)</b>	<b>18</b>	<b>10</b>
<b>Peripheral neuropathy (PN: all) (%)</b>	<b>67</b>	<b>43</b>
<b>Peripheral neuropathy (PN), grade <math>\geq 3</math> (%)</b>	<b>11</b>	<b>2</b>
<b>Lungtox grade <math>\geq 3</math></b>	<b>&lt;1</b>	<b>3</b>
<b>Neutropenia associated deaths (no G-CSF prophylaxis)</b>	<b>7</b>	<b>9</b>
<b>Lungtox associated deaths</b>	<b>11</b>	<b>13</b>

# HD18 for PET-2-negative patients

## Overall Survival



Pts. at risk

Time [months]	0	12	24	36	48	60
PET-, 8/6x eBEACOPP	504	476	438	363	298	207
PET-, 4x eBEACOPP	501	479	459	370	292	227

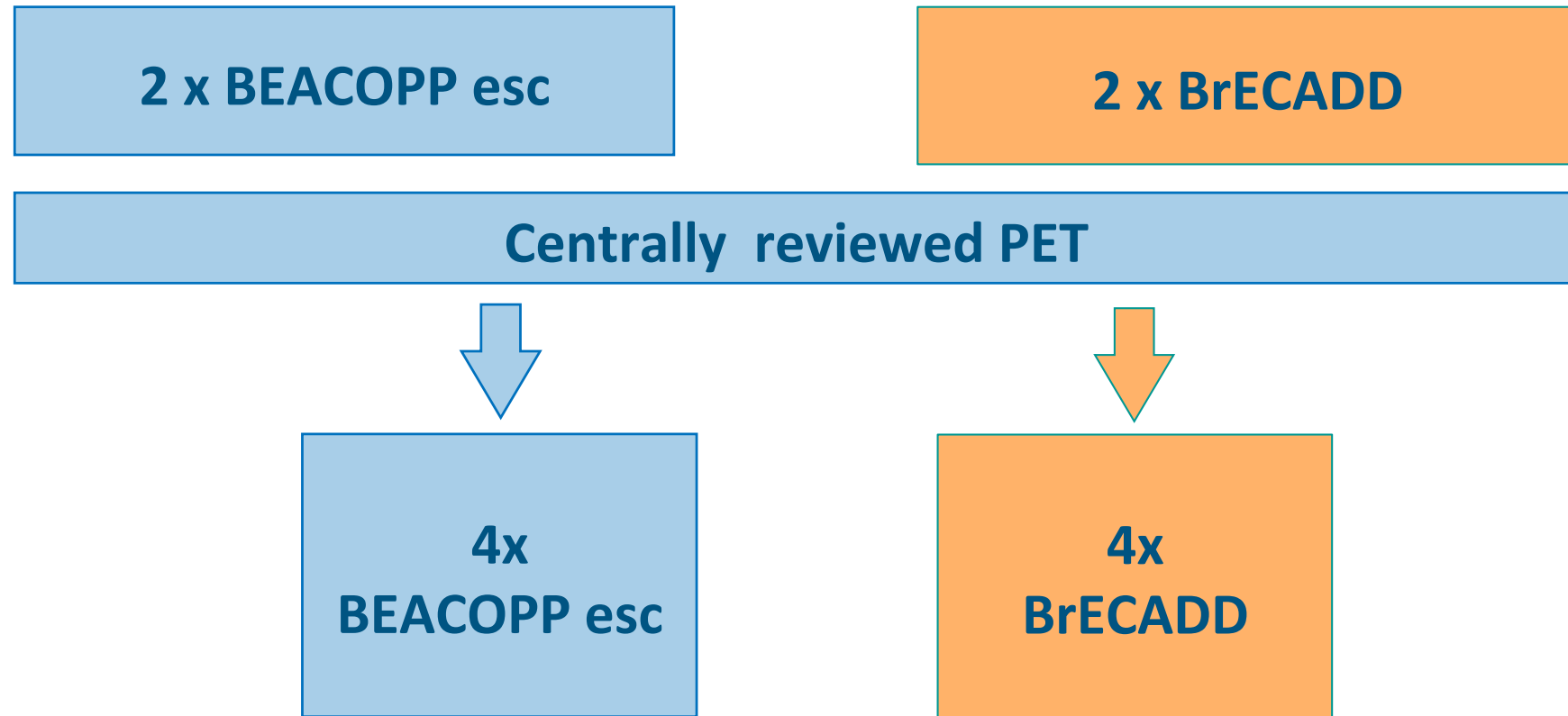
# Managing risk in advanced stage HL

## Key issues

- **Background**
- **Advanced Stages**
- **Perspectives**
- **Summary**

# The GHSQ perspective

## HD21: BV in advanced stage HL



End of therapy and residual nodes > 2.5 cm:

PET positiv:

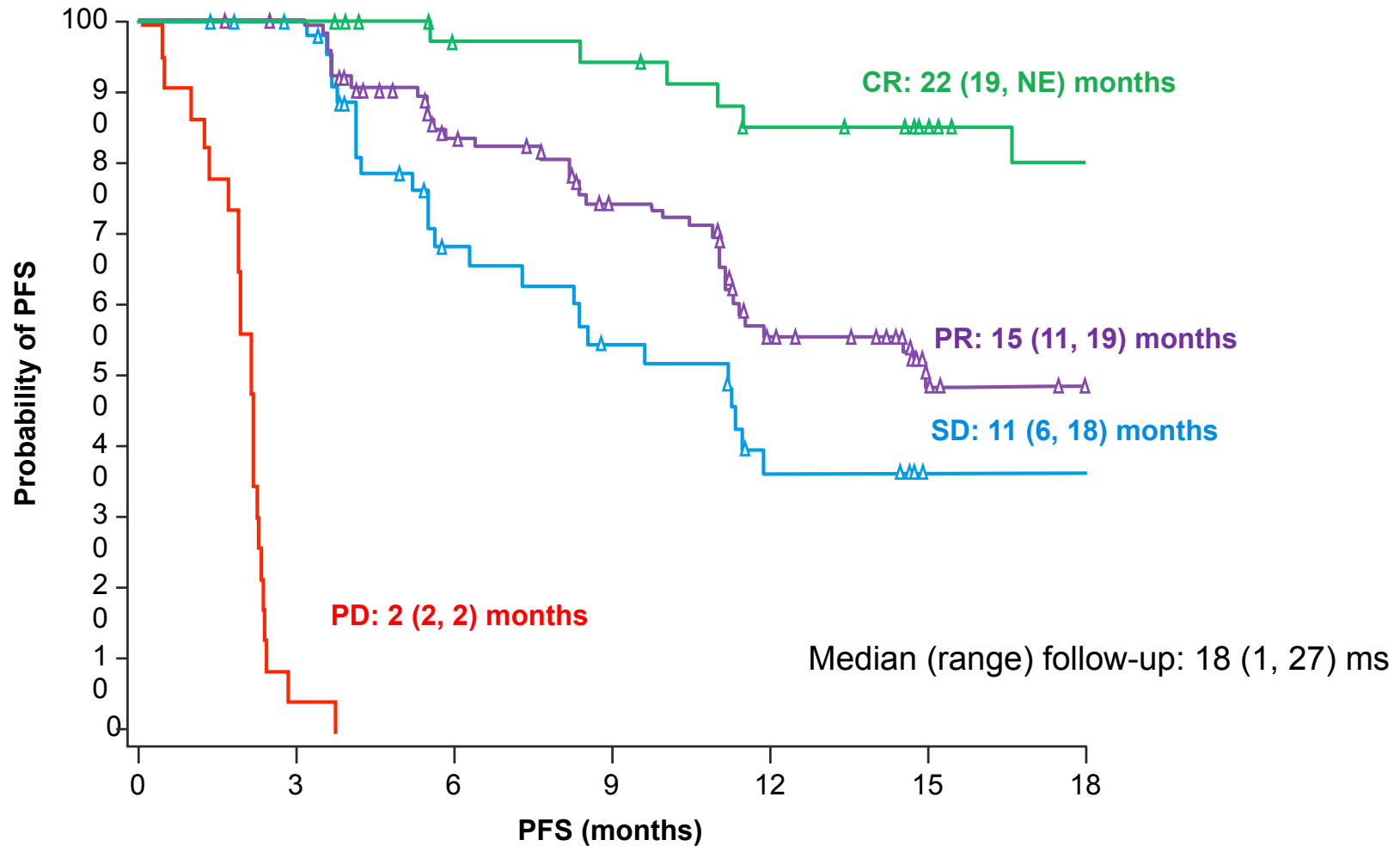
PET negative:

Rx

Follow up

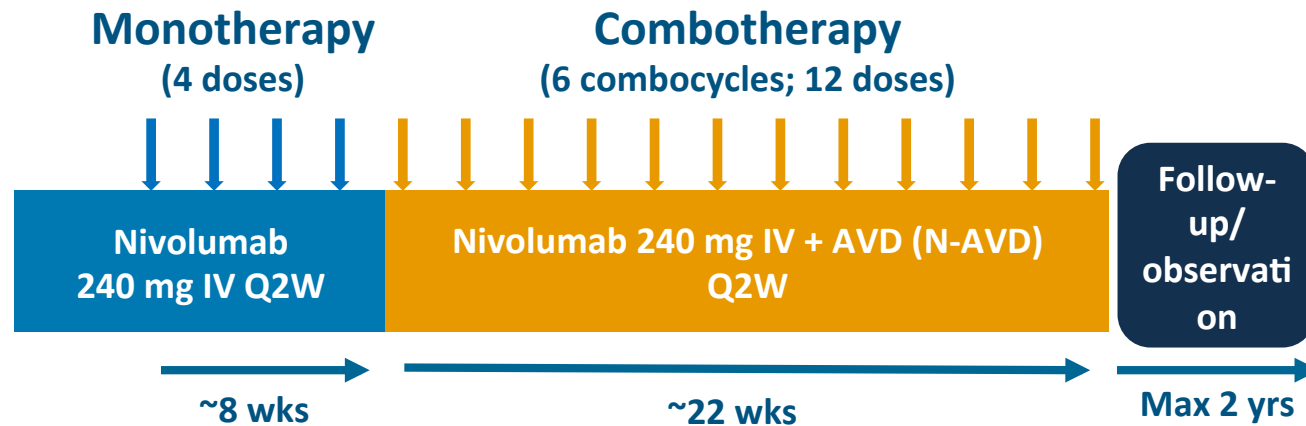
# Nivolumab for r/r cHL

PFS in CheckMate 205 trial



# CheckMate 205 Cohort D

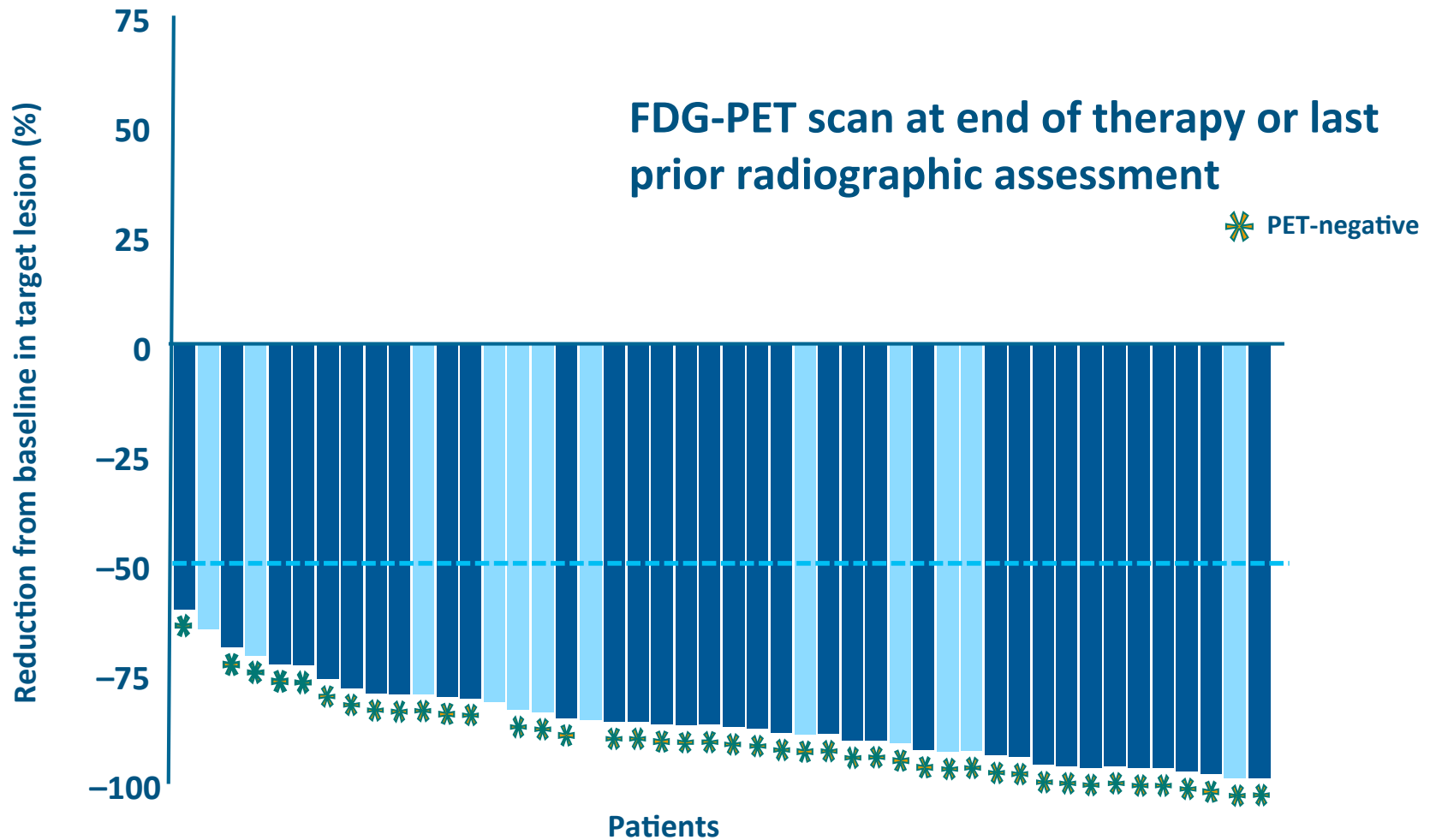
## Newly Diagnosed cHL



- 51 untreated advanced stage cHL pts (IIB, III, IV)
- Median follow-up 11.1 months (cut-off 31.8.17)
- Bleomycin excluded due to potential overlapping pulmonary toxicity
- Primary EP: G3-5 safety and tolerability
- Primary endpoint: safety and tolerability (G3–5 treatment-related AEs)

# Nivo-AVD in advanced stage cHL

## End of Combotherapy





# Managing risk in advanced stage HL

## Key issues

- **Background**
- **Advanced Stages**
- **Perspectives**
- **Summary**

# Advanced stage HL Summary

- **Advanced-stage HL became curable with multi-agent chemo**
- **B.esc gave 15-20% better PFS and 10-15% better OS than ABVD or variants; more hematotox and infertility**
- **B.esc not to be used in pts >40 ys and poor performance**
- **HD15: 6xB.esc: tumour control 89%, OS 95%**
- **HD18: only 4 cycles B.esc in PET- pts (3y FFTF 94.8%; OS 98.7%)**
- **ECHELON1 showed 4.9% better modified PFS for BV-AVD as compared with ABVD**
- **New trials evaluate targeted therapy including BV (HD21) and PD1 inhibitors**



# ISHL 11

**October 27 – 29, 2018**

[www.hodgkinsymposium.org](http://www.hodgkinsymposium.org)

**GHSG**   
[www.ghsq.org](http://www.ghsq.org)