German Hodgkin Study Group
Deutsche Hodgkin Studiengruppe

GHSG
www.ghsg.org

Problem Statement: What are the key issues in treating early stage HL

Andreas Engert, MD

Chairman, German Hodgkin Study Group
University Hospital of Cologne

Early stage Hodgkin Lymphoma
Key issues

- **Background**
- **Early stages**
- **Perspectives**
- **Summary**

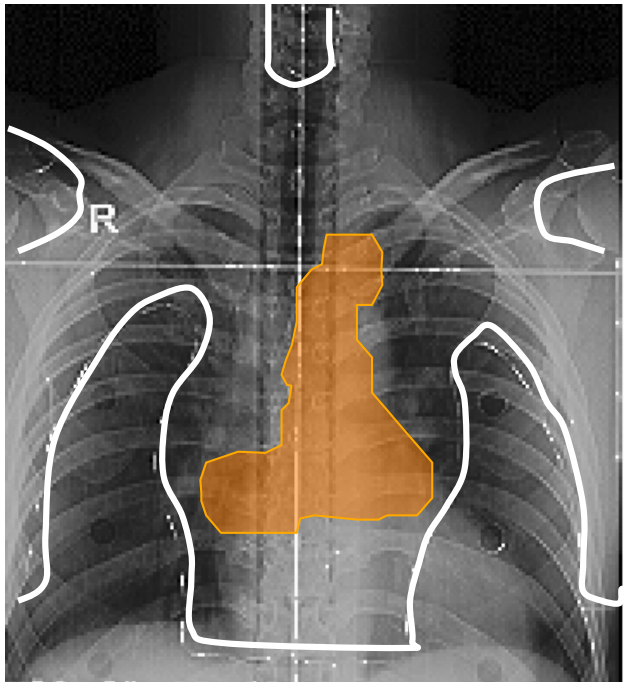
GHSG Risk Allocation for HL

GHSG
www.ghsg.org

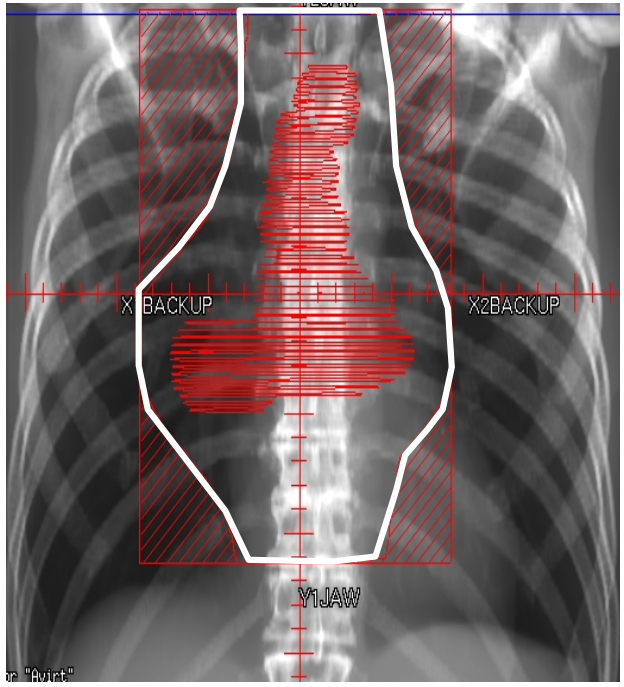
	Stage (Ann Arbor)			
Risk factors	**IA, IB, IIA**	**IIB**	**IIIA, IIIB**	**IVA, IVB**
None	**Early favorable**		**Advanced**	
≥ 3 LK- Areas	**Early unfavor-able**			
Elevated ESR				
Large Med Mass				
Extranodal disease				

Hodgkin Lymphoma
Evolution of Radiotherapy

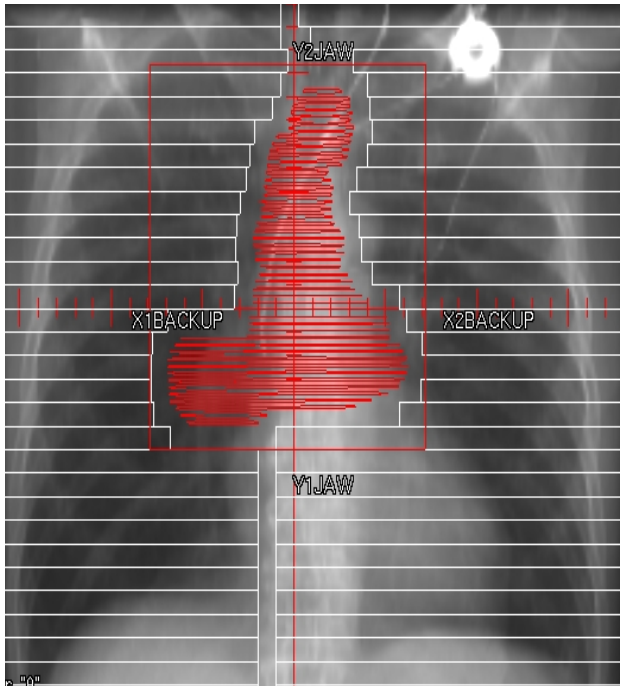
GHSG
www.ghsg.org



Mantle field



Involved Field

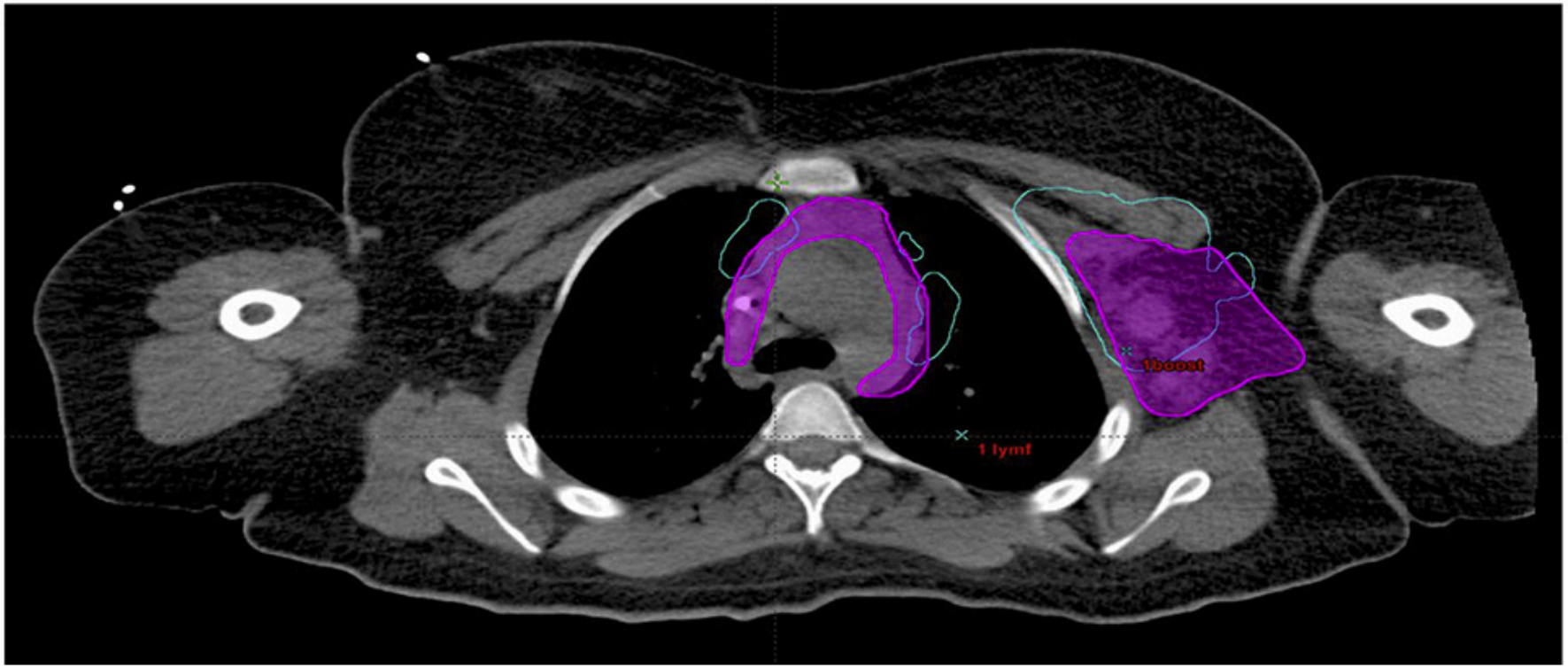


Involved Node

Courtesy R vd Maazen

IS-RT ILROG Guidelines
Target volume definition

E:

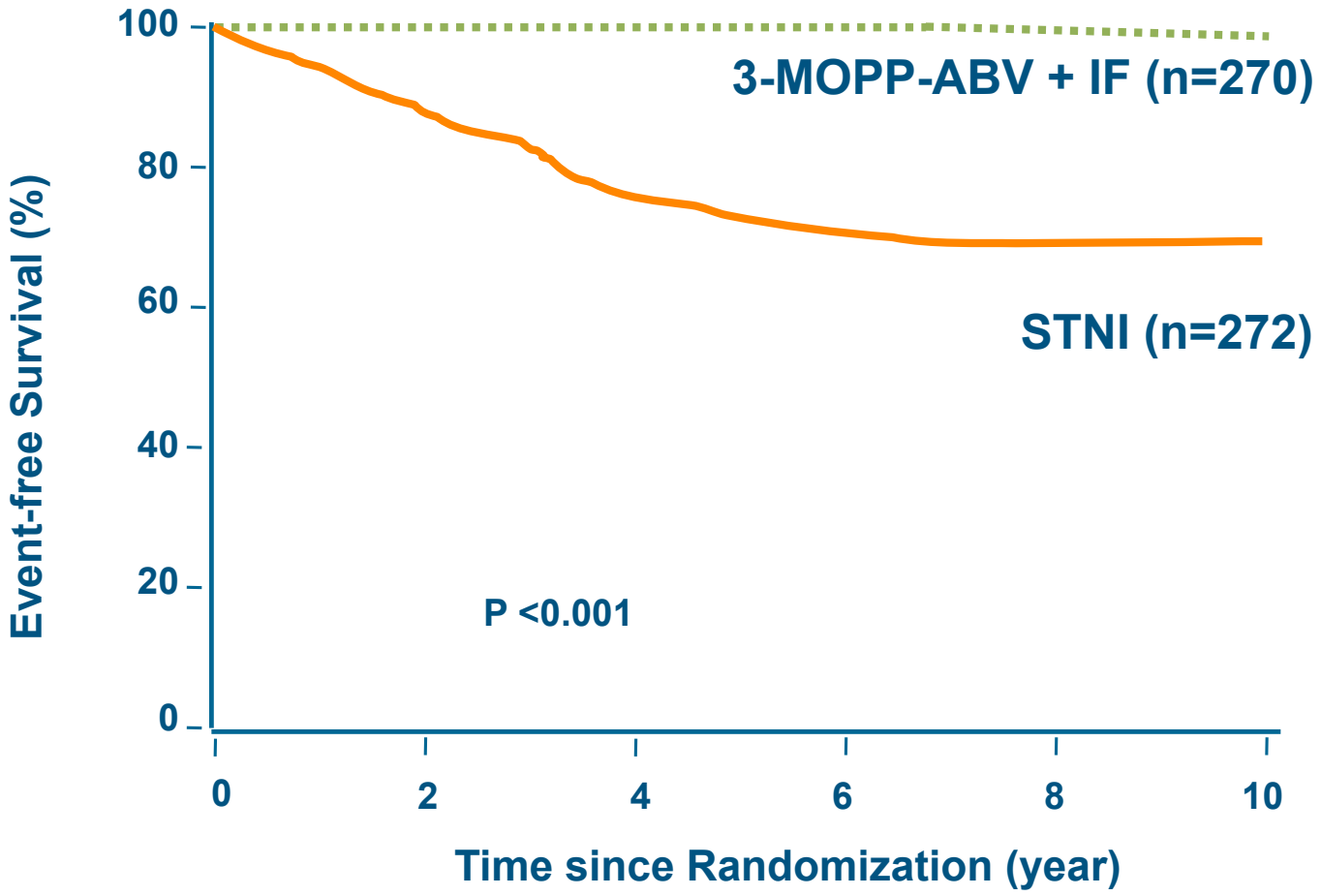


Fusion of GTV-CT-pre and GTV-PET-pre as well as response after chemo results in the CTV-post

Specht et al. Int J Rad Oncol Biol Phys 2014

EORTC H8F trial

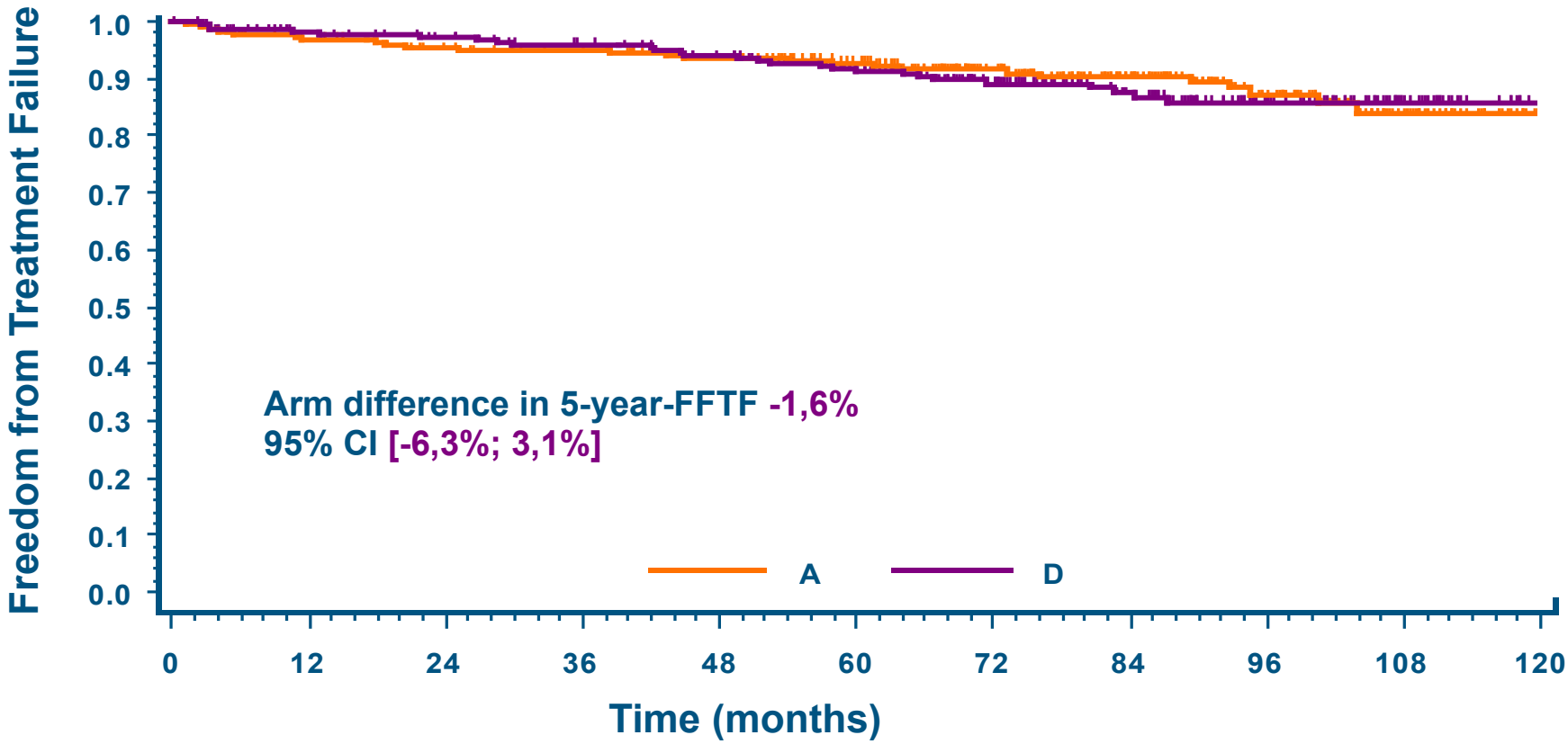
FFTF for pts with early favorable HL



Ferme et al NEJM 2007

GHSG HD10 Study

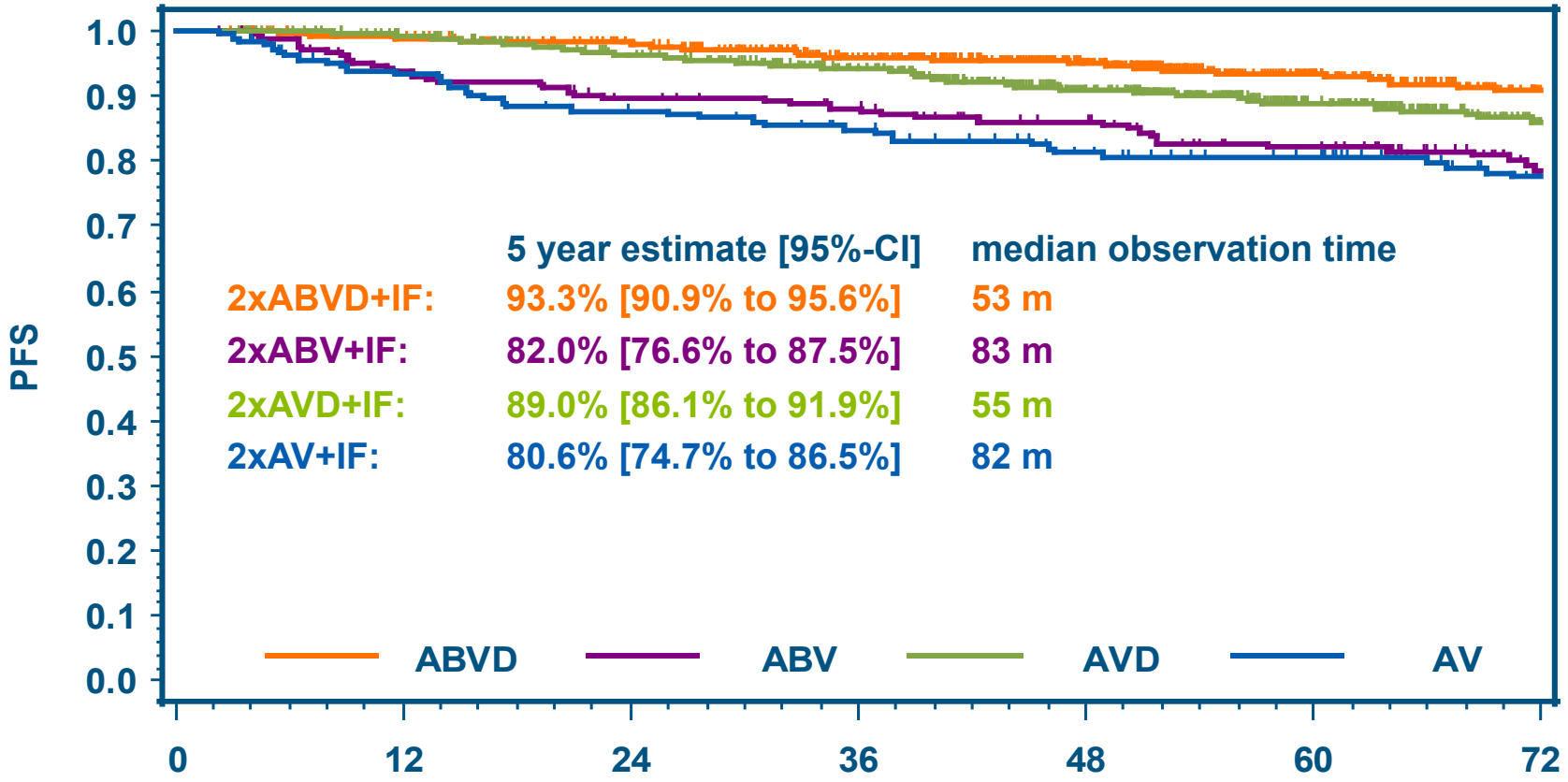
Weakest vs strongest arm (FFTF)



Engert et al NEJM 2010

HD13: Progression-free survival
All patients (ITT)

GHSG www.ghsg.org



Pts. at Risk							
ABVD	623	593	556	490	362	228	130
ABV	209	189	178	170	156	139	109
AVD	620	592	540	477	344	230	126
AV	186	166	153	144	128	118	93

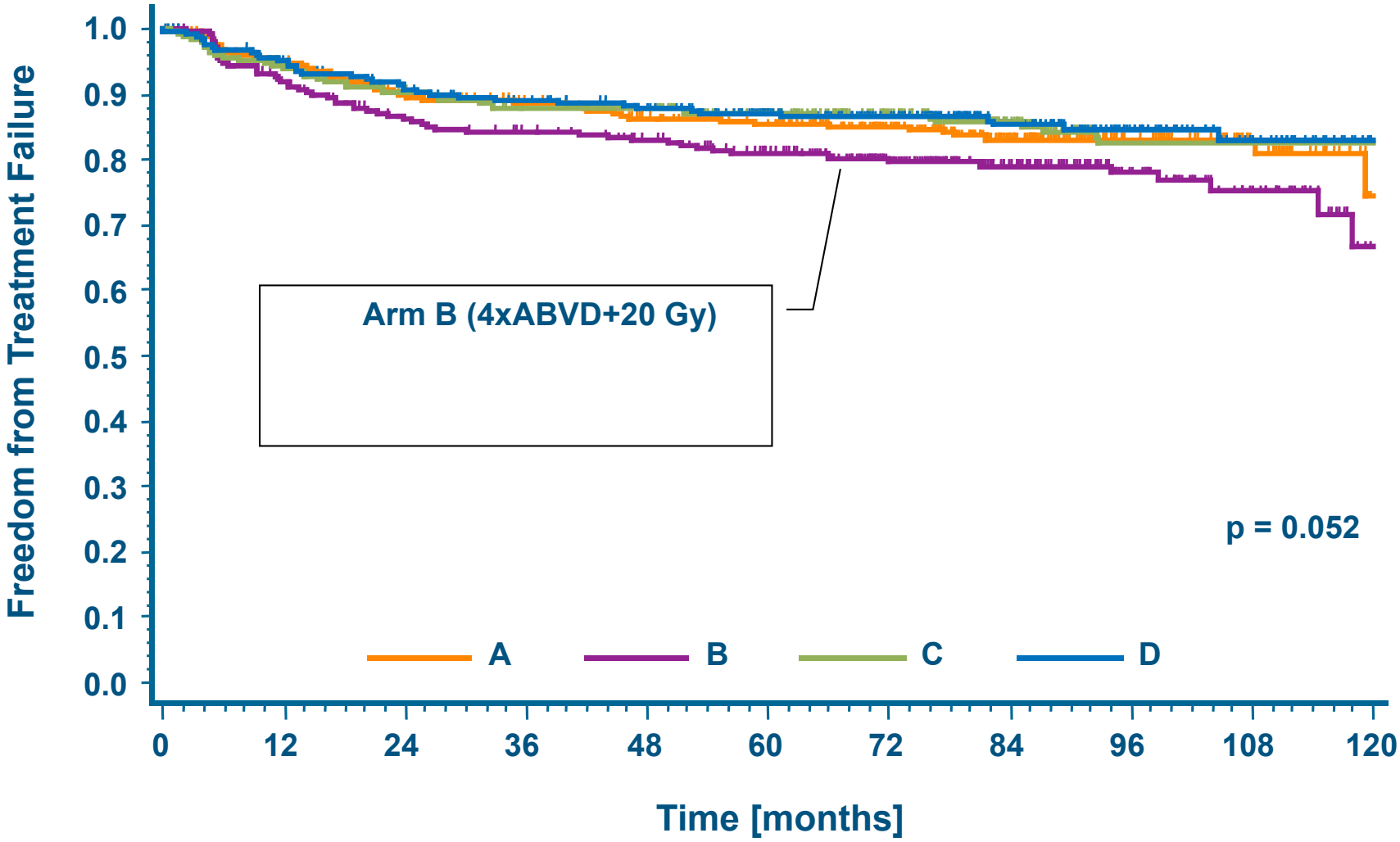
Behringer et al, Lancet 2014

GHSG Risk Allocation for HL

GHSG
www.ghsg.org

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

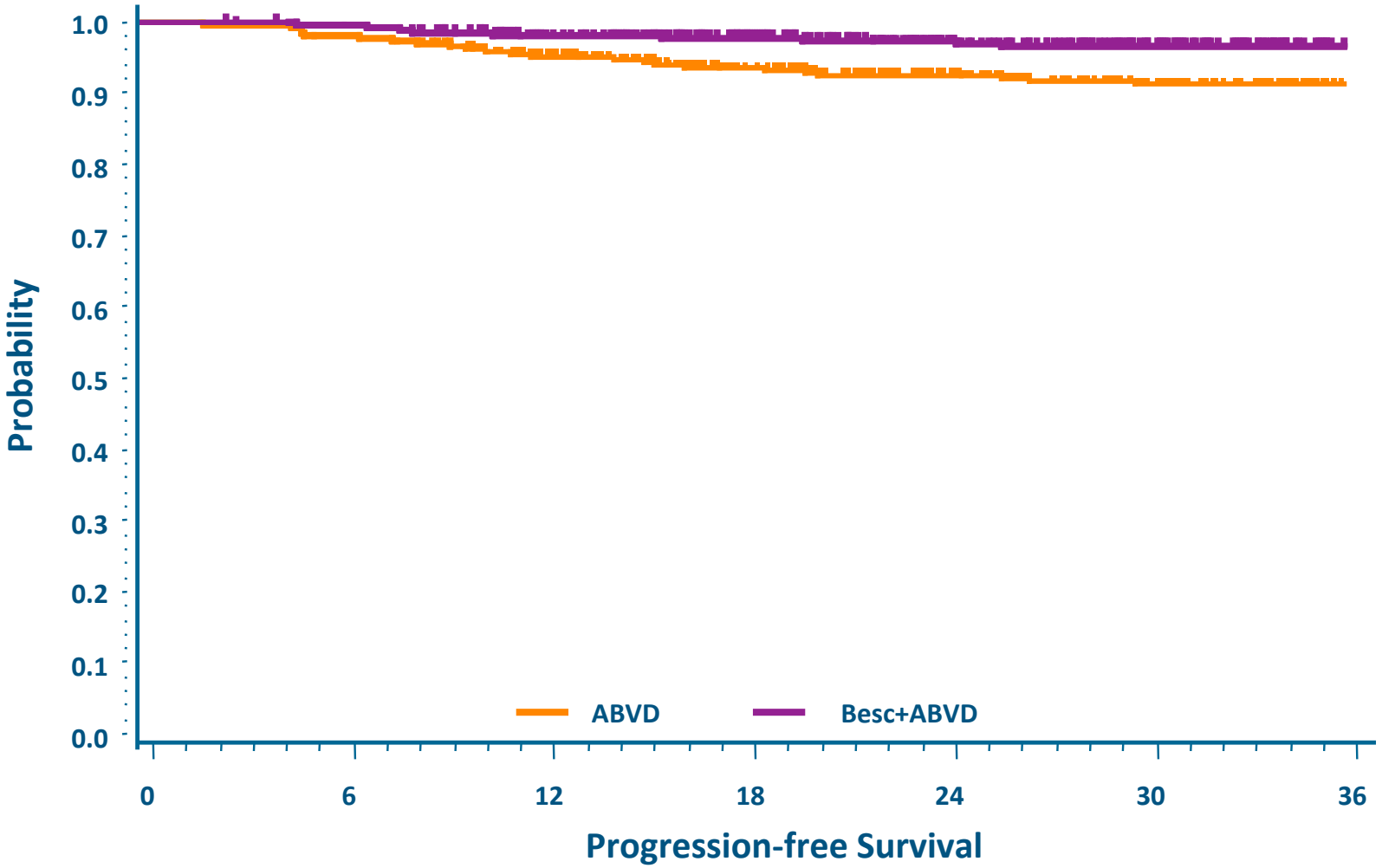
HD11 trial
FFTF – all 4 arms



Eich et al JCO 2010

HD14 Studie (GHSG)

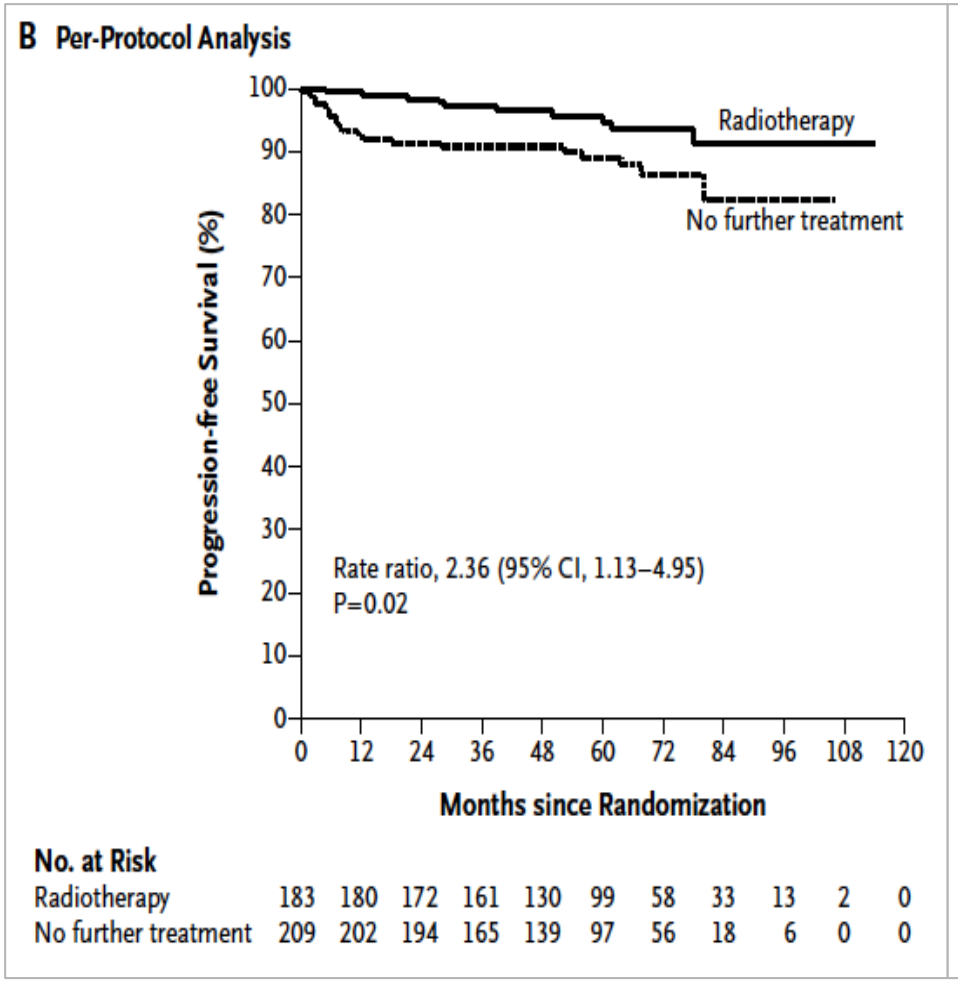
Early unfavorable HL (PFS)

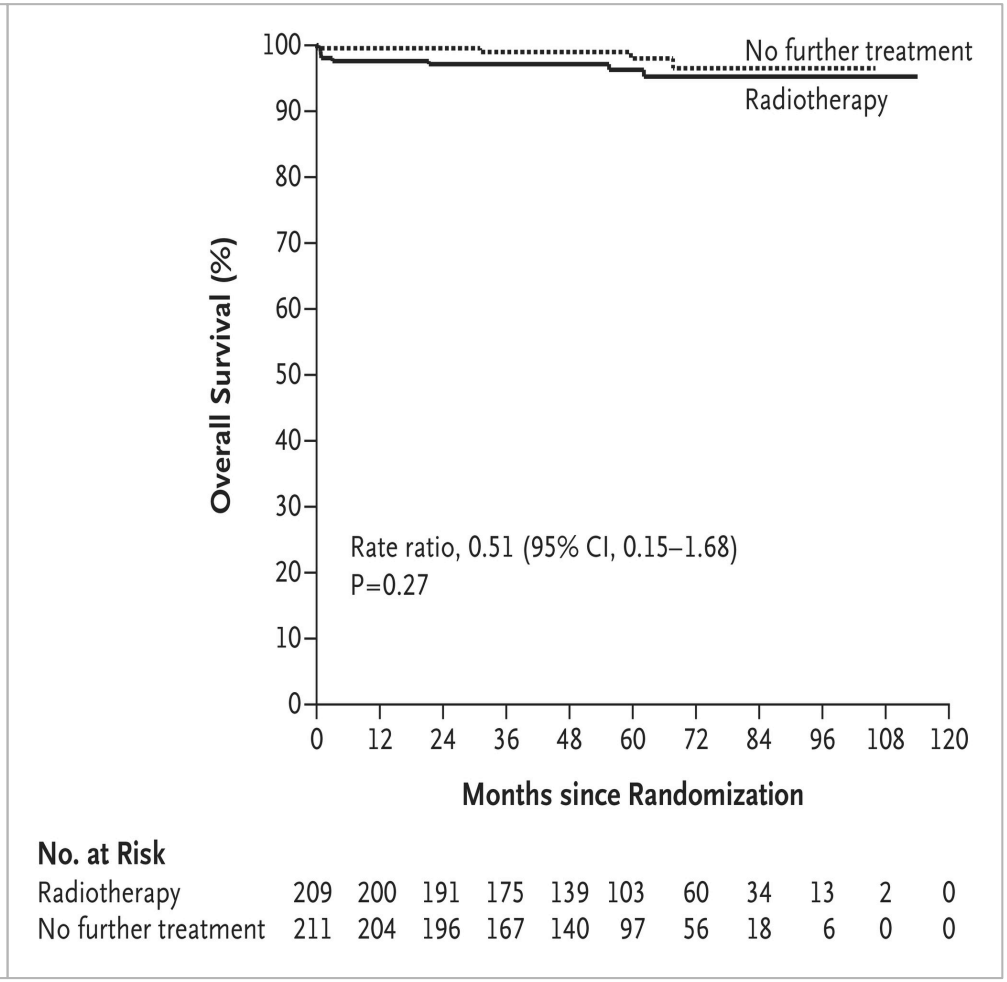


von Tresckow et al, JCO 2012

UK NCRI RAPID trial
Early stage HL

GHSG
www.ghsg.org

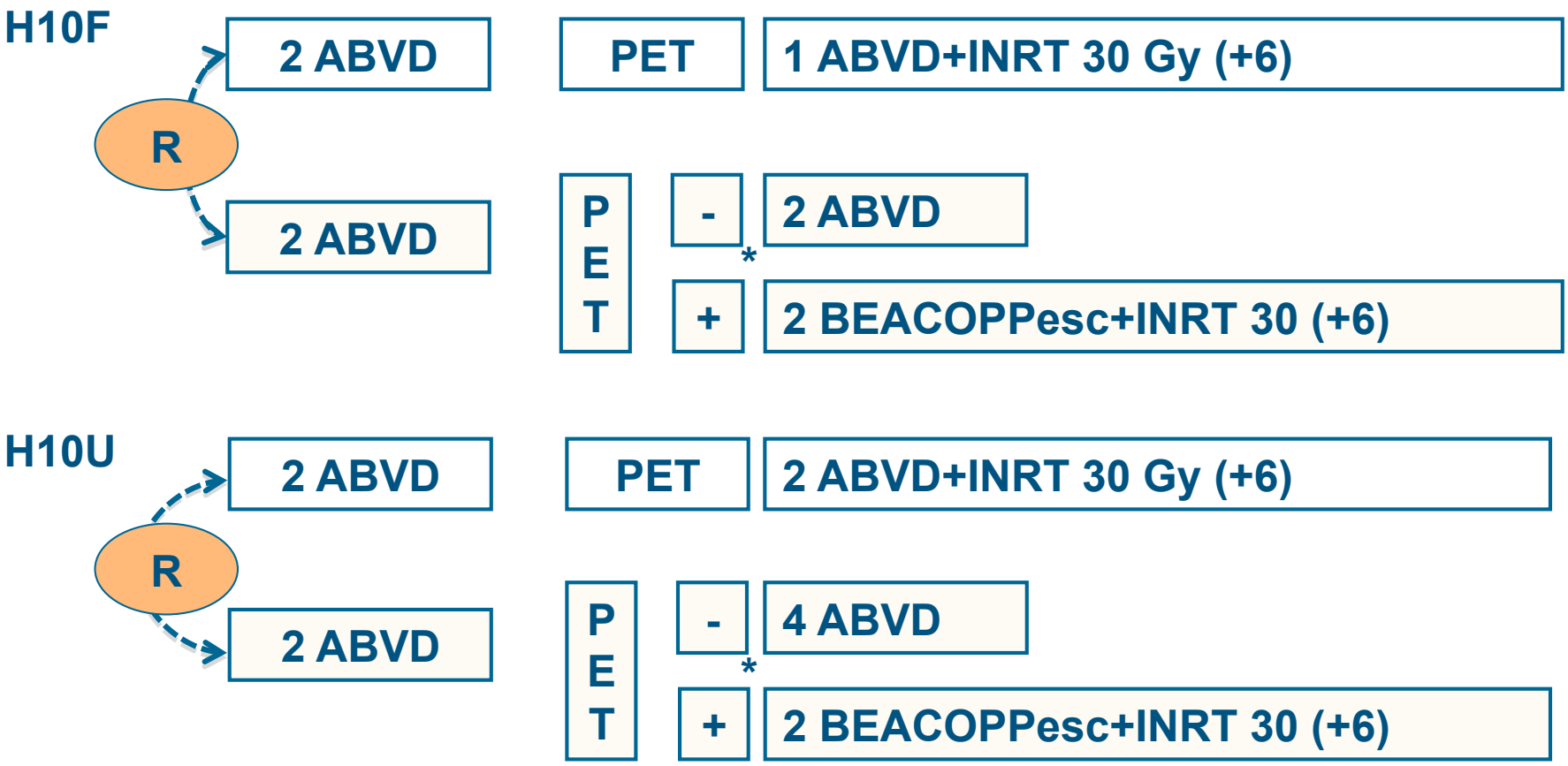




Radford J et al NEJM (2015) 372;17:1598-1605

EORTC/GELA/IIL H10 Study

Results of PET+ patients



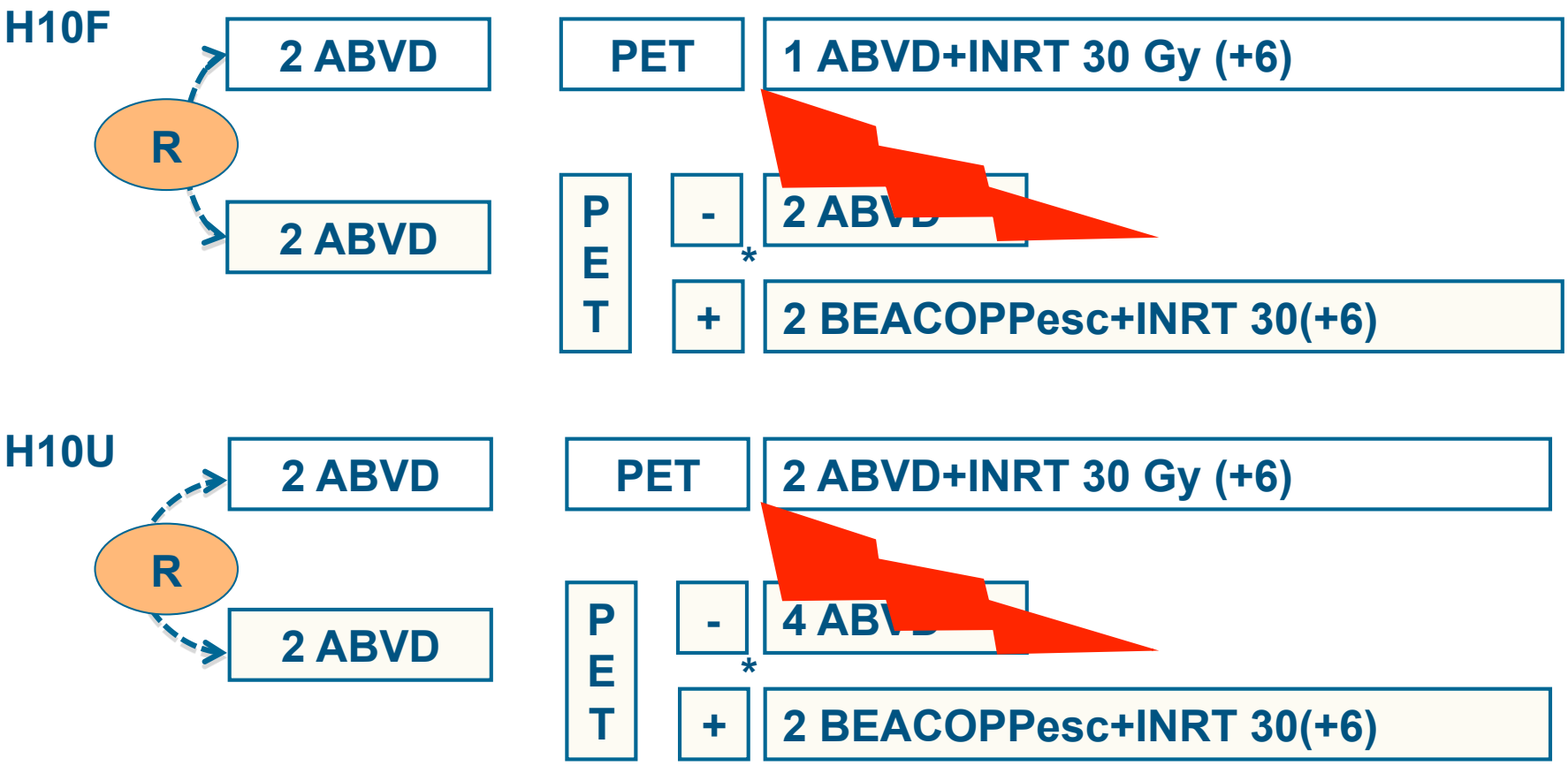
*PET-/+ according to protocol criteria

Hodgkin - CS I/II – untreated - 15-70 yrs – supradiaphragmatic - no NLPHL

EORTC/GELA/IIL H10 Study

For early favorable and unfavorable HL

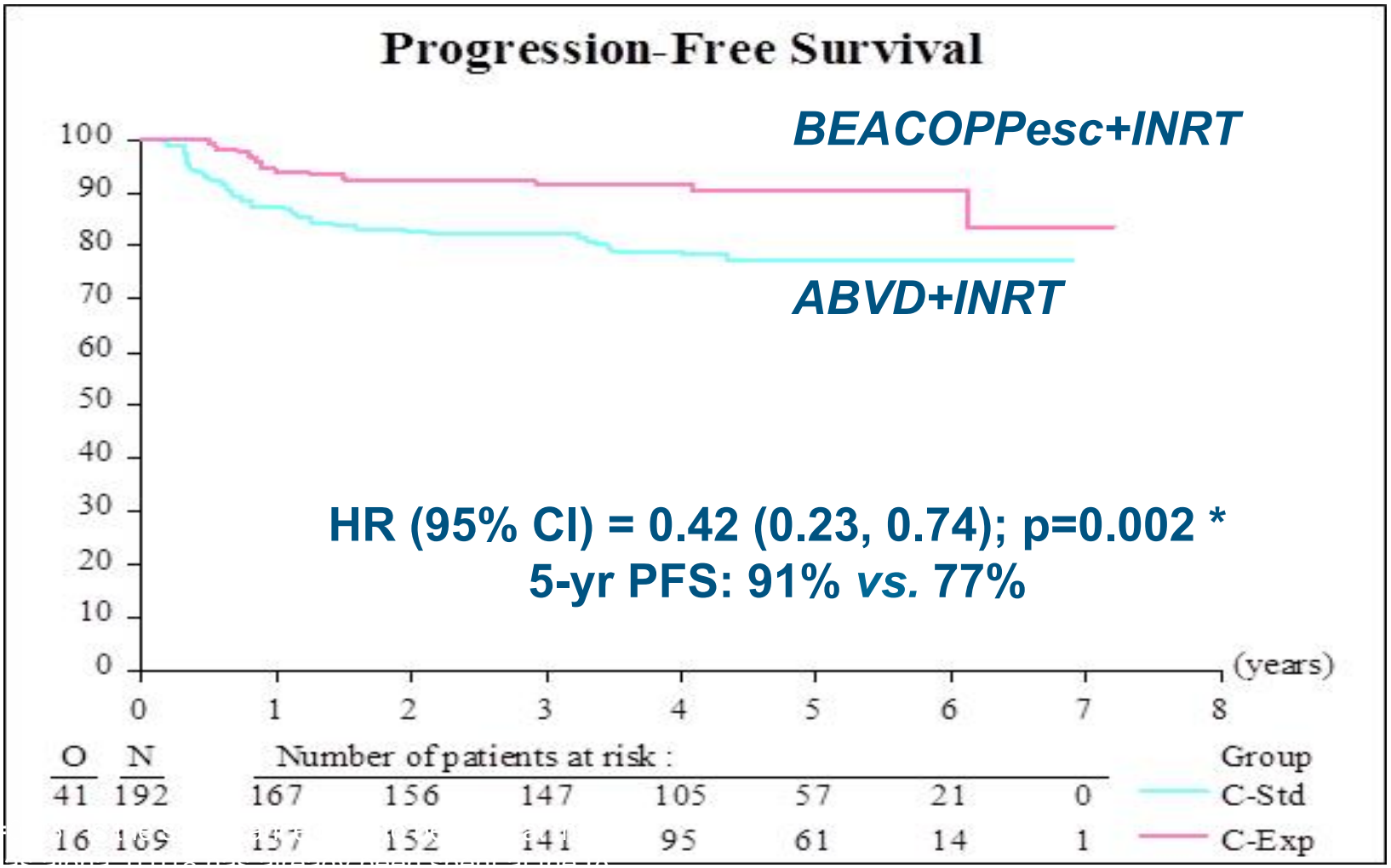
GHSG www.ghsg.org



*PET-/+ according to protocol criteria

Hodgkin - CS I/II – untreated - 15-70 yrs – supradiaphragmatic - no NLPHL

PET+ after 2xABVD: B.esc *vs.* ABVD
Progression-free survival (PFS)

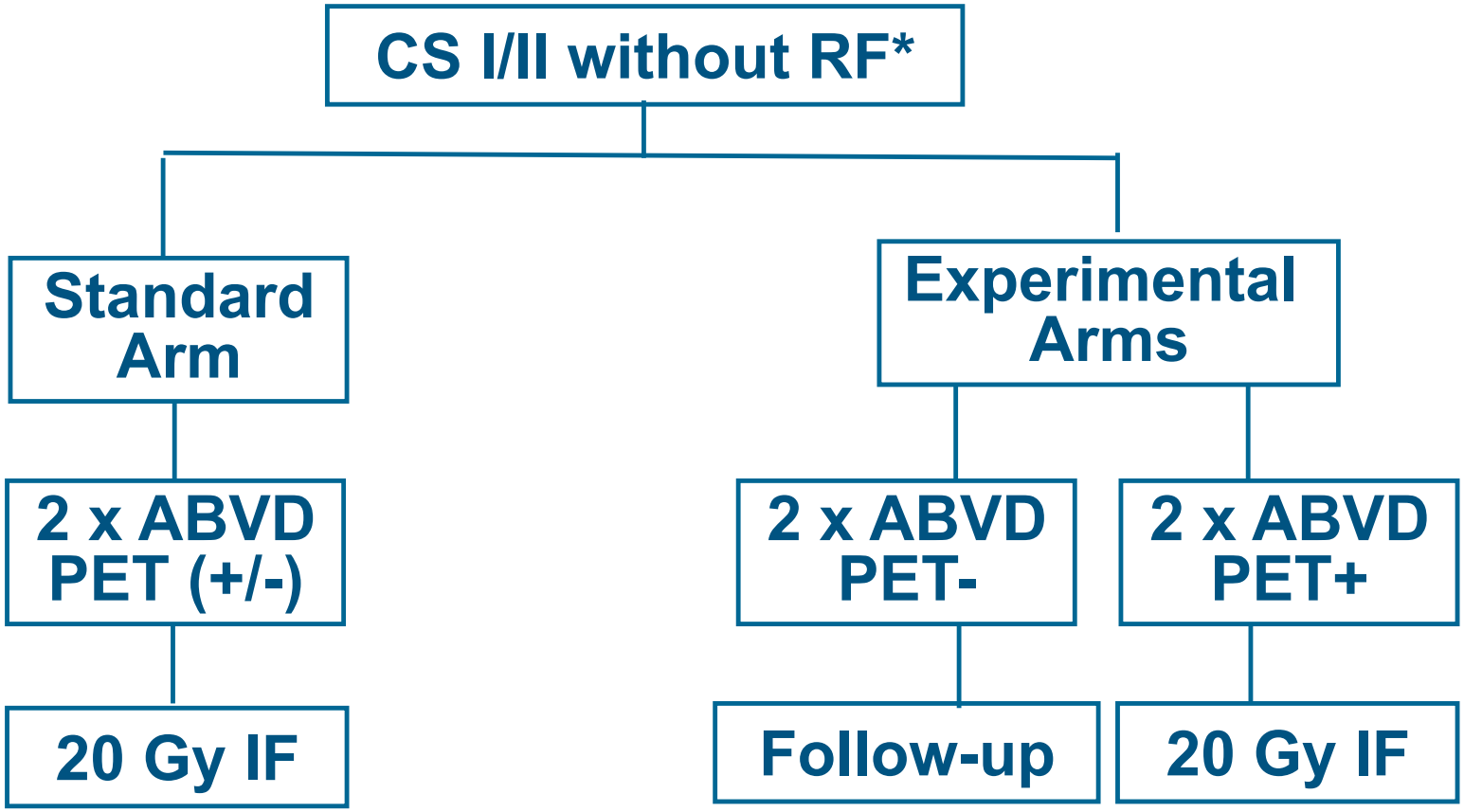


HR (95% CI) = 0.42 (0.23, 0.74); p=0.002 *
5-yr PFS: 91% *vs.* 77%

Raemaekers et at; ICML 2015

GHSG HD16 Trial

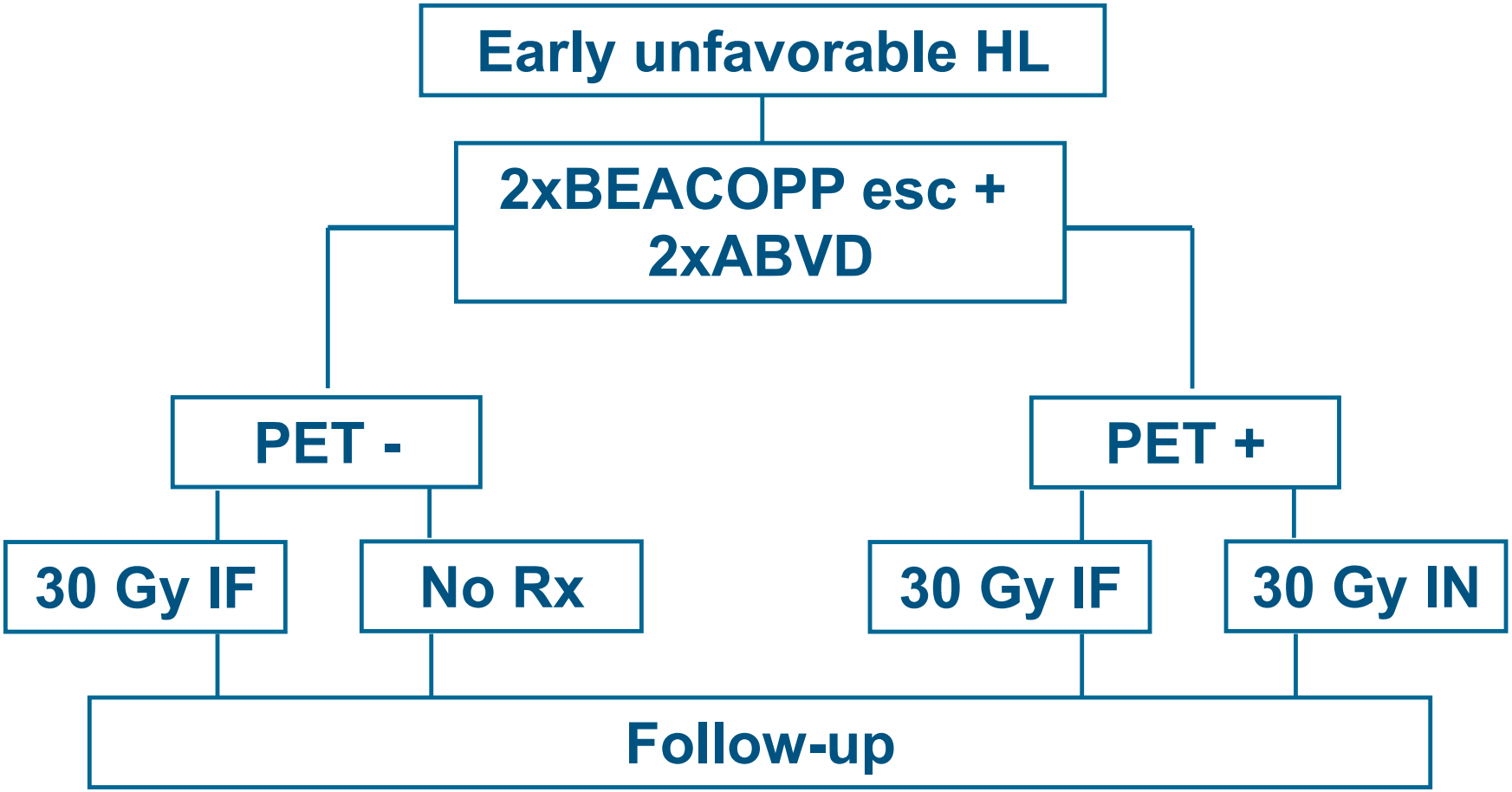
Early favorable HL



*a) large mediastinal mass; b) extranodal disease; c) high ERS; d) 3 or more areas

Ongoing GHSG trial
for early unfavorable (HD17)

GHSG
www.ghsg.org



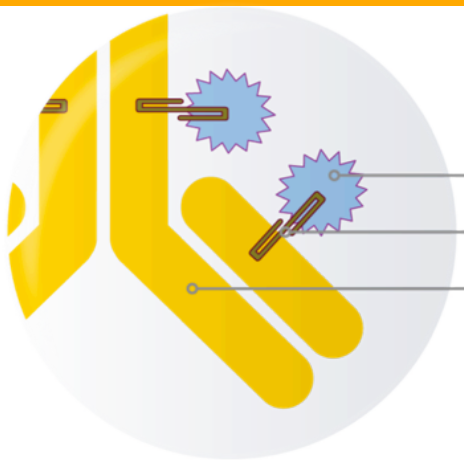
Early stage Hodgkin Lymphoma
Key issues

GHSG
www.ghsg.org

- **Background**
- **Early stages**
- **Perspectives**
- **Summary**

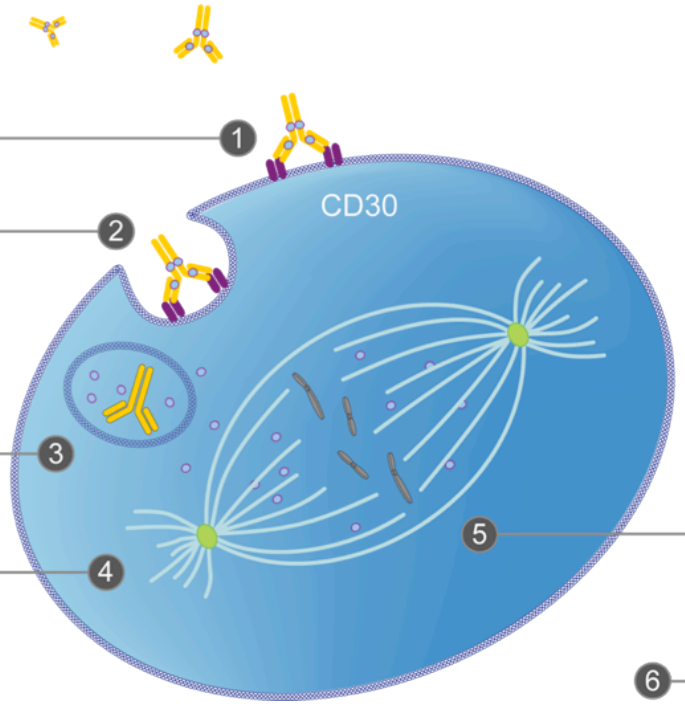
Brentuximab Vedotin
Mechanism of action

GHSG
www.ghsg.org



Brentuximab vedotin ADC

Monomethyl auristatin E (MMAE), potent antitubulin agent
Protease-cleavable linker
Anti-CD30 monoclonal antibody



ADC binds to CD30 — 1

ADC-CD30 complex traffics to lysosome — 2

MMAE is released — 3

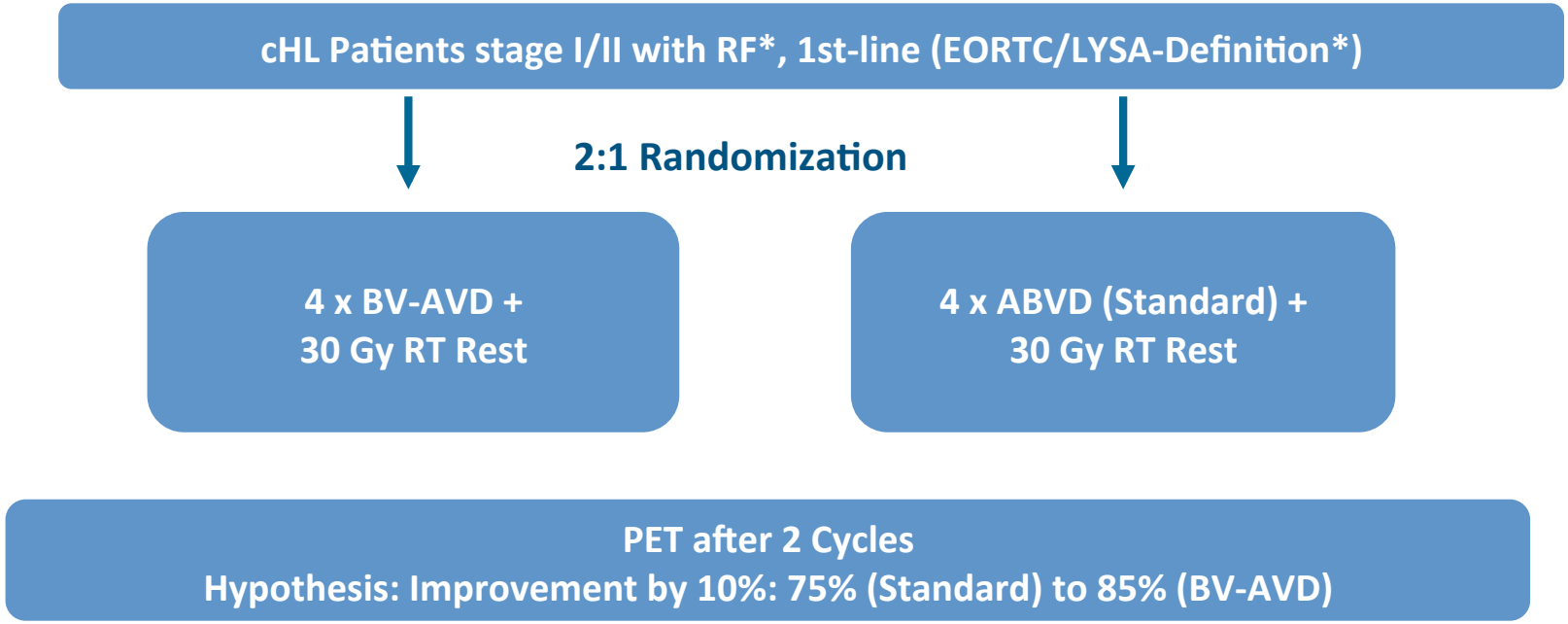
MMAE disrupts Microtubule network — 4

G2/M cell cycle arrest — 5

6 — **Apoptosis**

Hodgkin Lymphoma ASH 2017

Design BREACH Phase II study



* At least 1 RF: age ≥50J, mediastinal tumor, ≥4 LN regions ESR ≥50mm/h or ≥30 mm/h with B-symptoms

Fornecker et al, ASH 2017: A736

Hodgkin Lymphoma
Summary BREACH Phase II Study

GHSG
www.ghsg.org

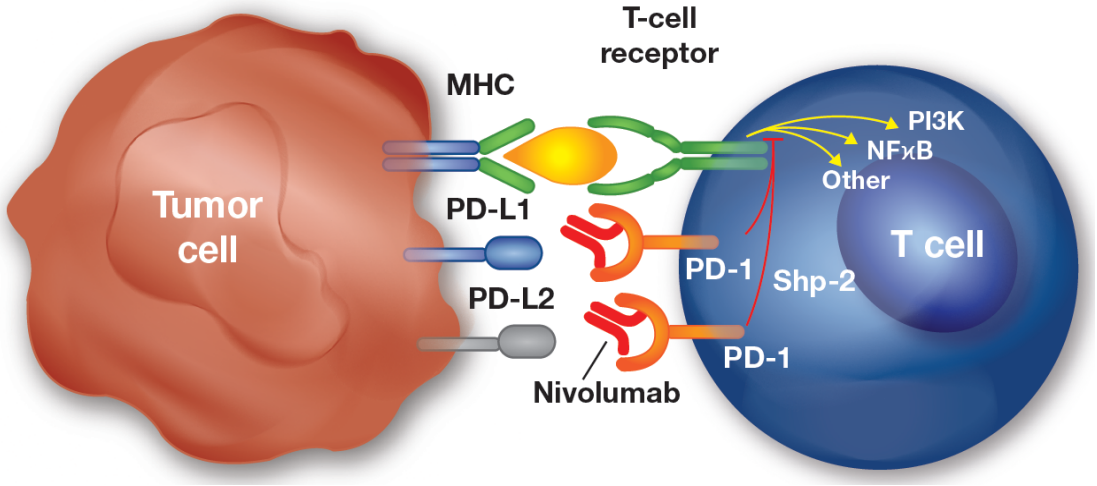
- **After 2 cycles, 82.3% in the BV-AVD were PET- (95% CI 75.3-88.0); Standardarm 75.4% (95% CI 64.3-84.5)**
- **Primary endpoint reached**
- **More tox in the BV-AVD arm, higher rate of grade 3-4 Aes and SAEs within first 2 cycles with BV-AVD**

Fornecker et al, ASH 2017: A736

PD1 Inhibition in Classical HL
Mechanism of action

GHSG
www.ghsg.org

- **Patients with cHL show high frequency of 9p24.1 alterations and overexpression of PD-L1 and PD-L2[1]**
- **Nivo and Pembro are fully human or humanized moabs targeting the programmed death-1 (PD-1) receptor immune checkpoint pathway**



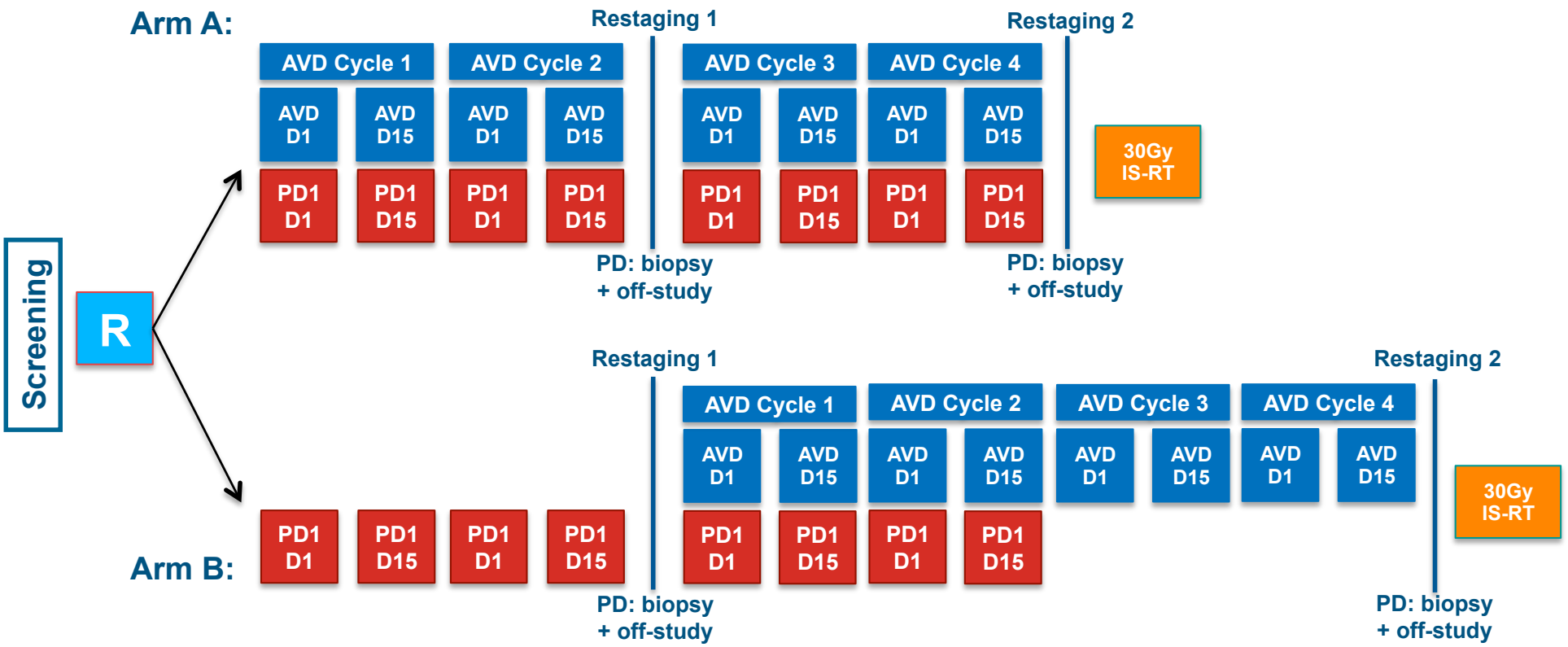
- **PD1 inhibitors block signaling through the PD-1 receptor**

Roemer MGM et al. *J Clin Oncol* 2016;34:260–7

HD20 Pilot

Randomized trial in early unfavorable HL

GHSG
www.ghsg.org



AVD: Adriamycin, Vinblastin, Dacarbazine; PD1: anti-PD1-antibody

Early stage Hodgkin Lymphoma
Key issues

GHSG
www.ghsg.org

- **Background**
- **Early stages**
- **Perspectives**
- **Summary**

Early stage HL
Summary

- **HL one of the best curable cancers; long-term side effects**
- **In early favorable, 2xABVD+20Gy IFRT; more chemo not better**
- **In early unfavorable, 2+2+IFRT or 4xABVD+IFRT; 6x chemo not better (H8U)**
- **CMT standard of care in early stage HL (OS better!)**
- **Rapid and H10 gave conflicting results; PET+ pts in H10 benefit from dose escalation with Besc.**
- **IFRT only in stage IA NLPHL**
- **Need to develop less toxic regimen; current trials evaluate targeted therapy including BV and PD1 inhibitors**


GÜRZENICH, COLOGNE
SAVE THE DATE
ISHL 11
October 27–29, 2018
www.hodgkinsymposium.org
GHSG
www.ghsg.org