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Hodgkin Lymphom

Update DGIM 2020

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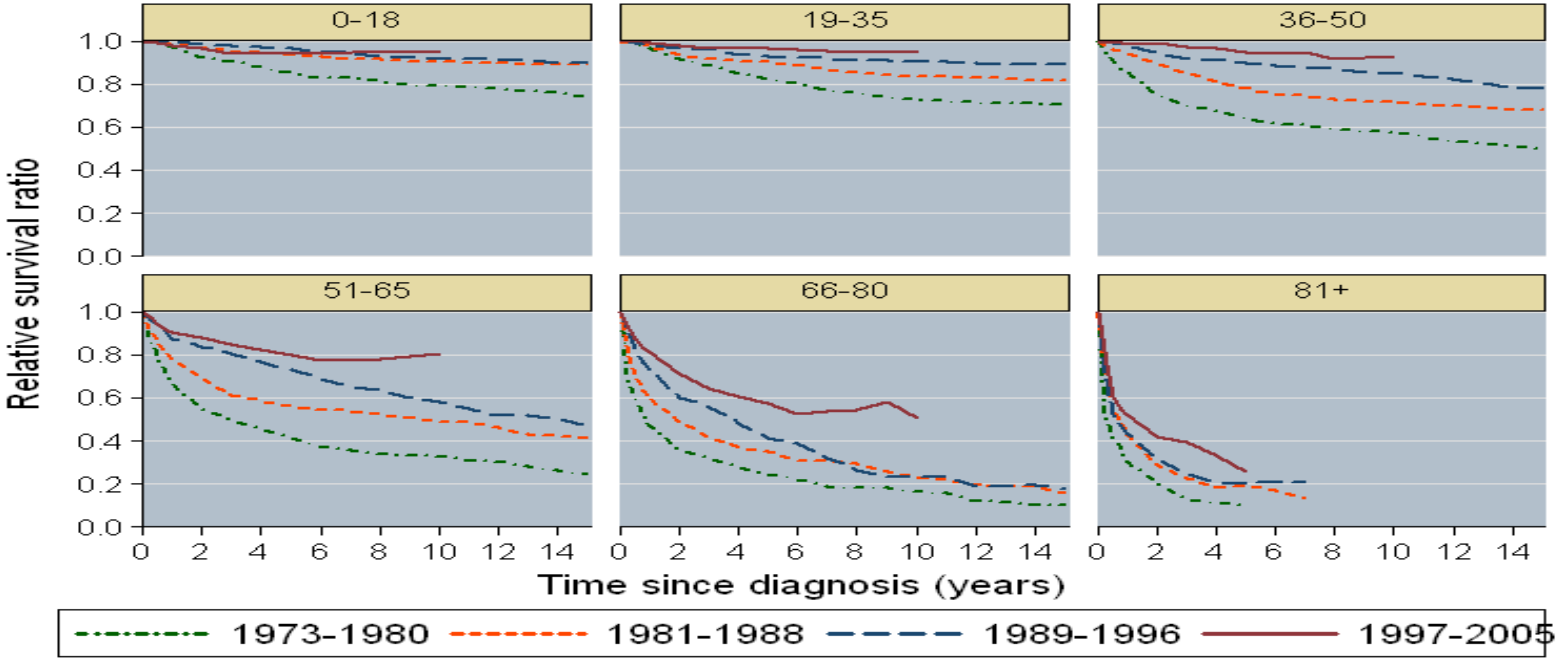
Disclosures Prof. A. Engert

Consultant or advisory role:	**BMS, Takeda, ADC Therapeutics**
Honoraria:	**BMS, Takeda, Novartis, MSD, Hexal, Chugai**
Research funding:	**BMS, Takeda, Affimed**

Hodgkin Lymphom
Kumulatives Relatives Überleben (Schweden)



Sjöberg et al, Blood 2012

Hodgkin Lymphom
Spätschäden nach Therapie

• 2nd NPL	AML NHL Solide Tumore
• Organschäden	Lunge Herz Schilddrüse
• Andere	Fertilität OPSI Fatigue

NPL, neoplasias; AML, acute myeloid leukemia; NHL, non-Hodgkin lymphoma; OPSI, overwhelming post-splenectomy infection

- **Höheres Risiko bei aggressiver Therapie**
- **Z.b. bei Behandlung mit BEACOPPesc**
- **Risiko bei autologer Transplantation**
- **Höheres Risiko bei allogener Transplantation**

NPL, neoplasias; AML, acute myeloid leukemia; NHL, non-Hodgkin lymphoma; OPSI, overwhelming post-splenectomy infection

Hodgkin Lymphom
Ein Update

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- **Frühe und mittlere Stadien**
- **Fortgeschrittene Stadien**
- **Rezidive, neue Ansätze**
- **Zusammenfassung**

GHSG Risk Allocation for HL

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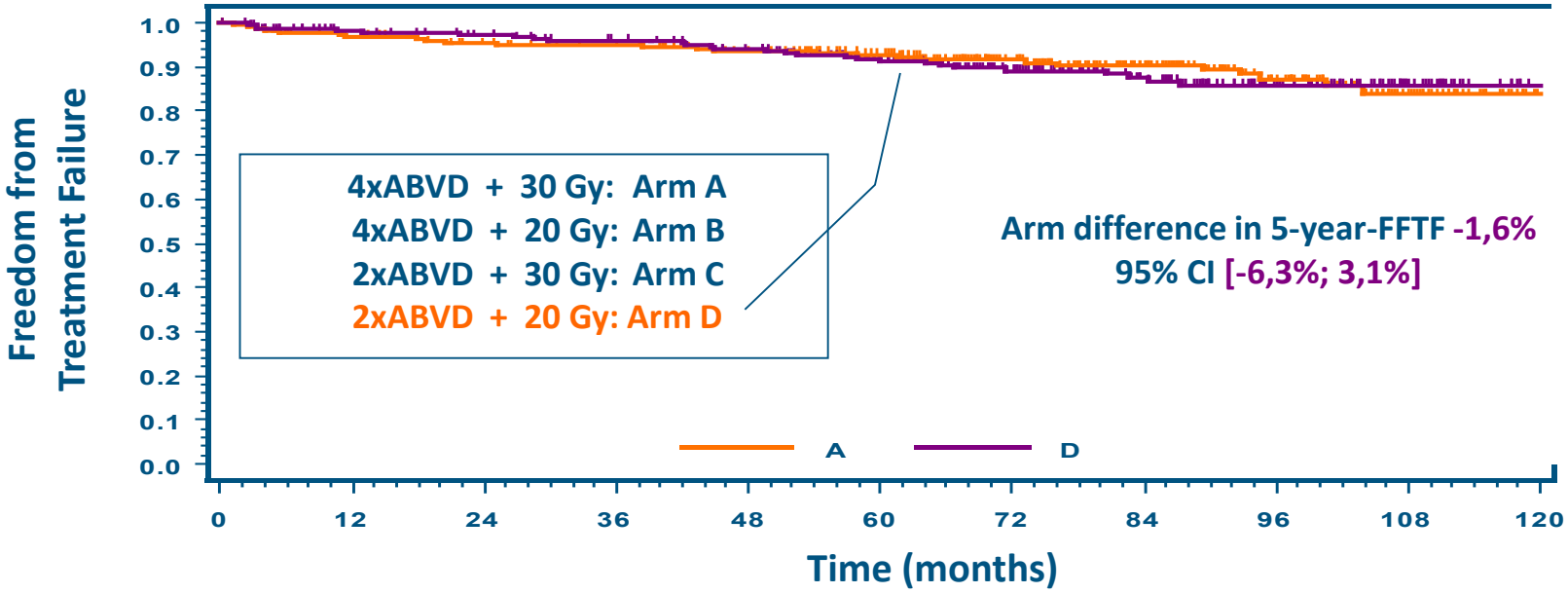
	Stage (Ann Arbor)			
Risk factors	**IA, IB, IIA**	**IIB**	**IIIA, IIIB**	**IVA, IVB**
None	**Early favorable**		**Advanced**	
≥ 3 LK- Areas	**Early unfavorable**			
Elevated ESR				
Large Med Mass				
Extranodal disease				

GHSG HD10 Studie: Early favorable HL
Weakest vs strongest arm (FFTF)



A indicates weakest arm; D, strongest arm.

Engert A, et al. N Engl J Med. 2010;363:640-652.

HD16: PFS

Behandlung mit 2xABVD+20Gy RT: DS1-3 vs DS4

PFS rate

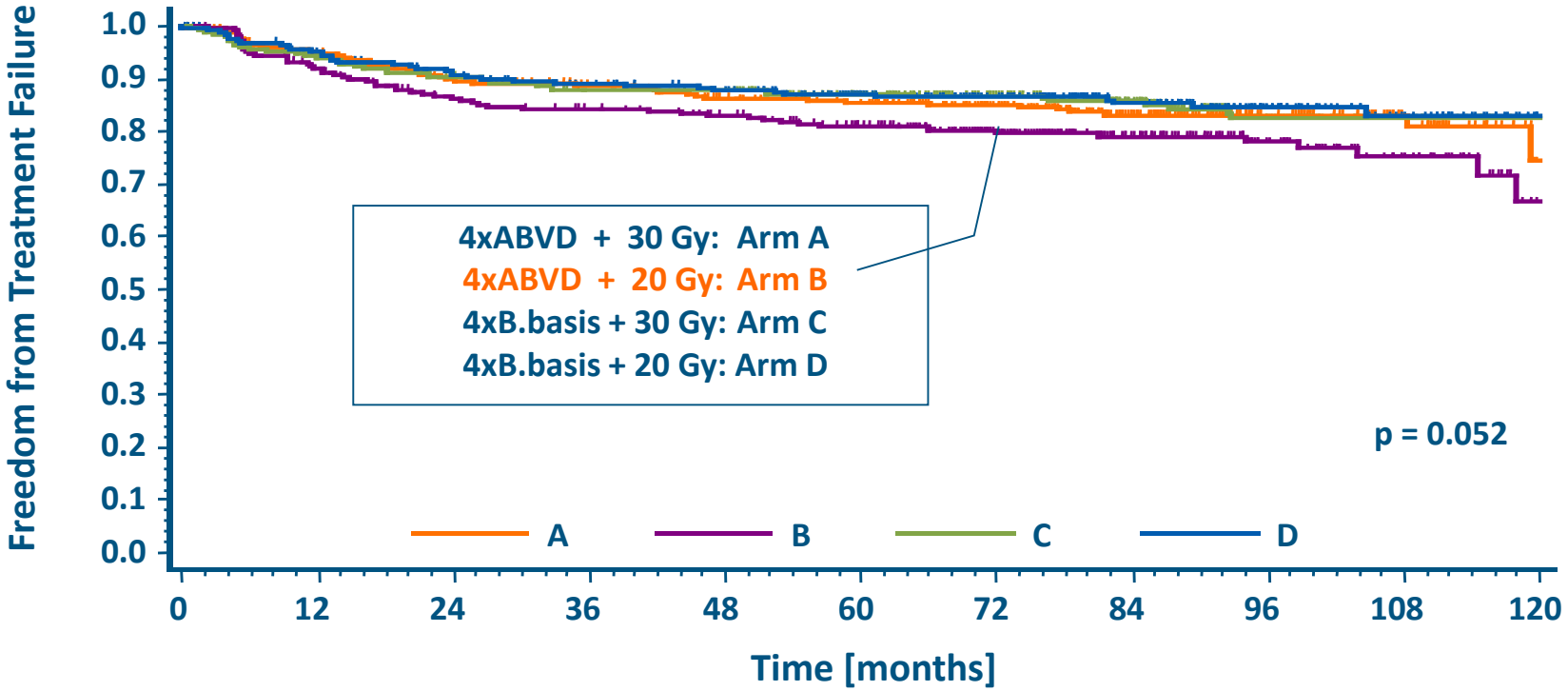
	5-year estimate [95% CI]
PET-negative (DS 1-3):	93.1% [90.7% to 95.5%]
PET-positive (DS 4):	80.9% [72.2% to 88.7%]
Difference:	-12.2% [-21.3% to -3.1%]
Hazard ratio [95% CI]*	2.94 [1.63 to 5.31], p=0.0004

Median observation time 46 months

*Cox model adjusted for stratification factors

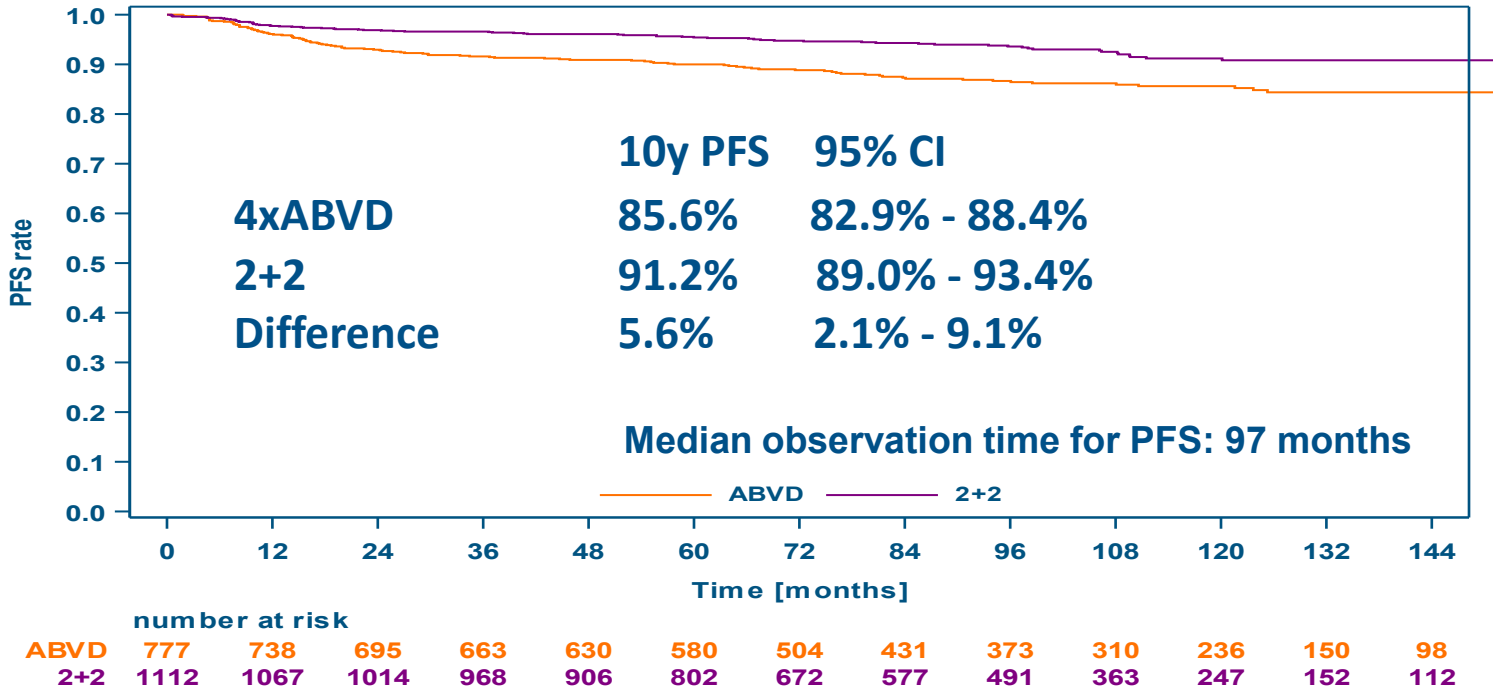
age, sex, B symptoms, localization of disease (supra- vs. infradiaphragmatic), albumin level (<4 g/dl vs. ≥4 g/dl) and bulky disease

HD11 Studie
Early favorable (FFTF – alle 4 Arme)



Eich HT et al, J Clin Oncol. 2010

Langzeit Follow-up der HD14 Studie
Progression-freies Überleben (ITT)



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HD15 Studie (fortgeschrittene Stadien)
Freedom from Treatment Failure (FFTF)

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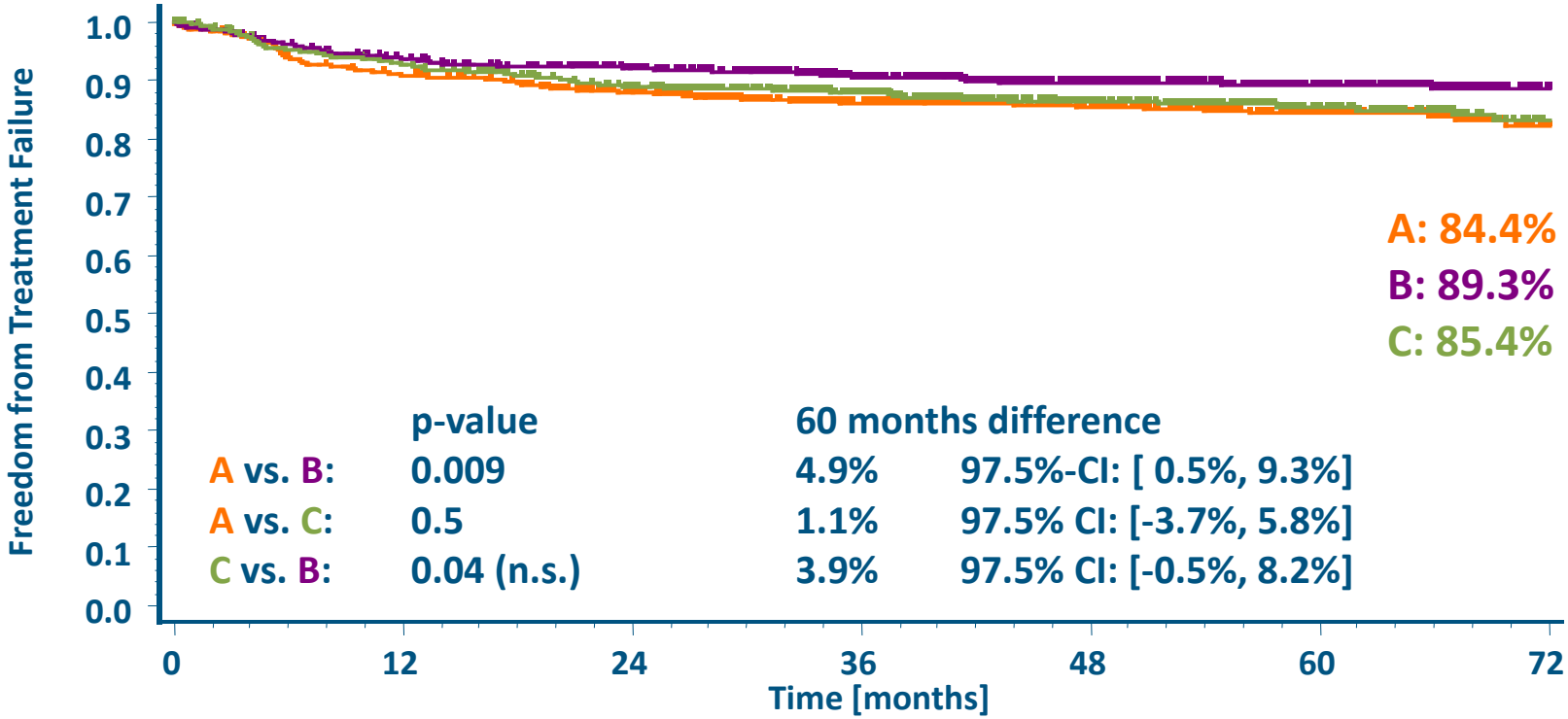

Engert A et al, Lancet. 2012

HD18 Studie für PET-2 negative Patienten
Finale Analysis (PFS)

PFS rate

	3-year estimate	5-year estimate
8/6x eBEACOPP	92.3% [89.8-94.8]	91.2% [88.5-94.0]
4x eBEACOPP	94.8% [92.8-96-8]	91.8% [89.0-94.6]
Difference	+2.5% [-0.7-+5.7]	+0.6% [-3.3-+4.5]
Hazard Ratio		0.88 [0.57 to 1.36]

Median observation time 53 months

Borchmann P et al, Lancet. 2018

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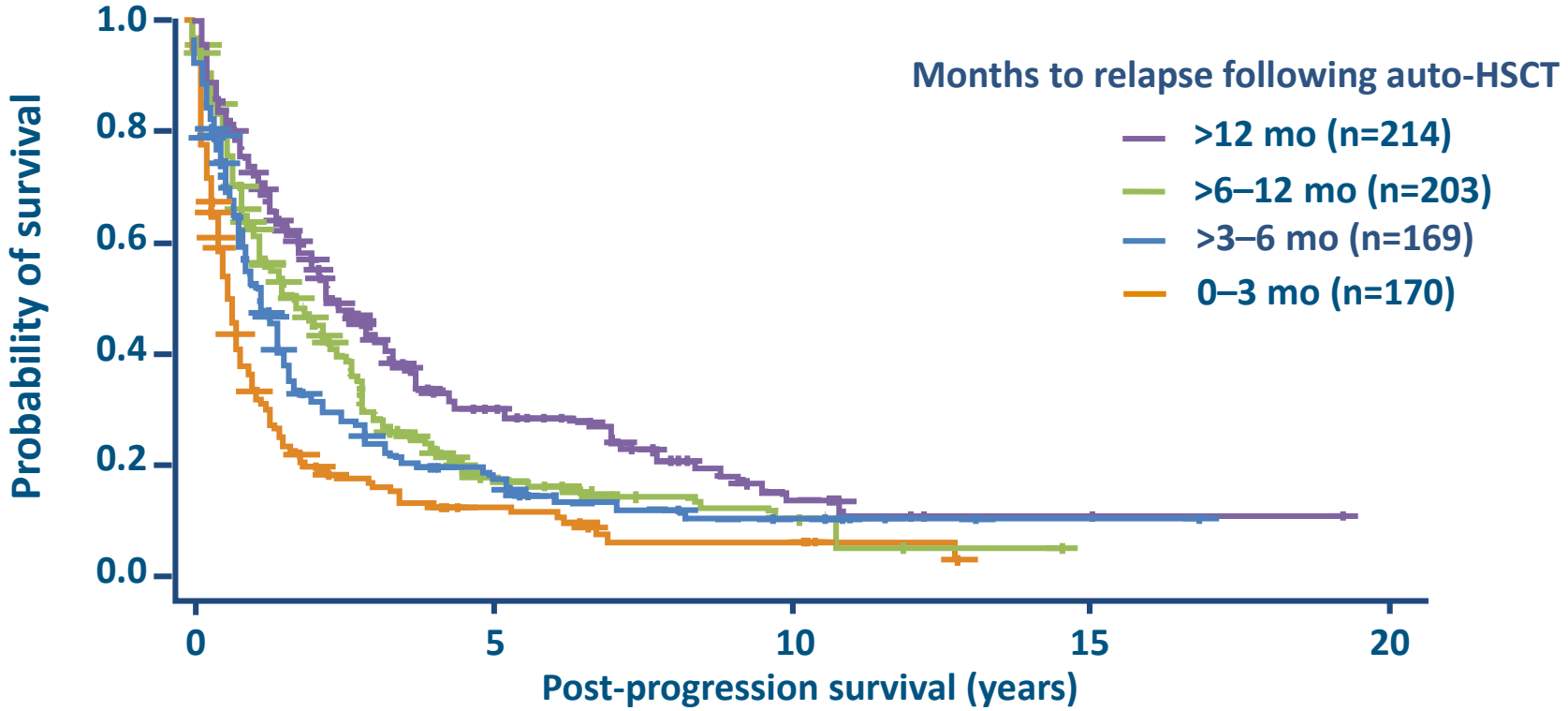
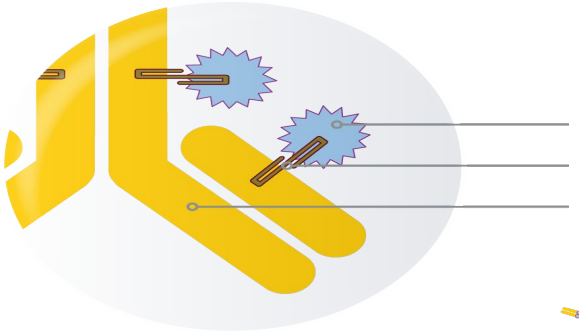
Hodgkin Lymphom
Prognose von rezidivierten Patienten nach HDCT



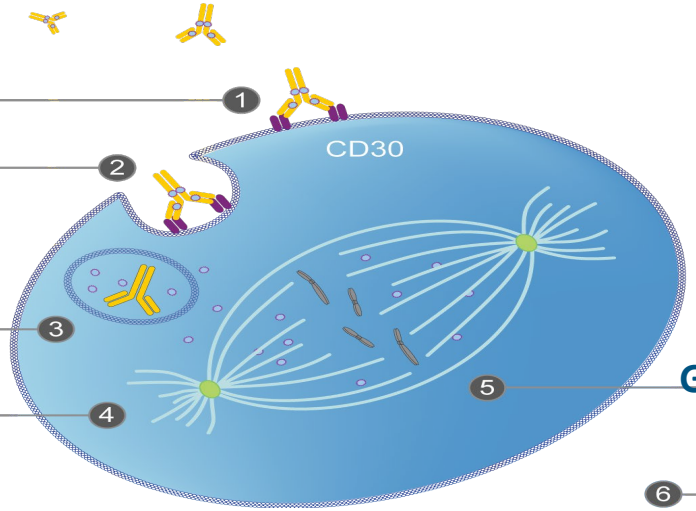
Arai S et al, Leukemia & Lymphoma 2013

Brentuximab Vedotin
Mechanism of action



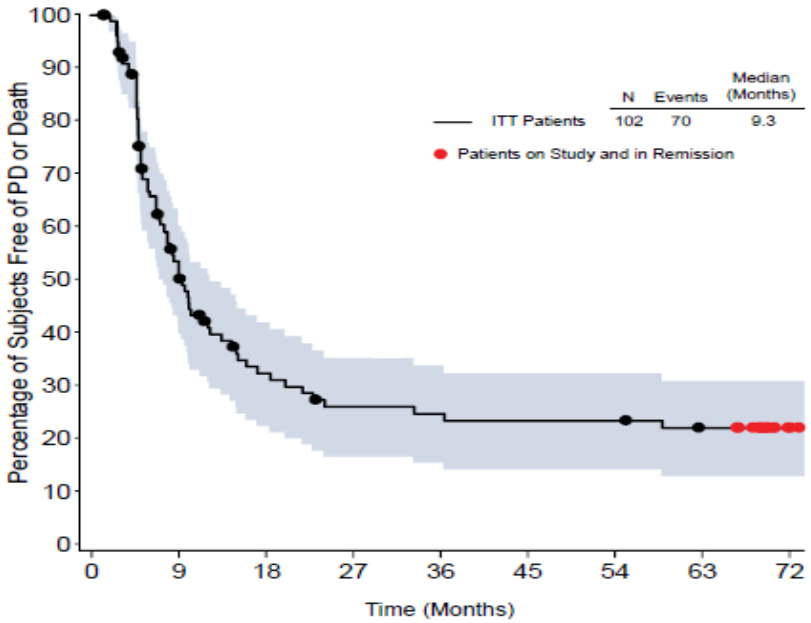
Brentuximab vedotin (ADC)

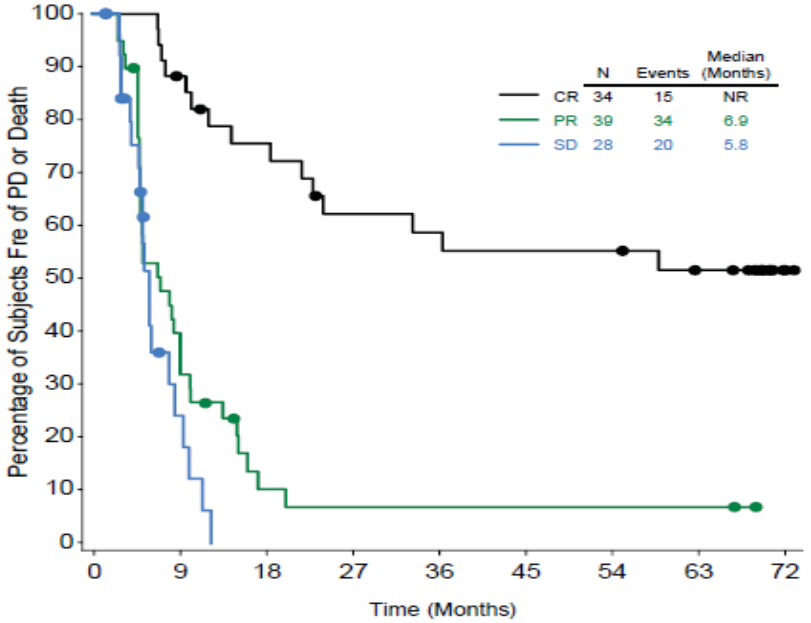
- Monomethyl auristatin E (MMAE), potent antitubulin agent
- Protease-cleavable linker
- Anti-CD30 monoclonal antibody



1. ADC binds to CD30
2. ADC-CD30 complex traffics to lysosome
3. MMAE is released
4. MMAE disrupts Microtubule network
5. G2/M cell cycle arrest
6. Apoptosis

Brentuximab Vedotin
Phase II Pivotal Study (PFS)

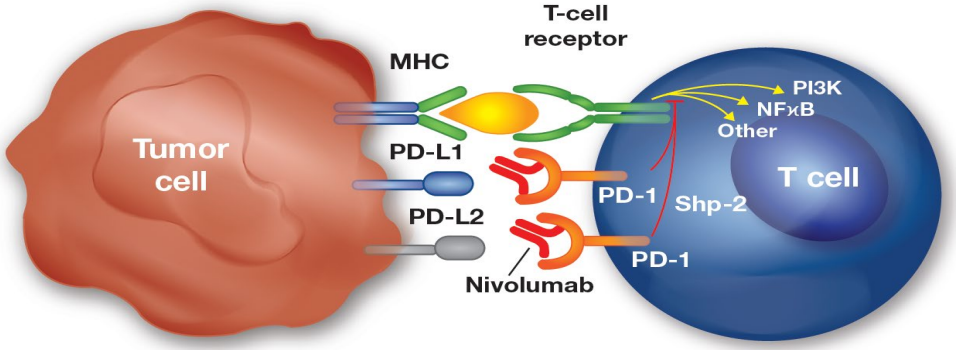




Chen, et al ASH 2015

PD1 Inhibition in classical HL
Mechanism of action

- **Patients with cHL show high frequency of 9p24.1 alterations and overexpression of PD-L1 and PD-L2[1]**
- **Nivolumab is a fully human immunoglobulin G4 monoclonal antibody targeting the programmed death-1 (PD-1) receptor immune checkpoint pathway**

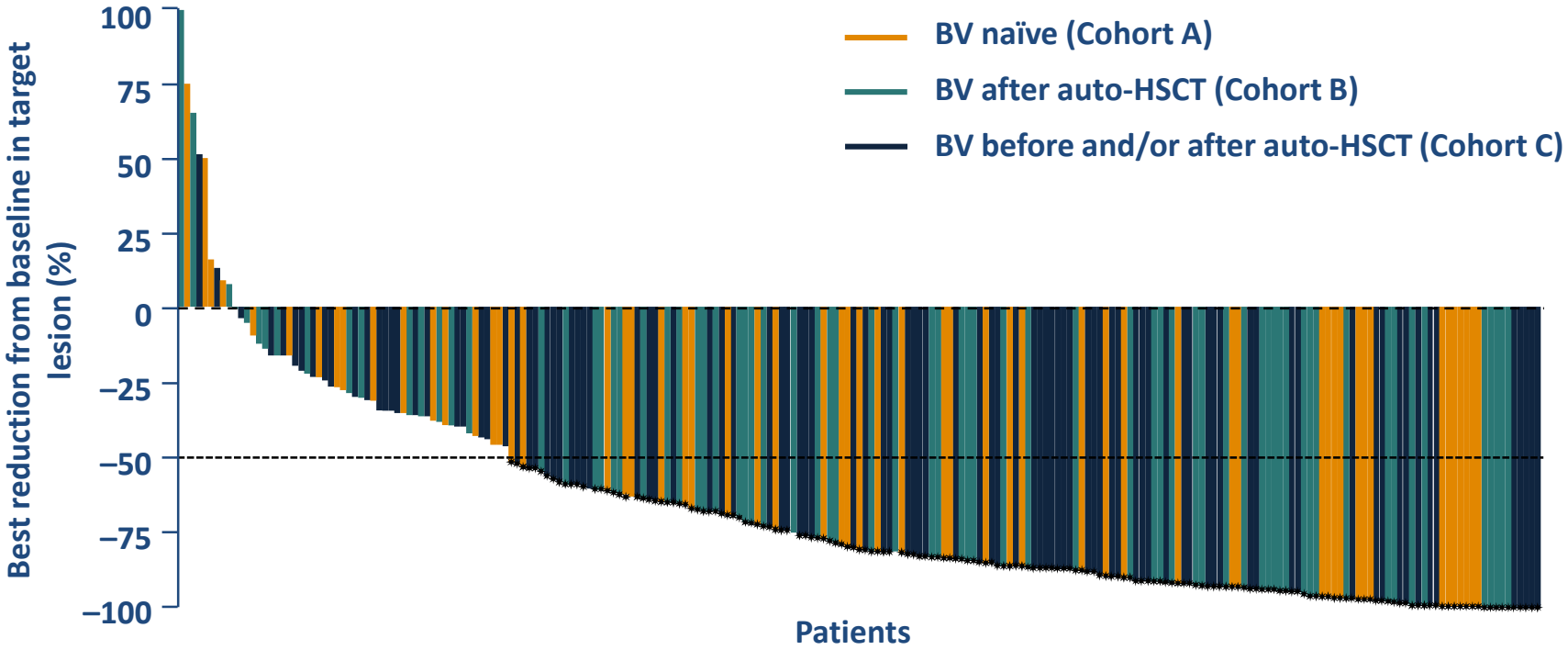


Nivolumab blocks signaling through the PD-1 receptor

cHL = classical Hodgkin lymphoma; MHC = major histocompatibility complex; NFκB = nuclear factor kappa B; PD-L1/2 = programmed death ligand 1/2; PI3K = phosphoinositide-3–kinase; Shp-2 = Src homology region 2-containing protein tyrosine phosphatase 2.

[1]Roemer MGM et al, J Clin Oncol 2016;34:2690–7

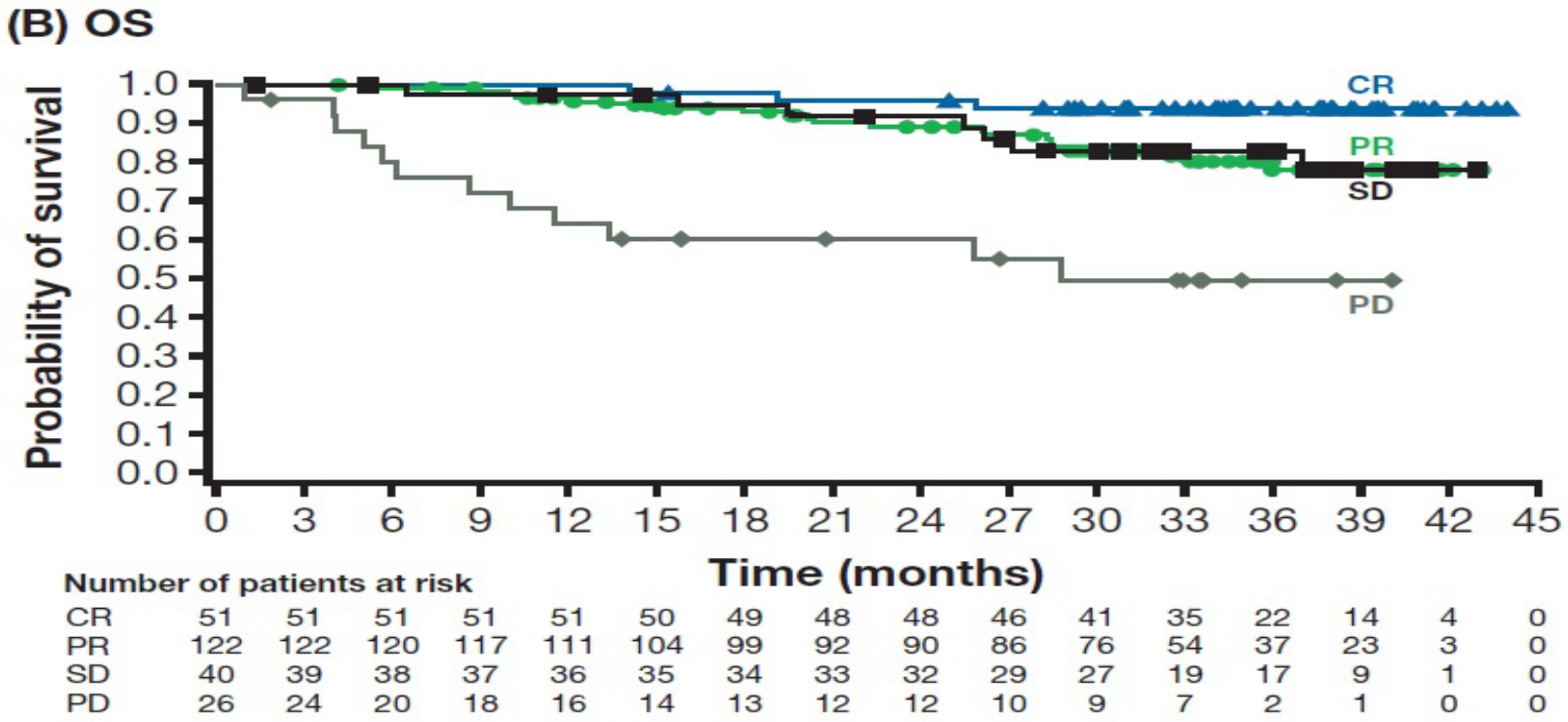
Phase 2 CheckMate 205 Studie
Targetläsion per IRC



Asterisks (*) denote responders

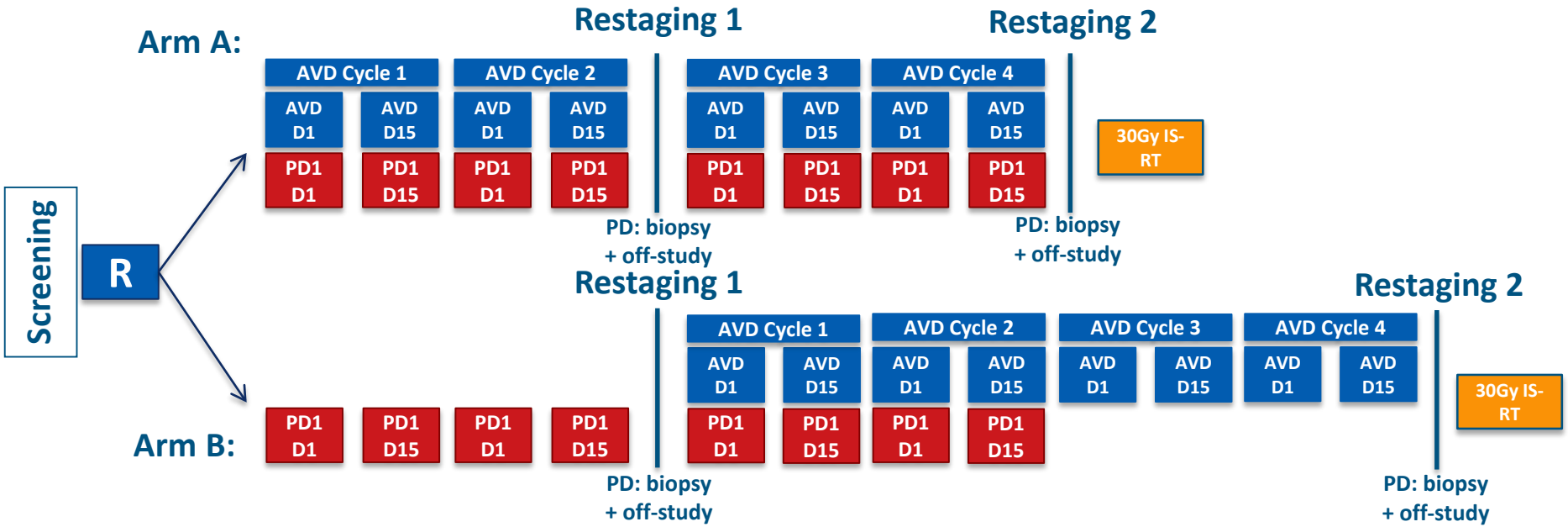
Engert A et al, EHA 2017

CheckMate 205 R/R beim cHL
OS nach BOR



PFS and responses were per IRC unless noted otherwise

NIVAHL: GHSG Pilotstudie
Randomisierte Studie beim early unfavorable HL



AVD: Adriamycin, Vinblastin, Dacarbazine; PD1: Nivolumab

NIVAHL: Outcome
Progression-Free Survival

PFS rate +/- 95%-CI

Median follow-up	12-month estimate	
Concomitant	9 months	100%
Sequential	9 months	98% [94-100]

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Zusammenfassung

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- **Etwa 90% der HL Patienten werden geheilt; Langzeittox problematisch**
- **Frühe Stadien: 2x ABVD+RT; mittlere Stadien: 2+2+RT PET gesteuert**
- **Fortgeschrittene Stadien: B.esk 15-20% besser im PFS und 10-15% im OS**
- **Nur 4x B.esk bei PET- Patienten (3y FFTF 94.8%; OS 98.7%)**
- **PD1 Inhibition in der Erstlinie (NIVAHL) und bei Rezidiven**
- **Aktuelle Studien mit anti-PD1 Moaks ersetzen zunehmend Chemo- und Strahlentherapie beim HL**

ISHL 12

October 24–26, 2020

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