Lymphom Kompetenz KOMPAKT

EHA2020 VIRTUAL
11. – 14. Juni 2020

Kompetenznetz Maligne Lymphome

Vernetzt forschen.
Gut informiert entscheiden.

Prof. Dr. med. Peter Borchmann

Hodgkin Lymphom

- Oberarzt der Klinik I für Innere Medizin, Uniklinik Köln
- Co-Chairman der Deutschen Hodgkin Studiengruppe (GHSG)
- Mitglied und Wissenschaftlicher Beirat im Kompetenznetz Maligne Lymphome e.V.

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT **EHA2020** wird in Kooperation mit fünf unterstützenden Firmen durchgeführt.
Diese Firmen haben keinen Einfluss auf die Inhalte dieses Vortrags. Meine weiteren Disclosures betreffen:

Art	Verbundenheit
Anstellungsverhältnis, Führungsposition	-
Beratungs-/Gutachtertätigkeit	Takeda, BMS, Roche, Amgen, Novartis, Celgene, Miltenyi Biotech, Gilead
Besitz von Geschäftsanteilen, Aktien, Fonds	-
Patent, Urheberrecht, Verkaufslizenz	-
Honorare	Takeda, Novartis, BMS, Roche, MSD, Celgene, Miltenyi Biotech, Gilead, Abbvie
Finanzierung wissenschaftlicher Untersuchungen	Takeda Oncology, MSD, Novartis
Andere (auch immaterielle)	-

Hodgkin Lymphom EHA 2020

1. PET-gesteuerte Bestrahlung bei intermediären Stadien? Endauswertung der HD17.
2. Fortgeschrittene Stadien HD18: 5 Jahre FU Ergebnisse.
3. Pembrolizumab oder Brentuximab vedotin für mehrfach rezidiverte oder refraktäre Patienten?

PET-gesteuerte Bestrahlung bei intermediären Stadien? Endauswertung der HD17.

–The German Hodgkin Study Group (GHSG) HD14 study has proven superior 5y PFS of intensified treatment with 2x eBEACOPP + 2x ABVD ("2+2") compared to 4x ABVD. [1]

–The 2+2 treatment led to more severe hem-tox and infections compared to 4x ABVD; however, treatment-related mortality (TRM), second primary malignant neoplasms (SPMN), and fertility for women and men were not different. [2,3]

➢*CMT with 2+2 plus 30 Gy IF-RT was thus established as GHSG SOC*

–However, a matter of concern for CMT are late sequelae arising from ionizing irradiation. It is known already that RT cannot be reduced without loss of tumour control when ABVD serves as backbone. [4,5]

[1] v.Tresckow et al., JCO, 2012
[2,3] Behrigner et al., Ann Oncol, 2012, Behringer et al., JCO 2013
[4,5] Eich et al., JCPO, 2010, Andre et al., JCO 2017

HD17 Trial Hypotheses and Objectives

For HD17, we thus hypothesized that

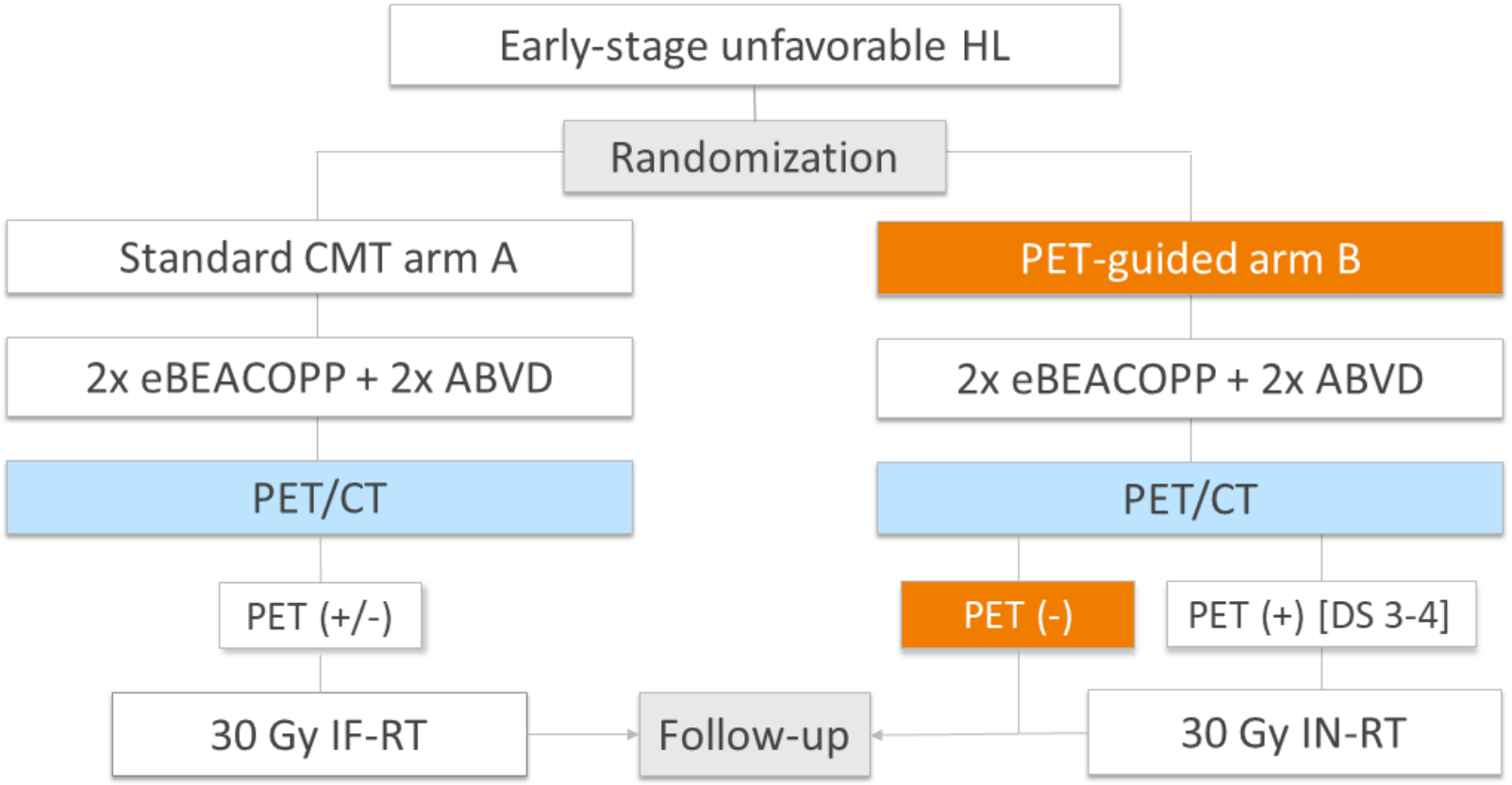
- the more effective systemic treatment with 2+2 might allow removing RT from CMT
- in an individualized approach for patients responding well to systemic treatment, as determined by Positron Emission Tomography (PET) after 4 cycles (PET4)

Primary objectives

- ***First primary objective:*** Is an individualized treatment strategy with PET-guided radiotherapy after 2+2 non-inferior to the standard CMT (with lower margin for inferiority set at 8%)?

GHSG

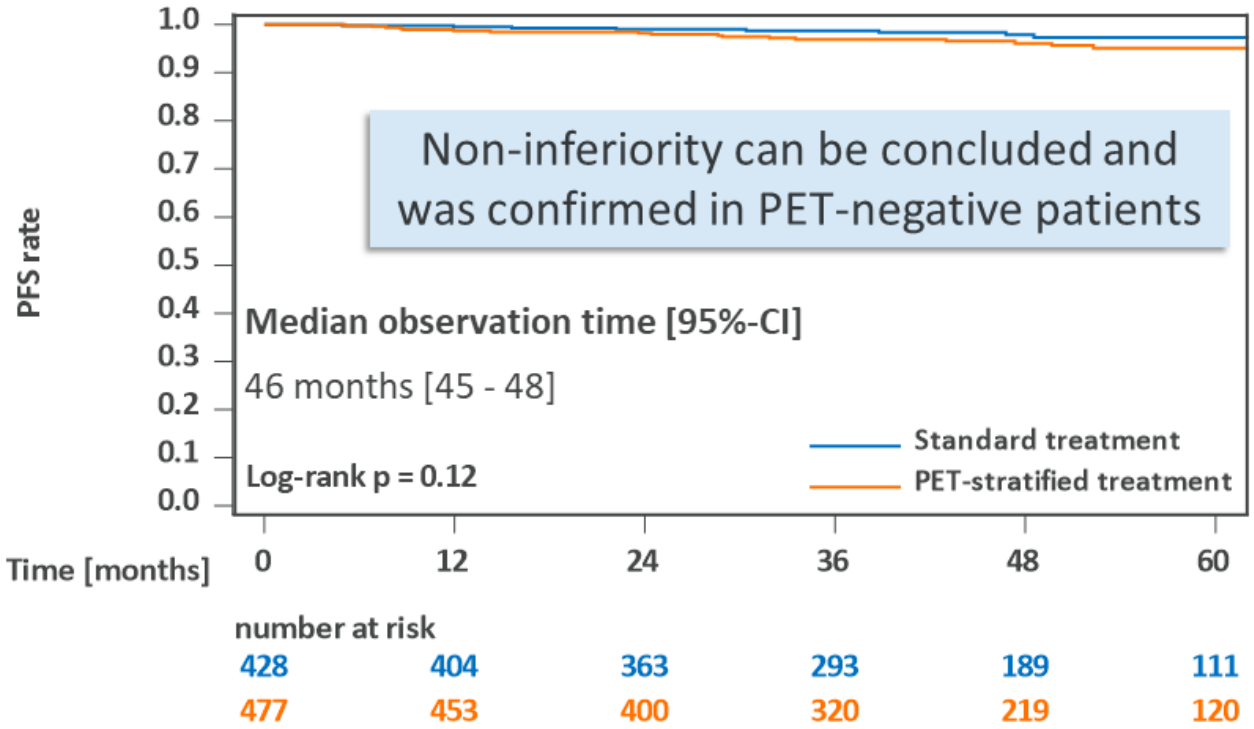
HD17 Trial Design



GHSG

6 | GHSG HD17 final analysis| Peter Borchmann on behalf of the GHSG

HD17 Trial PET guided treatment non-inferior to CMT?



5-year PFS [95%-CI]

Arm A: 97.3% [94.5 - 98.7]

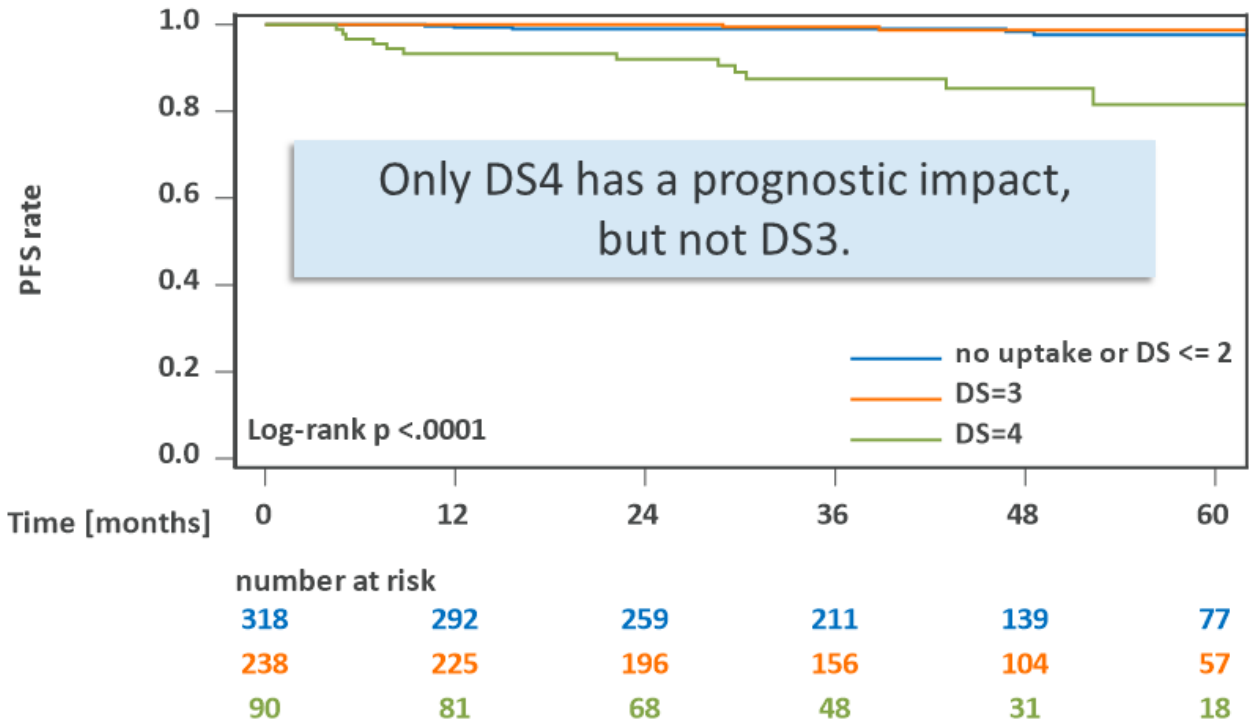
Arm B: 95.1% [92.0 – 97.0]

Difference in 5-year PFS [95%-CI]

2.2% [-5.3 - 0.9]

GHSG

HD17 Trial Prognosis per Deauville Score (DS)



5-year PFS		[95%-CI]
DS < 3:	97.6%	[94.0 – 99.0]
DS = 3:	98.8%	[95.0 – 99.7]
DS = 4:	81.6%	[67.9 – 89.9]

GHSG

HD17 Trial Summary and Conclusion

1. PET-guided treatment of early-stage unfavourable HL using the 2+2 backbone is non-inferior to CMT with 2+2 and 30 Gy consolidation RT.

   ➢ *The vast majority of early stage unfavourable HL patients can be treated with the brief and highly effective 2+2 chemotherapy alone.*

2. The PET-guided 2+2 strategy has no relevant HL- or treatment-related mortality and thus achieves 5y OS *not differing from the German normal population.*

3. PET-guided 2+2 is the new GHSG standard of care for intermediate stage HL

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Fortgeschrittene Stadien HD18: 5 Jahre FU Ergebnisse.

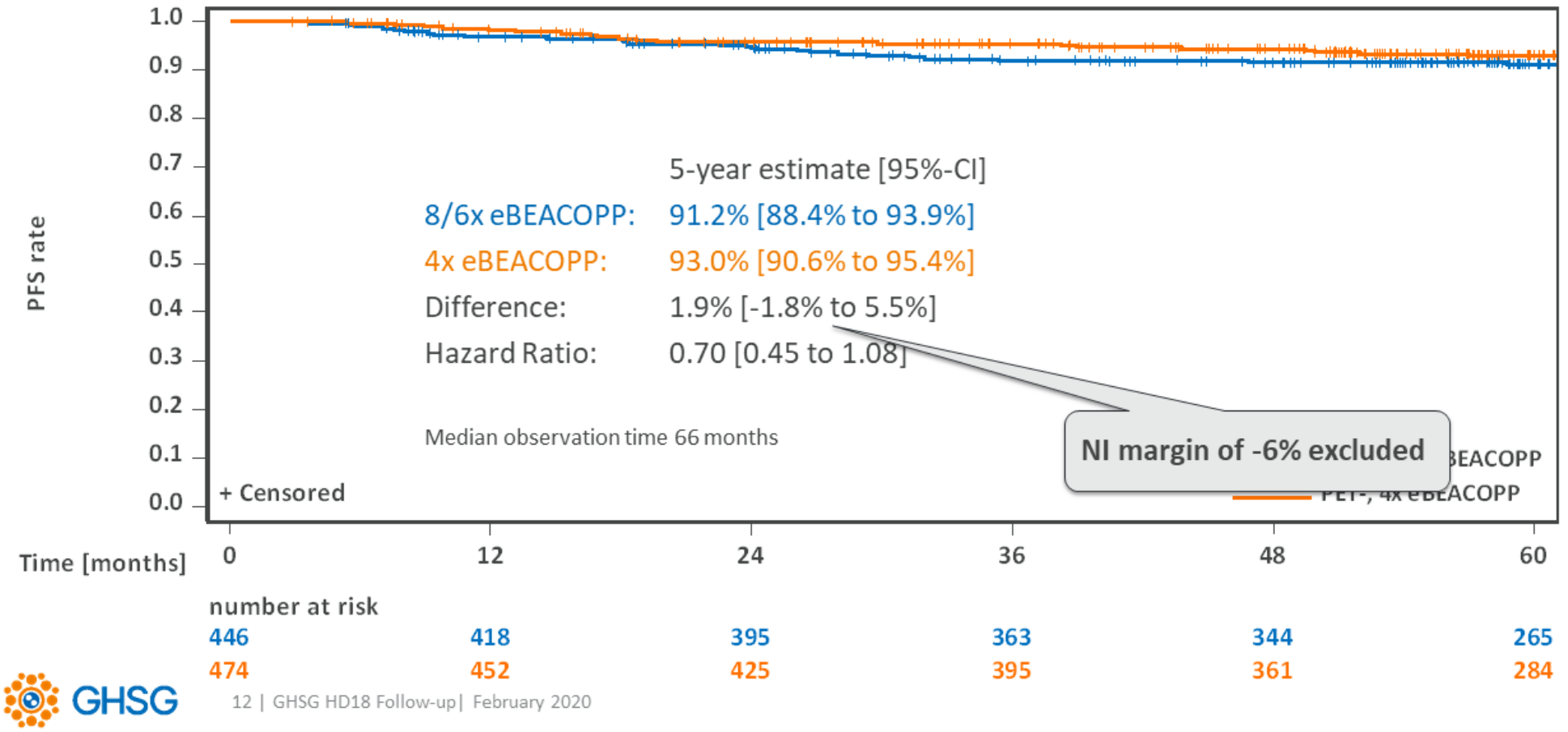
–The rationale behind the HD18 trial was to individualize and reduce therapy itensity by adapting it to early response assessed by PET/CT after 2 cycles of eBEACOPP.

–For PET-2 negative patients we intended to relevantly reduce the burden of therapy by reduction from 8 to 4 treatment cycles without compromising the patients' prognosis.

–However, HD15 results led to change of the SOC from 8 to 6 cycles while the trial was running.

➢ Can we still show non-inferiority of 4 compared to only 6 cycles?

HD18- (Per Protocol) PFS



GHSG

12 | GHSG HD18 Follow-up| February 2020

HD18 Trial Summary and Conclusion

1. The prolonged follow-up data establish the non-inferiority of only 4x eBEACOPP not only compared to 8 but also to 6x eBEACOPP in terms of PFS.
2. Thus, PET-guided eBEACOPP remains GHSG standard of care for patients with advanced-stage HL.
3. HD21 aims at further improving treatment tolerability for this particularly young patient cohort by modifying the intensive eBEACOPP regimen wit the use of Brentuximab vedotin (BrECADD)

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The management of mulitple relapsed Hodgkin Lymphoma

ICI vs Brentuximab vedotin: study concepts in r/r cHL

MK-3475-204/KEYNOTE-204
NCT02684292

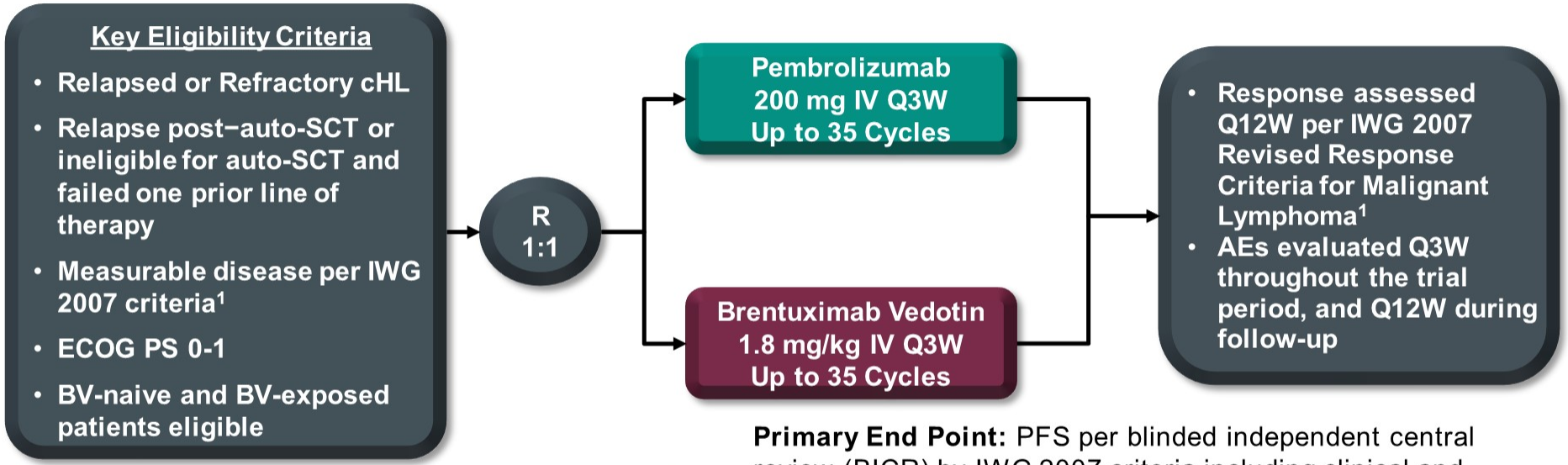
Brentuximab vedotin — R — Pembrolizumab

CheckMate 812
NCT03138499

Brentuximab vedotin — R — Brentuximab + Nivolumab

GHSG

KEYNOTE-204 Study Design (NCT02684292)

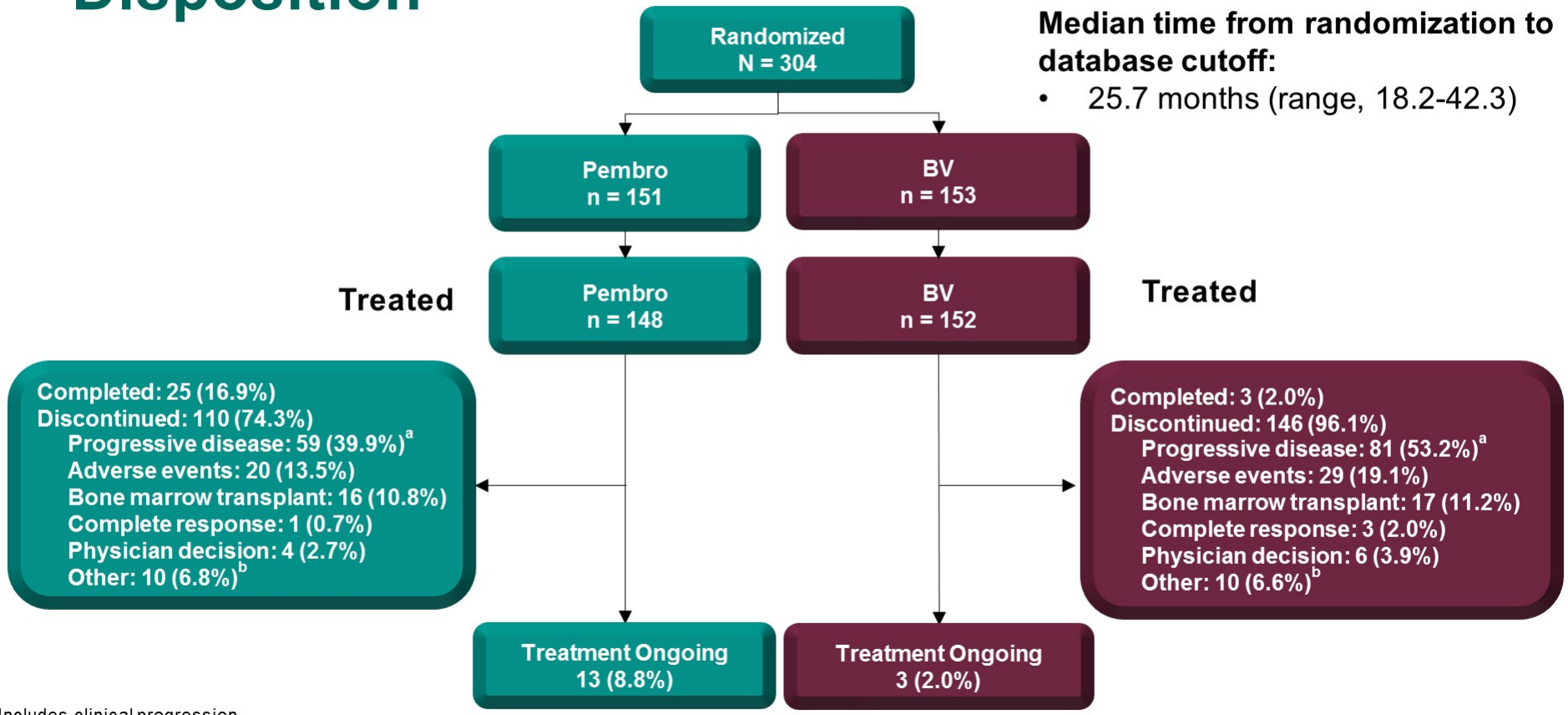


Primary End Point: PFS per blinded independent central review (BICR) by IWG 2007 criteria including clinical and imaging data following auto-SCT or allogeneic stem cell transplant (allo-SCT); OS

Secondary End Points: PFS per BICR by IWG 2007 criteria excluding clinical and imaging data following auto-SCT or allo-SCT; ORR by BICR per IWG 2007; PFS per investigator review; DOR; safety

1. Cheson BD et al. *J Clin Oncol*. 2007;25:579-586.

Disposition



Median time from randomization to database cutoff:

- 25.7 months (range, 18.2-42.3)

[a]Includes clinical progression.
[b]Other included nonstudy anticancer therapy, excluded medication, noncompliance, withdrawal by patient, and protocol deviations.
Data cutoff: January 16, 2020.

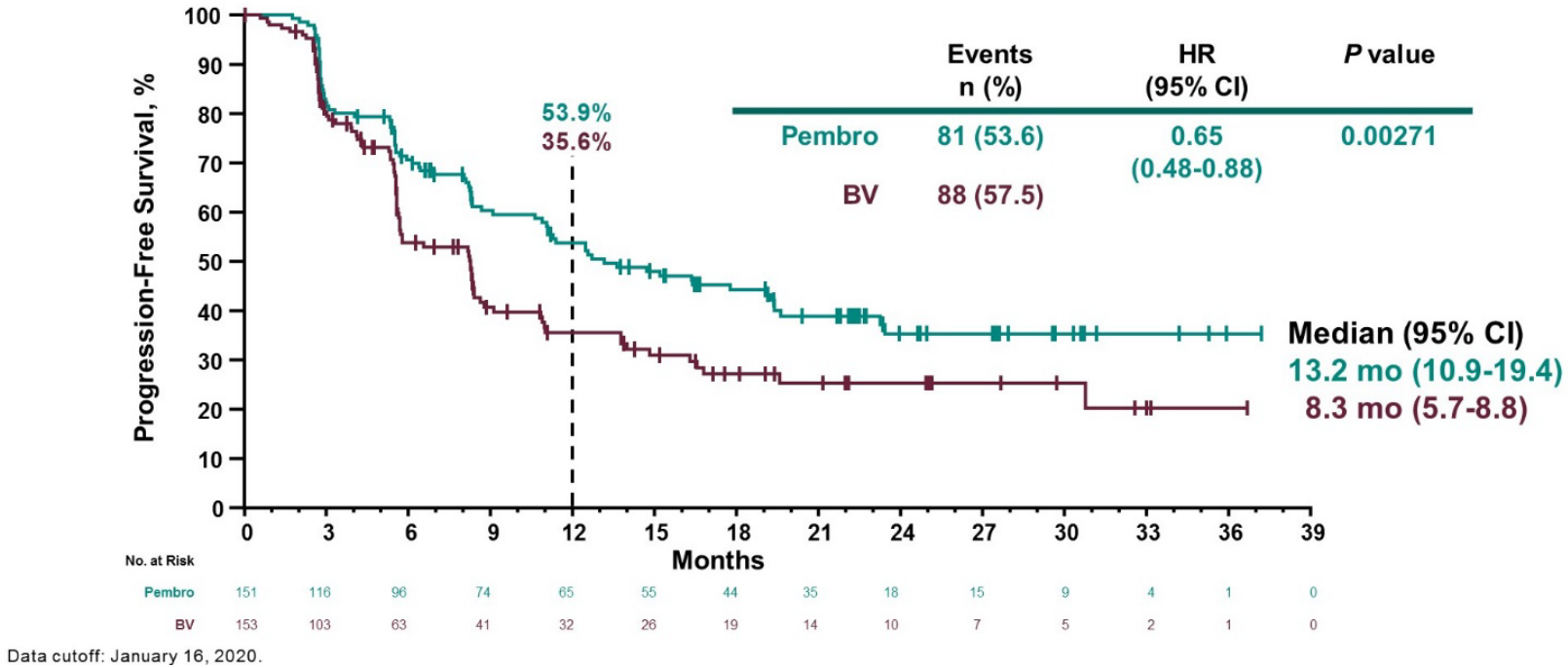
Keynote-204: randomized trial of BV versus Pembrolizumab in r/r cHL

Patient Characteristics (continued)

	Pembro n = 148	BV n = 152
Number of prior therapies, median (range)[a]	2 (1-10)	3 (1-11)
Subsequent SCT, n (%)		
Auto-SCT	30 (20.3)	34 (22.4)
Allo-SCT	14 (9.5)	13 (8.6)
Days on therapy, median (range)	305.0 (1-814)	146.5 (1-794)
Completed 2 years of treatment, n (%)	25 (16.9)	3 (2.0)
Treatment ongoing, n (%)	13 (8.8)	3 (2.0)

[a]Pembro: n = 151; BV: n = 153.
Data cutoff: January 16, 2020.

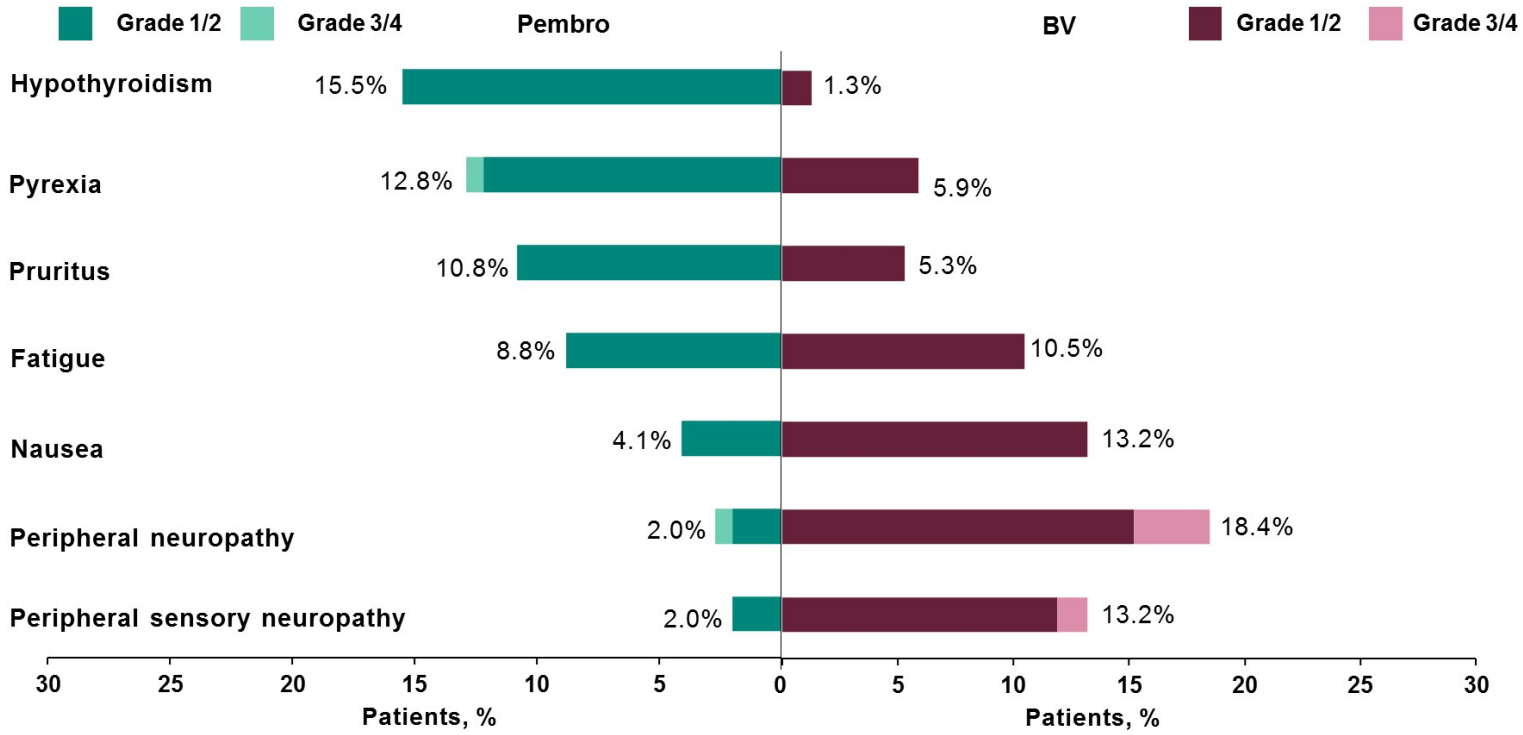
Keynote-204: randomized trial of BV versus Pembrolizumab in r/r cHL



Data cutoff: January 16, 2020.

Keynote-204: randomized trial of BV versus Pembrolizumab in r/r cHL

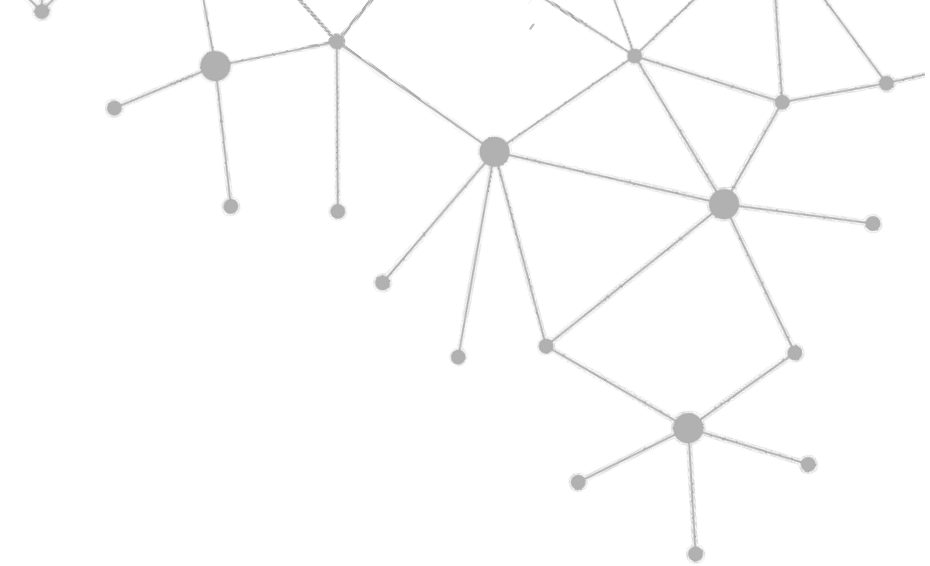
Treatment-Related AEs (≥10% Either Arm)



Data cutoff: January 16, 2020.

Keynote-204: randomized trial of BV versus Pembrolizumab in r/r cHL

- Pembrolizumab monotherapy showed statistically significant and clinically meaningful improvement in PFS versus brentuximab vedotin in patients with R/R cHL that have relapsed post auto-SCT or are ineligible for auto-SCT
  - PFS: 13.2 vs 8.3 months; (HR: 0.65 [95% CI, 0.48-0.88]; *P* = 0.00271)
- PFS benefit extended to key subgroups
  - Ineligible for auto-SCT (HR: 0.61)
  - Primary refractory disease (HR: 0.52)
  - BV naive (HR: 0.67)
- More durable responses were associated with pembrolizumab versus brentuximab vedotin
  - ORR: 65.6% vs 54.2%; DOR: 20.7 vs 13.8 months
- Safety was consistent with the known profiles of each agent
- Pembrolizumab should be considered the preferred treatment option and new SOC for the treatment of R/R cHL in patients that have relapsed post auto-SCT or are ineligible for auto-SCT



Die Kurzpräsentationen sind online unter

www.lymphome.de/eha2020

Für den Inhalt verantwortlich:

Prof. Dr. med. Peter Borchmann

Klinik I für Innere Medizin • Uniklinik Köln

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Diese hatten keinen Einfluss auf die Inhalte.

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