


Kompetenznetz
Maligne Lymphome

Lymphom Kompetenz KOMPAKT



KML KONGRESSE

Expert:innen berichten zu
Lymphomen & Leukämien



EHA2024 HYBRID



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Innere Medizin I | Uniklinik Köln

Hodgkin Lymphom (HL)

Offenlegung potentieller Interessenskonflikte

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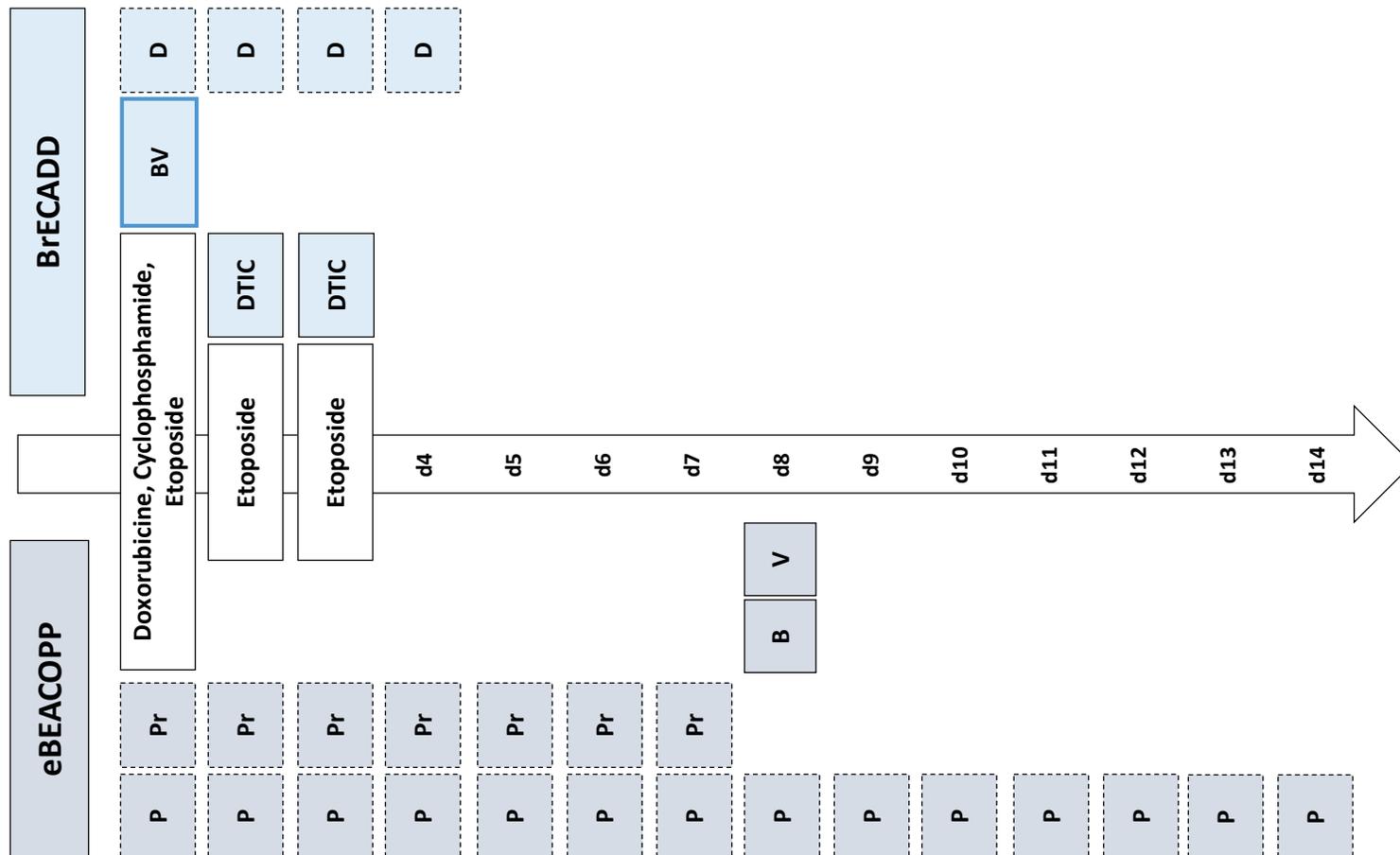
Kapitel 1

Können wir das eBEACOPP Schema durch Brentuximab vedotin modifizieren und relevant im Nutzen-Risiko Verhältnis verbessern?

GHSg HD21 Studie

S225: THE RANDOMIZED STUDY GHSg HD21 SHOWS SUPERIOR TOLERABILITY AND EFFICACY OF BREcADD VERSUS BEAcOPP IN ADVANCED STAGE CLASSICAL HODGKIN LYMPHOMA.

Peter Borchmann on behalf of all participating co-investigators



- The Kairos backbone **doxorubicin, cyclophosphamide, etoposide** was retained and *pre-defined dose de-escalation steps (DL 4, 3, 2, baseline)* were identical in both groups
- Introducing **Brentuximab Vedotin (BV)**, therefore omitting **Bleomycin (B, pulmonary toxicity)** and **Vincristin (V, neuropathy)**
- Replacing **Procarbazine (Pr)** with the **less geno- and gonadotoxic Dacarbazine (DTIC)**
- Replacing 14 days of **Prednisone (P)** to 4 days of **Dexamethasone (D)**

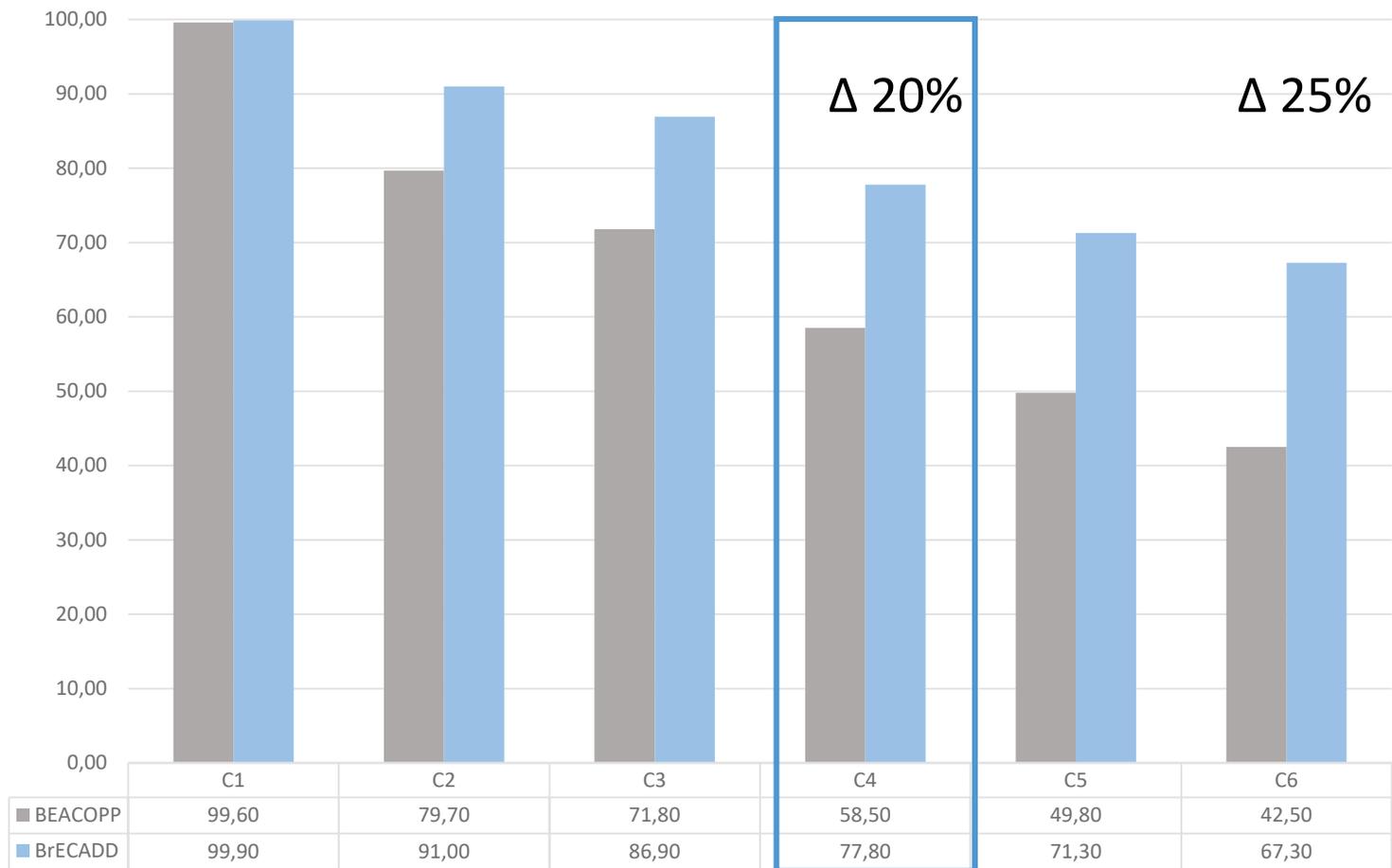
GHSG HD21 Studie

TRMB endpoint

1. The first part of the combined primary endpoint showed a **significant reduction of *acute and severe treatment related adverse events (TRMB) across all subgroups (IPS, sex, age) favouring***
 - **BrECADD** (312/738 patients [42%]) compared to the SOC
 - **eBEACOPP** (430/732 patients [59%]), relative risk 0.72; 95% CI 0.65–0.79, $p < 0.0001$
2. The observed significant reduction in acute TRMB is **clinically meaningful** with reduction of
 - **transfusion frequency** for red blood cells (from 52% with eBEACOPP to 24% with BrECADD) and platelets (from 34% to 17%, respectively), and
 - **peripheral sensory neuropathy** grade 2 (3) from 14% (2%) to only 6% (1%)
4. **Resolution of TRMB events** in 675/677 patients (> 99%) treated with BrECADD
5. **S228 GONADAL FUNCTION RECOVERY AND FERTILITY IN THE PHASE III GERMAN HODGKIN STUDY GROUP HD21 TRIAL**
6. **P1100 TREATMENT EFFECTS OF BRECADD ON HEALTH-RELATED QUALITY OF LIFE**

GHSB HD21 Studie

HD21: Improved tolerability of BrECADD results in more patients treated with full dose (cyclo, etoposide, doxo) per cycle (%)



Early termination of the tubulin inhibitors VCR and BV

BV in BrECADD:
18/738 patients, 2.4%

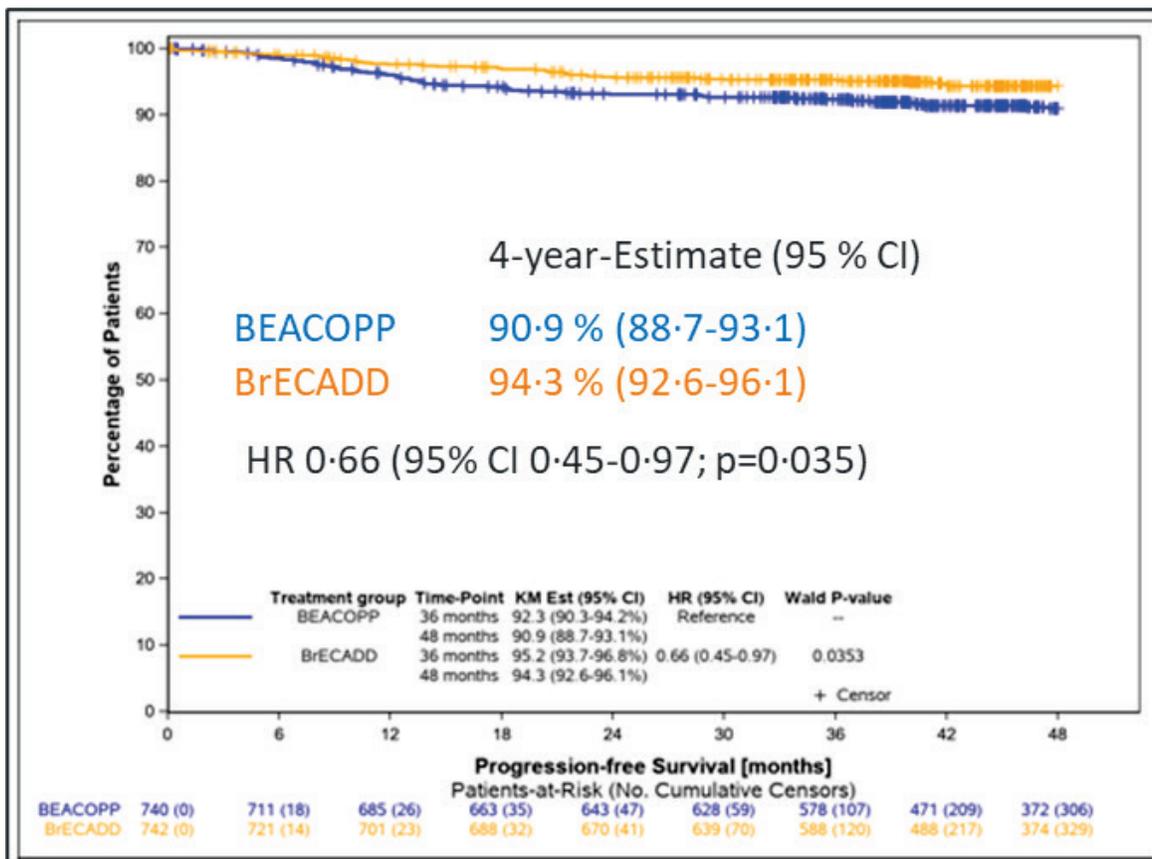
VCR in eBEACOPP:
132/732 patients, 18.0%

Δ **15.6%**

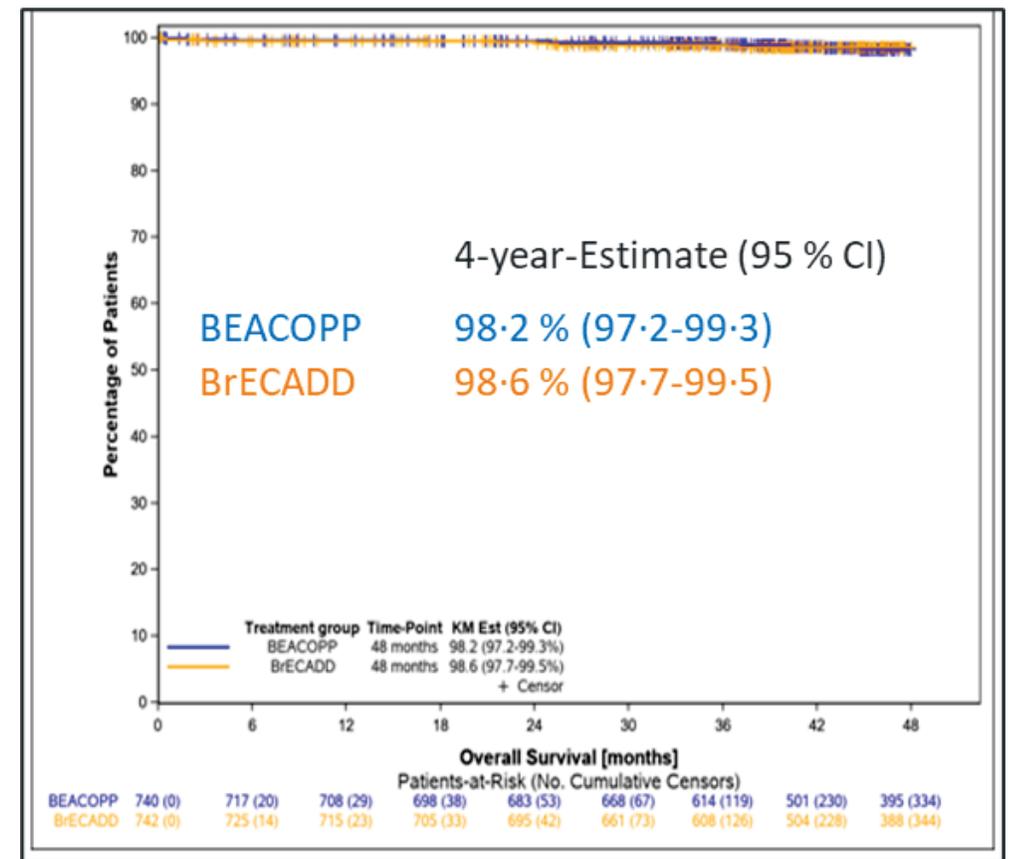
GHSB HD21 Studie

HD21 final analysis: BrECADD is superior to eBEACOPP (mFU 48 m)

Progression-free survival



Overall survival



GHSB HD21 Studie: Abs S228

S228: GONADAL FUNCTION RECOVERY AND FERTILITY IN THE PHASE III GERMAN HODGKIN STUDY GROUP HD21 TRIAL.

Justin Ferdinandus on behalf of all co-authors

Definitions:

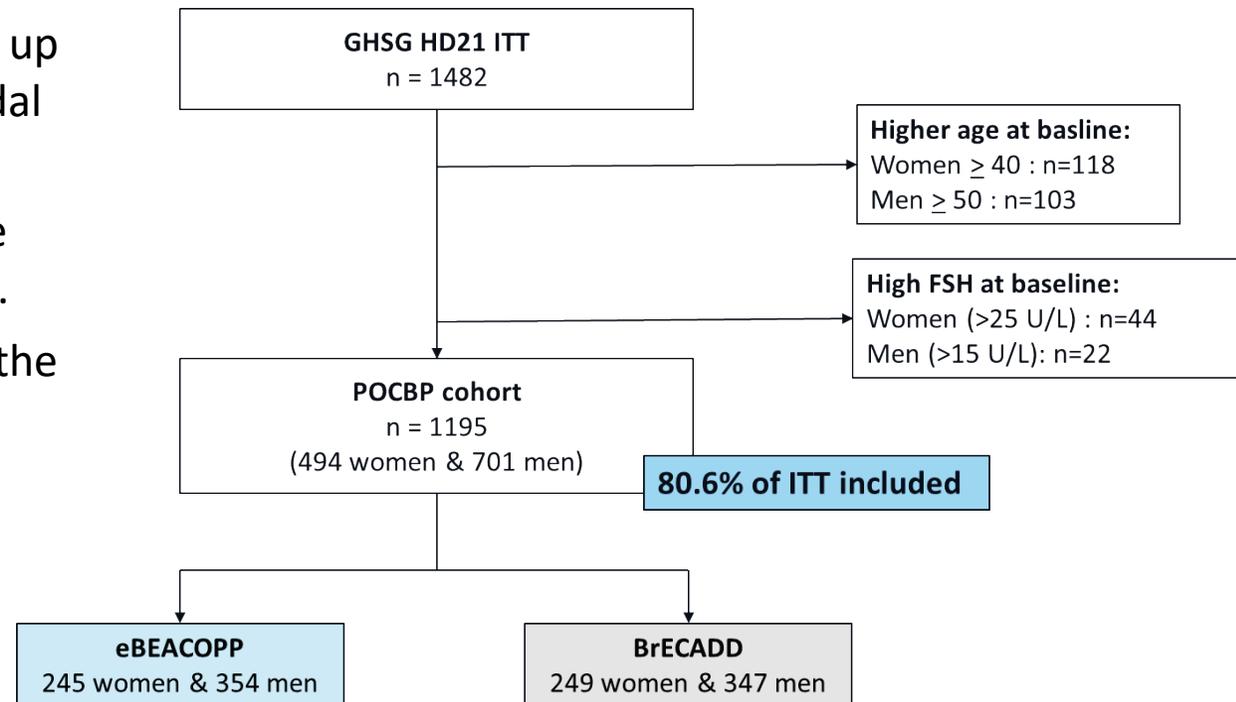
Patients of Childbearing Potential (POCBP) cohort: Women up to 40 and men up to 50 years of age without baseline gonadal function impairment

Gonadal function impairment: Follicle-stimulating hormone (FSH) serum levels >25 U/L for women and >15 U/L for men.

Time to gonadal function recovery: end-of-treatment until the first measurement of FSH level below threshold or last FSH measurement (censor)

Statistical methods:

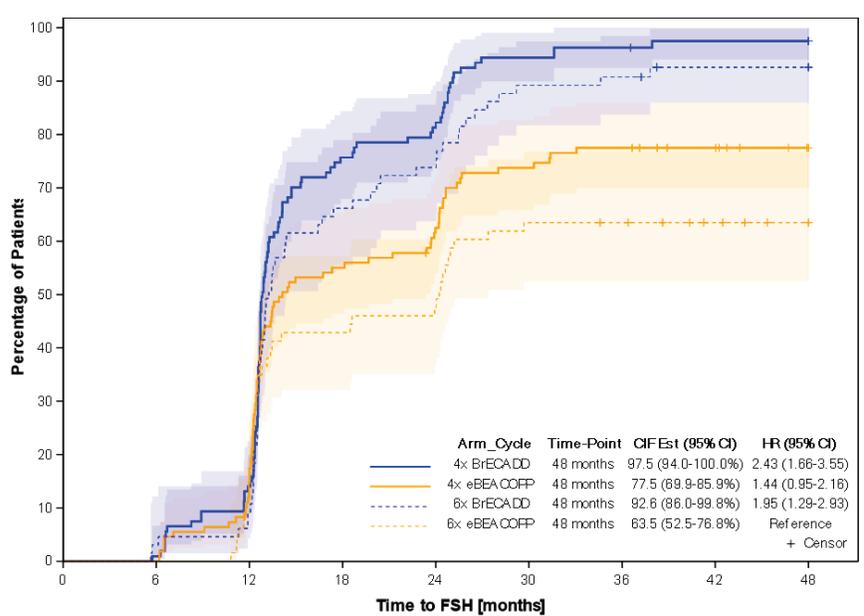
Cox regressions to compare time-to-event outcomes



GHSB HD21 Studie

S228: GONADAL FUNCTION RECOVERY AND FERTILITY IN THE PHASE III GERMAN HODGKIN STUDY GROUP HD21 TRIAL.

Women: Effect of number of cycles



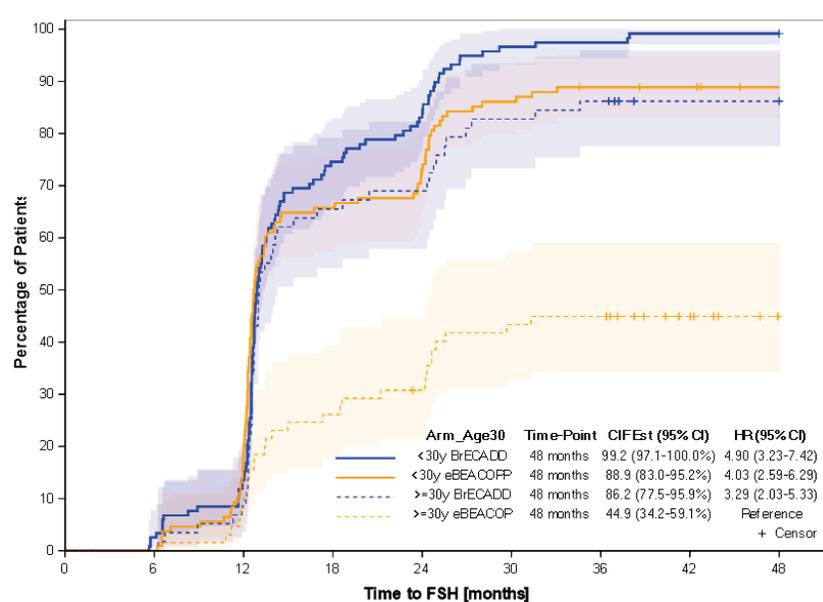
C4: 97.5 %
C6: 92.6%

C4: 77.5%

C6: 63.5%

	0	6	12	18	24	30	36	42	48
4x BrECADD	107 (0)	106 (0)	92 (0)	26 (0)	20 (0)	6 (0)	4 (0)	2 (1)	2 (2)
4x eBEACOPP	109 (0)	109 (0)	83 (0)	49 (0)	40 (1)	28 (1)	24 (1)	20 (5)	14 (11)
6x BrECADD	65 (0)	63 (0)	59 (0)	22 (0)	17 (0)	7 (0)	6 (0)	3 (2)	3 (3)
6x eBEACOPP	63 (0)	63 (0)	54 (0)	36 (0)	33 (0)	23 (0)	22 (1)	18 (5)	15 (8)

Women: Effect of age



<30y: 99.2 %

<30y: 88.9 %
>=30y: 86.2 %

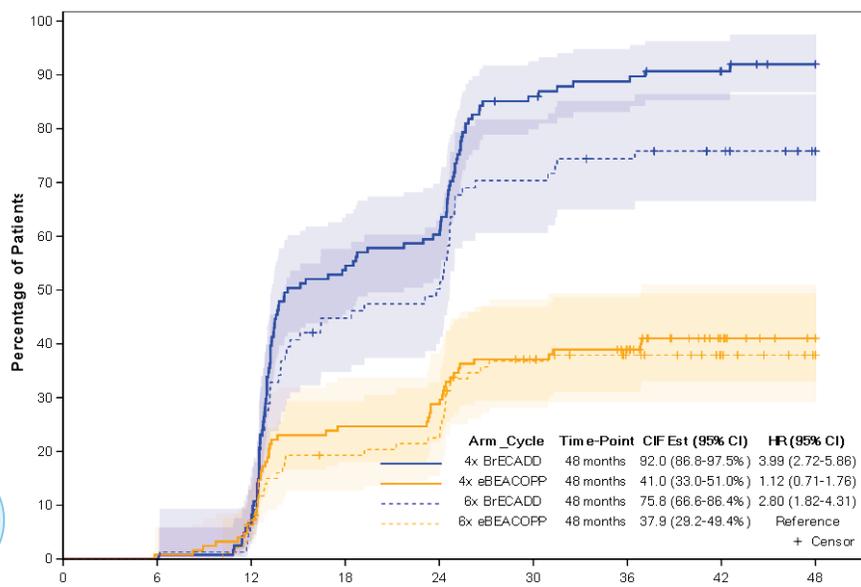
>=30y: 44.9 %

	0	6	12	18	24	30	36	42	48
<30y BrECADD	118 (0)	115 (0)	102 (0)	30 (0)	20 (0)	4 (0)	3 (0)	1 (0)	1 (1)
<30y eBEACOPP	108 (0)	108 (0)	88 (0)	37 (0)	29 (0)	15 (0)	11 (1)	10 (2)	7 (5)
>=30y BrECADD	58 (0)	58 (0)	53 (0)	20 (0)	18 (0)	10 (0)	8 (0)	4 (4)	4 (5)
>=30y eBEACOPP	65 (0)	65 (0)	60 (0)	48 (0)	44 (1)	36 (1)	35 (1)	28 (8)	22 (14)

GHSg HD21 Studie

S228: GONADAL FUNCTION RECOVERY AND FERTILITY IN THE PHASE III GERMAN HODGKIN STUDY GROUP HD21 TRIAL.

men: Effect of number of cycles



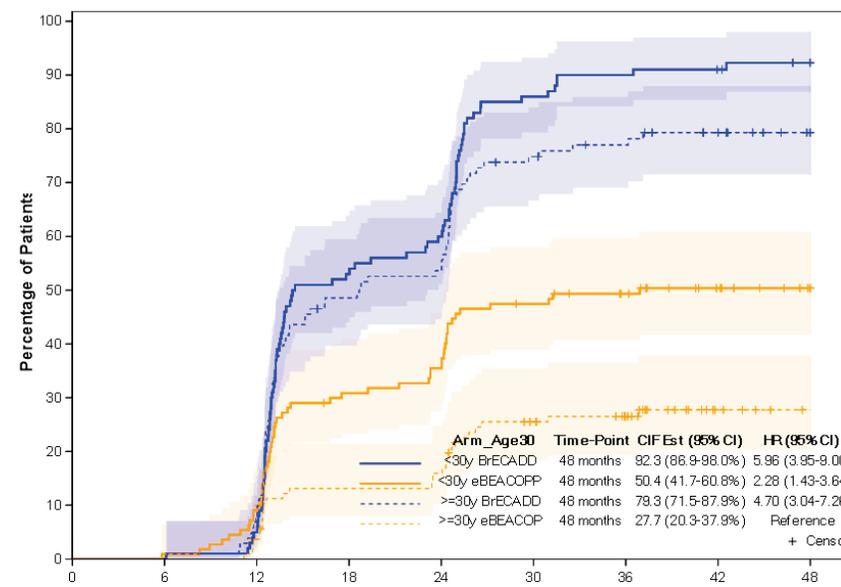
C4: 92.0 %

C6: 75.8%

C4: 41.0%
C6: 37.9 %

	0	6	12	18	24	30	36	42	48
4x BrECADD	121 (0)	121 (0)	113 (0)	56 (0)	48 (0)	18 (1)	12 (2)	8 (5)	3 (8)
4x eBEACOPP	123 (0)	122 (0)	115 (0)	81 (2)	86 (2)	72 (6)	64 (12)	43 (31)	33 (41)
6x BrECADD	76 (0)	76 (0)	71 (0)	41 (1)	37 (1)	22 (1)	18 (2)	14 (5)	9 (10)
6x eBEACOPP	84 (0)	84 (0)	87 (1)	74 (2)	71 (2)	57 (3)	51 (8)	43 (16)	37 (23)

men: Effect of age



<30y: 92.3 %

≥30y: 79.3 %

<30y: 50.4 %

≥30y: 27.7 %

	0	6	12	18	24	30	36	42	48
<30y BrECADD	100 (0)	100 (0)	95 (0)	47 (0)	40 (0)	14 (0)	10 (0)	8 (1)	5 (3)
<30y eBEACOPP	111 (0)	110 (0)	101 (0)	75 (2)	70 (2)	56 (3)	50 (7)	39 (17)	32 (25)
>=30y BrECADD	101 (0)	101 (0)	93 (0)	51 (1)	46 (1)	24 (2)	20 (4)	14 (9)	7 (15)
>=30y eBEACOPP	108 (0)	108 (0)	103 (1)	92 (2)	89 (2)	75 (6)	67 (13)	49 (30)	40 (39)

GHSB HD21 Studie: Abs P1100

TREATMENT EFFECTS OF BRECADD ON HEALTH-RELATED QUALITY OF LIFE: AN ANALYSIS OF PATIENT REPORTED OUTCOMES IN THE RANDOMIZED INTERNATIONAL PHASE III GERMAN HODGKIN STUDY GROUP HD21 TRIAL.

- In total, 917 patients consented to the HRQoL study and provided at least one valid HRQoL score.
- After two cycles of chemotherapy, patients reported with BrECADD significantly less sensory peripheral neuropathy ($\beta=-0.13$, $p<0.001$), cognitive fatigue ($\beta=-0.07$, $p=0.038$) and dyspnea ($\beta=-0.11$, $p=0.0016$) as compared to eBEACOPP .
- After four cycles, corresponding to the end of treatment for the majority of well-responding patients, we observed significant improvements with BrECADD in peripheral neuropathy, dyspnea, physical functioning and role functioning . These differences were not found in poor-responding patients treated with six cycles.
- In the first and second year after treatment, patients in the BrECADD group reported significantly less symptoms and higher functioning compared to eBEACOPP, most notable a higher global health status (1st year: $\beta=0.09$, $p=0.024$; 2nd year: $\beta=0.11$, $p=0.0089$).

GHSB HD21 Studie: Abs P1100

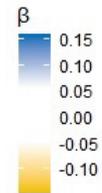
TREATMENT EFFECTS OF BRECADD ON HEALTH-RELATED QUALITY OF LIFE: AN ANALYSIS OF PATIENT REPORTED OUTCOMES IN THE RANDOMIZED INTERNATIONAL PHASE III GERMAN HODGKIN STUDY GROUP HD21 TRIAL.

Treatment effects of BrECADD vs. BEACOPP

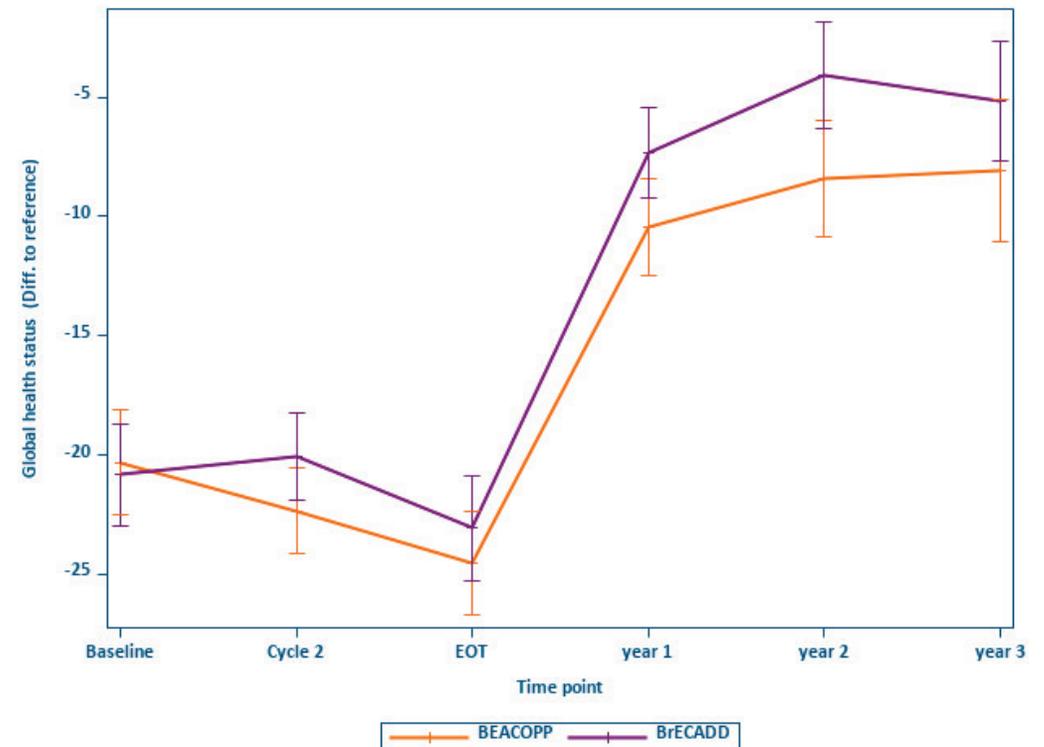
Global health status (positive numbers are favorable effects of BrECADD)					
Global health status (QLQ-C30)	c2	EOT-4	EOT-6	year 1	year 2
	0.05	0.04	0.02	0.09*	0.11**

Functioning (positive numbers are favorable effects of BrECADD)					
	c2	EOT-4	EOT-6	year 1	year 2
Cognitive functioning (QLQ-C30)	0.05	-0.01	0.08	0.03	0.1*
Emotional functioning (QLQ-C30)	0.06	0.04	0.01	0.04	0.16***
Physical functioning (QLQ-C30)	0.03	0.09*	-0.05	0.07	0.08
Role functioning (QLQ-C30)	0.03	0.11*	-0.04	0.03	0.04
Social functioning (QLQ-C30)	0.03	0.07	0.03	0.09*	0.11*

Symptoms (negative numbers are favorable effects of BrECADD)					
	c2	EOT-4	EOT-6	year 1	year 2
Sensory PNP (CIPN20)	-0.13***	-0.09*	-0.01	-0.04	-0.07
Motor PNP (CIPN20)	-0.06	-0.09*	-0.08	-0.05	-0.05
Physical Fatigue (FA12)	-0.03	-0.08	0.01	-0.02	-0.07
Emotional Fatigue (FA12)	-0.01	0	-0.05	-0.03	-0.11*
Cognitive Fatigue (FA12)	-0.07*	0.03	-0.01	0.03	0
Fatigue (QLQ-C30)	-0.03	-0.09	0.01	-0.03	-0.09*
Pain (QLQ-C30)	-0.06	-0.02	-0.06	-0.12**	-0.08
Dyspnoea (QLQ-C30)	-0.11**	-0.14**	-0.07	-0.05	-0.12**
Sleep (QLQ-C30)	-0.07	-0.02	-0.06	-0.12**	-0.15***



Global Health status in the BrECADD and BEACOPP group: deviations from German reference values over time



Zusammenfassung | Take-Home-Messages

Können wir das eBEACOPP Schema durch Brentuximab vedotin modifizieren und relevant im Nutzen-Risiko Verhältnis verbessern? Die GHSG HD21

- Das neue BrECADD-Schema ist besserverträglich als eBEACOPP (d.h. schwere organische oder hämatologische Toxizitäten)
 - > 99% der Patienten zeigen TRMB mehr nach einem Jahr, auch PNP hat sich dann praktisch komplett erholt.
 - Gonadale Funktion (FSH) erholt sich > 95% der Frauen und sehr gut vergleichbar zur Erholungsrate nach ABVD
 - QoL ist überlegen und erreicht die Referenzwerte der gesunden Kontrollpopulation
 - BrECADD ist wirksamer als eBEACOPP
 - Bisher bestes erreichtes PFS bei 4 Jahren von 94.3%.
 - PFS Benefit gilt für alle Risikogruppen.
 - 64% sind PET2 negative und benötigen nur 4 Zyklen BrECADD (12 Wochen). In dieser Subgruppe liegt das PFS sogar 96.8% nach 4 Jahren.
- Bisher unerreichtes Nutzen-Risiko Verhältnis von PET2-gesteuertem BrECADD. Wir empfehlen es als SOC für erwachsene PatientInnen mit Erstdiagnose eines klassischen Hodgkin Lymphoms in fortgeschrittenen Stadien.

Die Kurzpräsentationen sind online unter

www.lymphome.de/eha2024

Für den Inhalt verantwortlich:

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