Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

KML-Expert:innen berichten

17th ICML 2023 LUGANO

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Expert:innen berichten zu Lymphomen & Leukämien

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Hodgkin Lymphom (HL)

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – ICML2023 wird in Kooperation mit fünf unterstützenden Firmen durchgeführt.
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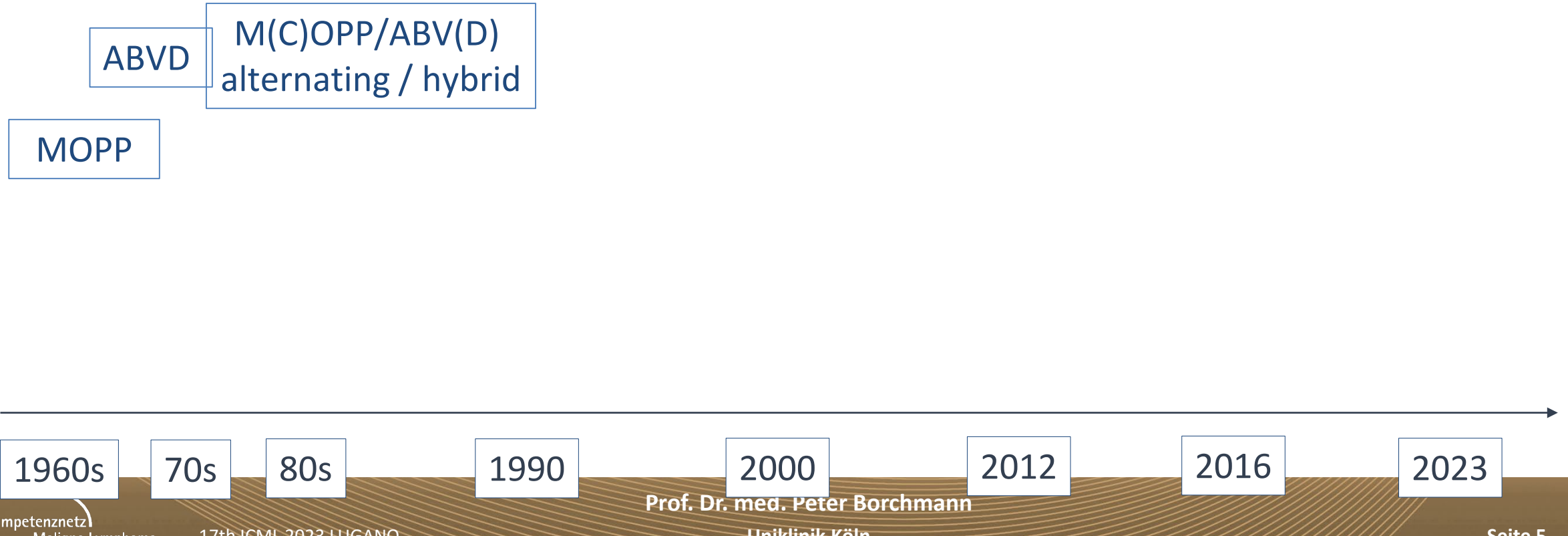
Honoraria	Takeda Oncology, Novartis, BMS, Roche, MSD, Celgene, Miltenyi Biotech, Gilead, Abbvie, Incyte
Funding scientific research	Takeda Oncology, MSD, Novartis, Incyte
Other financial relationships	–
Intangible conflicts of interest	–

Kapitel 1

Erstlinientherapie der fortgeschrittenen Stadien:
ICI-AVD, $ABVD_{DD\text{-}DI}$ oder BrECADD?

Academic research drives the treatment of Hodgkin lymphoma since decades



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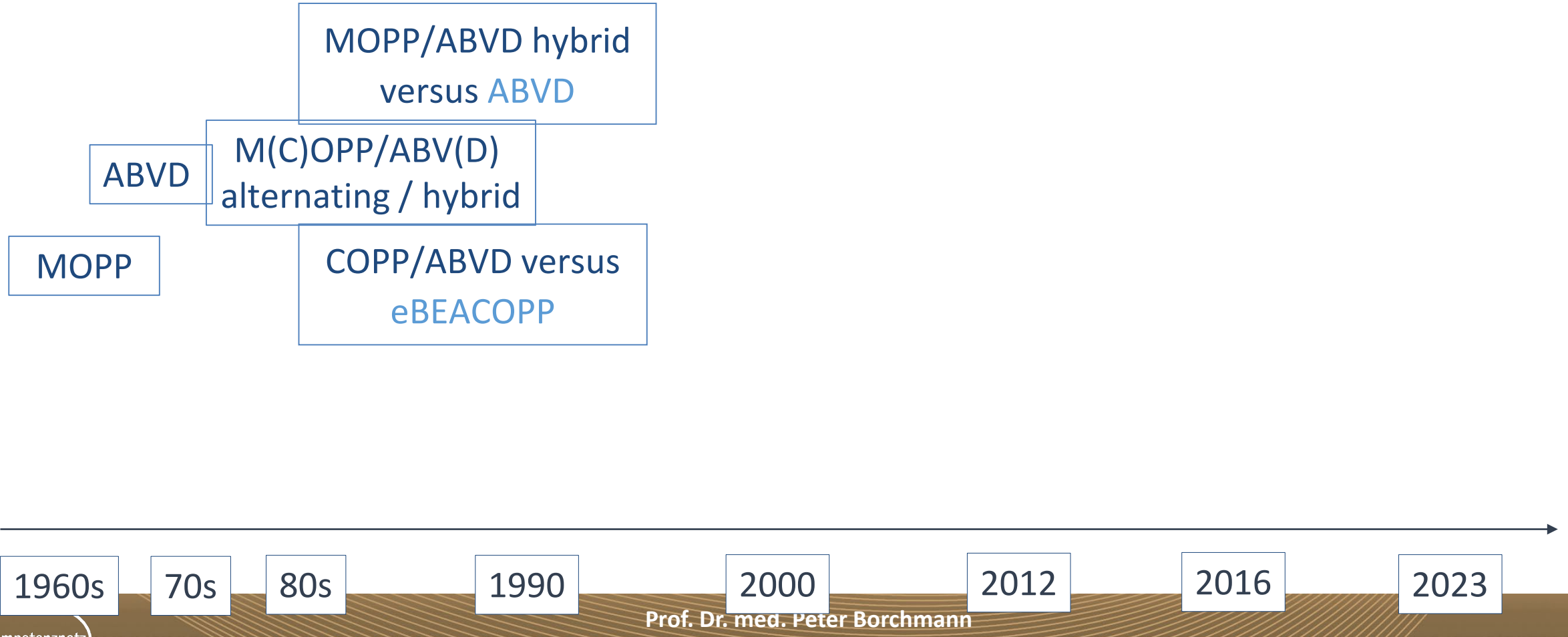

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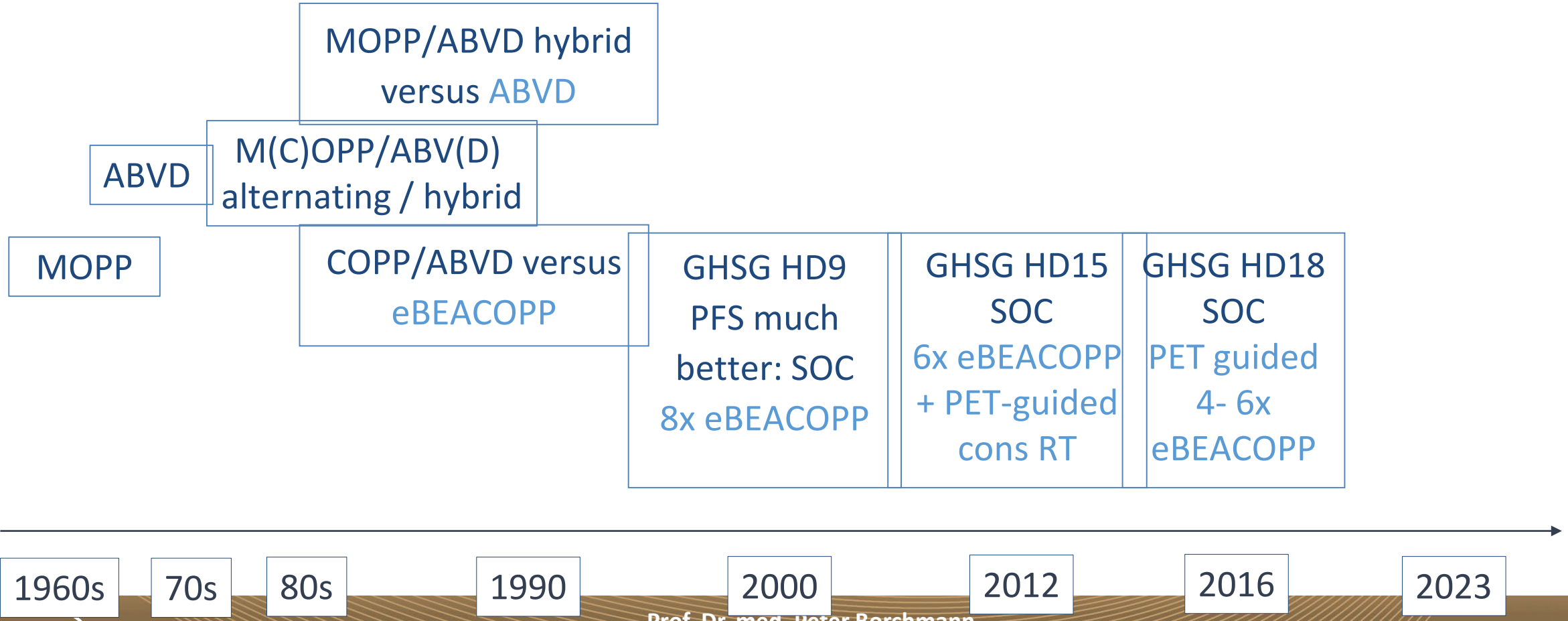

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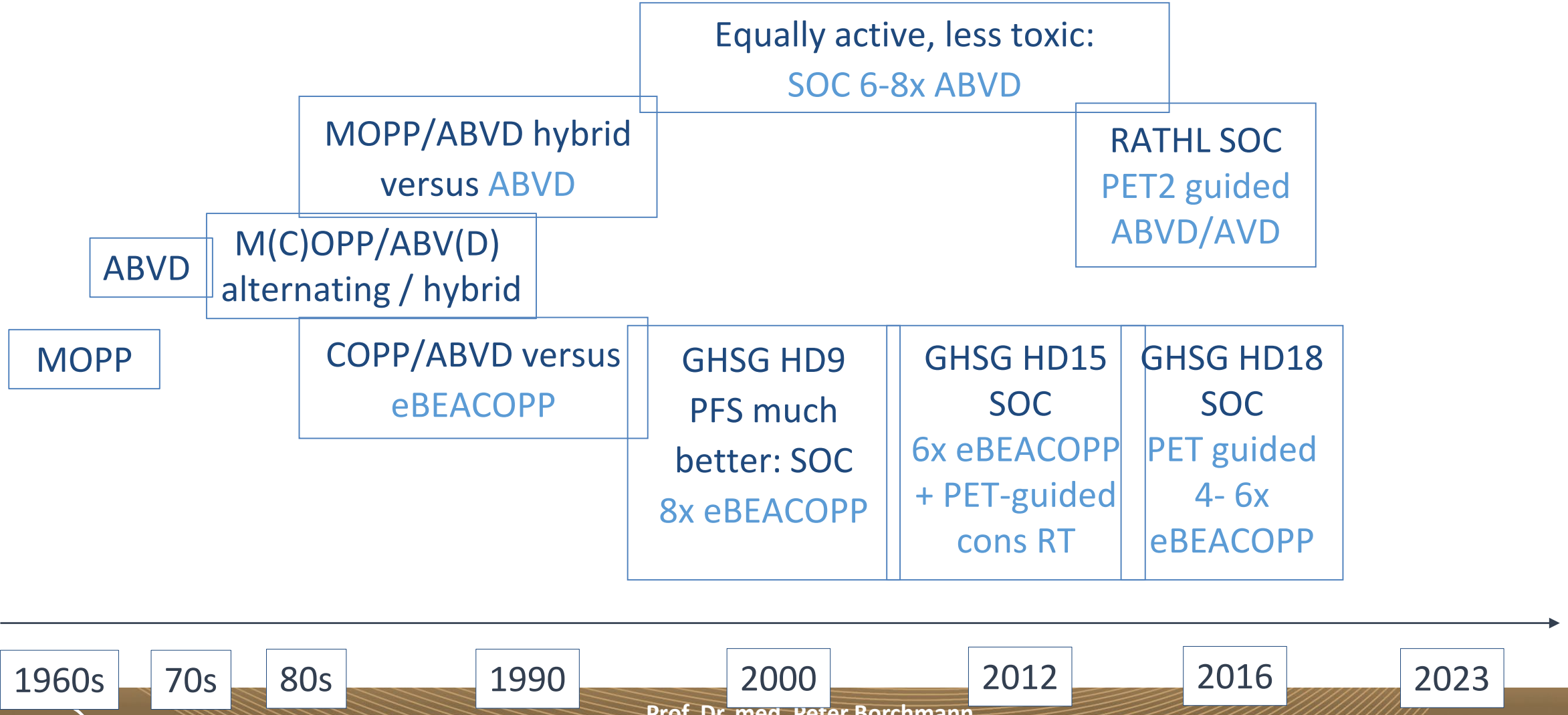

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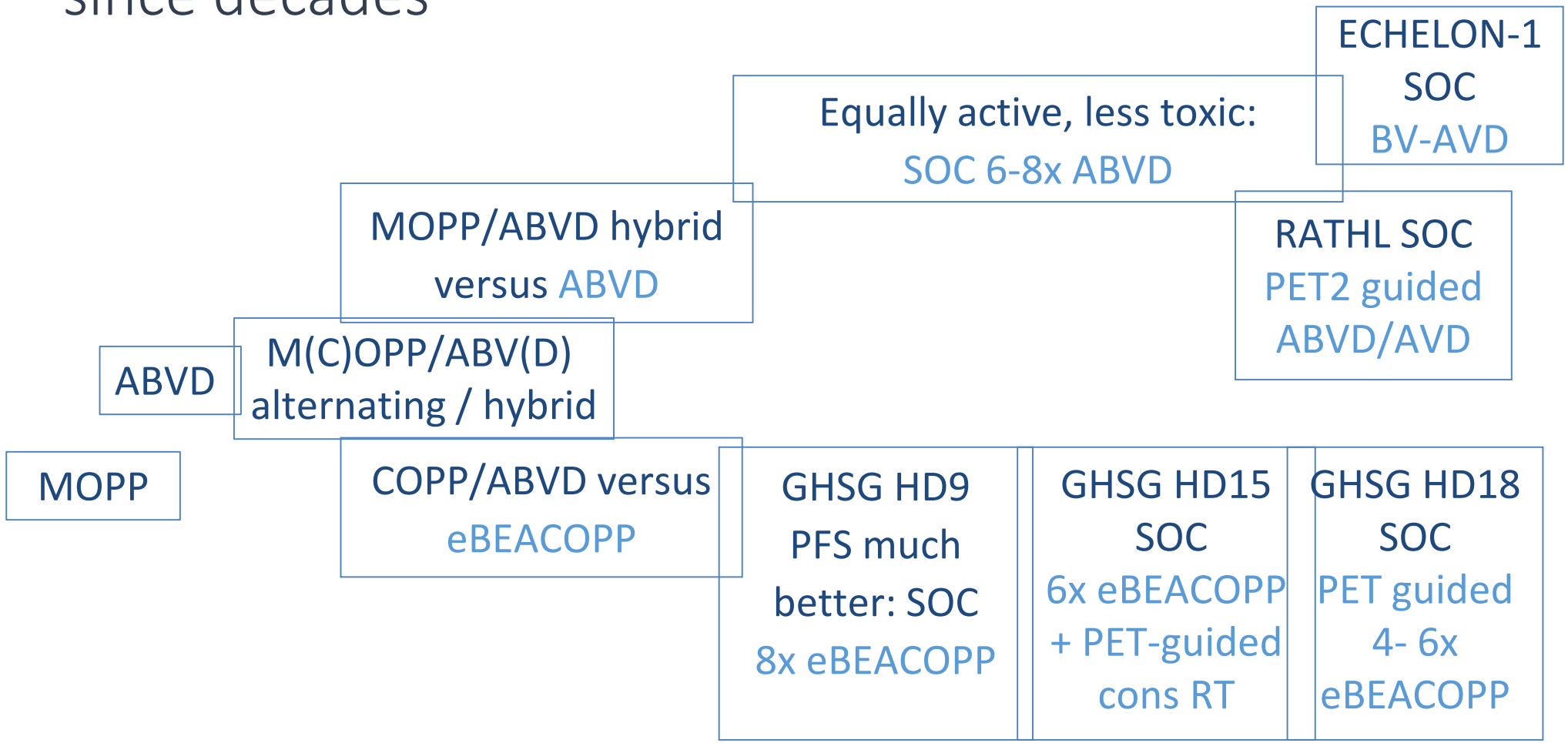

Academic research drives the treatment of Hodgkin lymphoma since decades

- 6x Nivo-AVD superior to 6x BV-AVD?

SWOG S1826
N-AVD > BV-AVD

- non-PET2-guided densified and intensified ABVD superior to PET2-guided A(B)VD?

FIL-Rouge
$ABVD_{DD-DI}$ > PET2-A(B)VD

- individualized PET2-guided BrECADD not inferior to PET2-guided eBEACOPP?

GHSG HD21
SOC
PET guided
4- 6x
BrECADD

1960s | 70s | 80s | 1990 | 2000 | 2012 | 2016 | 2023

Academic research drives the treatment of Hodgkin lymphoma since decades

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Abs No 4: Frontline intensified ABVD demonstrates superior efficacy than PET-adapted ABVD in advanced Hodgkin Lymphoma: the FIL-Rouge Phase 3 Trial by the Fondazione Italiana Linfomi

Abs 4 Pinto et al

Dose density & Dose intensity

ABVD DD-DI (repeated every 21 days) - Cycles 1 to 4			
Doxorubicin	35 mg/m^2	i.v.	days 1,11
Bleomycin	10,000 units/m^2	i.v.	days 1,11
Vinblastine	6 mg/m^2	i.v.	days 1,11
Dacarbazine	375 mg/m^2	i.v.	days 1,11
G-CSF	263 μg	s.c.	days 6-8, 17-19

Dose density

ABVD DD (repeated every 21 days) - Cycles 5 to 6			
Doxorubicin	25 mg/m^2	i.v.	days 1,11
Bleomycin	10,000 units/m^2	i.v.	days 1,11
Vinblastine	6 mg/m^2	i.v.	days 1,11
Dacarbazine	375 mg/m^2	i.v.	days 1,11
G-CSF	263 μg	s.c.	days 6-8, 17-19

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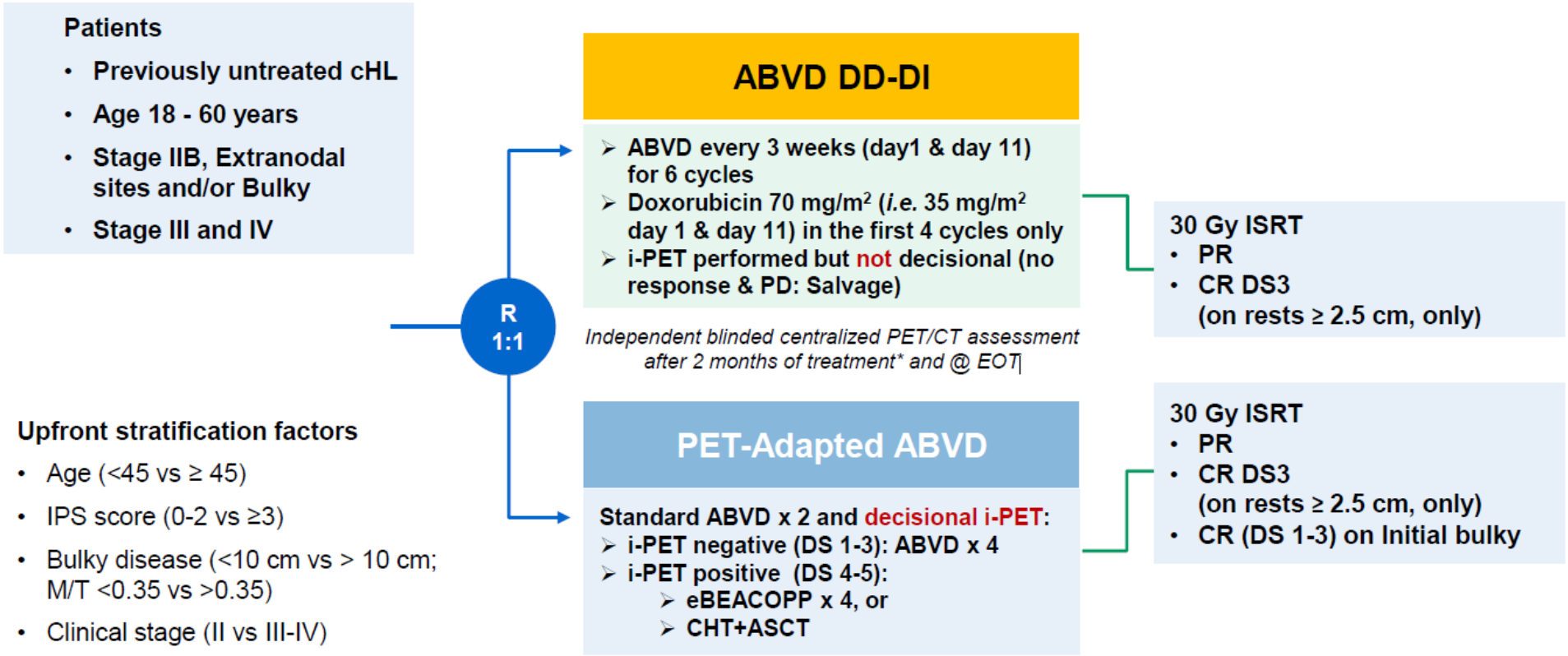

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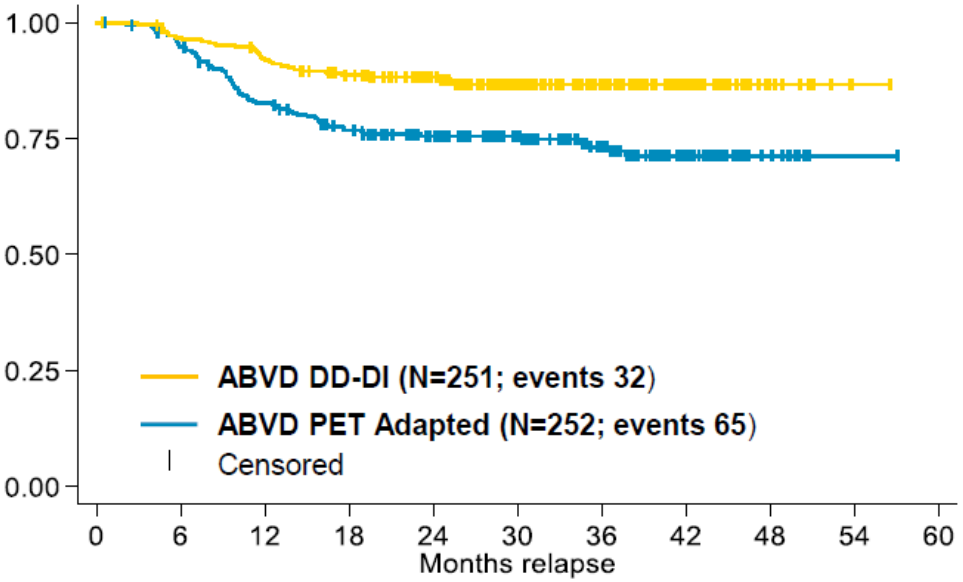


No. of patients at risk											
ABVD DD-DI	251	240	227	208	179	132	97	48	11	1	0
PET-adapted ABVD	252	236	203	182	150	121	85	48	11	1	0

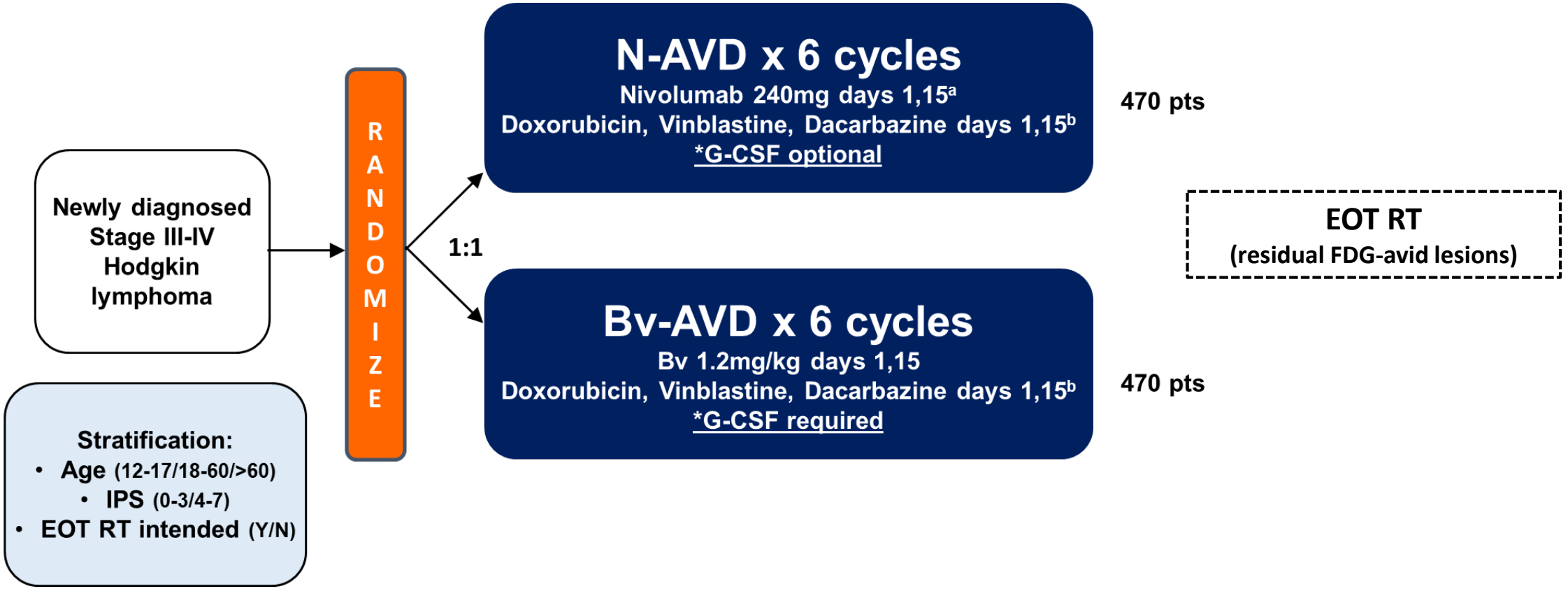
HR 0.44 (P<0.0002)
95% CI: 0.28 - 0.67

- ABVD DD-DI demonstrated a **56% reduction in the relative risk of disease progression, relapse, or death** versus PET-adapted ABVD

- **35-month PFS:**
  86.7% with ABVD DD-DI versus
  73.2% with PET-adapted ABVD
  (**Δ=13.46%**)

Nivolumab(N)-AVD Improves Progression-Free Survival Compared to Brentuximab Vedotin(BV)-AVD in Advanced Stage (AS) Classic Hodgkin Lymphoma (HL): Results of SWOG S1826

Herrera et al.



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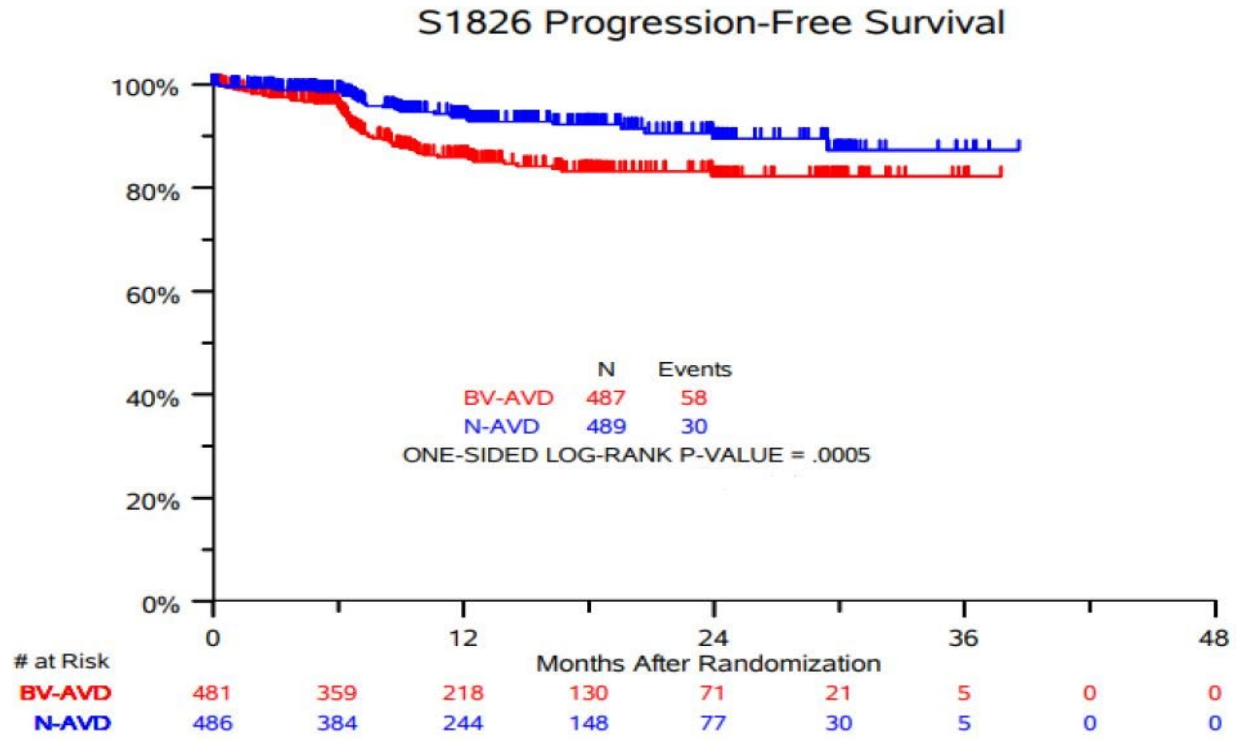


The 1-y PFS per ITT

N-AVD: 94%, versus BV-AVD: 86%

[HR 0.48, 99% CI 0.27-0.87, one-sided p=0.0005)

Nota bene:

significance was reached at a 99% CI due to interim analysis

cons RTx was used only in very few patients

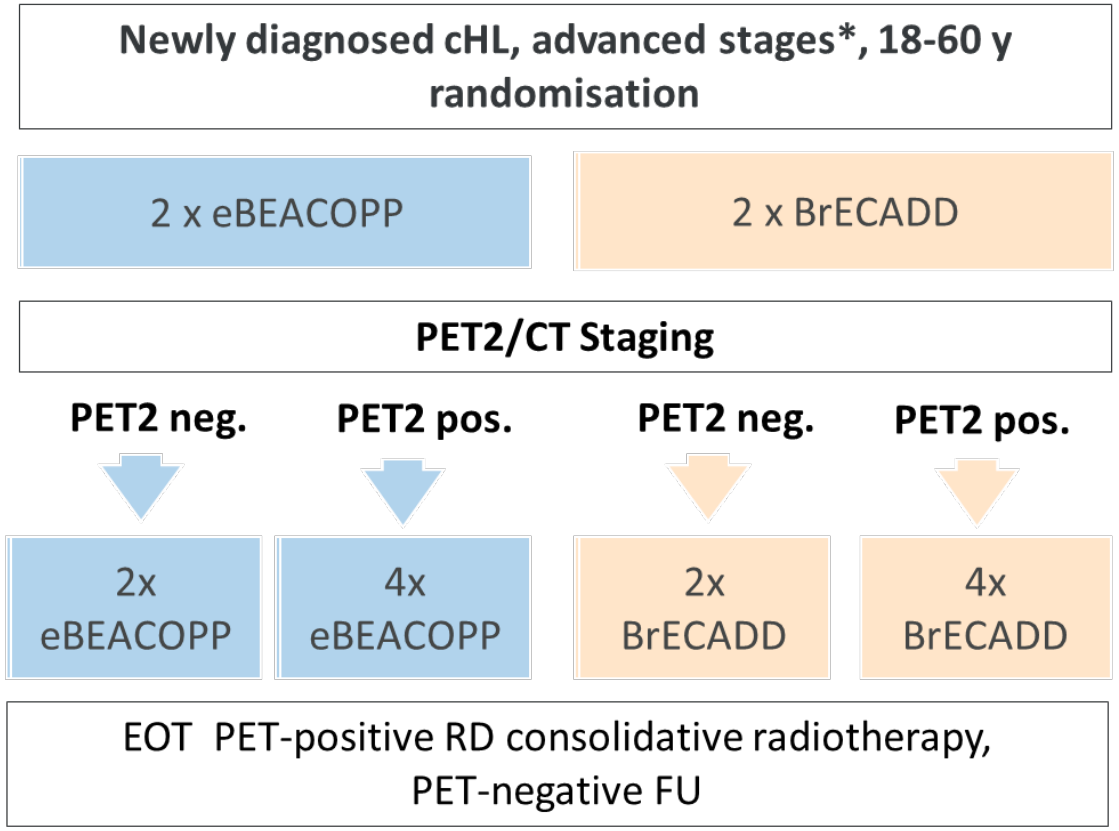
Nivolumab(N)-AVD Improves Progression-Free Survival Compared to Brentuximab Vedotin(BV)-AVD in Advanced Stage (AS) Classic Hodgkin Lymphoma (HL): Results of SWOG S1826

Herrera et al.

Toxicity	N-AVD n = 483		Bv-AVD n = 473	
	Any Grade No (%)	Grade ≥ 3 No (%)	Any Grade No (%)	Grade ≥ 3 No (%)
ALT increased	**156 (32%)**	**22 (5%)**	**194 (41%)**	**22 (5%)**
AST increased	**120 (25%)**	**12 (2%)**	**153 (32%)**	**13 (3%)**
Rash maculo-papular	51 (11%)	4 (1%)	58 (12%)	0 (0)
Hypothyroidism	**33 (7%)**	**1 (0%)**	**3 (1%)**	**0 (0)**
Rash acneiform	18 (4%)	0 (0)	12 (3%)	0 (0)
Pneumonitis	10 (2%)	2 (0%)	15 (3%)	10 (2%)
Gastritis	10 (2%)	3 (1%)	8 (2%)	0 (0)
Hyperthyroidism	**14 (3%)**	**0 (0)**	**0 (0)**	**0 (0)**
Colitis	5 (1%)	1 (0%)	6 (1%)	4 (1%)

BrECADD is non-inferior to eBEACOPP in patients with advanced stage classical Hodgkin Lymphoma: efficacy results of the GHSG phase III HD21 trial.

Borchmann et al.



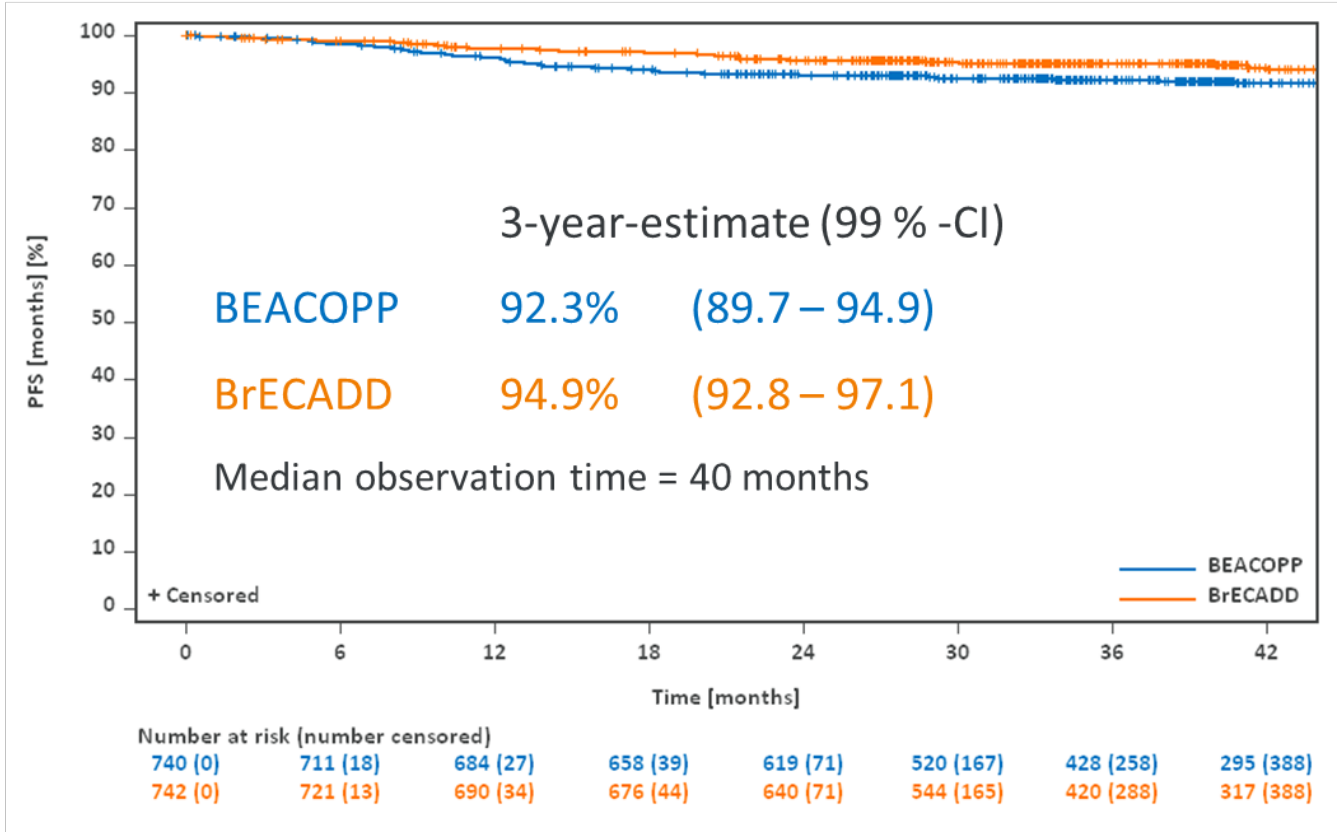
* Includes stage IIB with RF LMM or ED, and stage II and IV

Non-inferiority for efficacy (PFS, controlled by blinded central review)

- interim analysis of efficacy with estimated 36 months of median follow-up
- alpha spending function and actual information rate were used to calculate efficacy bounds for early stopping
- with an information rate of 65% (100 /154 events) and a pre-defined non-inferiority margin = 1.69 (90.5% BEACOPP/ 84.5 % BrECADD),
- *a point estimate of Hazard Ratio bound < 1,02 would show statistical significance of non-inferiority (termination of the trial for efficacy)*

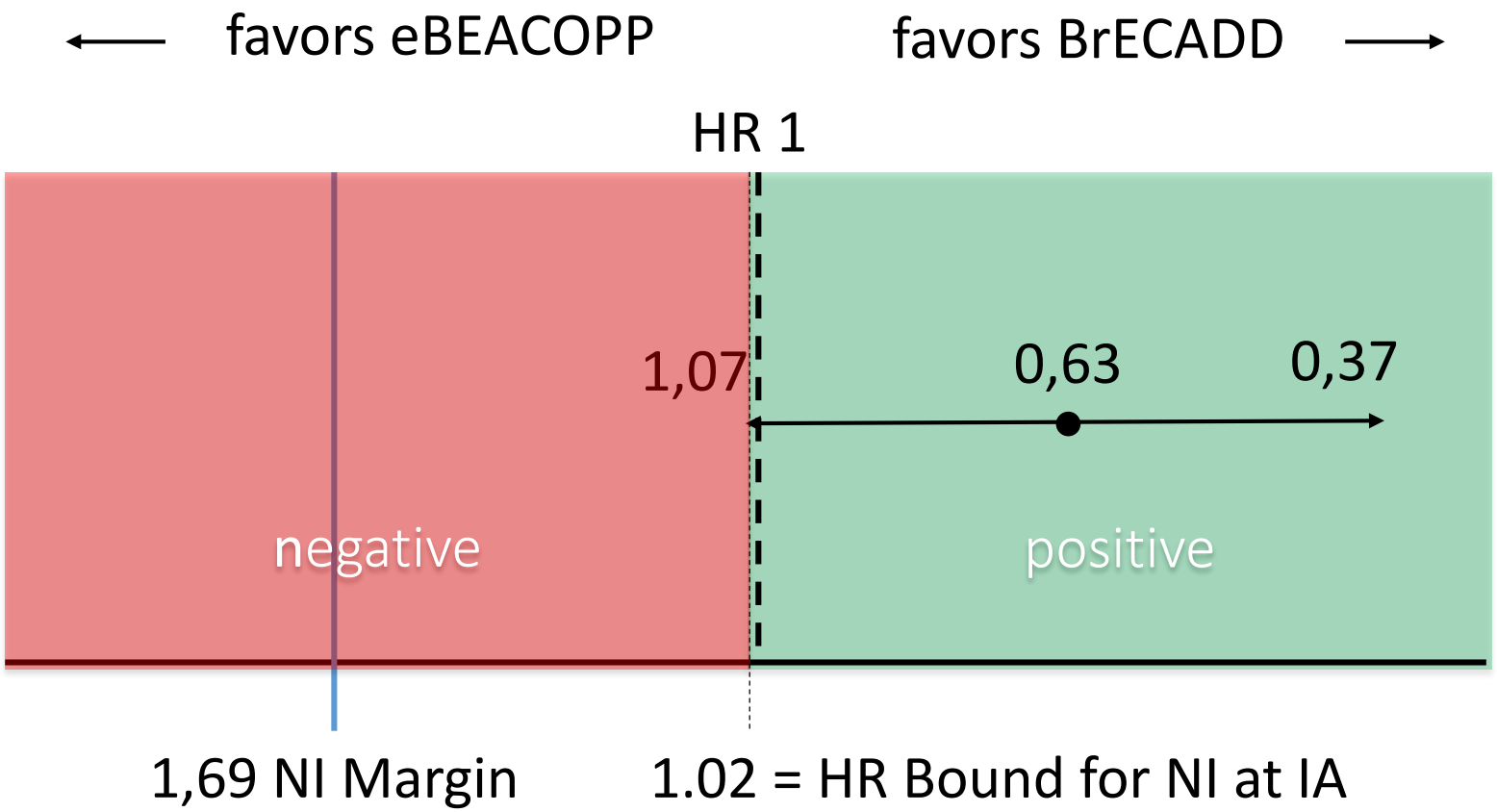
BrECADD is non-inferior to eBEACOPP in patients with advanced stage classical Hodgkin Lymphoma: efficacy results of the GHSG phase III HD21 trial.

Borchmann et al. HD21 PFS – ITT



	eBEACOPP N=740		BrECADD N=742	
	n	%	n	%
Progression/Relapse	55	**7.4**	32	**4.3**
Progression	14	**1.9**	5	**0.7**
Early Relapse, FU <= 1 year	23	**3.1**	11	**1.5**
Late Relapse, FU > 1 year	18	2.4	16	2.2
Death without previous PRO or REL	6	0.9	7	0.9
PFS events, total	**61**	**8.4**	**39**	**5.3**

HD21 Test of non-inferiority



- HR bound of 1,02 is excluded and *non-inferiority of BrECADD thus fully established*
- 99% CI for HR 1.07 – 0.37 indicates a *trend towards superiority* (to be determined at final analysis with 95% CI)

Kapitel 1 Erstlinientherapie der fortgeschrittenen Stadien: ICI-AVD, ABVDDD-DI oder BrECADD?

1. FIL-Rouge: ABVD DDDI ist effektiver als PET2-gesteuertes ABVD, aber: PFS von 86% nach 3 Jahren liegt doch deutlich unter dem PFS für das andere eskalierte Schema: eBEACOPP

2. S1826: N-AVD ist nach 1 Jahr besser als BV-AVD und hat ein relativ günstiges Toxizitätsprofil mit wenigen akuten AI-Phänomenen und etwa 10% terminaler Schilddrüsen-Insuffizienz durch Thyreoiditis. Die Kurve für N-AVD ist noch im Fallen begriffen, längere Nachbeobachtung obligat.

3. GHSG HD21: BrECADD ist sicher nicht unterlegen gegenüber eBEACOPP. Im Gegenteil sehen wir einen sehr starken Trend zur Überlegenheit in dieser Zwischenanalyse, die deswegen nun ein endgültiges Ergebnis gezeigt hat. Das Nutzen-Risiko Verhältnis von BrECADD ist ausgezeichnet, so das es denen neuen Standard setzt.

Die Kurzpräsentationen sind online unter

www.lymphome.de/icml2023

Für den Inhalt verantwortlich:

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Lymphom Kompetenz KOMPAKT

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