Two cycles of escalated BEACOPP followed by four cycles of ABVD utilizing early-interim PET/CT scan for patients with advanced high-risk Hodgkin's lymphoma

A. Avigdor, S. Bulvik, I. Levi, E. Dann, A. Nagler,

I. Ben-Bassat and A. Polliack

On behalf of the Israel Cooperative Lymphoma Group

GHLSG-HD9: escBEACOPP is superior to COPP/ABVD

	COPP/ ABVD	Escalated BEACOPP	p
	%		
CR	85	96	NS
Early progression (at 5 yr)	10	2	<0.01
FFTF (at 5 yr)	69	87	<0.01
OS (at 5 yr)	83	91	0.02

Adapted from Diehl V. et al.; NEJM, 2003.

The superiority of escBEACOPP is most evident in patients with a poor IPS

International Prognostic Index	COPP-ABVD	Standard BEACOPP	Increased-Dose BEACOPP
		percent	
Early progression†			
Good (0–1)	10	6	2
Fair (2–3)	11	9	2
Poor (4–7)	18	9	3
Freedom from treatment failure at 5 yr			
Good (0–1)	79	81	92
Fair (2–3)	67	72	87
Poor (4–7)	59	74	82
Overall survival at 5 yr			
Good (0–1)	92	93	95
Fair (2–3)	84	86	90
Poor (4–7)	67	81	82

Diehl V. et al.; NEJM, 2003.

8 X escBEACOPP have high incidence of acute and long term toxicities:

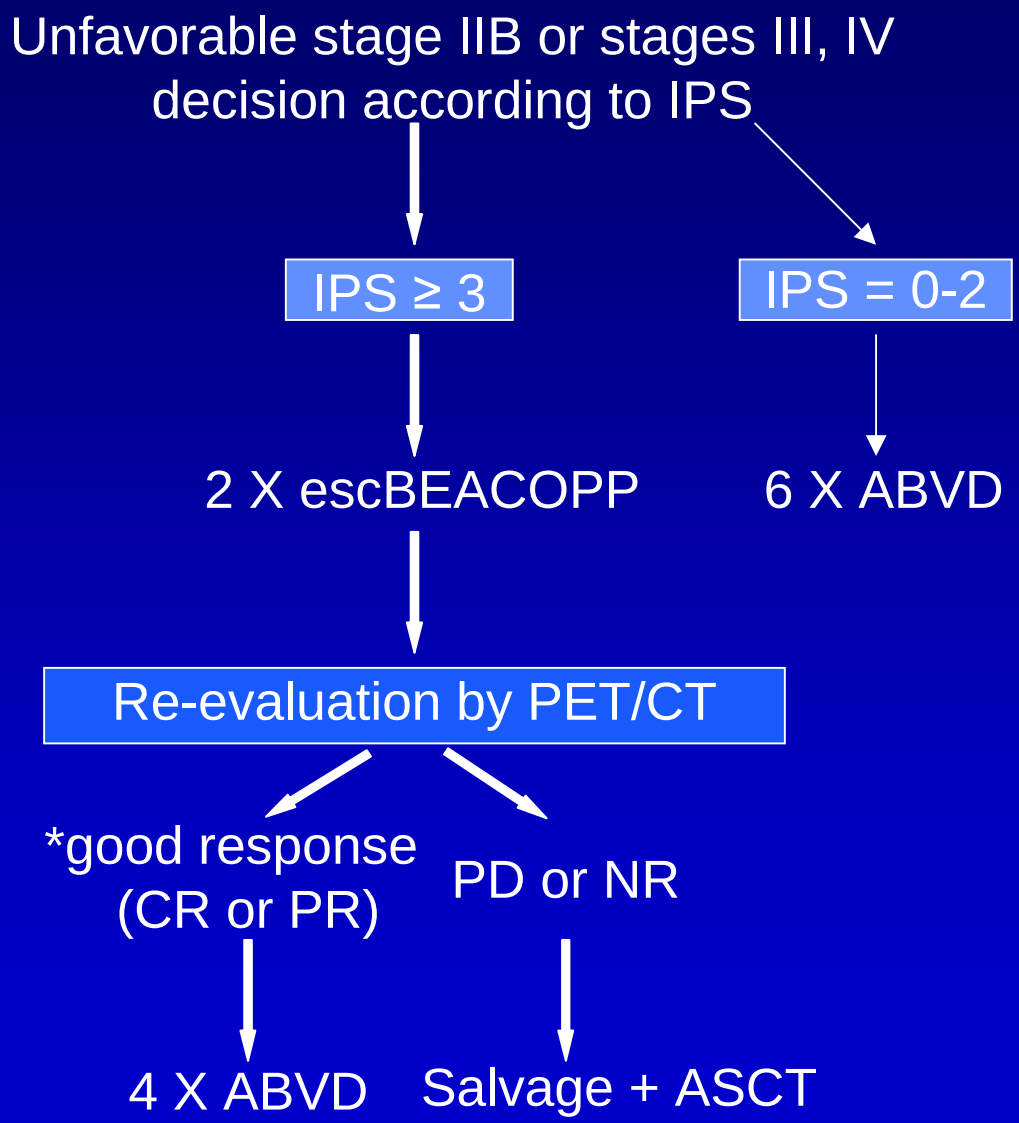
- Grade 3/4 leukopenia (98%), thrombocytopenia (70%), anemia (66%)
- Grade 3/4 infections - 22%
- AML (10 yr) - 3%
- Infertility -male: ~80%, female: ~100%

Two cycles of escBEACOPP followed by four cycles of ABVD in patients with advanced HL and high IPS score: a phase II study

Aims of the study:

- attempt to reduce toxicity while preserving improved initial tumor control
- employ the international prognostic score to tailor treatment at diagnosis
- collect data on early versus late responders according to the findings on PET scans, carried out early after 2 cycles of escBEACOPP

Combined escBEACOPP-ABVD - scheme



*__CR__- PET negative with residual mass of any size

__PR__- residual FDG uptake at previously involved sites & reduction of masses > 50%

PET/CT-FDG analyses

- **PET/CT scans were scored as positive or negative for disease activity based only on visual assessment. Semiquantitative analyses were not used.**
- **Definition of disease status:**
  - CR- PET negativity with or without a residual mass of any size
  - PR- presence of one or more PET-positive residual lesions at previously involved sites and a size reduction of the majority of large masses by >50%
  - PD- >50% increase in the largest diameter of any residual PET-positive lesion identified in the early interim PET/CT or when any new PET-positive findings developed

Characteristics of patients

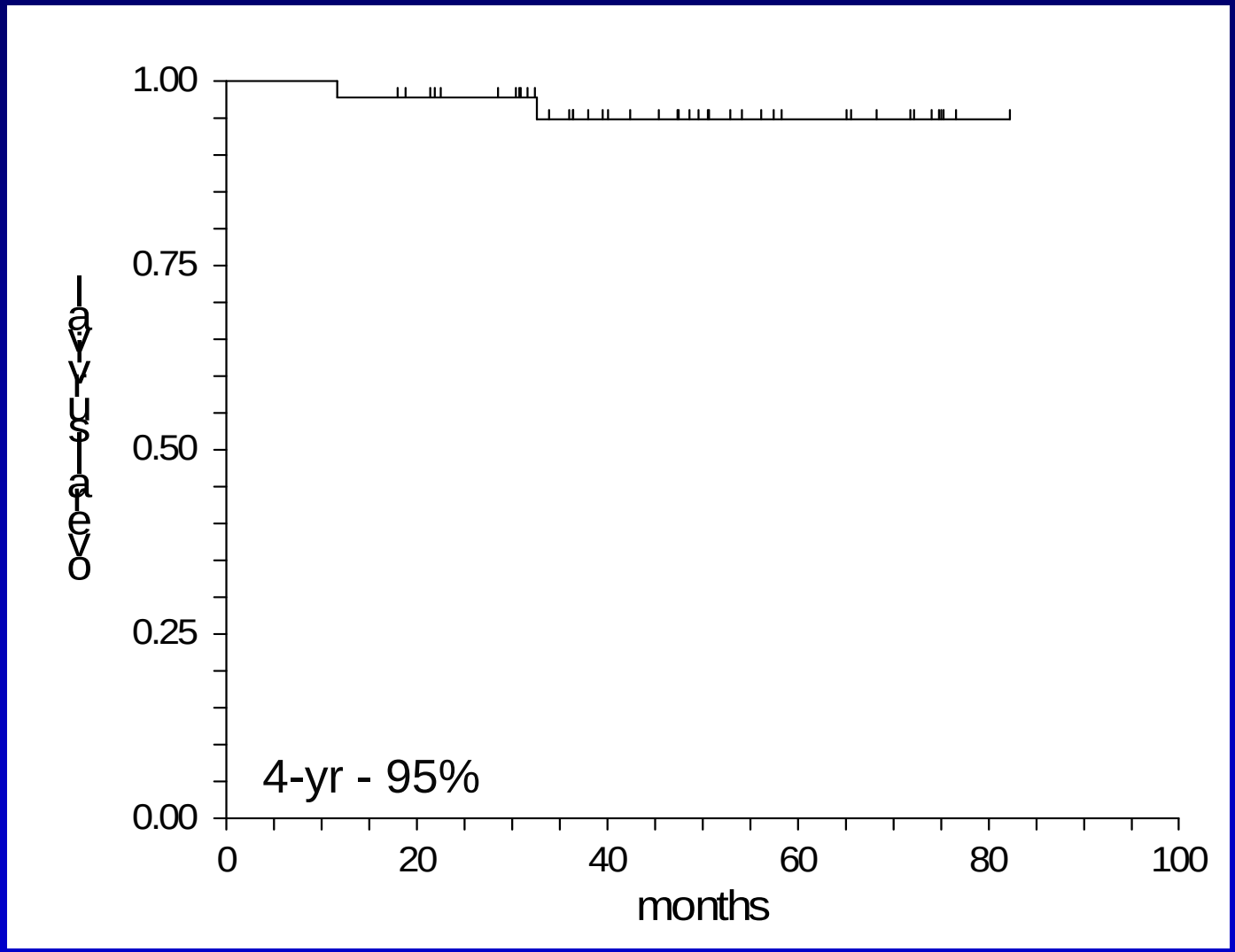
Total	45
Median age yrs (range)	27 (18-59)
Male sex n (%)	32 (71)
Histology: n (%)	
Nodular sclerosis	34 (75)
Mixed cellularity	7 (15)
Unclassified	4 (10)
Stages: n (%)	
IIB	3 (7)
III	9 (20)
IV	33 (73)
Bulky mediastinum n (%)	15 (33)
Extranodal involvement: n (%)	33 (73)
Bone marrow	15
Bone	22
Lung	9
Liver	5
International prognostic score n (%)	
3	31 (69)
4-5	13 (29)
6-7	1 (2)

Response after completing all therapy according to early-interim PET results

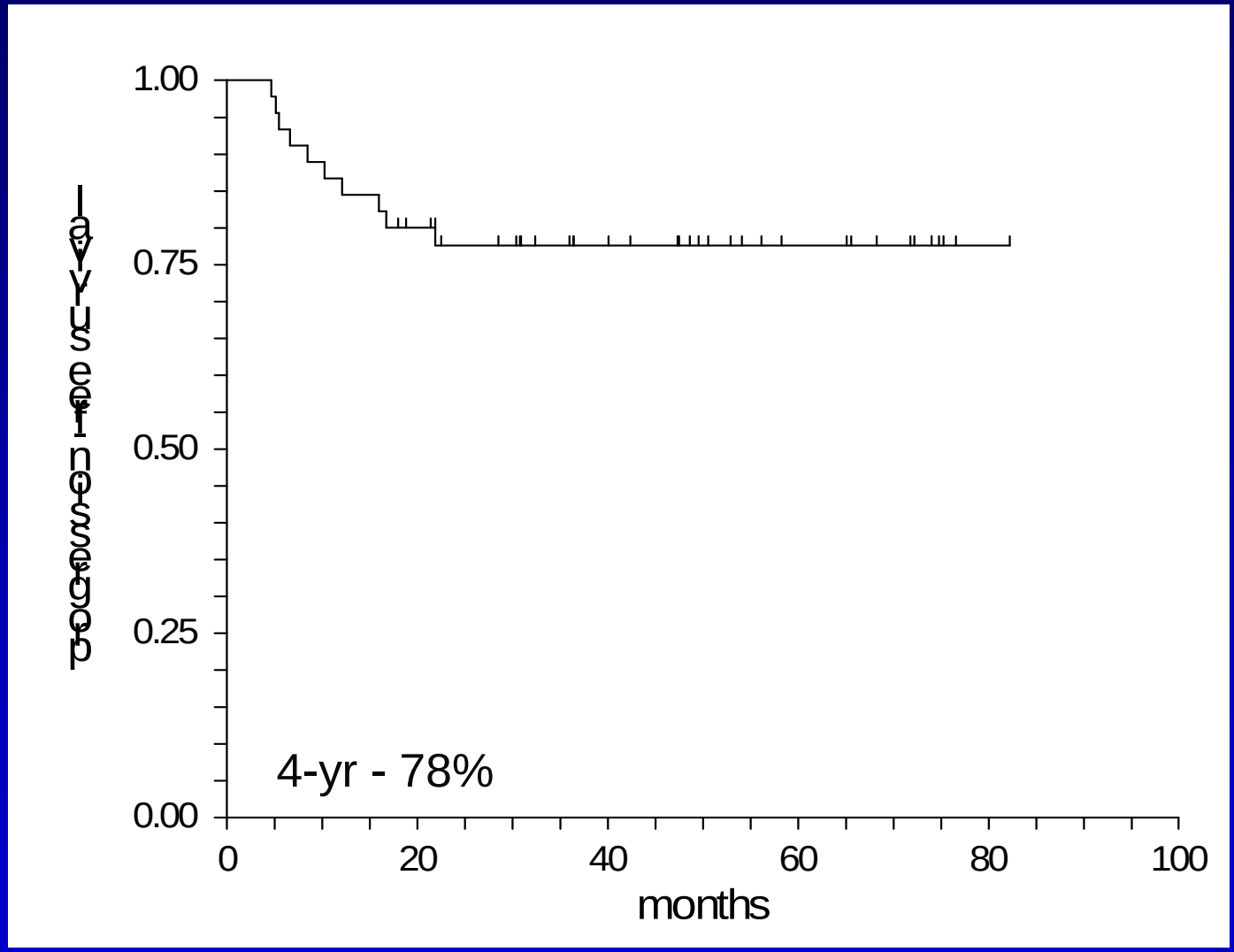
	Early interim PET results		
	Negative n=31 (71%)	Positive n=13 (29%)	Total* n=44
CR	30	9	39 (89%)
PR	-	3	3 (7%)
PD	1	1	2 (4%)

*One patient - non-FDG-avid disease at the time of diagnosis. CR at the end of therapy.

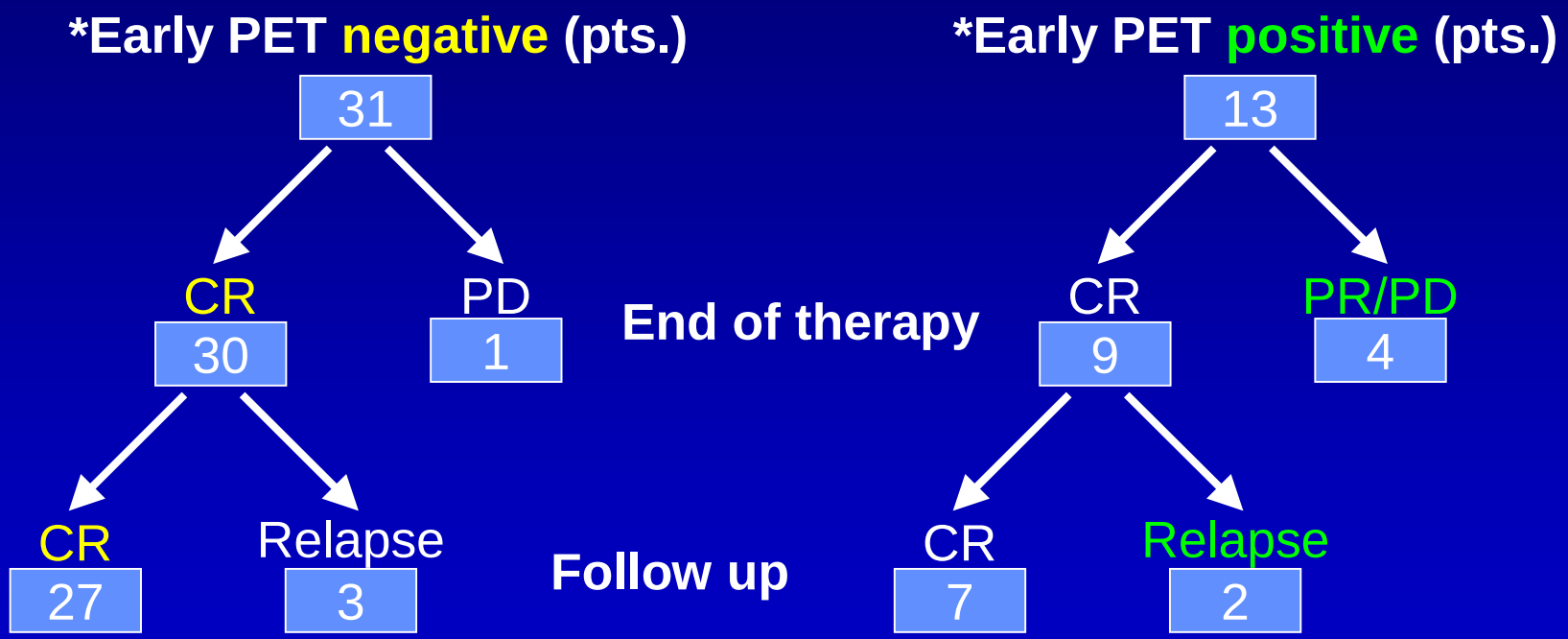
Overall survival



Progression-free survival

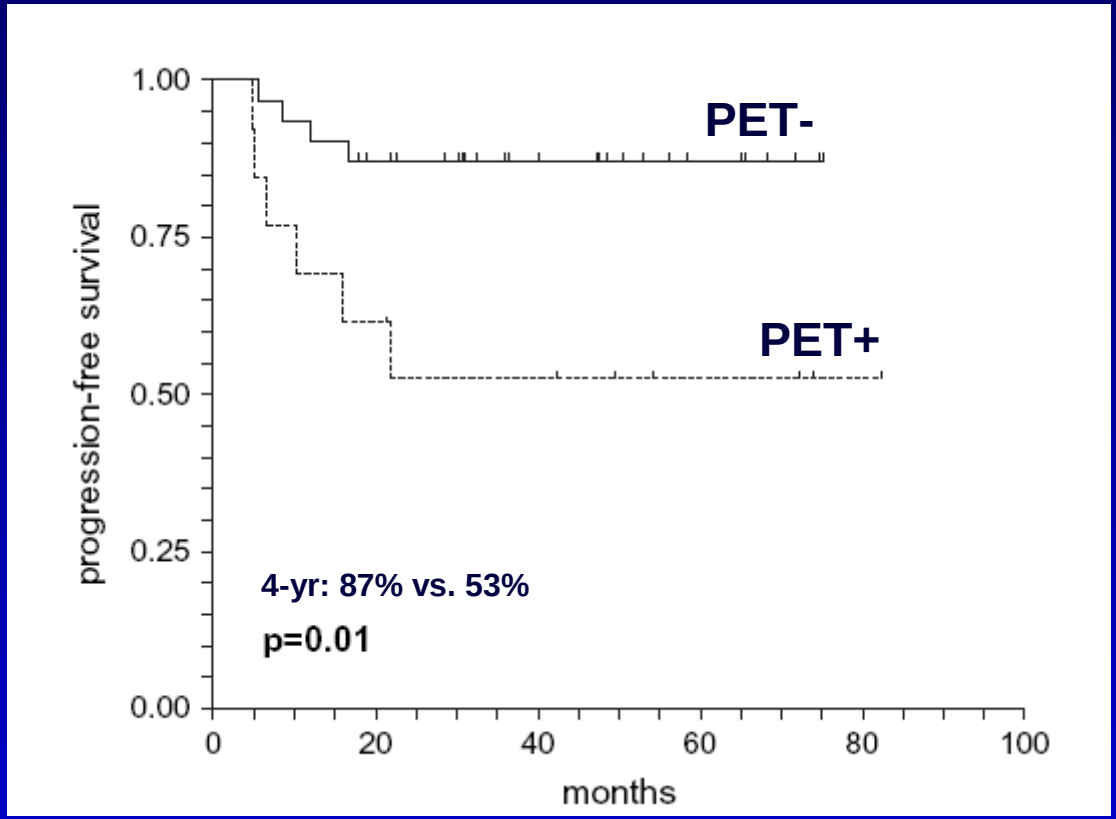


Outcome of patients according to results of early FDG-PET



*non FDG-avid – 1 patient.

The role of early-interim PET as predictive of progression-free survival



- Early PET predicted the outcome in 75% of patients (33/44)
- Positive predictive value – 45%
- Negative predictive value – 87%

Combined escBEACOPP - ABVD: adverse effects

	2 X escBEACOPP	ABVD	All therapy
Leukopenia grade 3-4 (%)	83	24	
Thrombocytopenia grade 3-4 (%)	23	4	
Infections grade 4 (%)	4	0	
Hospitalization (%)	44	12	
Avascular necrosis (n)			1
Cognitive impairment (n)			1
AML/MDS (n)			0
Toxic deaths (n)			0

Two cycles of escBEACOPP followed by four cycles of ABVD in patients with advanced HL and high IPS score: Conclusions

- Therapy is well tolerated and associated with relatively low rates of acute toxicities.
- Higher survival rates than expected for high risk advanced stage HL patients, receiving other ABVD containing regimens
- Early-interim PET had a relatively high NPV but a much lower PPV.
- The results of early-interim PET had a significant long-term prognostic role in the treatment of those patients receiving this regimen.

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