EHA-GBMTA-AHA Hematology Tutorial: New aspects in diagnostic choices and treatment options of hematological malignancies

Session: Hodgkin's Lymphoma

Igor Aurer

What's new in the therapy of Hodgkin's lymphoma?

Prof. Igor Aurer MD, PhD

University Hospital Centre Zagreb

Medical School, University of Zagreb

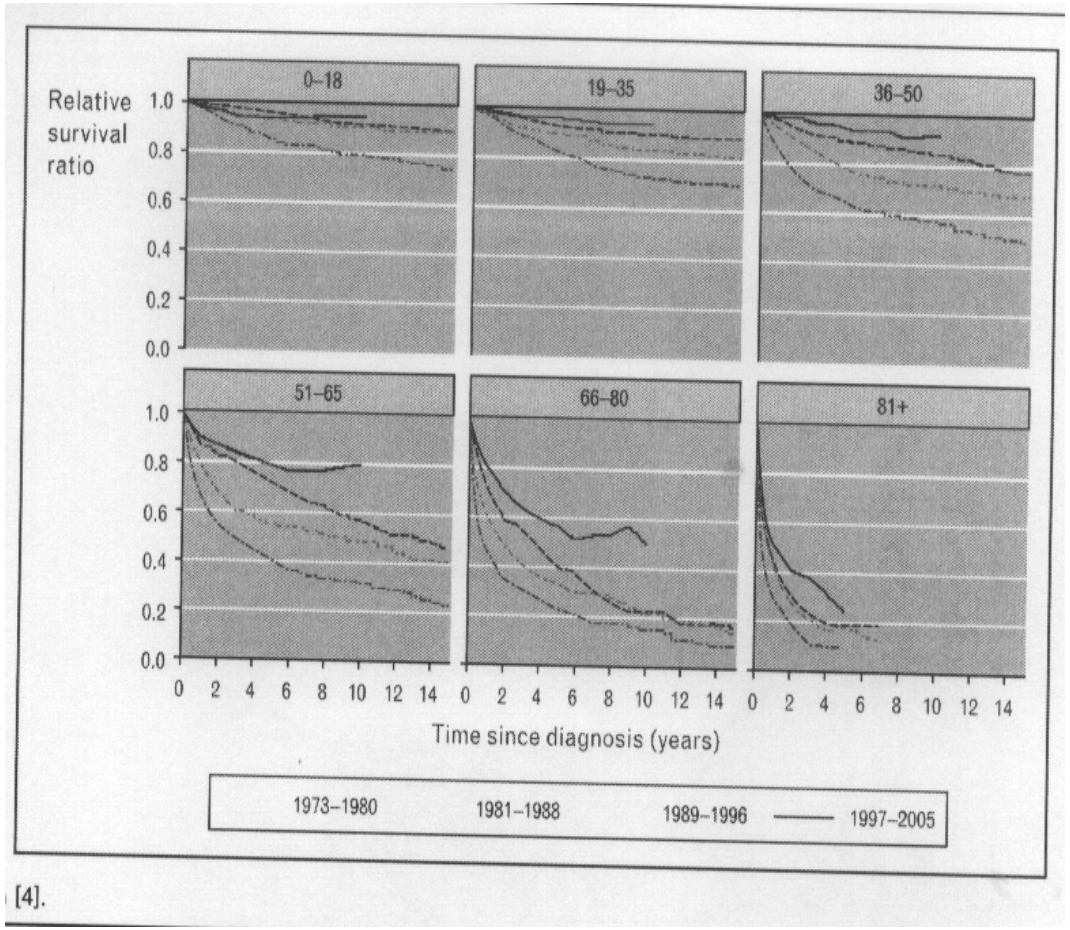
Croatia

Disclosures

Roche
Takeda
Janssen
Astra-Zeneca
Beigene
Eli Lilly
Sobi
Novartis / Sandoz
Genesis / Incyte
Swixx

Outcomes in HL depend on

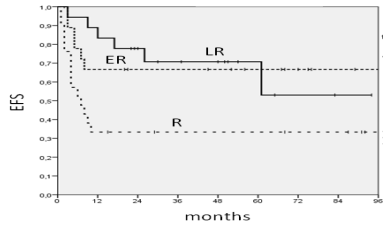
age



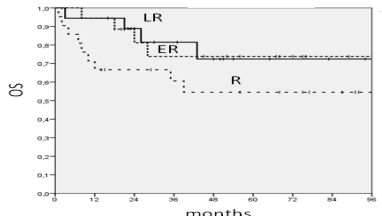
[4].

Bjorkholm et al, Curr Opin Onol 2011

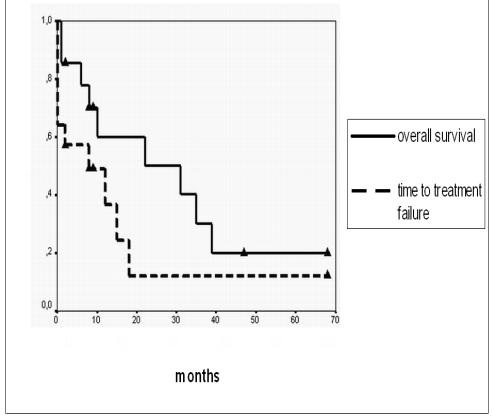
and treatment line



2nd line



Beyond 2nd line



Aurer et al. Ann Hematol 2016

Aurer et al, Onkologie 2005.

Health problems in responding patients

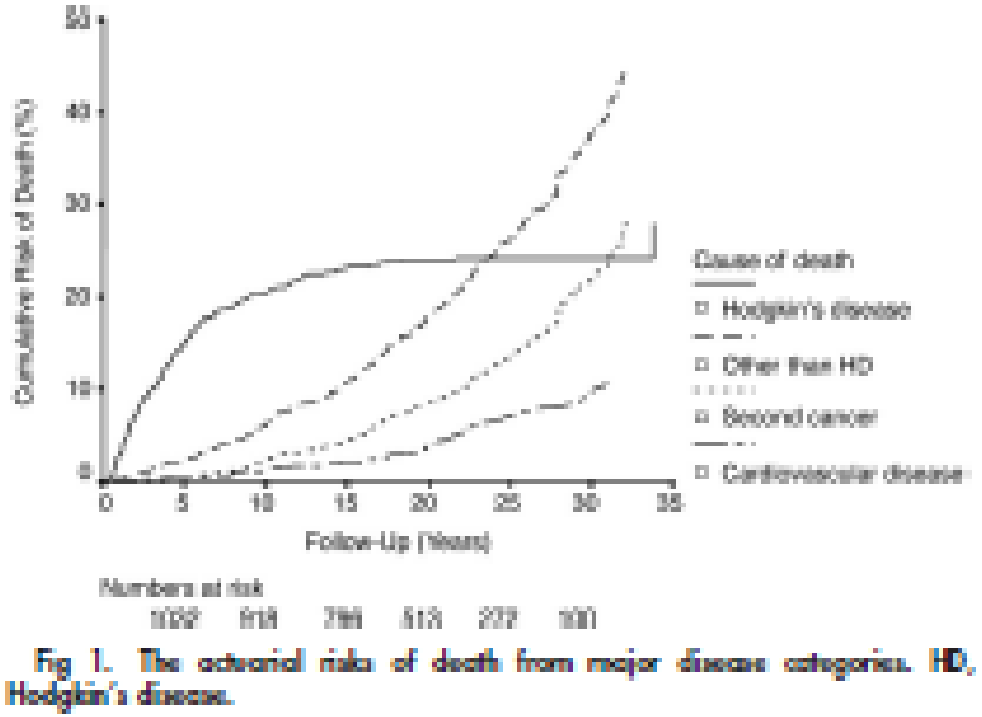


Fig 1. The actuarial risks of death from major disease categories. HD, Hodgkin's disease.

secondary cancers
heart disease

infertility
aseptic hip necroses
thyroid disease
chronic fatigue
...

Aleman et al, JCO 2003

What do we want from new treatment approaches?

Reduce long-term toxicity of front-line treatment in younger

Without jeopardizing efficacy

Improve efficacy of salvage treatments and front-line treatment of elderly

Aim for cure

Armamentarium

Chemotherapy

eBEACOPP, ABVD, AVD, dacarbazine, bendamustine, high-dose chemotherapy

Radiotherapy

3D – 4D linear accelerators

Conjugated monoclonal antibodies = targeted chemotherapy

Brentuximab vedotin

PD1 (checkpoint) blockers

nivolumab, pembrolizumab

Risk assessment

Front-line

Age: younger, fit elde

Stage: limited favora

Later lines

Primary refractory, e

Transplantable vs. n

GHSG criteria

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

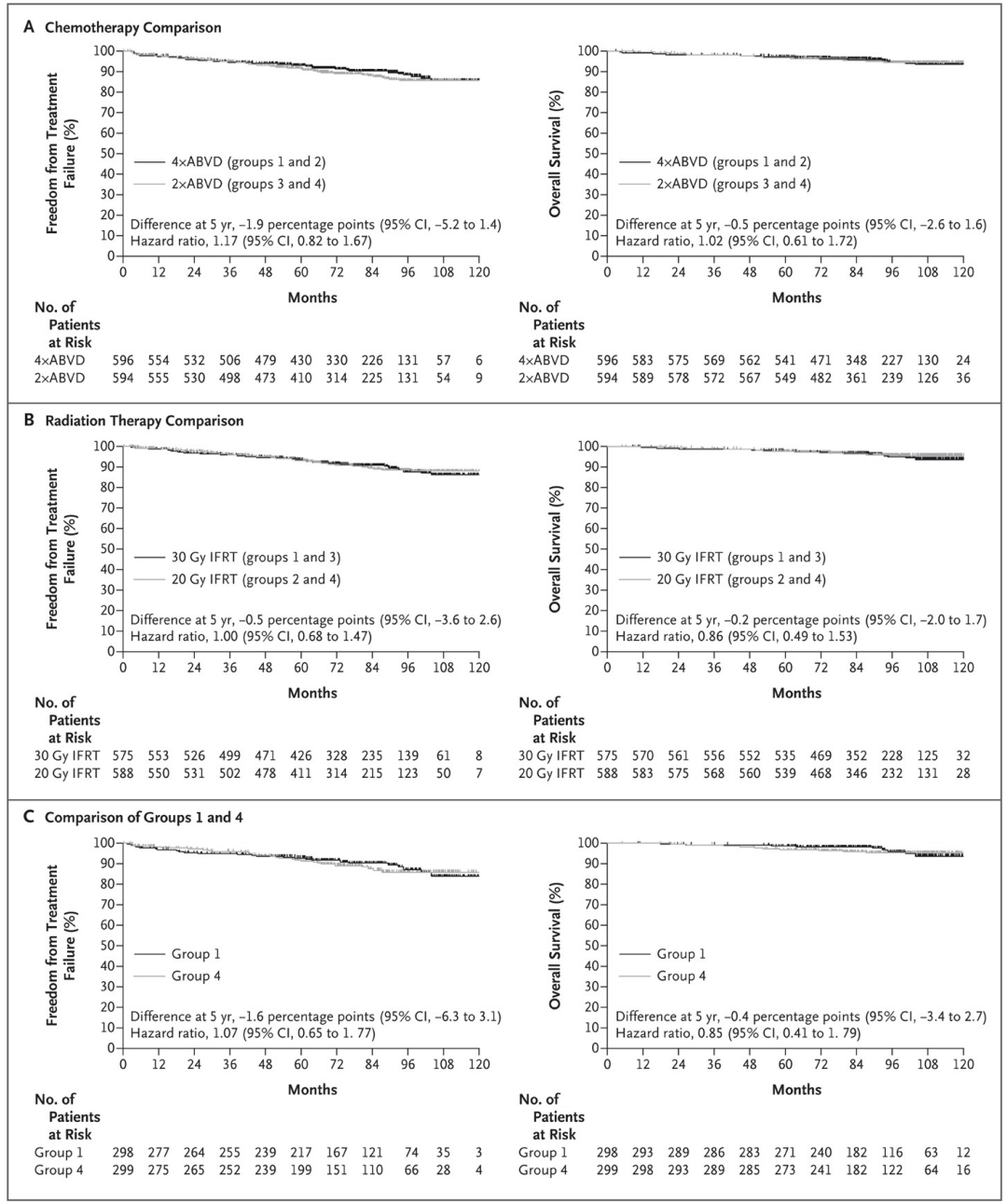
GHSG – German Hodgkin Study Group; HL – Hodgkin lymphoma; ESR - erythrocyte sedimentation rate

Limited stage favorable

2xABVD = 4xABVD

20 Gy RT = 30 Gy RT

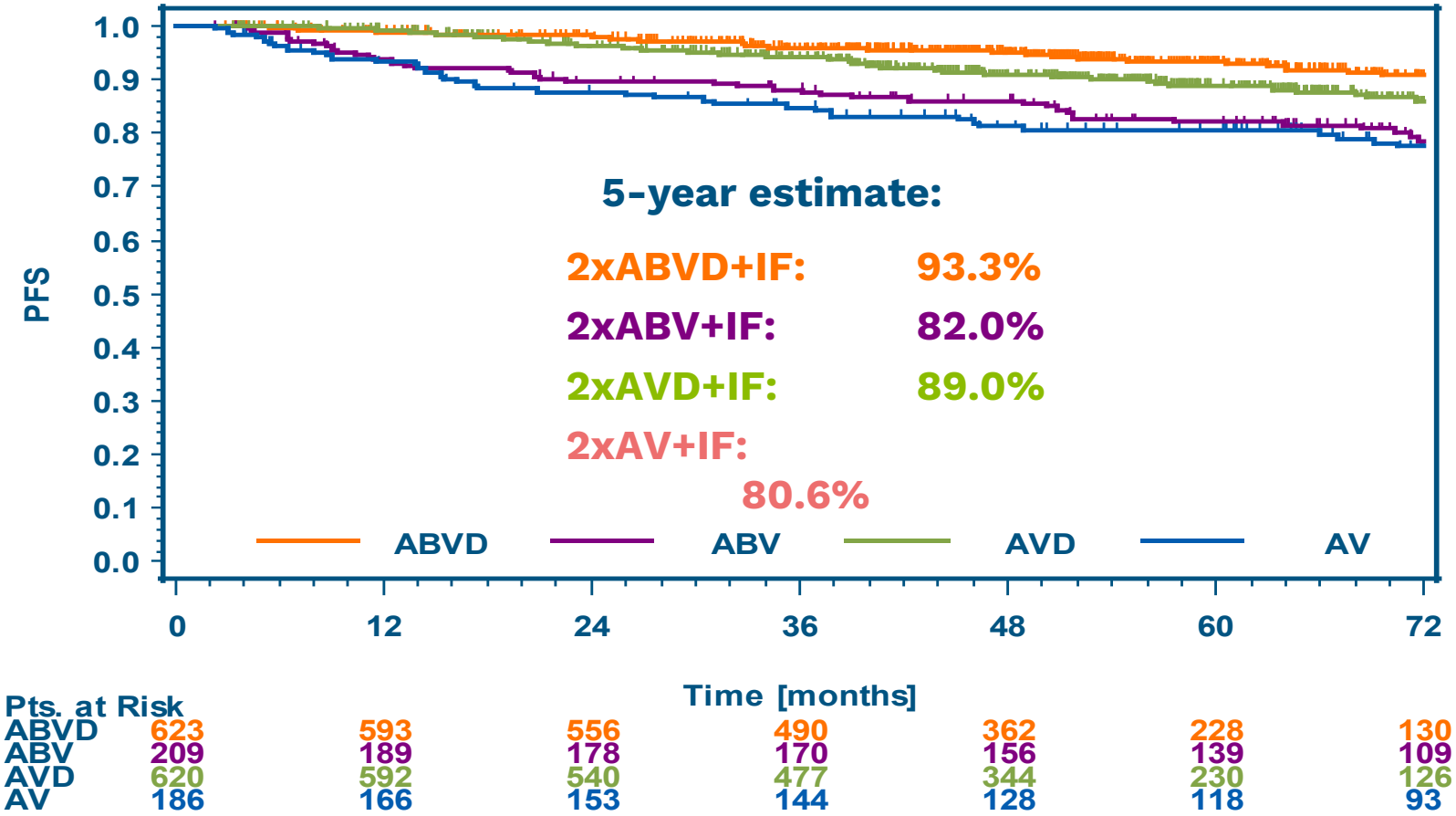
2xABVD + 20 Gy RT = 4xABVD + 30 Gy RT



Engert et al, NEJM 2010;

Reducing chemotherapy

GHLSG (H13): KT + 20 Gy RT - PFS

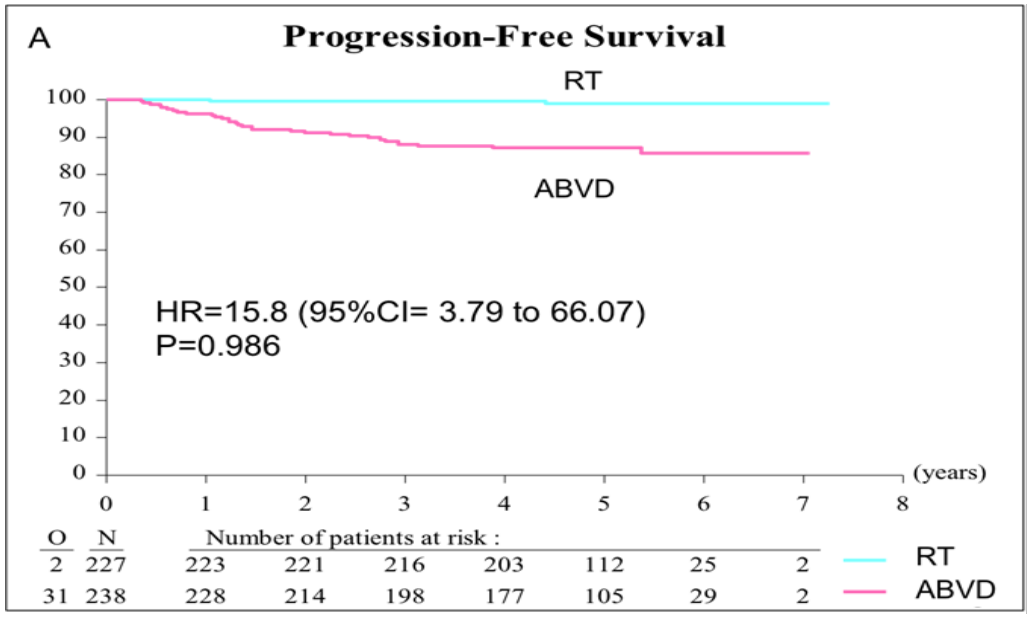


ABVD – doxorubicin, bleomycin, vinblastine, darcarbacine; ABV - doxorubicin, bleomycin, vinblastine; AVD - doxorubicin, vinblastine, darcarbacine; AV – doxorubicin, vinblastine; IF – involved field radiotherapy; pts – patients; PFS – progression free survival

Behringer et al, Lancet 20

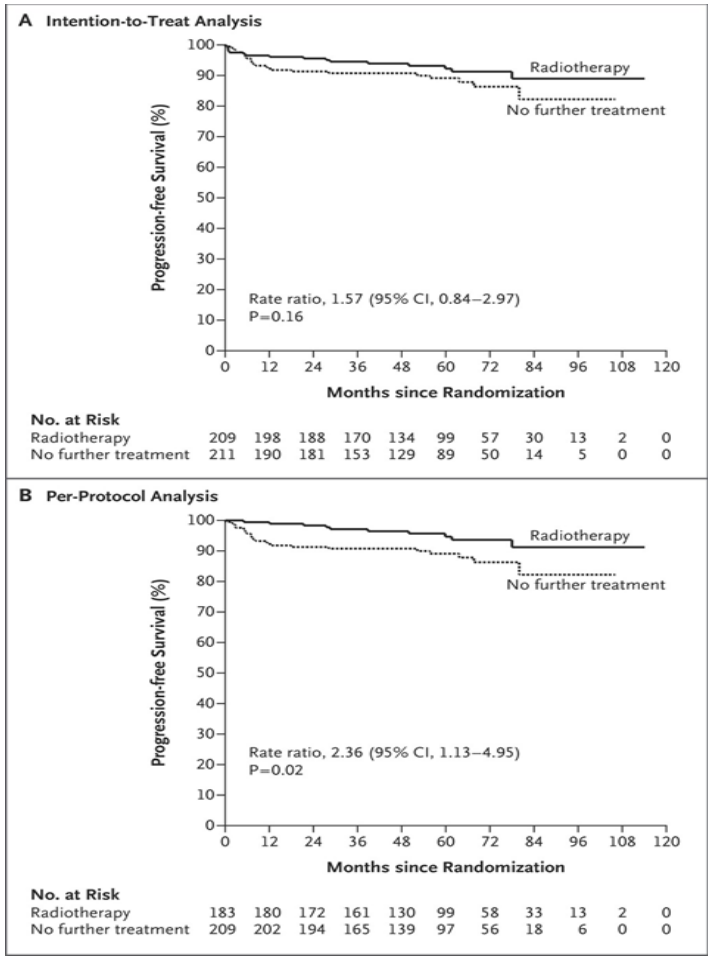
Reducing radiotherapy

H10 favorable



Raemaekers et al, ICML 2015

RAPID

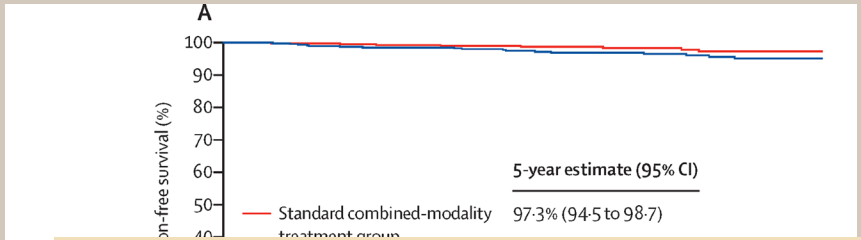


Radford et al, NEJM 2015

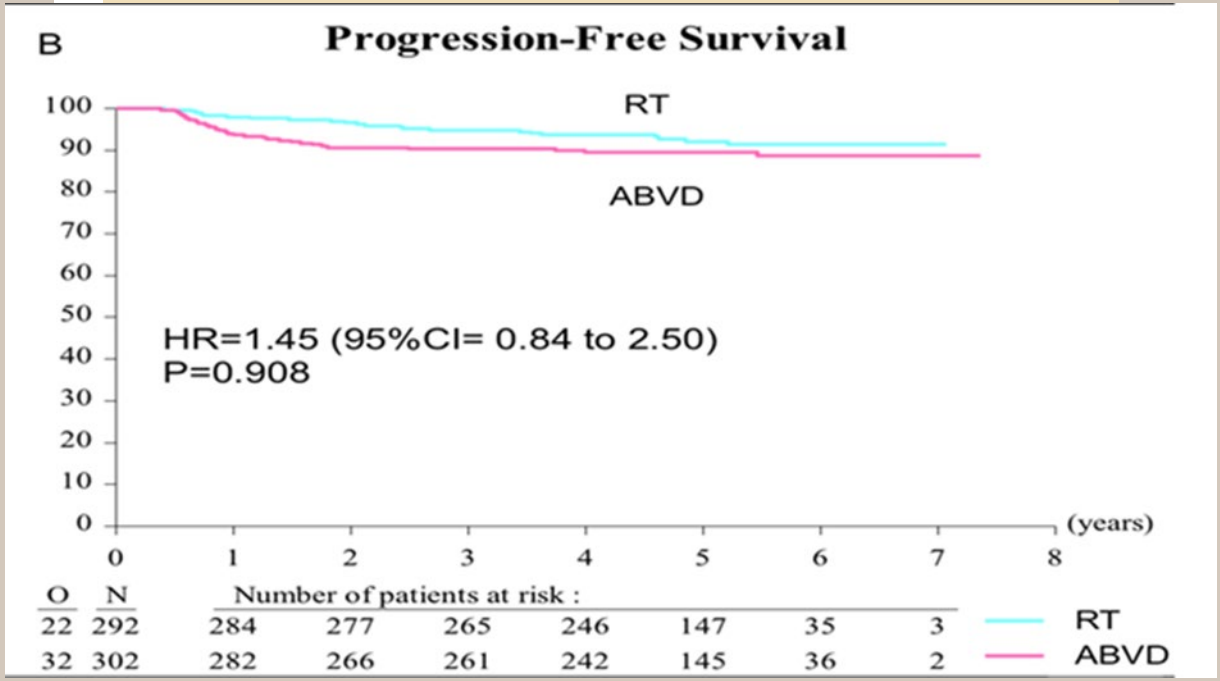
Limited stage, unfavorable

Borchmann et al, Lancet Oncol 2021

In pts. with localised unfavorable disease RT can safely be avoided if they are PET- after 2x eBEACOPP + 2x ABVD



But not after ABVD

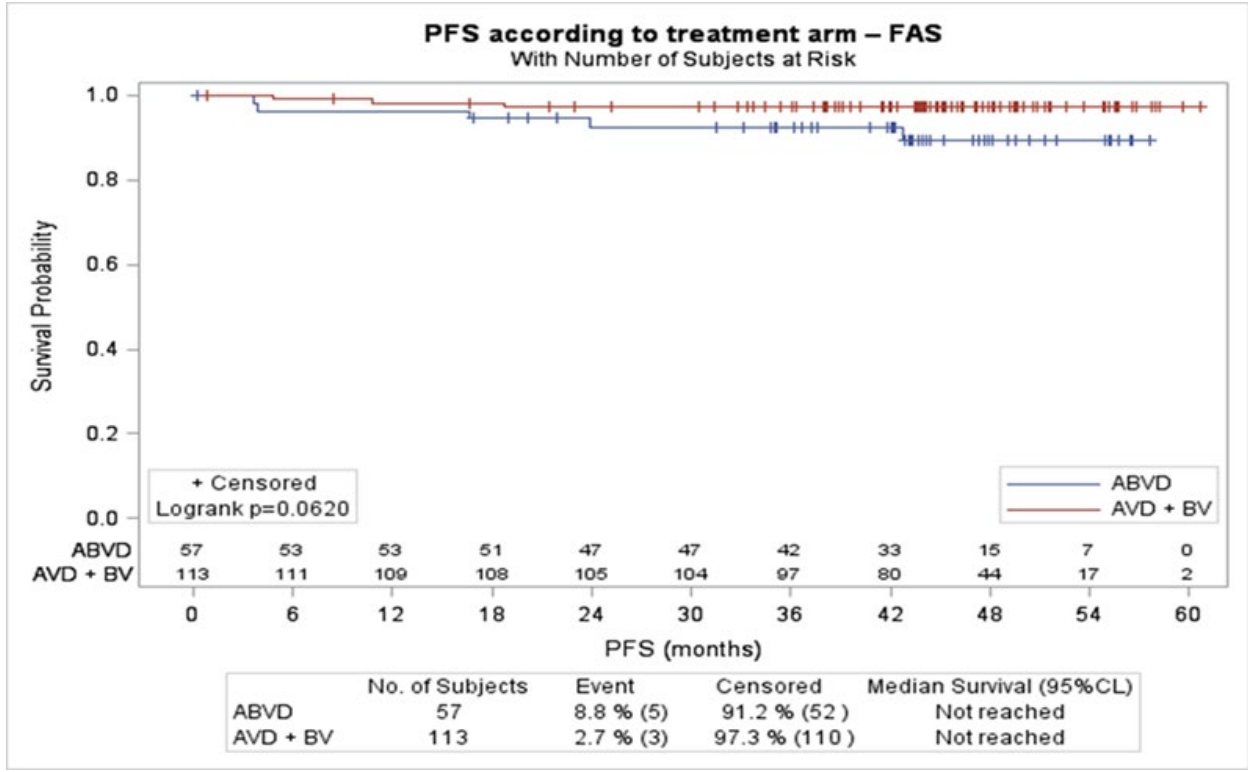


New agents in this setting

BREACH

4x AVD-Bv + RT 30 Gy

vs. 4x ABVD + RT 30 Gy



2y PFS 97% vs. 93%

Fornecker LM et al, JCO 2022

Advanced stage

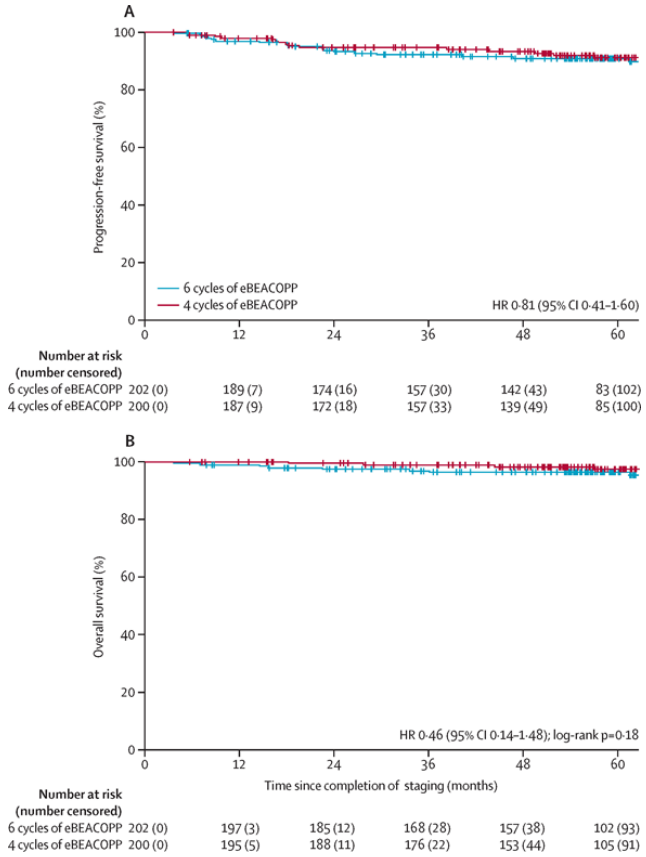
eBEACOPP

4 cycles if PET- after 2nd

- 5y PFS 91%
- 5y OS 98%

6 cycles ± RT if PET+ after 2nd

- 5y PFS 91%
- 5y OS 96%

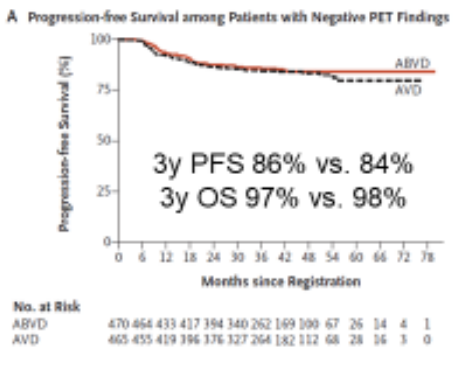


Kreissl S et al, Lancet Haematol 2021

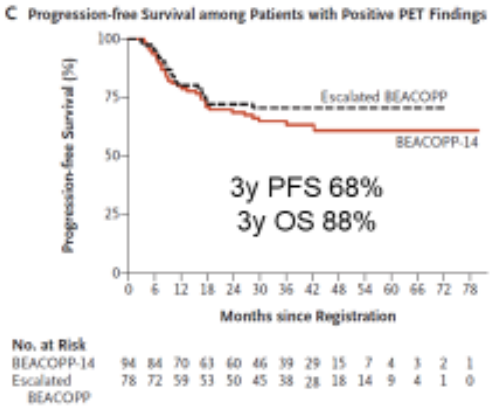
RATHL

ABVDx2 followed by iPET

PET- AVDx4

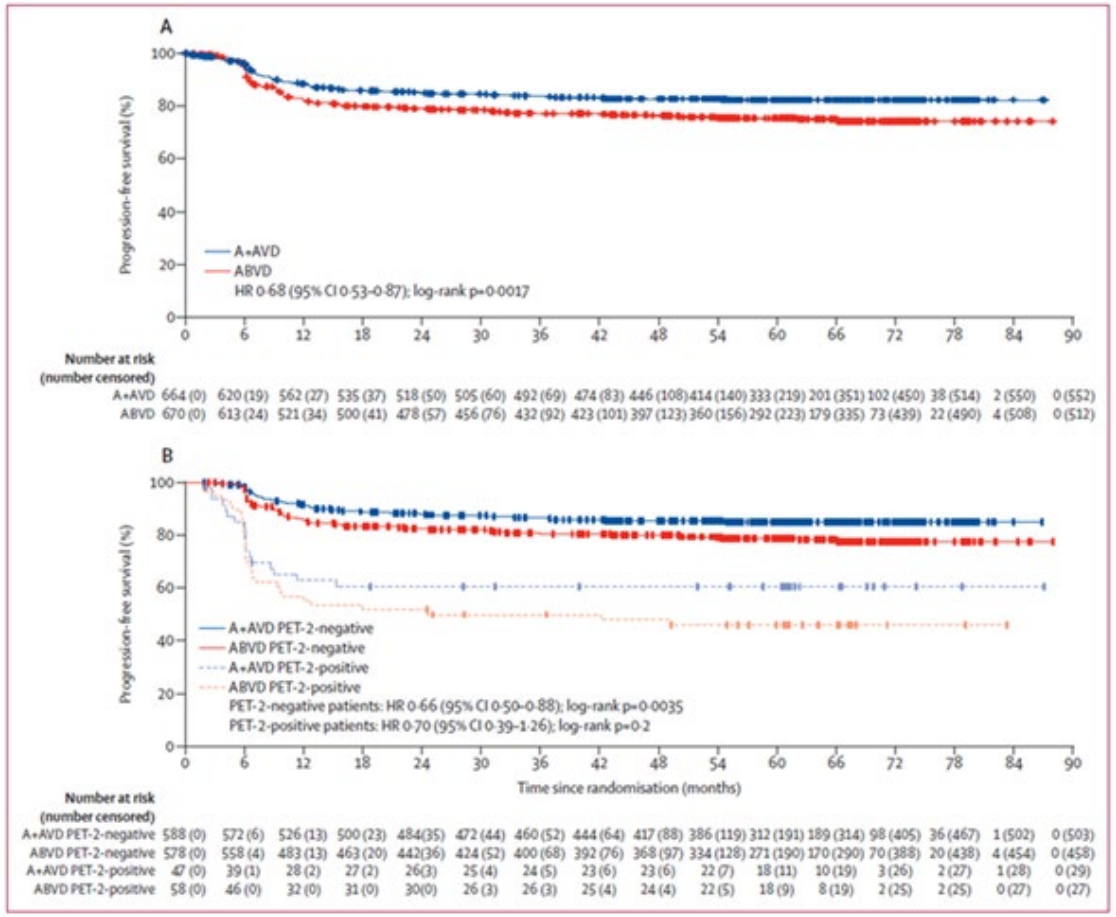


PET+ eBEACOPPx4



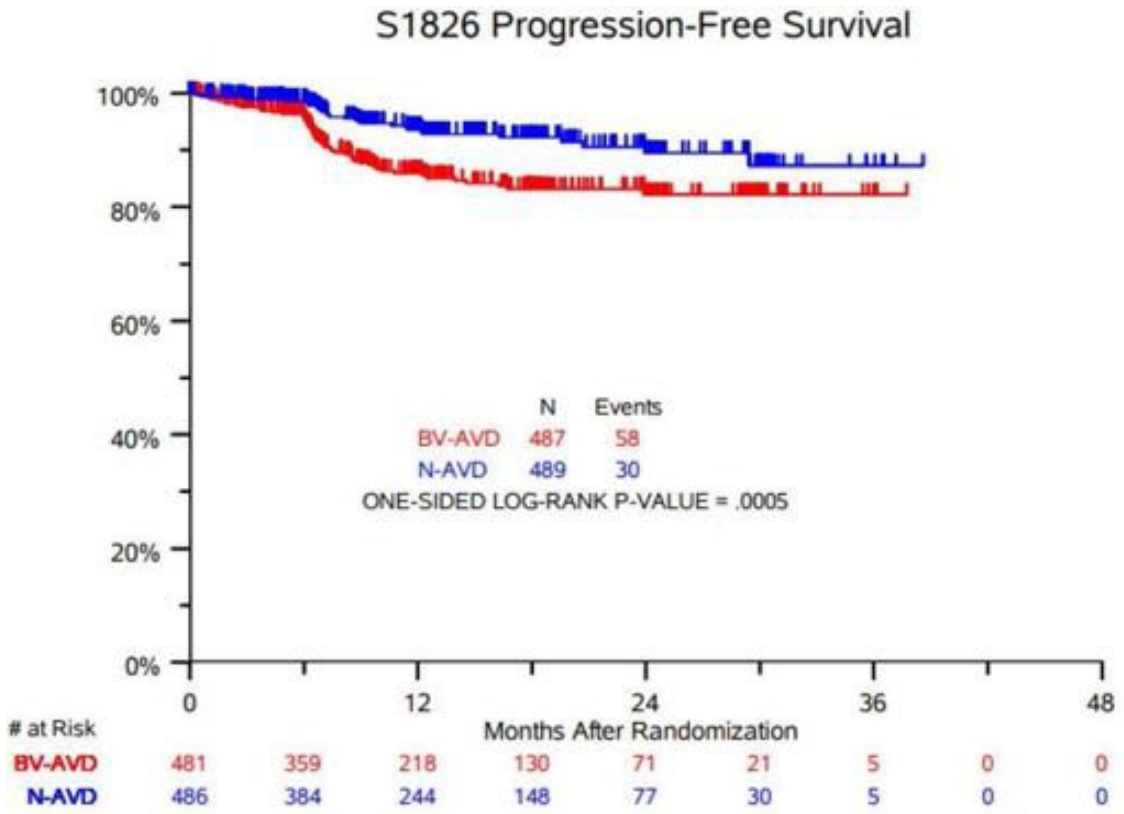
Johnson P et al, NEJM 2016

- ECHELON 1
- 6x AVD-Bv vs. 6x ABVD
- 5y PFS 82% vs. 75%



Straus DJ et al, Lancet Haematol 2021

PD-1 blockers



Herrera AF et al, ICML 2023

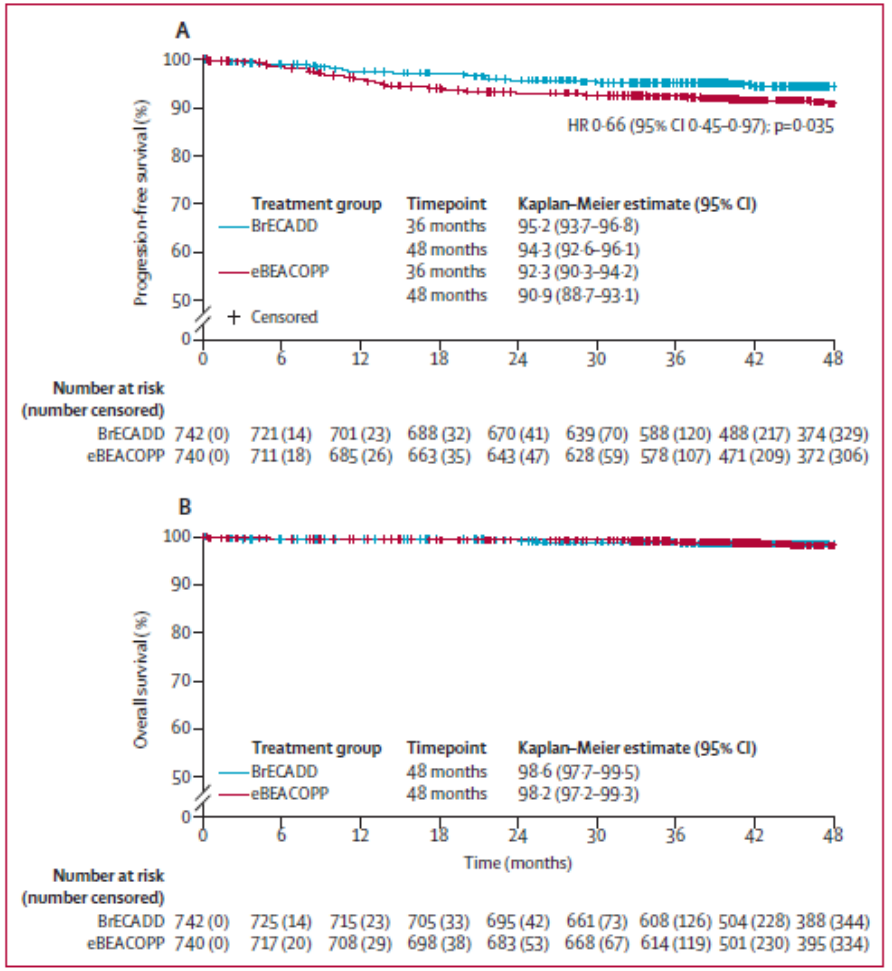
cHL stage III-IV, > 12y

6x AVD + nivo vs. 6x AVD + Bv

1y PFS 94% vs. 86%

BrECADD x 4-6 for advanced-stage cHL 18-60 y

		q 3 wks	day
Bv	1,8 mg/kg	1	
Etoposide	150 mg/m²	2-4	
Cyclophosph.	1250 mg/m²		2
Doxorubicin	40 mg/m²	2	
Dacarbazine	250 mg/m²	3-4	
Dexa	40 mg	2-5	
Peg-G-CSF	6 mg sc	5	



Borchmann P et al, Lancet 2024

HL in elderly – an unresolved problem

Pts > 60 do not tolerate >2 cycles of eBEACOPP

Pts > 70-75 do not tolerate >2 cycles of bleomycine

6 cycles of ABVD 5% (7%) lethal lung toxicity*

2 cycles ABVD 2% lung toxicity+

4 cycles ABVD 9% lung toxicity+

BV monotherapy is not the solution*

neuropathy

short DOR

BV + dacarbazine >

BV + bendamustine+

*Stamatoullas et al, BJH 2015
+Behringer et al, Lancet 2015

*Forero-Torres et al, Blood 2015
+Friedberg et al, Blood 2017

Classical front-line treatment options for elderly

60-70 (75) y: ABVD

> 70 (75) y: ?

CHOP, bendamustine, AVD, LVPP...

Zallio et al, Br J Haematol 2016; Walewski et al, Med Oncol 2010

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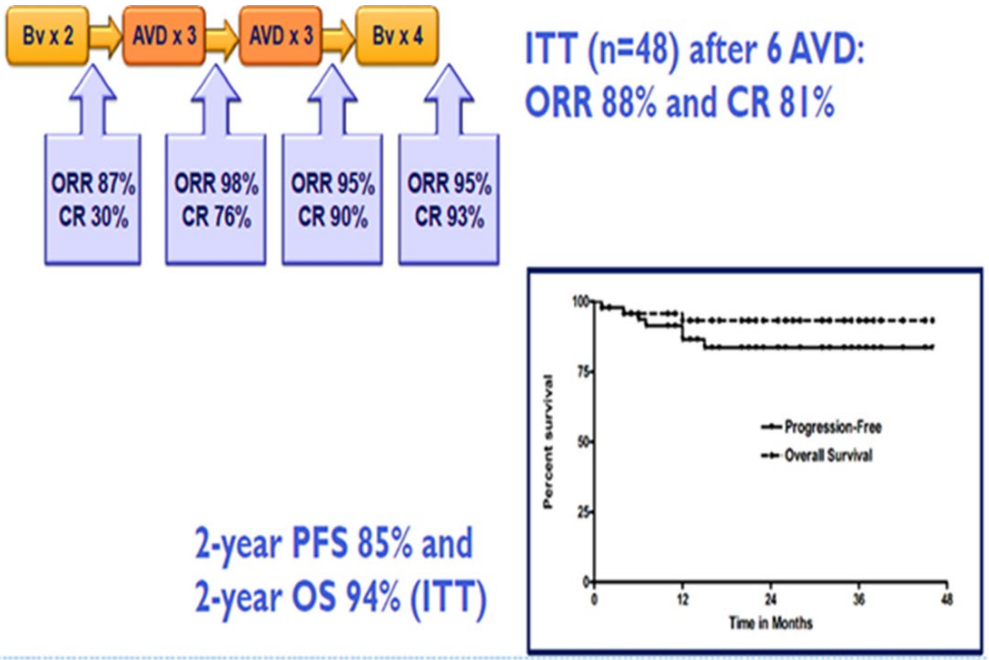
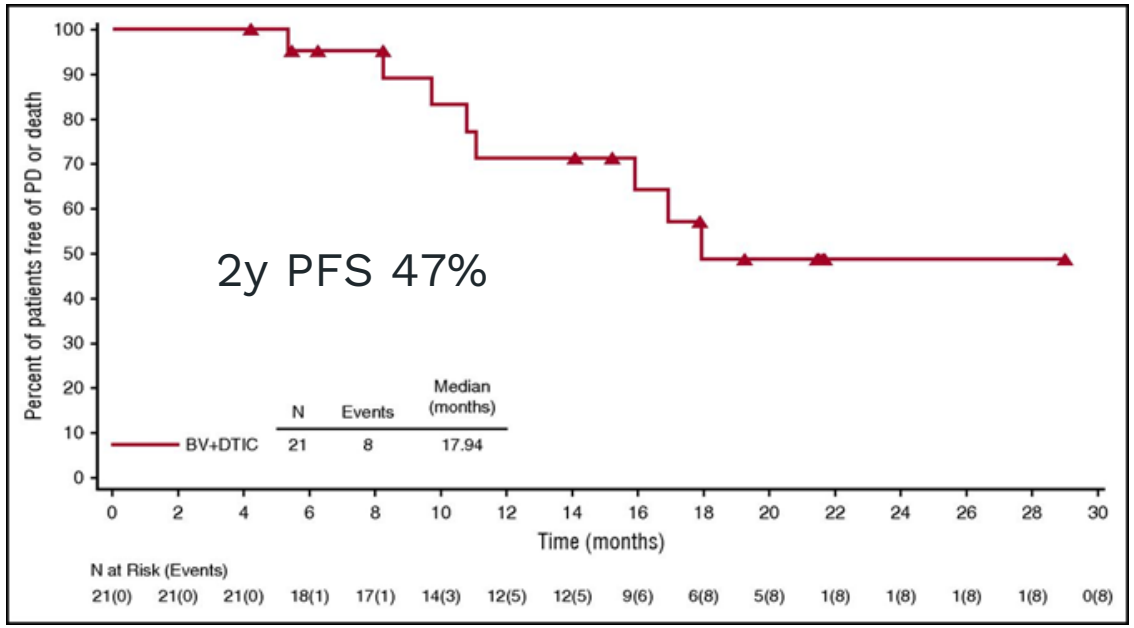
Elderly

Fit



Evens at al. 2018. J Clin Oncol 36:3015-3022

Unfit



Friedberg JW et al, Blood 2017

2nd line, transplantable

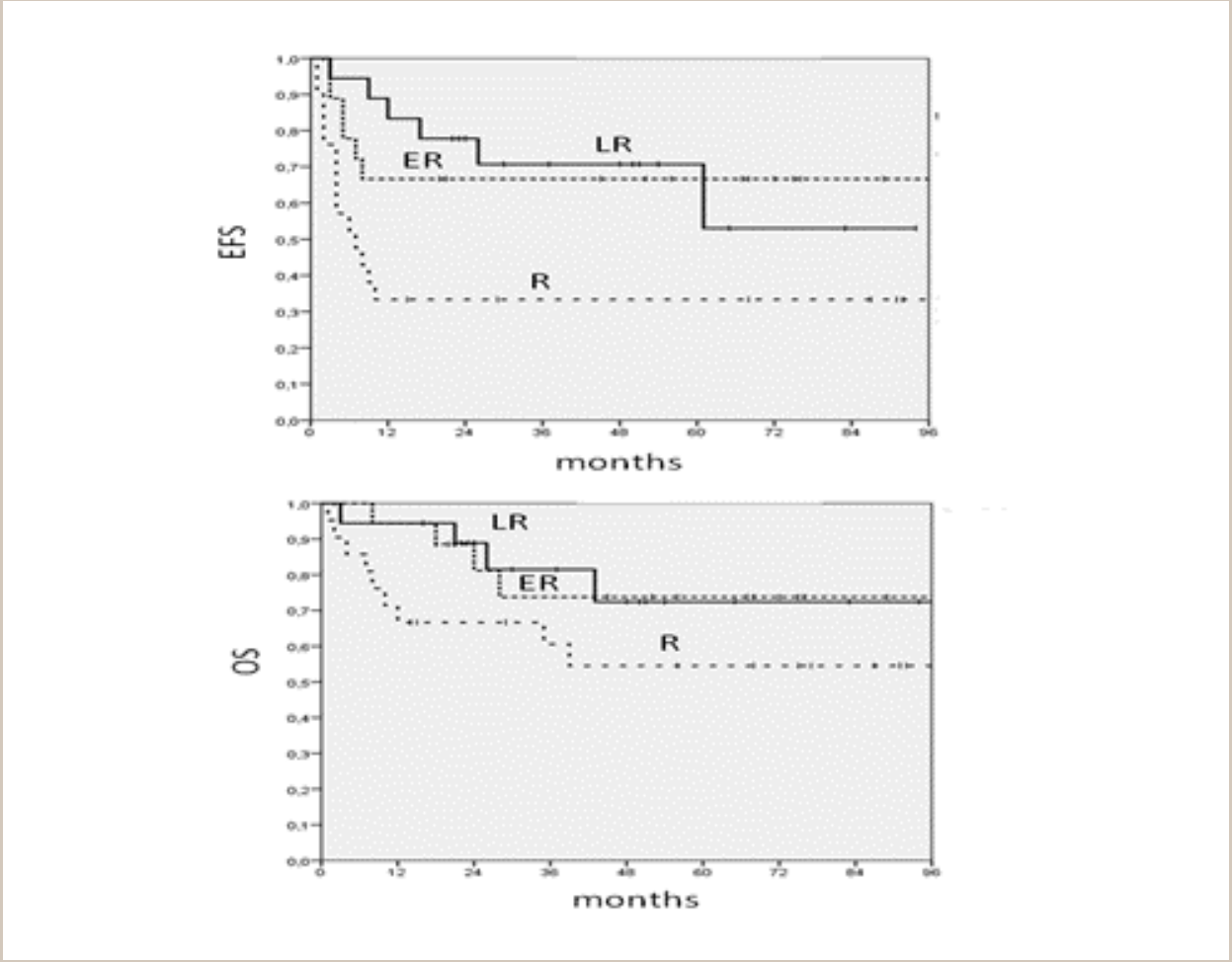
Old standard

HD-CT (DHAP, ICE, IGEV, HDIM, ESHAP)...

- All produce similar outcomes

ASCT in responding patients

RT consolidation

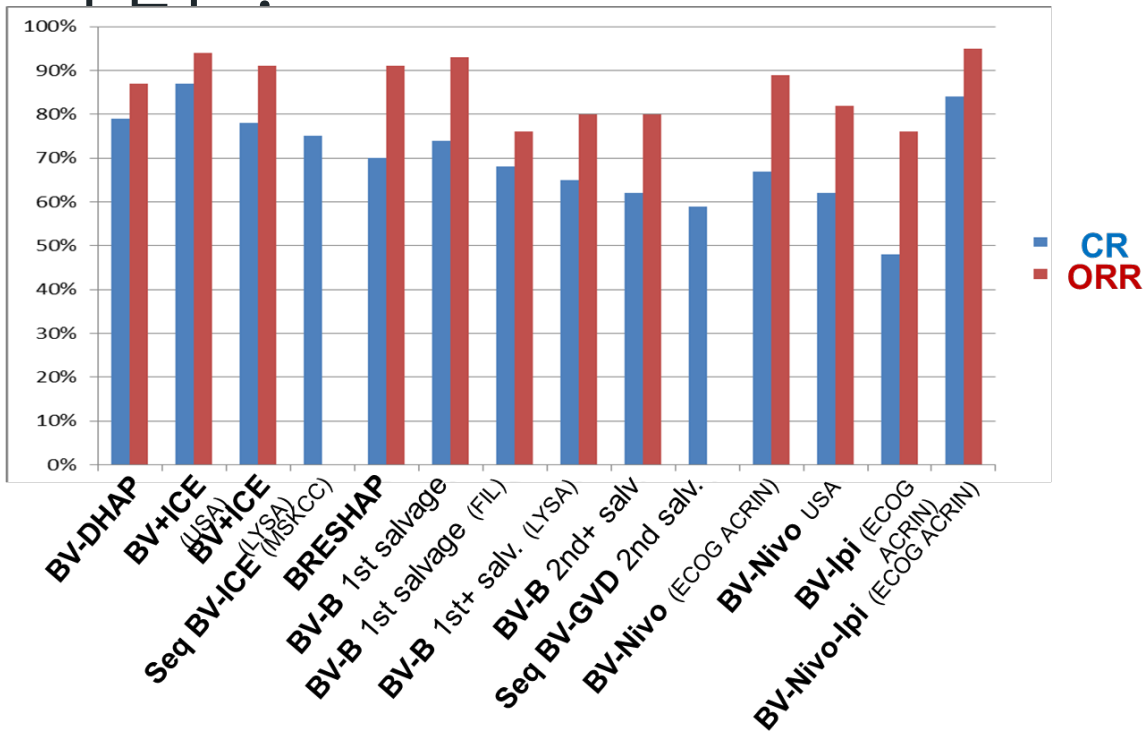


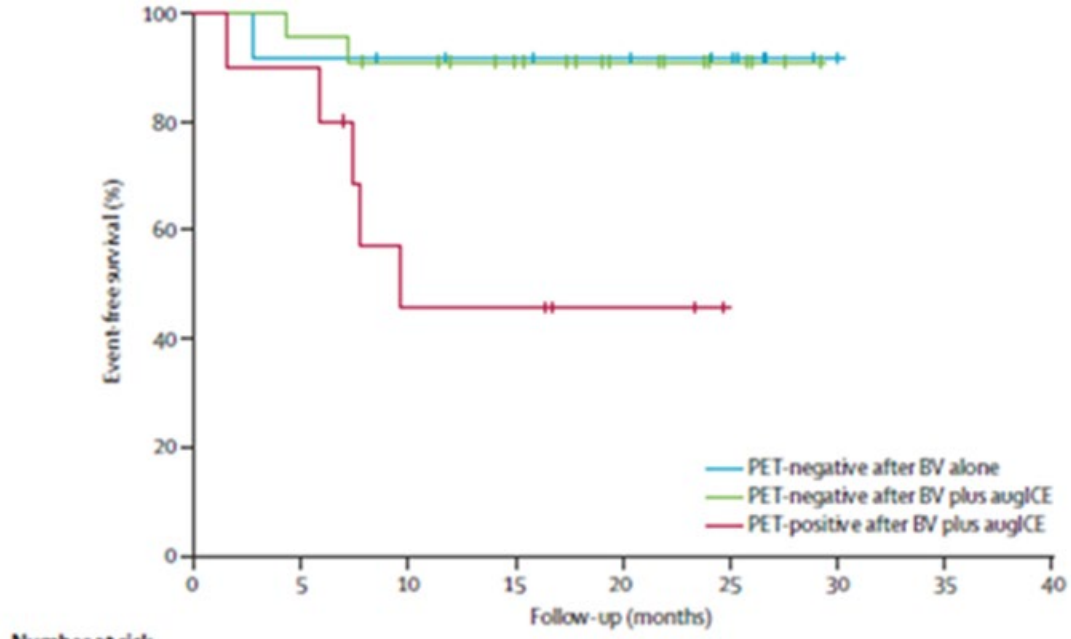
Aurer et al. Ann Hematol 2016

eha

Improvements in induction

The importance of being PET-!





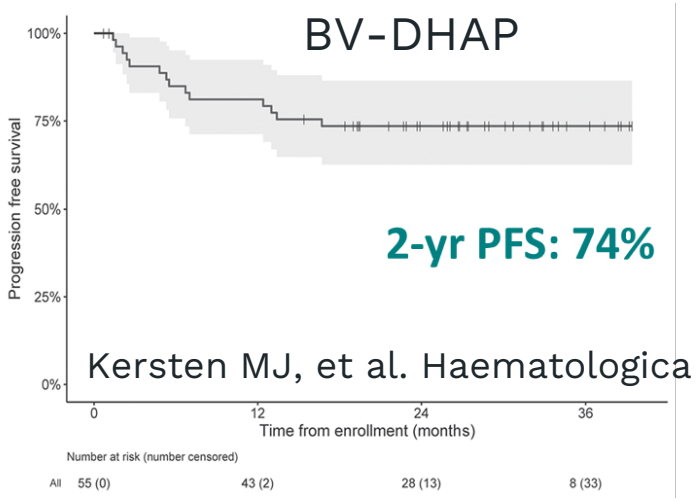
Number at risk							
BV PET negative	12	11	10	9	8	5	1
BV-augICE PET negative	22	21	19	15	9	4	0
BV-augICE PET positive	10	9	8	4	2	0	0

Moskowitz et al, Lancet Oncol 2015

Improvements in induction

PFS

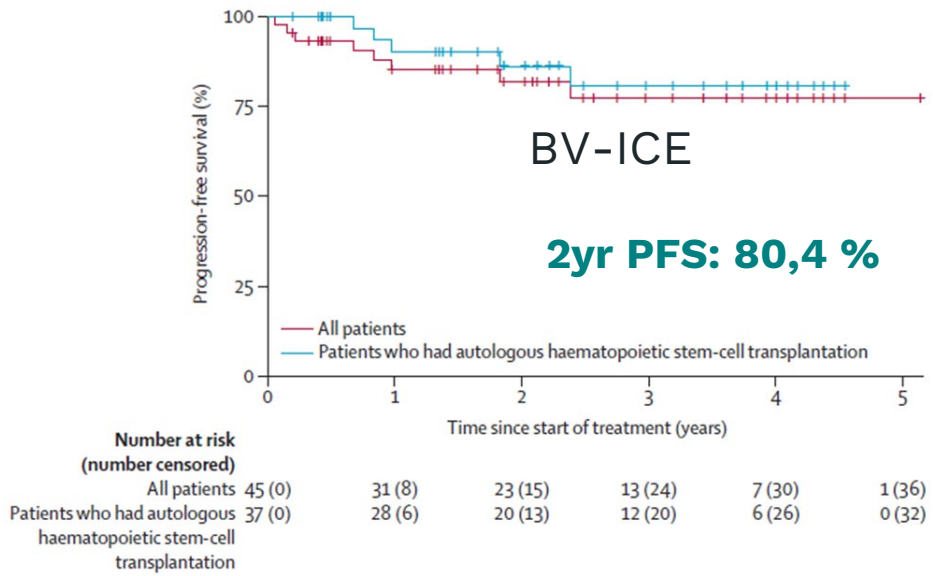
BV-DHAP



2-yr PFS: 74%

Kersten MJ, et al. Haematologica 2021

BV-ICE

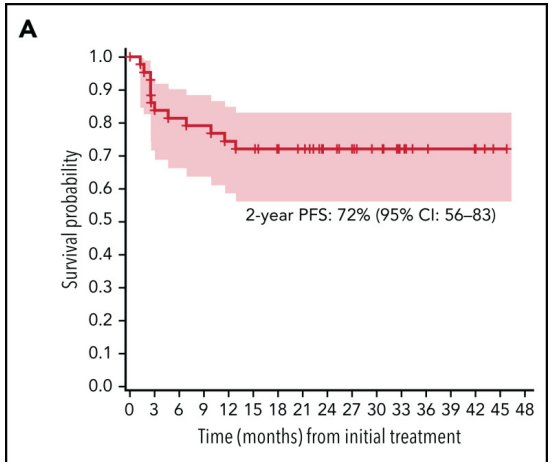


2yr PFS: 80,4 %

Lynch RC, et al. Lancet Haematol 2021

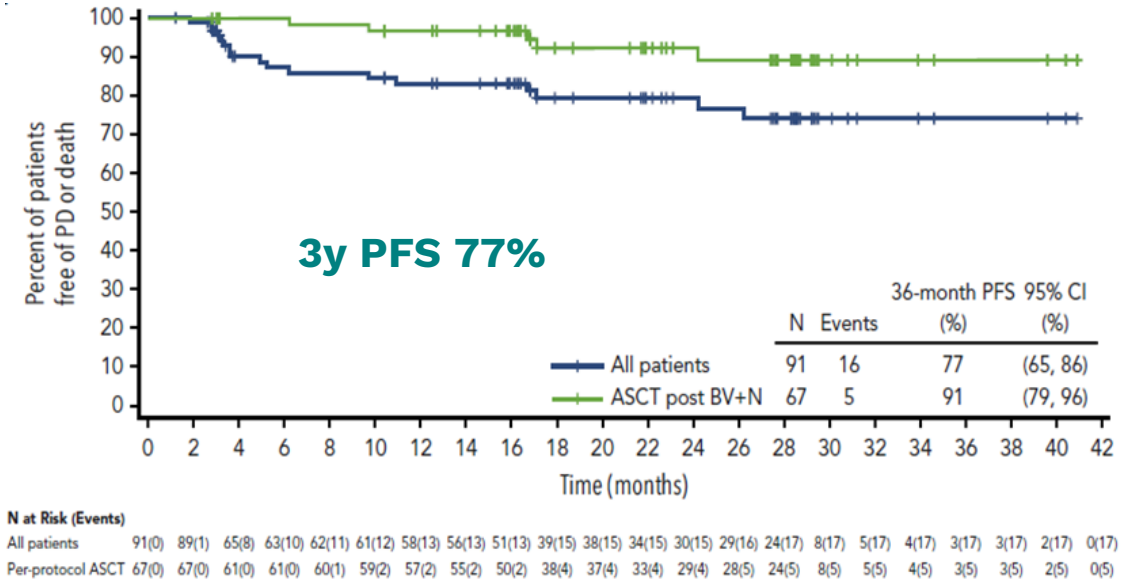
Nivo ± ICE

2y PFS 72%



Mei GM et al, Blood 2022

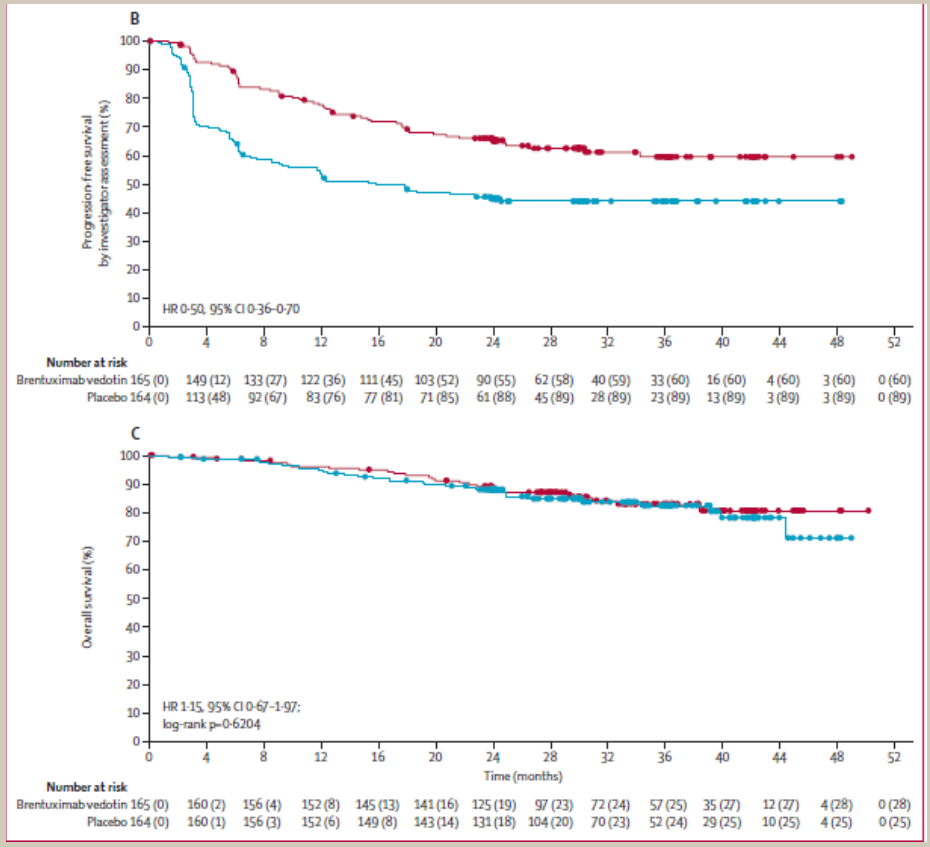
BV-Nivo



Advani R, et al. Blood 2021

BV after ASCT - AETHERA study

BV after ASCT improves PFS of high-risk patients: primary refractory, early relapse, stage IV at relapse



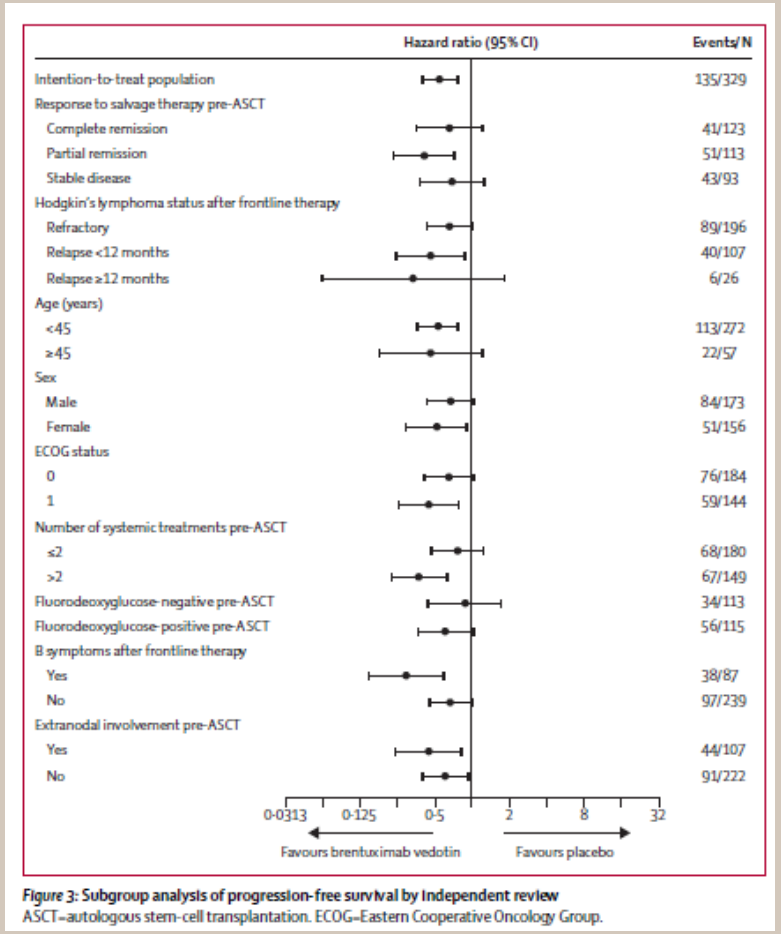


Figure 3: **Subgroup analysis of progression-free survival by Independent review**
ASCT=autologous stem-cell transplantation. ECOG=Eastern Cooperative Oncology Group.

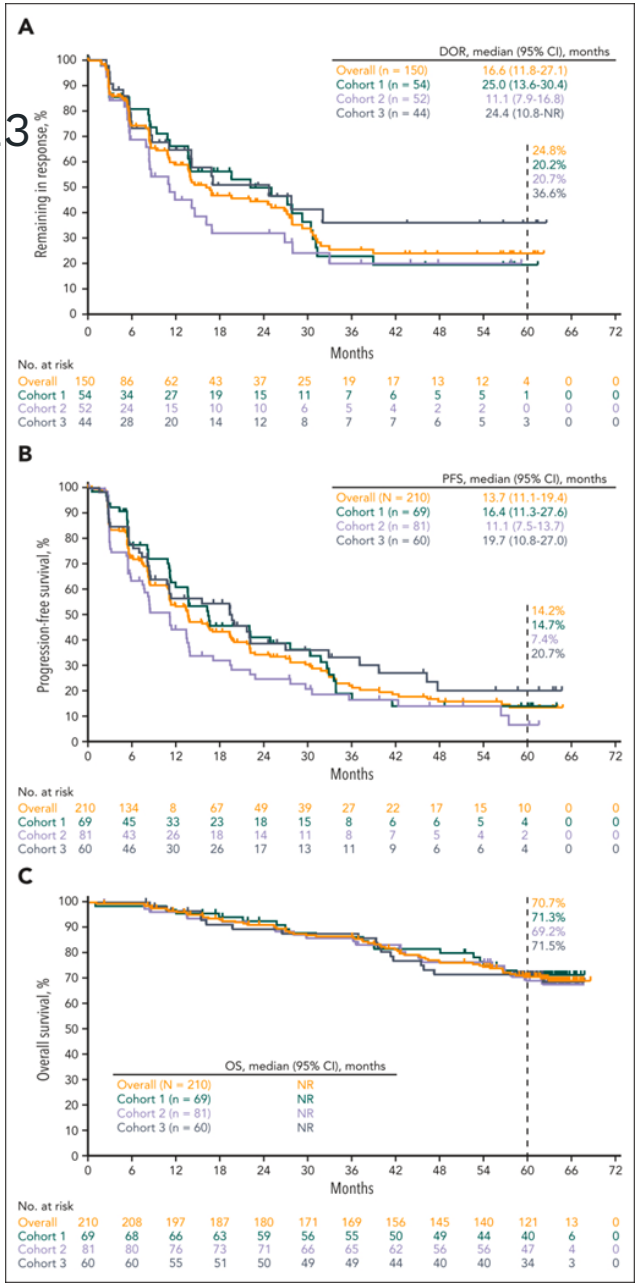
Moskowitz et al, Lancet 2015.

eha

Beyond 2nd line

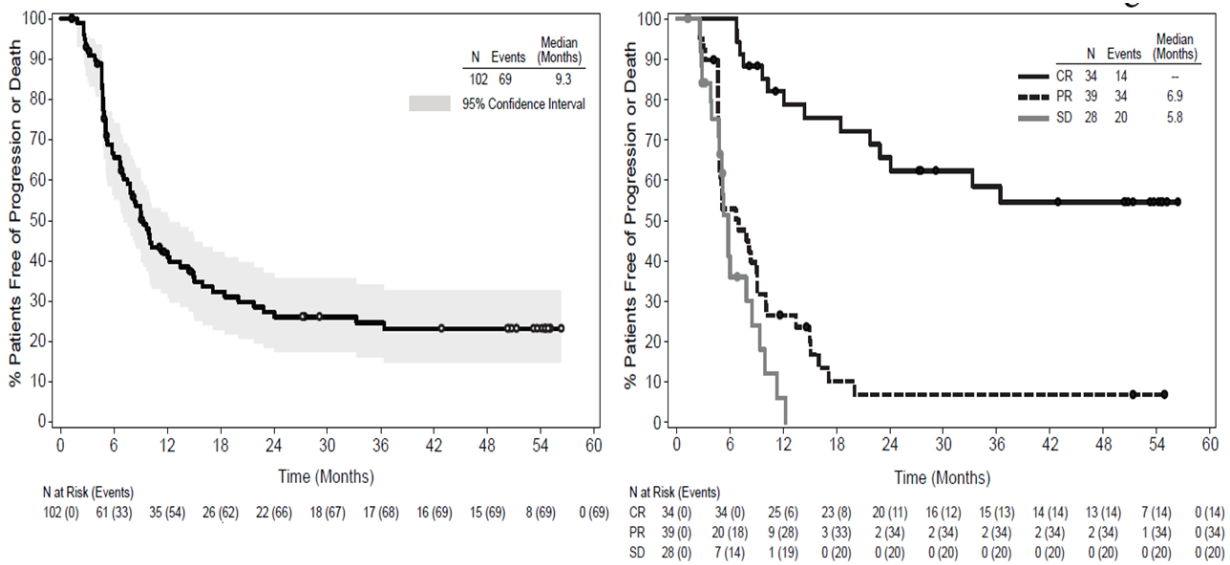
PD1 blockade

Armand et al, Blood 2023



Bv monotherapy

Gopal et al. Blood 2015



Bendamustine + Bv

- full doses of both agents q 3 wks
- well tolerated
- Sawas et al, ASH 2015: > 2nd line: RR 69%

How to cure the incurable?

Diseases desperate grown

By desperate appliance are relieved

Or not at all*

*Shakespeare W, Hamlet

RIC followed by HLA-(haplo)identical SCT

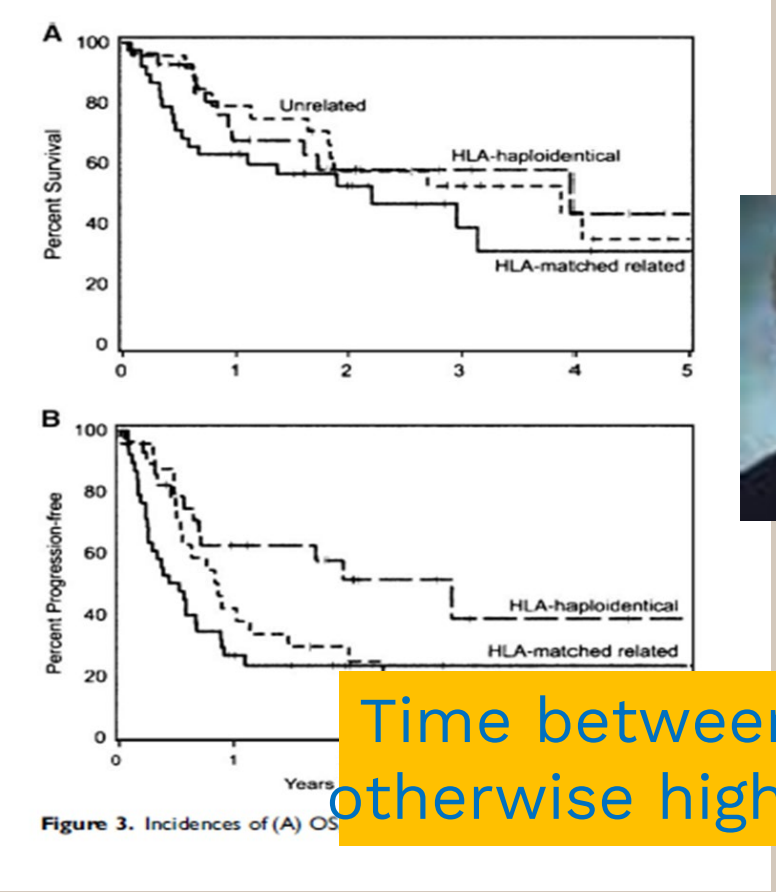
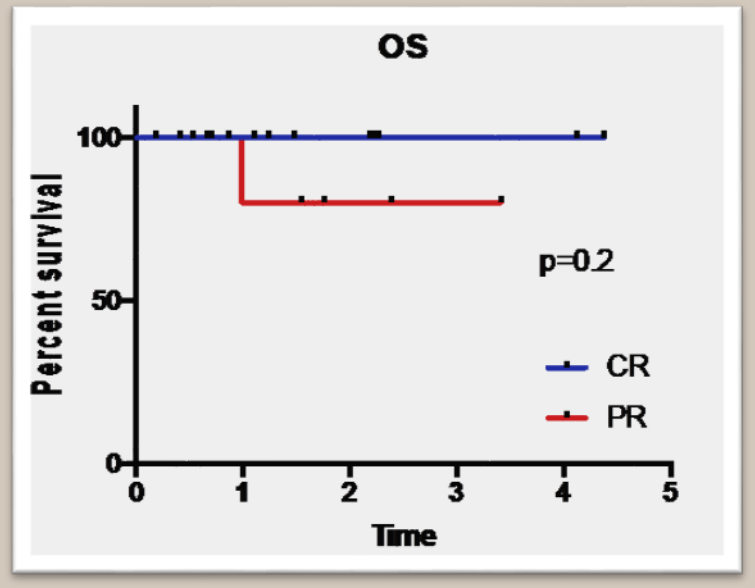
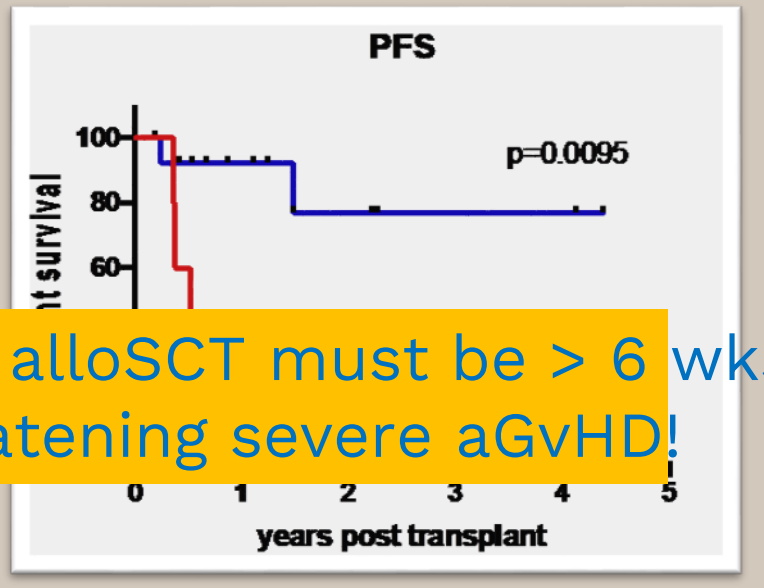


Figure 3. Incidences of (A) OS





Time between last dose of PD1i and alloSCT must be > 6 wks, otherwise high incidence of life-threatening severe aGvHD!

Burroughs et al, Biol Blood Marrow Transplant 2008

Duraković N et al, Clin Hematol Int 2021

Conclusions 1 – front-line therapy

With risk-adapted front-line therapy ≈ 90% newly diagnosed pts. < 60-70 y can be cured

eBEACOPP > AVD+Bv > ABVD

Front-line regimens including Bv or PD1i will become standard of care

BrECADD, AVD + PD1i

To ameliorate toxicity

Use peg-G-CSF for primary prophylaxis in all regimens > ABVD

Use sperm cryopreservation in men and GnRH analogues, oocyte or ovary tissue cryopreservation in women

Start routine breast imaging <7 y from th. start, consider LD lung-CT in smokers

Keep in mind, it’s not only RT that causes secondary cancer!

Irradiate only involved nodes or, at most, regions

Conclusions 2 – relapsed / refractory

HD-CT + Bv or PD1i seems more effective than HD-CT alone

Which group of pts benefits and role of ASCT currently unclear

Consolidation with Bv or PD1i after ASCT useful in high-risk patients

Do not forget RT!

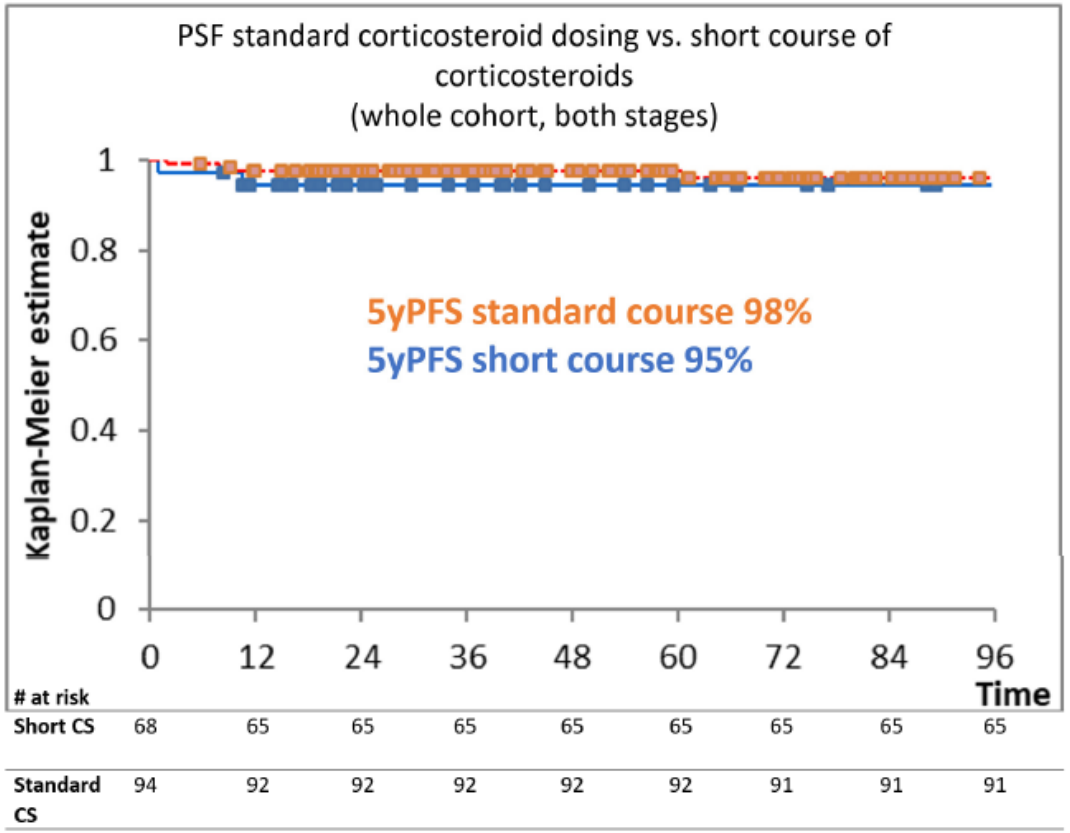
Do not stop PD1i until clinical progression

Allo SCT using haploidentical related donors and RIC can cure some, otherwise incurable, young pts. with treatment-sensitive disease

OPTIMAL APPROACH TO R/R cHL

Prevention

Cure the patient with front-line therapy!



Hude Dragičević I et al, Medicina 2024

KBC ZAGREB

HRVATSKO DRUŠTVO ZA HEMATOLOGIJU
HRVATSKOG LIJEČNIČKOG ZBORA

SVEUČILIŠTE U ZAGREBU MEDICINSKI FAKULTET

eha

KroHem
Hrvatska kooperativna grupa za hematološke bolesti

EHA LyG EHA Lymphoma Group