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How should we treat early unfavourable Hodgkin Lymphoma?

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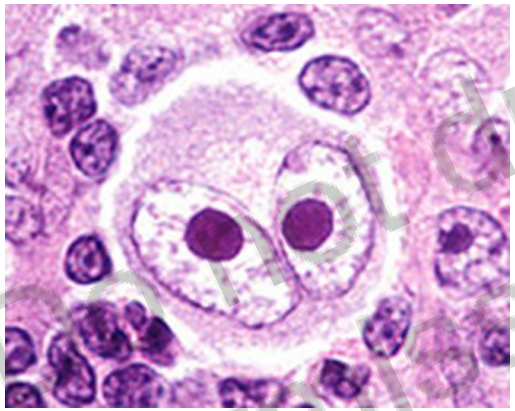
How should we treat early unfavourable Hodgkin Lymphoma?



Dr Wendy Osborne
Consultant Haematologist
Freeman Hospital
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April 2022

24 year old student

Presented August 2020with swelling left neck and sweats

ESR 31 mm/hr

Biopsy: classical Hodgkin, nodular sclerosis

Unfavourable prognosis in early stage HL

EORTC presence of one or more of the following	GHSG presence of one or more of the following
Large mediastinal adenopathy	Large mediastinal adenopathy
ESR ≥ 50 without B symptoms	ESR ≥50 without B symptoms
ESR ≥ 30 with B symptoms	ESR ≥30 with B symptoms
Age >50	E-disease
≥ 4 lymph node sites involved	≥ 3 lymph node sites involved

EORTC, European Organisation for the Research and Treatment of Cancer; GHSG, German Hodgkin's Study Group

Treatment options for Early Unfavourable HL

German HD11 : 4 X ABVD plus 30Gy

German HD14 : 2X esc beacopp 2X ABVD plus 30Gy

German HD17: 2X esc beacopp 2X ABVD PET guided RT

PET guided H10 (EORTC)

For stage IIB bulk RATHL/HD18 /AHL2011 are also options

HD14 trial design

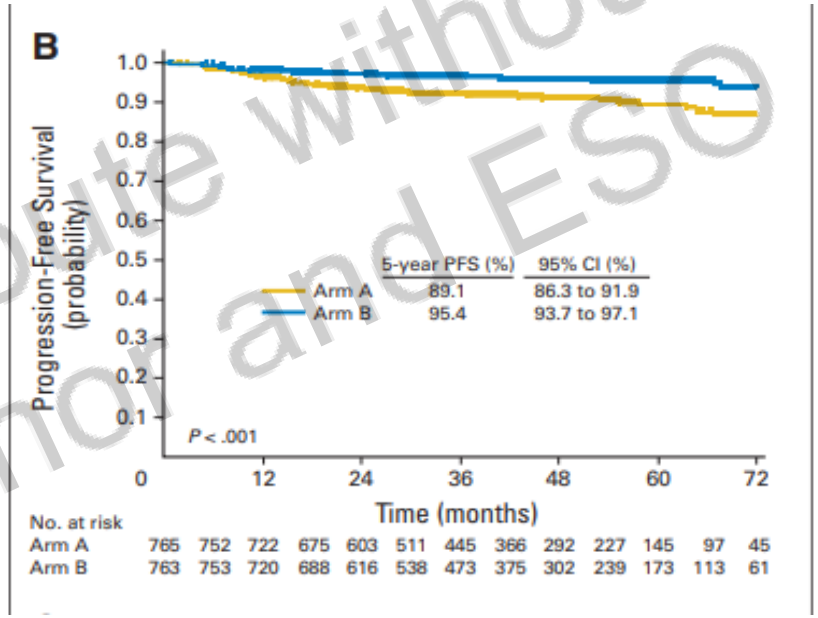
Early Unfavorable HL ≤60 years

CS I/II with RF*

randomization

Group A
4xABVD
+30Gy IFRT

Group B
2xBEACOPPesc+2xABVD
+30Gy IFRT



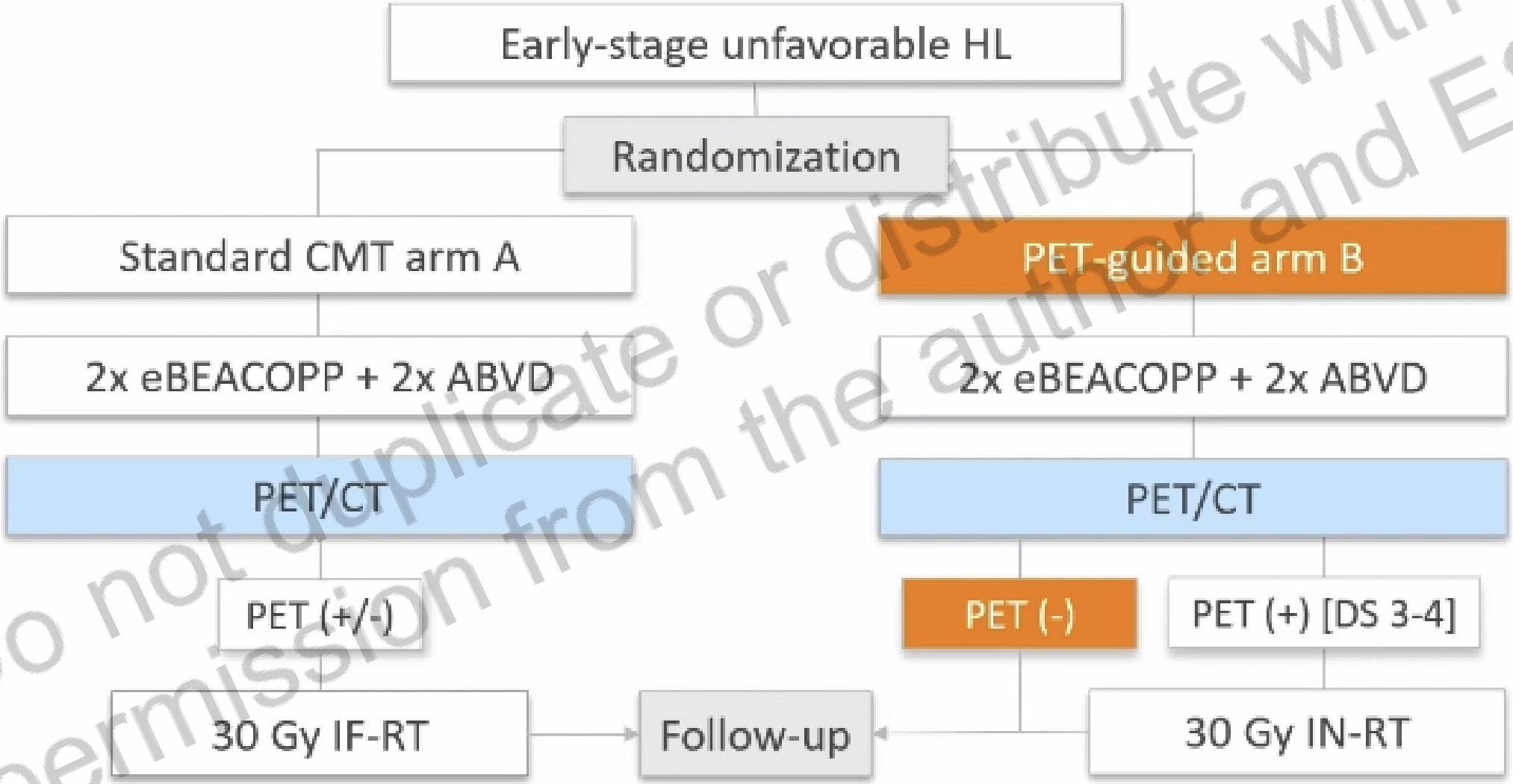
1528 pts

Arm B (esc beacopp arm) : 5yr PFS 95.4 % (6 % improvement)

More acute toxicity but no difference in TRM or secondary malignancy

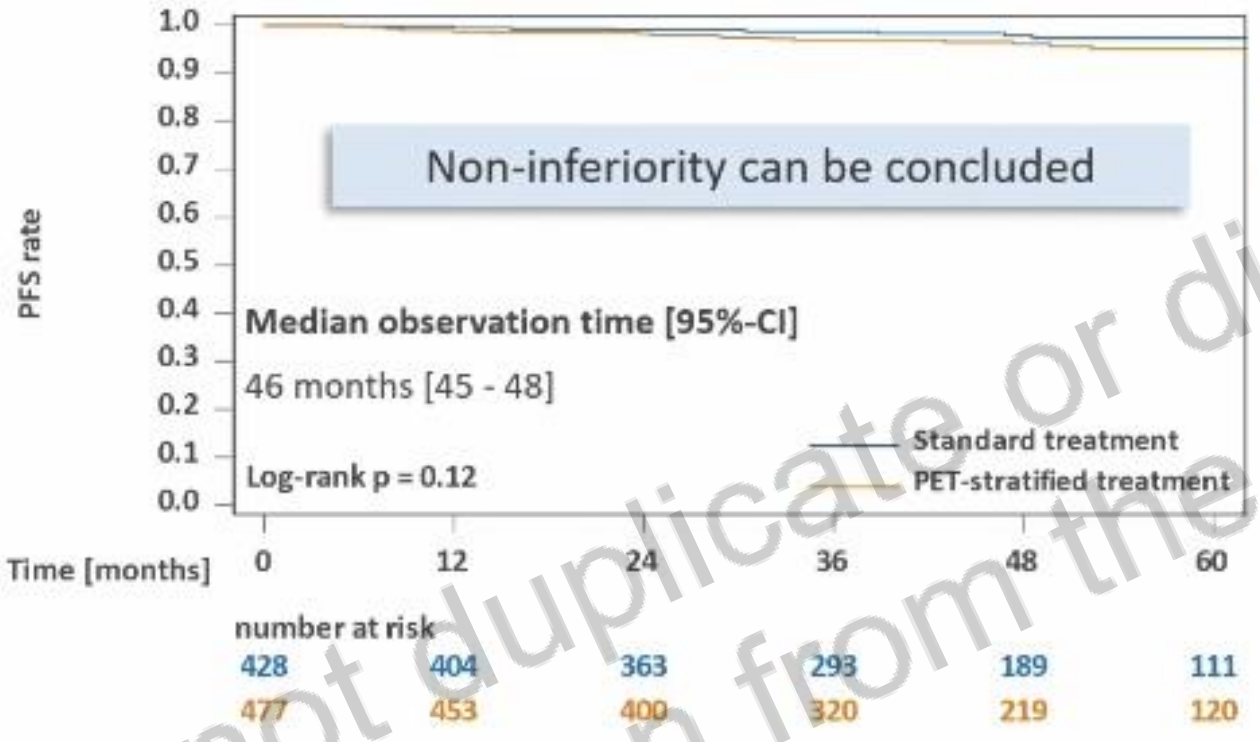
Von Trescow et al JCO 2012

HD17 Trial Design



Borchmann et al Lancet Oncology 2021;22: 223-234

HD17: 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]

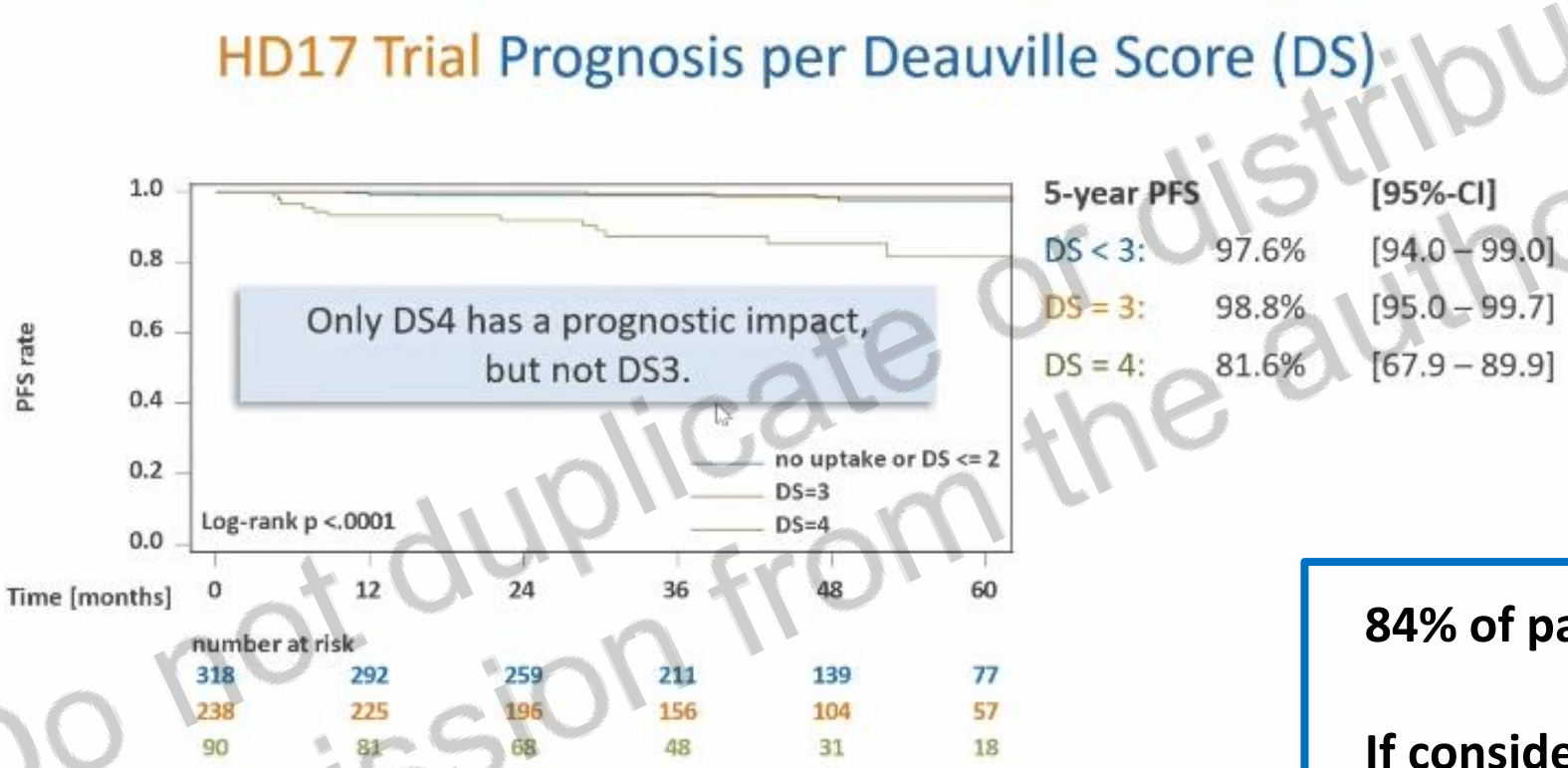
Difference in 5-year PFS [95%-CI]

2.2% [-5.3 - 0.9]

This is the first study to show that there is no reduction in PFS when radiotherapy removed (RAPID/ H10/ HD16 all did)

Borchmann et al Lancet Oncology 2021;22: 223-234

A positive PET4 scan is a predictive factor for progression free survival



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]

84% of patients are Deauville Score 1-3

If consider Deauville 4 or 5 to be positive then 16% of patients will be escalated to radiotherapy

Borchmann et al Lancet Oncology 2021;22: 223-234

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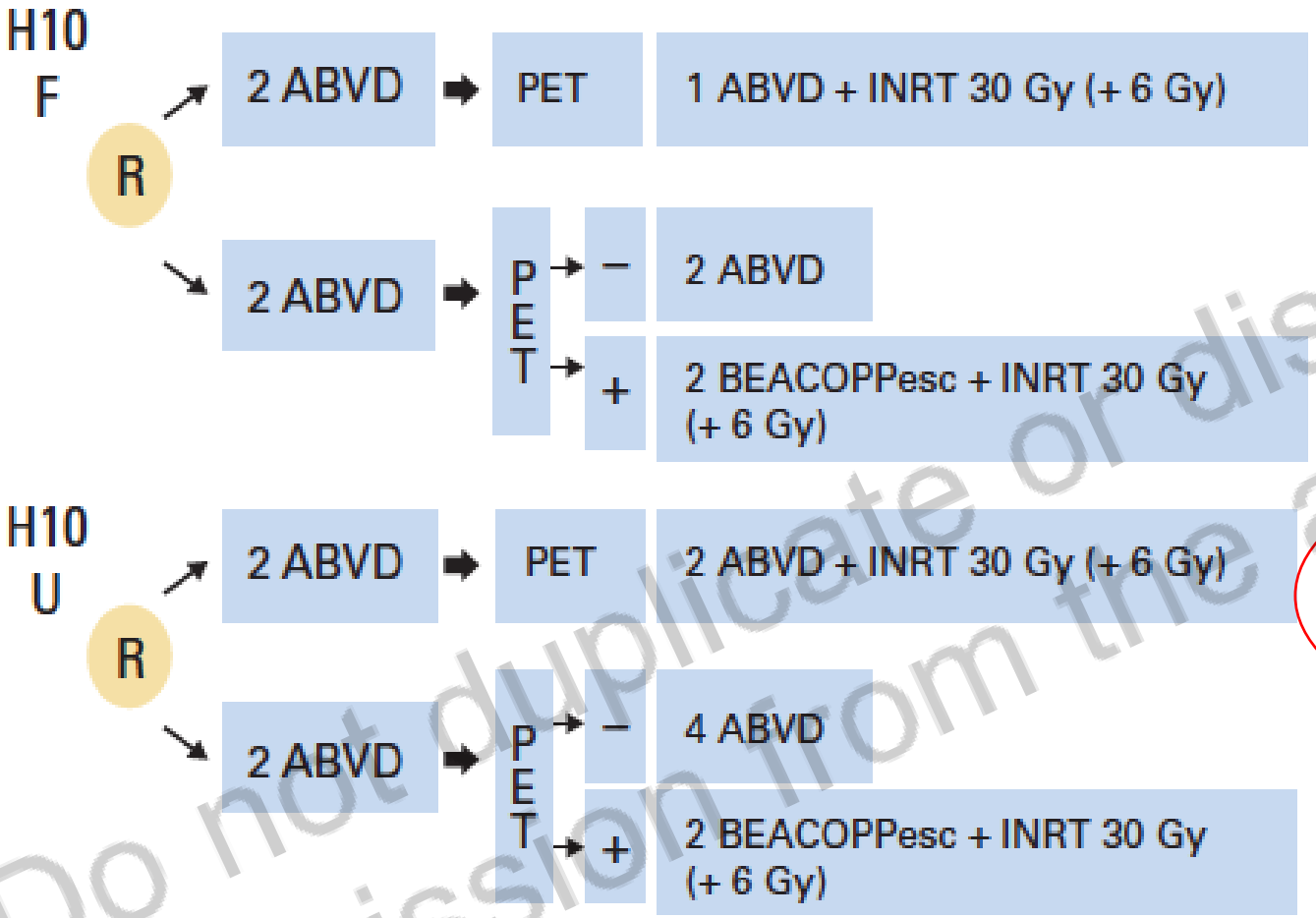
PET negative patients in H10



5 year PFS : F GROUP
RT: 99%
No RT: 87.1%

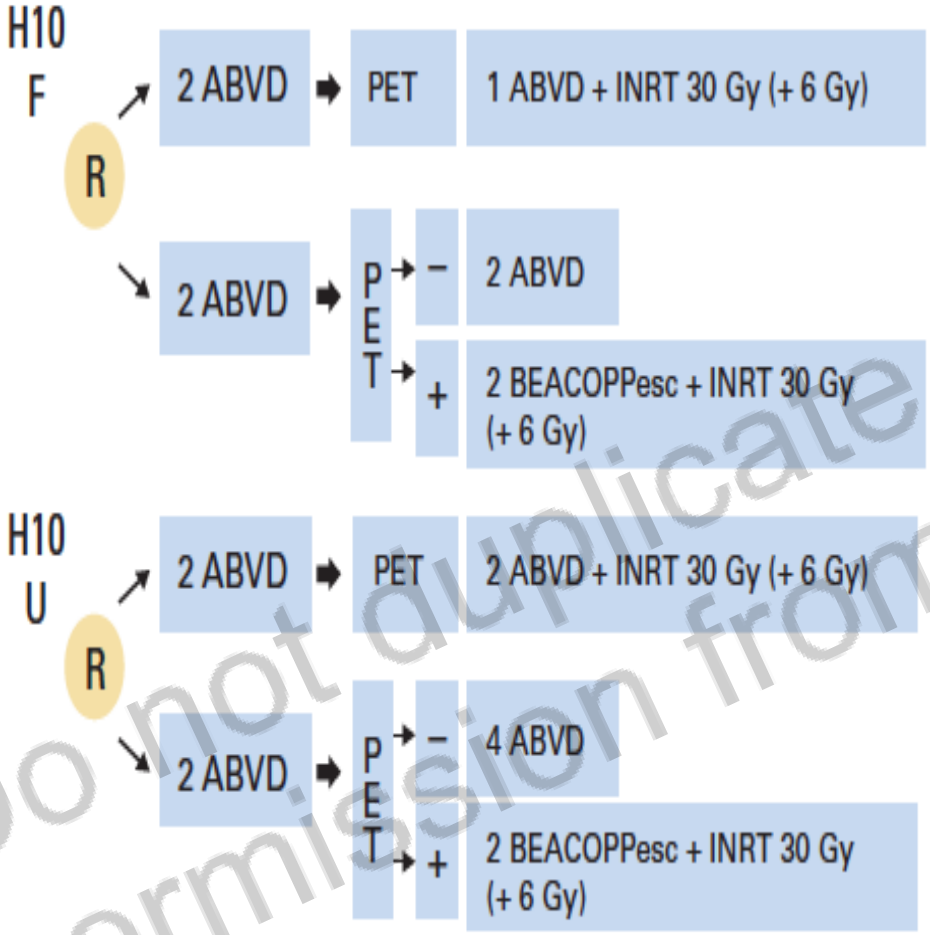
5 year PFS: U GROUP
RT: 92.1%
No RT: 89.6%

Compare this to:
HD14 10yr PFS 91%
HD17 5yr PFS 95% (PET4 negative)

F: Favourable, U: Unfavourable

Andre *et al* (2017) JCO: 35(16): 1786-1794

PET positive: 13% of F group and 22% of U group



5 yr PFS
ABVD+INRT: 77.4%
eBEACOPP+INRT: 90.6%
P=0.02

Compare this to:
HD17 5 year PFS 82% at PET 4 DS4

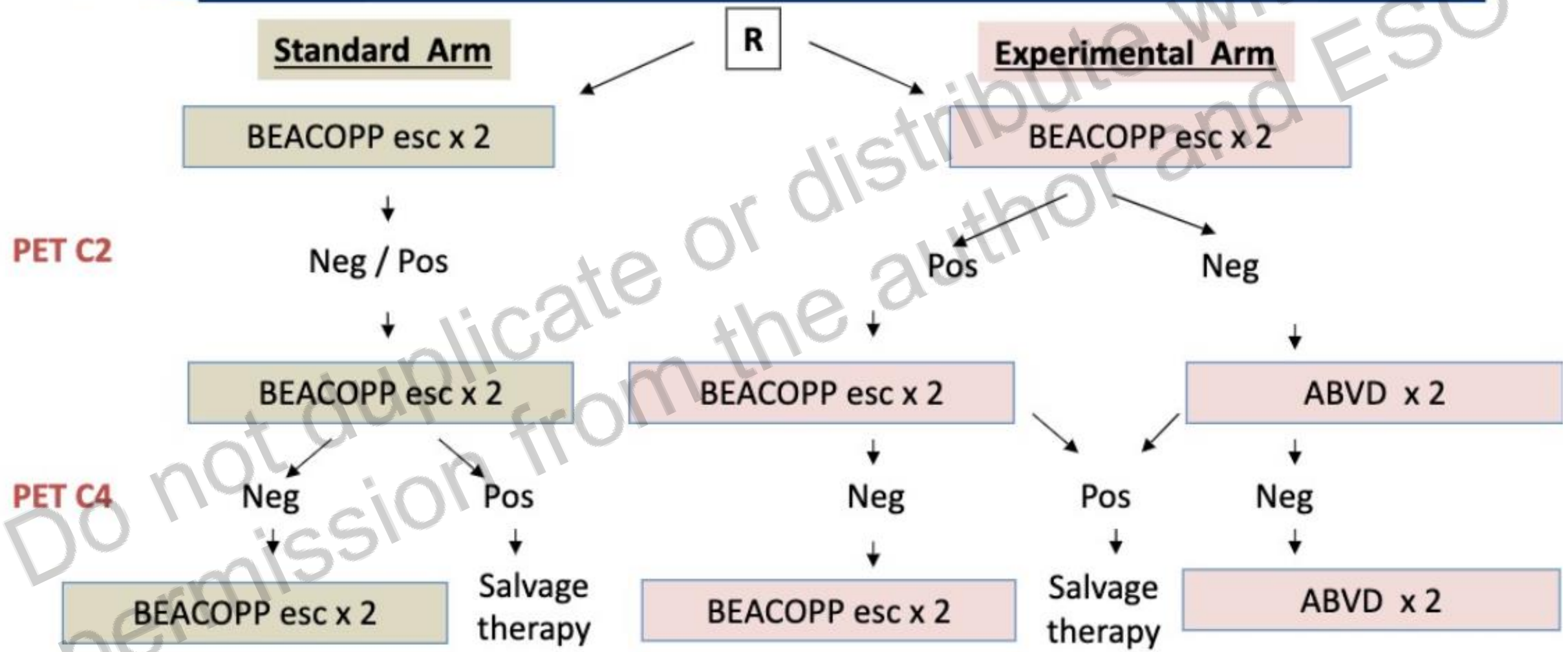
Andre *et al* (2017) JCO: 35(16): 1786-1794

Retrospective review of 148 patients <60 years with IIB and mediastinal bulk or extra-nodal localization (10% of pts)

Stage High risk IIB Hodgkin lymphoma treated in the H10 and AHL2011 trials: **similar efficacy** of both strategies and **prognostic impact** of baseline TMTV and PET2 response

Cédric Rossi, Marc André, Clémentine Joubert, Catherine Fortpied, Pauline Brice, Bénédicte Deau, Hervé Ghesquières, Luc Fornecker, Anne-Claire Gac, Julien Lazarovici, Aspasia Stamatoullas, John Raemaekers, Massimo Federico, Marie Maerevoet, Sarah Bailly, Salim Kanoun, Michel Meignan, Anne-Ségolène Cottereau, René-Olivier Casasnovas

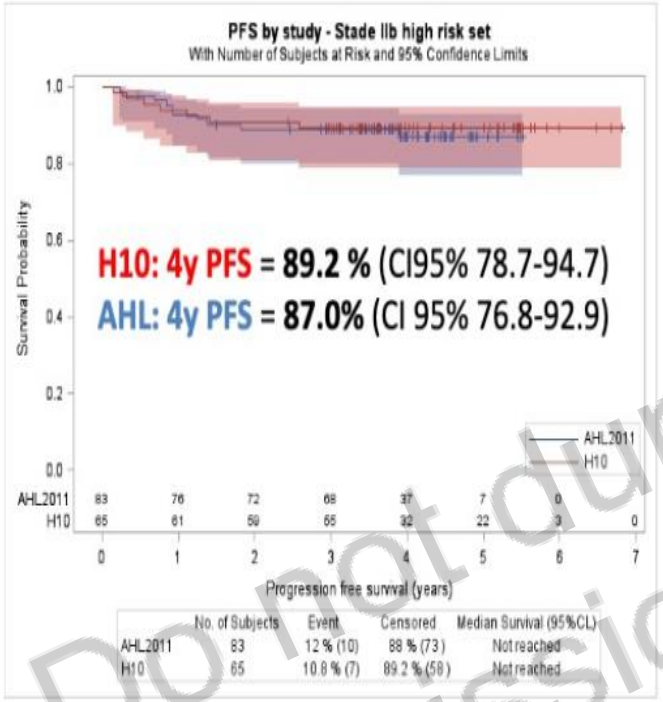
AHL2011 study (IIB high risk-III-IV stage)

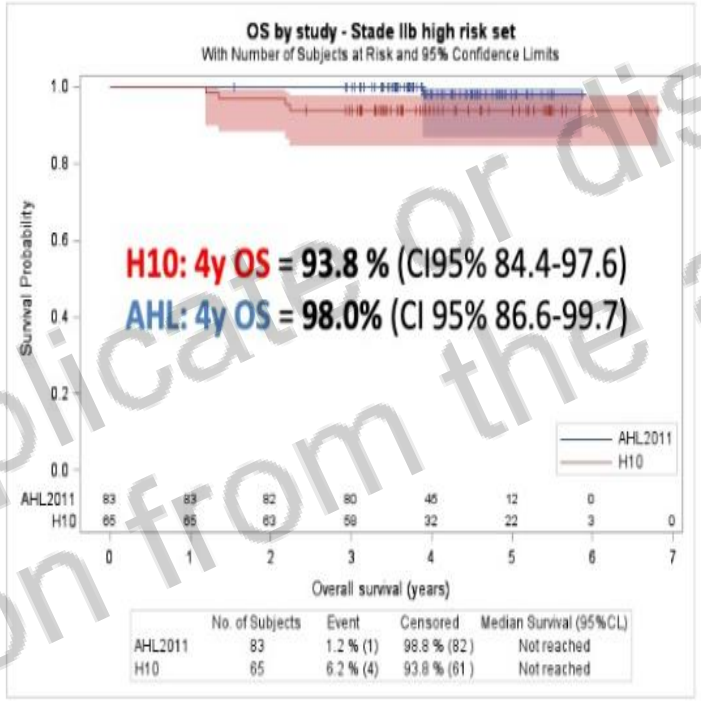


Casasnovas et al., Lancet Oncol., 2019

Outcome according to study

Median follow-up: **4.1 years** (95% IC 3.9-4.4)





Similar PFS between approaches

More severe disease at baseline in AHL 2011 group

TMTV >155mls and IPS >3 associated with inferior outcome with H10 approach

Could we use these predictive factors to select treatment upfront?

Treatment options for Early Unfavourable HL

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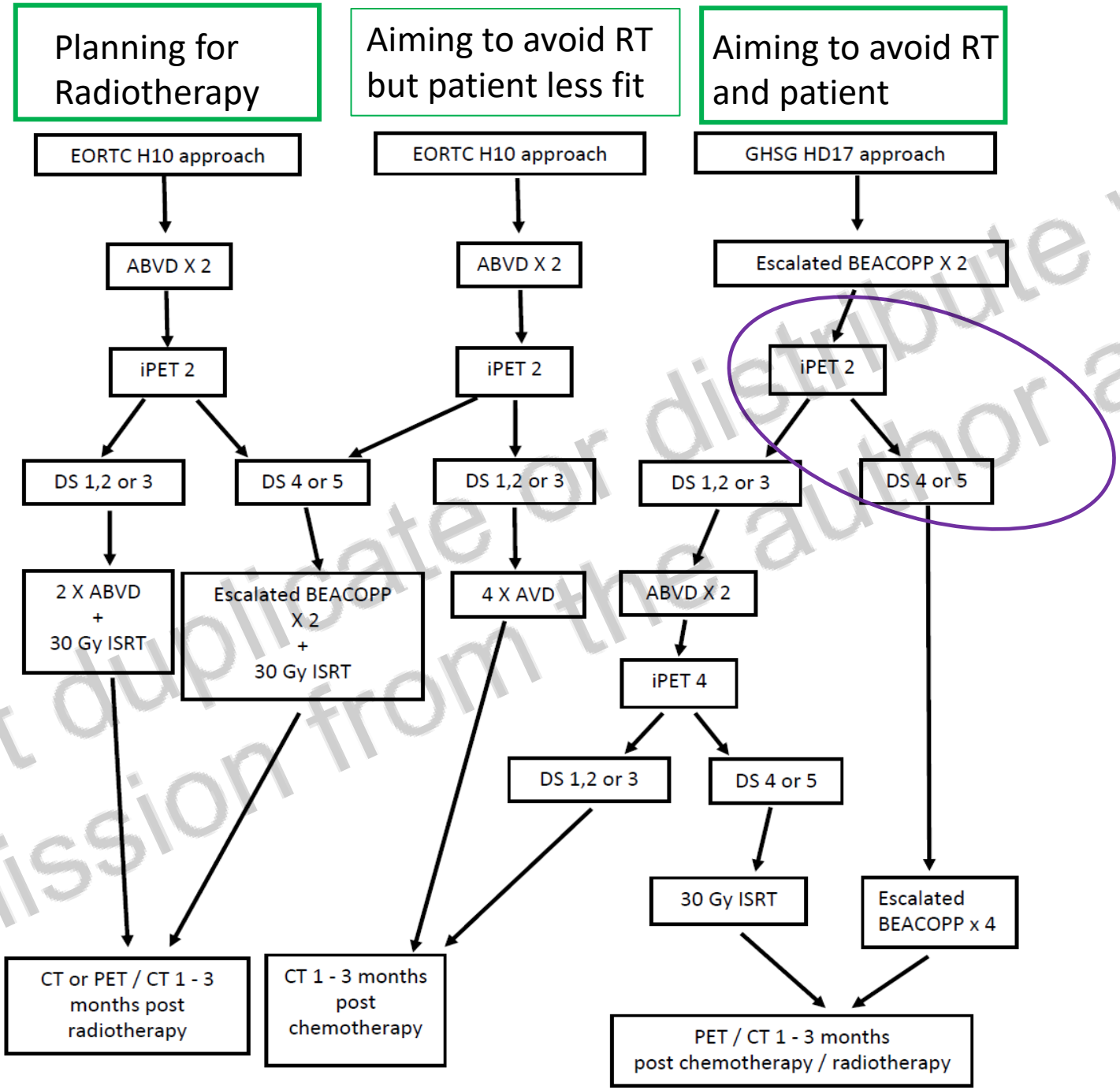
We are unable to compare the data from trials due to different patient populations and PET assessments

	HD17	H10	RATHL	HD18	AHL2011
% Early unfavourable patients	100%	100 % U arm	42%	14%	11%
% iPET2 positive	Not done (iPET4 9%)	22%	16%	25%	16% (SUV 140% liver)
PET neg PFS	95% at 5yrs if Pet4 neg	92% (4ABVD +30) 90% (6 x ABVD)	84% at 3 years (whole cohort)	95% at 3 years (whole cohort)	87% at 5 years (whole chort)
PET pos PFS	82% at 5 years if PET 4 pos	91% if escalated 77% if not (4 ABVD+30Gy)	68% at 3 years (whole cohort)	88% at 3 years (whole cohort)	75% at 5 years (whole cohort)
% pts having radiotherapy	9%	100% if IPET2 pos	7%	13%	<1%

Approach in Newcastle to Early Unfavourable HL



iPET is included to allow movement to HD18 if concerns about response

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Biopsy: classical Hodgkin, nodular sclerosis

MDT discussion, clinical oncology keen to avoid RT

H10 vs HD17 discussed with patient

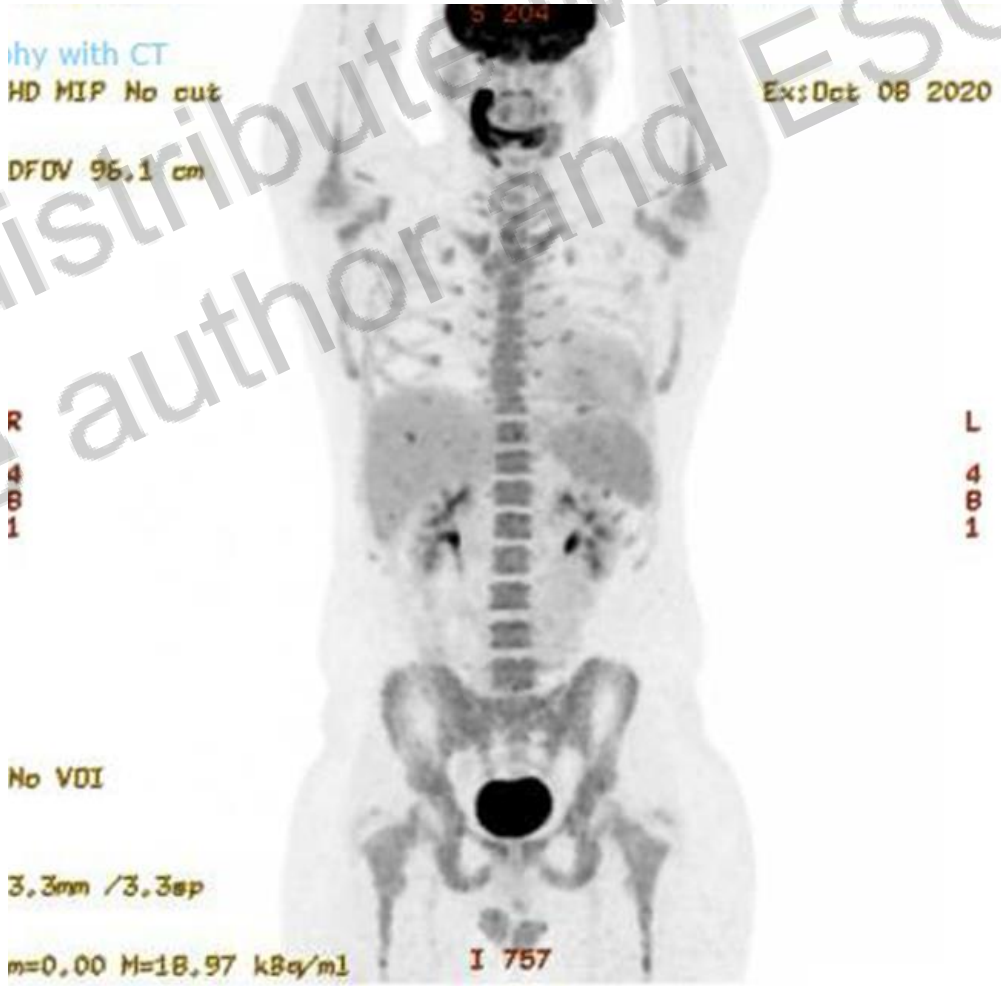
Elected for HD17

2 X Escalated BeacopDac

iPET 2 Deauville 3

2 X ABVD and no radiotherapy

EOT PET scan complete metabolic response



Conclusions: Clinical oncology opinion in MDT is essential, is the toxicity of radiotherapy acceptable?

Yes: **H10**

No: **HD17** 5 yr PFS in PET4 neg patients 95%

9% of patients will be PET4 positive, will need RT and 5 year PFS 82%

H10 77% of U pts were iPET2 neg in H10, had 5 yr PFS 90% with 6 X ABVD

RATHL 84 % of **whole** trial cohort iPET2 neg with 3 year PFS 84%

16 % of **whole cohort** were iPET2 positive and escalated with 3 yr PFS 68%

We need to understand how we can predict the iPET2 positive patients upfront