Guy's and St Thomas' NHS
NHS Foundation Trust

KING'S College LONDON
University of London

Combination of Baseline MTV & Deauville score >2 cycles improves prediction of PFS in DLBCL

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5th International workshop on PET in Lymphoma,

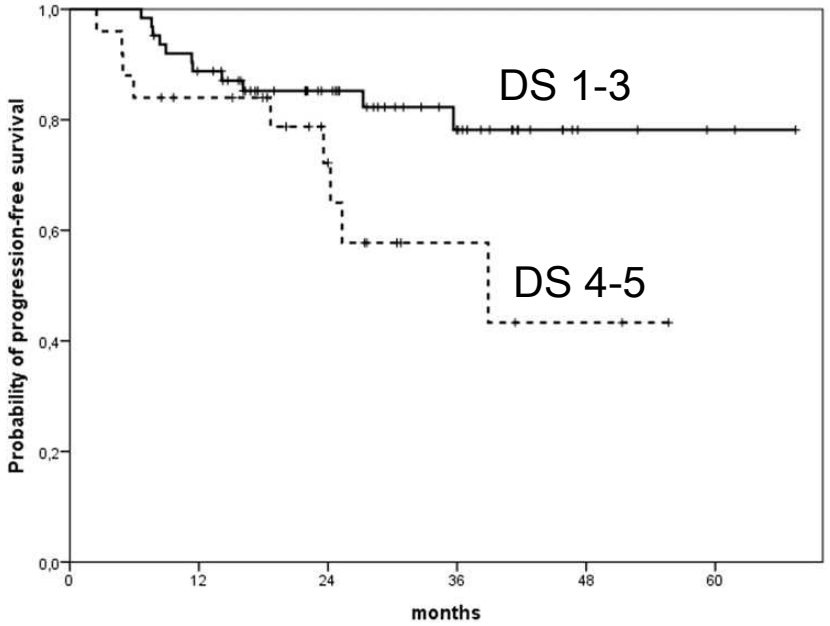
Menton, 19 Sept 2014

Background

- PET-CT using FDG demonstrates **early response** to chemotherapy in DLBCL.
- Previous studies using DS or ΔSUVmax alone showed **low PPV** and were not able to identify a group with sufficiently poor prognosis who may be candidates for testing early change in treatment.
- Prognosis of DLBCL is determined by many **other factors** in addition to early response to chemotherapy.
- Response assessment with DS or ΔSUVmax is based on assessing level of residual uptake after few cycles of chemotherapy but does not make full use of **baseline PET information**.

blood
JOURNAL OF THE AMERICAN SOCIETY OF HEMATOLOGY

PFS according to iPET (Deauville Score)



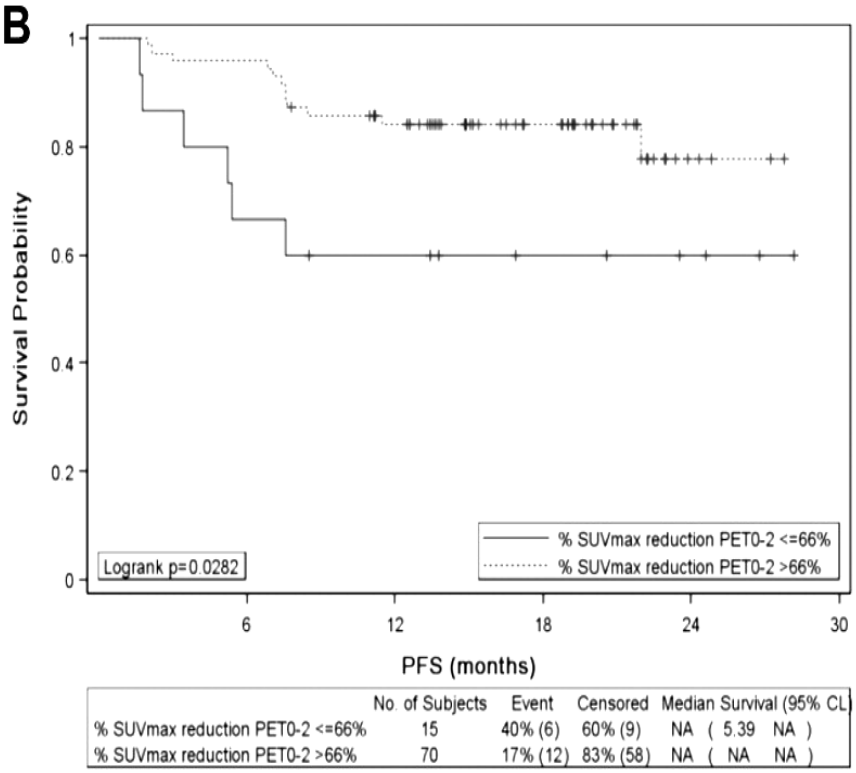
PFS = 85% for negative patients

& 72% for positive patient

P = .047

Pregno P et al. Blood 2012;119:2066

PFS of 85 patients according to %SUV max reduction

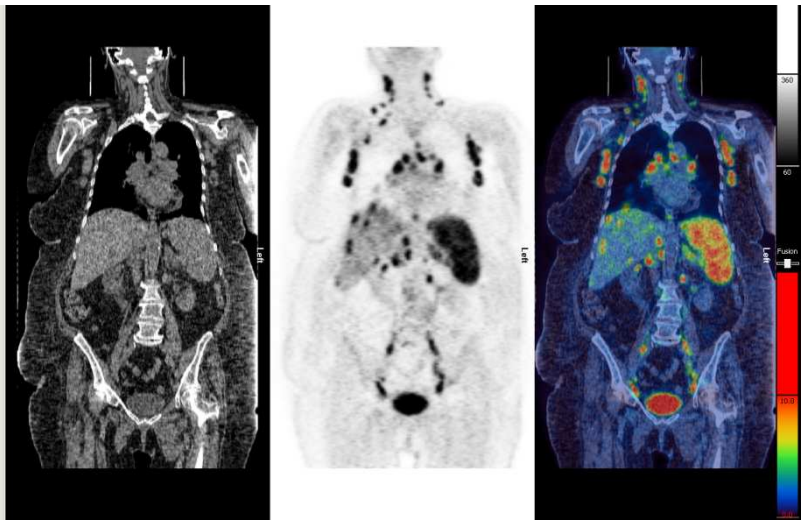


	No. of Subjects	Event	Censored	Median Survival (95% CL)
% SUVmax reduction PET0-2 <=66%	15	40% (6)	60% (9)	NA (5.39 NA)
% SUVmax reduction PET0-2 >66%	70	17% (12)	83% (58)	NA (NA NA)

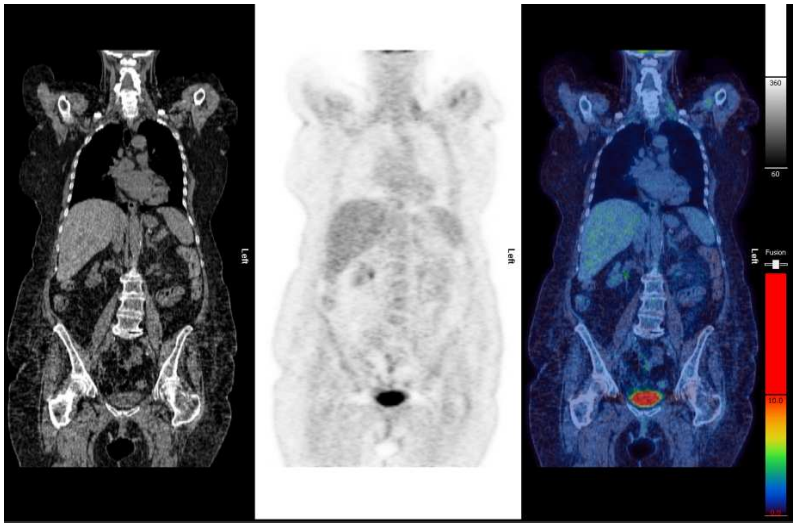
Casasnovas R et al. Blood 2011;118:37

Patient 1

Baseline

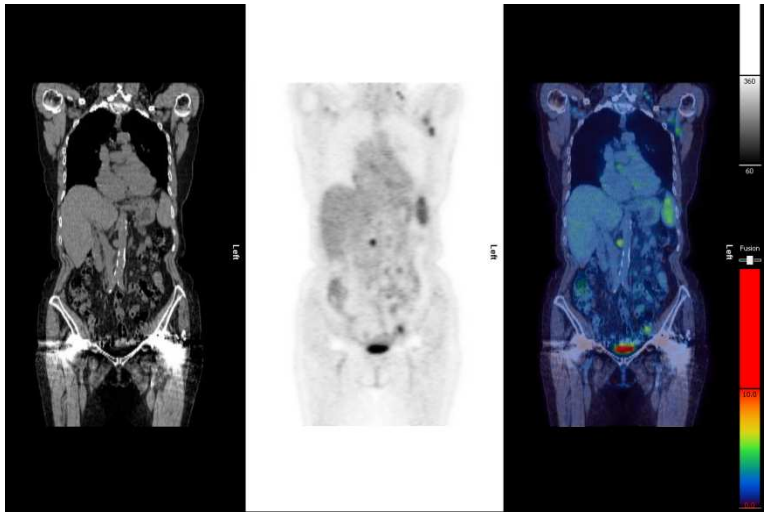


R-CHOP x 2

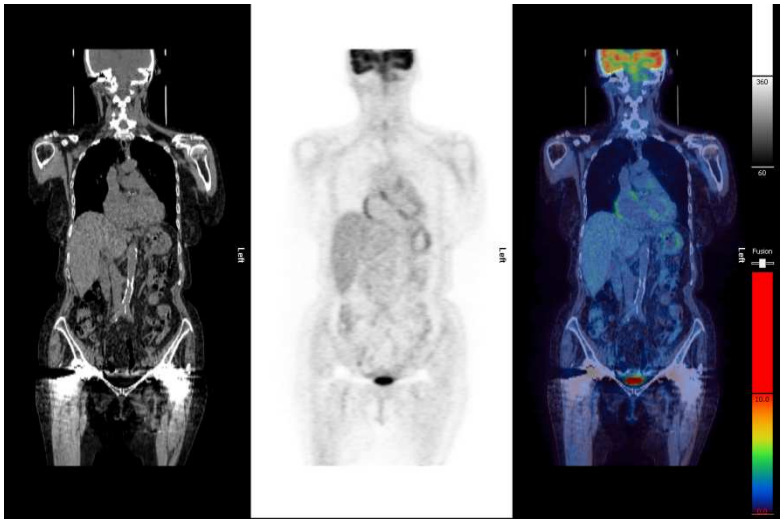


Patient 2

Baseline



R-CHOP x 2



Objectives

- Evaluate the prognostic value of quantitative parameters particularly metabolic tumour burden
- Test the hypothesis that *"combining measurement of metabolic tumour burden at baseline with early PET response could improve the prognostic ability of iPET in DLBCL"*.
- Identify a group of patients with sufficiently poor prognosis who may be candidates for testing alternative approaches.

Patient Population

147 patients treated at Guy's & St Thomas' Hospital, London.

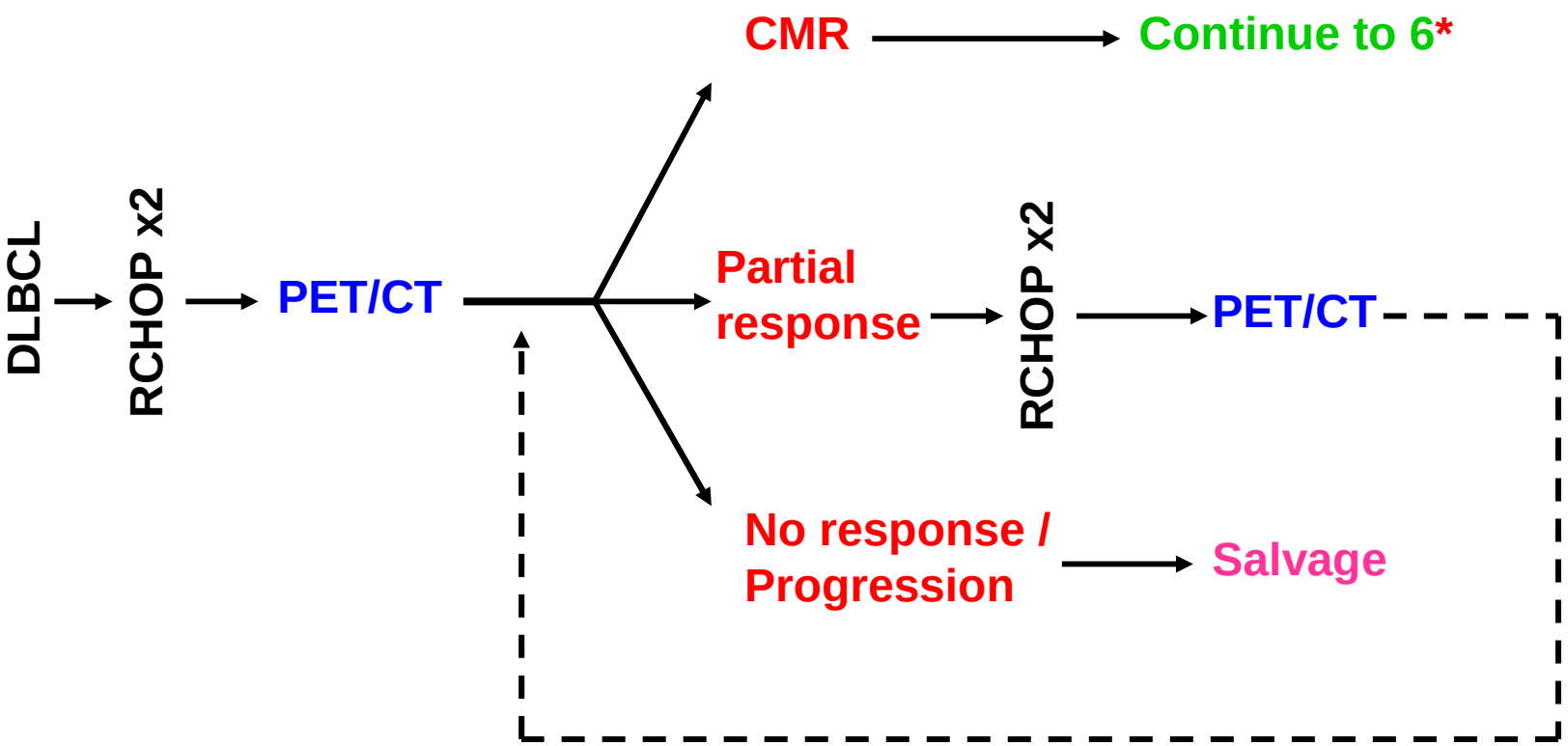
Inclusion

- New diagnosis DLBCL March 2005 - August 2012
- R-CHOP
- PET/CT at baseline and after 2 cycles
- Minimum FU 12 months

Exclusion

- Concurrent LGL or other malignancy
- Previous Anthracycline exposure
- No assessable disease on baseline PET/CT

Treatment Protocol



*If localised stage + non-bulky: 3-4 cycles + IFRT

Imaging

- FDG-PET/CT
  - FDG 350 MBq, 90 min uptake time
  - Reported by 2 NM physicians

- PET review: all scans reviewed (blindly) for study:
  - Sites of disease
  - Baseline staging
  - Deauville score after 2 cycles

- Segmentation
  - PETRRA software for automated segmentation
  - NM physician manually modified volumes to exclude physiological uptake.

Quantitative parameters

Baseline:

- **SUVmax-0:** baseline maximum Standardised Uptake Value
- **MTV-0** (Metabolic Tumour Volume): baseline total metabolic volume of all lesions, defined by SUV≥2.5 threshold
- **TLG-0** (Total Lesion Glycolysis): bMTV x mean SUV

>2 cycles:

- **SUVmax-2**
- **MTV-2**
- **TLG-2**

- **IPI**
- **Deauville score (DS)**

% change (% reduction from baseline)**:**

- **ΔSUVmax**
- **ΔMTV**
- **ΔTLG**

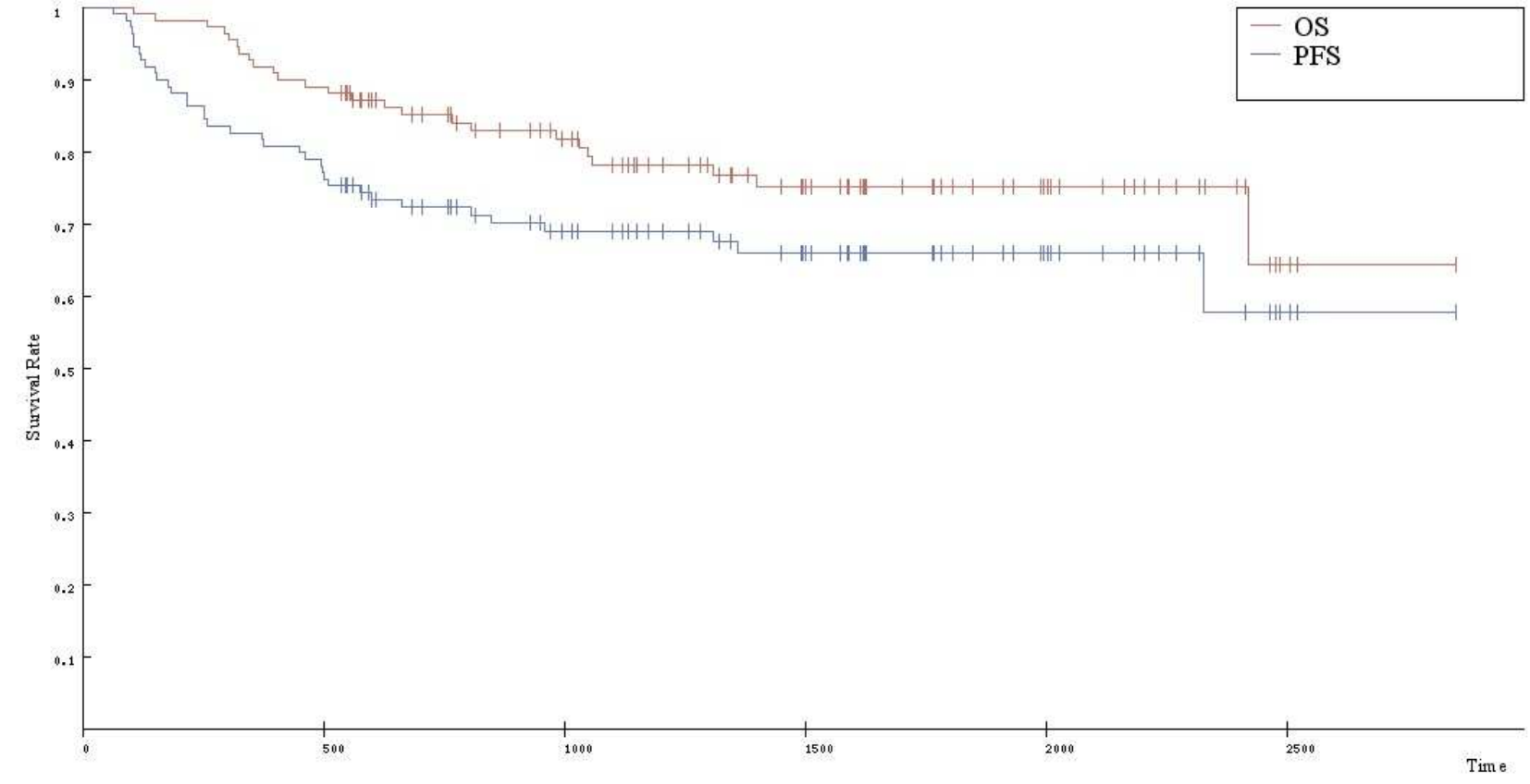
Statistical Analysis

- End point: PFS
- Cox regression:
  - to test the relationship between PFS and the study variables
  - Non-categorical data were grouped into tertiles
- Receiver Operator Characteristics (ROC) analysis :
  - to determine optimal cutoff
- KM survival analysis
  - using optimal cutoff
  - KM analysis of combined parameters to define worst prognostic group

Patient characteristics

Sex	Female	74
	Male	73
Age	Range	22 – 86
	Median	57
Stage	I	17 (11%)
	II	29 (20%)
	III	16 (11%)
	IV	85 (58%)
IPI	0/1	45 (31%)
	2	18 (12%)
	3	38 (26%)
	4/5	46 (31%)

PFS & OS for all patients



Univariate analysis

Baseline	> 2 cycles	
IPI	DS	
SUVmax-0	SUVmax-2	ΔSUVmax
MTV-0	MTV-2	ΔMTV
TLG-0	TLG-2	ΔTLG

Significant variables

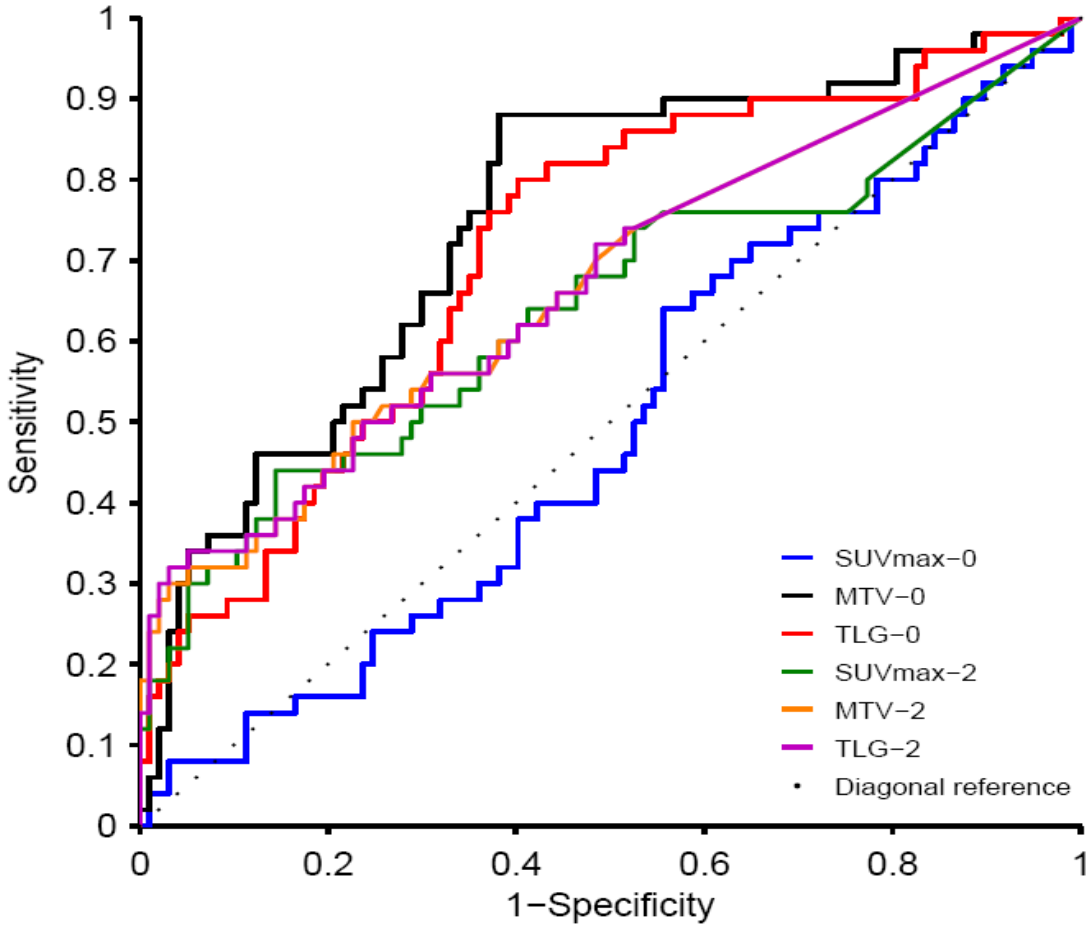
Baseline	> 2 cycles	
IPI	DS	
	SUVmax-2	ΔSUVmax
MTV-0	MTV-2	
TLG-0	TLG-2	

MVA

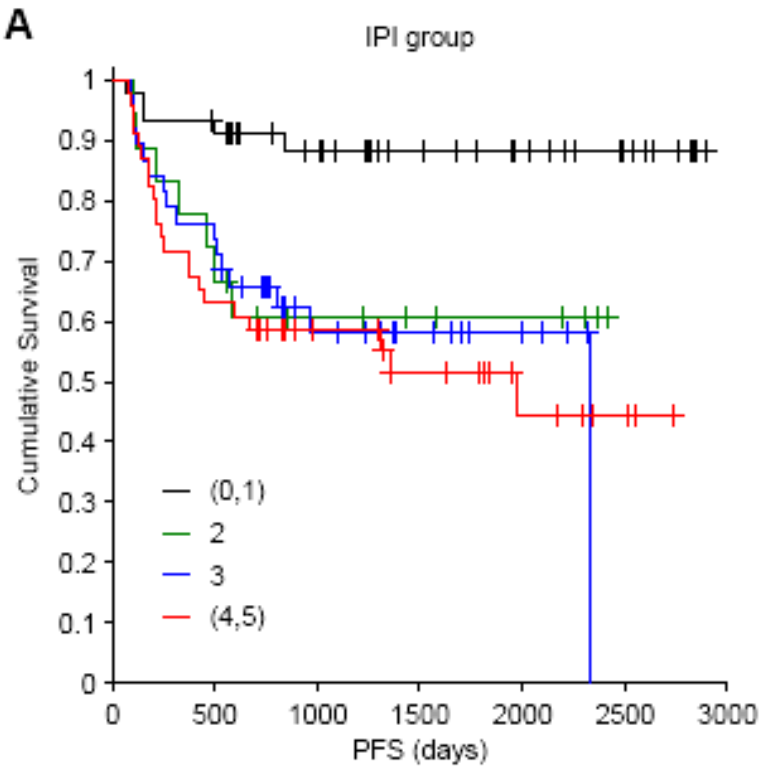
Baseline	> 2 cycles	
IPI	DS	
	SUVmax-2	ΔSUVmax
MTV-0	MTV-2	

MEASURE	LEVELS	CASES (n=147)	MULTIVARIATE HR	95% C.I for HR	
IPI groups	(0,1)	45	1.00		
	2	18	2.95	0.82	10.60
	3	38	2.30	0.74	7.21
	(4,5)	46	2.98	0.98	9.08
		TREND:	***χ^2 =***	***2.78***	***P-value =***	***.0955***
DS	1	34	1.00		
	2	18	0.21	0.04	1.09
	3	30	0.06	0.01	0.42
	4	47	0.09	0.01	0.62
	5	18	0.23	0.03	1.88
		TREND:	***χ^2 =***	***0.95***	***P-value =***	***.3303***
MTV-0 Tertiles	Lower	49	1.00		
	Middle	49	2.73	.89	8.40
	Upper	49	3.46	1.10	10.86
		TREND:	***χ^2 =***	***4.00***	***P-value =***	***.0454***
SUVmax-2 Tertiles	Lower	49	1.00		
	Middle	49	2.56	.20	33.22
	Upper	49	0.98	.06	16.10
		TREND:	***χ^2 =***	***2.40***	***P-value =***	***.1216***
MTV-2 Tertiles	Lower	59	1.00		
	Middle	39	4.16	.49	35.29
	Upper	49	8.08	.72	90.67
		TREND:	***χ^2 =***	***3.02***	***P-value =***	***.0820***
Δ SUVmax Tertiles	Lower	49	1.00		
	Middle	49	1.04	.32	3.31
	Upper	49	1.16	.32	4.17
		TREND:	***χ^2 =***	***0.09***	***P-value =***	***.7701***

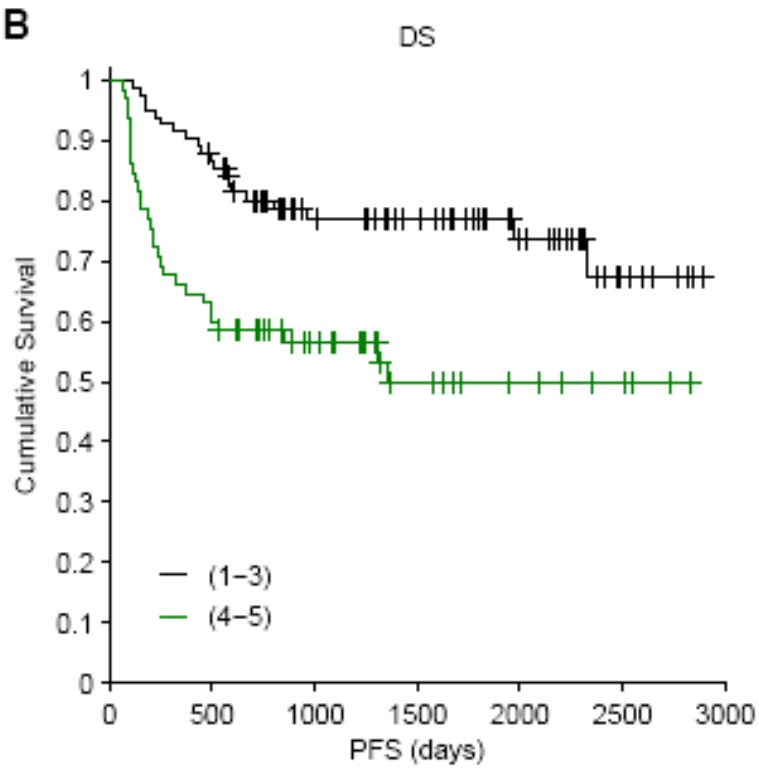
Receiver Operator Characteristic (ROC) analysis for continuous variables



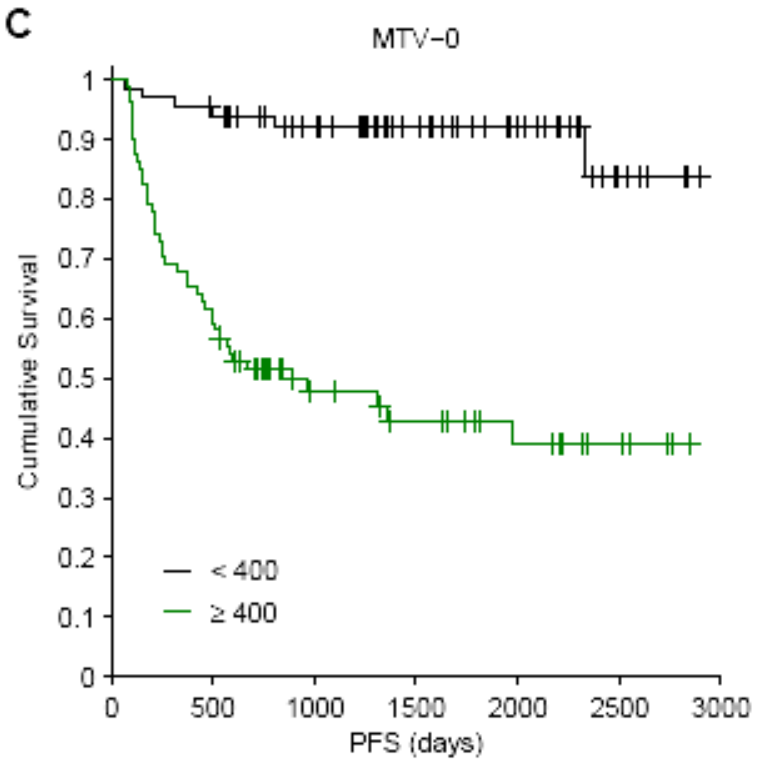
	Cut-off
MTV-0	**396**
TLG-0	**4541**
MTV-2	1.8
TLG-2	5.6
ΔMTV	99.8%
ΔTLG	99.9%


A
IPI group
Cumulative Survival
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
500
1000
1500
2000
2500
3000
PFS (days)
(0,1)
2
3
(4,5)

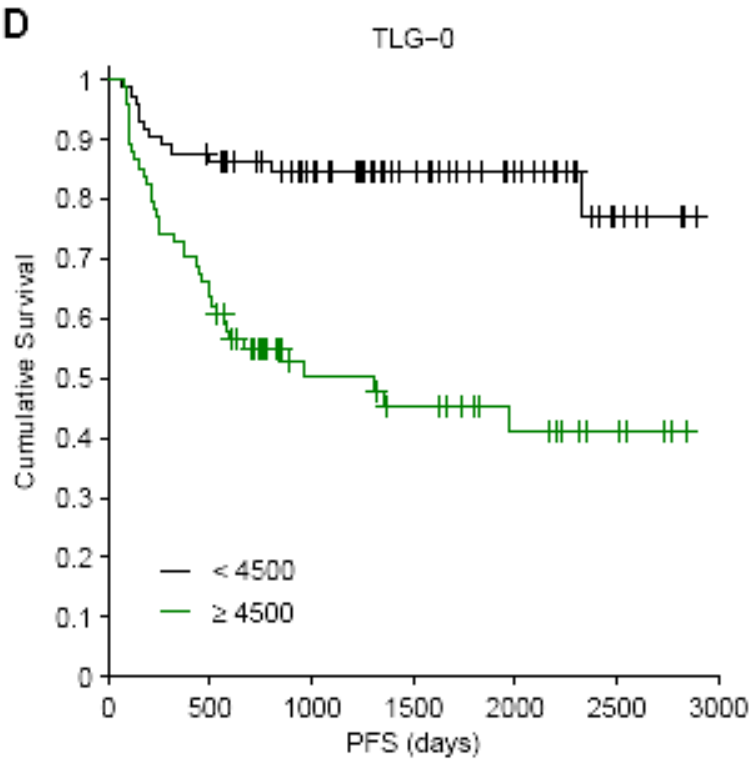
P<.0001


B
DS
Cumulative Survival
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
500
1000
1500
2000
2500
3000
PFS (days)
(1–3)
(4–5)

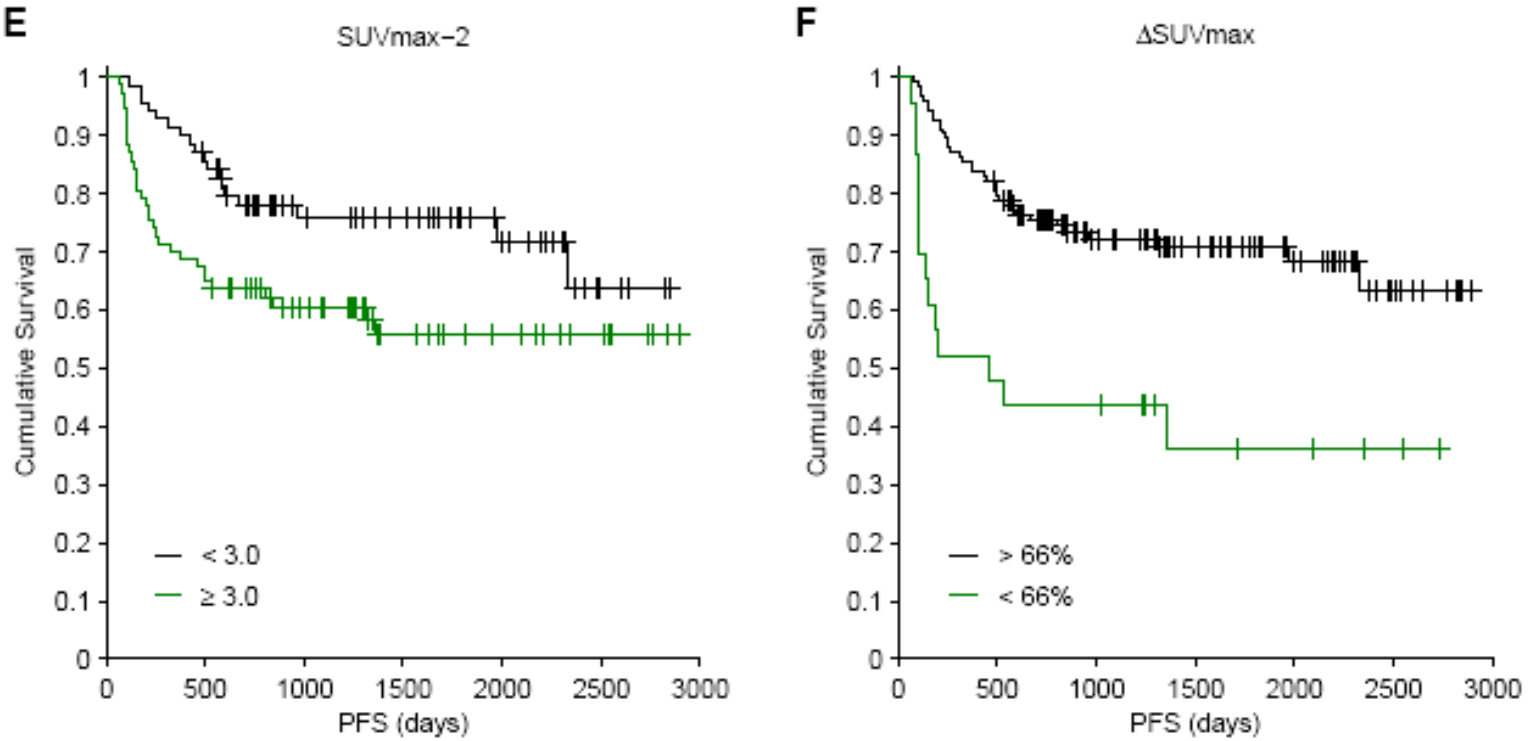
P=.001


C
MTV-0
Cumulative Survival
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
500
1000
1500
2000
2500
3000
PFS (days)
< 400
≥ 400

P<.001


D
TLG-0
Cumulative Survival
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
500
1000
1500
2000
2500
3000
PFS (days)
< 4500
≥ 4500

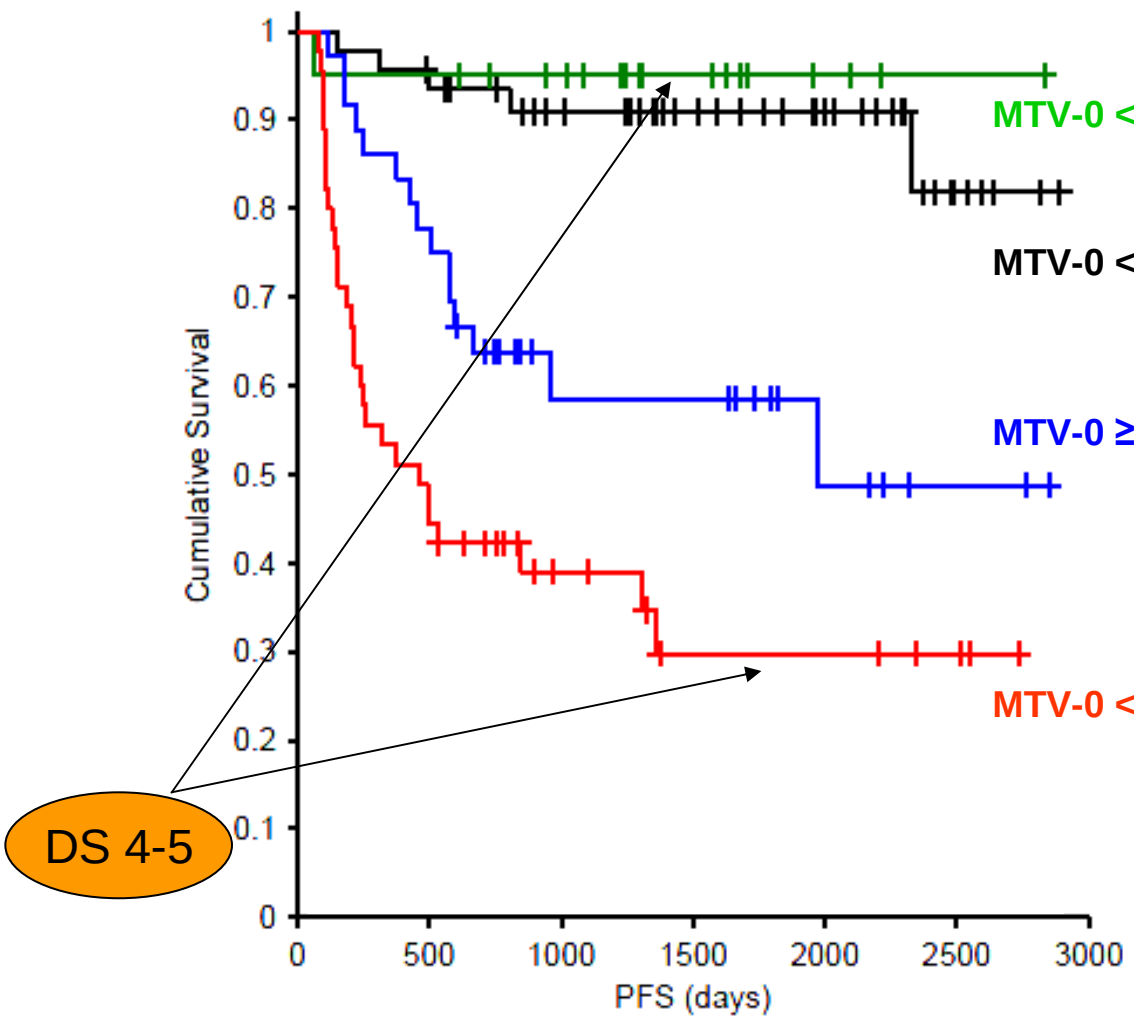
P<.001


E
SUVmax−2
Cumulative Survival
PFS (days)
< 3.0
≥ 3.0
F
ΔSUVmax
Cumulative Survival
PFS (days)
> 66%
< 66%

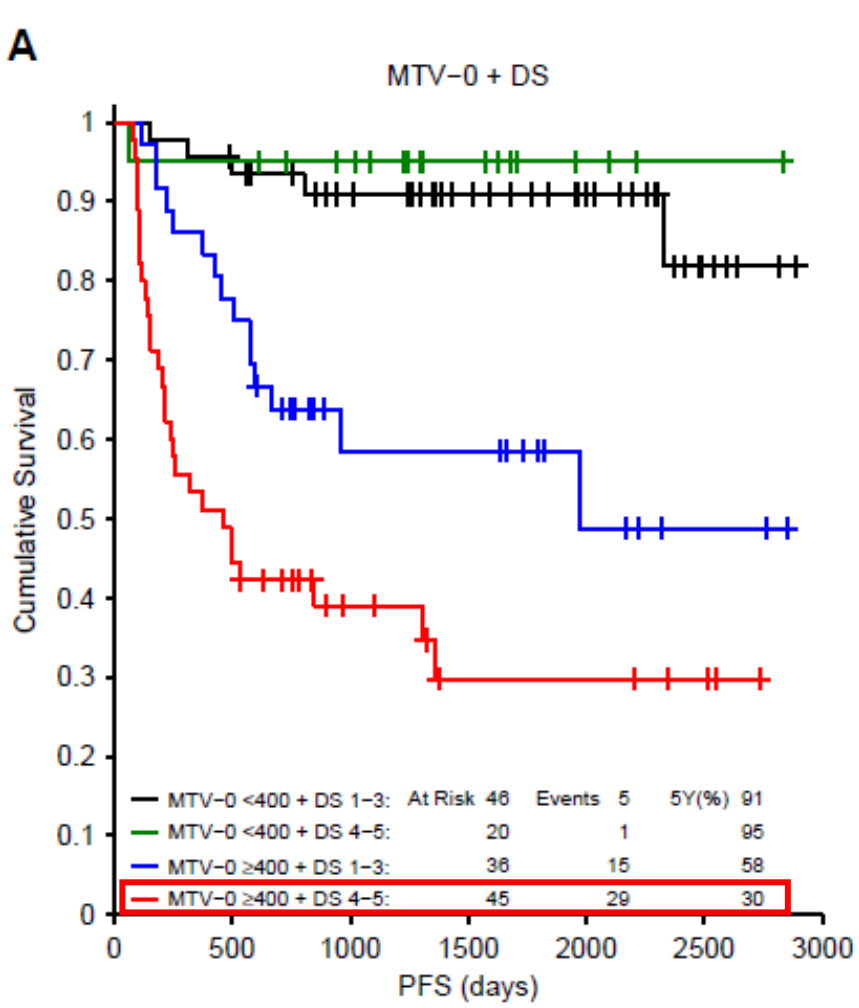
P=.02

P<.001

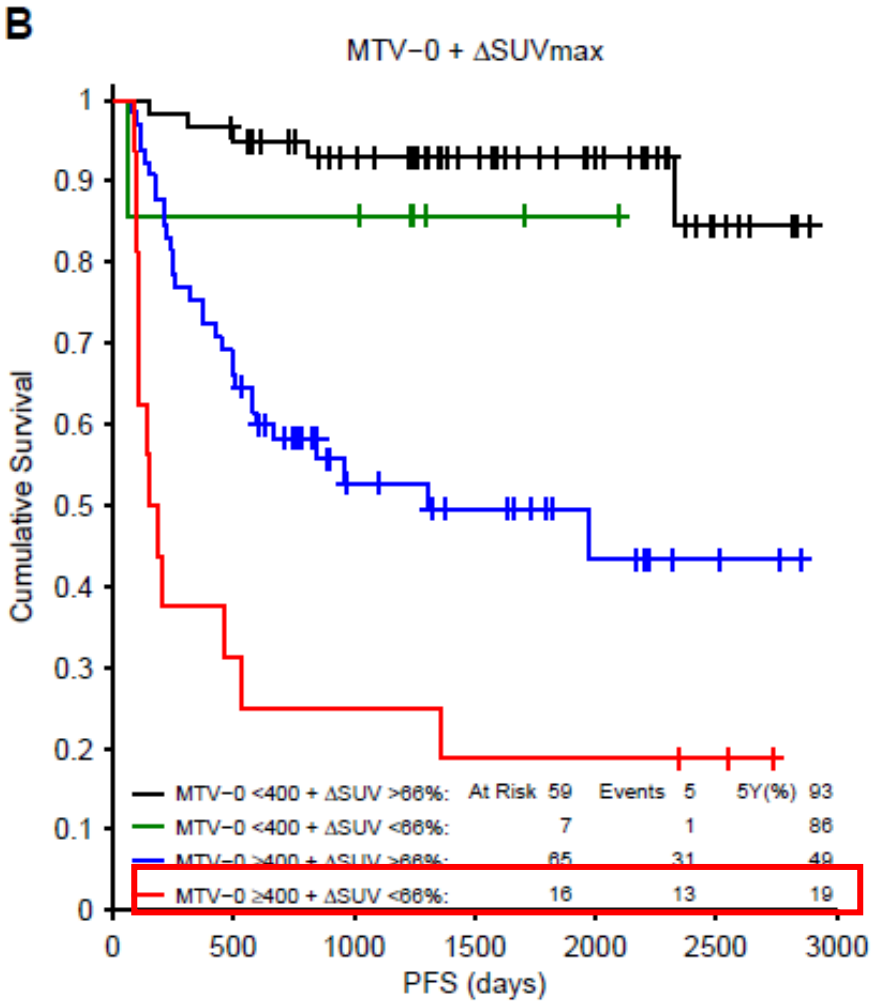
MTV-0 + DS



	At risk	events	5y-PFS
MTV-0 <400 + DS 4-5	20	1	95%
MTV-0 <400 + DS 1-3	46	5	90.9%
MTV-0 ≥400 + DS 1-3	36	15	58.5%
MTV-0 <400 + DS 4-5	45	29	29.7%



58% of events



26% of events

Summary & Conclusion

- Baseline MTV and TLG were strongly predictive of prognosis but the change in these parameters after 2 cycles of chemotherapy was not
- On MVA, baseline MTV was the only significant parameter
- A model combining MTV-0 and DS improves prediction of PFS and identifies a group with significantly low PFS, where most of the events occur.
- The results will be validated in the completed UK-NCRI prospective blinded study

Acknowledgment

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