

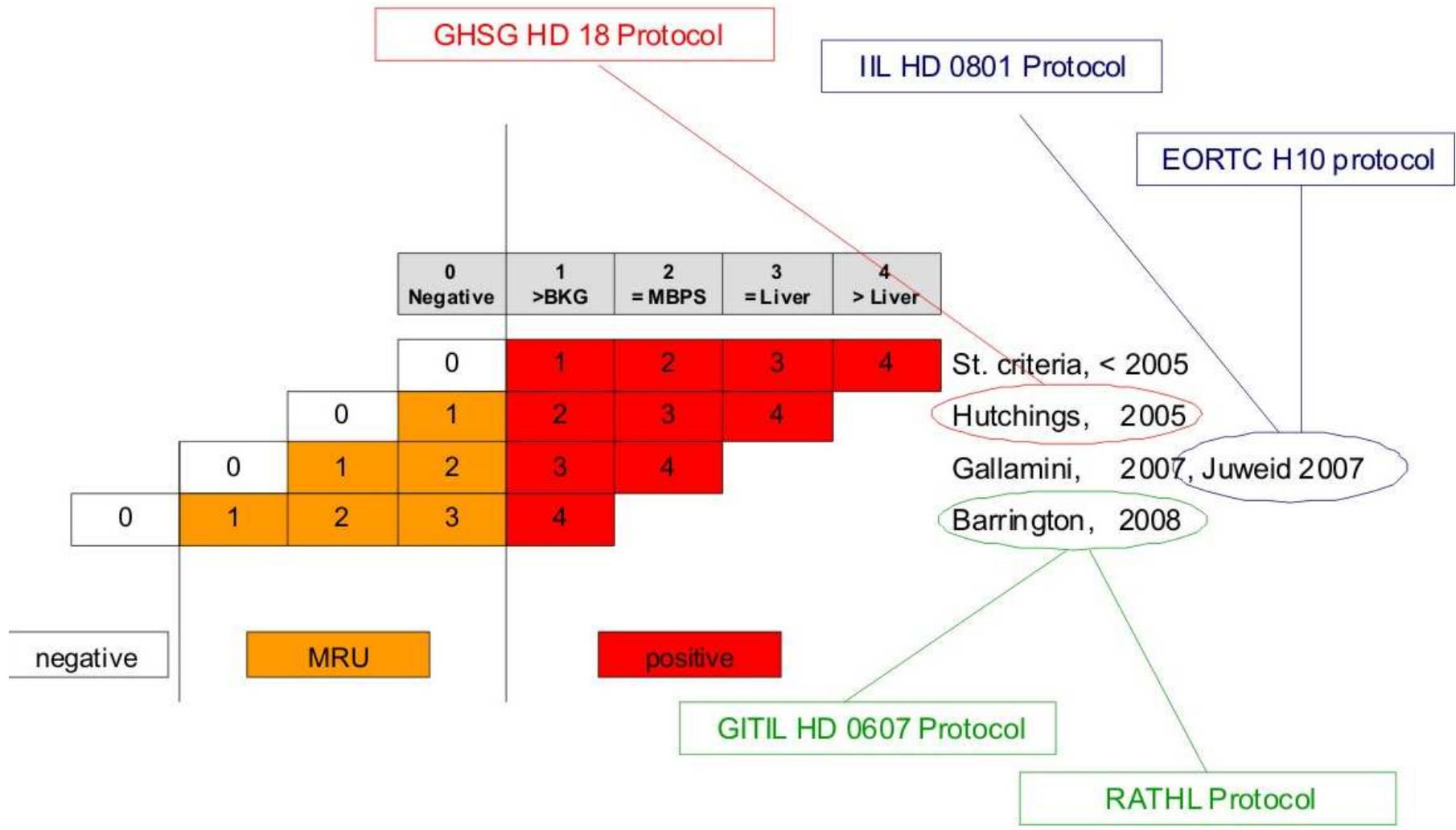
**How do we define a positive PET/CT for escalation of therapy is an issue not yet resolved. Therefore we performed a retrospective study and evaluated a functional dynamic scoring model to elucidate the significance of post-induction interim F<sup>18</sup>DG-PET/CT scanning in patients with Hodgkin Lymphoma .**

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# The MRU definition, as the time goes by.



Parameter	Data	Percent
Gender (M/F), number=96	49/47	51% / 49%
Median age, years (range)	30 (17-57)	
B symptoms, yes/no, number	43 / 53	45% / 55%
Bulky mediastinal mass, n	10	10%
<b>Early disease (Ia, IIa)</b>	<b>2/31</b>	<b>34%</b>
<b>Advanced disease Ann Arbor Stage - IB, IIB, III, IV</b> For these patients International prognostic score was applied	<b>63</b> <b>1/18/19/25</b>	<b>66%</b> -
<b>Initial chemotherapy regimen</b>		
<b>ABVD</b>	<b>33</b>	<b>34%</b>
Ann Arbor Stage (I,II) (III, IV)	25/8	76% / 24%
Radiation Therapy	22	67%
<b>BEACOPP</b>	<b>41</b>	<b>43%</b>
Ann Arbor Stage (I,II) (III, IV)	24/17	59% / 41%
Radiation Therapy	15	36%
<b>Escalated BEACOPP</b>	<b>22</b>	<b>23%</b>
Ann Arbor Stage (I,II) (III, IV)	3/19	14% / 86%
Radiation Therapy	2	9%

## 96 Patients assessed according to static visual score

Escalated BEACOPP N=22		Standard BEACOPP N=41		ABVD N=33	
Interim PET/CT		Interim PET/CT		Interim PET/CT	
Positive N=6	Negative N=16	Positive N=11	Negative N=30	Positive N=7	Negative N=26
5 CCR median: 50 months (36-64) 1 PPD	15 CCR median: 70 months (41-89) 1 PPD	9 CCR 7 following dose escalation median: 70 months (47-73) 2 PPD despite dose escalation	30 CCR median: 61 months (28-93)	5 CCR median: 54 months (43-79) 2 PPD (1 PPD despite dose escalation)	23 CCR median: 55 months (25-84) 1 PPD 2 relapses

**Fig. 1a**

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## Interim PET/CT dynamic visual score for HD patients

**0- No evidence of residual uptake.**

**1- Single site uptake.**

**2- More than one residual site with markedly decreased intensity compared to baseline in those sites.**

**3- No change in number of sites with pathologic uptake; however, reduced intensity of uptake in those sites compared to baseline.**

**4- No change in number of sites or intensity or appearance of new sites of uptake.**

## PET scoring criteria for a single site of HL at diagnosis

In case of a single focus of FDG uptake on the baseline PET/CT study, the response on the interim study will be defined as follows:

Score 0 – Negative PET (disappearance of uptake in the single site)

Score 1a – Residual uptake in a single site, reduced in area and intensity, compared to normal mediastinal or liver blood pool uptake)

Score 3a – Residual uptake in a single site, equal to or higher than uptake in normal mediastinal or liver blood pool uptake (the reference organ will be the hottest of these two), with or without change in uptake area.

Score 4a – No change in intensity or increase in intensity and area of FDG uptake in a single site, or the appearance of new foci of abnormal FDG uptake consistent with disease progression.

Table 3: EVALUATION OF DIFFERENT DYNAMIC SCORE CUT-OFF POINTS FOR DEFINITION OF NEGATIVE AND POSITIVE INTERIM FDG-PET/CT

<b>96 patients</b>	<b>Negative PV % and (95% confidence interval)</b>	<b>Positive PV% and (95% confidence interval)</b>	<b>Specificity % and (95% confidence interval)</b>	<b>Sensitivity% and (95% confidence interval)</b>	<b>Accuracy% and (95% confidence interval)</b>
<b>Score 0 versus 1-4</b>	<b>94% (89-99)</b>	<b>21% (4.6-37)</b>	<b>78% (69-70)</b>	<b>56% (23-88)</b>	<b>76% (67.4-84)</b>
<b>Score 0-1 versus 2-4</b>	<b>93% (87-98)</b>	<b>27% (1-53)</b>	<b>91% (85-97)</b>	<b>33% (2-64)</b>	<b>85% (78-92)</b>
<b>Score 0-2 versus 3,4</b>	<b>93% (88-98)</b>	<b>50% (10-90)</b>	<b>96% (93-100)</b>	<b>33% (2-64)</b>	<b>91% (85-96)</b>

STATIC VISUAL SCORE	SCORE	DYNAMIC VISUAL SCORE (CURRENT STUDY)	F <sup>18</sup> FDG UPTAKE > MEDIASTINAL BLOOD POOL	F <sup>18</sup> FDG UPTAKE > LIVER BLOOD POOL
No abnormal F <sup>18</sup> FDG uptake	0	No abnormal F <sup>18</sup> FDG uptake	No abnormal F <sup>18</sup> FDG uptake	No abnormal F <sup>18</sup> FDG uptake
	1	A single residual focus of abnormal F <sup>18</sup> FDG uptake.  If only a single site on baseline: a markedly decreased intensity compared to baseline.	<b>Residual mass ≥2cm:</b>  Lesion uptake < mediastinum	<b>Residual mass ≥2cm:</b>  Lesion uptake < liver
	2	More than one site of residual uptake but with a marked decrease in number of disease sites compared to baseline.	<b>Residual mass ≥2cm:</b>  Lesion uptake = mediastinum	<b>Residual mass ≥2cm:</b>  Lesion uptake = liver



Static visual score	Score	Dynamic Visual Score	F <sup>18</sup> FDG uptake >mediastinal blood pool	F <sup>18</sup> FDG uptake > liver blood pool as comparator
Any focus of abnormal F <sup>18</sup> FDG uptake (not related to physiologic or benign tracer uptake).	3	Reduced intensity of uptake with no change in their number compared to baseline	<p><b>Residual mass ≥2cm:</b> moderately increased uptake compared with mediastinum <b>OR</b></p> <p><b>Residual mass &lt;2cm:</b> any focus of abnormal F<sup>18</sup>FDG uptake</p>	<p><b>Residual mass ≥2cm:</b> lesion uptake moderately increased compared with liver <b>OR</b></p> <p><b>Residual mass &lt;2cm:</b> any focus of abnormal F<sup>18</sup>FDG uptake</p>
	4	No change in both number and intensity of sites or the appearance of new sites of disease.	<p><b>Residual mass ≥2cm:</b> markedly increased uptake compared with mediastinum <b>OR</b></p> <p><b>Residual mass &lt;2cm:</b> any focus of abnormal F<sup>18</sup>FDG uptake (not related to physiologic or benign uptake).</p>	<p><b>Residual mass ≥2cm:</b> Lesion uptake markedly increased compared with liver <b>OR</b></p> <p><b>Residual mass &lt;2cm:</b> any focus of abnormal F<sup>18</sup>FDG uptake (not related to physiologic or benign uptake).</p>

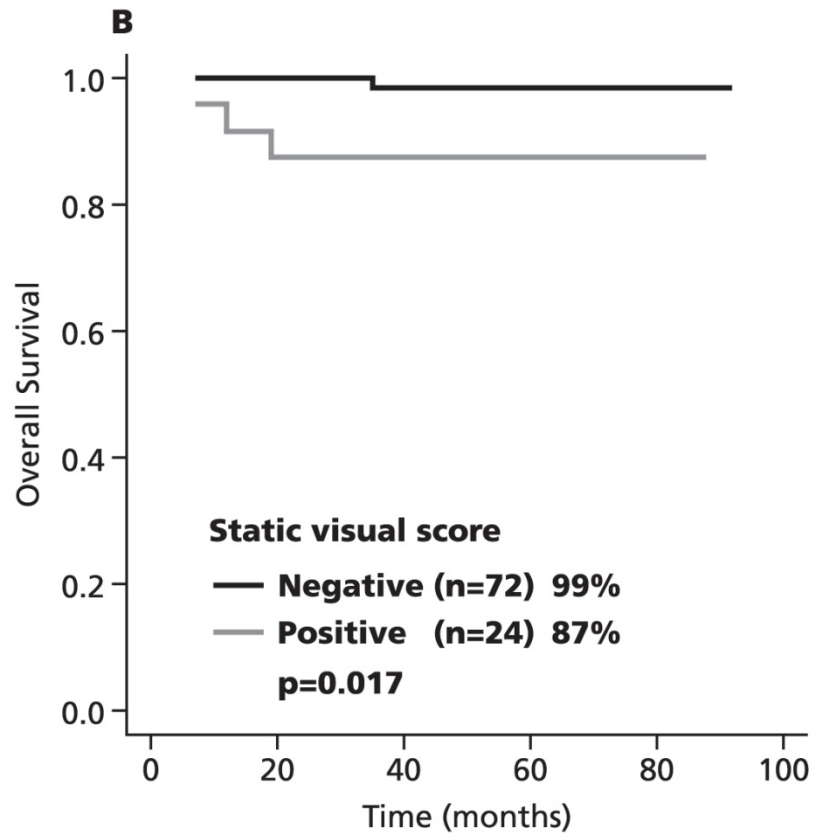
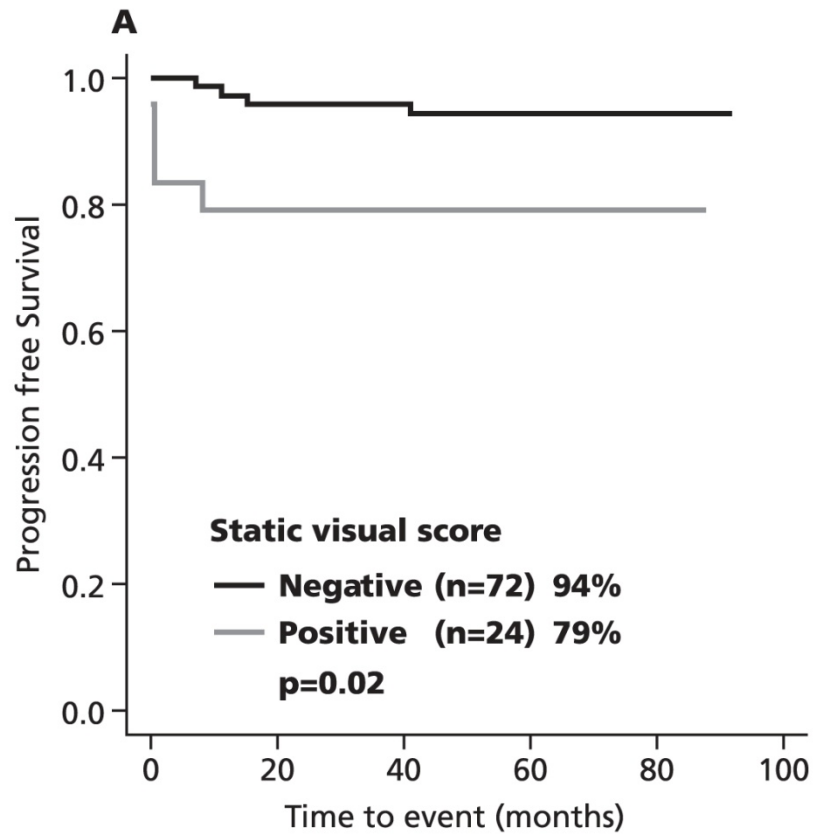
	Negative PV	Positive PV	Specificity	Sensitivity	Accuracy
<b>Static visual score</b>					
All patients (96)	(68/72) 94%	(5/24) 21%	(68-87) 78%*	(5/9) 55%	(73-96) 76%
<sup>®</sup> Modified cohort (n=88)	(68/72) 94%	(5/16) 31%	(68.79) 86%#	(5/9) 55%	(73/88) 83%
Static score by CIS	(70-75) 93%	(4/21) 19%	(70/87) 80%**	(4/9) 44%	(74/96) 77%*†
<sup>®</sup> Modified cohort	(69/74) 93%	(4/14) 28%	69/79) 82%###	(4/9) 44%	(73/88) 83%
Static score liver blood pool	(74/80) 92%	(3/16) 19%	(74/87) 85%	(3/9) 33%	(77/96) 80%*††
<sup>®</sup> Modified cohort (n=88)	(70/76) 92%	(3/12) 25%	(70/79) 88%	(3/9) 33%	(73/88) 83%
<b>Dynamic visual score</b>					
All patients (96)	(84/90) 93%	(3/6) 50%	(84/87) 96%	(3/9) 33%	(87/96) 91%

When compared to the dynamic visual score: \*p <0.0001, \*\* p = 0.001, @ p <0.01, #p<0.03, ##p<0.05

	Negative PV	Positive PV	Specificity	Sensitivity	Accuracy
<b>Static visual score</b> All patients (96)	(68/72) 94%	(5/24) 21%	(68-87) 78%*	(5/9) 55%	(73-96) 76%
BEACOPP (41)	(30/30) 100%	(2/11) 18%	(30/39) 77%#	2/2	
Escalated BEACOPP (22)	(15/16) 94%	(1/6) 17%	(15/20) 75%	1/2	
<b>Liver blood pool</b> All patients (96)	(74/80) 92%	(3/16) 19%	(74/87) 85%	(3/9) 33%	(77/96) 80%**
BEACOPP (41)	(35/36) 97%	(1/5) 20%	(35/39) 90%	1/2	
Escalated BEACOPP (22)	(16/18) 89%	(0/4) 0%	(16/20) 80%	0/2	
All patients (96) <b>Dynamic visual score</b>	(84/90) 93%	(3/6) 50%	(84/87) 96%	(3/9) 33%	(87/96) 91%
BEACOPP (41)	(38/38) 100%	(2/3) 66%	(38/39) 97%#	2/2	
Escalated BEACOPP (22)	(19/21) 90%	(0/1) 17%	(19/20) 95%	0/2	

When compared to the dynamic visual score: \*p < 0.0001, \*\* p = 0.001, @ p < 0.01,

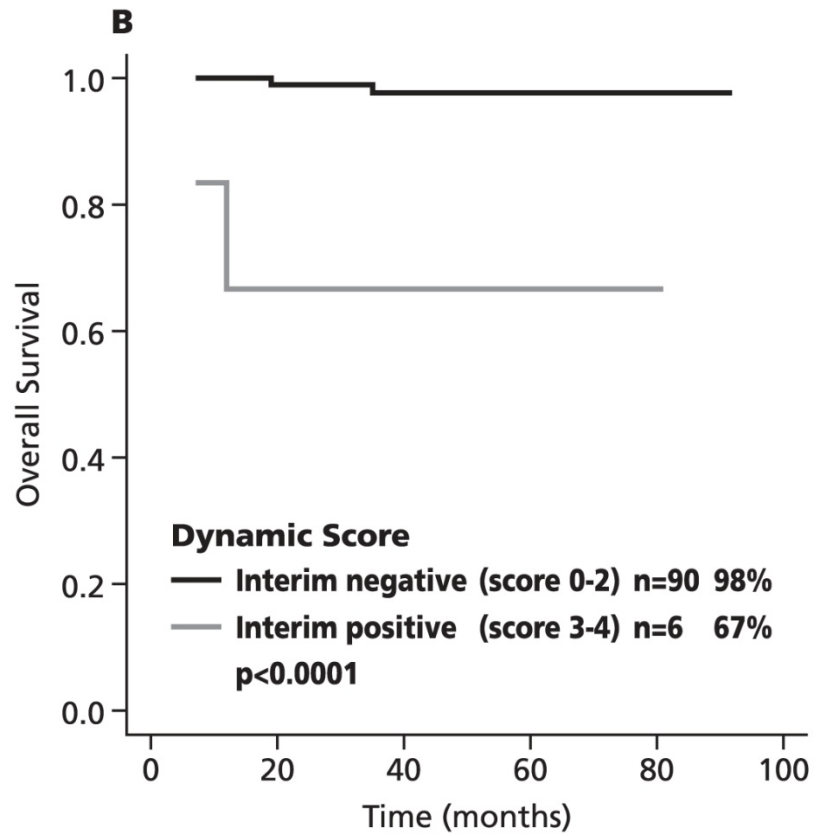
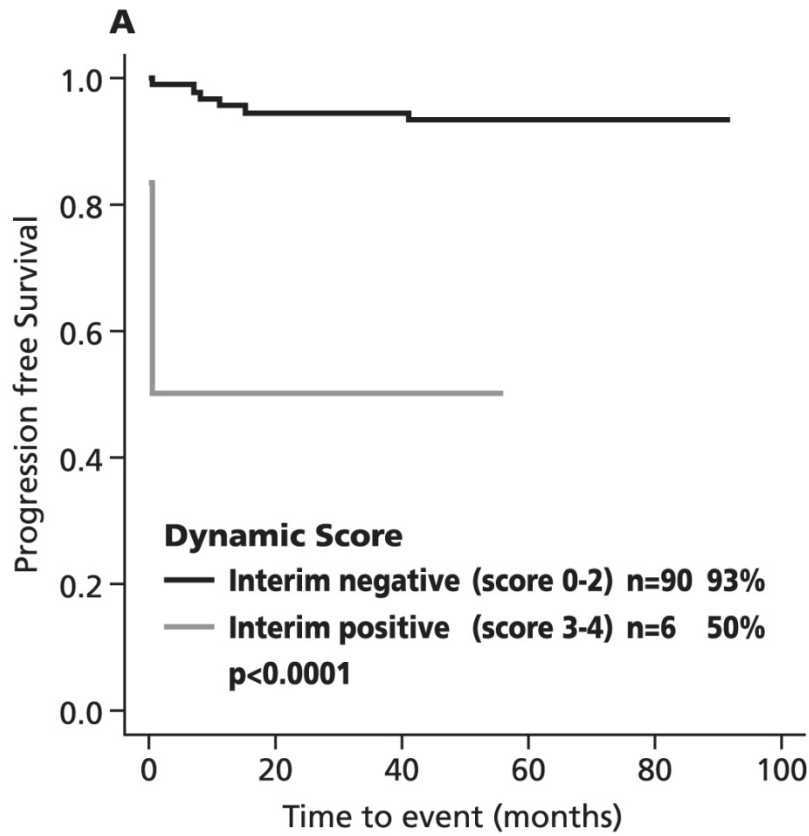
♣ p = 0.001, ♣♣ p = 0.006, # p < 0.03, ## p < 0.05



**Fig. 2**

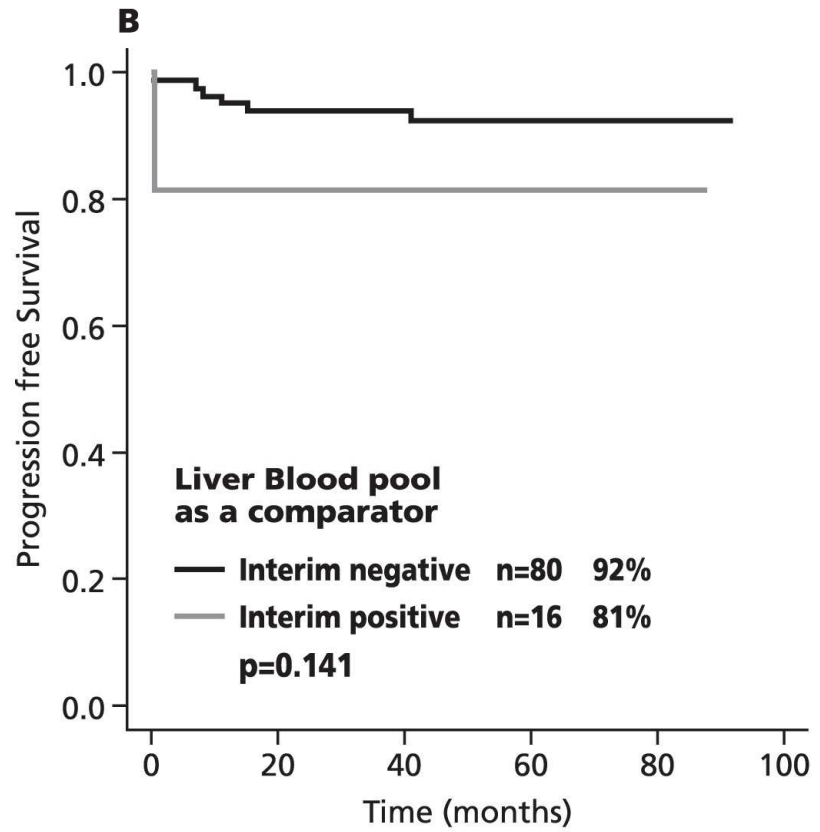
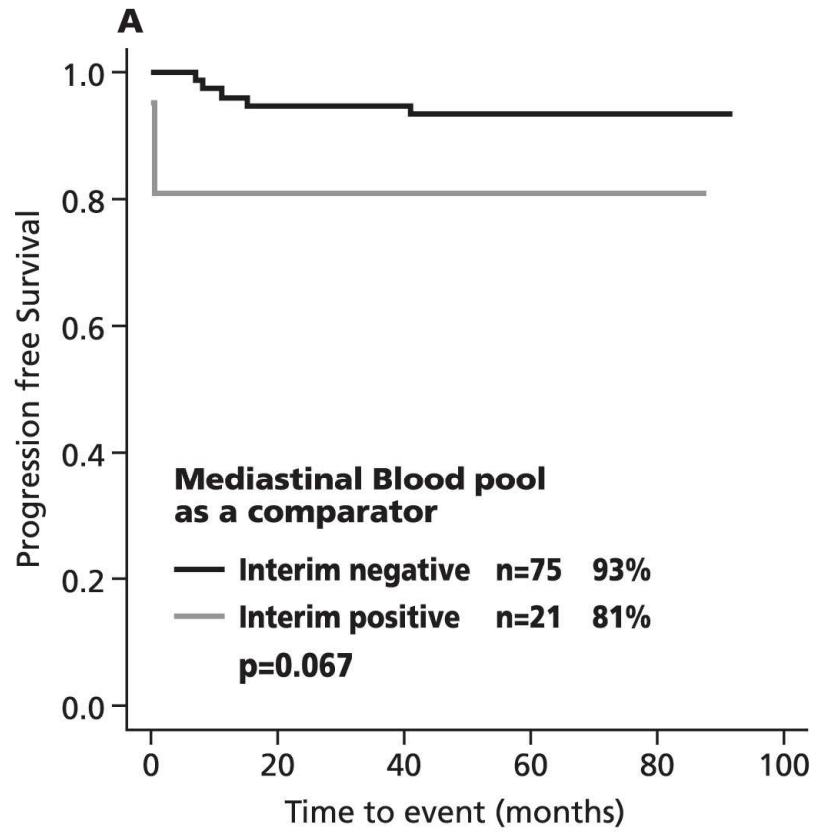
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**Fig. 3**

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**Fig. 4**

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# CONCLUSIONS

- Baseline PET/CT should be mandatory in any case when interim PET/CT is planned to be used for further therapeutic decision
- Number of residual disease sites is an important part of evaluation
- Probably, a single residual site following resolution of other sites of disease should not be considered as requiring augmentation of therapy
- Dynamic scoring model should be independently evaluated in other cohorts of patients