PROGNOSTIC VALUE OF INTERIM FDG-PET/CT IN 100 DIFFUSE LARGE B-CELL LYMPHOMA TREATED WITH R-CHOP ACCORDING TO INTERPRETATION CRITERIA AND PRETHERAPEUTIC PROGNOSTIC FACTORS

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INTRODUCTION : Positive interim PET-CT (iPET+) is an adverse prognostic factor in DLBCL. Positivity criteria are still debated. The aim of this study was to assess the prognostic value of interim PET-CT (iPET) according to qualitative criteria (Deauville 5 Points-Scale : $iPET_{5PS}$), quantitative criteria (Δ SUVmax : $iPET_{\Delta SUV}$), and to an algorithm combining those two ($iPET_{algorithm}$) in DLBCL. As previously reported, we also evaluated impact of other prognostic factors (IPI, genomic expression profile and Bcl2 status)[1,2].

METHODS : Retrospective analysis of first line DLBCL evaluated by PET-CT at baseline and after 2 to 4 cycles of R-CHOP (2: 17%; 3: 68%; 4: 15%), treated in our institute from 2006 to 2013, with no therapeutic change based on the results of interim PET. The response of the iPET was assessed by qualitative parameters ($iPET_{5PS}$ positive when score ≥ 4), ΔSUVmax ($iPET_{\Delta SUV}$ positive when ≤ 71%) and a combination of those 2. The algorithm criteria were identical to Deauville ones, except for score 4 : $iPET_{Algorithm}$ was considered negative when ΔSUVmax >71%, and positive when ΔSUVmax ≤ 71%. Pre-therapeutic factors including GCB gene expression profile (Hans classifier), Bcl2 status and IPI score were also studied. Results were correlated with EFS and OS using curves computed with Kaplan-Meier and compared with log-rank test. Predictive factors were finally selected with multivariate cox regression (IPI, GCB, Bcl2 status and iPET results).

Interim PET interpretation criteria	Baseline PET and interim PET after 2 to 4 chemotherapy cycles		
Deauville 5PS qualitative	**1-2-3** <liver background	**4** >liver background but $SUVmax_i$<5	**5** >>liver background
Quantitative if applicable*		**ΔSUVmax >71%**	**ΔSUVmax ≤ 71%**
PET algorithm **RESULTS**	**PET -**		**PET +**

Table1. PET algorithm interpretation combining qualitative and quantitative criteria

*Baseline SUVmax>10

RESULTS : One hundred patients were included with a median follow up of 40 months 95%CI [36,1-44,5]. Overall 3-years EFS and OS were 63,7% and 75,8%. Every PET criteria was significantly discriminating for outcome in terms of EFS and OS (p<0,0001), slightly less in OS discrimination using quantitative criteria (p=0,0082). Three-years and 5-years EFS were respectively 83,1% and 73,9% in $PET_{Algorithm}$ negative vs 14,3% and 0% in $PET_{Algorithm}$ positive, 3-years and 5-years OS were respectively 85,8% and 85,8% in $PET_{Algorithm}$ negative versus 50% and 43,8% in $PET_{Algorithm}$ positive.

Evaluation of pre-therapeutic factors showed significantly different EFS and OS in GCB versus non GCB (respectively p=0,087 and p=0,031), as well as in low IPI (1,2,3) versus high IPI (4,5), respectively p=0,014 and p=0,031. BCl2 Status did not show any significant statistical difference in terms of EFS (p=0,13). In multivariate cox regression, positive $iPET_{algorithm}$ (Hazard ratio=11.7) and GCB status (HR=0.431) were independent risk factor of EFS. Combining algorithm and GCB status split sample in 3 groups with significant different 5-years EFS and OS respectively, 93% and 93% in the (GCB & negative $iPET_{algorithm}$) group; 60% and 81% in the (nonGCB & negative $iPET_{algorithm}$) group, and 0% and 44% in the (positive $iPET_{algorithm}$ & non GCB) group, p<0.0001.

CRITERIA	3y-EFS		p	3y-OS		p
IPI (0,1,2 vs 3,4,5)	75%	54%	0,0143	83%	69%	0,0305
Bcl2- vs Bcl2+	73%	57%	0,1304	82%	72%	0,13
GCB vs nonGCB	71%	58%	0,087	86%	69%	0,0305
$iPET_{5PS}$ neg vs pos	87%	36%	<0,0001	91%	58%	<0,0001
$iPET_{\Delta SUV}$ neg vs pos	78%	29%	<0,0001	82%	61%	0,0082
$iPET_{algorithm}$ neg vs pos	83%	14%	<0,0001	86%	50%	<0,0001
Combined GC-TEPneg vs nonGC-TEPpos	93%	0%	<0,0001	93%	44%	<0,0001

Table2. Main results EFS and OS according to prognostics criteria

	HR	IC 95%	p
GCB status:			
- **GCB**	0,43	0,22 – 0,83	0,0128
- **Non GCB**	1	-	
TEP algorithm :			
- **Negative**	1	-	<0,0001
- **Positive**	6,09	5,80-23,65	

Table3. Cox regression model : multivariated analysis

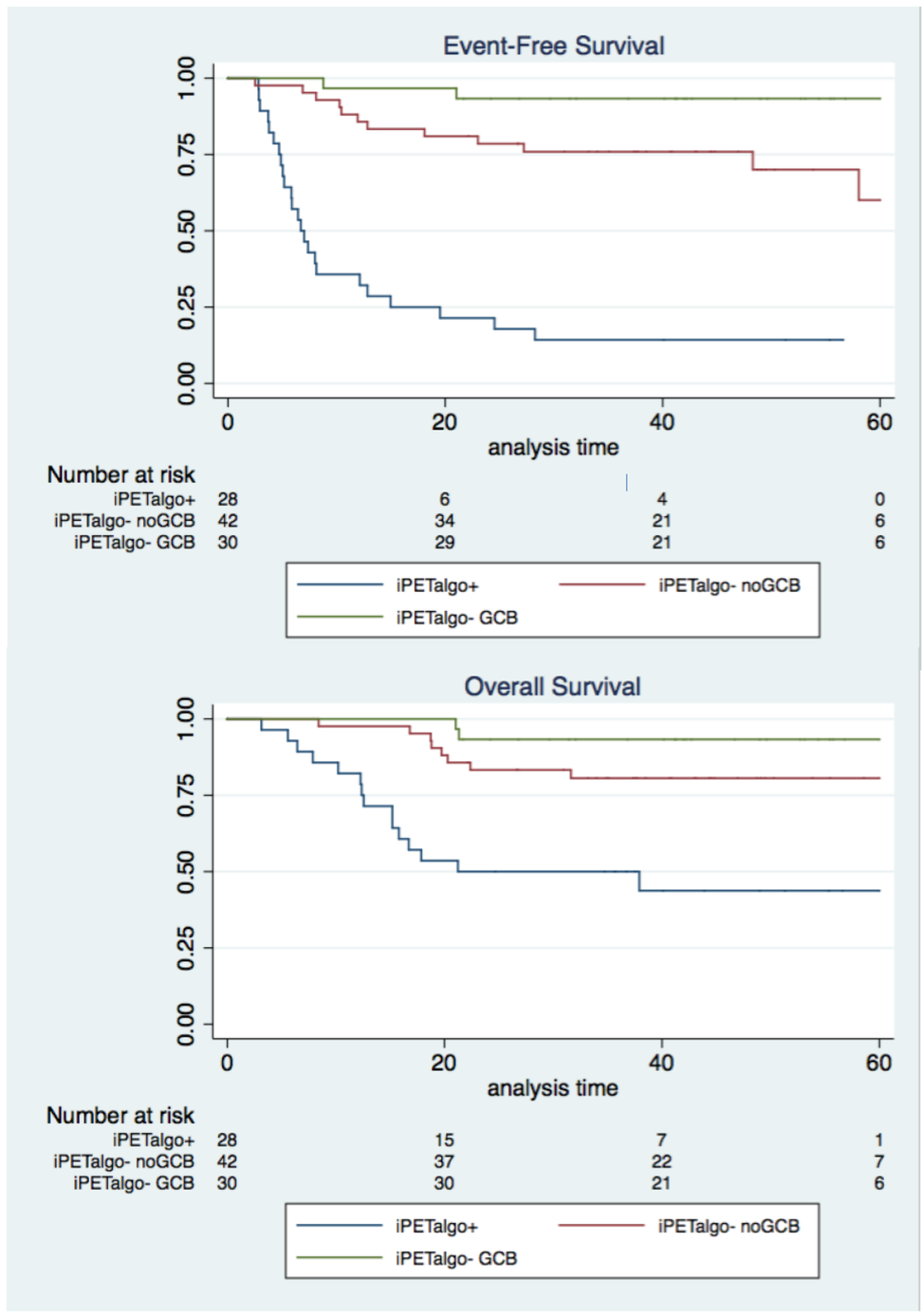

Fig 1. EFS and OS curves combining PET algo and GC status

CONCLUSION : The algorithm we proposed, successfully stratified patients according to EFS and OS. Integrating genomic expression profiles study improves the outcome prediction. Negative iPET in GCB DLBCL had an excellent prognosis whereas iPET+ non GC had a particularly poor one.

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