

**Gene expression profile and the interim PET scan are two complementary and independent tools to predict the outcome of diffuse large B-cell lymphomas treated by rituximab(R) and anthracyclines-based chemotherapy**

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# GCB /ABC signature : a well recognized prognosis factor

## WHO classification of DLBCL

### Classifications

#### DLBCL, not otherwise specified (NOS)

Common morphologic variants

Centroblastic

Immunoblastic

Anaplastic

Rare morphologic variants

Molecular subgroups

Germinal center B cell-like (GCB)

Activated B cell-like (ABC)

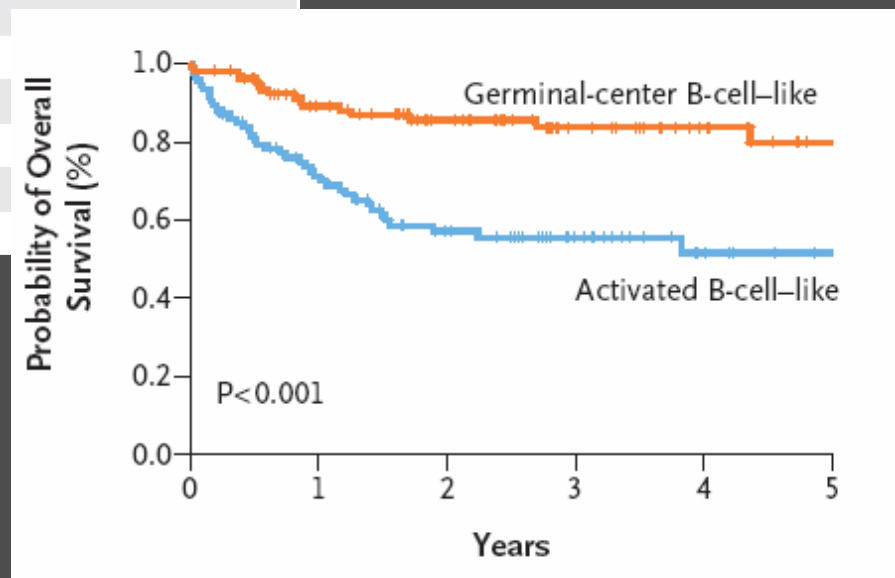
Immunohistochemical subgroups

CD5-positive DLBCL

Germinal center B cell-like (GCB)

Nongermlinal center B cell-like (non-GCB)

#### Diffuse large B-cell lymphoma subtypes



*Lenz et al. NEJM 2008*

# Objectives

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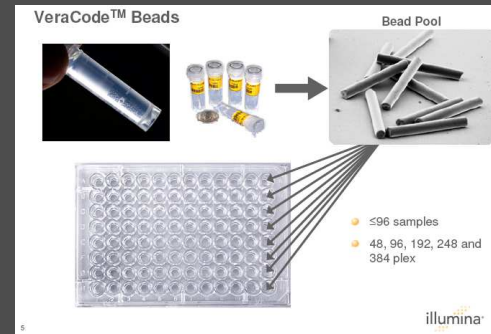
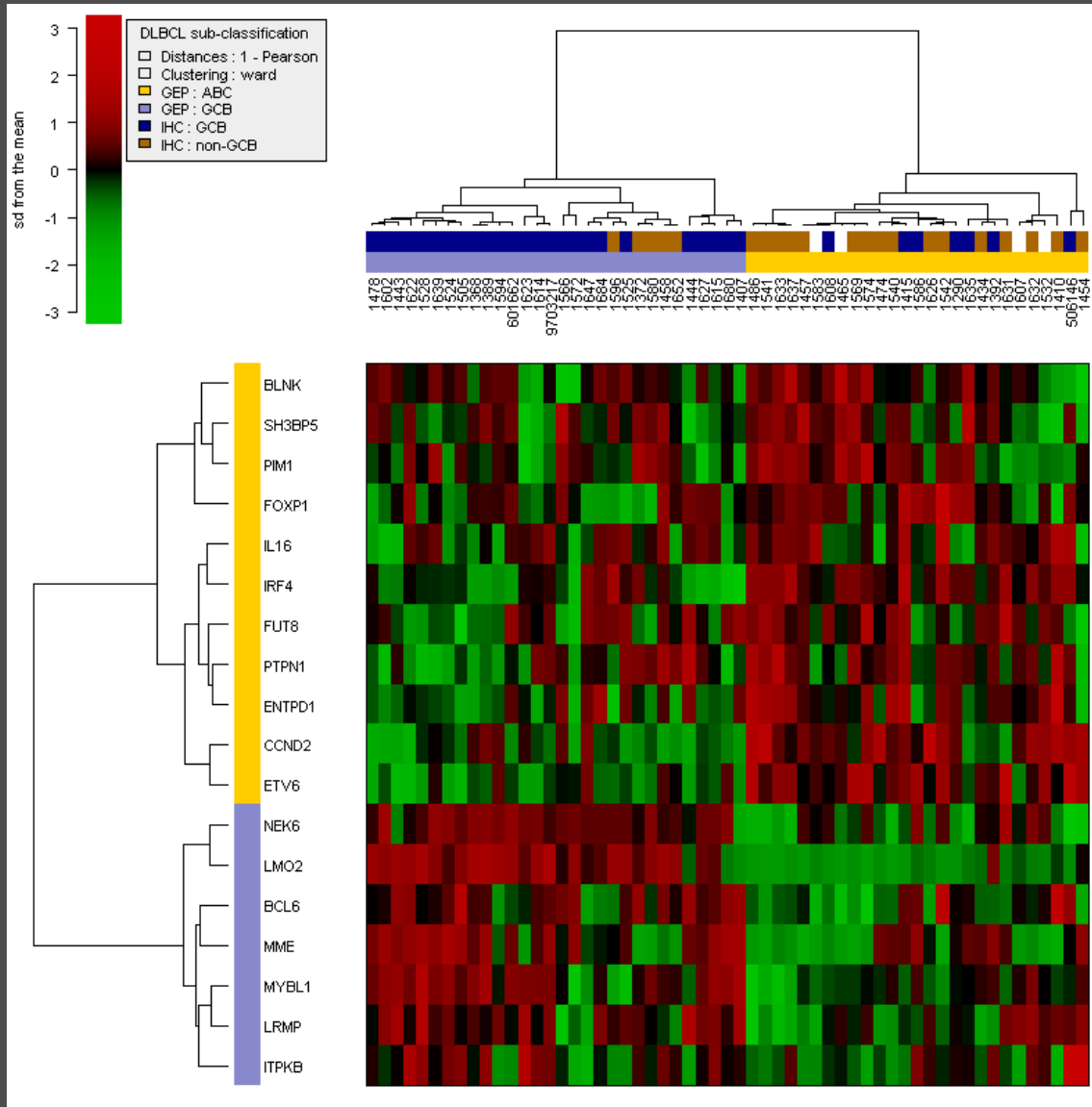
- ( 1) To determine the relationship between gene expression profiles, Glucose transporter gene expression and PET scan features (SUV max base line)
- (2) To determine the respective prognosis value of GCB /ABC subclassification and interim Pet assessed by semi-quantitative method

## Patients and methods

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- 57 cases treated by CHOP/CHOP-like+R
- PET scan results at diagnosis (SUVmax), following 3/4 cycles of chemotherapy (interim PET) and at the end of treatment (final PET)
- Expression profile of 18 genes related to GCB/ABC signatures
- Expression of 5 genes coding for glucose transporters (GLUT)
- GCB / non-GCB phenotype assessed by immunohistochemistry (IHC) according to Hans algorithm.

# GCB / ABC subclassification with DASL technology

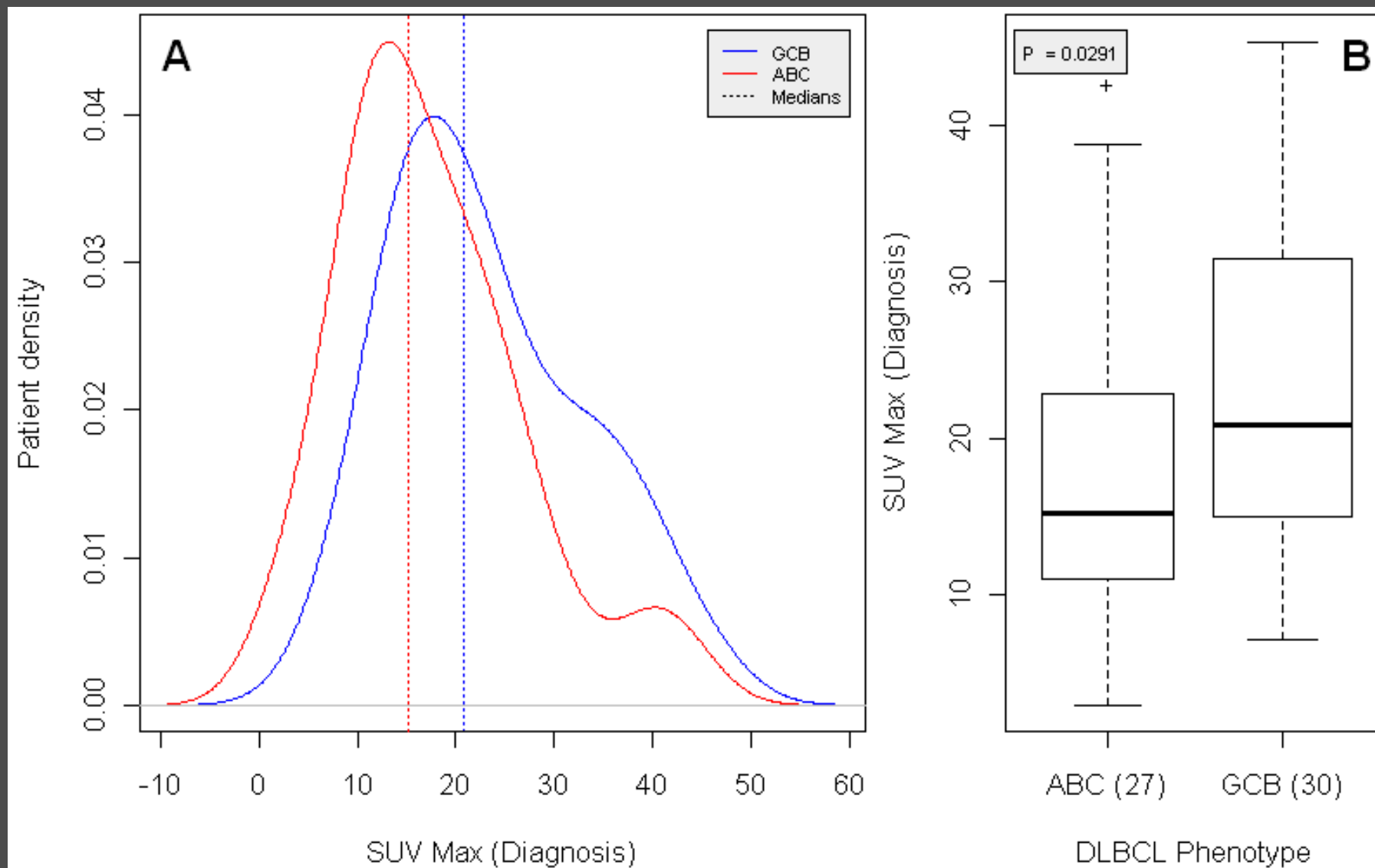


27 ABC (48%)  
30 GCB (52%)

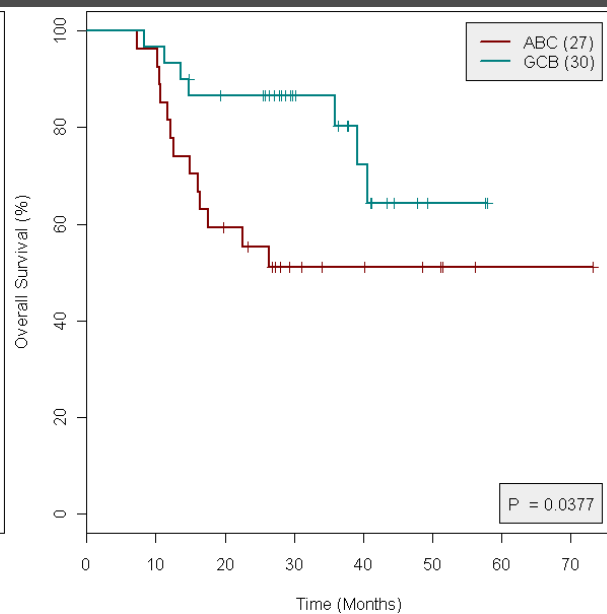
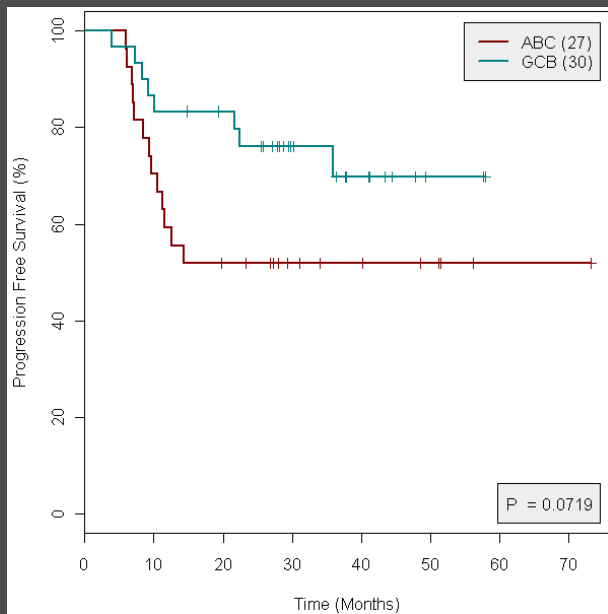
21 non-GCB (39%)  
32 GCB (61%)

Hans concordance  
77%

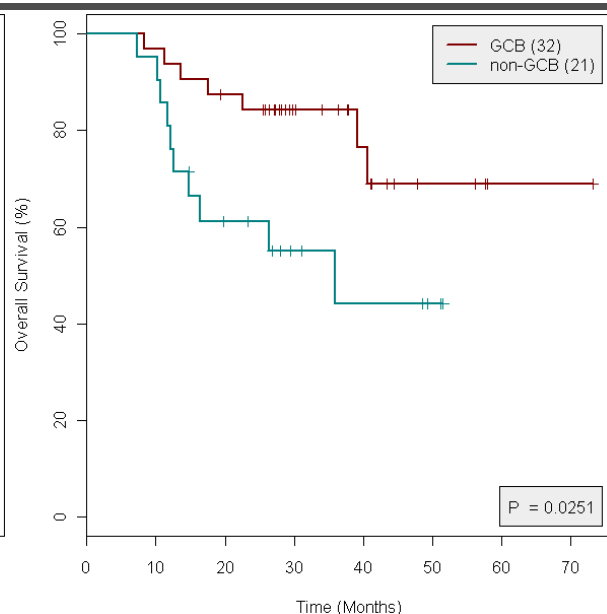
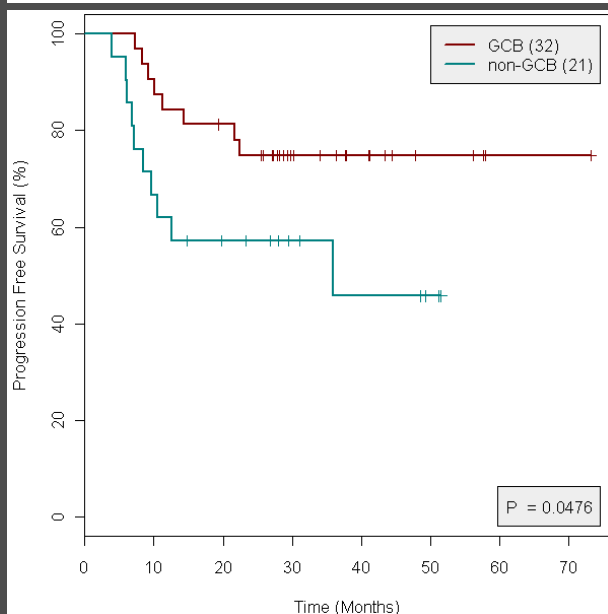
# GCB/ABC subtype and SUV max at baseline



# Survival according GCB/ABC classification

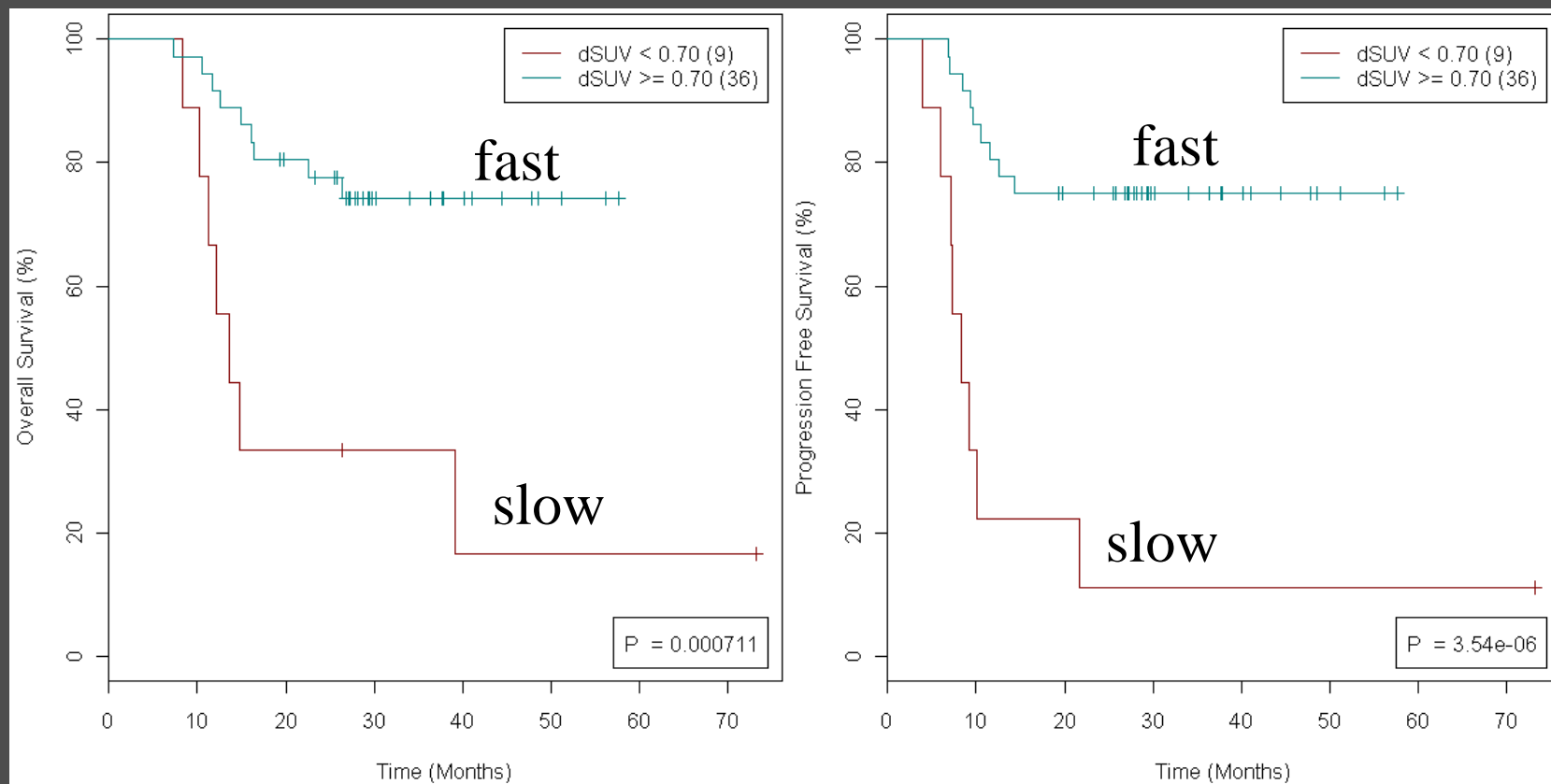


ABC/GCB



Non-GCB/GCB

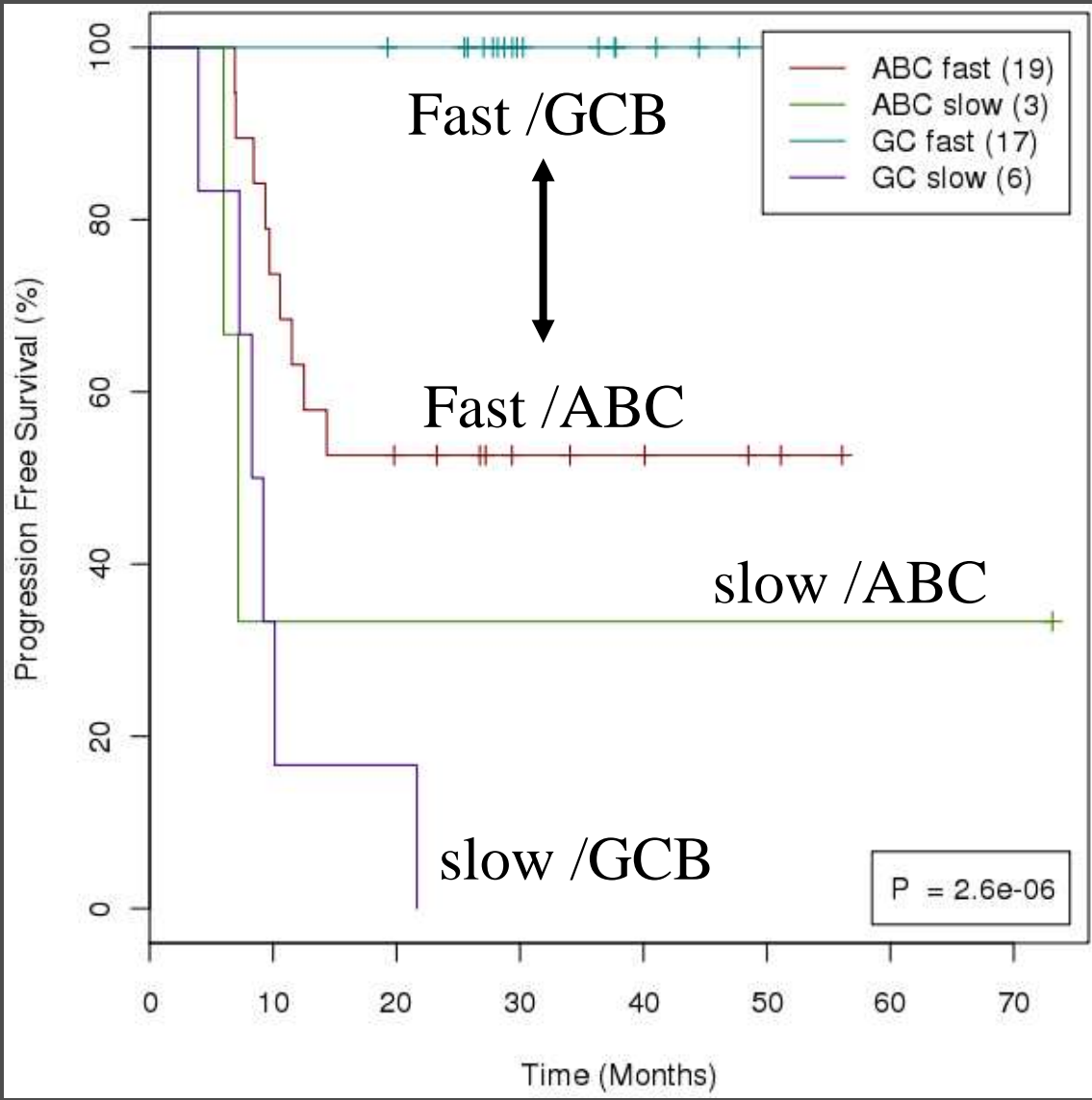
## Survival according Interim-Pet (Delta SUV < or > 70%)



Fast responders (delta SUV > 70% : 36 (80%))  
Slow responders (delta SUV < 70% : 9 (20%))



# Fast responders and GCB/ABC subtypes



Good risk group

Fast / GCB

Poor risk group

Slow GCB and ABC

## Multivariate analysis

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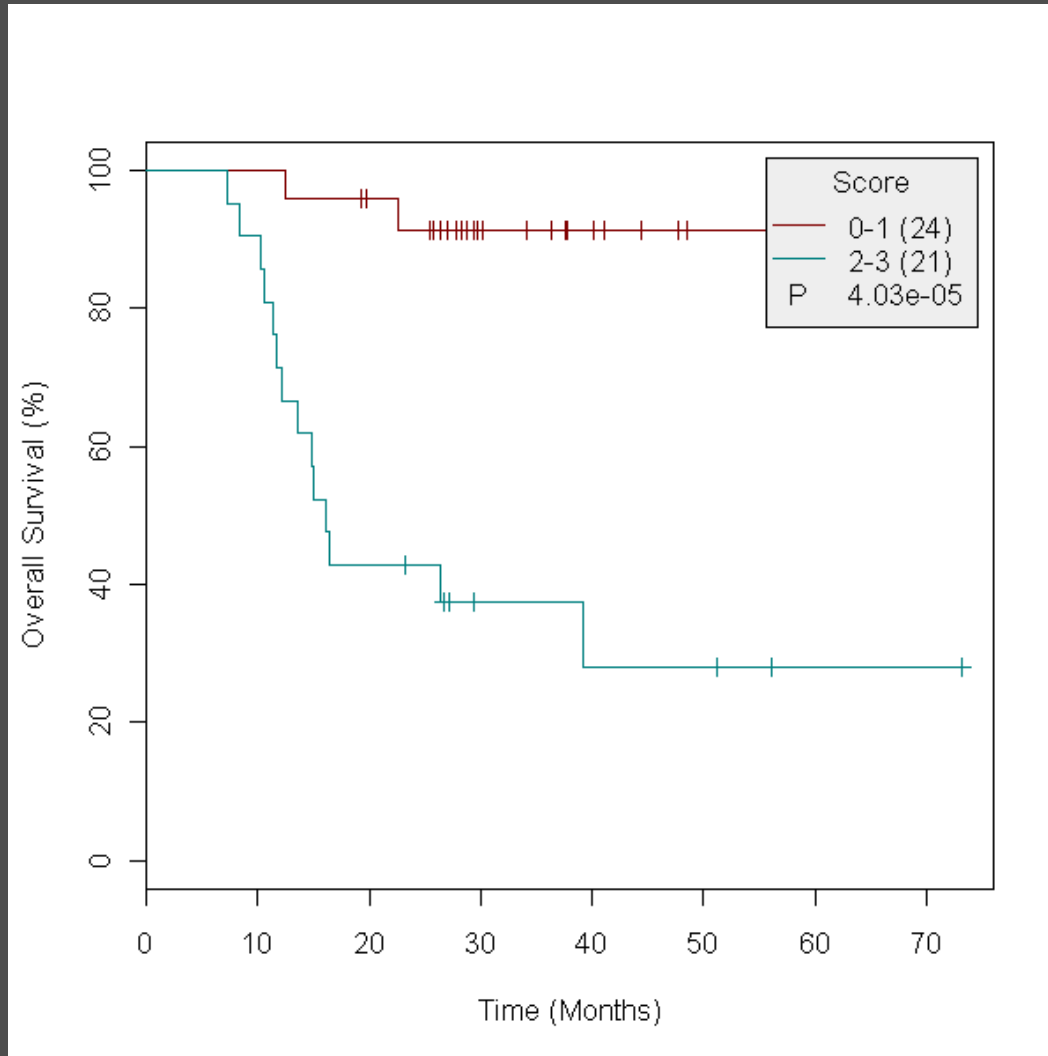
- > interim PET scans (slow/fast),
- > phenotype (GCB/ABC subtypes)
- > age-adjusted IPI (aaIPI)

aaIPI (**HR = 7.1**, CI 95% of 1.4-35.3%,  $p = 0.017$ )

GCB/ABC subgroups (**HR = 5.2**, CI 95% of 1.6-16.7%,  $p = 0.006$ )

slow/fast responders (**HR = 0.1**, CI 95% of 0.03-0.3%,  $p < 0.001$ )

# Overall survival according aaIPI/GCB-ABC/ interim-Pet

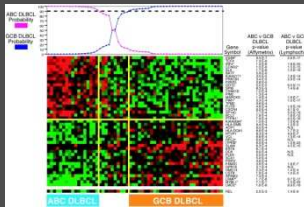


## Prognosis Score

1. IPI<sub>aa</sub> (0-1/2-3)
2. GCB/ABC
3. Slow/fast

# Practical conclusion

**ABC**

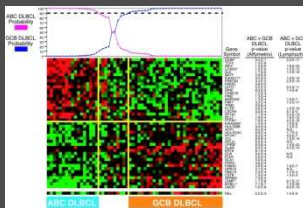


**Interim-PET**

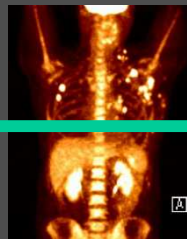


**Alternative strategy**

**GCB**



**Interim-PET +**



# Aknowledgements



INSERM U918 - Quantif (LITIS EA 4108)

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