Quantitative pre-treatment PET in Follicular Lymphoma

Preliminary data from the PET Folliculaire Trial

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How we used to look at FL

1. Indolent B-cell lymphoma of mostly elderly
2. Watch and wait an accepted approach
3. Good response to treatment
4. Constant relapses
5. Shorter duration of subsequent remissions
6. Risk of transformation into aggressive NHL

The changing face of FL in recent years

1. Common lymphoma – and >60yrs is not so old!
2. Pre-treatment prognostic indices – assist in triaging who to W+W
3. Excellent reponse to immuno-chemotherapy
4. Duration of remissions prolonged by maintenance Rituximab
5. Risk of transformation into aggressive NHL
6. Death from lymphoma becoming a later event

Follicular lymphoma: Recognised Heterogeneity

Histology

- Grade 1-3a correlates poorly with outcome
- Poor reproducibility 3a vs. 3b (transformation)

Heterogeneity in patient outcomes

- FLIPI (>4 Nodal areas / LDH / Age>60 / Stage III-IV / Hb<12) *Solal-Celigny 2004*
  - 5yr OS 91 vs. 53%, Low vs. High risk
- FLIPI2 (B_2M>ULN / LoDLIN>6cm / BMI / Hb<12 / Age>60)
  - 3yr PFS 89 vs. 57%
  - 3yr OS 99 vs. 82% *Federico 2009*

Can FDG-PET add clinically useful information to initial staging?

- Almost universally but not uniformly FDG avid

  Elstrom 2003, Blum 2003, Wohrer 2006, Weiler-Sagie 2010,Tychy-Pinel 2011, Dupuis 2011

- Poor correlation of SUV_{max} with histologic grade

  Wohrer 2006, Karam 2006

- No clear cut-off defines transformation

  SUV_{max} <11.7 = indolent, SUV>17 = transformation

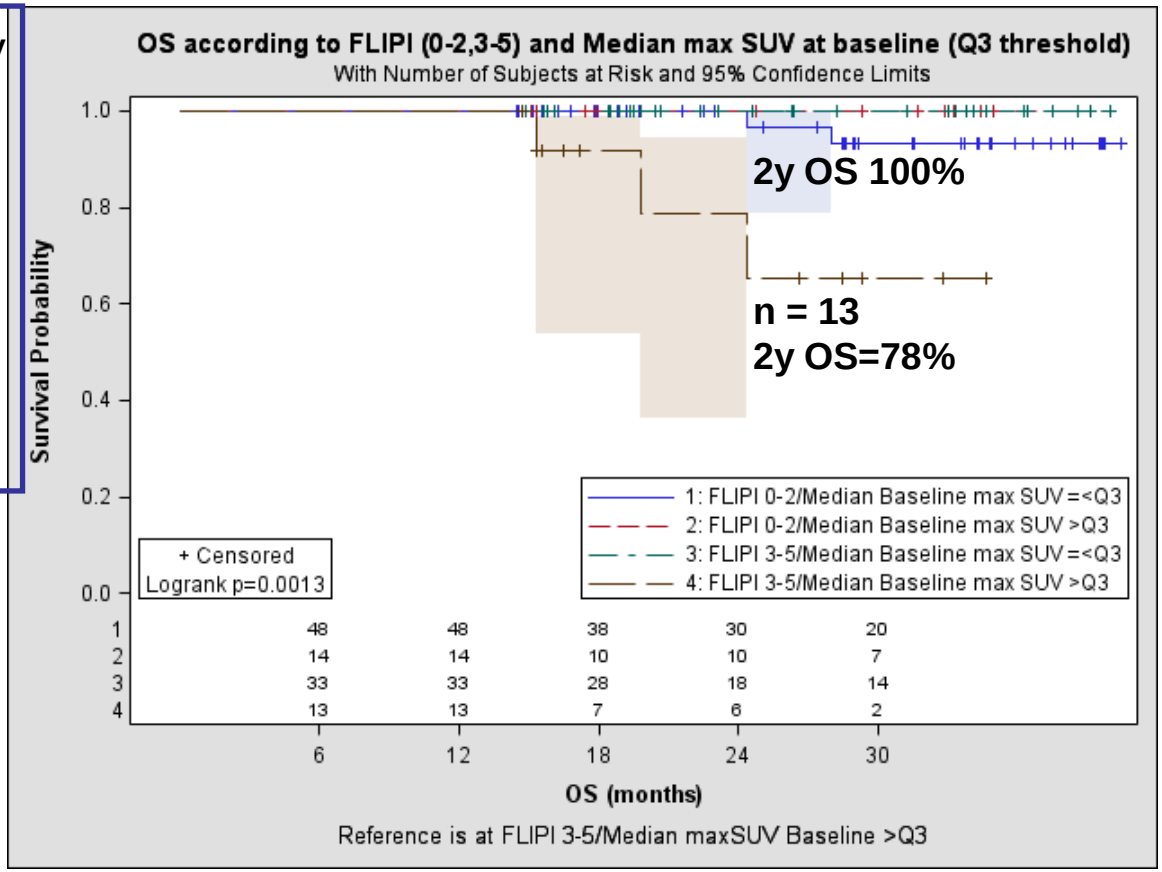
  Bodet-Milin 2008

PET-Folliculaire:

Pre-treatment SUV_{max}>13.7(>75thpercentile) & FLIPI in two classes

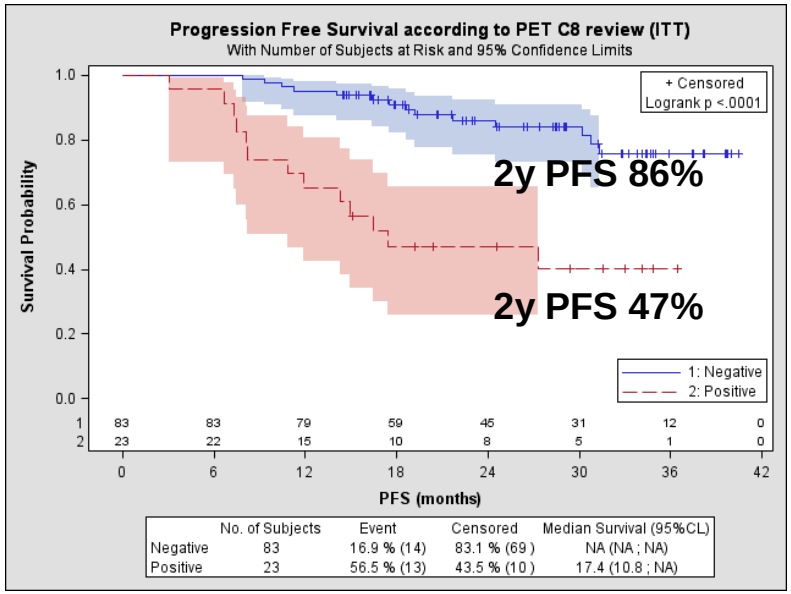
Prospective GELA/LYSA study
- n =109
- high tumour burden FL
- 6 R-CHOP+2 Rituximab

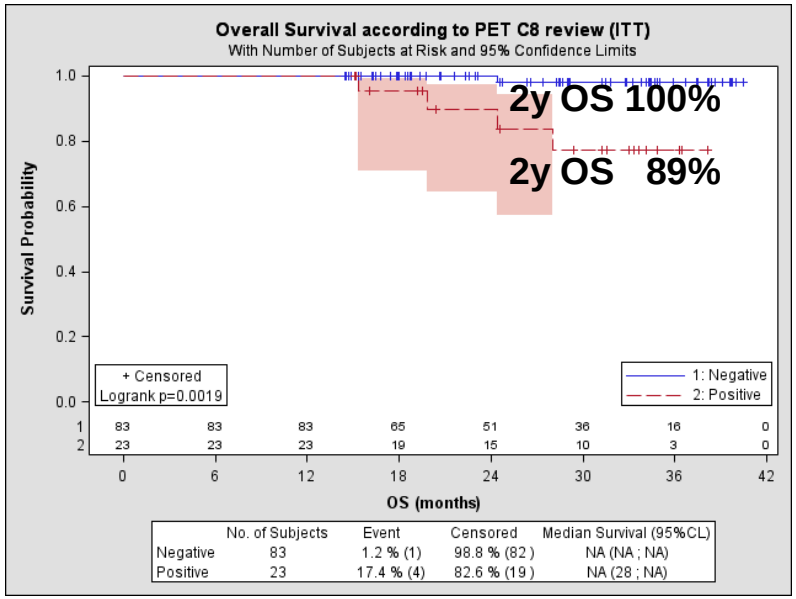
Baseline SUV max
- mean = 11.4
- range 3.3-34



Dupuis J et al, PET-Folliculaire study

Postinduction PET
Deauville score (5PS) ≥4

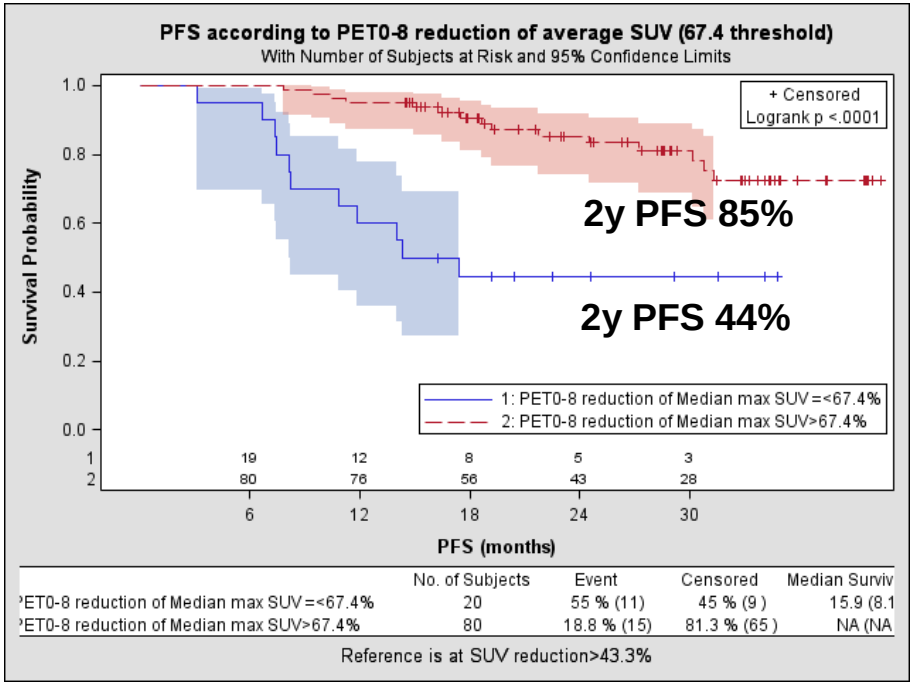


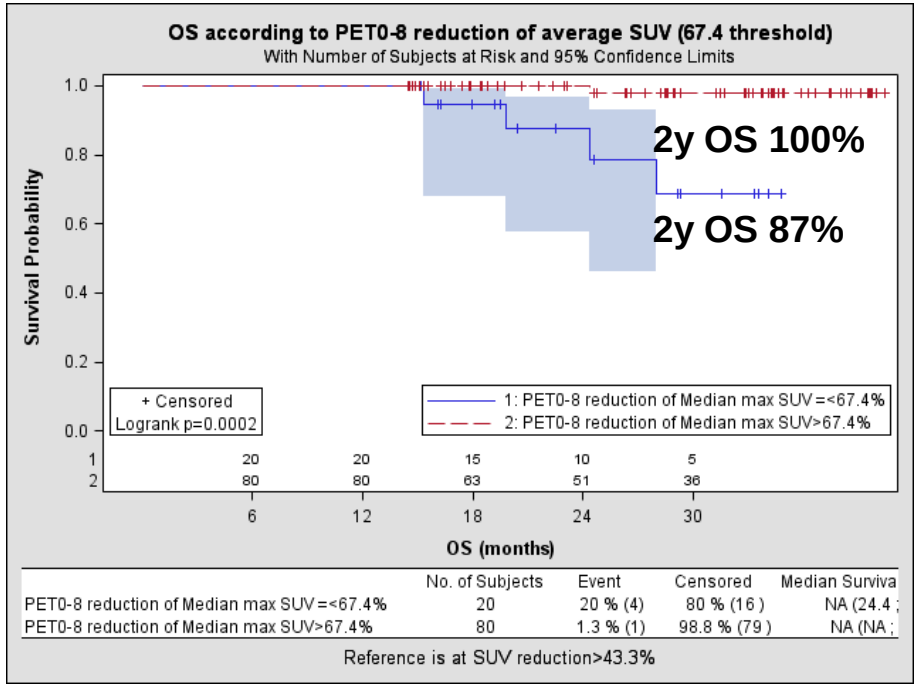


n = 106 patients
Med FU = 28 months

Dupuis J et al, J Clin Oncol 2012

Quantitative assessment of postinduction PET (ΔSUVmax 67%)





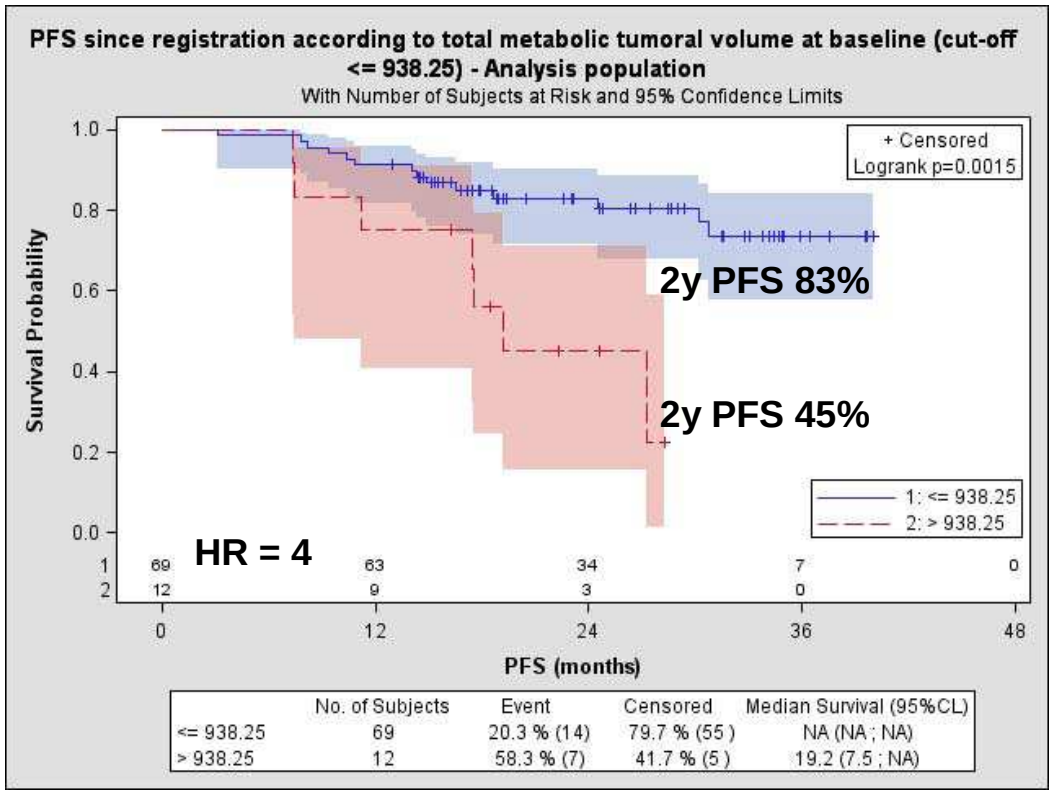
Total metabolic tumour volume and Total Lesion Glycolysis

- TMTV
  - Computed using the SUV_{max} 41% threshold
  - Sum of the local metabolic volumes

Meignan, EJNMMI, 2014

- TLG
  - Sum of local metabolic volumes times their local SUV_{max}

Baseline TMTV prognostic value



n = 81 (fused PET-CT images)

TMTV
- mean = 462
- median = 303
- range 1-2401
- AUC 0.63 Cut-off TMTV >938cm^3
  12/81 (15%)

Of the 12 patients:
- 9 had stage IV disease
- 9 in int-high FLIPI group
- more nodal sites
- bulk >7cm % similar in both groups

Population with SUV_{max}>13.7
- n=21
- all had MTV <938cm^3

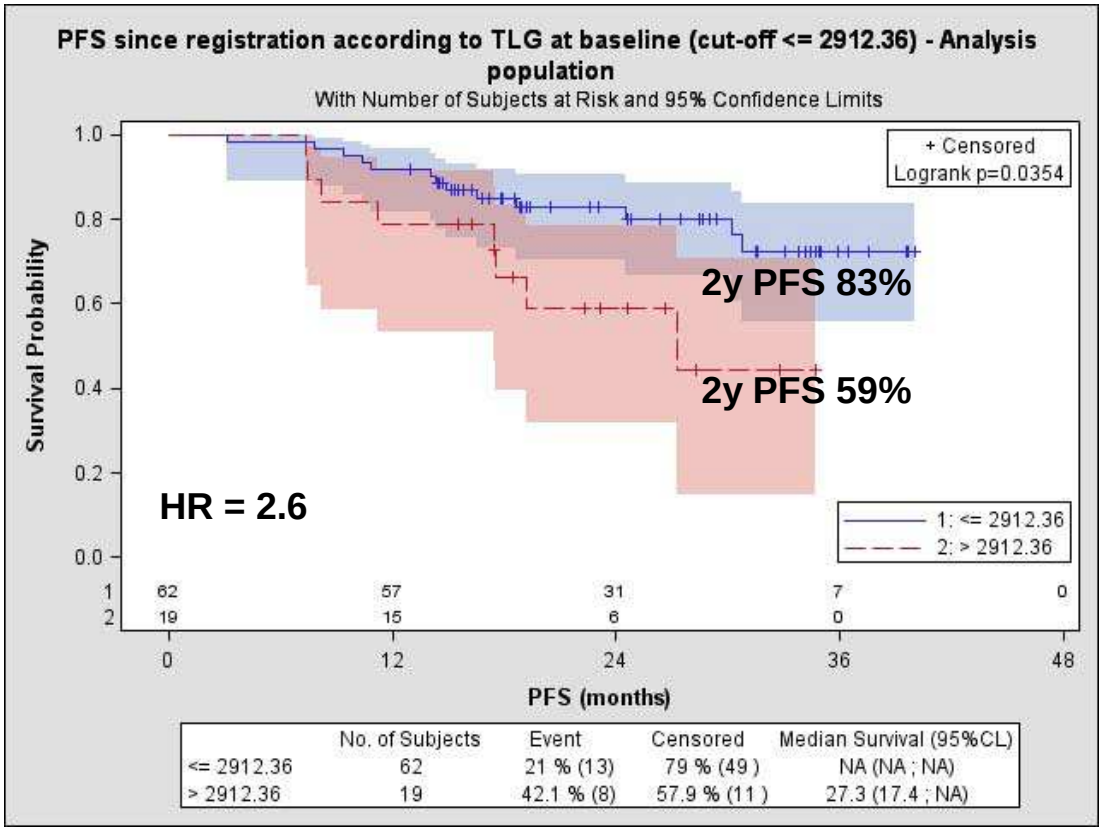
On planned multivariate analysis…

In 81 patients with only 28mo follow-up, on

univariate analysis of TMTV & GELF factors, and
univariate analysis of TMTV & FLIPI factors,

only TMTV was a significant predictor of PFS: HR 4.

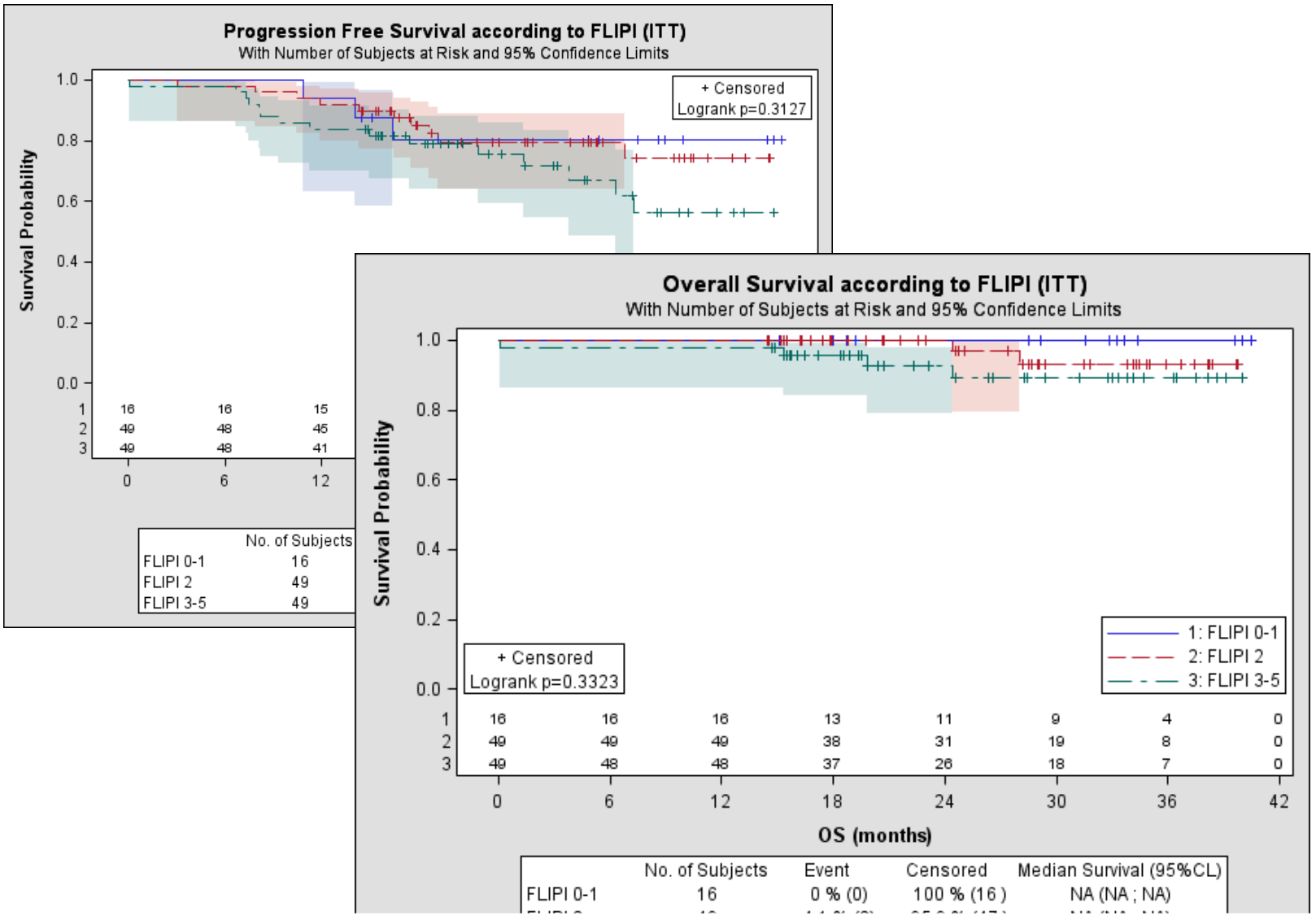
Baseline TLG prognostic value



TLG
- mean =2022
- median = 1464
- range 4-9396
- AUC only 0.56 for best cut-off TLG >2912

Population with SUV_{max}>13.7
- n=21
- 5/19 had TLG >2912

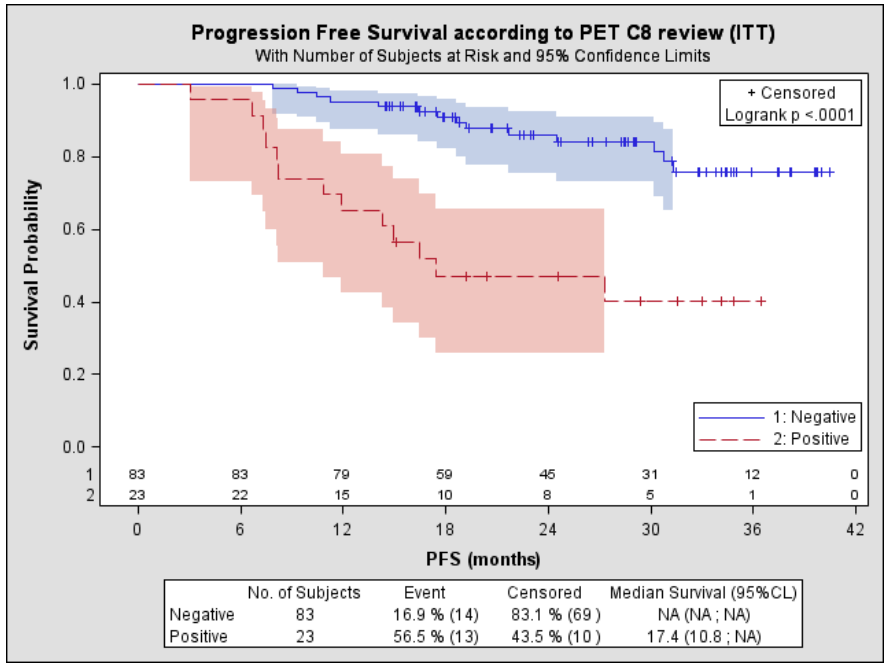
… should we persevere in examining TMTV in Follicular Lymphoma?



The new “gold standard” vs. TMTV

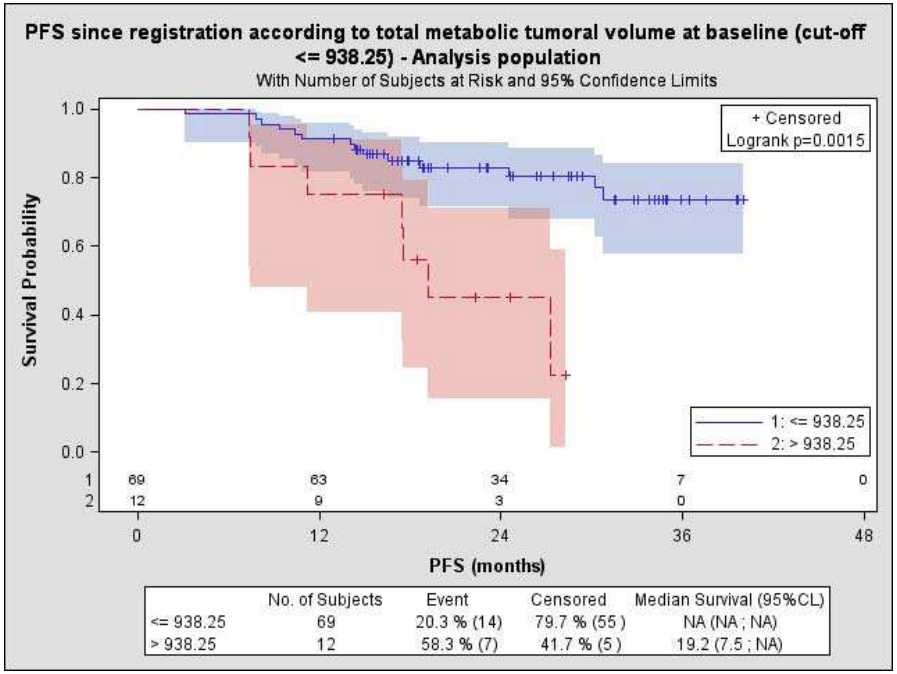
Post-induction:

5PS Cut-off ≥4



Pre-induction:

TMTV



Yes, we should persevere!!

… in larger populations (both symptomatic and asymptomatic)

... with longer follow-up

… with differing therapies

Potential for exploratory studies within existing large scale trials (already with years of follow-up) using Bendamustine, Obinutuzumab, lenalidomide: …

BRIGHT, GALLIUM, RELEVANCE, FOLL12

… so before we all retire we may obtain robust OS data based on pre-treatment PET to better identify the small but significant population for whom follicular lymphoma is not an indolent disease.