PET2 negative/ PET4 positive patients in the AHL2011 study

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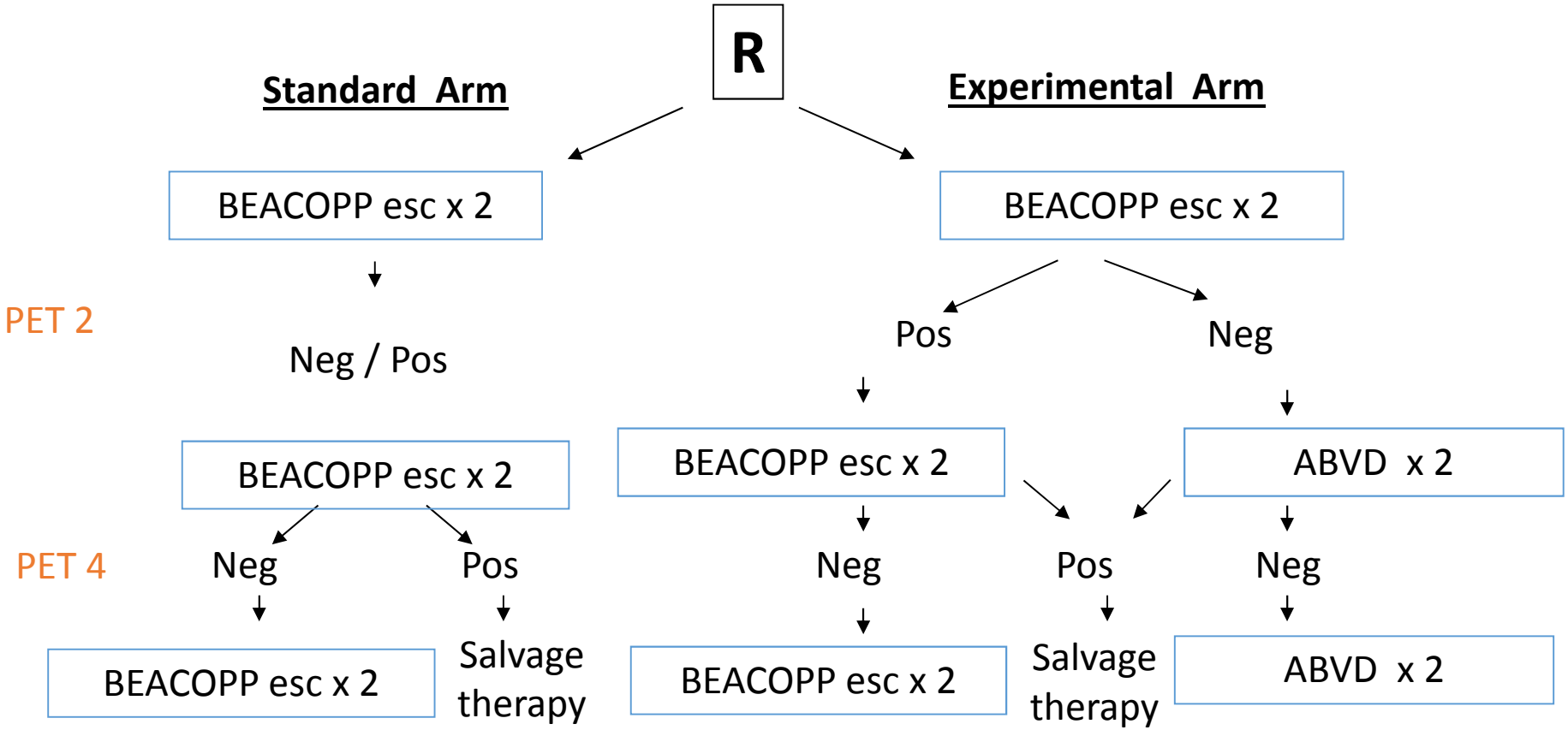
AHL 2011

- 823 patients enrolled from France and Belgium in 3 years (2011-2014)
  - **Diagnosis of classical Hodgkin lymphoma according to the WHO 2008 classification**
  - **Age between 16 to 60 years inclusive**
  - **Ann Arbor stages:**
    - **IIB with mediastinum/thorax > 0.33 or extra nodal localization**
    - **III**
    - **IV**
  - **Baseline 18-FDG PET scan (PET0) performed before any treatment with at least one hypermetabolic lesion**

- 782 patients included in the pre-planned interim analysis

AHL 2011: study design

NCT01358747



Non inferiority of the experimental arm
Standard arm : 85% 5y-PFS ; Experimental arm: 5y-PFS > 75% (HR=1.77)

AHL2011: PET Review criteria

Local and review interpretations had to follow the 5PS criteria modified as following:

The 5-point scale:

- 1. No uptake.
- 2. Uptake ≤ mediastinum.
- 3. Uptake > mediastinum but ≤ liver.
- 4. Uptake moderately more than liver uptake, at any site.

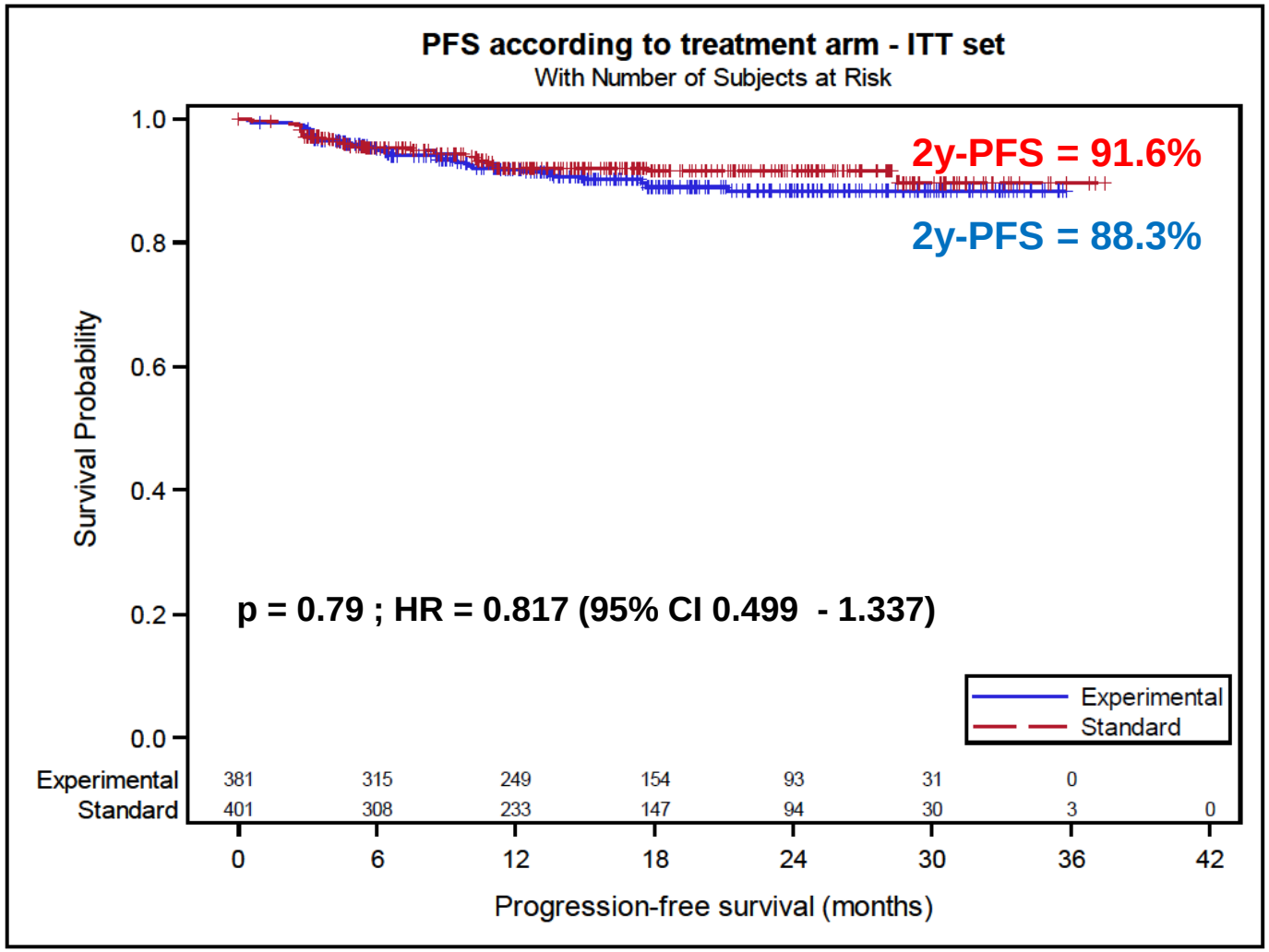
  ***A moderately uptake** more than liver uptake **is define as an uptake more or equal than 140% of SUV max liver** (assessed on 3 slides on the liver middle region)*

- 5. Markedly increased uptake at any site or new sites of disease.

  ***A markedly uptake** more than liver uptake **is define as an uptake more or equal than 200% of SUV max liver** (assessed on 3 slides on the liver middle region)*

- ➢ **PET positive** is defined by scale level 4 and 5 (as described above)
- ➢ **PET negative** is defined by scale level 1, 2 and 3.

AHL 2011: PFS according to treatment arm



Median follow-up = 16.3 months (0.1 – 37.4)

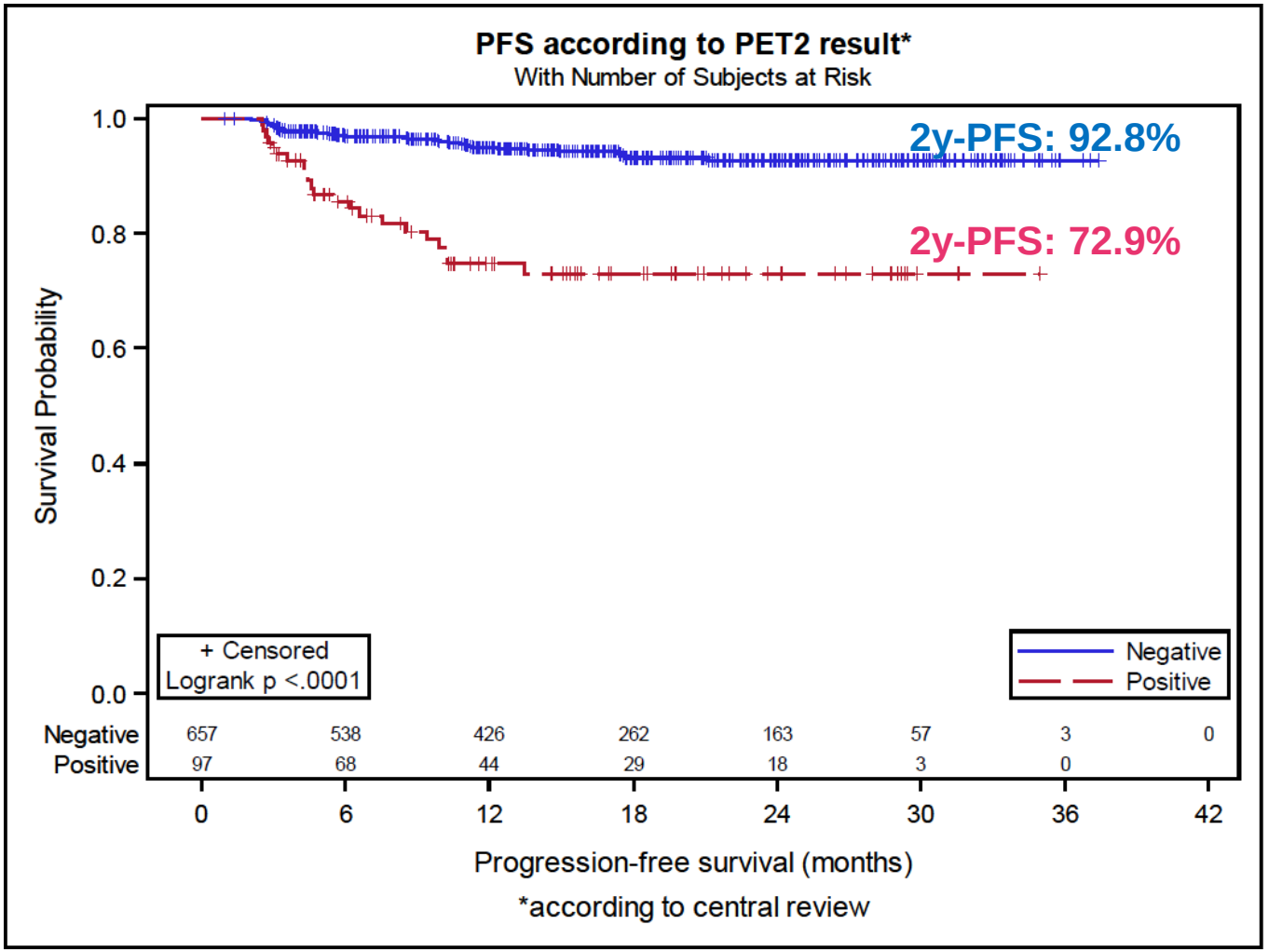
Casasnovas et al, ASH 2015, Abs 577

AHL2011: PET2 results (central review)

	Treatment arm					
	Standard		**Experimental**		**All**	
	n = 401		**n = 381**		**n = 782**	
PET2						
Evaluable	386	96%	368	97%	754	96%
Negative	**338**	**88%**	**319**	**87%**	657	87%
Positive	48	12%	49	13%	97	**13%**

Casasnovas et al, ASH 2015, Abs 577

AHL 2011: PFS according to PET2 result



Casasnovas et al, ASH 2015, Abs 577

AHL2011: interim PET results (central review)

		Treatment arm					
		Standard		Experimental		All	
		n = 401		n = 381		n = 782	
PET2							
	Evaluable	386	96%	368	97%	754	96%
	Negative	**338**	**88%**	**319**	**87%**	657	87%
	Positive	48	12%	49	13%	97	**13%**
PET4							
	Evaluable	373	93%	348	92%	721	92%
	Negative	**347**	**93%**	**332**	**95%**	679	94%
	Positive	26	7%	16	5%	42	**6%**

Lysa THE LYMPHOMA STUDY ASSOCIATION

Lysarc THE LYMPHOMA ACADEMIC RESEARCH ORGANISATION

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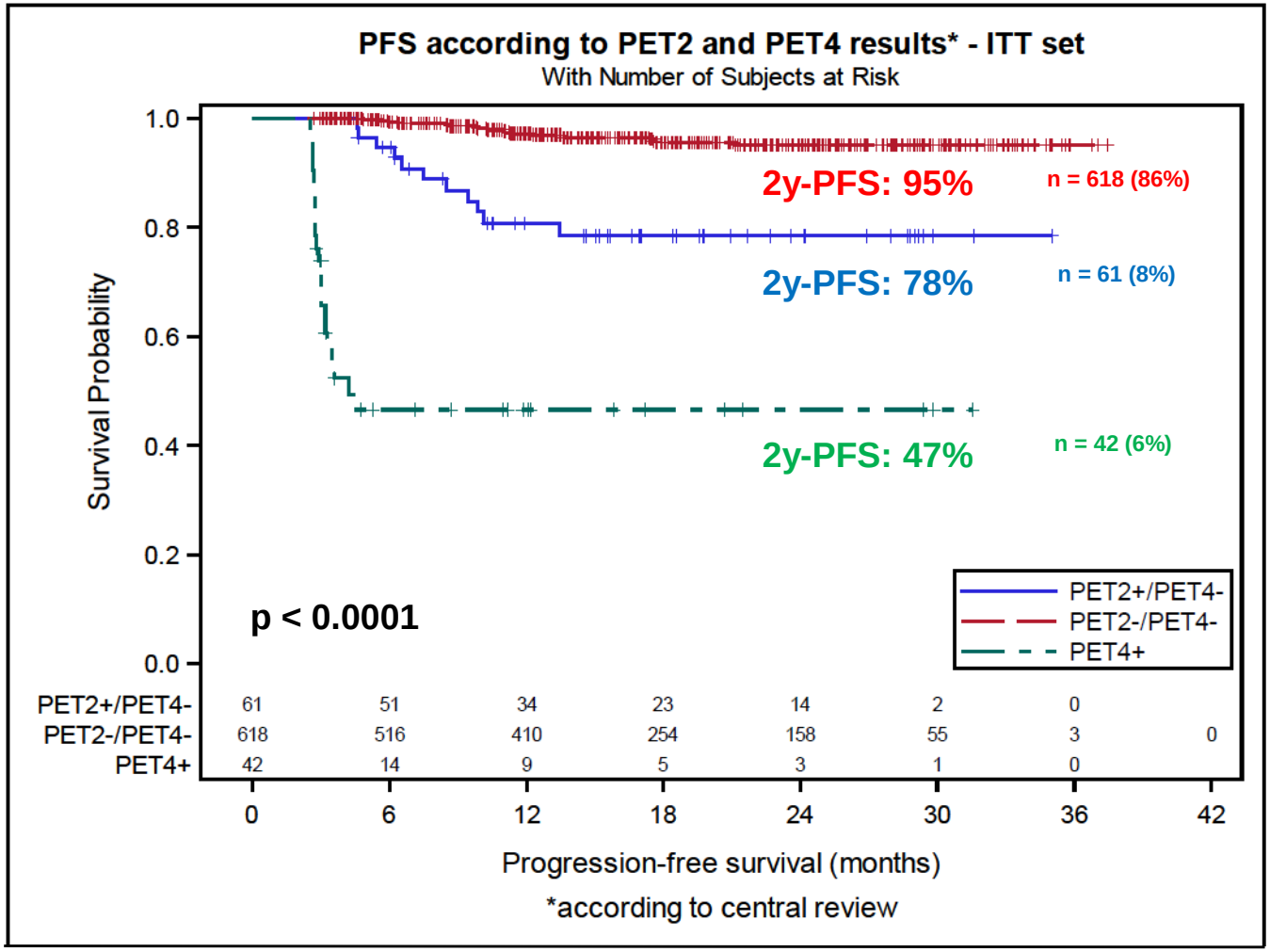
AHL2011: PET4 positive patients

- Among the 42 (6%) PET4 positive patients
  - 29 had a positive PET2
  - 13 (31%) had a negative PET2
    - This subset represents:
      - 1.7% of the whole cohort
      - 2% of PET2 negative patients

- PET2-/PET4+ and PET2+/PET4+
  - had similar baseline characteristics
  - 6 of 13 (46%) PET2-/PET4+ were in the experimental arm and received 2 x BEACOPPesc + 2 x ABVD
  - The 29 PET2+/PET4+ all received 4 x BEACOPPesc
  - So far no difference of outcome

AHL 2011: PFS according to the PET driven strategy



Casasnovas et al, ASH 2015, Abs 577

AHL 2011: PFS according to the PET driven strategy

Risk factors		n (%)	2y-PFS % (95%CI)	Univariate analysis HR	Univariate analysis p	Multivariate analysis HR	Multivariate analysis p
PET2/PET4	PET2-/PET4-	618 (86%)	95.1 (92.3-96.9)				
	PET2+/PET4-	61 (8%)	78.4 (64.2-87.4)	5.89	<0.0001	5.248	<0.0001
	PET4+	42 (6%)	46.5 (30.2-61.3)	32.23	<0.0001	31.285	<0.0001
B symptoms	No	250 (34%)	93.2 (88.2-96.1)				
	Yes	532 (68%)	88.3 (84.7-91.1)	2.011	0.0218	2.049	0.0567
IPS	0-2	322 (42%)	92 (87.2-95.1)				
	≥3	443 (58%)	88.3 (84.4-91.2)	1.897	0.0195	1.493	0.1995

Casasnovas et al, ASH 2015, Abs 577

Summary

- The proportion of patients shifting from a negative PET2 to a positive PET4 is weak (2% of PET2 negative patients)

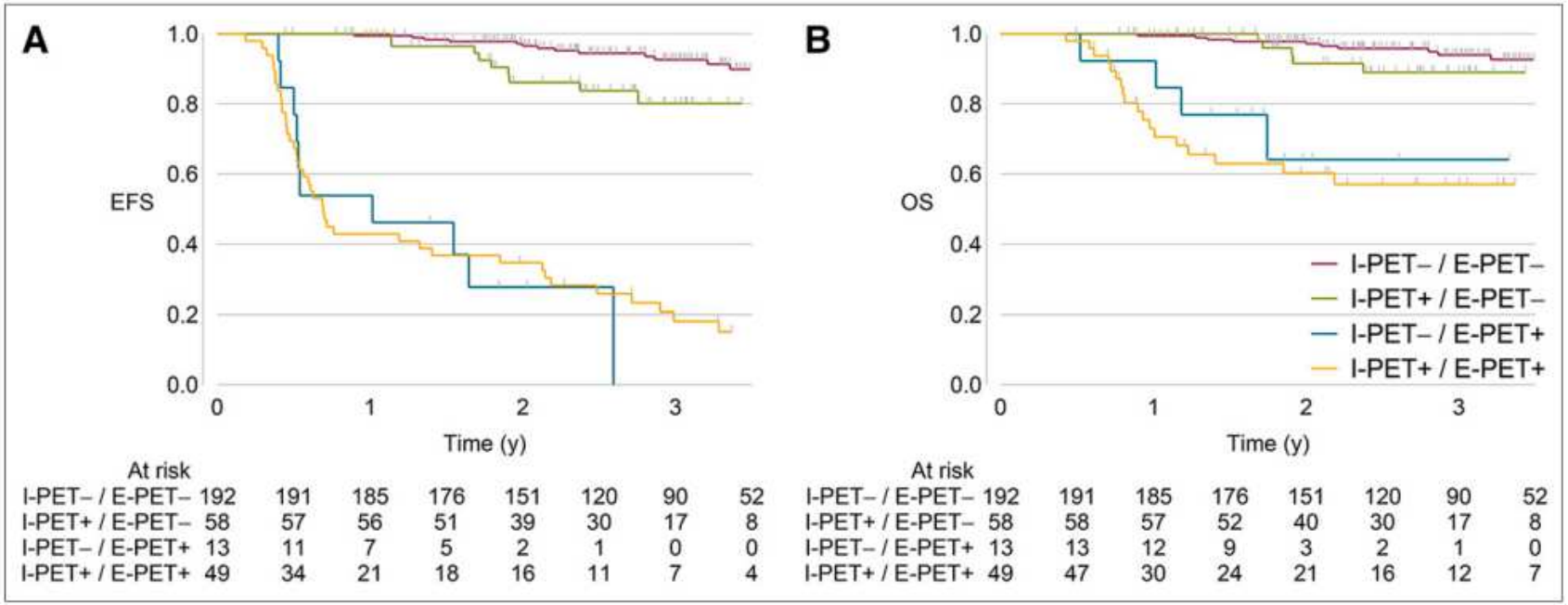
- No baseline characteristics differences between PET2-/PET4+ and PET2+/PET4+ patients but the TMTV analysis in these 2 subsets is ongoing

- The risk of PET4 positivity in PET2 negative patients is similar in both randomization arms

- Does this 2% risk of response loss justifies the systematic PET4 assessment in PET2 negative patients?

Backup

iPET and / or EOT PET?



49 (79%) of 62 PET EOT positive patients had a positive iPET

58 (54%) of 107 of iPET positive patients shift to negative PET at the EOT

Carr et al, JNM 2014