Characteristics and clinical outcome of patients with acute promyelocytic leukemia and increased body mass index treated with the PETHEMA Protocols

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On behalf of the PETHEMA, HOVON, PALG, and GATLA cooperative groups

Background

- Overweight and obesity was related to:
  - Higher incidence of differentiation syndrome:
    - Obesity (BMI ≥30) independent predictor of DS (n=39)
    - 4% in BMI<25 vs. 21% in BMI ≥ 25 (n=144)
  - Increase CIR at 5 years (n=144)

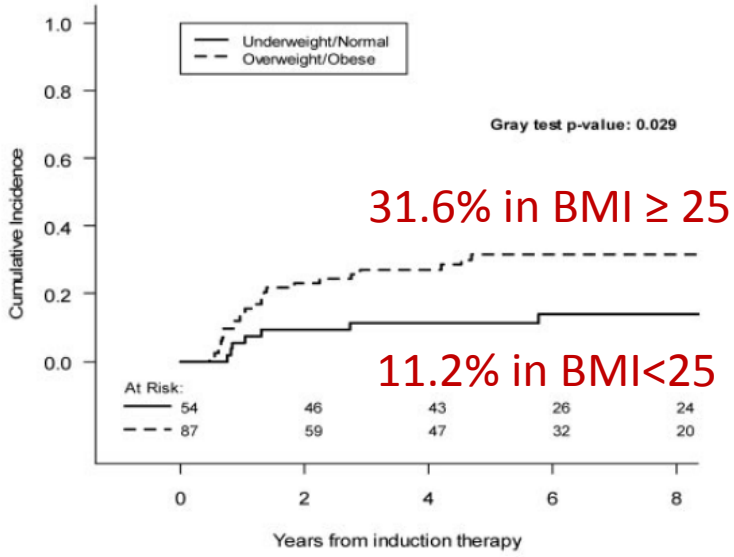


Figure 2. Cumulative incidence of relapse according to BMI.

Jeddi R et al. Heatology 2010
Breccia et al. Blood 2012 Blood.

Aims

Analyze in a large series of adult patients (≥18 yr.) with genetically confirmed *de novo* APL, homogeneously treated with three consecutive multicenter PETHEMA trials:

- The characteristics at diagnosis of overweight/obese patients
- The impact of BMI on clinical outcome

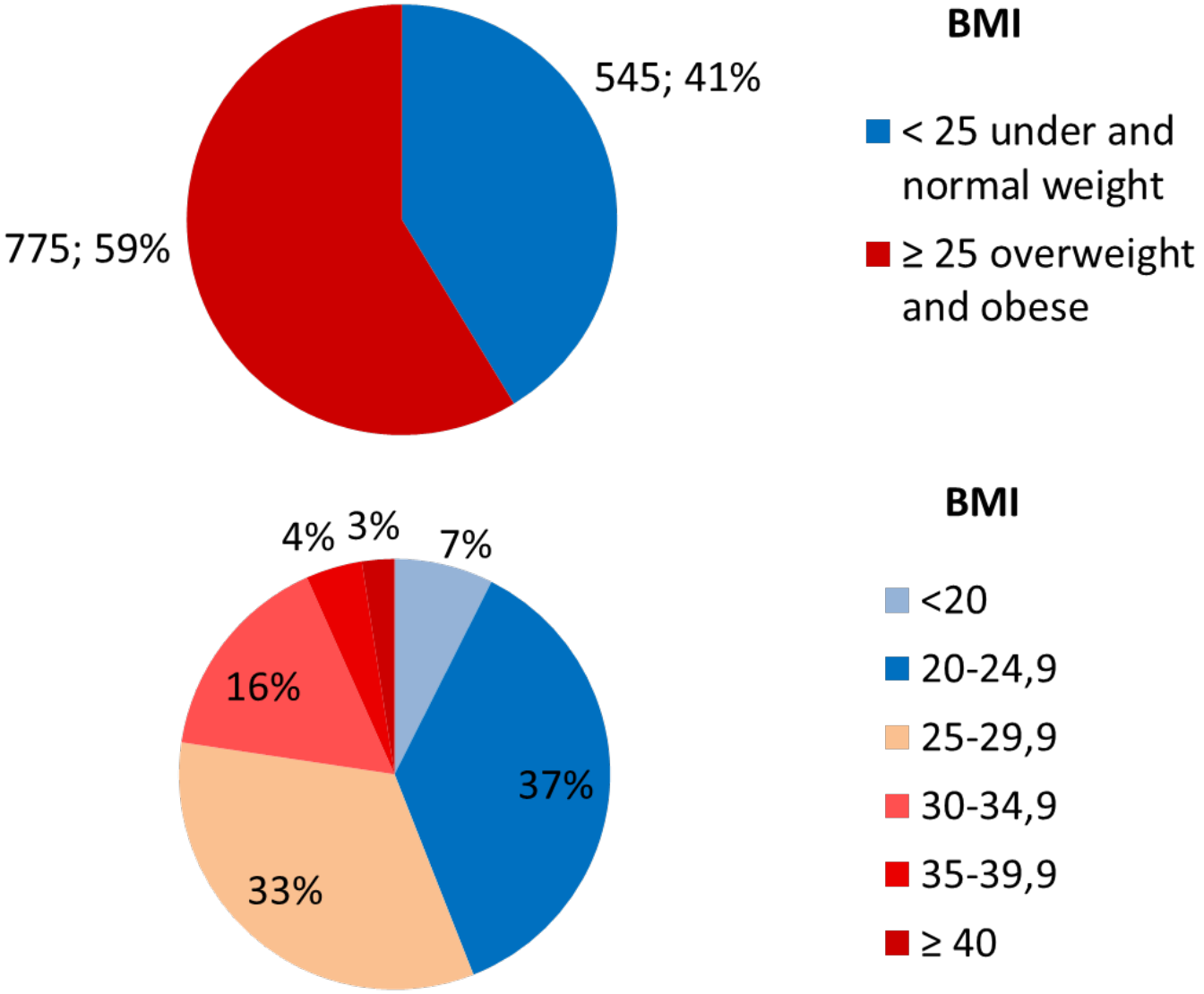
Material and Methods

- Between 1996 and 2012, 1419 consecutive adult patients were enrolled in the PETHEMA LPA 96, LPA 99, and LPA2005 trials
- 1320 (93%) patients have available height and weight data, and were included in this analysis

Material and Methods

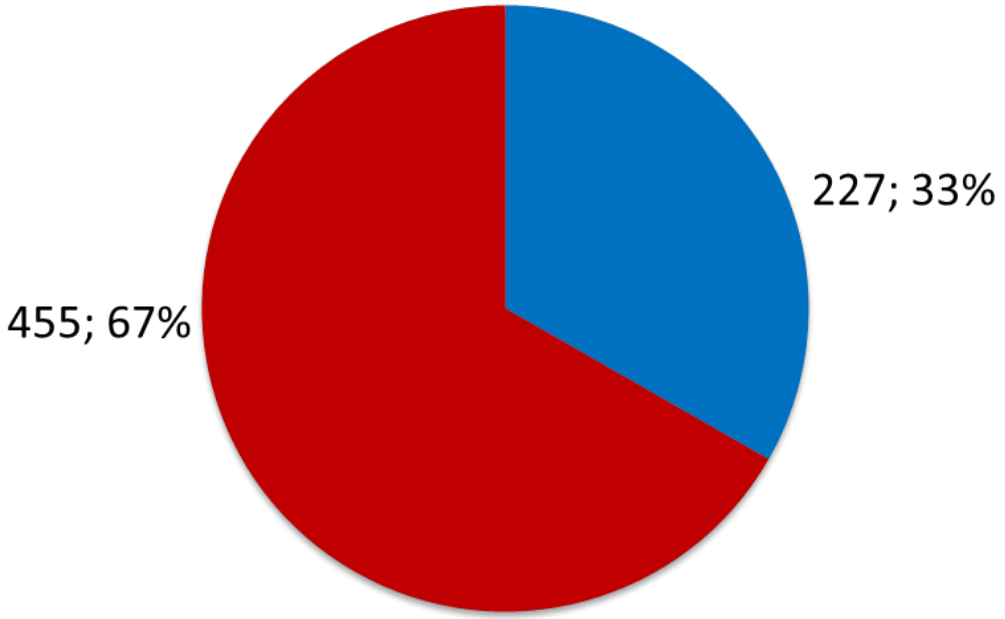
- Induction and consolidation following the multicenter trials LPA96, LPA99 & LPA2005
  - Induction: AIDA
  - Consolidation → 3 risk-adapted courses
    - ATRA + idarrubicine or mitoxantrone ± cytarabine
  - Maintenance: intermittent ATRA and low dose methotrexate and 6-mercaptopurine.

Results
Overweight and obesity frequency



Baseline characteristics

Male, n= 682



p<0,0001

Baseline characteristics

	BMI < 25 N= 534	BMI ≥ 25 N=775	P
	Mean (range)	Mean (range)	
Age (years)	38 (18-83)	48 (18-84)	<0.0001
Creatinine (mg/dl)	0.8 (0.3-12)	0.9 (0.2-13)	<0.0001
Urea (mg/dl)	29 (8-154)	35 (8-299)	<0.0001
Uric acid (mg/dl)	3.8 (0.8-11.7)	4.5 (1.1-11.6)	<0.0001
Bilirrubin (mg/dl)	0.7 (0.1-3.3)	0.8 (0.1-4.3)	0.002
Cholesterol (mg/dl)	175 (52-305)	189 (76-1276)	<0.0001
Triglycerids (mg/dl)	160 (39-850)	191 (22-700)	<0.0001

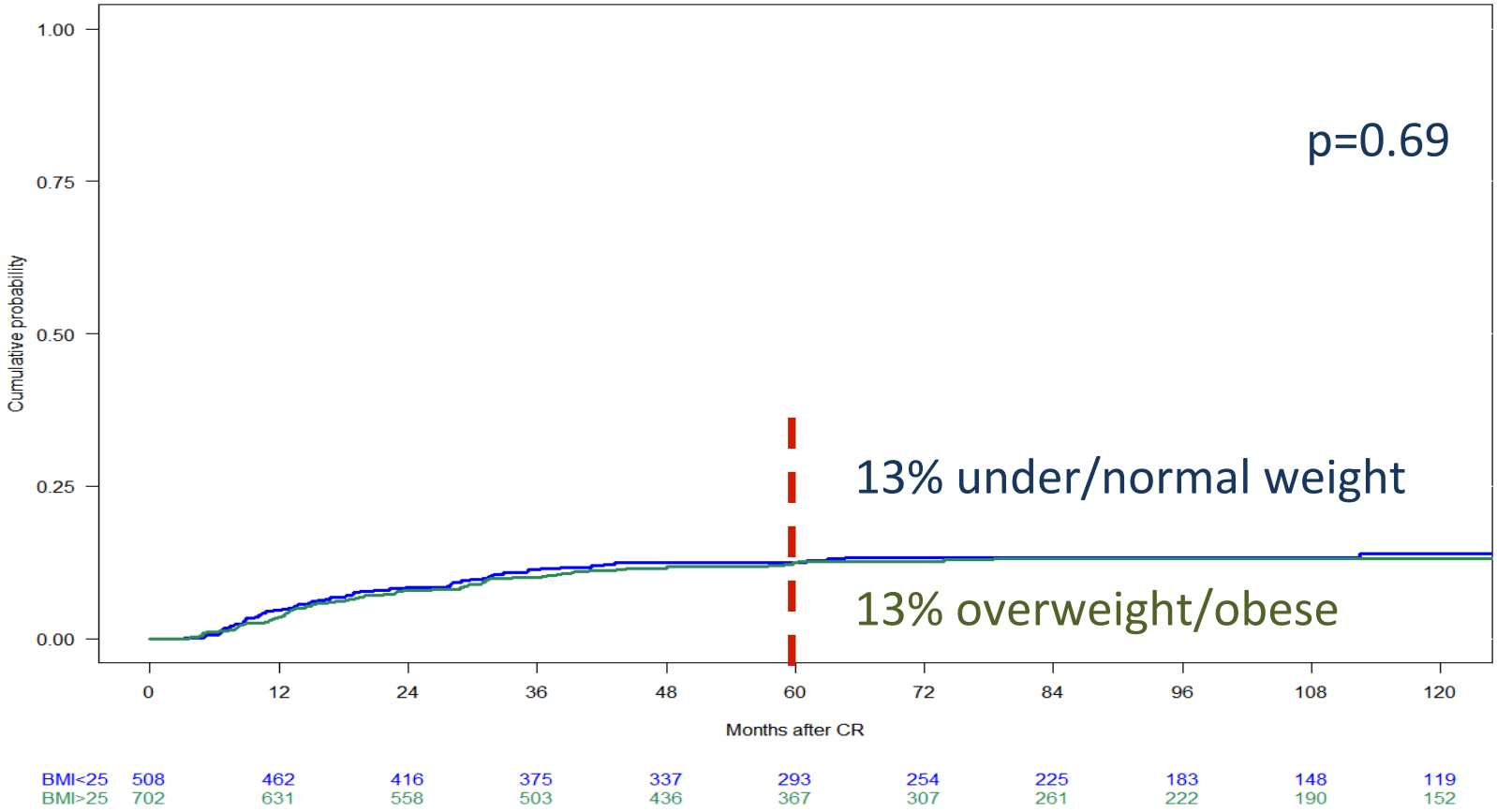
- No differences in FLT3, BCR3, and other markers distribution

Clinical outcome during induction

	BMI < 25 N= 543	BMI ≥ 25 N= 775	p
	N (%)	N (%)	
Thrombosis	29 (5)	63 (8)	0.06
Bleeding	436 (80)	608 (78)	0.5
Mortality	35 (6)	74 (10)	0.04
Differentiation syndrome*	143 (26)	221 (29)	0.4

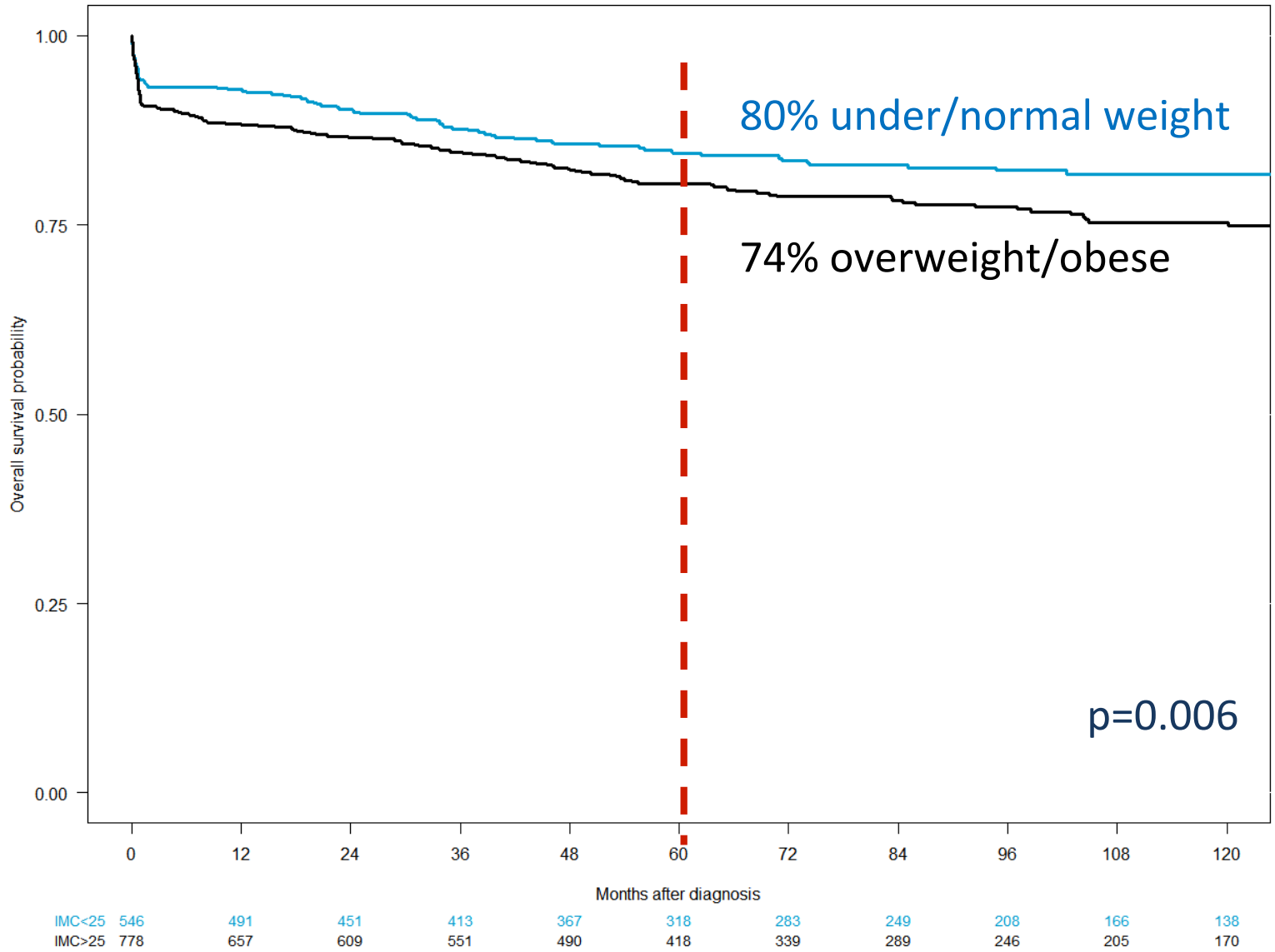
DS* under/normal/overweigh vs. obese (BMI ≥ 30): 26% vs. 32% (p=0.06)

Cumulative incidence of relapse according to BMI

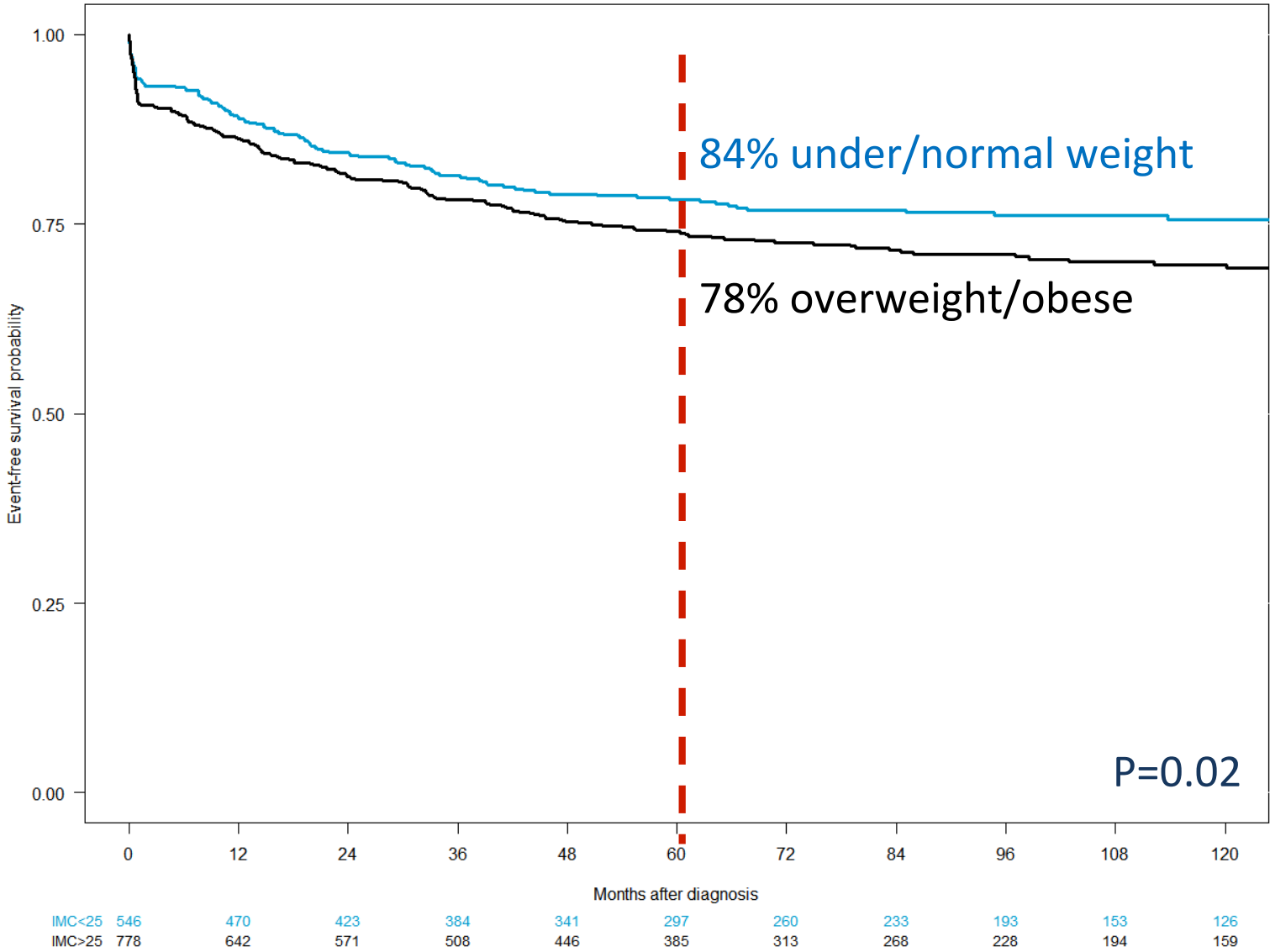


CIR at 5 years in obese (BMI ≥ 30) vs. under/normal/overweight: 13% vs. 12% (p=0.58)

Overall survival according to BMI



Event-free survival according BMI



Multivariate analysis
Overall survival

Adverse Risk factor	P value
Overweight/obese (BMI ≥ 25)	0.46
Older age	<0.0001
High relapse-risk	<0.0001
PETHEMA trials LPA 96/99	0.001

Conclusions

- We confirm the reported relationship between male gender, older age, and other known laboratory abnormalities in overweight/obese patients
- We could not confirm the higher incidence of DS in patients with BMI ≥25, but there was trend in obese patients
- In this large series, there was not difference in the relapse rate according BMI
- The univariate analysis showed worse OS in overweight and obese patients, but BMI was not an independent factor in the multivariate analysis

Aknowledgements

All the participating institutions of the PETHEMA, HOVON,

GATLA and PALG groups