



7<sup>th</sup> INTERNATIONAL SYMPOSIUM ON  
ACUTE PROMYELOCYTIC LEUKEMIA  
ROME, September 24-27, 2017

Chairmen: F. Lo-Coco, M.A. Sanz  
Honorary President: F. Mandelli

# RETROSPECTIVE ANALYSIS OF **EARLY MORTALITY** IN A COHORT OF PATIENTS WITH ACUTE PROMYELOCYTIC LEUKEMIA

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# Objective and Methods



- Objective: Compare characteristics between patients who died and survived induction chemotherapy.
- Methods:
  - Data of newly diagnosed APL patients from **January 2009 to February 2017** in one center → Total of **63 patients**
  - Sanz score was used to divide patients into risk groups
  - Treatment protocol in our institution consists of **AIDA protocol**

# Results



- Median follow-up of 66 months and **71% overall survival**
- Thirteen (**21%**) patients **died before induction was completed**:
  - 8 from CNS vascular events (5 hemorrhagic)
  - 5 from infection
- **All** induction survivors achieved **complete remission** in the end of induction treatment- **26% with molecular remission**
- 4 deaths occurred after induction: 2 from CNS events (1 hemorrhagic), 1 from infection and 1 from accidental trauma

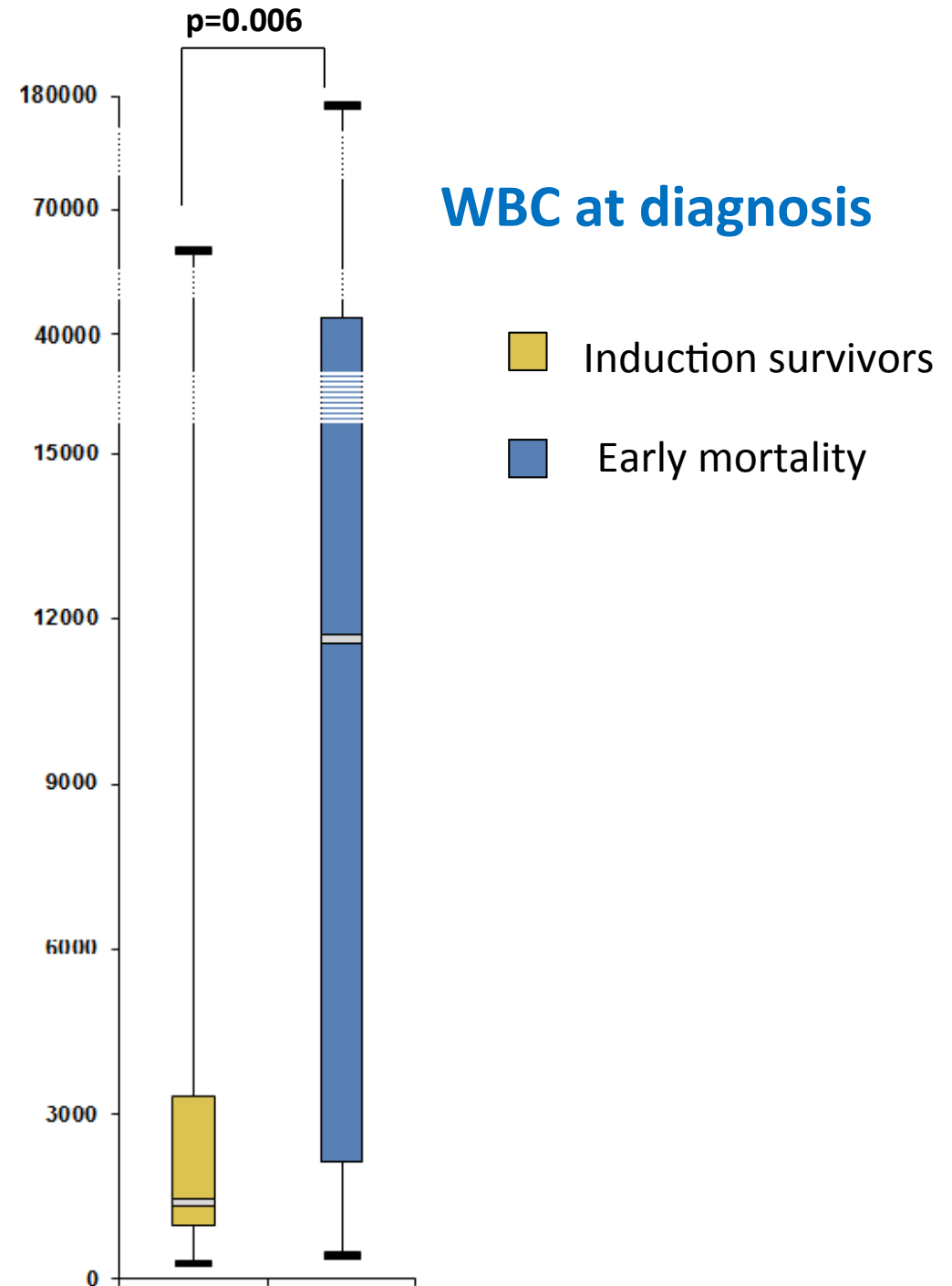
# Cohort characteristics

	Induction Survivors (n=50)	Early Deaths (n= 13)	P value
<b>Age</b> Median [min;max]	53 [24;78]	66 [33;80]	0.096
<b>Gender</b> Female %	52	69	0.265
<b>BMI</b> Median [min;max]	26 [14;39]	28 [23;35]	0.392
<b>Risk %</b> Low Intermediate High	18 66 16	15 31 54	<b>0.015</b>
<b>Platelets at diagnosis</b> Median [min;max]	20 [5;120]	23 [5;106]	0.905
<b>White Blood Count</b> Median [min;max]	1.40 [0.29;66.84]	11.65 [0.43;178]	<b>0.006</b>
<b>LDH</b> Median [min;max]	307 [132;1244]	308 [297; 901]	0.400



# Cohort characteristics

→ Prognostic Factors



# Cohort characteristics

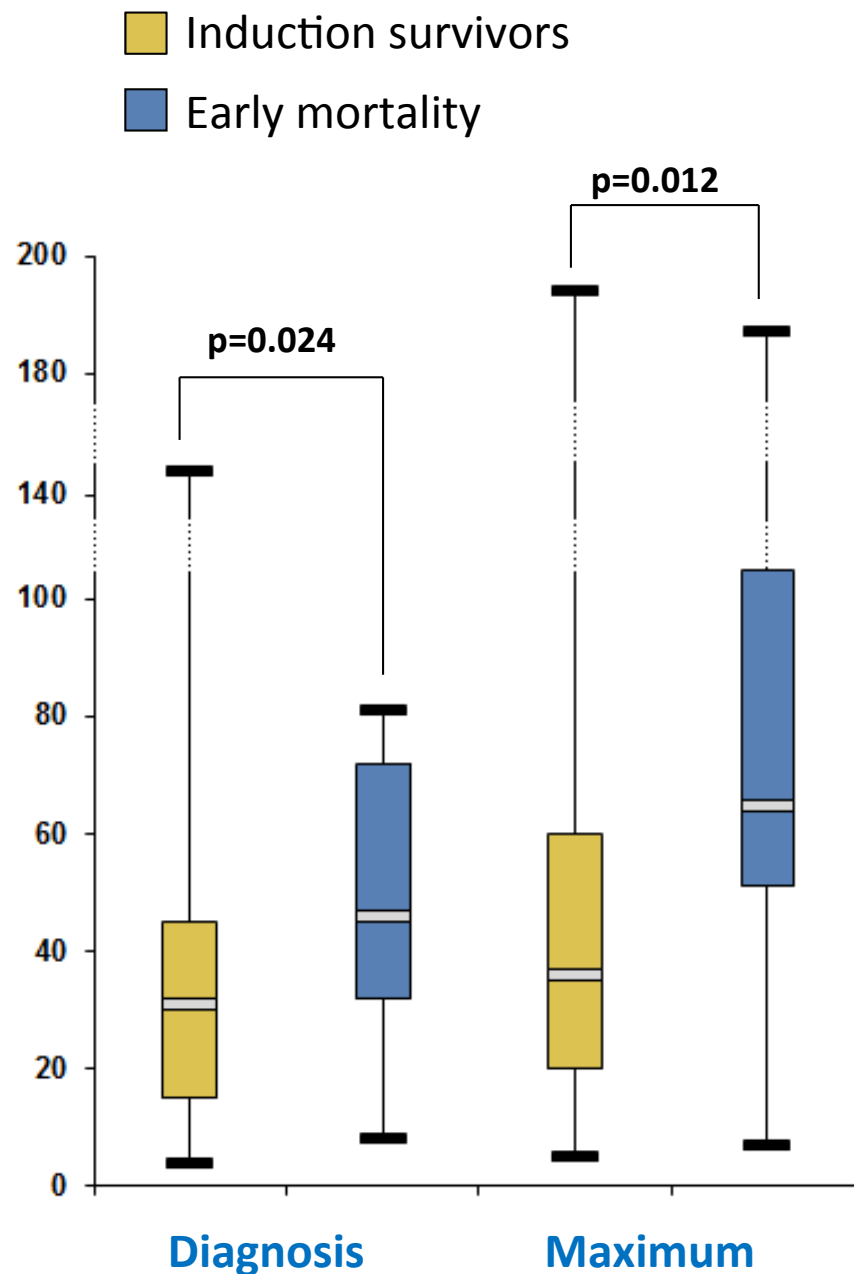
	Induction Survivors (n=50)	Early Deaths (n= 13)	P value
<b>Blasts BM %</b> Median [min;max]	80 [65;95]	68 [40;93]	0.829
<b>CD34 + %</b>	22	31	0.720
<b>BCR %</b>			
BCR 1	56	31	0.099
BCR 2	6	-	
BCR 3	36	61	
Other	2	-	
Unknown	-	8	
<b>Caryotype %</b>			
t(15,17)	80	79	0.773
Normal	6	7	
No metaphases	12	7	
Unknown	2	7	

# Cohort characteristics

	Induction Survivors (n=50)	Early Deaths (n= 13)	P value
<b>D- dimers</b> microgr/mL Median [min;max]			
At Diagnosis	31 [4;144]	46 [8;81]	<b>0.024</b>
Maximum	35 [5;194]	65 [7;187]	<b>0.012</b>
<b>Fibrinogen</b> mg/dL Median [min;max]			
At Diagnosis	156 [68;396]	141 [65;310]	0.241
Maximum	127 [56;277]	131 [39;252]	0.728

❖ **D-dimers levels** at diagnosis and during treatment were **higher for those with early mortality**

## D-dimers



## Cohort characteristics

→ Prognostic Factors



# Cohort characteristics

		Induction Survivors (n=50)	Early Deaths (n= 13)	P value
<b>Infection</b> at diagnosis	%	36	61.5	0.096
<b>Hemorrhage</b> at diagnosis	%	76	84.6	0.506

Hemorrhage Degree	Number (%)
<b>No (0)</b>	14 ( 22%)
<b>Mild (1)</b>	<b>35 ( 56%)</b>
<b>Severe (2)</b>	8 ( 12%)
<b>Potentially Fatal (3)</b>	6 ( 10%)

Rates of infection  
and hemorrhage at  
diagnosis were  
**similar** in both  
groups

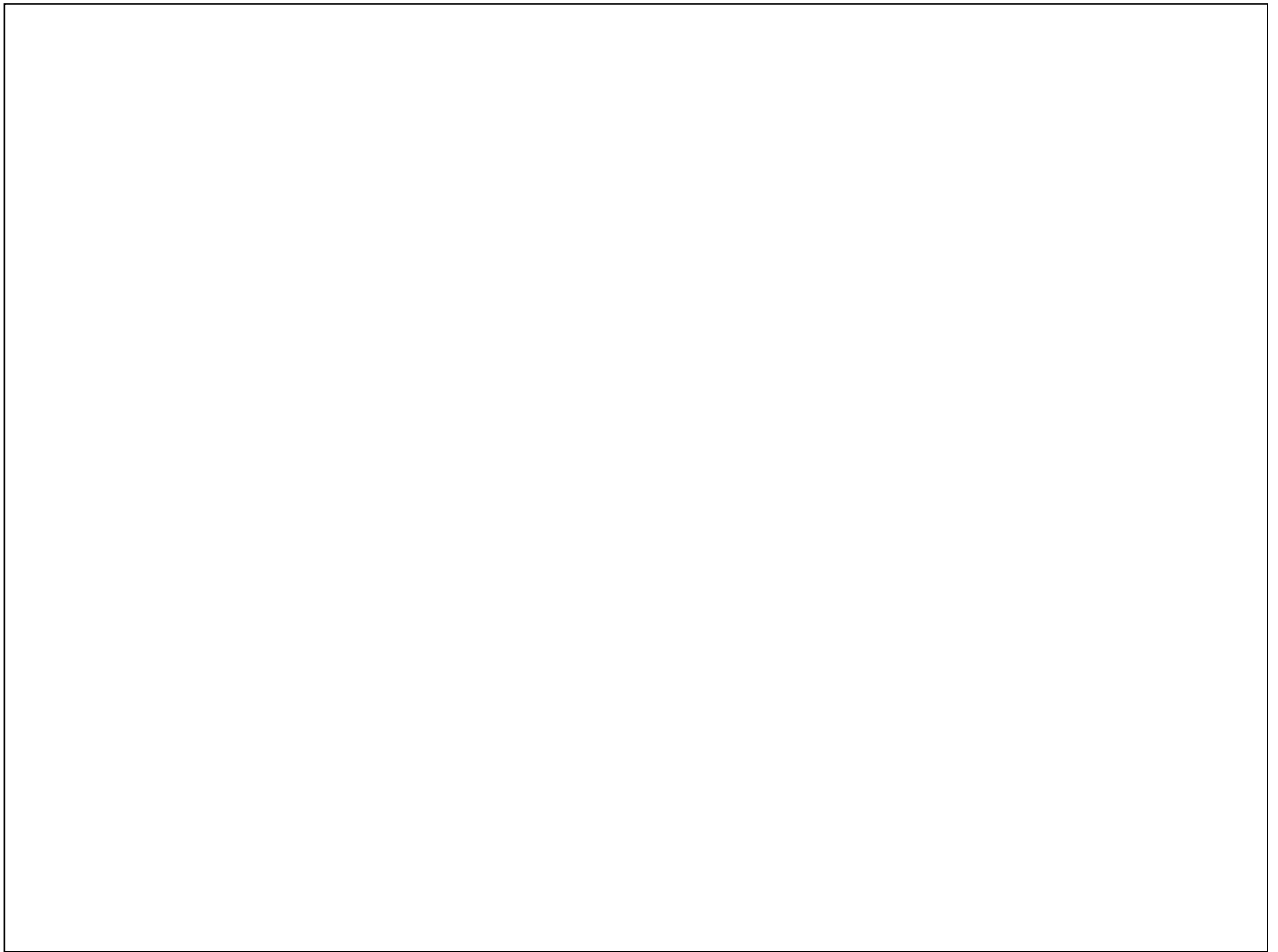
# Conclusion



- Our cohort of real-life APL patients had an **early mortality** rate of **21%**, mostly secondary to **CNS vascular events**
- **High leukocyte count** and **D-dimers level** were the main **determinants for early death**
- »» **higher index of suspicion**
- »» **prompt referral to specialized centers**
- supportive care and **targeted treatment as soon as possible** to avoid excess death at APL presentation

Thanks for your attention!







		Crude OR		Adjusted OR	
		OR	[95% CI]	OR	[95% CI]
Age	≤40 years	Ref		---	
	>40 years	2.59	[0.51-13.07]		
Gender	Male	Ref		---	
	Female	2.08	[0.57-7.64]		
Leucocytes	≤20000	Ref		Ref	
	>20000	<b>5.11</b>	<b>[1.08-24.30]</b>	4.12	[0.76-22.35]
D-dimers	≤70	Ref		Ref	
	>70	<b>10.67</b>	<b>[1.69-67.21]</b>	<b>10.67</b>	<b>[1.69-67.21]</b>
Fibrinogen	≥150	Ref		---	
	<150	1.73	[0.50-6.04]		
BMI	<30	Ref		---	
	≥30	0.56	[0.11-2.89]		
BM blasts	<80	Ref		---	
	≥80	0.78	[0.09-6.98]		
BCR	Not bcr1	Ref		---	
	With bcr1	0.37	[0.10-1.34]		
CD34	Negative	Ref		---	
	Positive	1.62	[0.42-6.26]		
Hemorrhage	Grade 0-2	Ref		Ref	
	Grade 3-5	2.85	[0.75-10.77]	2.61	[0.57-11.97]
Infection	No	Ref		Ref	
	Yes	2.93	[0.835-10.30]	1.53	[0.33-7.00]
Differentiation	No	Ref		---	
	Yes	0.88	[0.21-3.69]		
Sanz modified	Low/int	Ref		Ref	
	High/ultra	<b>5.08</b>	<b>[1.02-25.29]</b>	2.37	[0.40-14.04]

## Multivariate Analysis

Quanto doentes do grupo morte precoce estavam a fazer ATRA?

-Todos

-Quanto morreram nas primeiras 48 horas?

-- cinco dos 13