GET – LAP
Groupe d'Etude et de Travail
Sur les Leucémies Aigues
Promyélocytaires

Arsenic Trioxide (ATO) and ATRA with Limited Chemotherapy (CT) in Newly Diagnosed Standard Risk APL in the Elderly. a Report By the French Belgian Swiss APL Group (APL 2006 trial)

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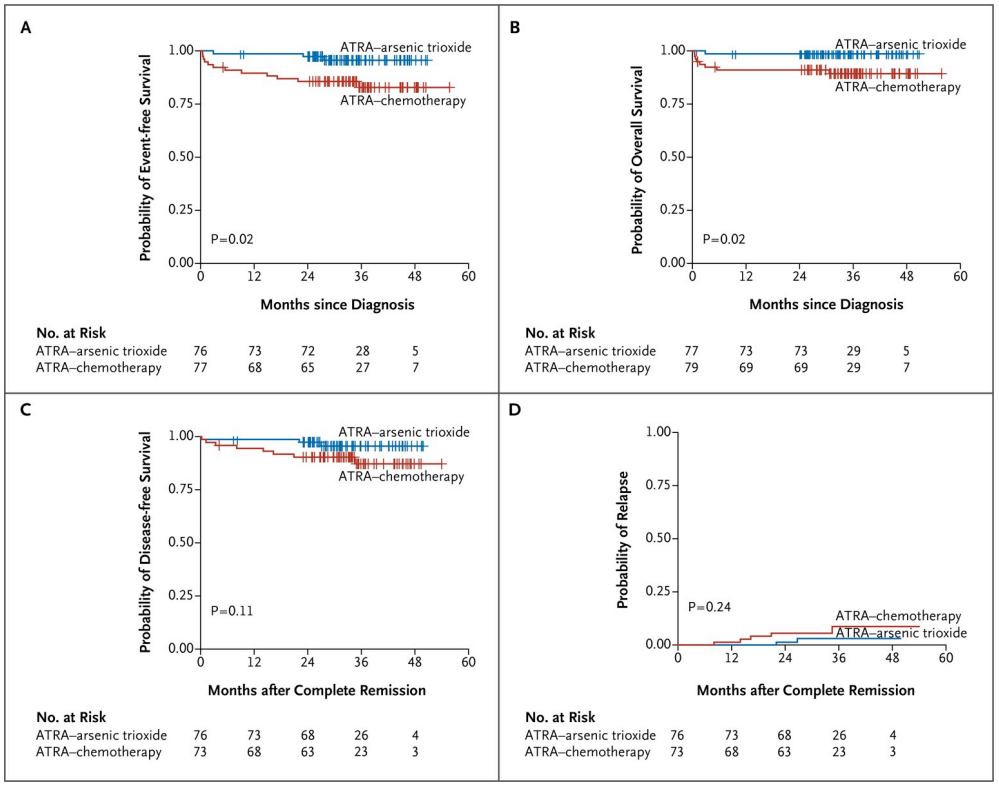
Introduction

- In the elderly, the treatment of APL with conventional ATRA-anthracycline based CT regimens is associated with :
  - A relatively high early death rate
  - Limited number of relapses
  - and a high rate of deaths in CR (21% in our experience)

Leukemia (2014) 28, 2422–2424;
Blood 2010 115:1690

Introduction

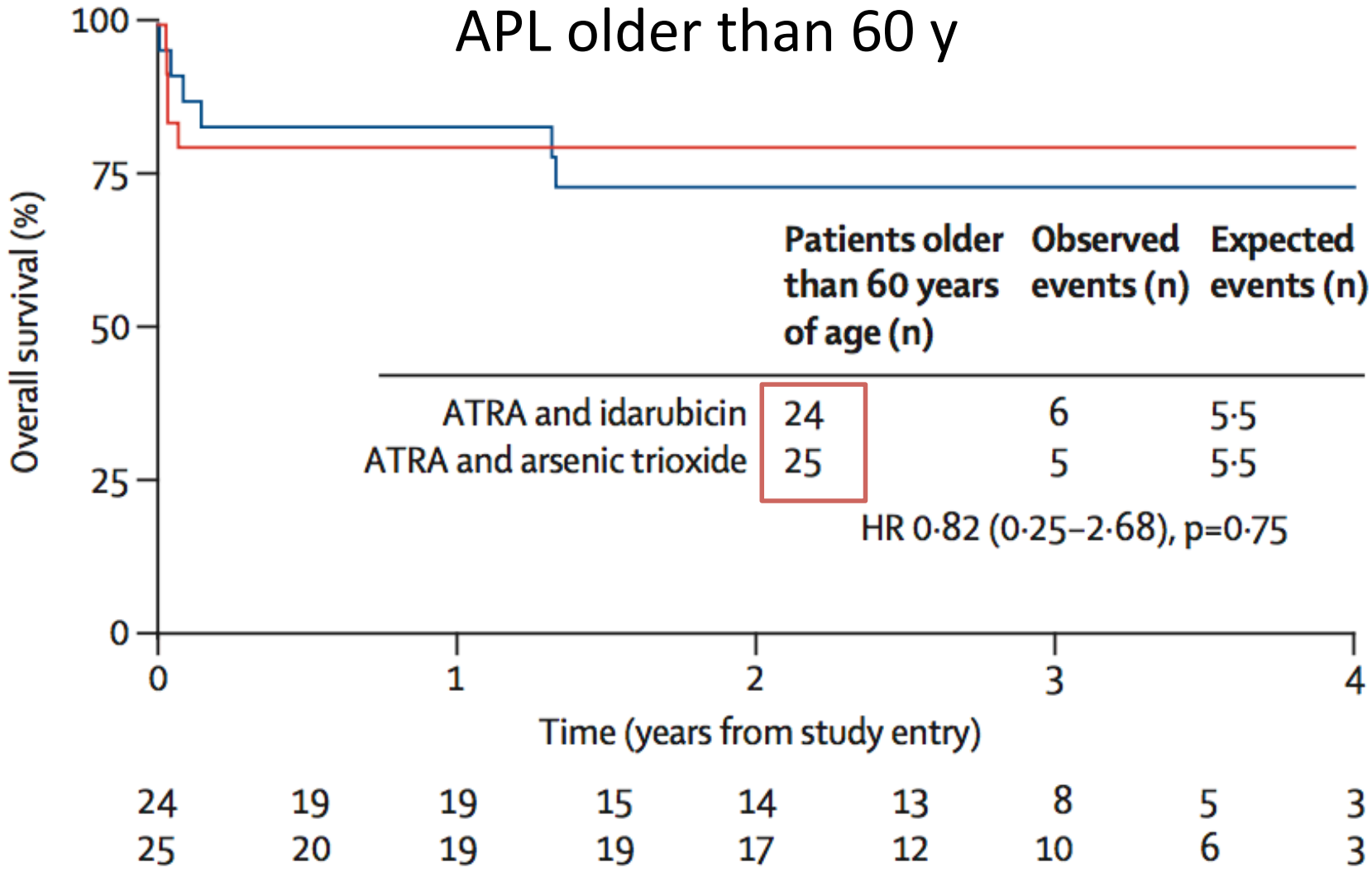
ATO-ATRA is highly effective in newly diagnosed standard risk younger APL



Lo-Coco F et al. N Engl J Med 2013;369:111-121

Introduction

APL older than 60 y



Burnett, Lancet Oncol 2016

Introduction

- We present results of APL 2006 trial
  - where we combined ATO to ATRA
  - and reduced CT
  - in patients aged older than 70 years
  - with standard risk APL (WBC <10G/L)

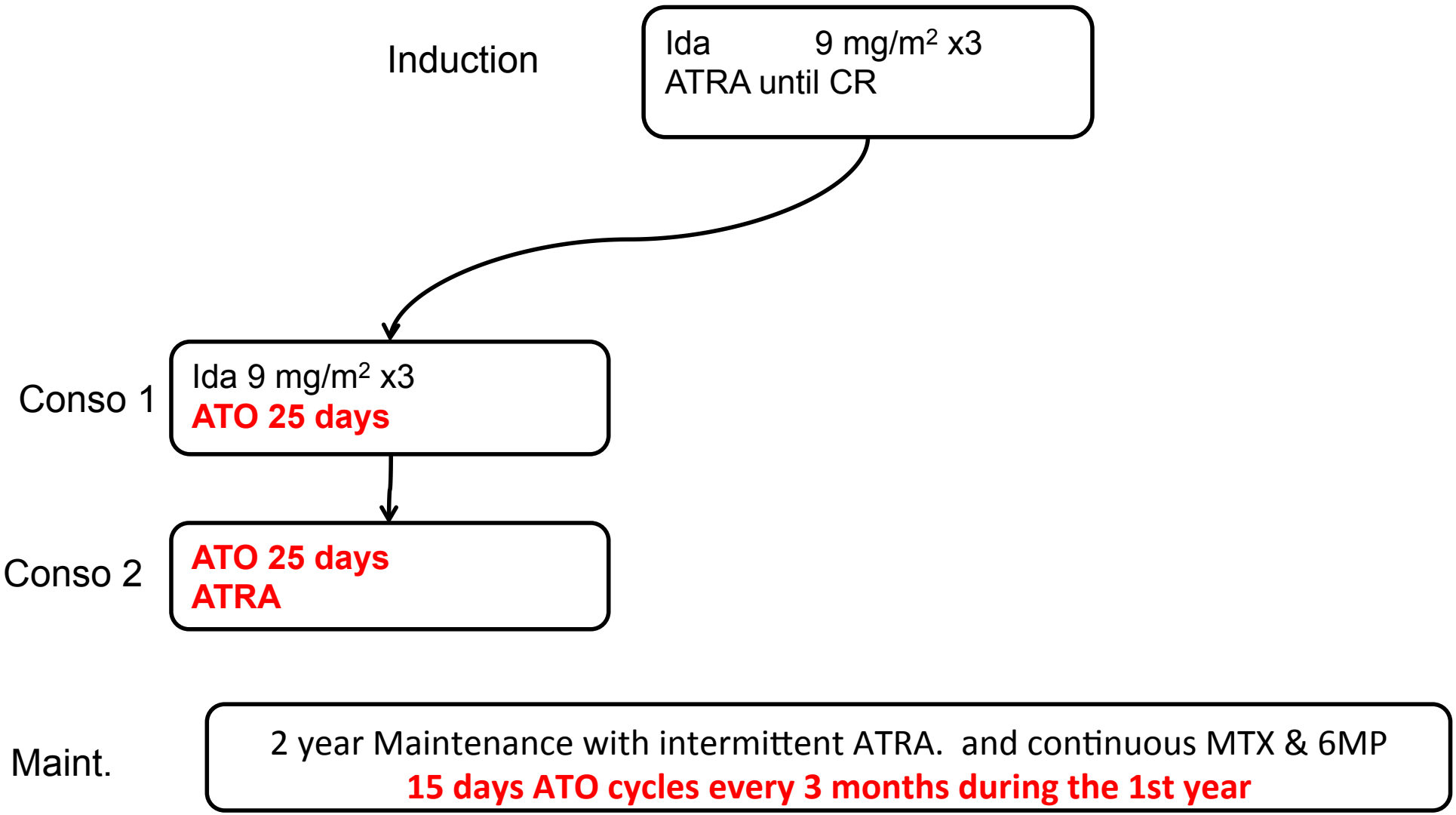
Inclusion criteria

- Newly diagnosed APL patients
  - Subsequently confirmed by
    - Conventional cytogenetic
    - And/or presence of PML-RARA transcript
- >70 years
- WBC count < 10 G/L
- No contra-indication to ICT or ATO

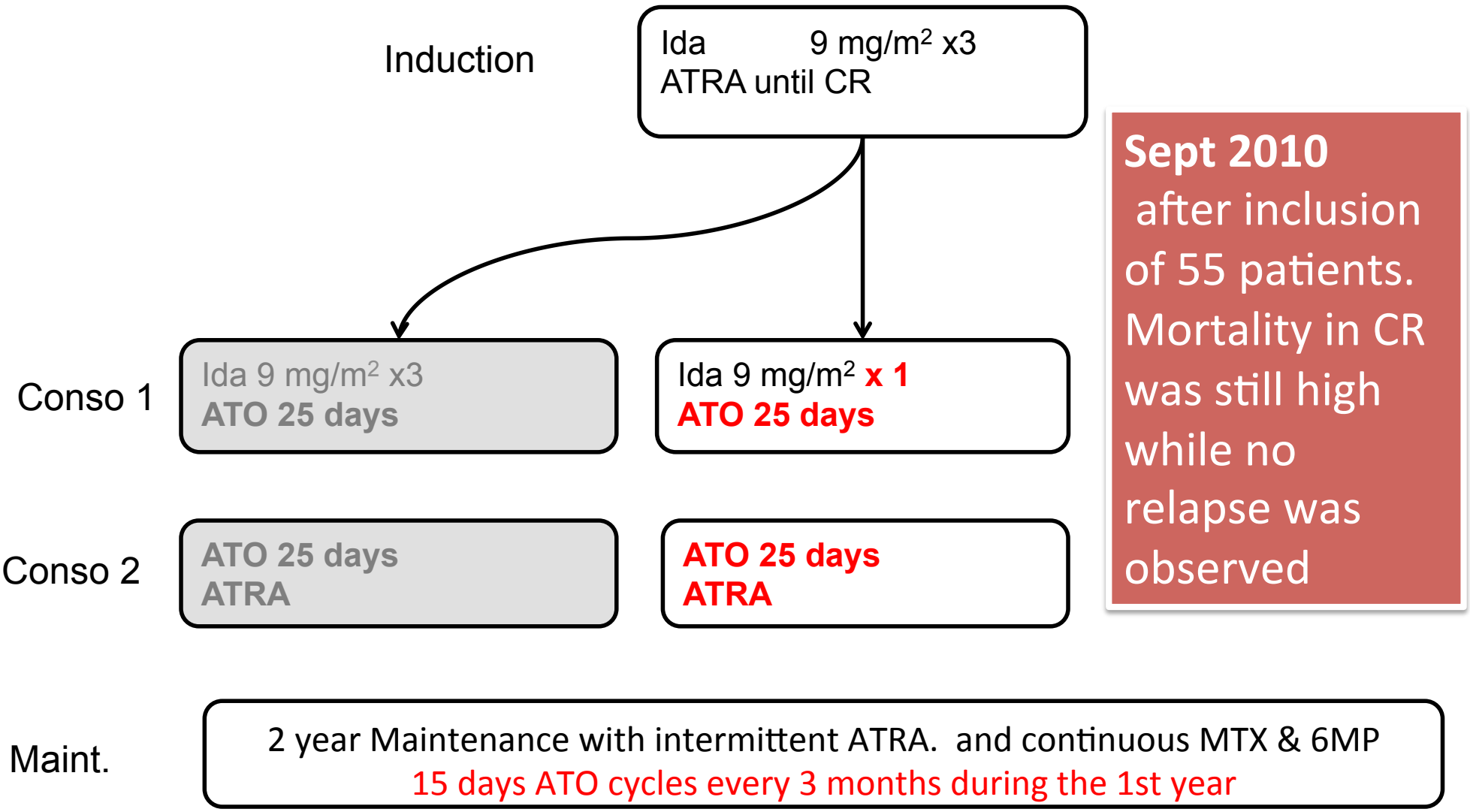
Analysis

- Inclusion period: 2006 to 2015
- Analysis :
  - made at the reference date of 1st Jan 2016
  - In 124 pts aged > 70 years included in 43 centers
- With a median Follow-up of 44 months

Treatment schedule



Treatment schedule

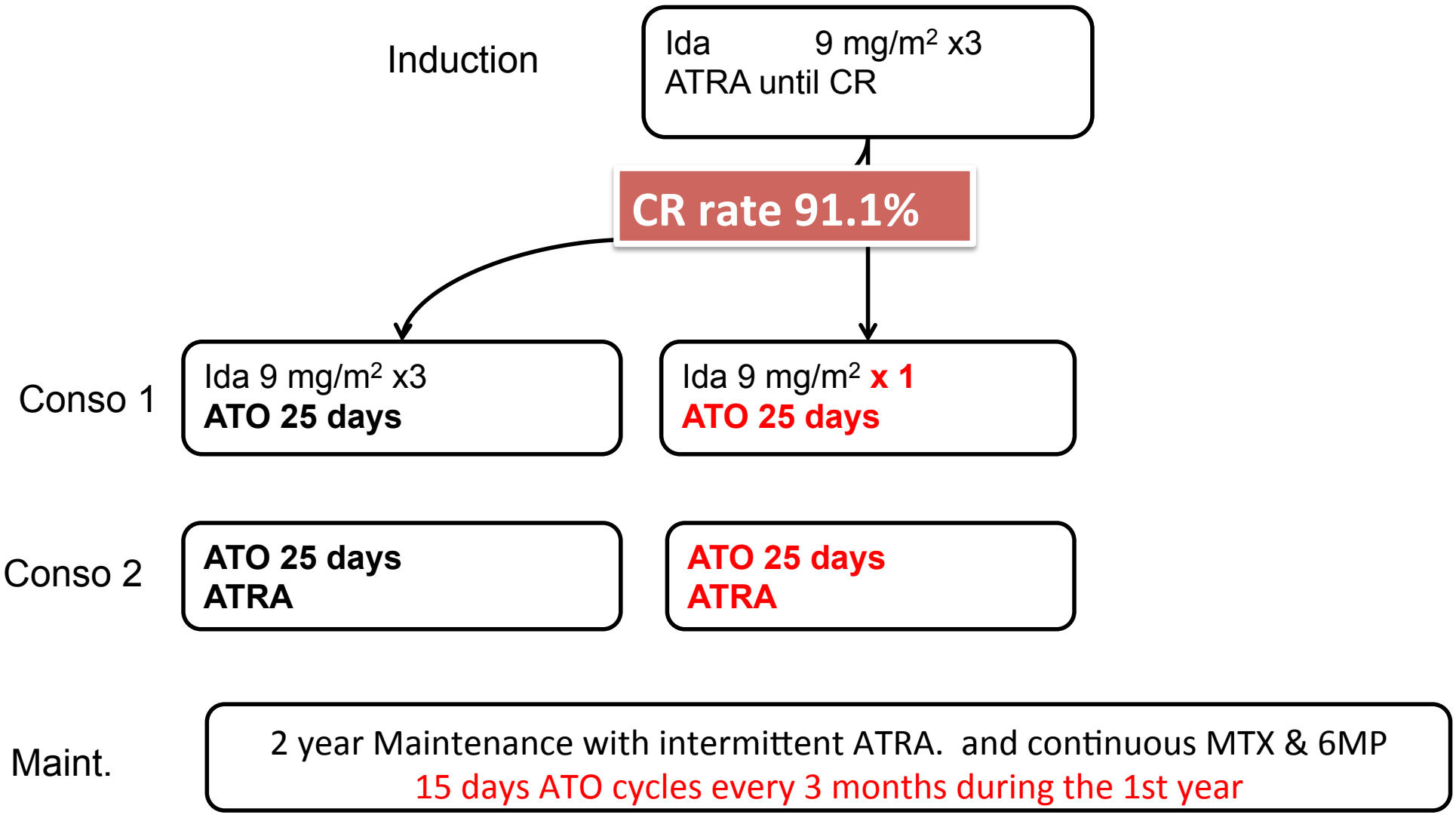


Sept 2010 after inclusion of 55 patients. Mortality in CR was still high while no relapse was observed

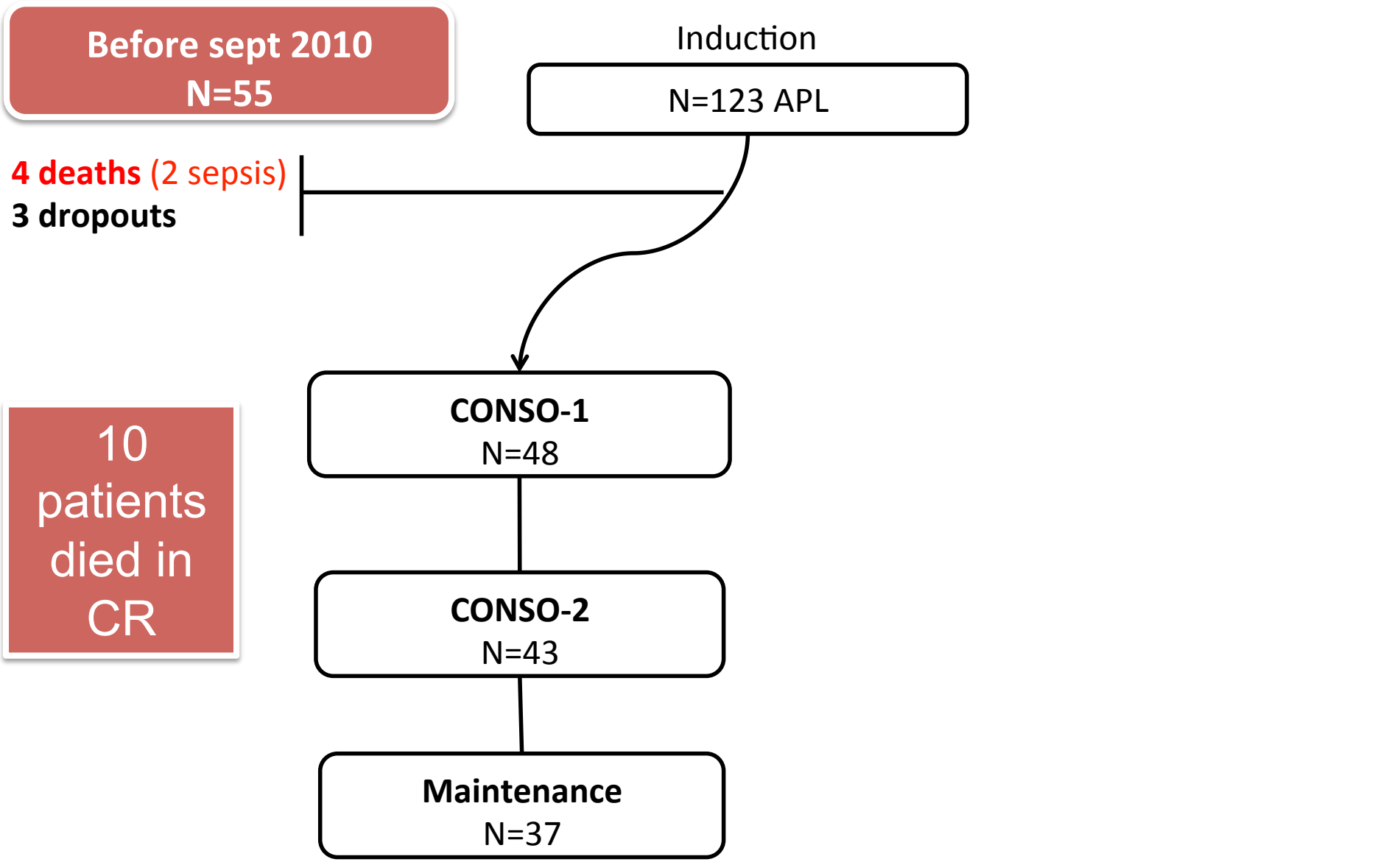
Patient characteristics

Median [Q1-Q3]	N=124
Age (y)	73.5 [71.8; 77.9]
WBC (G/L)	1.1 [0.8; 1.8]
Platelets(G/L)	44.0 [22.5; 87.5]
Fibrinogen (g/l)	2.3 [1.6; 3.3]
%M3v	5%
%Previous cancer	35%

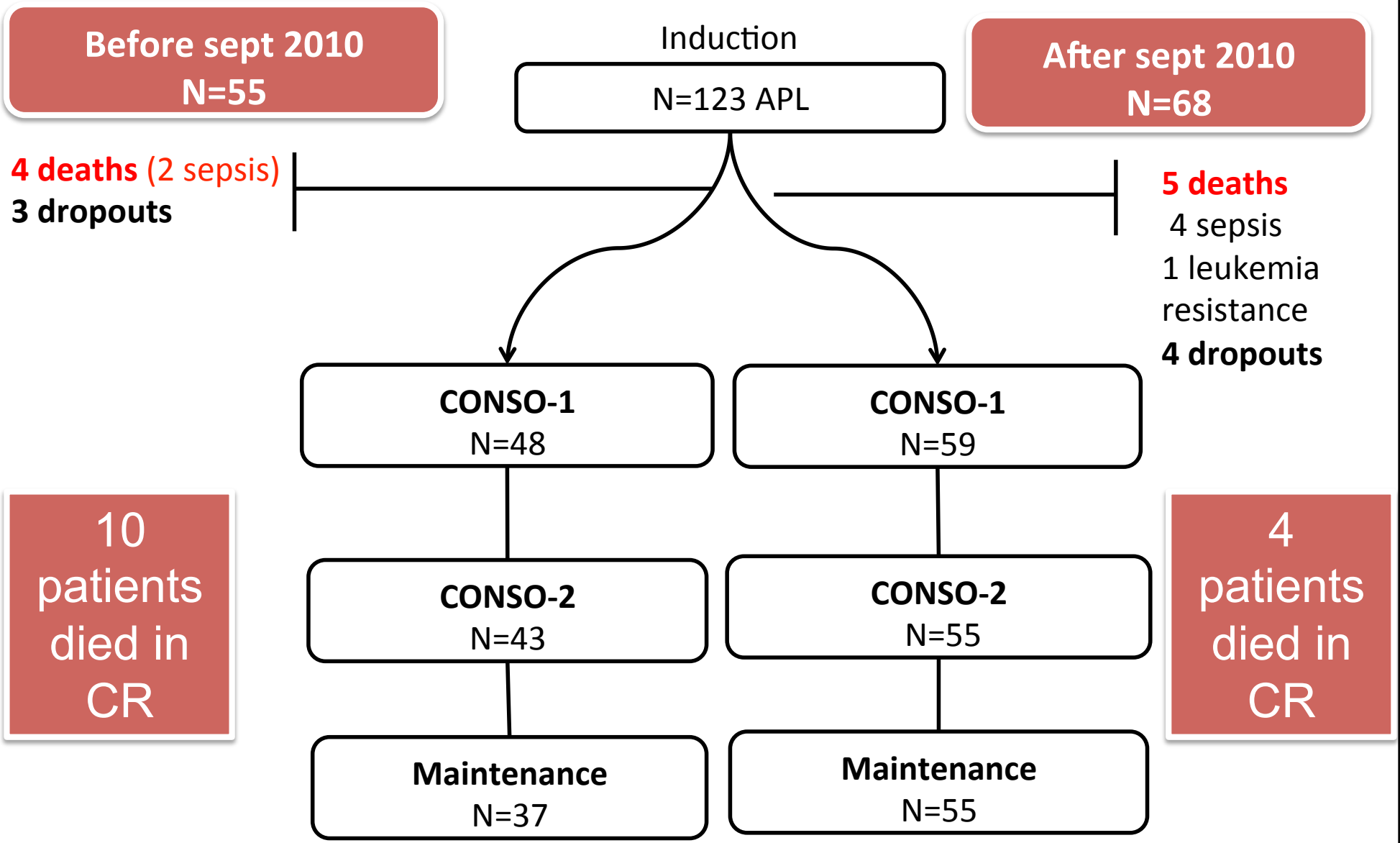
Response Rate



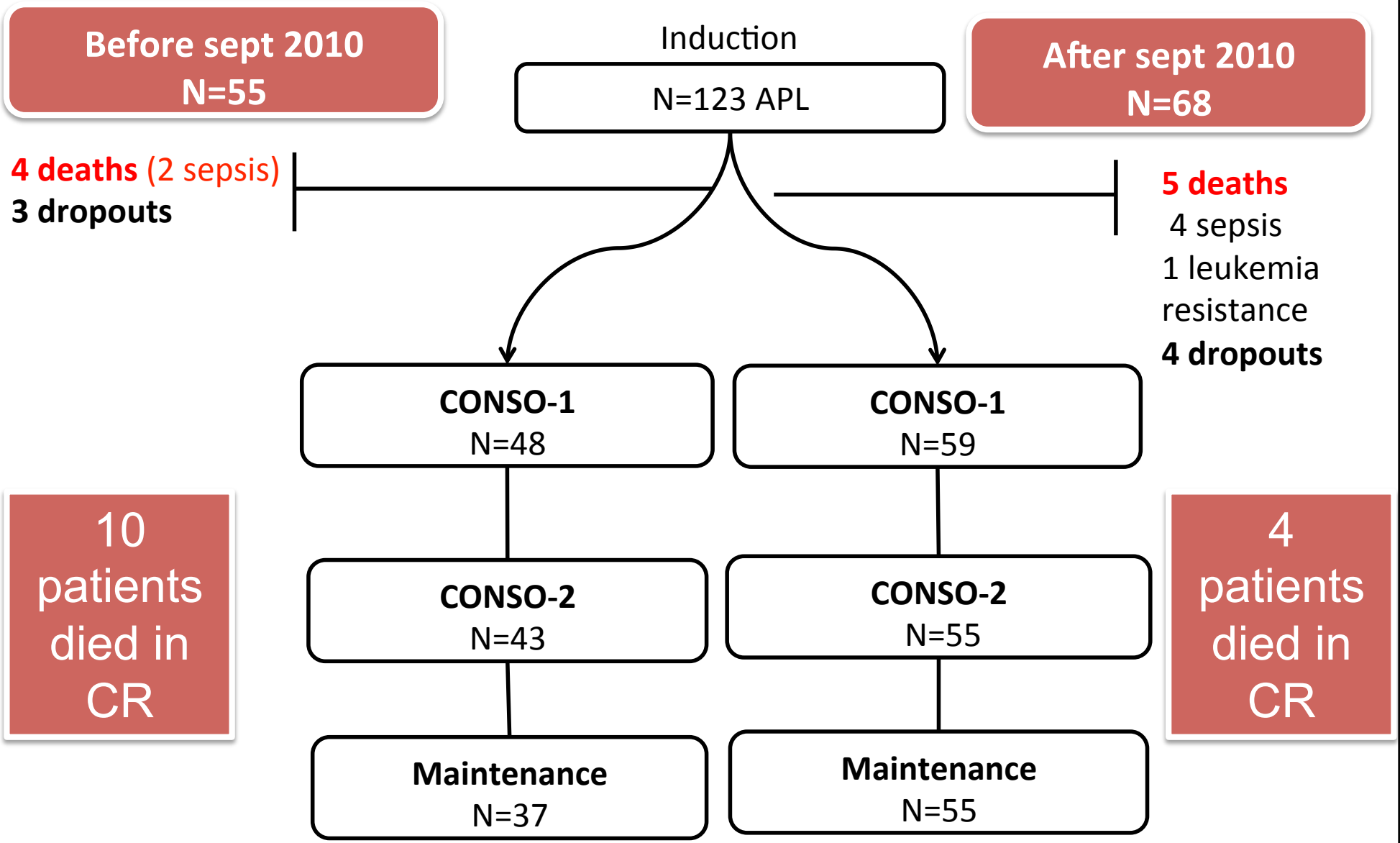
Deaths during the study



Deaths during the study



Deaths during the study



Death in CR

Death in CR rate :

- 20% before Amendment
- 4% After Amendment

P=0.045

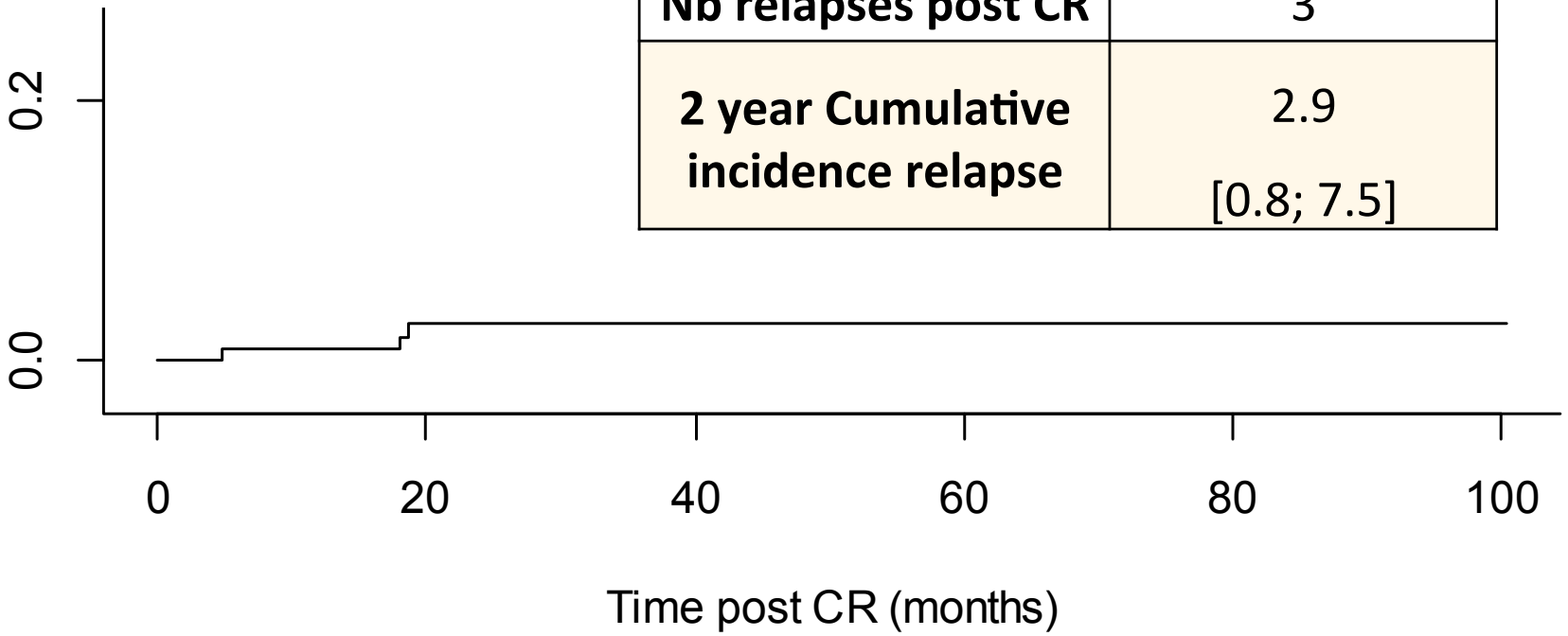
Causes of death in CR were :

- Sepsis
  - n=4 before amendment
  - n=2 after amendment
- Bleeding
  - n=5 before amendment
  - n=1 after amendment
- Other cause (n=2)

Cumulative incidence of Relapse

With a median FU of 44.3 months

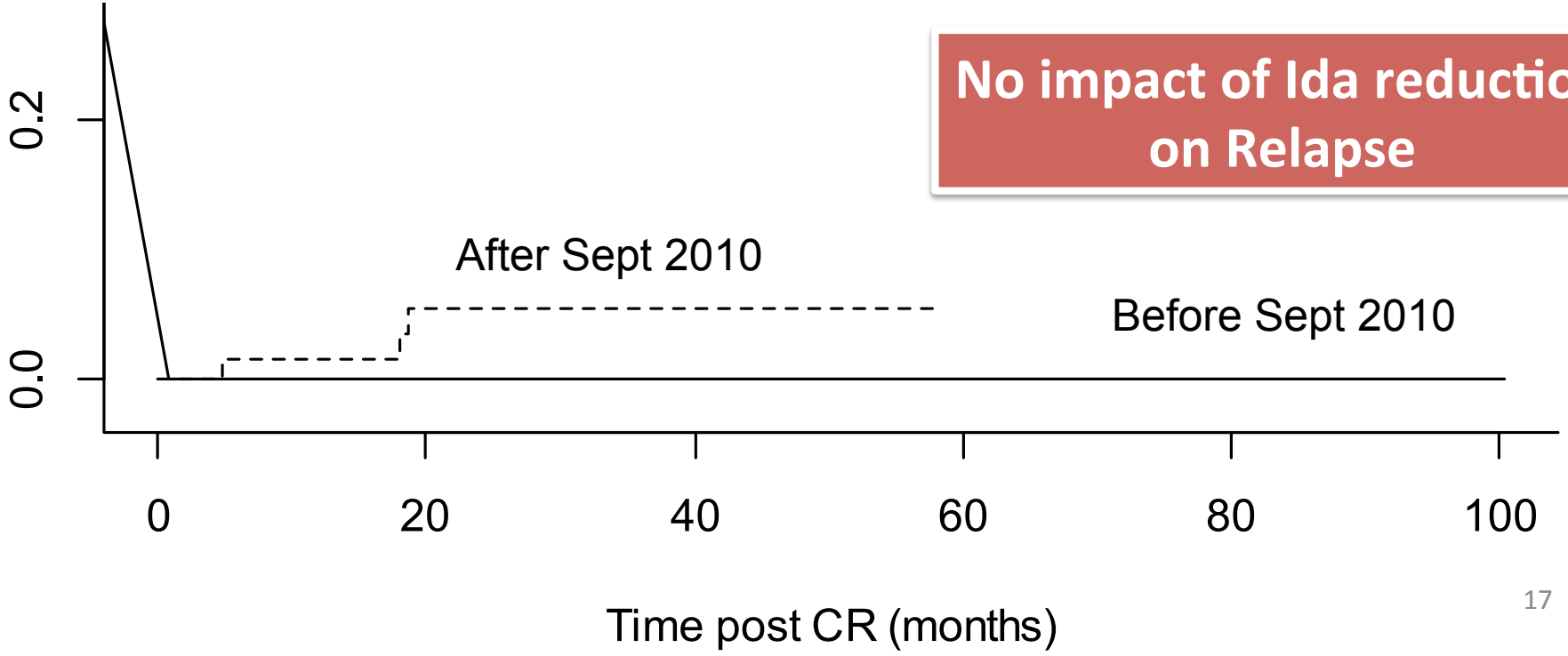
	Overall N=124
Nb relapses post CR	3
2 year Cumulative incidence relapse	2.9 [0.8; 7.5]



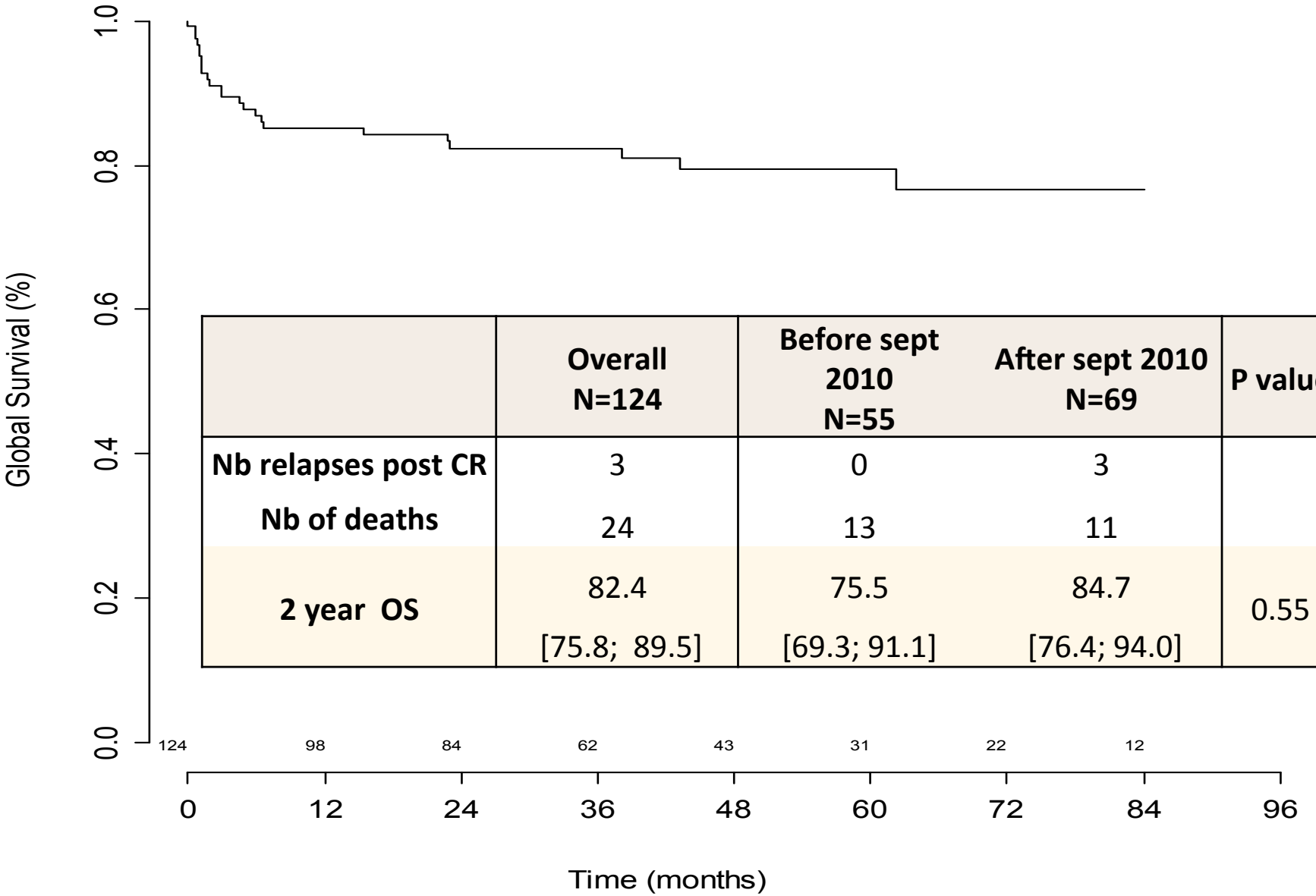
Cumulative incidence of Relapse

	Overall N=124	Before sept 2010 N=55	After sept 2010 N=69	P value
Nb relapses post CR	3	0	3	
2 year Cumulative incidence relapse	2.9 [0.8; 7.5]	0	5.5 [1.4; 13.8]	0.1

No impact of Ida reduction on Relapse

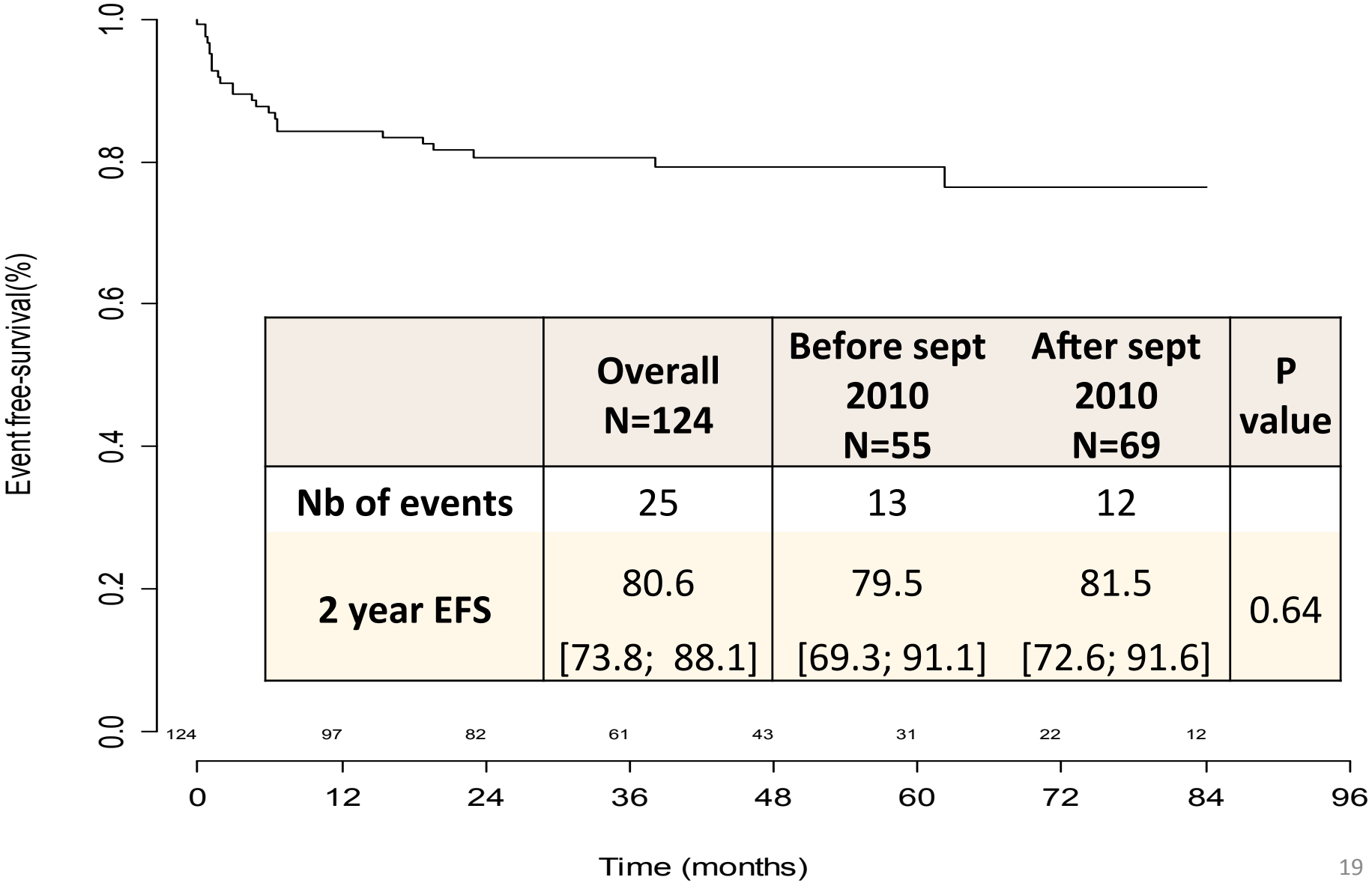


Overall Survival



	Overall N=124	Before sept 2010 N=55	After sept 2010 N=69	P value
Nb relapses post CR	3	0	3	
Nb of deaths	24	13	11	
2 year OS	82.4 [75.8; 89.5]	75.5 [69.3; 91.1]	84.7 [76.4; 94.0]	0.55

Event free survival



	Overall N=124	Before sept 2010 N=55	After sept 2010 N=69	P value
Nb of events	25	13	12	
2 year EFS	80.6 [73.8; 88.1]	79.5 [69.3; 91.1]	81.5 [72.6; 91.6]	0.64

Hematological toxicity

Mean	Before sept 2010	After sept 2010	p-value
days w/ Antibiotics 1st Consolidation	6.2	3.8	0.22
RBC transfusion 1st Consolidation	2.9	1.2	<0.0001
Time to platelet > 50 G/l 1st consolidation	5.6	4	<0.0001
Time to ANC > 1 G/L 1st consolidation	16.2	11.9	<0.0001

Conclusions

- In older patients with standard risk APL, addition of ATO, with limited amount of CT was associated with :
  - high CR rates,
  - without any increase in the relapse rate compared to our previous experience with ATRA–CT regimens.
- Reduction of mortality in CR was only seen when consolidation CT was reduced to one single day of Ida.

Acknowlegments

- **Centers of the European APL group in France, Switzerland and Belgium**
  - Xavier Thomas, Agnès Guerci, Arnaud Pigneux, Norbert Vey, Emmanuel Raffoux, Sylvie Castaigne, Olivier Spertini, Dominique Bron, Jean Pierre Marolleau,,Gandhi Damaj, Dominique Bordessoule
  - And many more
- **Statistical analysis**
  - Julie Lejeune, Sylvie Chevret
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  - Pierre Fenaux