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Update of APL 2006 trial results

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Objective

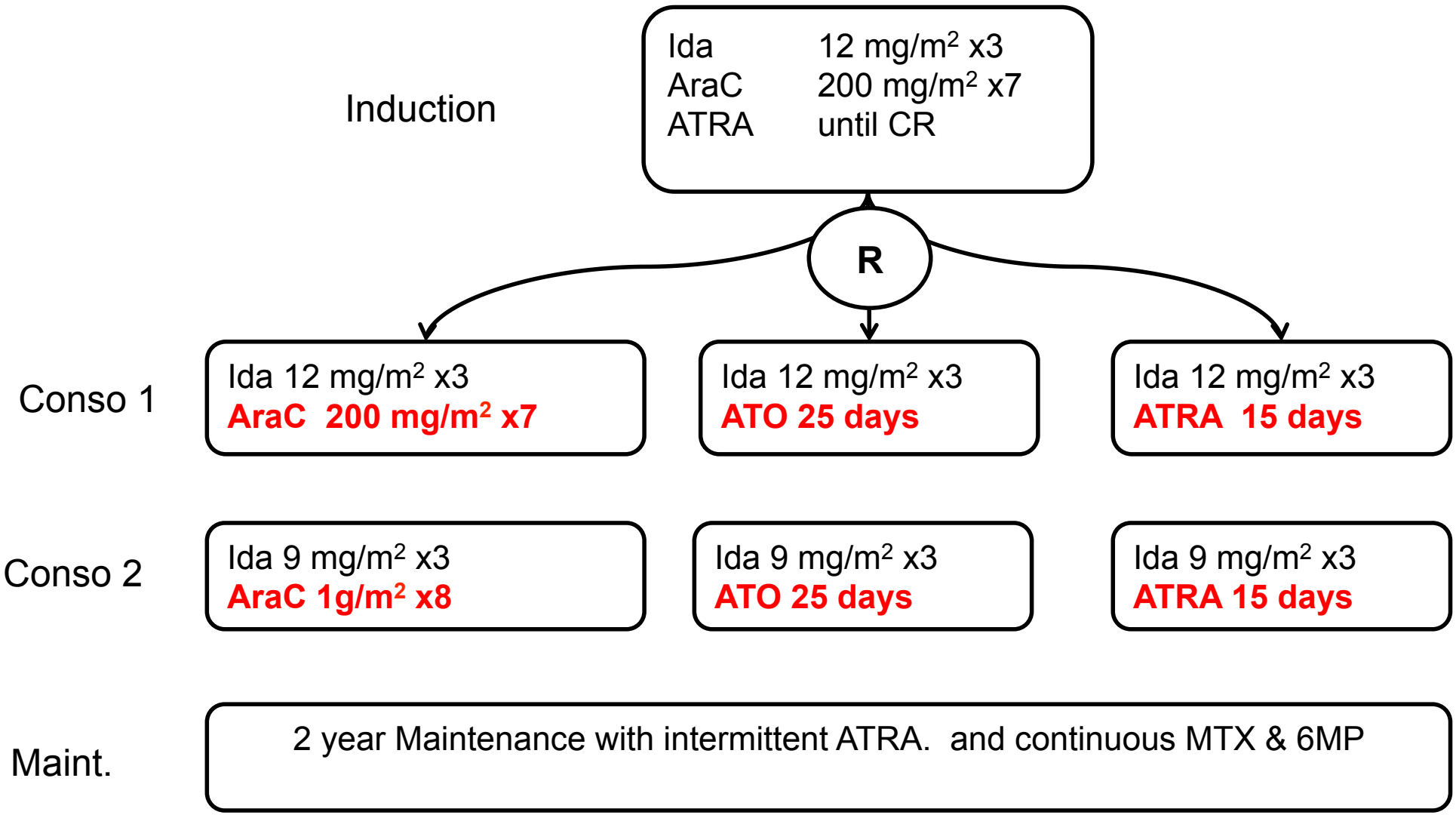
- APL 2006 trial aimed at testing the role of ATO in APL
- during consolidation treatment
- in standard
- and higher risk APL

Inclusion criteria

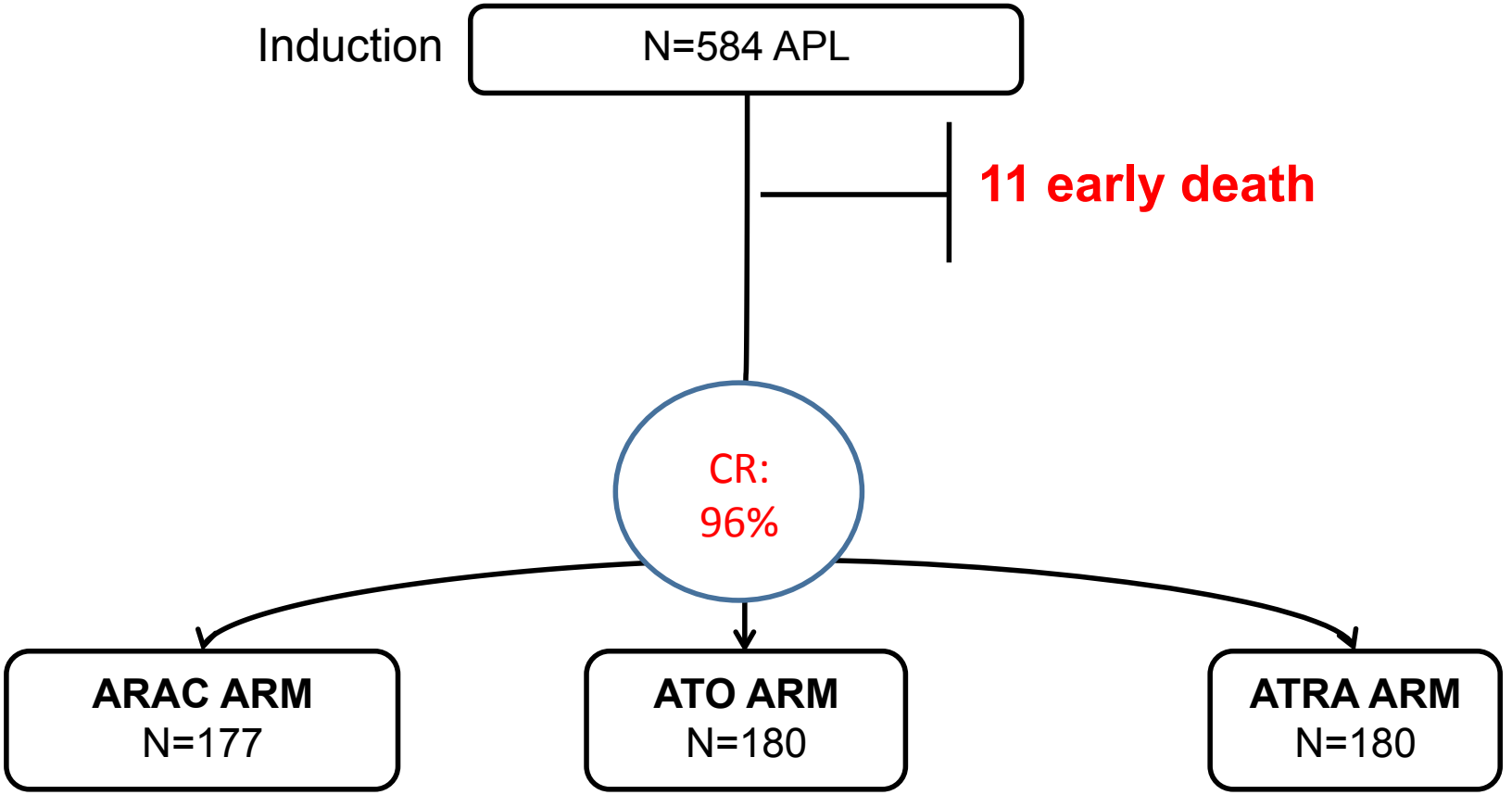
- Newly diagnosed APL patients
  - Subsequently confirmed by
    - Conventional cytogenetic
    - And/or presence of PML-RARA transcript
- <70 years
- No contra indication to ICT or ATO

Standard Risk APL

Treatment schedule (n=584)



Induction


Induction
N=584 APL
11 early death
CR:
96%
ARAC ARM
N=177
ATO ARM
N=180
ATRA ARM
N=180

Patient characteristics

Median [Q1-Q3]	AraC Arm N=178	ATO Arm N=180	ATRA Arm N=180
Age (y)	45.4 [32.45 ;55.95]	49.4 [38.85 ;57.8]	50.5 [38.4 ;60.8]
WBC (G/L)	1.3 [0.8 ;2.3]	1.4 [0.95 ;2.615]	1.51 [0.8 ;3.45]
Platelets(G/L)	47 [25 -74]	50 [25-80]	42 [20-69]
Fibrinogen (g/l)	44.5 [25 ;71]	46 [20.75 ;77]	42 [20 ;68]
%M3v	3%	8%	5%
Previous cancer	12%	12%	9%

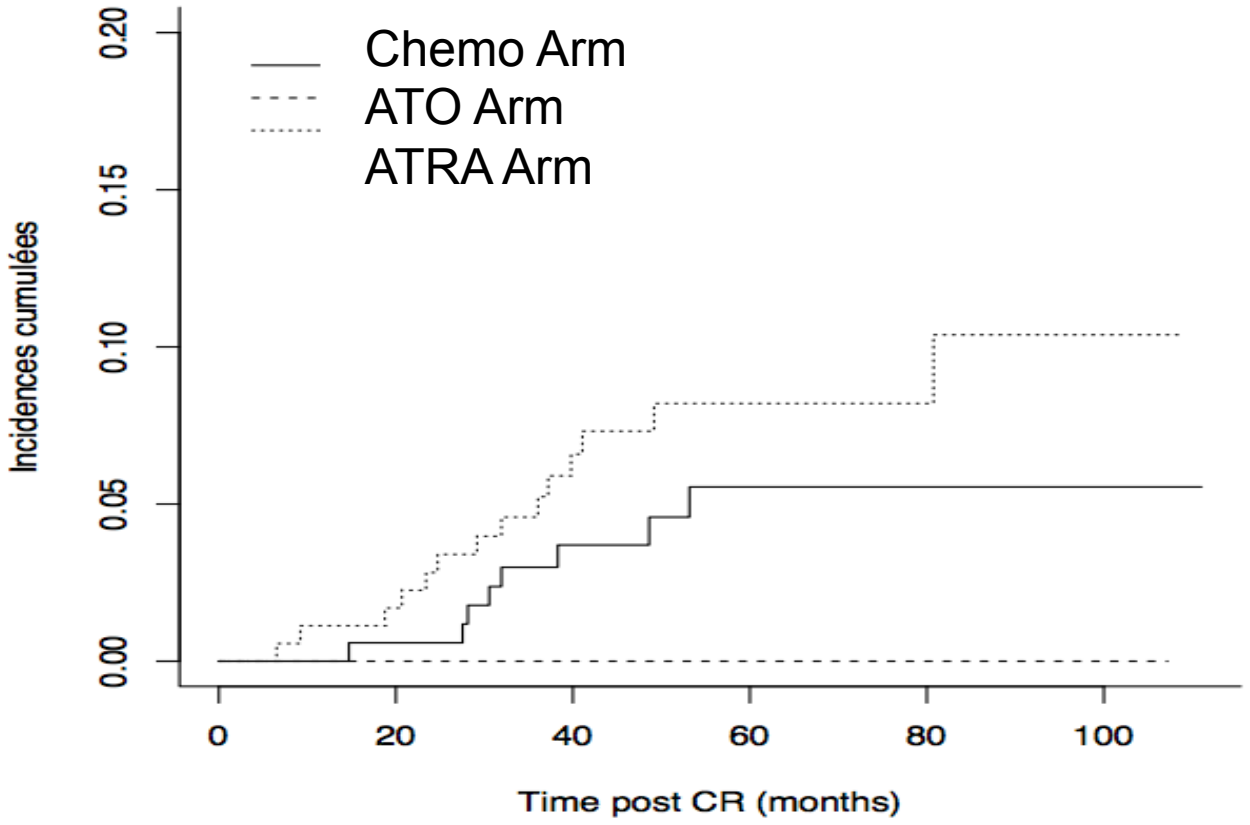
Outcome

With a median FU of 58 months

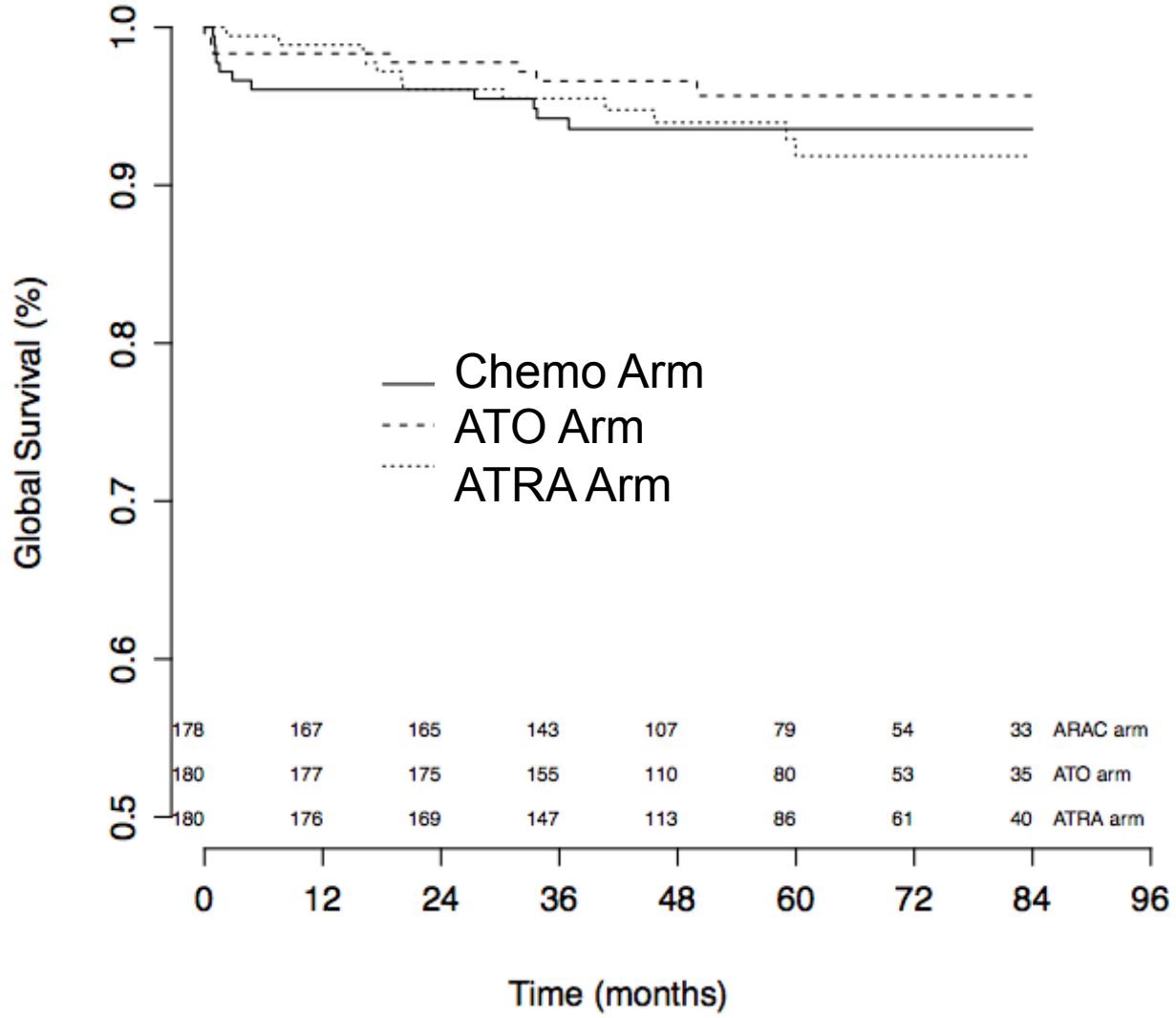
	AraC Arm N=178	ATO Arm N=180	ATRA Arm N=180	P value
Nb of relapse	8	0	14	
Nb of deaths	12	7	14	
5 year EFS	88.7%	95.7%	85.4%	**0.006**
5 year OS	94	96	92	0.349

Cumulative incidence of relapse

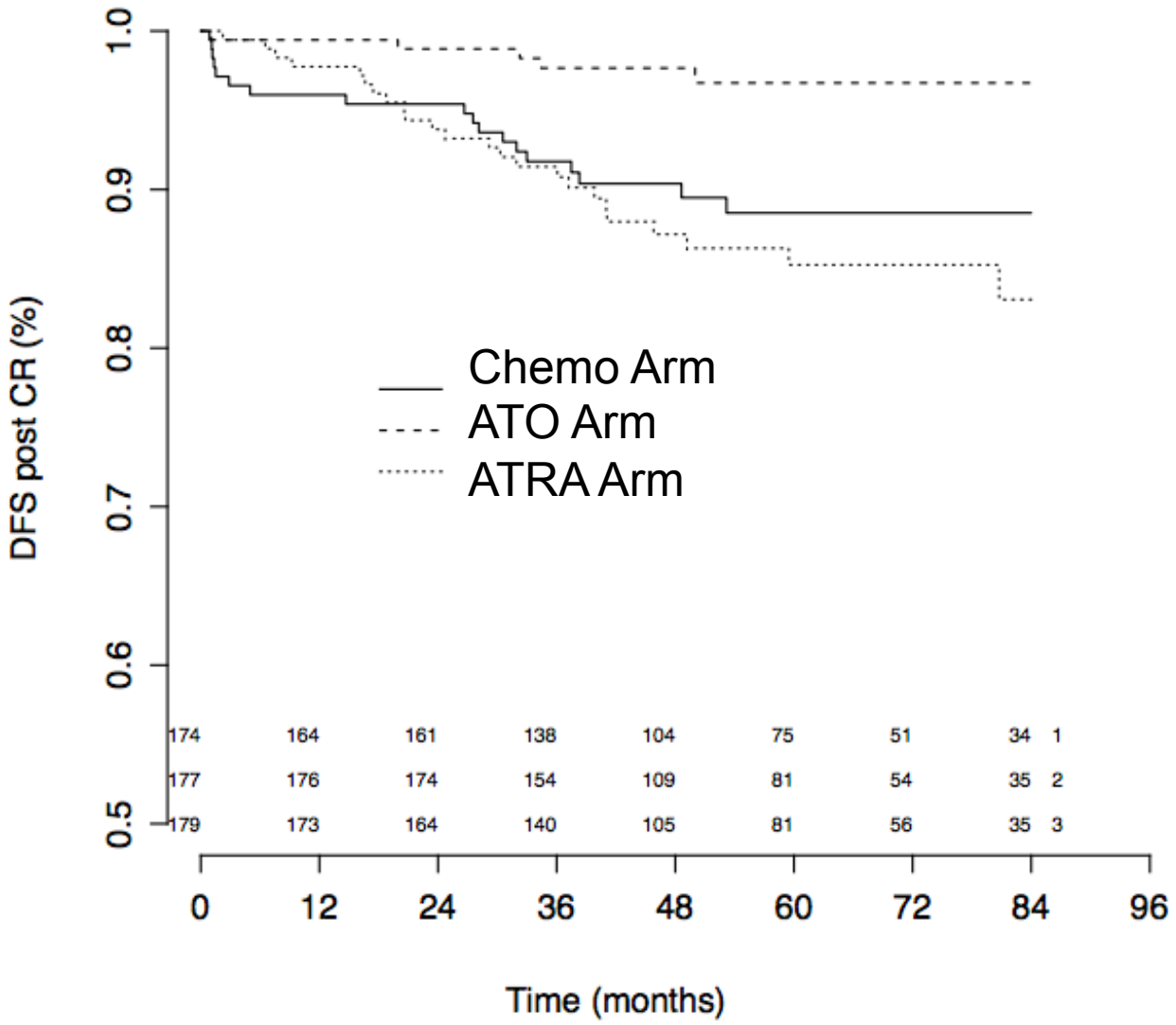
5y CIR was 5.54% %, 0% and 8.2% in the AraC, ATO and ATRA arms, respectively.
p=0.001



Overall Survival



Event free survival



Hematological toxicity

Median [Q1-Q3]	ARAC Arm	ATO Arm	ATRA Arm
days w/ Antibiotics			
1st Consolidation	17	9.9	6.8*
2nd Consolidation	14	7	6*
RBC transfusion			
1st Consolidation	5.8	3.9	2.96*
2nd Consolidation	4.7	1.5	1.6*
Hospitalization (days)			
1st Consolidation	31	32	19.5*
2nd Consolidation	28	29	16.5*

* : $p < 0.001$

Conclusion

- Very high CR rates are obtained in standard risk APL using classical ATRA and anthracycline based CT combinations. with very few relapses.

- Our results strongly suggest that relapse rates observed with regimens without ATO, can be significantly further reduced by addition of ATO.

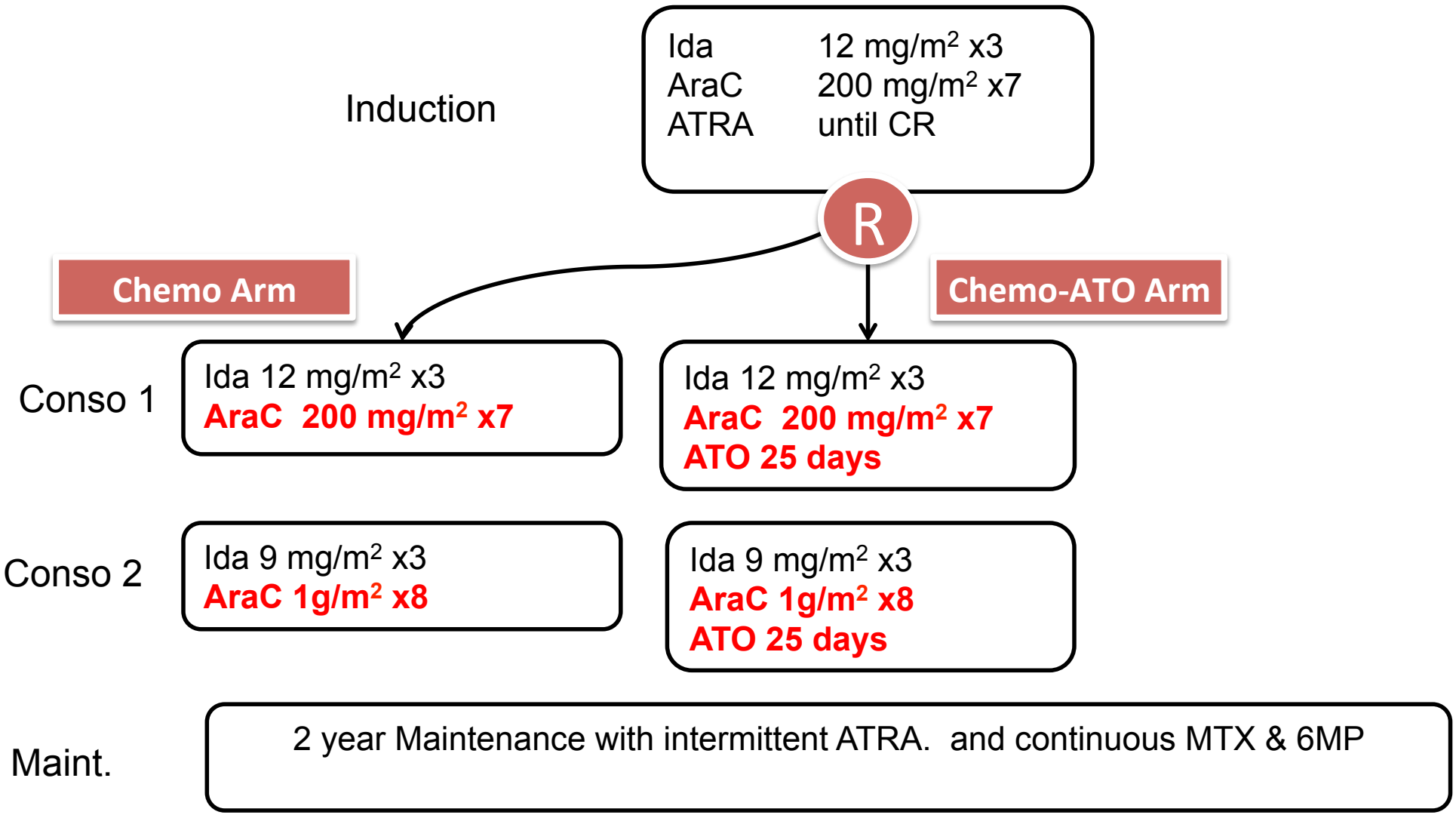
Higher Risk APL

Treatment schedule

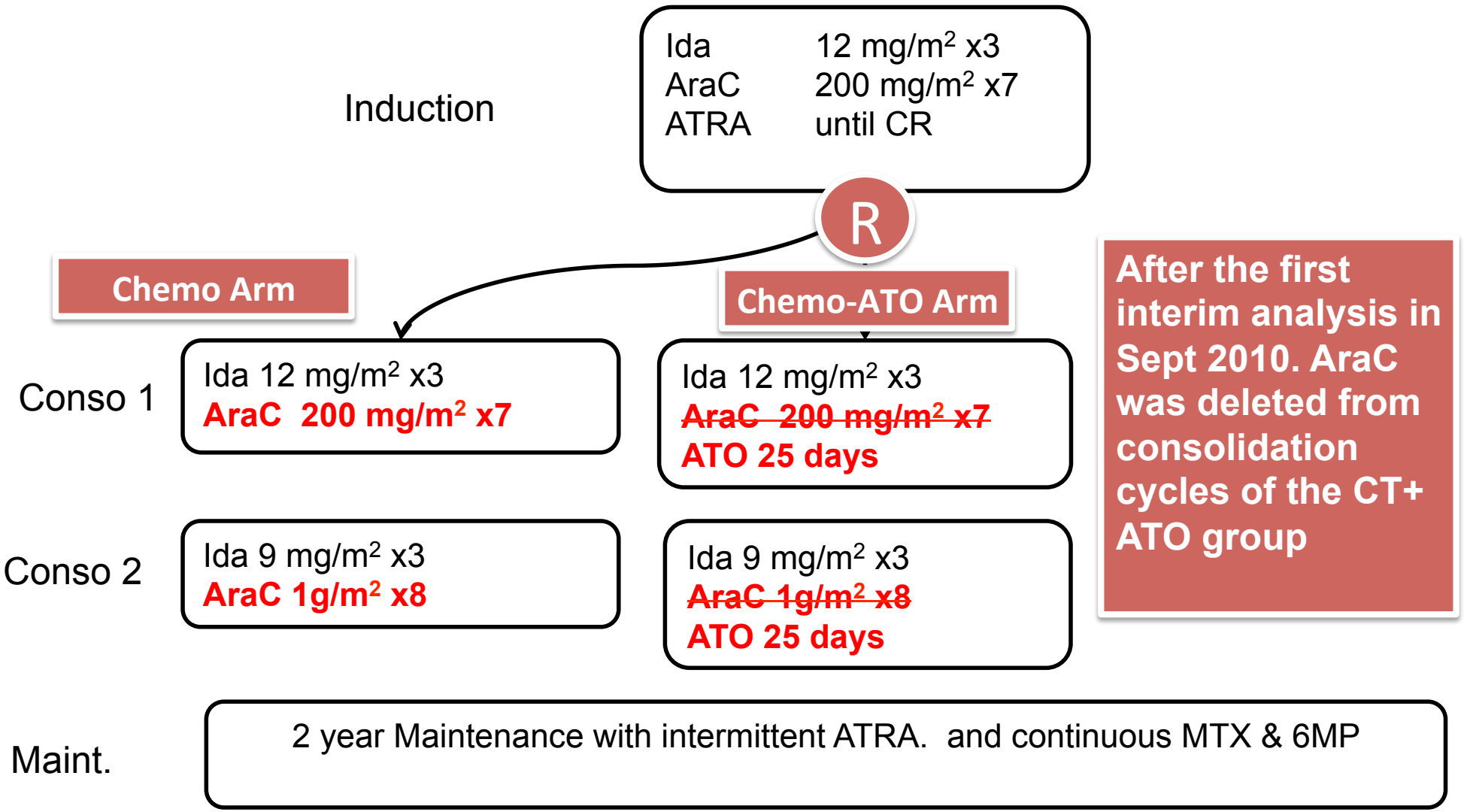
Induction

Ida	12 mg/m^2 x3
AraC	200 mg/m^2 x7
ATRA	until CR

Treatment schedule



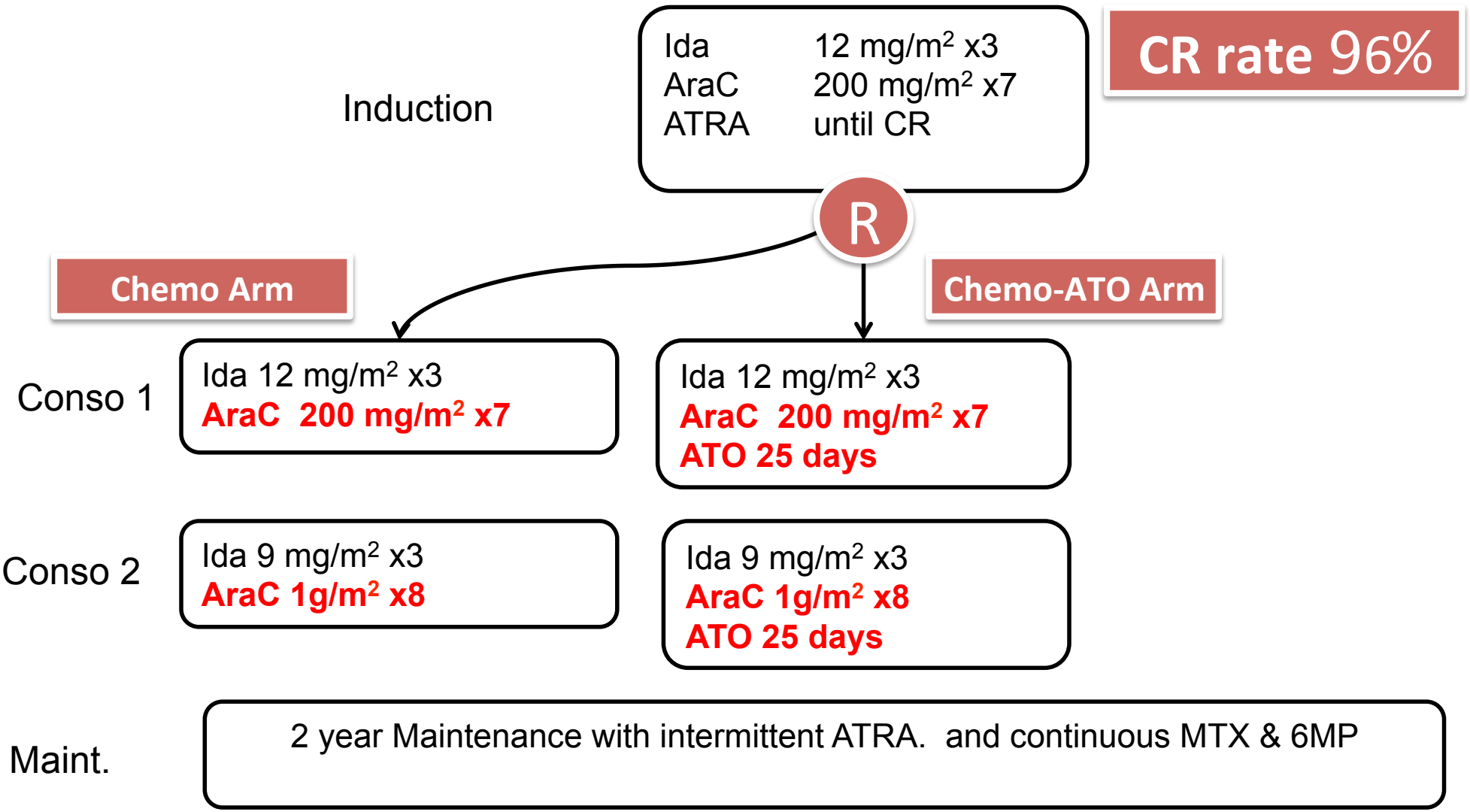
Treatment schedule



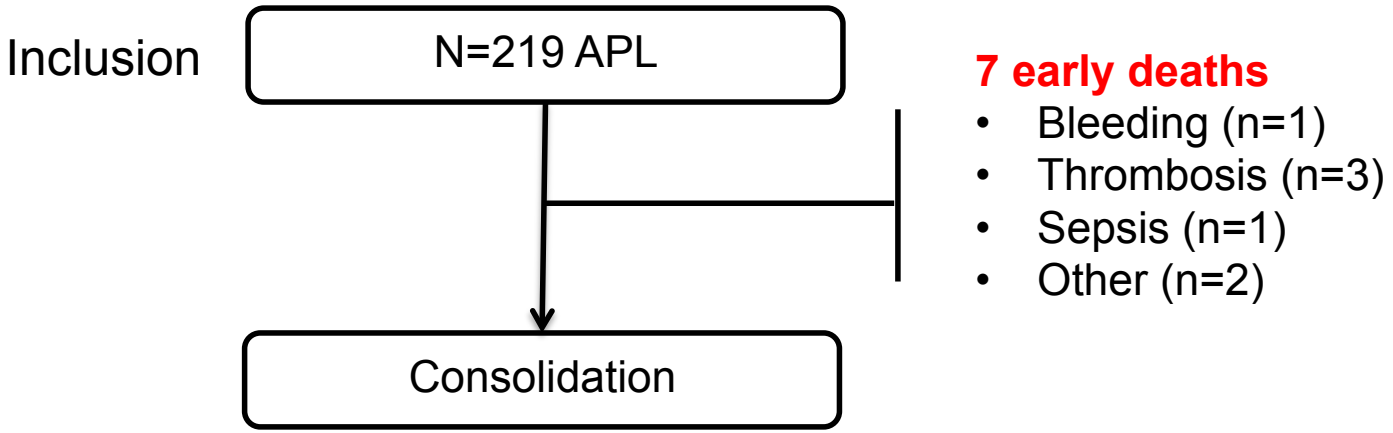
Patient characteristics (219 pts)

Median [Q1-Q3]	Chemo Arm	Chemo ATO Arm
Age (y)	39.2 [29.6 ; 54.2]	45.0 [34.2; 58.9]
WBC (G/L)	23.7 [14.9; 40.5]	19.7 [13.0; 33.9]
Platelets (G/L)	27.0 [13.8; 48.3]	30.0 [18.0 ; 50.5]
Fibrinogen (g/l)	1.3 [1.1; 1.7]	1.4 [0.9; 1.8]
%M3v	35%	28%
% Previous cancer	8%	12%

Response Rate



Deaths during the study



9 pts had died in CR

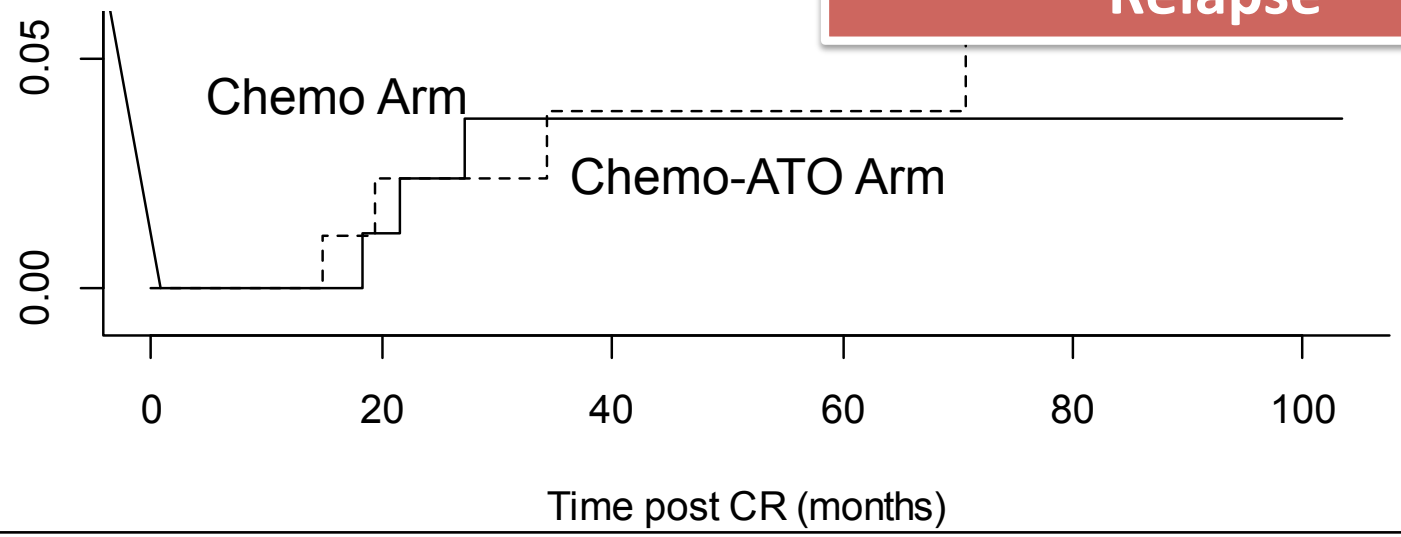
- 7 (7.8%) in the Chemo Arm
- 2 (5.1%) in the Chemo including AraC -ATO Arm
- 0 (0%) in the Chemo-without Arac-ATO Arm

P=0.04

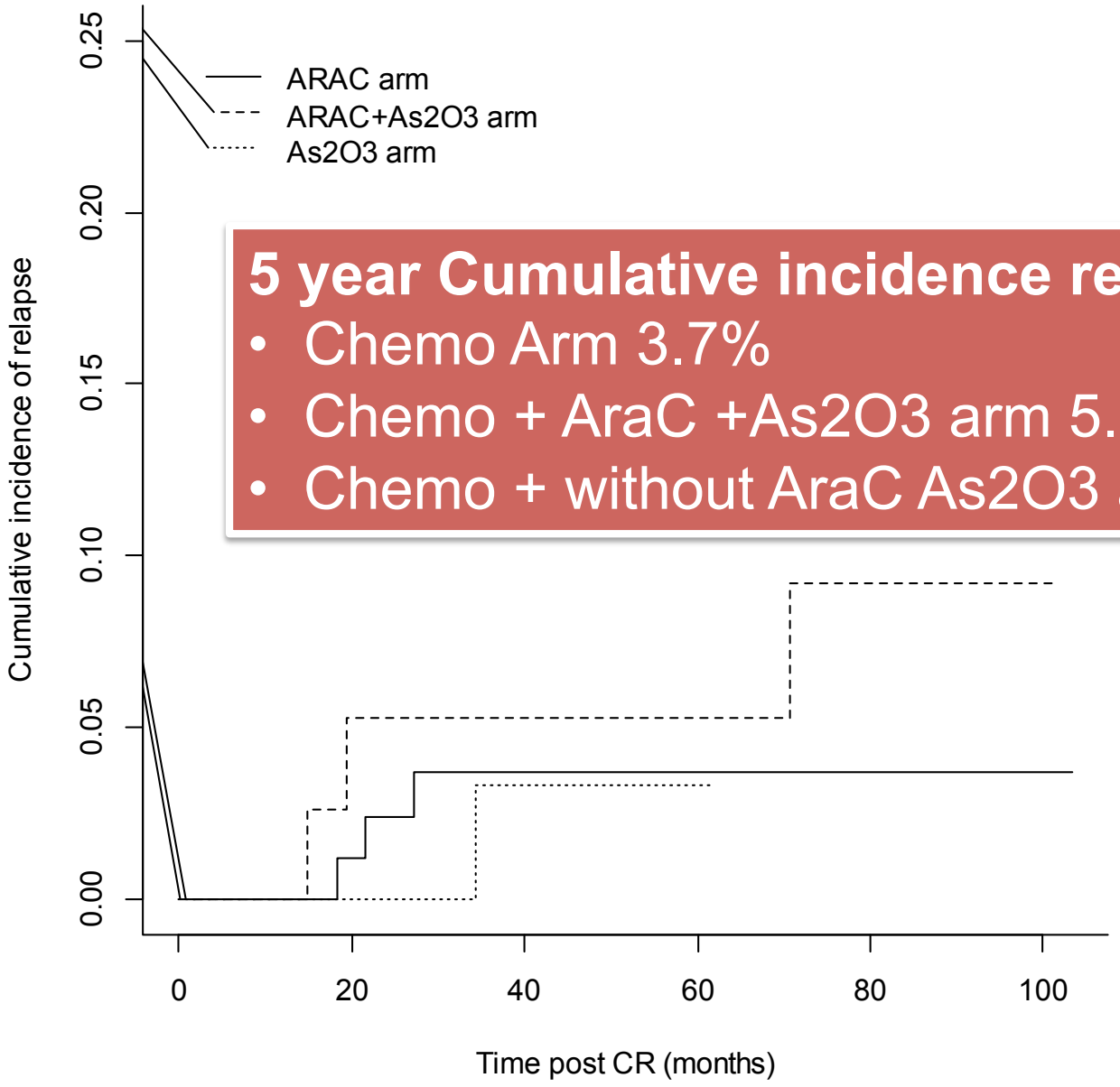
Cumulative incidence of Relapse

	Chemo Arm	Chemo ATO Arm	P value
Nb of relapses post CR	3	4	
2 year Cumulative incidence relapse	3.7 [1.0; 9.6]	3.9 [1.0; 10.0]	0.69

No difference in terms of Relapse



CIR – impact of omission of AraC after amendement

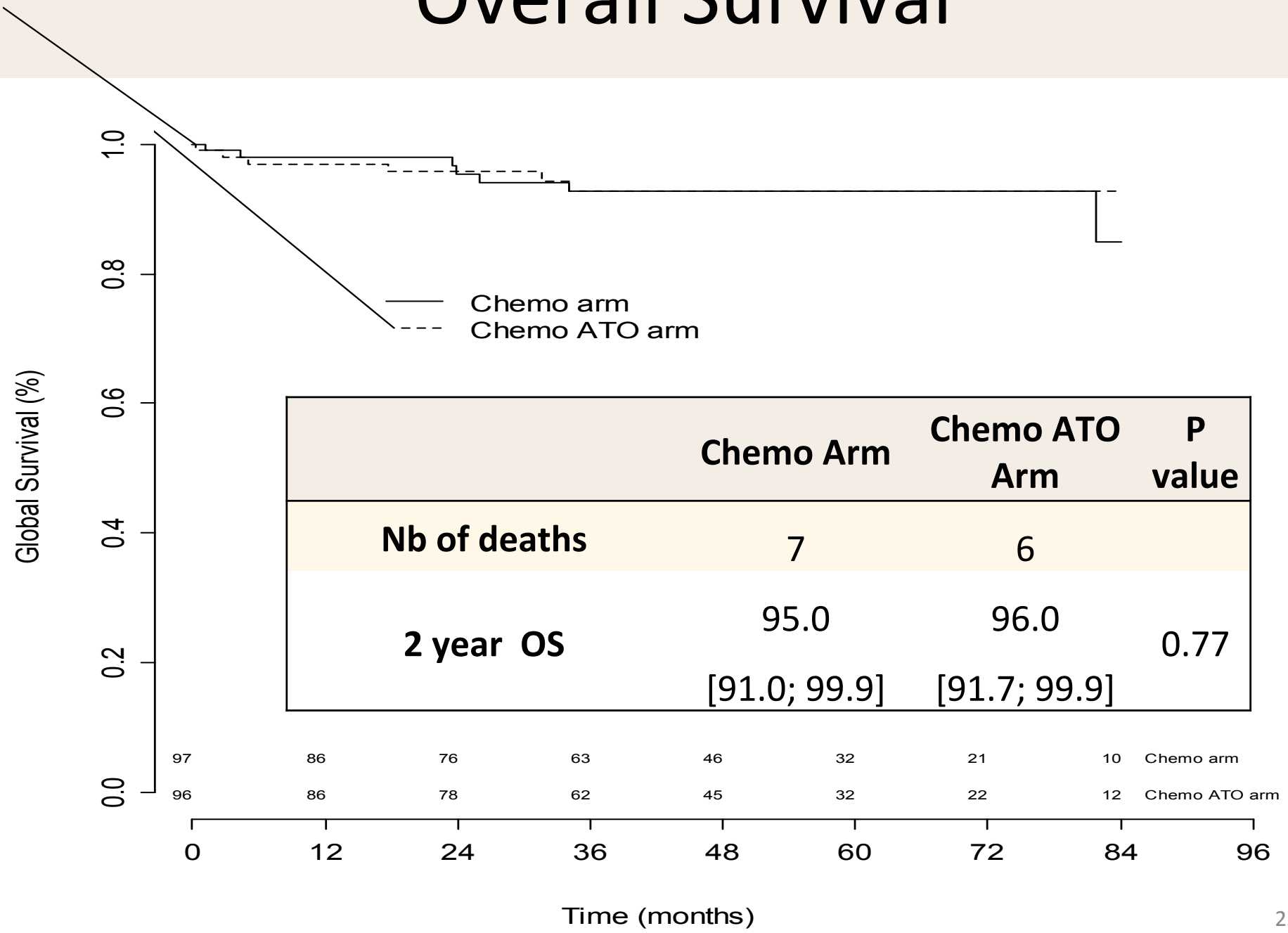


5 year Cumulative incidence relapse

- Chemo Arm 3.7%
- Chemo + AraC +As2O3 arm 5.3 %
- Chemo + without AraC As2O3 arm 3.3 %

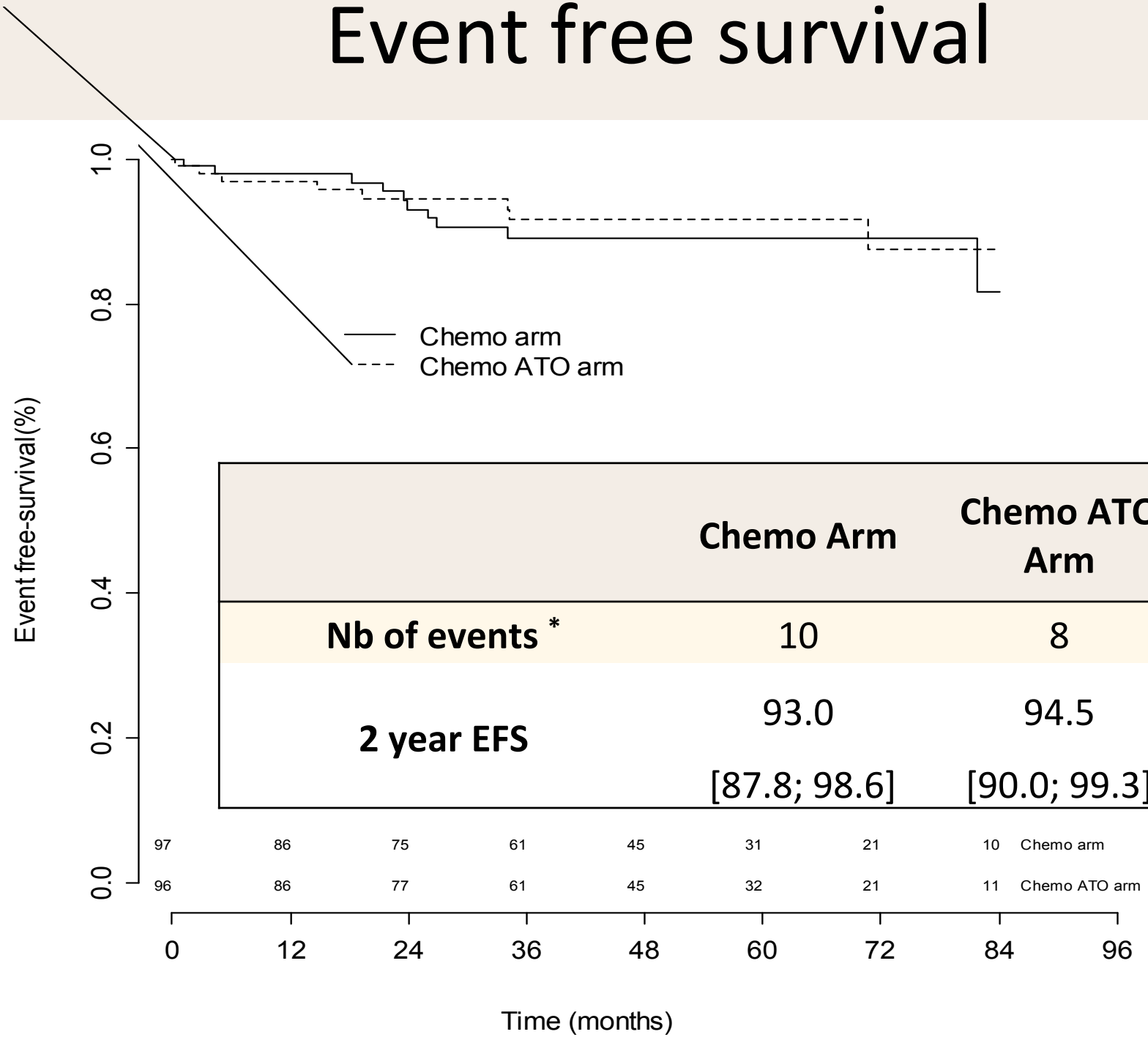
p=0.62

Overall Survival



	Chemo Arm	Chemo ATO Arm	P value
Nb of deaths	7	6	
2 year OS	95.0 [91.0; 99.9]	96.0 [91.7; 99.9]	0.77

Event free survival



	Chemo Arm	Chemo ATO Arm	P value
Nb of events *	10	8	
2 year EFS	93.0 [87.8; 98.6]	94.5 [90.0; 99.3]	0.63

Hematological toxicity

Median	Chemo Arm	ATO-Chemo Arm Before sept 2010	ATO chemo Arm after sept 2010
days w/ Antibiotics			
1st Consolidation	15.0	18.0	**10.0 ***
2nd Consolidation	10.0	14.5	**10.0 ***
RBC transfusion			
1st Consolidation	4.0	4.0	**2 ***
2nd Consolidation	4.0	4.0	**1.0***
Time to ANC > 1G/L	22	25	**19***
Time to Platelet > 50 G/L	24	26	**20***

* : p <0.001

Conclusions

- Addition of ATO to ATRA-CxT regimen did not reduce relapses, and added some myelosuppression
- However, if ATO was added and AraC omitted from consolidation cycles, relapses were not increased, while myelosuppression and deaths in CR were reduced.
- ATO therefore appears useful in high risk APL.

Acknowlegments

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