CHEMO-FREE POST-INDUCTION THERAPY FOR ALL APL PATIENTS

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Disclosures

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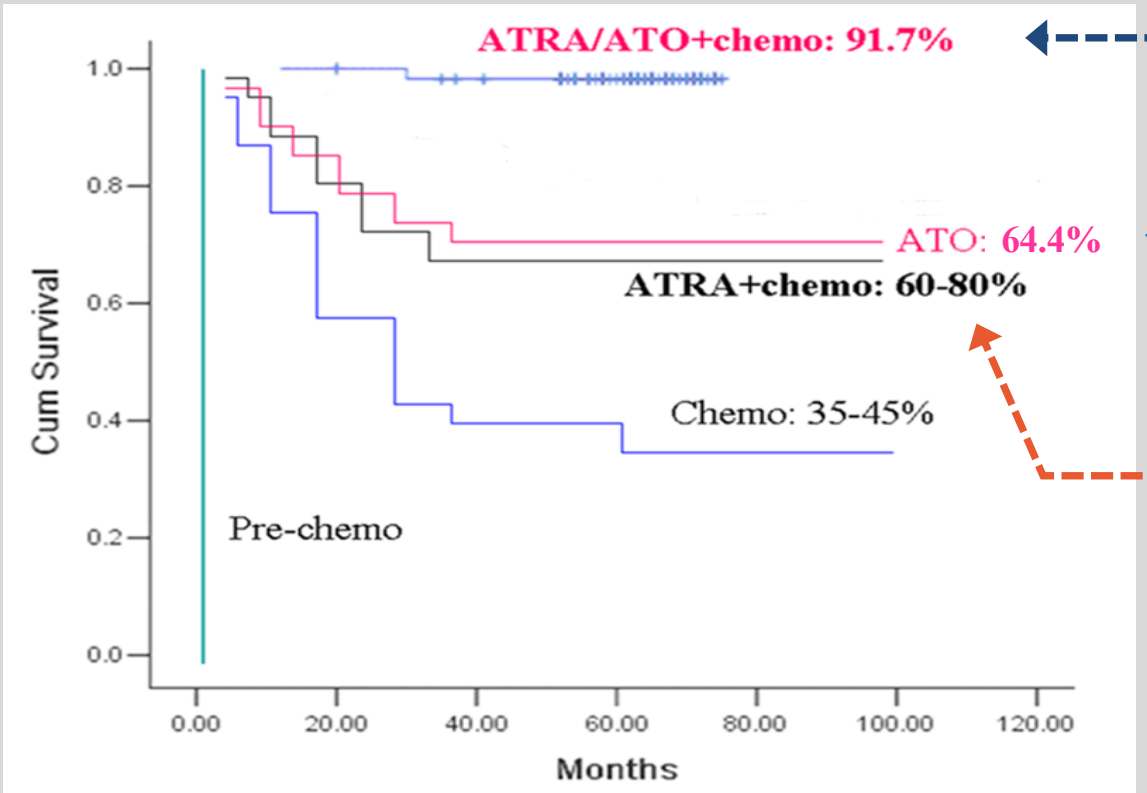
Therapies for APL

- ATRA and ATO combination therapy has made acute promyelocytic leukemia (APL) highly curable.



Synergistic target therapy: a cure of APL

PNAS,2009

ATO: Improve the prognosis of newly and relapsed patients

Blood 1997; JCO, 2011

ATRA+Chemo: improve CR rate and survival

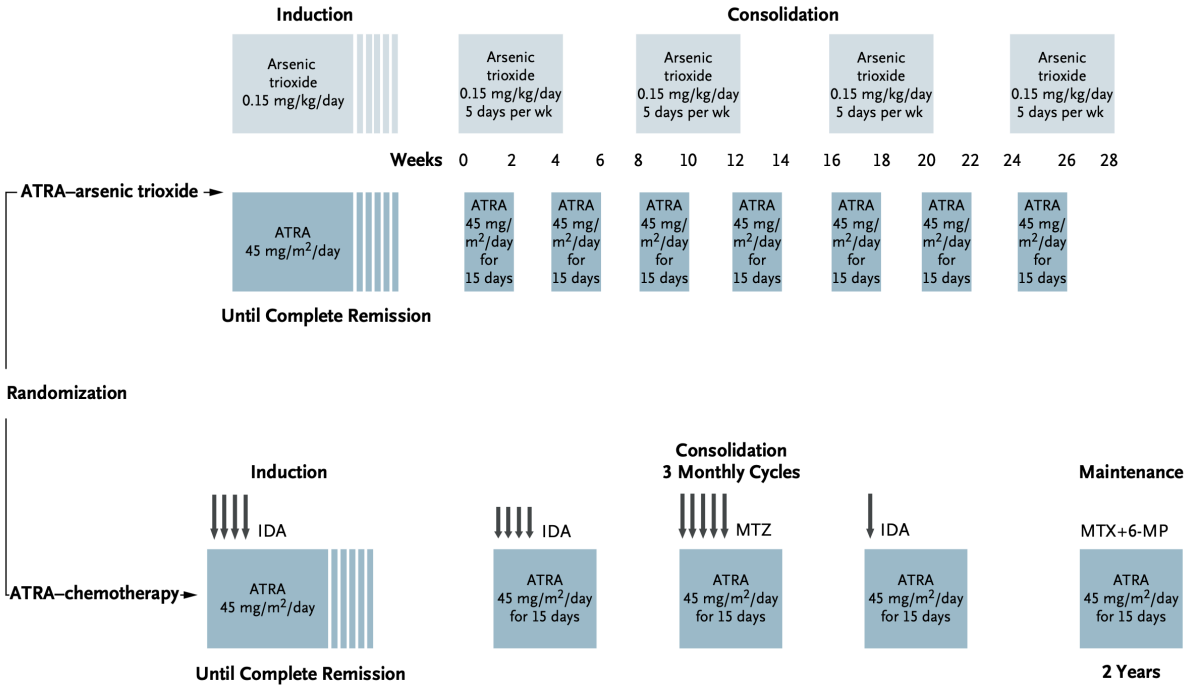
Blood,1988; Blood, 2008

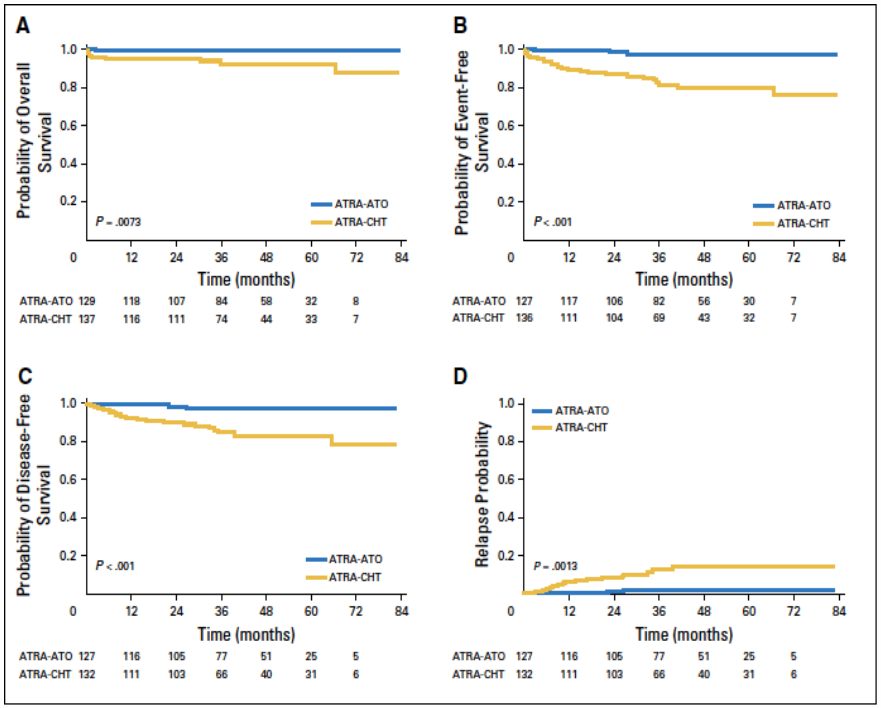
Blood 2011;117:6425-37
PNAS 2009;106: 3342-3347

Chemo-free therapy for APL

- The chemo-free concept has become a reality for almost all low-risk and partly high-risk patients.

APL0406 confirmed better long-term remission in ATRA-ATO group for low-to-intermediate risk APL

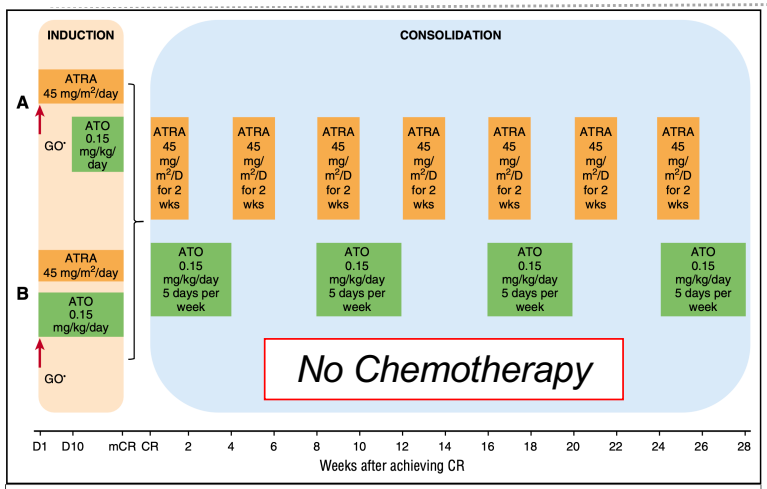


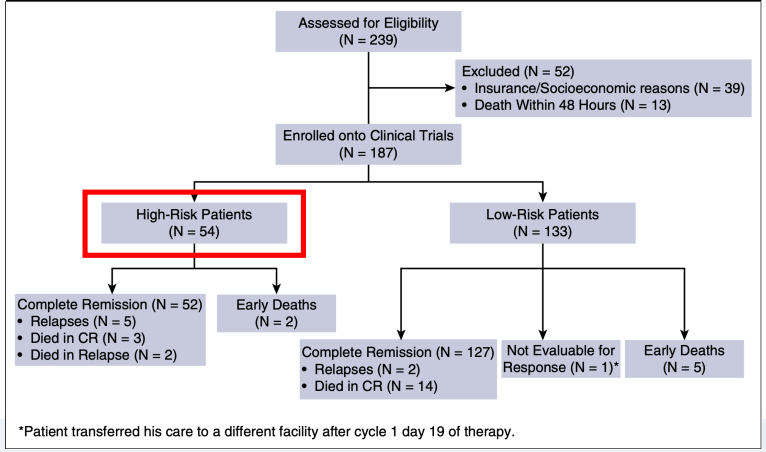


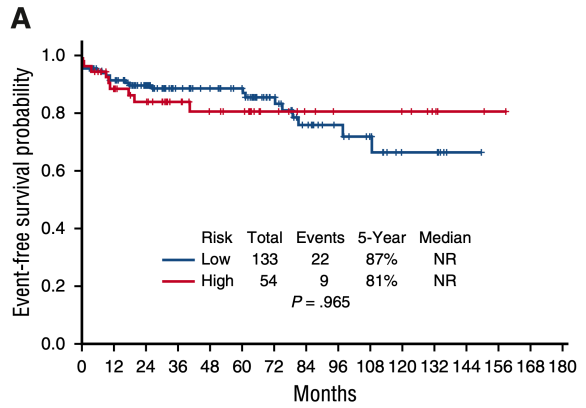
Lo-Coco F, et al. N Engl J Med. 2013;369(2):111-121.
Platzbecker U, et al. J Clin Oncol. 2017;35(6):605-612.

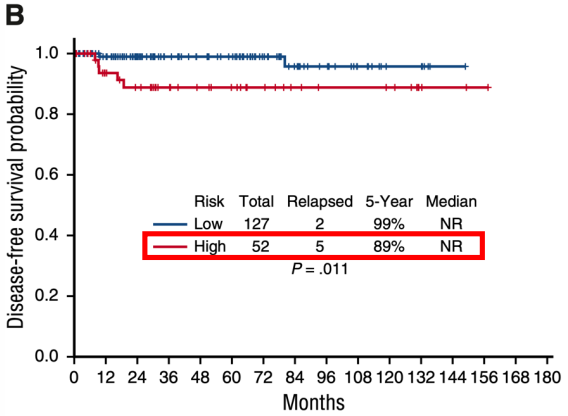
Chemo-free therapy for APL

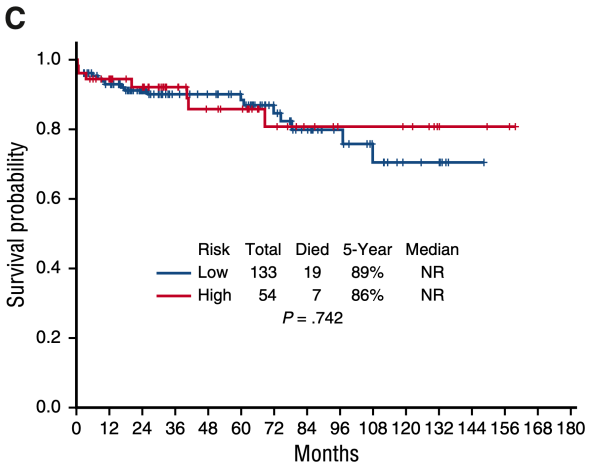
M.D. Anderson Cancer Center: ATRA+ATO±GO for APL at all risks











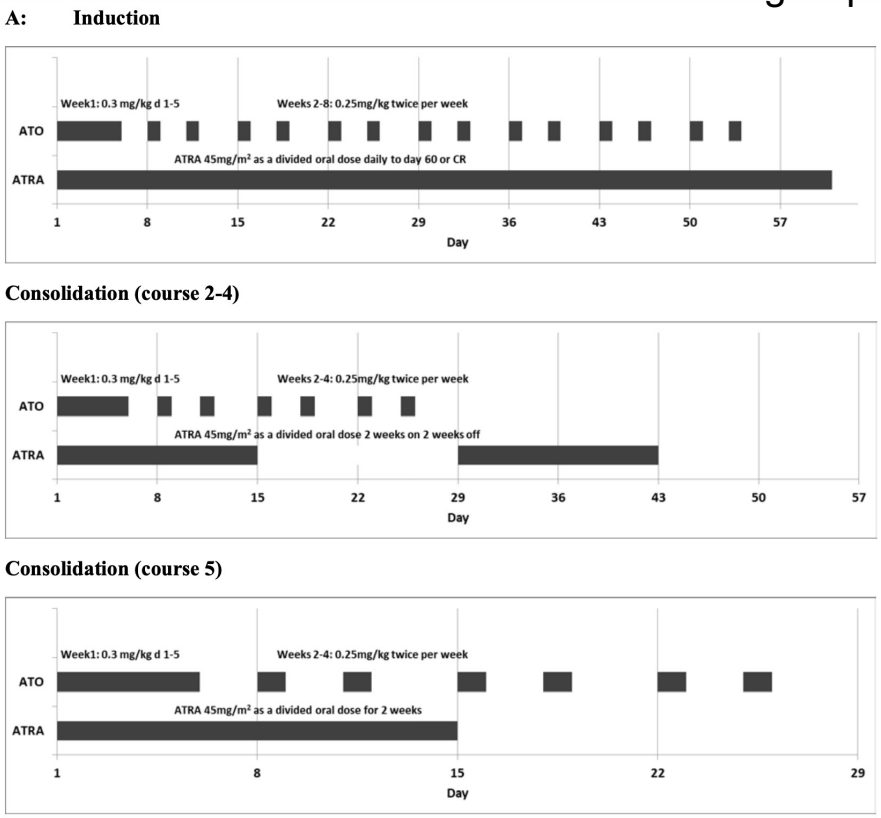
- ATRA+ATO±GO was effective and safe, providing long-term and durable leukemia-free survival for both standard-risk and high-risk patients,

Abaza Y, et al. Blood. 2017;129(10):1275-1283.

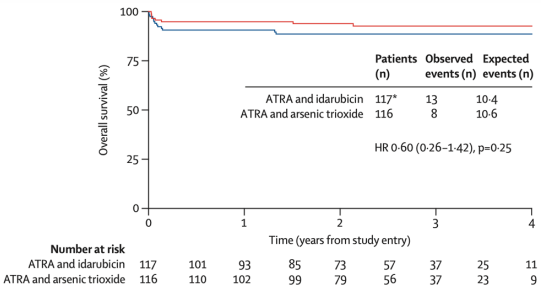
Chemo-free therapy for APL

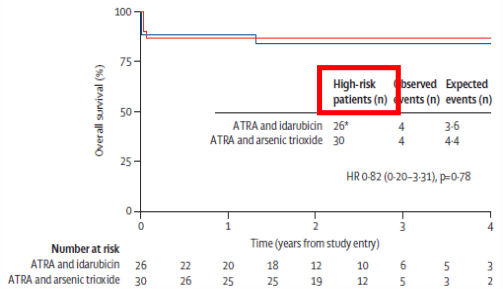
UK AML17: phase III randomized trial containing high-risk, ATRA/ATO *vs.* AIDA

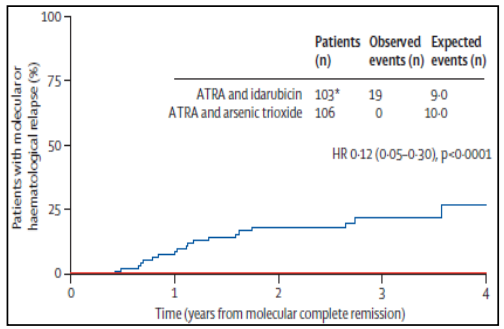
- Treatment Schedules - ATRA/ATO group

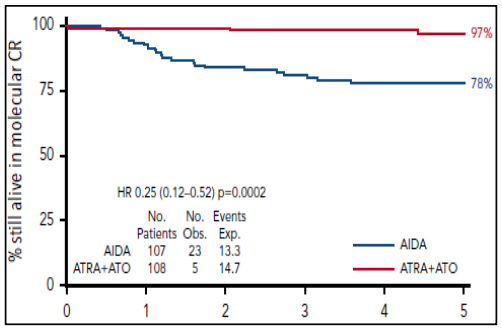


- Lower incidence of relapse in ATRA/ATO group
- High-risk 5y RFS: 100% (ATRA/ATO) vs. 83% (AIDA), *P*=0.03







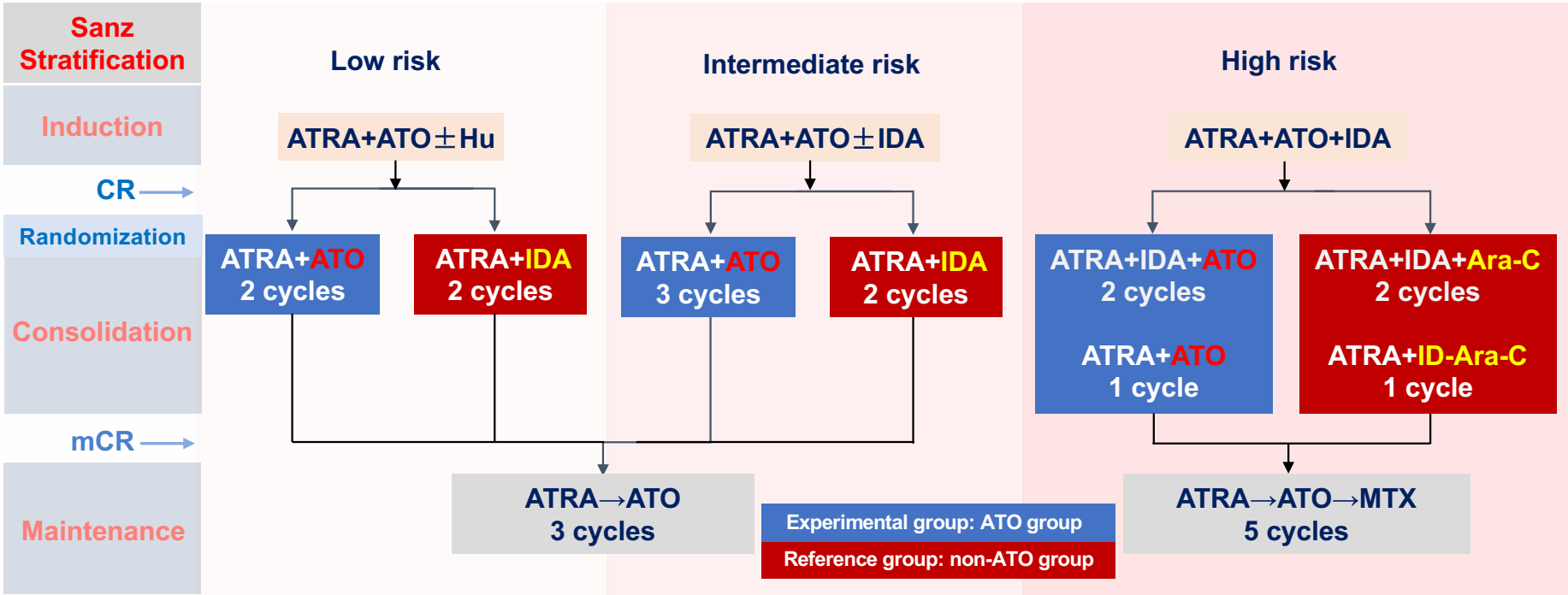


Burnett AK, et al. Lancet Oncol. 2015;16(13):1295-1305.
Russell N, et al. Blood. 2018; 132(13): 1452–1454.

Chemo-free therapy for APL

APL2012 trial - a prospective, multiple-center, randomized, non-inferiority clinical trial from 2012 to 2017 at 22 hospitals in China

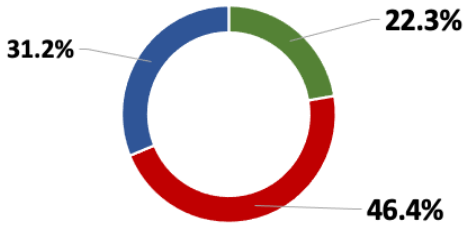
- Aimed to see if CHT could be replaced by ATO in low-, intermediate-; reduced in high-risk patients in consolidation therapy.



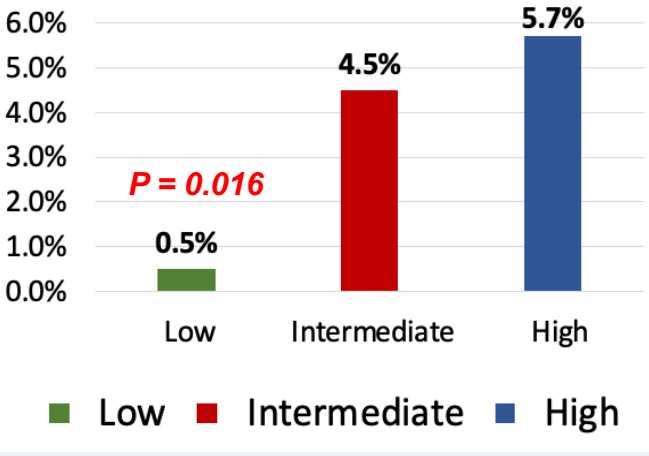
Chen L, et al. Proc Natl Acad Sci U S A. 2021;118(6).

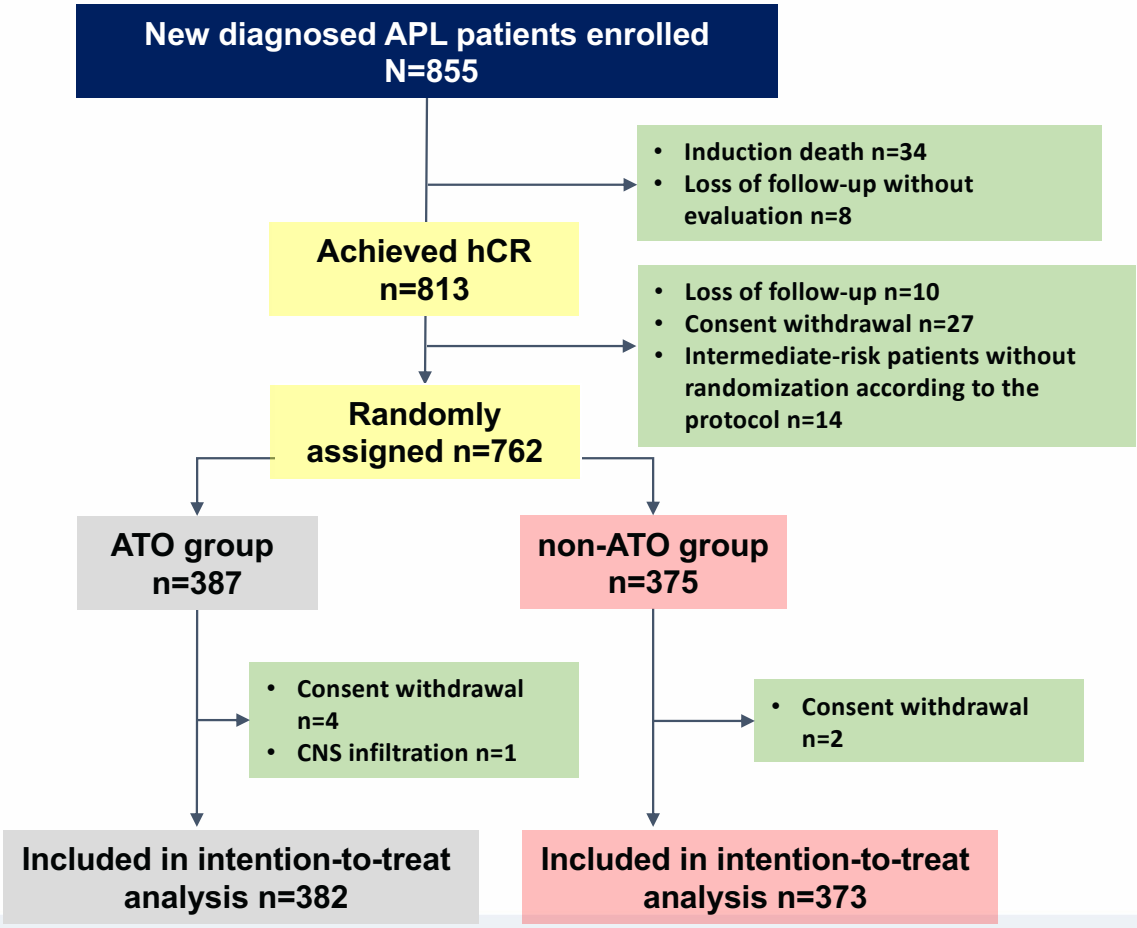
APL2012 trial
Enrollment and patient characteristics

- **Sanz risk, %**



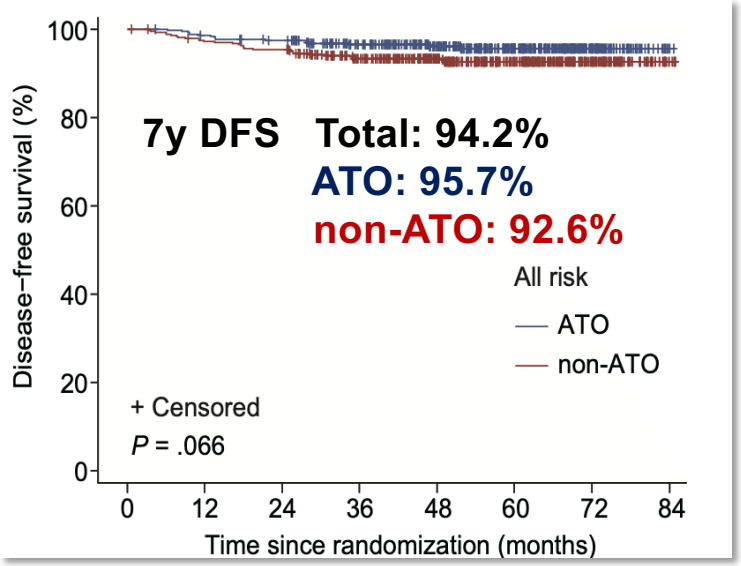
- **Early death rate, %**

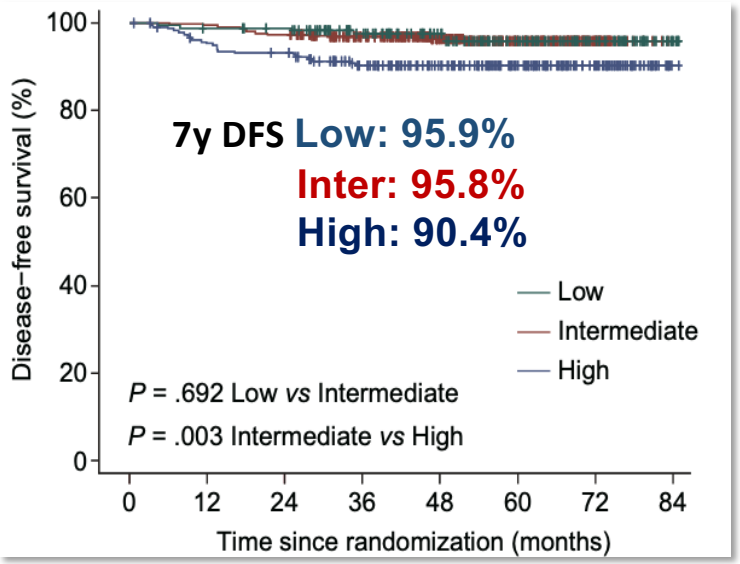




APL2012 trial - survival

- Primary endpoint: DFS
- Median follow-up: 54.9 months after CR



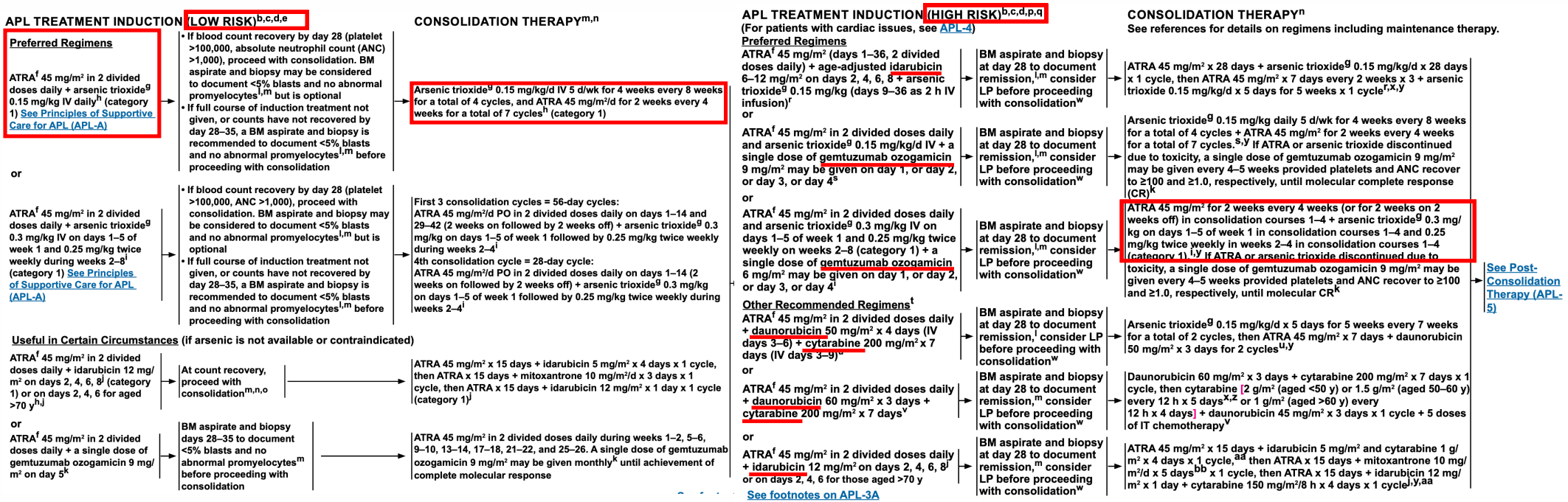


7y DFS	number	Low %	Inter %	High %
ATO group	382	100	95.2	93.2
non-ATO group	373	91.6	96.5	87.4
P value		0.012	0.781	0.14

Chen L, et al. Proc Natl Acad Sci U S A. 2021;118(6).

Chemo-free therapy for APL

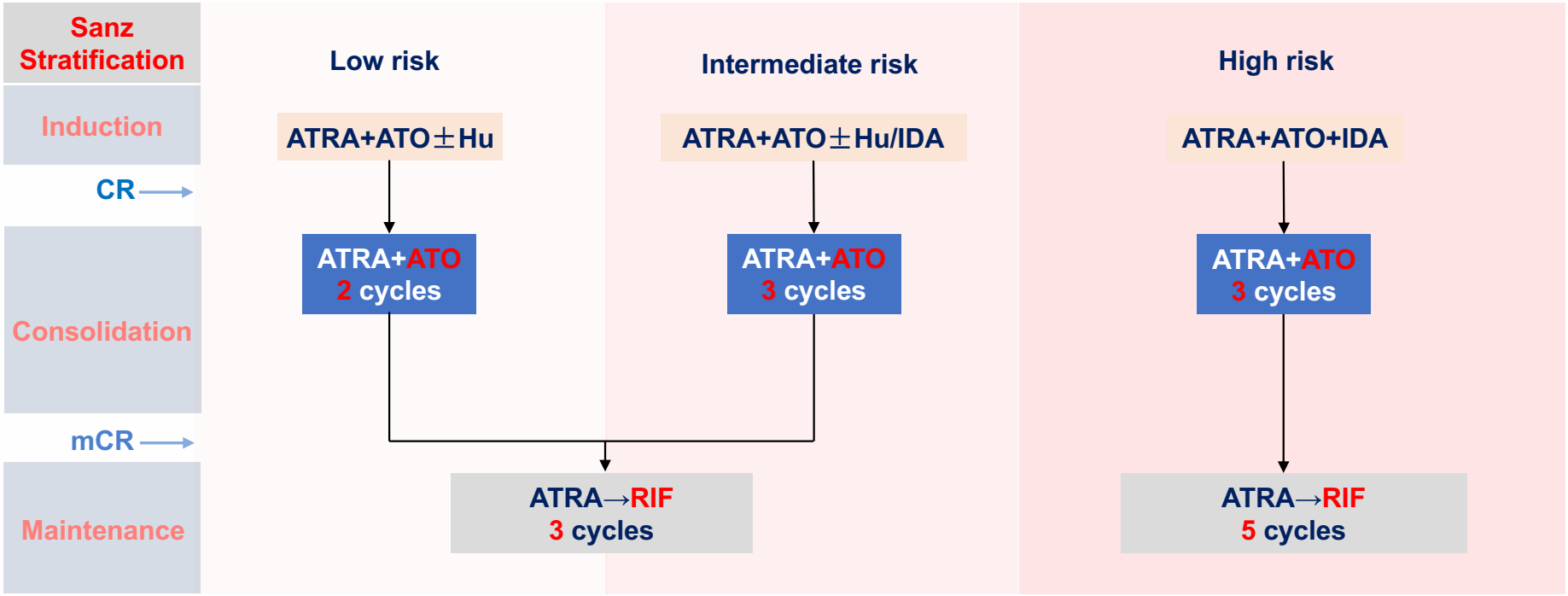
NCCN guideline



- Chemotherapy-free is hardly achievable during induction phase for high-risk APL, but feasible during post-induction phase.

APL2018 trial - protocol

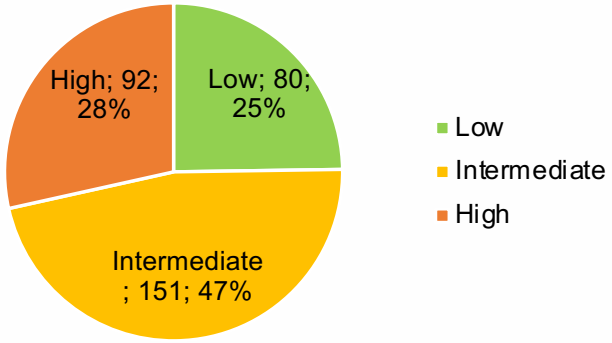
- APL2018 single-arm trial: adjusted post-induction therapy based on the ATO-group of APL2012.
  1. Totally removing CHT from consolidation therapy for high-risk patients;
  2. Replacing ATO with oral arsenic Realgar-Indigo naturalis formula (RIF) in maintenance therapy;
  3. Methotrexate was removed from maintenance therapy.



APL2018 trial - outcome

- N=323

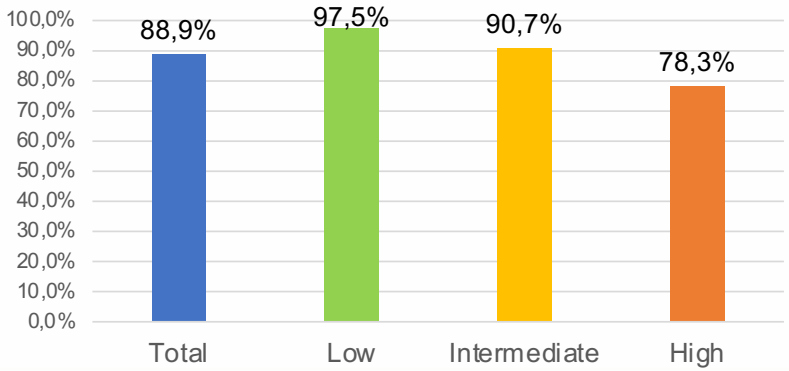
Sanz risk, n, %



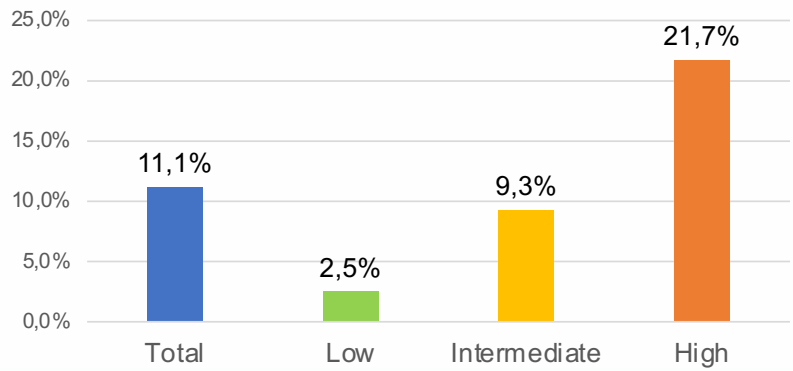
Causes of early death

Total	36	100%
Cerebral bleeding	24	66.7%
Differentiation syndrome	6	16.7%
Infection	3	8.3%
DIC	2	5.6%
Cardiac attack	1	2.8%

CR rate, %



Early death rate, %



APL2018 trial - survival

- Median follow-up: 29.2 months

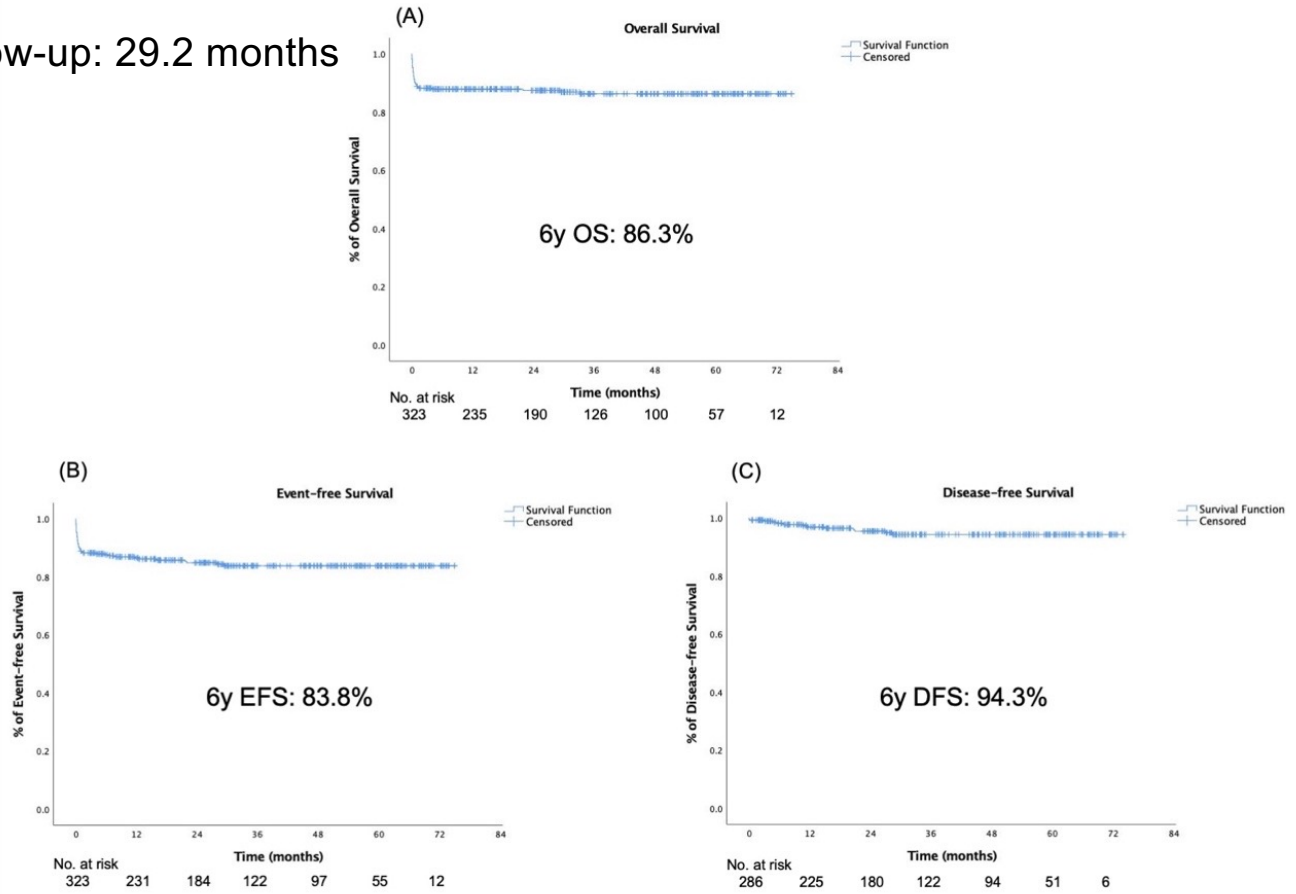


Figure 1 Survival of all patients. (A) OS (B) EFS (C) DFS

APL2018 trial - survival

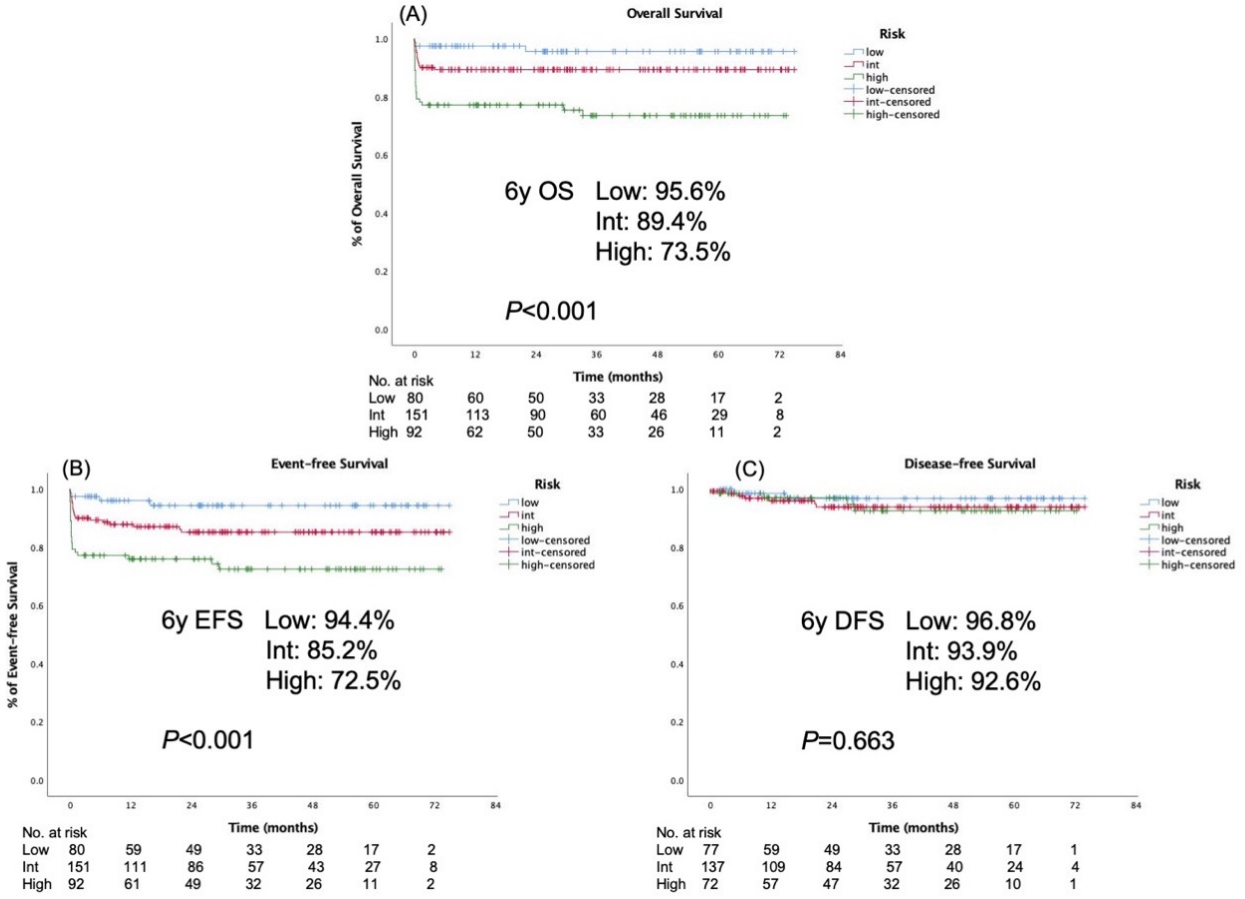
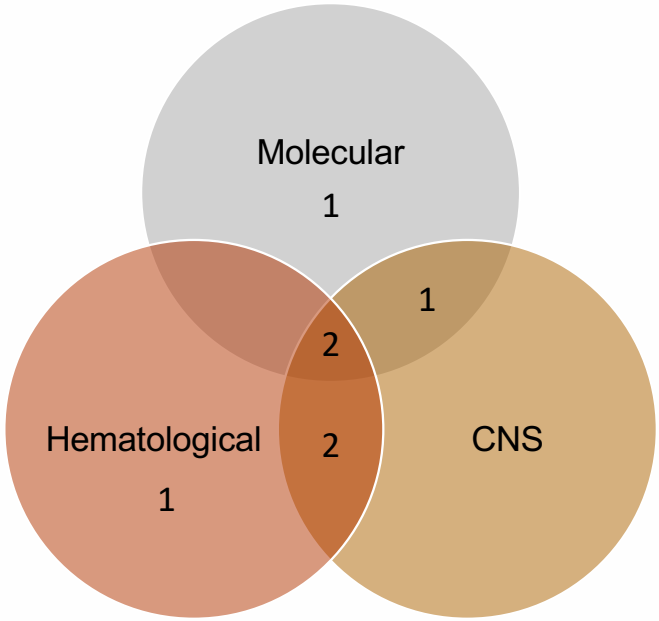


Figure 2 Survival of patients at low-, intermediate- and high-risk. (A) OS (B) EFS (C) DFS

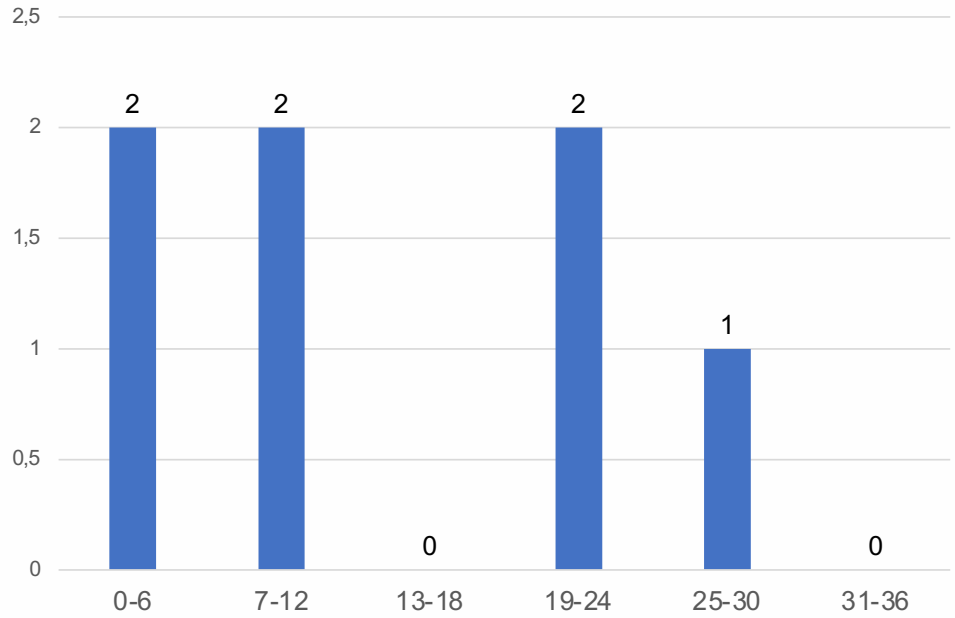
APL2018 trial - relapse

- N=7 (Intermediate-risk 5, High-risk 2)

Type of Relapse



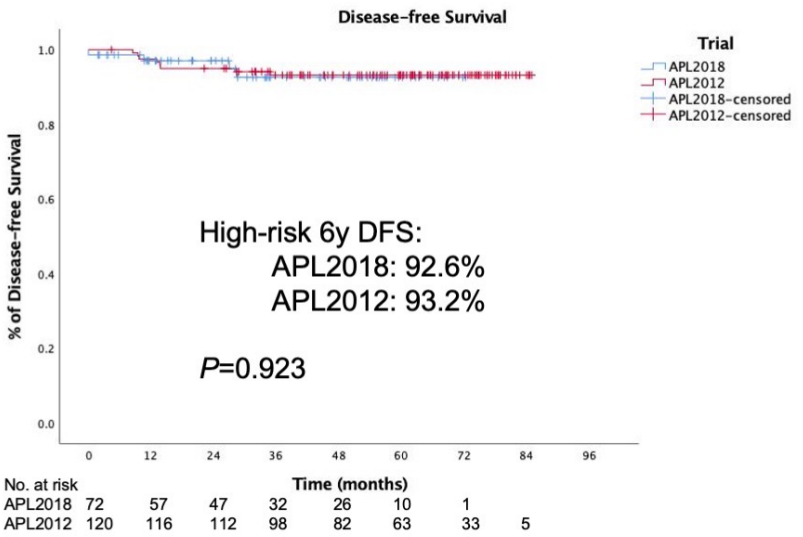
Time from CR to relapse (months)



Median time: 10.6 (range, 3.0 – 27.0) months from CR

APL2018 trial - high-risk DFS

Trial/Center	Post-induction treatment	Cumulative dosage of ATO (mg/kg; days)	No.	DFS rate
APL2018	ATRA+ATO* (Consolidation) ATRA+RIF# (Maintenance)	ATO 13.4; 84; max 840mg RIF 8400; 140	72	92.6% (6Y)
MDACC[1]	ATRA+ATO	12; 80	52	89% (5Y)
Zhu HH[2]	ATRA+RIF#	RIF 6720; 112	54	93.8% (2Y)
AML17[3]	ATRA+ATO	12; 44	30	100% (5Y)
AAML1331 (Pediatric)[4]	ATRA+ATO	12; 80	56	96.4% (2Y)
APML4[5]	ATRA+ATO (Consolidation) ATRA+MTX+6MP (Maintenance)	8; 53	19	95% (5Y)
APL2012[6]	ATRA+ATO+IDA (Consolidation) ATRA+ATO+MTX (Maintenance)	29; 182 Max 1820mg	120	93.2% (7Y)



*ATO 0.16mg/kg/d, maximum 10mg/d
#RIF 60mg/kg/d equals to ATO 0.15mg/kg/d

1. Abaza Y, et al. Blood. 2017;129(10):1275-1283.
2. Ma YF, et al. J Hematol Oncol. 2022;15(1):148.
3. Russell N, et al. Blood. 2018; 132(13): 1452–1454.
4. Kutny MA, et al. JAMA Oncol. 2022;8(1):79–87.
5. Iland HJ, et al. Lancet Haematol. 2015;2(9):e357-66.
6. Chen L, et al. Proc Natl Acad Sci U S A. 2021;118(6).

Conclusion

1. APL2018 trial confirmed the possibility of chemo-free post-induction therapy for APL patients at all risks.

2. How to determine the end-time of post-induction therapy should be further focused.

THANK YOU!

Acknowledgements:

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