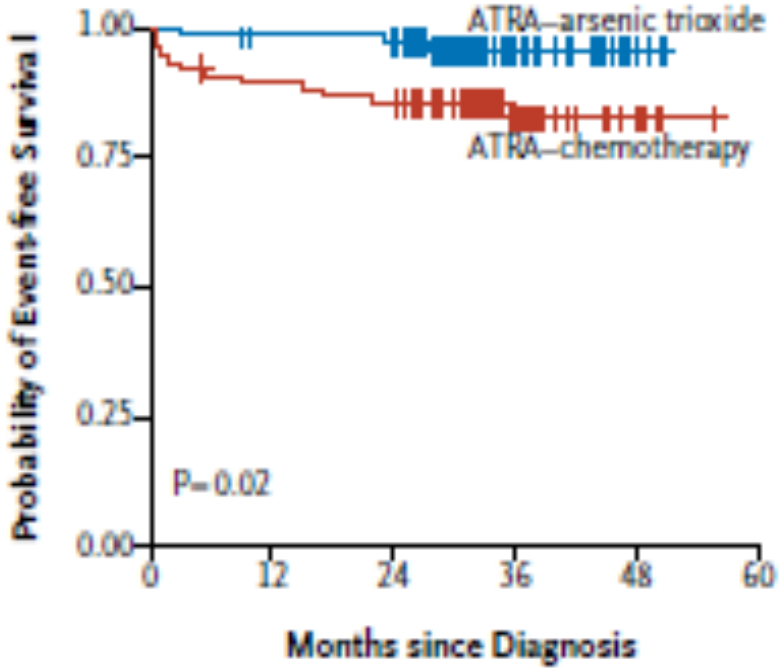
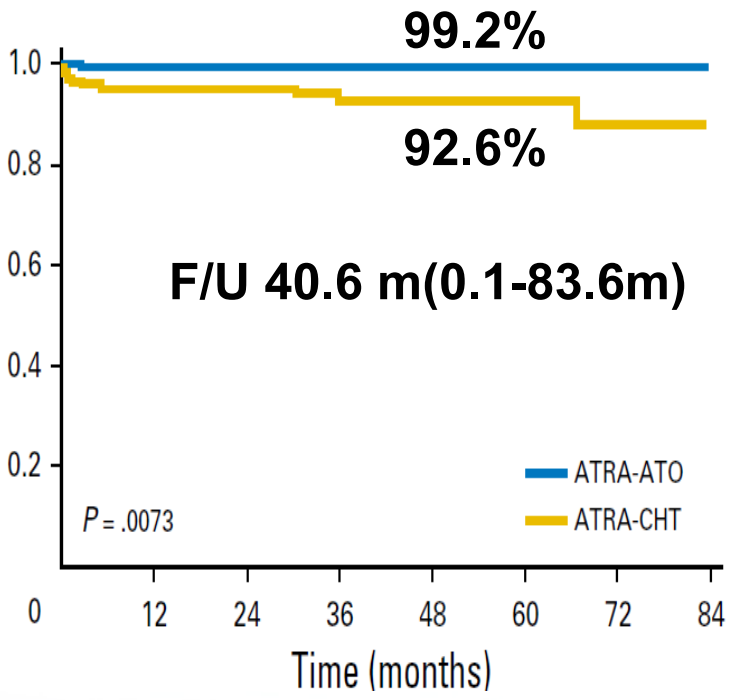
Oral Arsenic and Retinoic Acid for Children with Non-high-risk APL

Hong-Hu Zhu

Peking University Institute of Hematology (PUIH)
Peking University People's Hospital, Beijing, P.R.C.

Adult patients with APL have a higher cure rate in a chemo-free model





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

Platzbecker U, et al. JCO 35:605

The standard treatment model is still ATRA+Chemo

Diagnosis and management of acute myeloid leukemia in children and adolescents: recommendations from an international expert panel

*Ursula Creutzig,[1] *Marry M. van den Heuvel-Eibrink,[2] Brenda Gibson,[3] Michael N. Dworzak,[4] Souichi Adachi,[5] Eveline de Bont,[6] Jochen Harbott,[7] Henrik Hasle,[8] Donna Johnston,[9] Akitoshi Kinoshita,[10] Thomas Lehrnbecher,[11] Guy Leverger,[12] Ester Mejstrikova,[13] Soheil Meshinchi,[14] Andrea Pession,[15] Susana C. Raimondi,[16] Lillian Sung,[17] Jan Stary,[18] Christian M. Zwaan,[2] †Gertjan J. L. Kaspers,[19] and †Dirk Reinhardt,[1] on behalf of the AML Committee of the International BFM Study Group

Recommendations

In children, ATRA at 25 mg/m^2 per day should already be started if APL is suspected, as it reduces the risk of fatal hemorrhage. It should be used throughout treatment. The intensive, risk-adapted chemotherapy regimen in APL should be based on anthracyclines, cytarabine, and ATRA to avoid excessive anthracycline exposure.

ATRA+Chemo in Children with APL

Year	2010	2010
Group	BFM	Japanese Childhood AML Cooperative Study
Induction Therapy	ATRA+IDA+VP /CA+VP+DNR	ATRA+IDA+CA
No. of Pts	81	58
Consolidation Therapy	CA+IDA+HD-CA+VP16	HD-CA+MTZ+ATRA+PIRARUBICIN+ACLARUBICIN
EFS (%)	73 (5 years)	91 (7 years)
OS (%)	89 (5 years)	93 (7 years)

Chinese experiences in pediatric APL:ATO as first-line treatment

Author	Year	N. pts	Age yrs	Induction	CR (%)	Post-induct.	Outcome
Zhang	1999-2012	65	13 (med.)	ATRA±ATO	90.8	CHT	5-y EFS 77.5% 5-y OS 88.9%
Zhou	2001-11	19	4-15 (range)	ATO	89.5	ATO	5-y EFS 72.7% 5-y OS 83.9%%
Wang	2000-11	35	NA	ATO±ATRA	85.7	CHT	5-y EFS 78.3% 5-y OS 82.7%
Zhang	2003-12	37	2-14 (range)	ATRA±ATO	94.6	CHT	5-y EFS 79.2% 5-y OS 91.5%

Chemo-based protocol brings long-term adverse on children

Subclinical Anthracycline Cardiotoxicity in Patients With Acute Promyelocytic Leukemia in Long-Term Remission After the AIDA Protocol

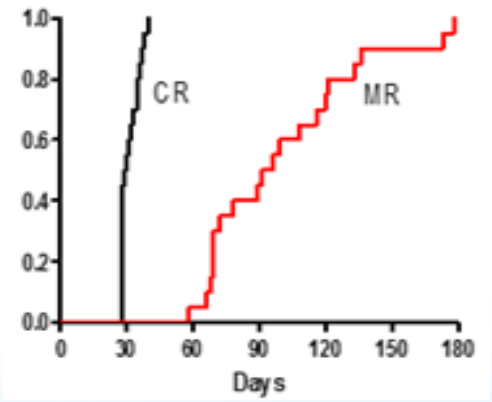
Pierpaolo Pellicori, MD;[1] Angela Calicchia, MD;[1] Francesco Lococo, MD;[2] Giuseppe Cimino, MD;[2] Concetta Torromeo, MD[1]

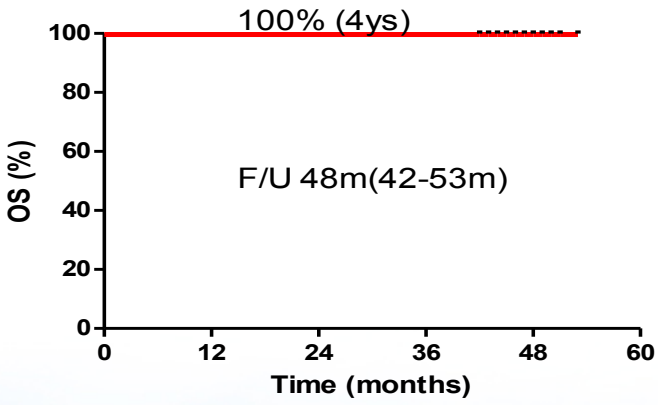
late cardiotoxicity of anthracycline regimens. Late subclinical cardiotoxicity was observed in 52% of the adult survivors of APL treated on the GIMEMA AIDA-0493 and-2000 protocols.[54] To reduce the risk of

A 5ys girl with APL was crying for fearing about chemo and wanted to school with her friends

Home-based treatment become reality in non-high-risk APL (Beijing Protocol)

ATRA Oral arsenic	15 days in hospital	8 months treatment	4,675$ Medical cost





+2 ms since treatment

Zhu HH, et al. NEJM 2014; 371：2239

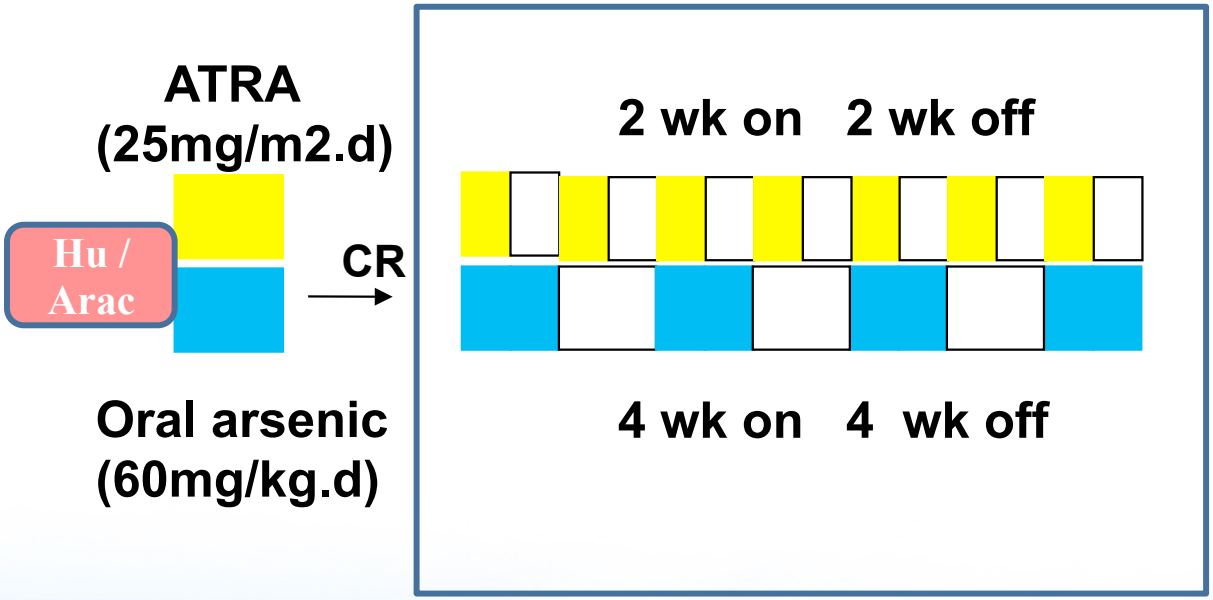
Home-based treatment is an ideal model for Children

Question

- Whether our Beijing Protocol in non-high-risk APL also benefit for children

Purpose and Protocol

- To evaluate the efficacy and safety of oral arsenic and ATRA for children with non-high-risk APL.



oral tetra-arsenic tetra-sulphide formula (Realgar-Indigo naturalis formula, RIF)

Inclusion criteria

- Newly diagnosis of de novo APL
- <18 years old;
- WBC <10×10^9/L before treatment ;
- Adequate hepatic and renal reserve
- Performance Status (PS) score 0-2(WHO);
- provide written informed consent.

Endpoints

- **Primary endpoint:**

  Complete molecular remission (CMR) rate at 6 months

- **Secondary endpoints:**

  CR ; EFS; Safety;

  Hospitalized days

Results

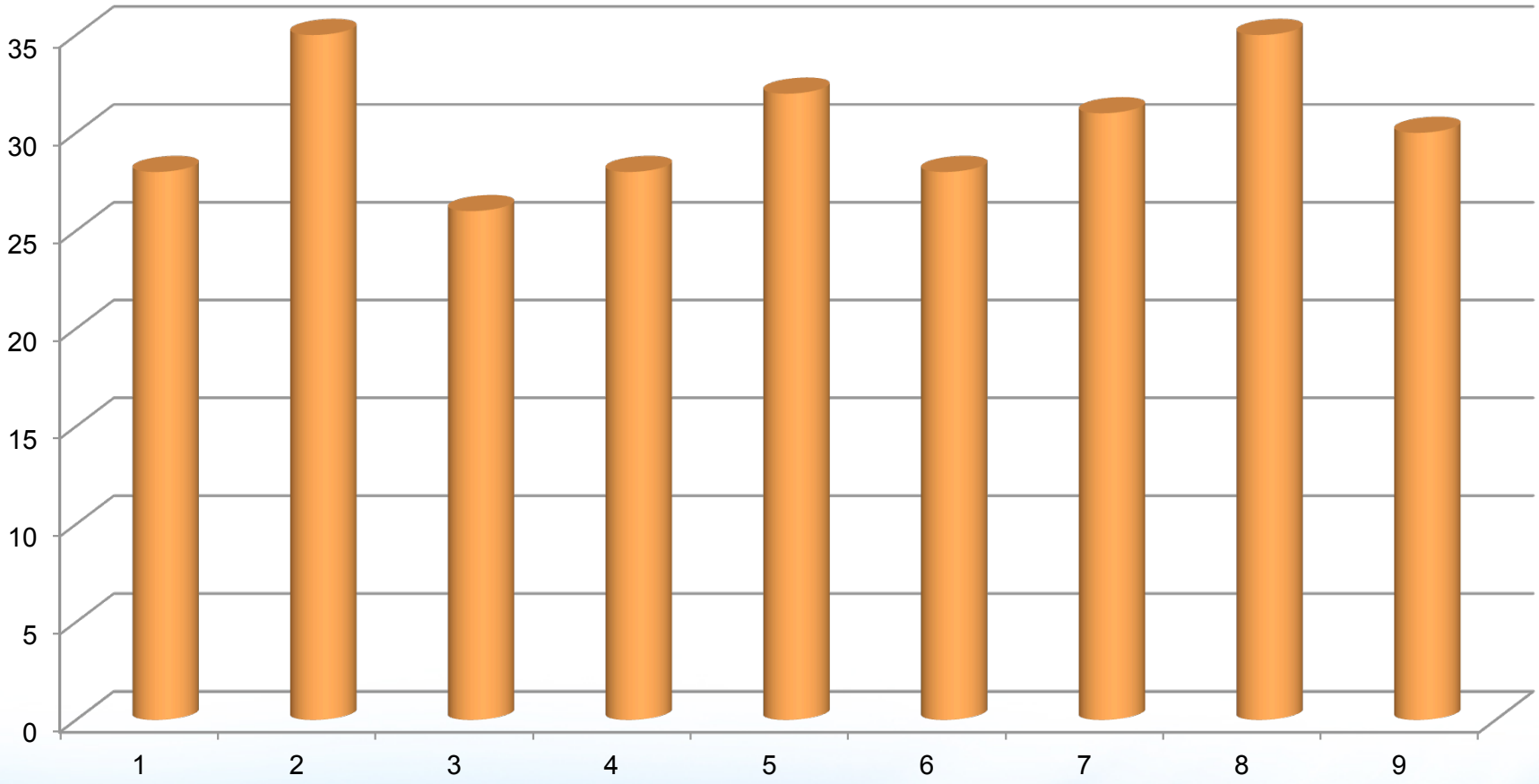
- Enrollment time: 2014.4-2016.12
- Numbers of patients: 9

Results

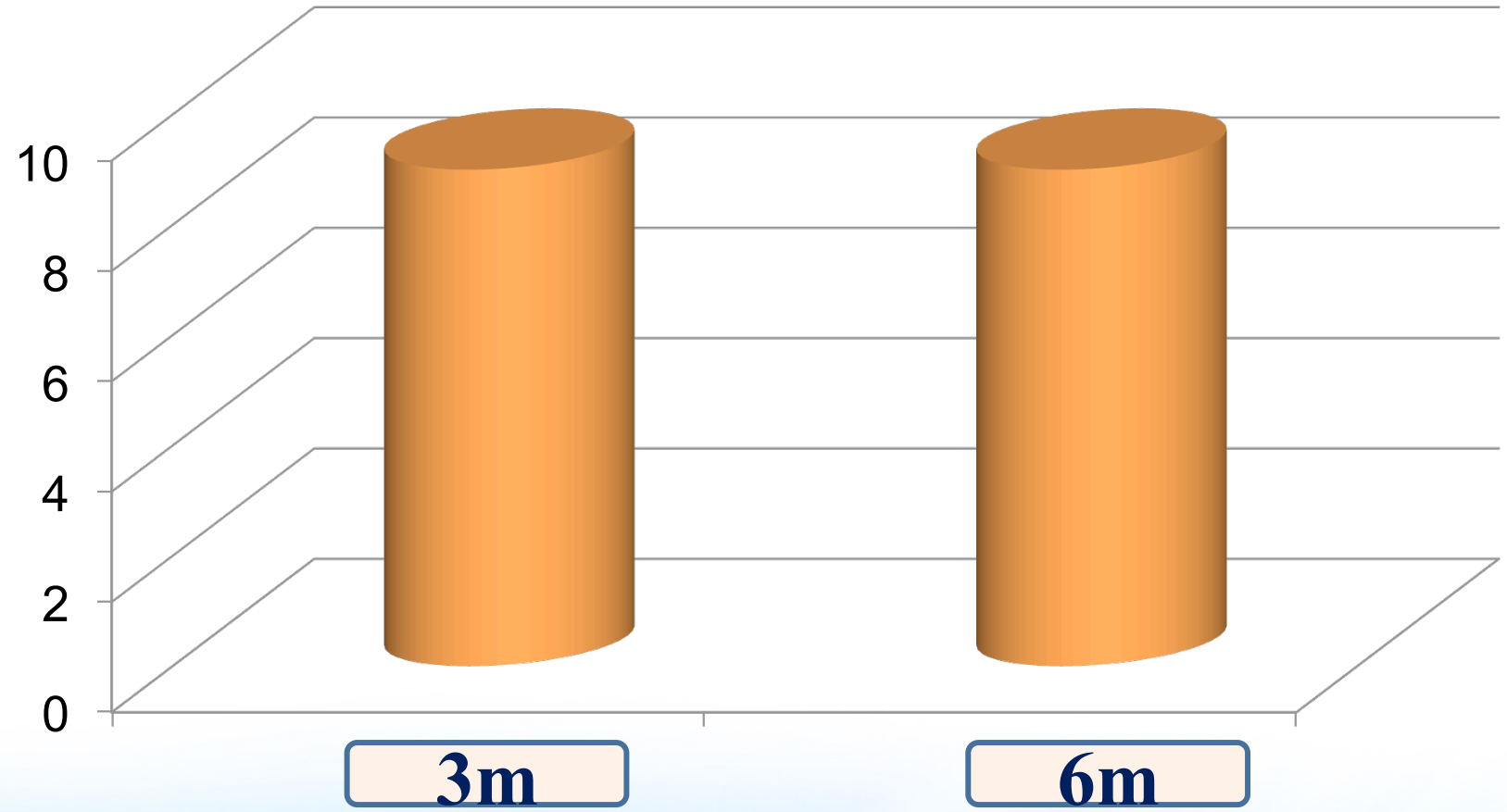
- Age: 16 years old (range 13-18)

  (RIF, 60 mg/kg) and ATRA (25 mg/m^2)
- Hydroxyurea and/or cytarabine (without anthracyclines) were used to diminish the increased WBC during induction treatment.

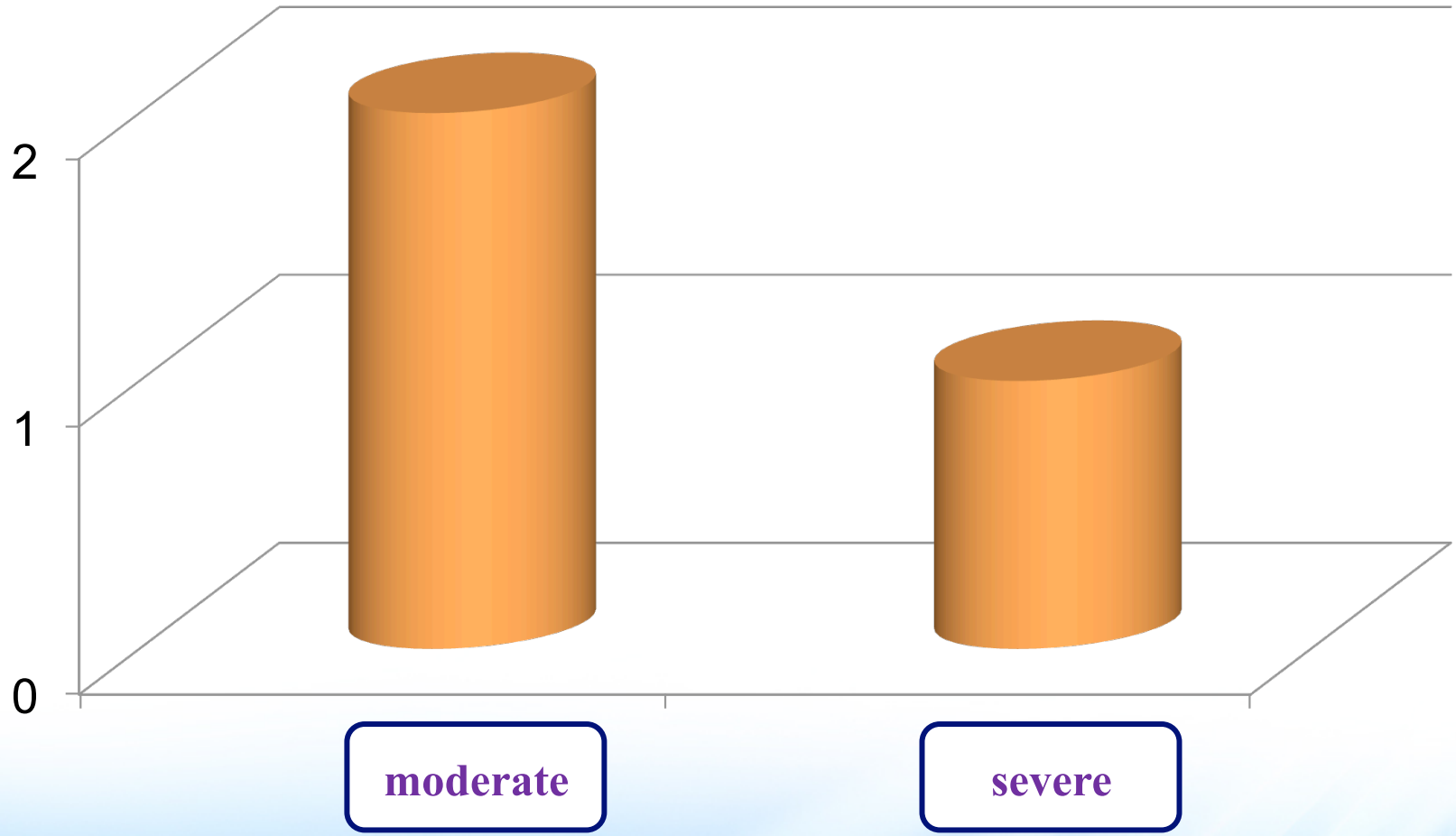
Days achieving CR of 9 patients



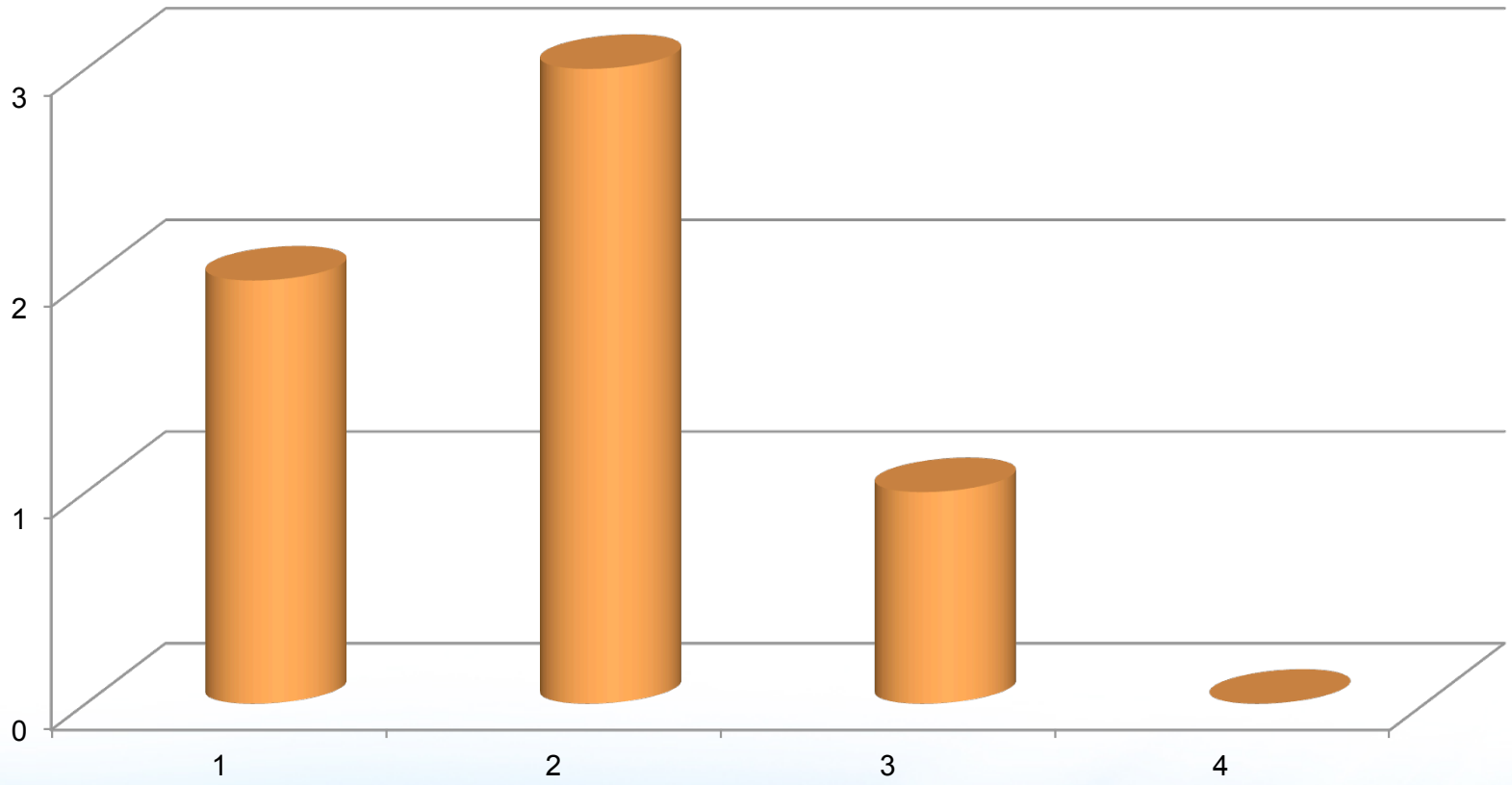
Molecular remission at 3 and 6 months



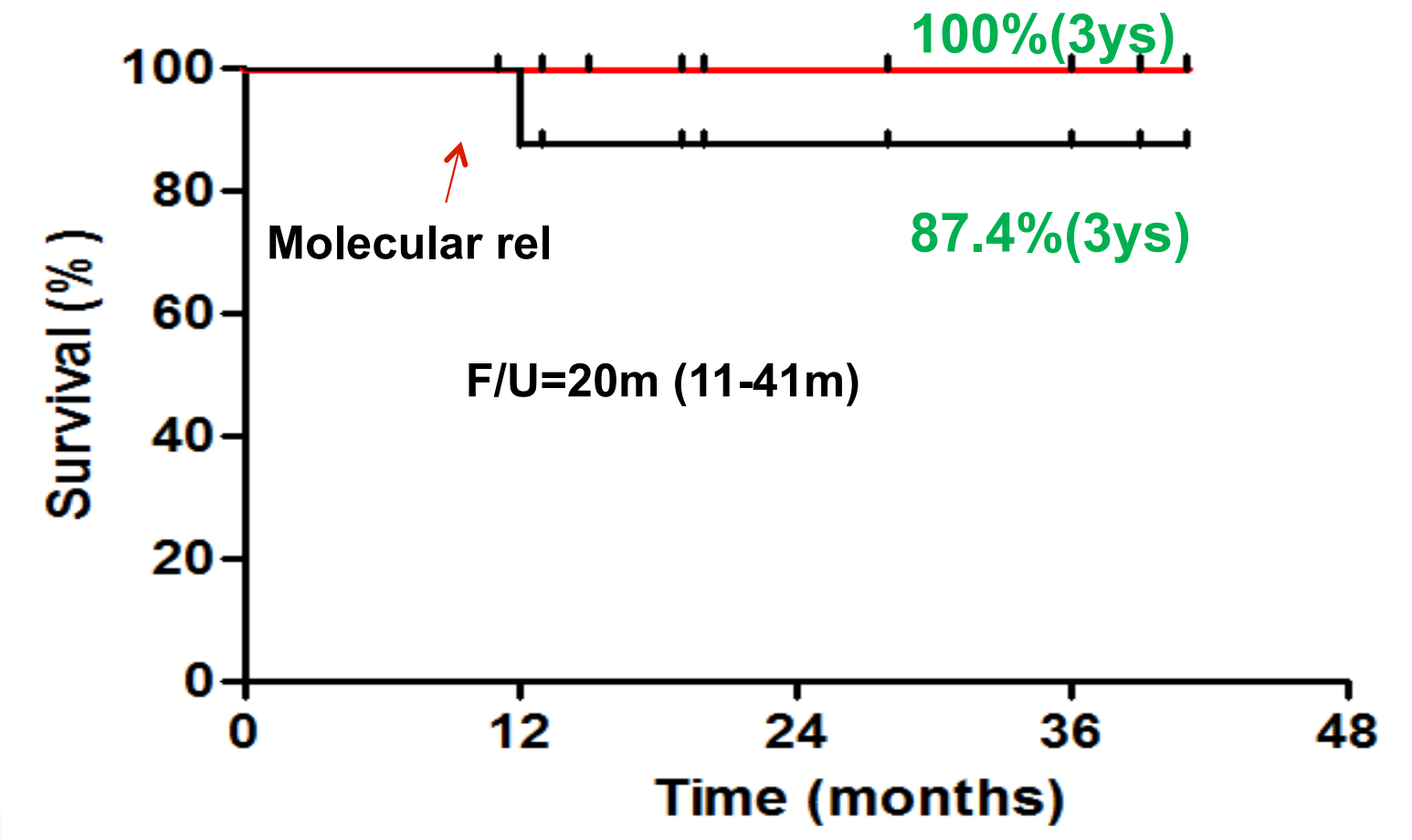
DS during induction



Liver damage during induction



Os and EFS


100%(3ys)
87.4%(3ys)
Molecular rel
F/U=20m (11-41m)
Survival (%)
100
80
60
40
20
0
0
12
24
36
48
Time (months)

Conclusions

- A largely home-based treatment protocol with complete oral regimen, chemo-free in children with low-risk APL, proved to be effective, safety and convenient

- This approach exemplifies an ideal model for the treatment of children patients with low-risk APL

“I am vey happy .
I can go to school as others”

Diagnosed

1 month later

I love you, boys and girls

Home-based treatment becomes reality for Children

Acknowledgements

- All the patients and theirs parents involved in this study

- My colleagues

Thanks for your attention