A Predictive Model for Intensive Chemotherapy Outcomes in Newly Diagnosed Elderly Patients with AML

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A Predictive Model for Intensive Chemotherapy Outcomes in Newly Diagnosed Elderly Patients with AML

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BACKGROUND

Not all Elderly "fit" Patients are "fit" for Intensive Chemotherapy: Results of ECOG 2906* Trial

	7+3@	Clofarabine
CR/CRi^	43.8%	42.8%
Day 30 Mortality	8.5%	7.9%
Day 60 Mortality	14.9%	13.1%
Grade 3-4 Non Hematological Toxicity	27%	19%

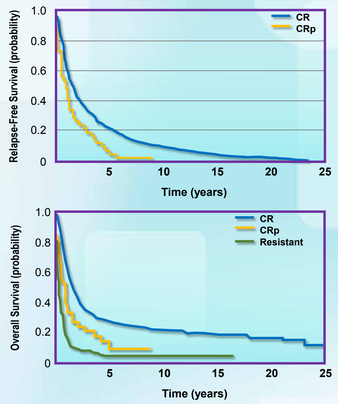
...Is this good enough?

*Foran, J. M., Sun, Z., Claxton, D. F., Tallman, M. S. (2015). North American Leukemia, Intergroup Phase III Randomized Trial of Single Agent Clofarabine As Induction and Post-Remission Therapy, and Decitabine As Maintenance Therapy in Newly-Diagnosed Acute Myeloid Leukemia in Older Adults (Age ≥60 Years): A Trial of the ECOG-ACRIN Cancer Research Group (E2906). Blood, 126(23), 217

@ 7+3, Daunorubicin and cytarabine

^ CRi, Remission with incomplete platelet recovery (<100,000)

Remission: A True Surrogate to Survival



Walter, Kantarjian et al, JCO 2010

Attainment of remission is an important milestone in long term survivorship. An effective induction strategy is very crucial to achieve this milestone.

STUDY OBJECTIVES AND METHODS

Predict outcomes to decide choice of induction strategy: standard chemotherapy or "something else"

- Quantify the role of various pre-treatment variables in the attainment of complete remission (CR) in elderly patients.
- Validation of a hypothesized risk scoring system to predict remission outcomes in the elderly age group.

The Data Source:

- Retrospectively analyzed 95 elderly patients with AML treated with intensive chemotherapy at Penn State Hershey Medical Center from 2010-2015.

INCLUDED	EXCLUDED
7+3	Hypomethylating agents
CLAG/M	Investigational agents on clinical trials
MEC	Best supportive care
Clofarabine	Promyelocytic leukemia
Cytarabaine	Age <60 years

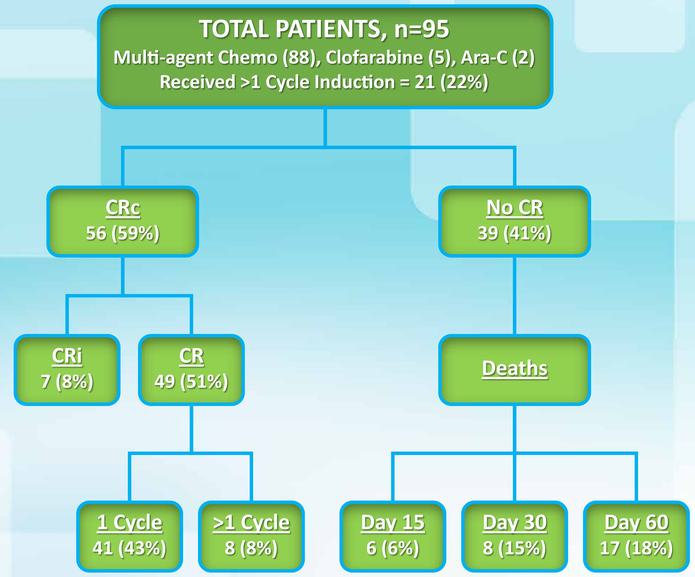
The Predictors of Response

	Variable	Hypothesized Odds Ratio (OR) For Not Achieving Remission
1	**Age (years)**	
	60-65	1
	66+	1.61
2	**CD34 expression**	
	Negative	1
	Positive	1.82
3	**NPMI mutation status**	
	Mutated	1
	Wild Type	2.82
4	**Serum WBC (per uL)**	
	<10000	1
	>10000	1.47
5	**Serum LDH (IU/L)**	
	<700	1
	>700	1.56
6	**Karyotype**	
	Inetermediate	1
	Favorable	0.25
	Non complex adverse	1.37
	Complex (>4 changes)	3.17

Treatment Failure Score (TFS) = A x B x C x D x E x F

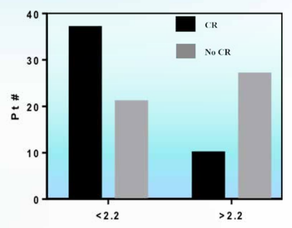
Based on Rollig et al, Blood 2010

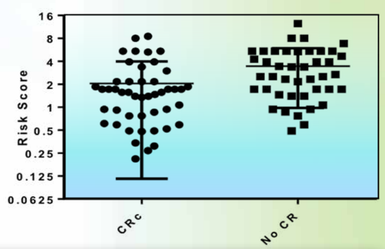
RESULTS



Treatment Failure Score (TFS) & Remission					
TFS	CRc (CR+CRi)	No CR	OR	(95% CI)	(95% CI)
> 2.2	10	27	4.75 (1.93-11.72) p=0.0004	64% (50-76)	73% (56-86)
< 2.2	37	21			
TOTAL	47	48			

- A TFS of > 2.2 was significantly associated with "no CR" with almost 5 times less likelihood of achieving CR.
- A TFS of > 2.2 is also associated with a significantly higher day 60 mortality (28% vs 10%) with intensive chemotherapy.





CONCLUSIONS & SUGGESTIONS

- Our algorithm was statistically predictive of the remission outcomes after intensive chemotherapy in patients > 60 years of age.
- A Treatment Failure Score (TFS) was constructed using six pre-treatment variables: Age, CD34 expression, NPM1 mutation status, Karyotype, Serum WBC and Serum LDH.
- A TFS of > 2.2 was not only associated with a low likelihood of achieving remission (OR 4.75, P=0.0004) but also higher day 60 mortality (28% vs 10%)" in this elderly population receiving intensive chemotherapy
- All components being available in ~7 days from diagnosis, will allow assignment of intensive vs less intensive (and toxic) therapy in this difficult patient population.
- This approach will improve remission rates and hence survivorship.
- Further refinement and validation of this approach may follow study of an increased sample size or ideally, a prospective study.