Hematologics

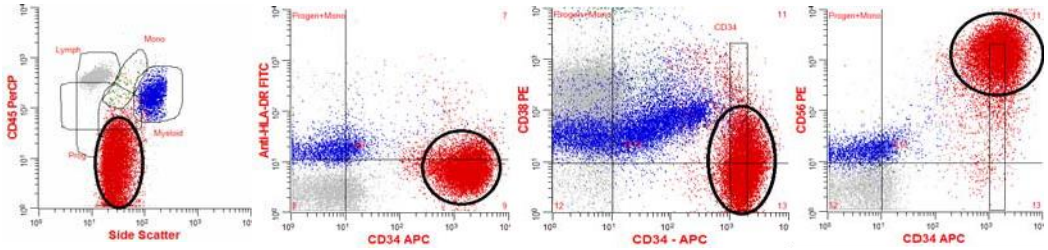
3161 Elliott Avenue, Suite 200, Seattle, WA 98121 Phone: (800) 860-0934 Fax: (206) 223-5550 www.hematologics.com

Are you screening for RAM immunophenotype and CBFA2T3-GLIS2 in pediatric AML?

Hematologics has identified a unique recurrent Immunophenotype at diagnosis that identifies a high-risk pediatric AML (RAM)[1]

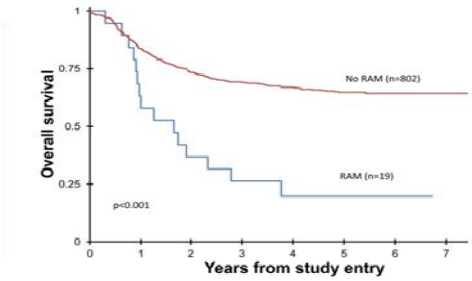
- **ΔN:™** (Difference from Normal) Flow Cytometry provides a definitive diagnostic RAM phenotype,which is an independent predictor of poor outcome in pediatric AML

RAM phenotype expresses high intensity CD56 expression, lack of HLA-DR, dim to negative expression of both CD38 and CD45.



- RAM phenotype can be identified rapidly at diagnosis, allowing clinicians to predict failure before initial therapy, thereby allowing more effective alternative therapies.

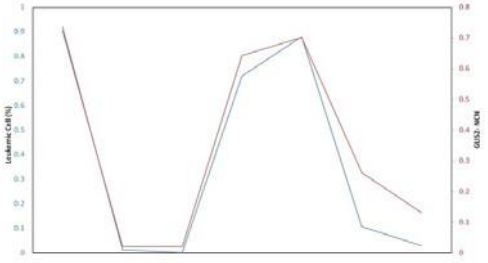
- Survival of patients with the RAM phenotype is like, or worse than those with high-risk molecular features and does not respond to standard therapy.



Patients with RAM AML have significantly worse overall survival compared to patients with non-RAM AML.

NO RAM (n=802)
RAM+ (n=19)

- Patients ≤ 5 years old or have AMKL (M7 megakaryoblastic) should be screened and monitored for RAM and CBFA2T3-GLIS2[2] (both have bad prognoses).



Tracking tumor percentage by both flow and GLIS2 fusion transcripts by RQ-PCR shows tumor load. (Case Study)

Percent Leukemia by Flow
GLIS2 Normalized Copy Number

- The CBFA2T3 -GLIS2 fusion transcript is a common feature in pediatric AML (M7) in patients having normal cytogenetic findings and confers a poor prognosis.[3]

- FAB M7 classification might not be poor risk if RAM phenotype patients are considered independently.

Best for Your Patient—Best for You

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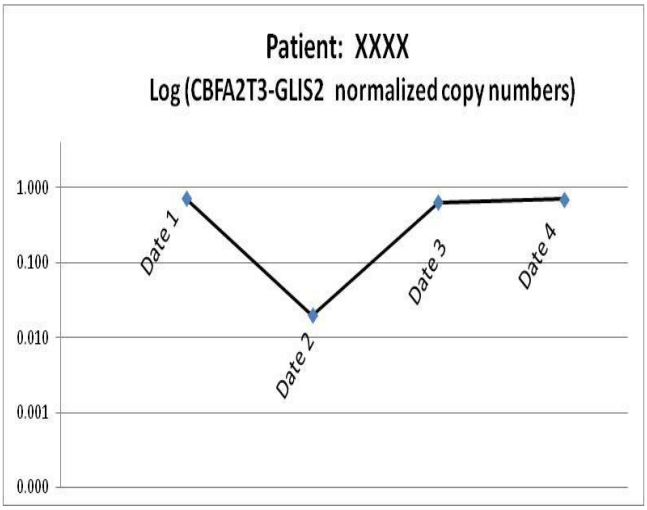
SAMPLE MOLECULAR ANALYSIS REPORT

CBFA2T3-GLIS2 RT-PCR Results: POSITIVE

Date	HLID#	Specimen	CBFA2T3-GLIS2 NCN	% Reduction	Log Reduction
Date 1	HLID1	BMA	0.724	Baseline	Baseline
Date 2	HLID2	BMA	0.020	97.2	1.6
Date 3	HLID3	BMA	0.643	11.2	0.1
Date 4	HLID4	BMA	0.702	3.0	0.0



NCN (normalized copy numbers): 0.702 - Quantitative assay units: CBFA2T3-GLIS2 transcript levels are reported as a ratio of fusion gene transcript to ABL reference gene transcript.

Analysis/Conclusions: The specimen tested positive for CBFA2T3 fusion transcripts, which are the molecular result of the cryptic chromosome 16 inversion [inv(16)(p13.3q24.3)], associated with a poor prognosis in AML.

- **The quantitative CBFA2T3-GLIS2 NCN value of 0.702 is reduced by 3.0% (log reduction 0.0) in comparison to the patient's baseline specimens.**

This PCR test can detect the CBFA2T3-GLIS2 transcript with sensitivity up to 1 in 10e5 transcripts (0.001%). Note: Control gene amplification indicated good RNA quality.

References:

1. Eidenschink Brodersen L. et al. "A Recurrent Immunophenotype at Diagnosis Independently Identifies High Risk Pediatric Acute Myeloid Leukemia: A report from Children's Oncology Group." Leukemia. 2016. 30(10):2077-2080.
2. Gruber, TA et al. An Inv(16)(p13.3q24.3)-Encoded CBFA2T3-GLIS2 Fusion Protein Defines an Aggressive Subtype of Pediatric Acute Megakaryoblastic Leukemia, Cancer Cell 22, 683-697, November 13, 2012 Elsevier, Inc.
3. Masetti R. et al. CBFA2T3-GLIS2 fusion transcript is a novel common feature in pediatric, cytogenetically normal AML, not restricted to FAB M7 subtype BLOOD, 25 APRIL 2013 x VOLUME 121, NUMBER 17