

Prognostic impact of RAS and C-KIT mutations (Single Vs. Multiple) in core-binding factor acute myeloid leukemia (CBF AML) treated with fludarabine, cytarabine, G-CSF (FLAG) based regimen

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Background

- Core-binding factor acute myeloid leukemia (CBF-AML), including inv (16) and t (8;21) AML, represent 15%-20% of all adult AML patients (pts) and is generally recognized as favorable AML subgroups.
- Despite being favorable, up to 30-50% of patients with CBF-AML eventually relapse.
- Both RAS (particularly multiclonal) and KIT mutations in CBF-AML have been associated with poor outcomes.
- We demonstrated that optimal reduction of disease defining transcripts (RUNX1-RUNX1T1 and CBFB-MYH11) by qPCR at end of induction and end of consolidations, has the most impact on the relapse free survival (RFS) of these patients.

Objective

We studied the prognostic impact of RAS and KIT mutation, including number of mutations on RFS in CBF AML and on attainment of optimal transcript reductions at the end of induction and end of treatment (EOT).

Materials & Methods

- Pts aged ≥ 18 years (yrs) with de novo CBF-AML, treated with FLAG (fludarabine, cytarabine, GCSF) regimen in combination with idarubicin or gemtuzumab ozogamicin between April 2013 and December 2019 at our center were included in this analysis.
- RAS and KIT mutations were tested by next generation sequencing.
- qPCR for disease-specific transcripts was monitored at the end of C1 and end of therapy (EOT).
- Optimal response was considered as qPCR transcripts < 0.1% post C1 and <0.01% at EOT.

Results

Mutations		N (%)
RAS	Positive	32 (35%)
	➢ One mutation	16 (50%)
	➢ More than one mutation	16 (50%)
KIT	Positive	30 pts (33%)
	➢ One mutation	25 (83%)
	➢ More than one mutation	5 (17%)

Results

- 91 pts with CBF AML were included in this analysis
- Median age was 52 yrs (range, 22-79).
- 41 of the pts were females (45%).
- Only KIT mutation was associated with lower odds (0.33, 95% CI 0.11-0.9) of optimal EOT response.
- The presence of single versus multiple KIT or RAS mutation did not affect optimal PCR responses.

- At a median follow up of 53.1 months:-

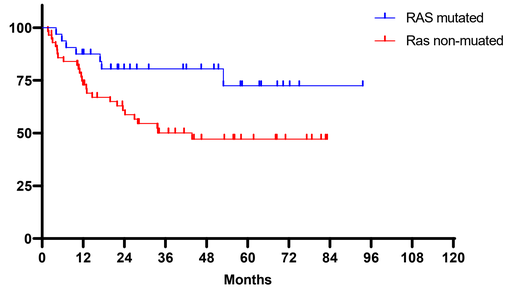
> The median relapse free survival (RFS) for the whole cohort was 27.7 months (range,1.7-93.6).

> RAS mutated pts had longer RFS compared to non-mutated pts (not reached vs. 43.78 mos, p=0.02).

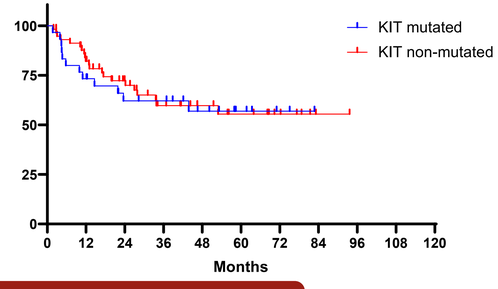
> KIT mutation did not affect RFS.

>The number of the RAS or KIT mutation (One mutation vs. multiple mutations) did not impact RFS.

RFS of RAS mutated vs RAS non-muated



RFS of KIT mutated vs KIT non-mutated



Conclusion

- ➢ KIT mutation might negatively affect attainment of optimal qPCR responses at end of FLAG based therapy, but it lacked significant impact on RFS.
- ➢ Single versus multiple KIT or RAS mutations do not seem to have an impact on relapse free survival.