Effect of Cytarabine/A anthracycline/Crenolanib Induction on Minimal Residual Disease (MRD) in Newly Diagnosed FLT3 Mutant AML

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Background

- FLT3-ITD and TKD mutations are known to be associated with a poor prognosis in AML.
- Clinical trials have demonstrated that a single induction cycle of cytarabine/anthracycline/crenolanib leads to MRD negativity by multi-parameter flow cytometry (MFC), and the rate of early relapse in this drug is with newly diagnosed FLT3-ITD AML.

Methods

- This abstract includes 29 consecutively treated, newly diagnosed, FLT3-ITD AML pts, who achieved CR one cycle of cytarabine/anthracycline/crenolanib. Pts received 7+3 induction with cytarabine 100 mg/m2 x 7 days and either daunorubicin (<60 y: 90 mg/m2; ≥60y: 60 mg/m2) or idarubicin 12 mg/m2 x 3 days. Crenolanib 100 mg tid x 7 days in FLT3-ITD pts.
- FLT3-ITD and TKD mutations were identified by targeted NGS. FLT3-ITD pts received 20% Crenolanib 100mg TID starting day 7. FLT3 TKD pts received 80% Crenolanib 100mg TID starting day 9. FLT3-ITD TKD pts received 40% Crenolanib 100mg TID starting day 9.
- Induction chemotherapy regimen included Cytarabine/Idarubicin/Crenolanib (Cytarabine + idarubicin + crenolanib) (Ivey et al., NEJM 2016). HLA-identical sibling or umbilical cord blood transplant was performed in 4 (13%) patients. 4 (13%) patients were non-responders. 2 (6%) patients achieved PR after first induction and CR after second.
- All patients with MRD positive state after first induction achieved MRD negativity after second induction cycle (Ivey et al., ASH 2015).
- Treatment-naïve patients received induction chemotherapy regimen of Cytarabine/Idarubicin/Crenolanib (Cytarabine + idarubicin + crenolanib).
- FLT3-NPM1/DNMT3A mutations are known to be associated with a poor prognosis in AML.

Response Rate

- 26/95 (28%) patients achieved CR after first induction.
- 15/26 (58%) patients achieved CCR after first induction.
- 2 (2%) patients achieved CR after first induction and CR after second.
- 14/15 (93%) patients achieved CR after CR after second.
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Hematologic Reconstitution after Induction

- Median WBC at count recovery was 4.6 x 10^9/L. Median platelet count at count recovery was 100,000 /µL.
- 3 (7%) patients were > 100,000 /µL at count recovery.
- Hematologic recovery was achieved within 22 weeks.

Results

- Median follow-up of 2.8 months.
- 20/24 (83%) patients achieved CR/CRi with MRD negativity.
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- All CR patients with high WBC counts at baseline achieved MRD negativity with a single cycle of cytarabine/anthracycline/crenolanib.
- Multivariate analysis was performed by multi-parameter flow cytometry.

Conclusions

- Cytarabine/anthracycline/Crenolanib induction is associated with a high rate of complete remission by multi-parameter flow cytometry.
- MRD was assessed by multi-parameter flow cytometry using bone marrow aspirates at count recovery.
- CR/CRi patients with MRD assessment (n=24) achieved CR/CRi after induction chemotherapy.
- Bone marrow samples at count recovery were assessed.
- MRD assessment was performed by multi-parameter flow cytometry.
- Even patients who were at high risk (WBC ≥100,000/µL or CD34+ > 1%) achieved MRD negativity with a single cycle of cytarabine/anthracycline/crenolanib.
- FLT3-NPM1/DNMT3A mutations are known to be associated with a poor prognosis in AML.
- 20/24 (83%) patients achieved CR/CRi after induction chemotherapy.
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