Bortezomib and rituximab in de novo adolescent/adult CD20-positive,Ph-negative pre B-cell acute lymphoblastic leukemia:Updated 3-year result

Vasu Babu Goli D.M[1],Hasmukh Jain D.M[1],Manju Sengar D.M[1],Jayashree Thorat M.D[1],Prashant Tembhare M.D[2],Dhanalaxmi Shetty M.D[3],Avinash Bonda V.N D.M[4],
Lingaraj Nayak D.M[1],Subramanian P.G M.D[2], Bhausaheb Bagal D.M[1], Nikhil Patkar M.D[2], Sumeet Gujral M.D[5]

[1]Department of Medical oncology,Tata Memorial Centre,Mumbai,India.[2]Department of Hematopathology ACTREC,Navi Mumbai,India.[3]Department of cytogenetics,ACTREC , Navi Mumbai, India.
[4]Department of Medical oncology, Homi Bhabha Cancer Hospital and Research Centre,Visakhapatnam, India.[5]Department of Pathology,Tata Memorial Centre, Mumbai, India

Background

- CD20 expression in B-cell precursor acute Lymphoblastic leukemia (B-ALL) is associated with inferior outcomes.[1]
- Treatment approaches involve incorporation of Rituximab (variable doses and scheduling between trials), intensification of chemotherapy and allogeneic stem cell transplant in patients who continue to remain MRD-positive post induction.
- Treatment intensification with chemotherapy or allogenic stem cell transplantation for EOI MRD positive patients is limited in resource constraint areas due to cost and infection related morbidity and mortality.
- Hence, there is an unmet need to identify active and safe drugs to improve EOI MRD negative rates which can reduce the need for transplant and chemotherapy intensification.
- Given bortezomib's activity in relapsed ALL and its synergism with rituximab in B-cell lymphomas, the addition of bortezomib to rituximab and chemotherapy may provide an incremental benefit in CD20 positive precursor B-ALL.[2,3]

Objective

- To test the activity of bortezomib and rituximab in combination with a paediatric-inspired regimen during induction therapy in newly diagnosed adolescents and adults (aged >14 years) with CD20 positive, Philadelphia-negative precursor B-ALL. Here we present updated results with longer follow up.

Materials & Methods

- **Design:** Single-centre, phase 2, nonrandomized open-label trial (Simon's two-stage design) conducted between December 2017 and August 2019.
- **Main Outcome measures:** The primary end point of the study was the rate of (end of induction) EOI BM-MRD negativity. Secondary end points were EFS and OS.

Summary

- A total of 35 patients were enrolled between December 2017 and August 2019.
- EOI MRD negative rates were 70.1% compared with 51.7% in historical cohort treated with chemotherapy.
- On longer follow up (median follow up 38months), 3-year EFS and OS rates were 75.6% (95% CI 62.3-91.9%), and 75.6% (95% CI 62.3-91.9%) respectively.
- 3-year rates of EFS based on post-induction (week 4) MRD status was 55.6% (31-99.7%) in MRD positive group compared with 86.1% (72.7-100%) in MRD negative group.
- 3-year rates of OS based on EOI MRD status was 55.6% (31-99.7%) in MRD positive group compared with 86.1% (72.7-100%) in MRD negative group.
- The median OS for patients who attained CR was not reached versus 8months in patients who fail to achieve CR.

Conclusion

- On longer follow up, the activity of combination of bortezomib and rituximab is maintained without any new safety concerns.
- EOI MRD positivity and lack of complete remission post induction are strong predictors of poor outcomes.

Reference

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