CORRESPONDENCE

Ibrutinib to Allogeneic Stem Cell Transplant in a Case of Refractory Mantle Cell Lymphoma

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Dear Editor,

Mantle Cell Lymphoma (MCL) remains difficult to treat despite of availability of intensive chemo-immunotherapies with number of patients experience relapse or refractory disease. Possible cure in a relapsed/refractory (R/R) case of MCL has been described after allogeneic hematopoietic stem cell transplantation (alloSCT) [1].

Ibrutinib, a bruton's tyrosine kinase inhibitor, acts by blocking B cell receptor signaling and has been approved by FDA as a single agent in R/R MCL cases for its favorable efficacy and toxicity profile [2–4].

Maintenance of higher PFS rates in these R/R MCL cases on Ibrutinib requires lifelong treatment with good adherence to dosing schedule. Ibrutinib monotherapy is found to be associated with (a) financial burden, (b) possible relapse in the first 2 years of treatment, and (c) acquired resistance after prolonged therapy; demonstrating poor clinical outcomes [4], which calls for different treatment strategies. These pitfalls of Ibrutinib monotherapy could be salvaged with alloSCT as reported in our current case. Here, we report a case of refractory MCL with prior three lines of chemotherapy before successful treatment with Ibrutinib followed by AlloSCT.

A 53 year old male presented with jaundice, significant weight loss, hepatosplenomegaly, large lymphnodal masses at porta and peripancreatic region, and obstructive biliopathy. Lymph node histopathology with immunohistochemistry confirmed MCL, while whole body PET-CT

showed extensive disease including extranodal sites and bone marrow infiltrates. Patient was planned for 6 cycles chemotherapy with R-CHOP alternating with R-DHAP followed by autologous SCT (ASCT). He received one cycle of R-CHOP and R-DHAP each, to which he developed grade-IV toxicities (abdominal pain, abdominal distension, loose stools) which required prolonged repeated hospitalization. Therefore, treatment was changed to Rituximab–Bendamustine (R–B) chemotherapy regimen which he tolerated well. Post 4 cycles of R–B chemotherapy, patient showed progression in extent of lymphoma. Further, he received bortezomib and lenalidomide based therapy for 2 cycles but again he showed progressive disease.

Patient was considered for Ibrutinib monotherapy followed by alloSCT. He tolerated Ibrutinib therapy well and attained complete remission (CR) after 1 month of therapy. Thereafter, he was received reduced intensity conditioning (Fludarabine and Melphalan) and matched sibling donor peripheral blood stem cell transplantation with Methotrexate and Cyclosporine-A (CSA) for GVHD prophylaxis.

Neutrophils and platelets were engrafted on day + 11 post alloSCT. Serial monitoring for CMV DNA was negative. There was no graft versus host disease while the CSA was tapered off by day 180 post transplant. Serial PET-CT at post transplant 90 days and 18 months showed CR. At 25 months of follow up post alloSCT, patient is disease free.

Primary refractory MCL is not uncommon and is a challenge to treat. Ibrutinib is a promising agent for such cases of MCL which has shown a response in nearly 2/3rd of R/R MCL patients [2, 5], but its long term utility is limited by high cost, indefinite therapy and poor long-term survival owing to loss of response because of acquired

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resistance. High dose therapy and ASCT has been ineffective in this group [5].

AlloSCT post high dose chemotherapeutic regimen in R/R setting of MCL case has been associated with long term PFS and a possible cure [1]. In order to maintain a longer PFS followed by Ibrutinib therapy, alloSCT appears to be a viable option. This case is one example where refractory MCL achieved CR with Ibrutinib and maintained it using alloSCT resulting into longer PFS.

In conclusion, alloSCT post Ibrutinib monotherapy may emerge as a promising therapeutic approach in patients with refractory MCL. This observation opens new perspectives in the utility of alloSCT post ibrutinib in refractory MCL disease.

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Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964

Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by our Institutional Review Board.

Informed Consent The informed consent was obtained from the individual participant included in the study.

References

1. Kroger N, Hoffknecht M, Kruger W, Zeller W, Renges H, Stute N et al (2000) Allogeneic bone marrow transplantation for refractory mantle cell lymphoma. *Ann Hematol* 79:578–580
2. Wang ML, Blum KA, Martin P, Goy A, Auer R, Kahl BS et al (2015) Long-term follow-up of MCL patients treated with single-agent ibrutinib: updated safety and efficacy results. *Blood* 126(6):739–745
3. Wang ML, Rule S, Martin P, Goy A, Auer R, Kahl BS et al (2013) Targeting BTK with ibrutinib in relapsed or refractory mantle-cell lymphoma. *N Engl J Med* 369(6):507–516
4. Wang M, Goy A, Martin P, Ramchandren R, Alexeeva J, Popat R et al (2014) Efficacy and safety of single-agent ibrutinib in patients with mantle cell lymphoma who progressed after bortezomib therapy. *Blood* 124(21):4471
5. Chiron D, Di Liberto M, Martin P, Huang X, Sharman J, Bleau P et al (2014) Cell cycle reprogramming for PI3 K inhibition overrides relapse-specific C481S BTK mutation revealed by longitudinal functional genomics in mantle cell lymphoma. *Cancer Discov* 4(9):1022–1035