Sitagliptin: A promising DPP-4 inhibitor for prevention of acute graft versus host disease

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Madam, allogeneic haematopoietic stem cell transplant (HSCT) remains a life altering cure to exceptionally challenging diseases ranging from haematologic malignancies to primary immunodeficiencies and blood cancers. One of its adversities includes graft versus host disease (GVHD), a lethal immunologically mediated condition wherein the donor's T-cells attack the host's tissues. The presentation can be classified as acute or chronic. Acute GVHD is divided into four grades. Despite current prophylaxis, including a combination of calcineurin inhibitor with either methotrexate or sirolimus, the incidence of grade-II or higher GVHD is between 30% to 80%, with grade-IV GVHD approaching mortality rates up to 90%.[1]

A recent phase II trial by Farag et al. addresses the issue by introducing a novel combination of sitagliptin – a specific DPP-4 inhibitor used to manage type 2 diabetes in adults – along with tacrolimus and sirolimus for prevention of GVHD.[2] Using the new blend, an overall marked reduction in the risks of grade-II to IV (5%) and grade-III to IV (3%) acute GVHD was shown, compared to previous studies using only sirolimus and tacrolimus.[3] Moreover, no adverse effects were associated with the drug during the period of study.

Advancements in the field of HSCTs are particularly crucial in developing countries such as Pakistan. The high prevalence of consanguineous marriages and insufficient genetic counselling make the country especially vulnerable to diseases like thalassemia, bone marrow failure syndromes and immunodeficiency states. Up to 9000 children require transplantation each year due to the high prevalence of beta- thalassemia major.[4] The situation is further complicated by limited resources and few stem cell transplant centres, which are limited to major cities.

Although HSCT efficiently treats numerous life-threatening conditions, only 719 patients underwent HSCT till mid-2017 cumulatively in Pakistan.[4] In accordance with the aforementioned factors, the number of transplants performed heavily outnumbers their demand, making it essential to tackle a complication as deadly as acute GVHD. In a 2005 study conducted in Rawalpindi by Hashmi et al., the overall incidence of acute GVHD grade-II to IV after standard immunosuppressive therapy was 44.2%.[5] While the results were comparable to other studies, the high morbidity and mortality rates necessitates alternate treatment courses.

Sitagliptin, a locally manufactured, cost-effective drug, will be an appropriate choice of medication in Pakistan where average income amounts to a meagre US$1000 per year.[4] However, randomized trials are needed to further investigate its role in the prevention of acute GVHD.

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