Belatacept: Good, but not good enough?

Sir,

We read with great interest the excellent review on belatacept,[1] the latest addition to immunosuppressive agents used in kidney transplantation. We would also like to bring to your kind attention that:

Belatacept has brought about a 'paradigm shift' in the maintenance immunosuppression after solid organ transplantation, in that it is the first biologic agent approved for use for long-term maintenance immunosuppression for solid organ transplantation. Biologic agents (Basiliximab, thymoglobulin, etc.) already have an established role as induction immunosuppressive agents at the time of kidney transplantation but there are several issues to be tackled before a biologic agent can be accepted as a viable option for long-term maintenance immunosuppression. Such an agent should inhibit the immune system in a nondepleting manner without creating excessive immunodeficiency, should not have initial and prolonged immunogenicity, should not require therapeutic drug monitoring, and should offer an acceptable administration route and interval between doses. Belatacept satisfies all these requirements, except that it requires intravenous (IV) administration.

Although it is not yet made available in India, belatacept appears to be the first immunosuppressive drug used in kidney transplantation for which phase III trials were conducted on Indian subjects as well, before marketing the drug.

Although belatacept is indeed a very promising drug, there are certain concerns-other than the safety issues discussed in the article-which need to be addressed before the drug receives whole hearted endorsement from the transplantation community.

Because of purely technical reasons, the BENEFIT trial[2] compared belatacept with cyclosporine. However, this does not represent current clinical practice where cyclosporine has been largely replaced by tacrolimus as the calcineurin inhibitor (CNI) of choice in kidney transplantation. Tacrolimus is known to be less nephrotoxic compared to cyclosporine and reduces the incidence of acute rejection compared to CsA.[3] Belatacept needs to be compared against tacrolimus in a clinical trial.

The need to be administered IV is a major disadvantage. After the initial few weeks of transplantation, the

recipients are as healthy as any normal individual and are able to lead a near normal life. Although the need for IV administration is touted as an advantage when it comes to ensuring patient compliance, the same may not apply in India. The major reason for noncompliance among kidney transplant recipients in India is economic concerns[4] and belatacept is expected to be more expensive than the current immunosuppressive drugs available in the market. The need for IV administration will only add to the expense. A significant number of patients travel long distances to their transplant centers, and patients may be forced to travel every month only for the sake of IV administration of the drug, especially if the drug cannot be reliably administered at a local hospital. Post-transplantation immunosuppression being lifelong, the need for IV administration of belatacept indefinitely is expected to create problems for both patients and care givers.

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