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Clinical Expert Summary

Belatacept (Nulojix®▼) for prophylaxis of graft rejection in adults receiving a renal transplant, in combination with corticosteroids and a mycophenolic acid

1. Existing guidelines

Consensus guidelines about the potential use of belatacept internationally following phase III and regulatory trials were mentioned, but experts were unaware of existing national guidelines. It was highlighted that the manufacturer has indicated the appropriate dosing frequency for prescribing, and local patient factors would be considered in the development of guidelines.

2. Disease prevalence

Experts agreed that there are 150-160 new transplants per year in the Cardiff Transplant Unit. A proportion of them is EBV positive to negative so they are not eligible a priori. About 20% are immunologically high risk and it was definite that these patients should be cared with other regimes at the moment. One expert suggested that approximately half of these patients might be appropriate for treatment with belatacept.

3. Current treatment options

There are numerous treatment options that are tapered to the individual necessities of the transplanted patient. Experts however agreed that most renal transplant recipients receive induction therapy with an Il-2 blocking monoclonal antibody (basiliximab), followed by triple immunosuppression with a CNI (usually tacrolimus), antiproliferative agent (usually mycophenolate mofetil) and steroid (prednisolone). One expert highlighted that for most patients, steroids are weaned from 3 months. Another expert noted that a number of patients after 3-6 months are converted to sirolimus to preserve or maintain renal function.

Patients at high immunological risk receive induction with a T cell depleting antibody (either alemtuzumab or polyclonal anti-thymocyte globulin).

The regimen may also be modified for the elderly, those at high risk of diabetes and those who have had a previous malignancy.

Patients for whom belatacept would not be considered are those at immunological high risk, or EBV negative.

4. Unmet needs

It was agreed that although transplantation has dramatically progressed in recent years, there is still a prevalent loss of kidney transplants (quoted by one expert as around 5% per year) that is related to either chronic toxicity from current immunosuppressive medication or to chronic rejection. Any development that can potentially improve this would be welcome.

Experts agreed that an advantage of the use of belatacept was seen as the significant improvement in renal function (compared to the CNI cyclosporin) following both standard and extended criteria cadaveric renal transplantation. One expert highlighted the

increasing use of donated kidneys from older patients with more co-morbidities, and an immunosuppressive regimen that is both effective at preventing rejection and promotes optimal renal function is desirable.

There was expert opinion that weight gain, new onset diabetes and lipid abnormalities are frequent following transplantation in the Welsh population and it was suggested there is evidence that these are all ameliorated by the use of belatacept rather than the current alternative, a calcineurin inhibitor (trial comparator cyclosporine, tacrolimus usually prescribed locally).

The fact that the pivotal trials have been performed with Neoral-Cyclosporine rather than tacrolimus was mentioned. With regards to the trial data one expert stated; 'there is a small penalty of increased rejections in the belatacept arm but those did not result to increased graft loss'.

It was suggested that belatacept provides a simplified treatment for patients since it is given initially in monthly and then bimonthly doses.

5. Knowledge of product in given indication

One expert highlighted that the introduction of belatacept would require discussion within the department, and agreement from the Consultant body to determine its place amongst the other drugs already available. In addition, that the necessary infrastructure to administer regular intravenous infusions to recipients would also need to be developed (which was also highlighted by other experts). It was mentioned by one expert that the logistical issues associated to the route of administration are likely to affect widespread prescription.

It was viewed that belatacept should be one of the available options and likely to be initially used in selected patients. To be considered for patients at low immunological risk, EBV+, high risk of the metabolic syndrome and post-transplant diabetes, recipient of extended criteria donor kidney. One suggestion was that it might be appropriate to provide belatacept as a treatment alternative for younger patients who have a high degree of incompliance with transplant medication and patients who require a non nephrotoxic regime and do not have a very high immunologic risk.

It was also suggested that since it is a causes co-stimulator blockade it can also, in the future, form part of a tolerogenic protocol for selected patients.

One expert expressed that 'the availability of belatacept would undoubtedly enable us to continue to develop minimally nephrotoxic immunosuppressive regimens, thus increasing graft longevity and patient health'.

The fact that there are further studies of belatacept underway using Alemtuzumab induction to avoid the risk of early rejection was also mentioned.

Declarations of interest were made, and were of a non-personal, non-specific interest and also of a personal non-specific interest.