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COCHRANE COMMENTARIES

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Belatacept for kidney transplant recipients

What is this review about?

This review is about the use of belatacept as part of a primary immunosuppressive regimen for kidney transplant recipients.

What are the findings?

Belatacept is associated with similar risks of acute rejection, graft loss and death as conventional therapy with calcineurin inhibitors (CNI) when used in a primary immunsuppression

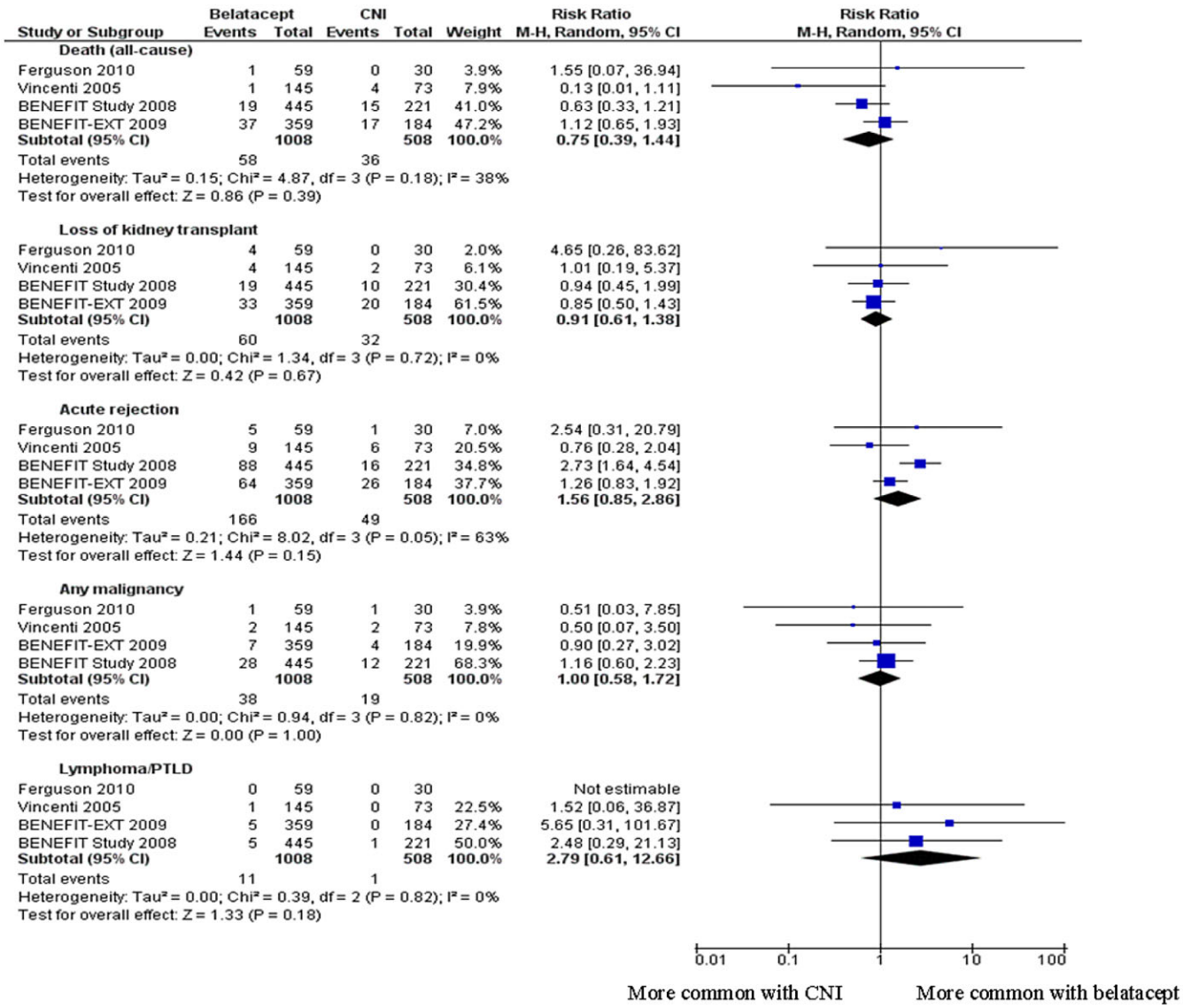

Fig. 1 Belatacept *versus* calcineurin inhibitor based regimens for primary immunosuppression of kidney transplant recipients (dichotomous outcomes).

regimen. However, recipients treated with belatacept had less chronic kidney scarring, better kidney function, better blood pressure and lipid profiles, and a lower incidence of diabetes compared with recipients treated with a calcineurin inhibitor. The belatacept dosage used (high or low), type of kidney donor (standard *vs* extended criteria), and whether recipients received tacrolimus or cyclosporine as the calcineurin inhibitors made no difference to kidney survival, acute rejection or kidney function. Important questions remain unanswered with current evidence, specifically how belatacept affects the risk of post-transplant lymphoproliferative disorder (PTLD). In addition, we could only synthesize data up to 3 years following kidney transplantation, and so whether short-term advantages of treatment with belatacept are maintained over the medium- to long-term or affect cardiovascular outcomes and kidney transplant survival remains unclear.

What are the findings based on?

A total of five trials involving 1535 randomized kidney recipients older than 18 years of age.

Three trials (478 participants) compared belatacept with cyclosporine and two trials (43 participants) compared belatacept with tacrolimus. Co-interventions varied among trials and included basiliximab (four trials, 1434 participants), anti-thymocyte globulin (one trial, 89 participants), alemtuzumab (one trial, 12 participants), mycophenolate mofetil (five trials, 1509 participants), sirolimus (one trial, 26 participants) and prednisone (five trials, 1535 participants). Recipients were generally not immunologically sensitized with a panel reactive antibody titre of <20%. Fifty per cent of recipients received a standard criteria donor kidney. Methodological quality was good, although selective reporting was suspected in the three largest trials for the outcome of PTLD, the main safety concern surrounding the use of belatacept. Despite enquiry, we were not able to access more complete data about this potential harmful effect.

Implications for practice

- Belatacept and CNI-treated kidney recipients have a similar risk of dying, losing their kidney transplant and returning to dialysis or having an episode of acute rejection.
- Recipients treated with belatacept are less likely to have chronic kidney scarring, and more likely to have better kidney transplant function than recipients treated with a calcineurin inhibitor.
- Blood pressure and lipid profiles for up to 3 years post transplant are better among recipients receiving belatacept than recipients receiving a calcineurin inhibitor.
- New-onset diabetes after transplant occurs less commonly in recipients treated with belatacept than recipients treated with a calcineurin inhibitor.
- The effect of belatacept on PTLD risk remains unclear on data currently available

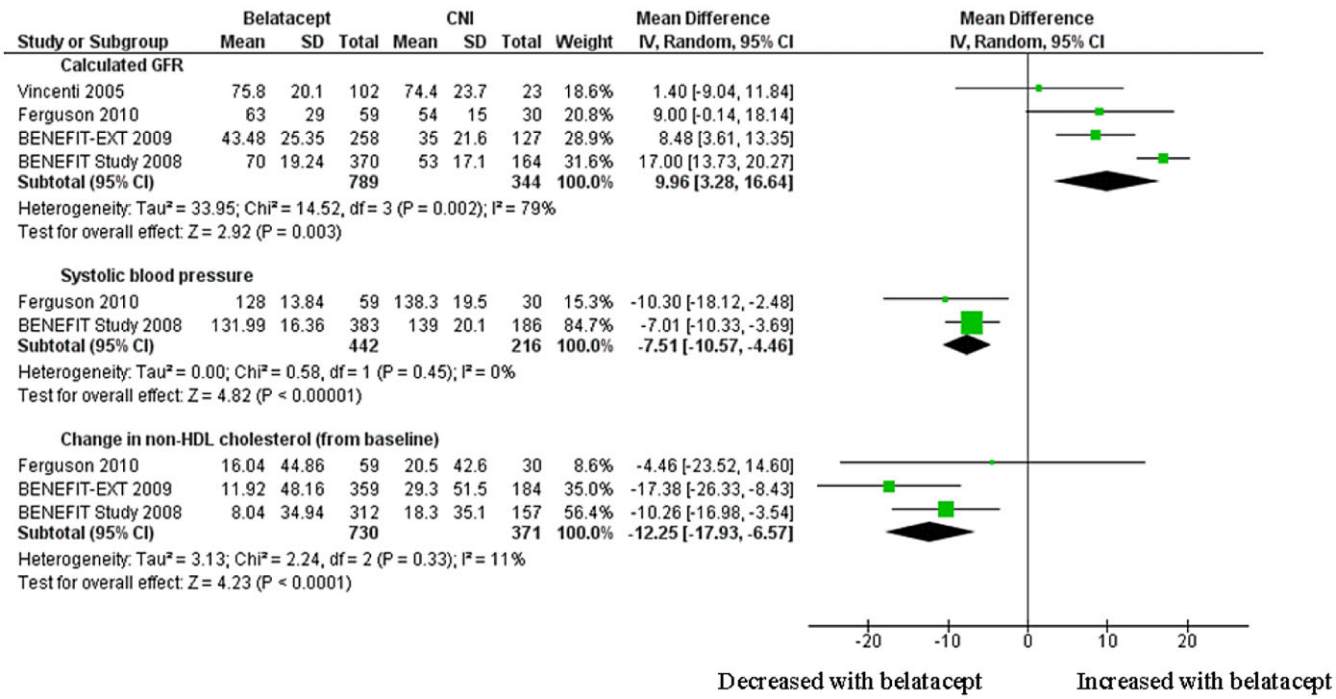

Fig. 2 Belatacept *versus* calcineurin inhibitor based regimens for primary immunosuppression of kidney transplant recipients (continuous outcomes).

Clinical perspective

This systematic review supports the cautious use of belatacept as an alternative to a calcineurin inhibitor based regimen as primary immunosuppression in carefully selected kidney transplant recipients (Figs 1,2). The favourable side-effect profile of belatacept – particularly the lower observed incidence of diabetes, better blood pressure control and lipid profile – means that its use should be considered as an option in primary immunosuppression regimens for recipients at high cardiovascular risk. Future research of immunosuppressive regimens requires larger pragmatic collaborative trials, with clinically relevant, long-term follow-up outcomes to fully clarify risks and eventual harms of treatments, particularly PTLD.

Masson P, Henderson L, Chapman JR, Craig JC, Webster AC. Belatacept for kidney transplant recipients. *Cochrane Database of Systematic Reviews* 2014, Issue 11, Art. No.: CD010699. DOI: 10.1002/14651858.CD010699.pub2