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Ihr Zeichen	Ihre Nachricht vom	Unser Zeichen	Datum:
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Biometrical Consultation: Pharmacological Tie2 activation in kidney transplantation

Dear Dr. Thamm,

you asked for biometrical consultation on the 15th of June, 2016, and on the 23rd of June, 2016, you presented your research paper on the above mentioned topic. You stated a need of evaluation of the statistical analysis you have conducted.

1. Experimental design

You investigate the therapeutic potential of vasculotide (VT) - a Tie2 activating therapeutic - in kidney transplantation. Therefore you performed a mice experiment and used a murine MHC-mismatched renal transplant model (C57Bl/6 male into Balb/c female). The kidneys of Eight week-old male C57Bl/6 mice were transplanted into 23 Balb/c mice and replaced the left kidney. The donor mice received 500 ng VT (n=11) or vehicle (PBS) (n=11) intraperitoneally (i.p.) 1h prior to surgery. Recipients were injected with 500 ng VT or vehicle respectively directly and on day 3 after kidney transplantation i.p.. The right native kidney was removed on post-transplantation day 4 so that survival became graft dependent. Blood was taken on days 0, 6, 14, 21, and 28. Survivors were sacrificed 28 days after transplantation.

As endpoints you assessed serum creatinine, urea level and Lactate dehydrogenase at days 0, 6, 14, 21, and 28. Survival has been monitored daily and histological changes have been assessed at day 28 in the surviving mice (vehicle: n=3, VT: n=5) with histological categories regarding interstitial inflammation and glomerular injury. Additionally you assessed expression levels of Intercellular adhesion molecule (ICAM-1), Vascular cell adhesion protein 1 (VCAM-1), Transforming growth factor β (TGFβ), collagen-1, collagen-3 and fibronectin in kidney homogenates via RT-qPCR at day 28 after harvesting the kidneys of surviving mice (vehicle: n=3, VT: n=5) and at day 0 for donor mice (n=3).

2. Analysis

- To compare VT group and vehicle group regarding serum creatinine, urea level and Lactate dehydrogenase you used an unpaired t-test. This method is adequate if normality assumption for serum creatinine, urea level and lactate dehydrogenase is justified.
- To compare VT group and vehicle group regarding survival you adequately used the Kaplan-Meier-estimates and the log-rank test.
- To compare VT group and vehicle group regarding histological changes assessed by your categorizations the Mann-Whitney-U test is adequate.
- You compared donor mice at day 0 (n=3) to vehicle group at day 28 (n=3) and VT group at day 28 (n=5) regarding levels of intercellular adhesion molecule (ICAM-1), vascular cell adhesion protein 1 (VCAM-1), transforming growth factor β (TGFβ), collagen-1, collagen-3 and fibronectin in kidney homogenates. The Mann-Whitney-U Test is adequate for each of these comparisons.

3. Further biometrical remarks

- Since all analyses are exploratory, a correction of type-I-error is not necessary.
- Between transplantation and day 28 most of the mice died. You need to set your results in perspective regarding the high mortality and discuss the observed mortality rate overall and separately for each group.

If you have any further queries, please do not hesitate to contact us.

With kind regards,

(Florian Lasch)