Reviewer’s report

Title: Kidney Injury Molecule-1 Expression in Human Kidney Transplants With Interstitial Fibrosis and Tubular Atrophy

Version: 2 Date: 30 October 2014

Reviewer: David Nikolic-Paterson

Reviewer’s report:

Major Compulsory Revisions
1. Please clarify whether this study constitutes an entirely separate cohort of patients to that previously published by the authors in two papers on the exactly the same topic (KIM-1 expression in renal transplant biopsies).

2. I disagree with the conclusion of the study that, “KIM-1 represents a potential biomarker of kidney allograft fibrosis”. Firstly, KIM-1 levels in the kidney are increased in virtually all types in renal injury involving the tubulointerstitial compartment, and thus KIM-1 has no selectivity for renal fibrosis. Second, the level of KIM-1 is much more related to the severity of tubular damage than to any specific cause of tubular damage. As a result, it is difficult to see how measuring KIM-1 in urine samples could be used to define kidney graft fibrosis and avoid the need for a biopsy.

3. The method of scoring KIM-1 immunohistochemistry staining is not clear. Is each tubular cross-section in the biopsy given a 0-3+ score and then averaged, or is each biopsy simply graded as 0-3+? The actual data for KIM-1 staining compared to biopsy diagnosis is not provided, so this is difficult to interpret.

Minor Essential Revisions
1. The graphs in Figure 1 are difficult to read due to the low resolution. This needs to be improved.

2. Some low power views of the biopsy tissue should be provided in Figure 2 since it is very difficult to see why 2(a) was scored 3+ while 2(b) was considered only 2+. Similarly, all of the tubules are positive in 2(c), but this is only scored as 1+.

3. It is important to discuss the data in term of the enormous variation in KIM-1 mRNA levels in biopsy samples (over a 3 log range) and in urine sediment cells (2 log range), and the great overlap in KIM-1 mRNA levels in biopsy tissue from AR, ATN and IF/TA. This type of data makes it difficult to see how measuring KIM-1 could possible distinguish between these quite different causes of graft dysfunction.

4. Please clarify the statistical analysis used to find that KIM-1 mRNA levels in biopsies from IF/TA are higher than in AR.

5. It is important to discuss whether the current manuscript provides any new findings compared to the previous 2 papers on this topic by the authors.
6. The phrase “molecular expressions” does not mean anything. I suggest using “mRNA levels”.

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I have no competing interests.