Author’s response to reviews

Title: Histological diagnosis of immune checkpoint inhibitor induced acute renal injury in patients with metastatic melanoma: a retrospective case series report

Authors:

Sebastian Hultin (sebastian.hultin@doctors.org.uk)
Kazi Nahar (kazi.nahar@melanoma.org.au)
Alexander M Menzies (alexander.menzies@sydney.edu.au)
Georgina V Long (georgina.long@melanoma.org.au)
Suran L. Fernando (susan.fernando@health.nsw.gov.au)
Victoria Atkinson (victoria.atkinson@health.qld.gov.au)
Jonathan Cebon (j.cebon@onjcri.org.au)
Muh Geot Wong (muhgeot.wong@sydney.edu.au)

Version: 2 Date: 16 Jul 2020

Author’s response to reviews:

Dr Hayley Henderson
Editor-in-Chief
BMC Nephrology

Dear Dr Henderson,

We thank you for the reviewers’ constructive comments. Based on these comments, we have revised the manuscript titled “Histological diagnosis of immune checkpoint inhibitor induced acute renal injury in patients with metastatic melanoma: a retrospective case series report” and have listed the itemised changes blow.

Please find attached a document with tracked changes alongside a clean version.

The revised manuscript has been seen, reviewed and approved by all contributing authors. I hope this will meet your editorial approval.

Sincerely yours,

Dr Sebastian Hultin

Renal Fellow Royal North Shore Hospital
Reserve Road. St Leonards NSW2065.
We agree with reviewer’s comments highlighting selection bias and possible high rate of losses of patients with AKI attributable to other causes. Although we took every effort to identify patients with Renal IrAE through close collaboration with our oncology colleagues, case identification ultimately relied on the presence of a creatinine rise >50% not attributable to other causes than immunotherapy and subsequent referral to our nephrology service.

In order to address the reviewers concerns of selection bias and to moderate the conclusion about interstitial nephritis, the statement of limitations has been expanded page 12 line 15-17. The conclusion has been changed to specify interstitial nephritis to apply to biopsy proven renal IrAE and acknowledging the potential for selective bias to miss other causes of kidney injury. (section page 12 line 31-41)

Recovery from AKI was defined as recovery of all renal dysfunction or return to pre-renal IrAE baseline kidney function. This has been added into methods section. Page 4 line 29-31.

Consistent with KDIGO I criteria, a creatinine rise of >26umol/L has been added into the methods section page 4 line 16-17.