

Rechallenge in Immune Checkpoint Inhibitors Associated Renal Tubular Acidosis



To the Editor: In this journal, we recently reported a novel form of renal tubular acidosis (RTA), which we termed Type V RTA, associated with immune checkpoint inhibitors (ICIs).¹ We demonstrated that ICI-associated RTA was a unique immune-related adverse event.

Rechallenge with an ICI in more common kidney-limited immune-related adverse events, such as interstitial nephritis, has been debated but may be acceptable on the basis of risks and benefits.² However, little is known about rechallenge in a rare immune-related adverse event, such as ICI-associated RTA. Here, to the best of our knowledge, we report the first case of ICI rechallenge in ICI-associated RTA.

A 46-year-old woman with metastatic lung cancer and squamous cell cancer of the tonsil developed RTA after 6 months of anti-programmed death-1 (PD1) immunotherapy, pembrolizumab, that resolved after

pembrolizumab discontinuation, as reported previously.¹ One year later, the patient developed a progression of her disease. Because of the excellent antitumor response to ICI therapy previously, the decision was made to treat her with a different ICI anti-PD1 immunotherapy, nivolumab. During 8 months of follow-up, she has not developed recurrent Type V RTA (Figure 1).

Our findings highlight 2 important findings. First, ICI rechallenge with a different ICI may be safe and not result in the recurrence of the RTA. Second, the finding that one ICI, but not another, both of which had anti-PD1 actions, induced RTA suggests that this effect may be an idiosyncratic effect and not a direct effect of the anti-PD1 action on kidney tubules. We speculated previously that interference of the proximal tubule ammoniogenesis as the likely mechanism of ICI-induced Type V RTA.¹ Still, the factors leading to such a condition that only affects certain patients remain unidentified. Further studies are warranted to better understand the pathophysiological mechanism of this condition.

1. Shah CV, Lee HW, Clapp WL, Weiner ID. A novel form of renal tubular acidosis associated with immune checkpoint

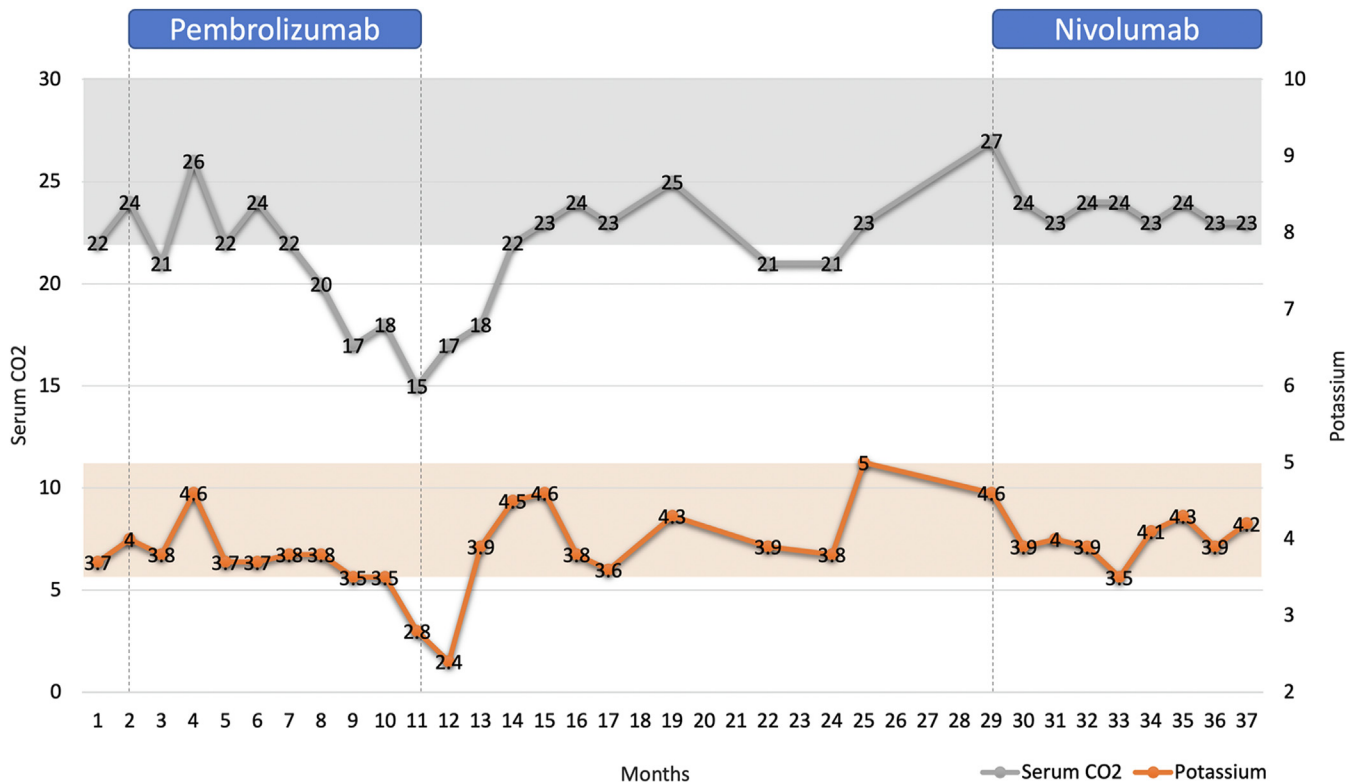


Figure 1. Rechallenge with a different immune checkpoint inhibitor (ICI) anti-PD1 immunotherapy, nivolumab, did not lead to a recurrence of ICI-associated renal tubular acidosis (ICI-RTA).

inhibitors. *Kidney Int Rep.* 2023;8:197–201. <https://doi.org/10.1016/j.ekir.2022.10.019>

2. Shirali AC. Is rechallenge appropriate in patients that develop immune checkpoint inhibitor-associated AKI?: commentary. *Kidney360.* 2022;3:806–808. <https://doi.org/10.34067/KID.0005592021>

Chintan V. Shah¹ and I. David Weiner^{1,2}

¹Division of Nephrology, Hypertension, and Renal Transplantation, University of Florida College of Medicine, Gainesville, Florida, USA and ²Nephrology and Hypertension Section, Gainesville VAMC, Gainesville, Florida, USA

Correspondence: Chintan V. Shah, Division of Nephrology, Hypertension, and Renal Transplantation, University of Florida College of Medicine, 1600 SW Archer Road, Room CG-98, Gainesville, Florida 32610, USA. E-mail: shahc@ufl.edu

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