

Renal side-effects of immune checkpoint inhibitors and their therapeutic consequences in patients with malignancies

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Background

Immune checkpoint inhibitors (ICIs) are a novel group of immune stimulating drugs that rapidly has improved the outcome of several malignancies. With the increasing use of ICI treatment, Immune-related Adverse Events (irAEs) are becoming an important challenge for clinicians. IrAEs can affect all organ systems, including the kidneys. An important question is whether or not patients can continue ICI treatment when severe renal irAEs occur.

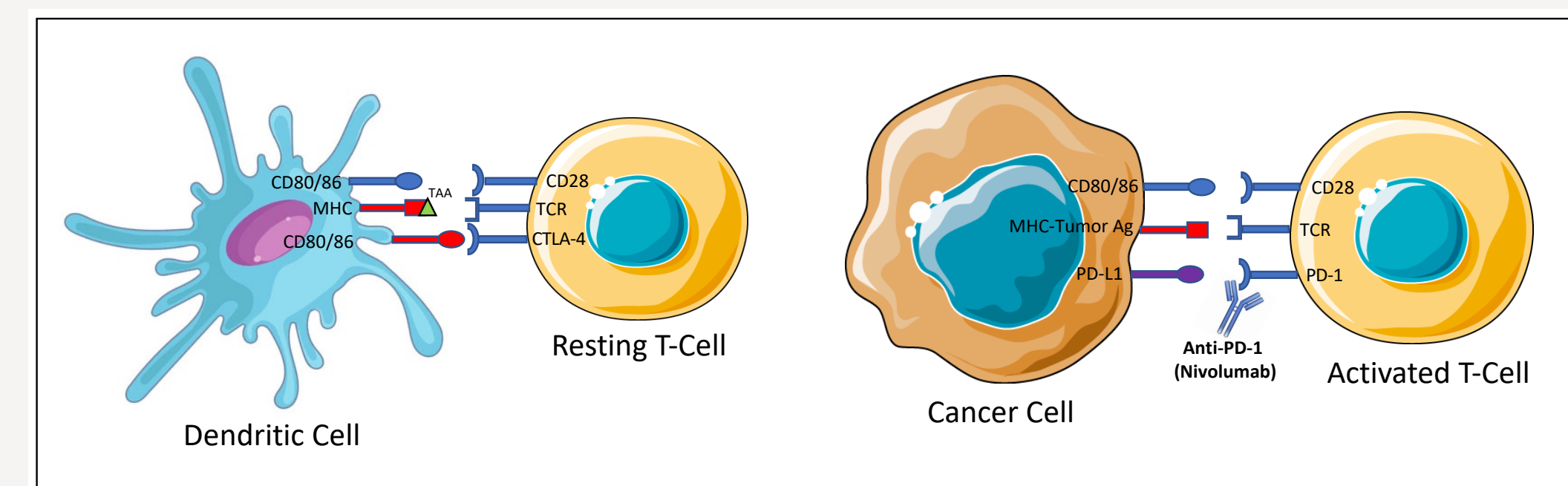


Figure 1 Effect of ICI on T-Cell: Antigen-presenting cells, like Dendritic cells, presents tumor associated antigens (TAA) to the T-cell receptor (TCR) of a T-lymphocyte. Interaction between TTA and TCR as well as co-stimulation by CD28 to CD80/86 lead to activation of the T-cell. In peripheral tissue, the activated T-cell can be de-activated by binding between PD-1 and PD-L1. PD-L1 can be found on cancer cells. Nivolumab is an Anti-PD-1 which target the PD-1 so the cancer cell can't de-activate the T-cell.

Method

Literature search: We used databases like UpToDate and Cochrane to find general information about the topic, followed by a more thorough search in PubMed to find more published literature that gave information about the research question. Guidelines from KDIGO, NCCN, CTCAE and ASCO was also used to give an overview of the current recommended handling of renal irAEs.

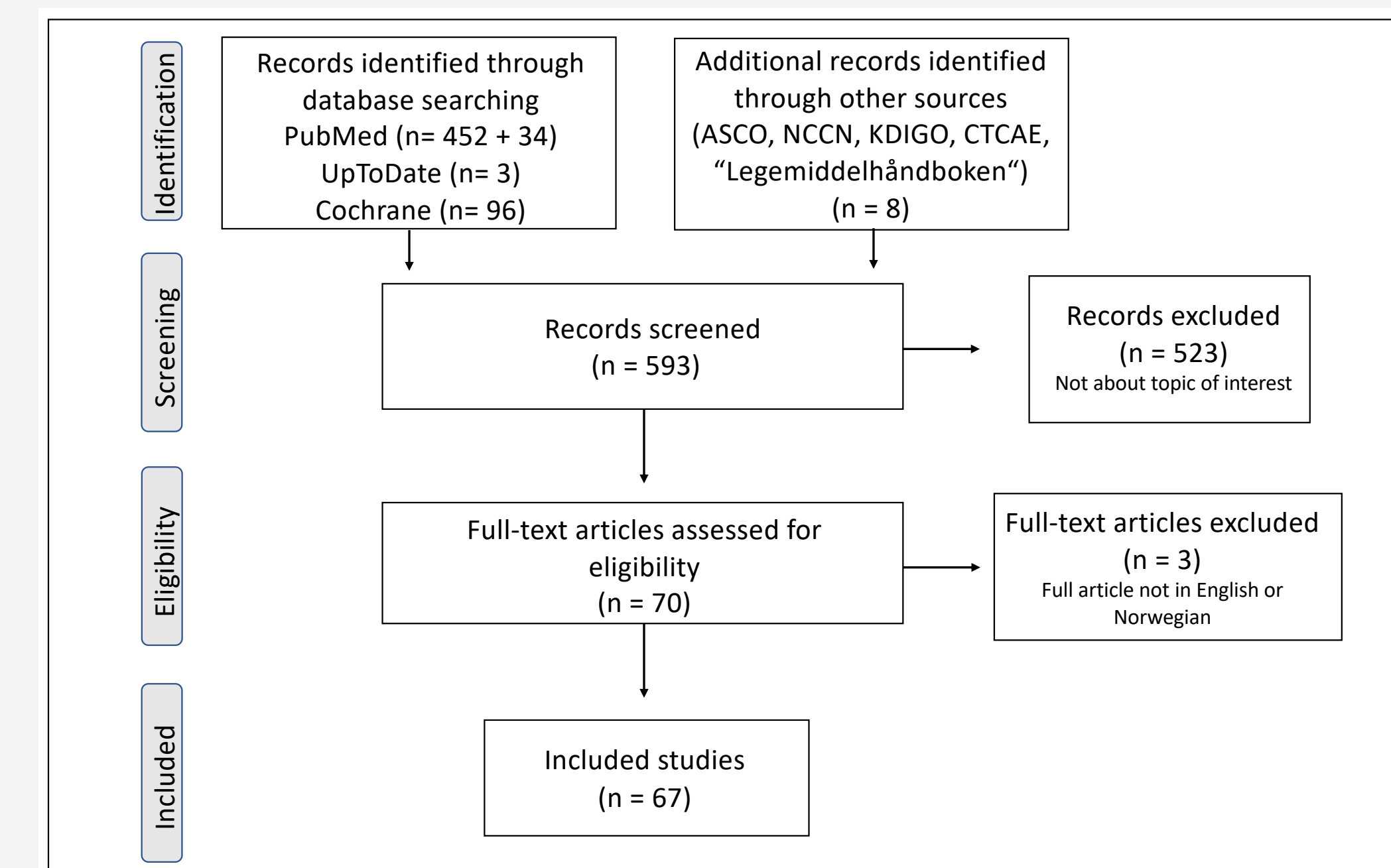


Figure 2 Flow chart of literature search process: The search led to 67 articles being picked out as relevant for the research question.

Results

Renal irAEs usually presents as acute kidney injury (AKI), with the most common histological finding being acute interstitial nephritis (AIN). It is routine to stop ICI treatment and empirically start steroid treatment when renal irAEs are suspected. Rechallenge is usually considered when low grade AKI occur and when the initial renal irAE have resolved. The literature largely supports rechallenge of ICI treatment.

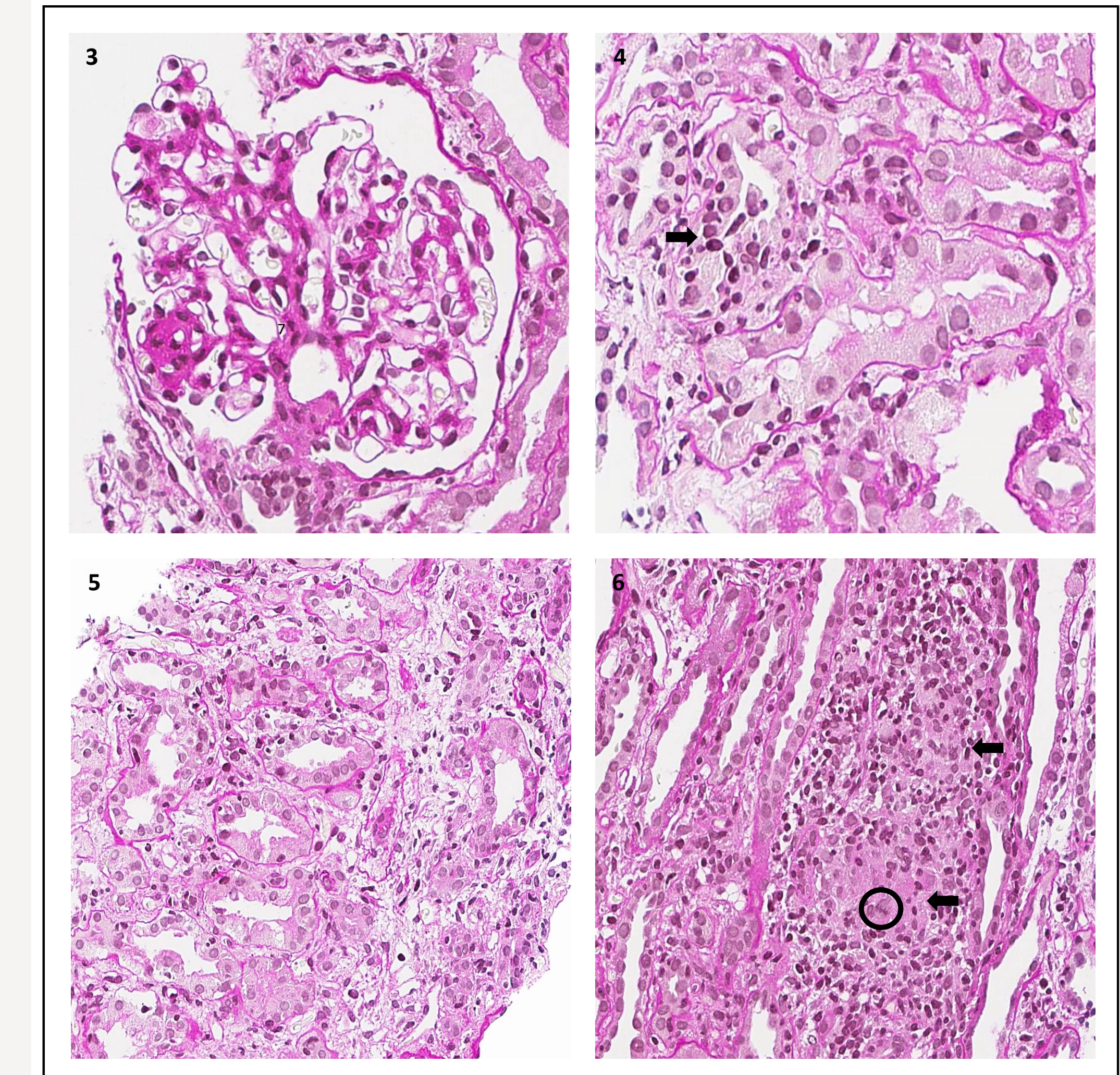


Figure 3 Histology of kidney biopsy with Periodic acid schiff staining: Picture 3 shows a normal glomerulus which means there are no sign of glomerulonephritis. The arrow in picture 4 points at lymphocytes invading the epithel cells of a tubuli causing a tubulitis, as well as breaking the basal membrane and entering the lumen of the tubuli. Picture 5 shows general invasion of inflammatory cells and edema in the tissue. The two arrows in picture 6 shows two granulomas, and the circle shows a mitosis.

Conclusion

The published literature shows significant renal irAEs and rechallenge of ICI treatment after renal irAEs has shown that treatment can be re-continued with acceptable safety.

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