

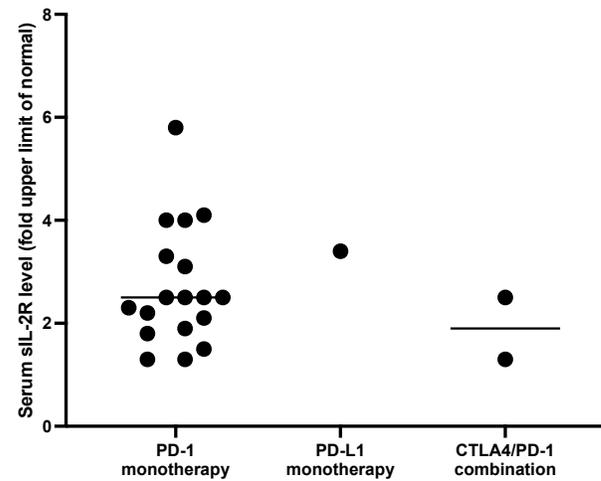
Supplemental Figure 1. sIL-2R levels of ICI-nephritis cases by ICI class

Figure S1. sIL-2R levels of ICI-nephritis cases by ICI class. PD-1 monotherapy includes cemiplimab, nivolumab and pembrolizumab; PD-L1 monotherapy includes atezolizumab; CTLA-4/PD-1 combination includes ipilimumab/nivolumab. Symbols represent unique individuals; bars represent median.

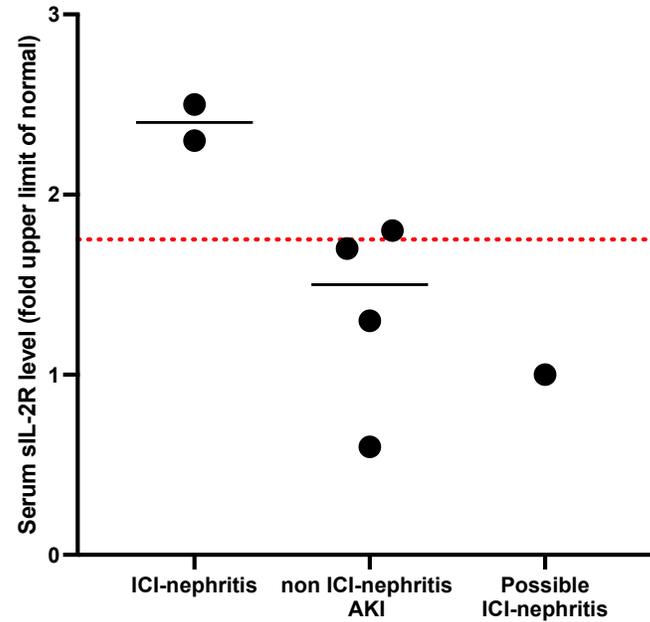
Supplemental Figure 2. External validation cohort for diagnostic performance of sIL-2R in ICI-treated patients who developed AKI

Figure S2. External validation cohort for diagnostic performance of sIL-2R in ICI-treated patients who developed AKI. ICI-nephritis include biopsy-proven ICI-nephritis (N=1) and clinically adjudicated ICI-nephritis (N=1); non ICI-nephritis AKI include biopsy-proven acute tubular necrosis (N=1) and clinically adjudicated hemodynamic AKI (N=3).

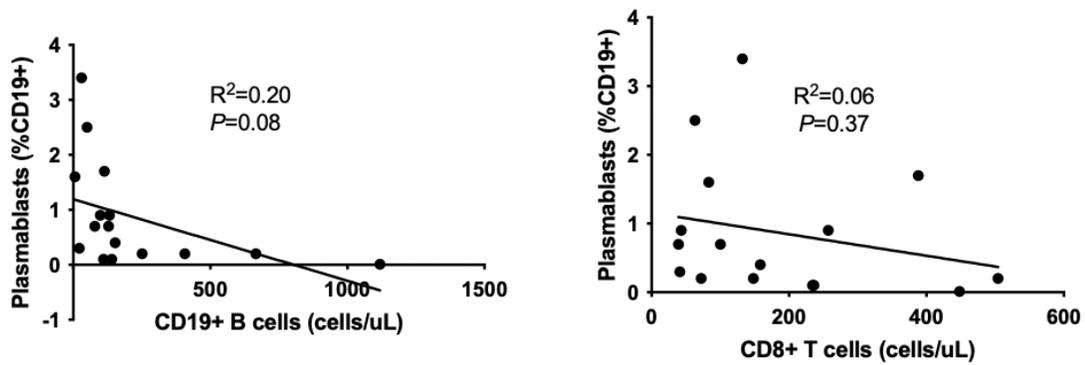
Supplemental Figure 3. Linear correlation between B cell phenotypes and CD8+ T cells and within different B cell phenotypes

Figure S3. Linear correlation between percentage of plasmablasts and total CD19+ B cell count (left), percentage of plasmablast and CD8+ T cells (right). Symbols represent unique individuals; straight line represents fitted regression line; R^2 and P values are indicated in the graphs.

Supplemental Figure 4. Comparison of sIL-2R level, peripheral T and B cell markers in patients with ICI-nephritis who were diagnosed with kidney biopsy and who were diagnosed by clinical adjudication

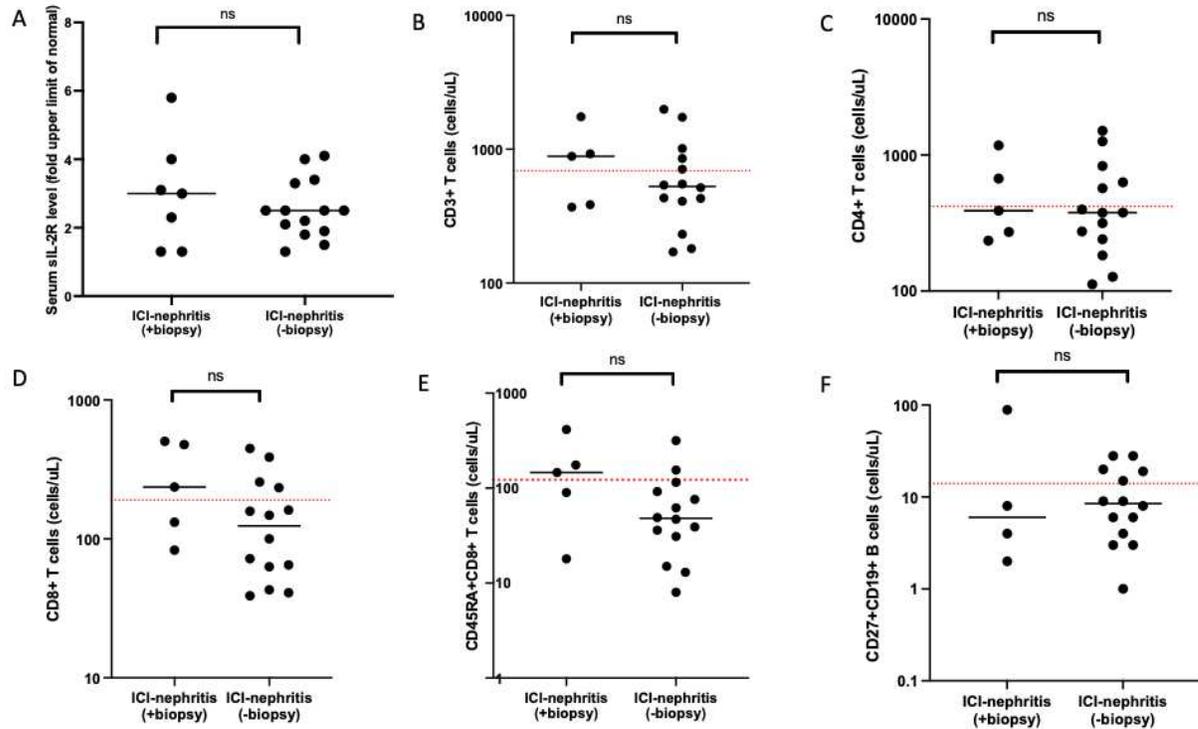


Figure S4. (A) Fold ULN of serum sIL-2R level were compared between patients with ICI-nephritis (N=7) who were diagnosed with kidney biopsy and who were diagnosed by clinical criteria (N=14). (B–F) Absolute total lymphocyte counts as indicated (cells/uL), shown in log scale, were compared between patients with ICI-nephritis who were diagnosed with kidney biopsy (N=5) and who were diagnosed by clinical criteria (N=14) who received concurrent chemotherapy (N=4). Symbols represent unique individuals; bars represent geometric means (95% confidence intervals) of total indicated patients; red dotted line represent lower limit of normal of the assay. ns=non-significant

Supplemental Figure 5. Comparison of peripheral T and B cell markers in patients with ICI-nephritis who received concurrent chemotherapy with ICI or who received ICI therapy alone

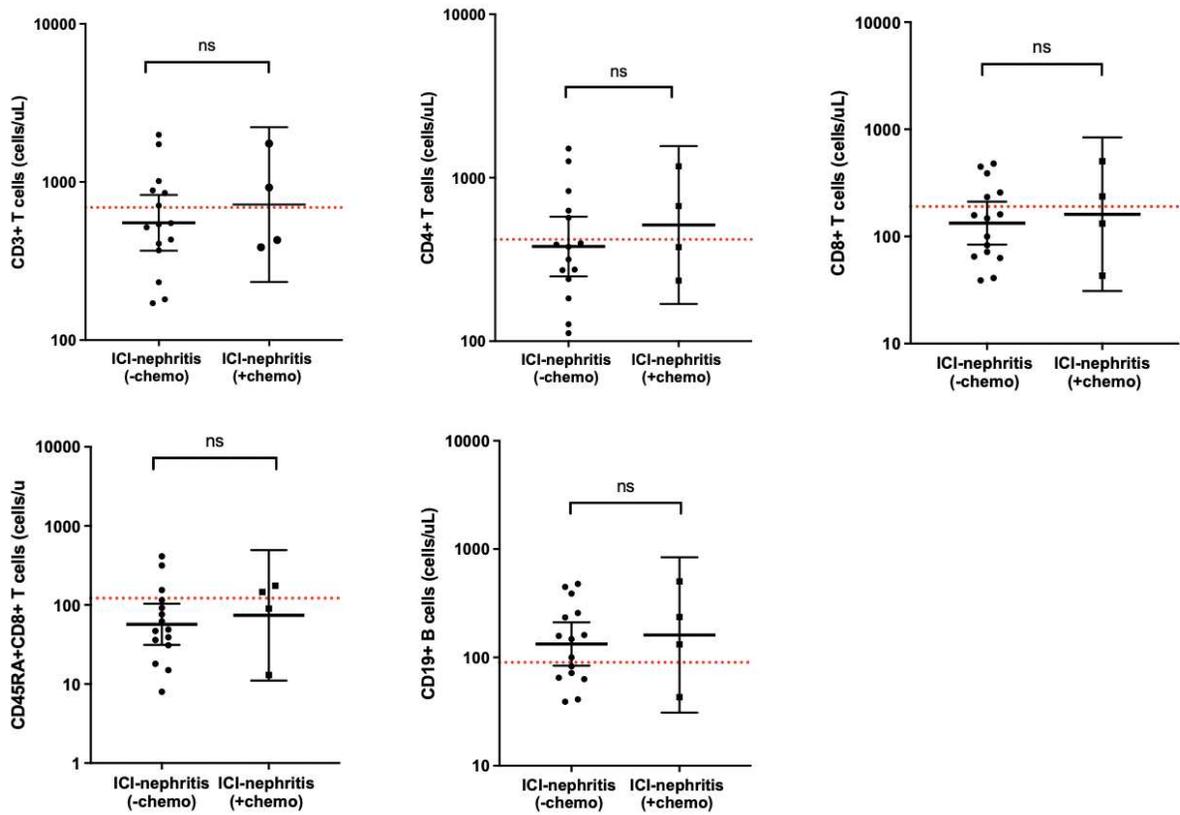


Figure S5. Absolute total lymphocyte counts as indicated (cells/uL), shown in log scale, compared between patients with ICI-nephritis who were treated with ICI alone (N=15) and who received concurrent chemotherapy (N=4). Symbols represent unique individuals; bars represent geometric means (95% confidence intervals) of total indicated patients; red dotted line represent lower limit of normal of the assay. ns=non-significant.

Supplemental Table 1. Case summaries for hemodynamic AKI control group

Patient ID	Age/race	Baseline creatinine (mg/dL) ^a	Peak creatinine (mg/dL)	sIL-2R (fold ULN)	Diagnosis
1	80-90 yo HF	1.3	3.0	1.1	Cardiorenal syndrome
2	70-80 yo WM	1.2	Required RRT	1.7	Ischemic ATN
3	40-50 yo WF	0.7	2.3	0.5	Myoglobin cast nephropathy
4	50-60 yo AM	1.5	3.4	0.8	Ischemic ATN
5	50-60 yo BM	1.0	4.4	1.0	Ischemic ATN
6	70-80 yo HM	1.4	1.9	0.7	Ischemic ATN

Table S1. Case summaries for hemodynamic AKI control group. a. case 3,4 and 6 do not have pre-AKI creatinine available within 90 days. Their baseline creatinine was imputed from creatinine nadir during hospitalization. Age ranges in 10-year intervals are used to protect patients' confidentiality. Abbreviations: sIL-2R=soluble interleukin 2 receptor; HF=Hispanic female; WM=White male; WF=White female; AM=Asian male; BM=Black male; HM=Hispanic male; RRT=renal replacement therapy; AKI=acute kidney injury; ATN=acute tubular necrosis; CKD=chronic kidney disease

Supplemental Table 2. Case summaries for non-ICI AIN group

Patient ID	Age/race	Baseline creatinine (mg/dL)	Peak creatinine (mg/dL)	sIL-2R (fold ULN)	Diagnosis
1	50-60 yo WF	0.8	1.6	1.2	TINU syndrome
2	70-80 yo AM	1.5 ^a	5.3	4.1	IgG4-related disease
3	30-40 yo WF	0.9	2.7	2.5	TINU syndrome
4	30-40 yo WF	0.9	1.1	2.8	TINU syndrome
5	70-80 yo BM	3.0	4.5	1.6	PPI-associated AIN

Table S2. Case summaries for non-ICI-nephritis group. a. case 2 does not have pre-AKI baseline creatinine available within 90 days. Baseline creatinine was imputed from creatinine nadir during follow-up course. Age ranges in 10-year intervals are used to protect patients' confidentiality. Abbreviations: sIL-2R=soluble interleukin 2 receptor; WF=White female; AM=Asian male; BM=Black male; TINU=tubulointerstitial nephritis and uveitis syndrome; PPI=proton pump inhibitor; AIN=acute interstitial nephritis

Supplemental Table 3. Genes included in IL-2 family pathway score and T cell receptor pathway score

IL-2 family pathway score	T cell receptor pathway score	
<i>HAVCR2</i>	<i>CD247</i>	<i>IL5</i>
<i>IL15</i>	<i>CD28</i>	<i>INPP5D</i>
<i>IL2</i>	<i>CD3D</i>	<i>JUN</i>
<i>IL21</i>	<i>CD3E</i>	<i>LCK</i>
<i>IL21R</i>	<i>CD3G</i>	<i>LCP2</i>
<i>IL2RA</i>	<i>CD4</i>	<i>MAPK11</i>
<i>IL2RB</i>	<i>CD40LG</i>	<i>MAPK12</i>
<i>IL2RG</i>	<i>CD45R0</i>	<i>MAPK13</i>
<i>IL5</i>	<i>CD45RA</i>	<i>MAPK14</i>
<i>INPP5D</i>	<i>CD45RB</i>	<i>NFATC1</i>
<i>JAK1</i>	<i>CD8A</i>	<i>NFATC2</i>
<i>JAK2</i>	<i>CD8B</i>	<i>NFKB1</i>
<i>JAK3</i>	<i>CHUK</i>	<i>NFKBIA</i>
<i>LCK</i>	<i>CSF2</i>	<i>PDCD1</i>
<i>PIK3CD</i>	<i>CTLA4</i>	<i>PIK3CD</i>
<i>PTPN6</i>	<i>FOS</i>	<i>PPP3CA</i>
<i>STAT1</i>	<i>FYN</i>	<i>PSMB10</i>
<i>STAT3</i>	<i>HAVCR1</i>	<i>PSMB8</i>
<i>STAT4</i>	<i>HLA-DPA1</i>	<i>PSMB9</i>
<i>STAT5A</i>	<i>HLA-DPB1</i>	<i>PSME1</i>
<i>STAT5B</i>	<i>HLA-DQA1</i>	<i>PSME2</i>
<i>SYK</i>	<i>HLA-DQB1</i>	<i>PTPN22</i>
	<i>HLA-DRA</i>	<i>PTPN6</i>
	<i>HLA-DRB1</i>	<i>PTPRC</i>
	<i>HLA-DRB3</i>	<i>RAF1</i>
	<i>ICOS</i>	<i>RELA</i>
	<i>IFNG</i>	<i>SLA</i>
	<i>IKBKB</i>	<i>TNF</i>
	<i>IKBKG</i>	<i>TRAF6</i>
	<i>IL10</i>	<i>TRAT1</i>
	<i>IL2</i>	<i>TRDC</i>
	<i>IL4</i>	<i>TRDV3</i>
		<i>ZAP70</i>

Supplemental Table 3. The pathway score is equal to the first principal component of the gene set.

Supplemental Table 4. Case summaries for external validation cohort

Patient ID	Age/race	Baseline creatinine (mg/dL)	Peak creatinine (mg/dL)	Cancer Type	ICI therapy	sIL-2R (fold ULN)	Diagnosis
1	60—70 yo AM	0.9	3.3	SCC of larynx	Pembro	2.5	ICI-nephritis (biopsy proven)
2	70—80 yo WF	1.6	2.9	Sacral sarcoma	Pembro	2.3	ICI-nephritis (clinically diagnosed)
3	70—80 yo WM	1.1	1.8	Peritoneal mesothelioma	Ipi/nivo	1.8	ATN (biopsy proven)
4	60—70 yo WM	1.1	3.7	Lung adenocarcinoma	Pembro	0.6	Ischemic ATN (clinically diagnosed)
5	60—70 yo WF	1.2	2.2	Pleural mesothelioma	Ipi/nivo	1.7	Pre-renal AKI
6	60—70 yo HM	1.2	1.9	Metastatic RCC	Nivo	0.3	Pre-renal AKI
7	60—70 yo WF	0.9	1.4	Metastatic RCC	Ipi/nivo	1.0	Possible ICI-nephritis

Table S4. Case summaries for the external validation cohort. Age ranges in 10-year intervals are used to protect patients' confidentiality. Abbreviations: sIL-2R=soluble interleukin 2 receptor; AM=Asian male; WF=White female; WM=White male; HM=Hispanic male; SCC=squamous cell cancer; RCC=renal cell carcinoma; pembro=pembrolizumab; ipi/nivo=ipilimumab/nivolumab; AKI=acute kidney injury; ATN=acute tubular necrosis