JASN
Journal of the American Society of Nephrology
Kidney Week Edition

ABSTRACT Supplement

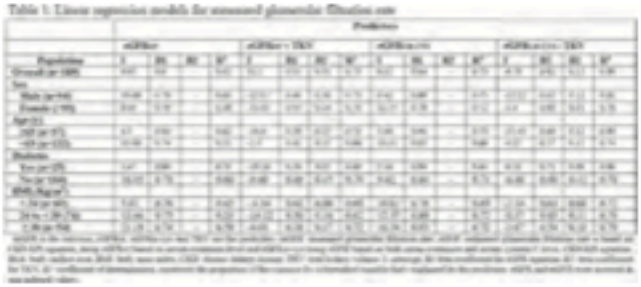
KIDNEY WEEK 2021

Methods: We enrolled 181 cancer patients treated at an academic tertiary cancer hospital in Brazil (Instituto do Câncer do Estado de São Paulo), who had undergone abdominal imaging and measurement of GFR by plasma clearance of 51Cr-EDTA within 60 days. eGFR was determined based on the CKD-EPI equation using Scr (eGFRcr) and Scr combined with Scys (eGFRcr-cys). eGFR and mGFR were non indexed for body surface area. Total kidney volume (TKV) was measured using a semi-automatic segmentation program, excluding non-functional tissues. The correlations between mGFR and TKV as well as mGFR and eGFR were calculated using the Pearson correlation coefficient. Linear regression models for mGFR having TKV and eGFR equations as predictors were built.

Results: Patients were 55 (14.0) y, 50.3% male. Most common cancer sites were breast (22.7%), male genital (21.8%) and gastrointestinal (20.9%). ECOG levels 0/1 corresponded to 95% of patients. Mean (SD) Body mass index was 27.18 (5.18). Mean (SD) mGFR, eGFRcr and eGFRcr-cys were 84.8(27.23), 90.4 (24.9), and 83.8 (25.9), ml/min, respectively. Mean (SD) TKV for both kidneys was 302.2 (77.9) cm3. PCC for mGFR-TKV, mGFR-eGFRcr and mGFR-eGFRcr-cys were 0.76, 0.78 and 0.85, respectively. TKV improved the coefficient of determination of the linear regression models when added to both eGFRcr and eGFRcr-cys, in overall and assessed subgroups (Table 1).

Conclusions: In conclusion, our results suggest that measurement of TKV is a reliable predictor of mGFR in cancer patients with the potential to be incorporated to the current eGFR equations used in clinical practice.

Table 1: Linear regression models for measured glomerular filtration rate



PO1889

Modifications of Renal Function in Cancer Patients Undergoing Repeated and Frequent Administrations of Iodinated Contrast Medium (CM): A Multicentric Retrospective Study from Italy

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Background: Contrast-enhanced computed tomography (CECT) is the imaging of choice for the diagnosis, staging, and follow-up of cancer patients, not to take into account its role to evaluate response to oncological treatments; in fact, it has been estimated that 47% of all CECTs are prescribed by Oncologists. Comorbidities, nephrotoxic concomitant medications, as well as chronic dehydration from different causes (nausea and vomiting, diarrhea, etc …) expose cancer patients to a higher risk of developing acute kidney injury (AKI) from CM. Risk factors, definition (PC-AKI vs CI-AKI) and preventive measures have been recently reconsidered, ultimately downsizing the incidence of this adverse event.

Methods: Aim of this study was to retrospectively assess the effects on renal function of repeated CM administrations in 407 oncological patients on active treatment, collected from 5 Italian oncology departments; patients should have undergone at least 3 CECT (on the average 3.5) within a single year (Fig I).

Results: According to our study, neither significant differences in eGFR values (calculated with the CKD-EPI formula) between the baseline and the different post-CECT timepoints, nor AKI cases (defined according to the RIFLE criteria), were recorded.

Conclusions: Repeated CM administrations in cancer patients did not lead to a worsening of renal function, confirming that CI-AKI has a significantly lower incidence than previously thought. Notably, 80% of the patients examined were found to be at low-risk, highlighting some kind of reluctance of Medical Oncologists and Radiologists to perform CECTs in these patients. On the contrary, the administration of CM could, and should, be freely used, in cancer patients, even in those at a higher risk.

Age	>65 <65	183 (45%) 224 (55%)
Sex	Male Females	228 (56%) 179 (44%)
Heart disease	Yes No Unknown	79 (19%) 274 (67%) 54 (13%)
Nephrectomy	Yes No	171 (42%) 236 (58%)
Diabetes	Yes No Unknown	73 (18%) 313 (77%) 21 (5%)
Hypertension	Yes No Unknown	195 (48%) 196 (48%) 16 (4%)
Kidney failure	Stages I and II Stadio IIIa Stadio IIIb Stage IV Stage V	281 (69%) 85 (21%) 33 (8%) 8 (2%) 0 (0%)
Type of Tumor	Genitourinary Gastro-intestinal Lung Head-neck Cute Udder Other	199 (49%) 57 (14%) 45 (11%) 3 (0,8%) 16 (4%) 41(10%) 46 (11, 2%)
Type of oncology therapy	Cytotoxic chemotherapy Drugs with molecular target Immunotherapy Hormone therapy	175 (43%) 184 (59%) 342 (55%) 16 (4%)

PO1890

Proliferative Glomerulonephritis with Monoclonal Immunoglobulin Deposits: Searching for the Underlying Clone

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Background: The pathophysiological mechanisms of proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID) are still largely unknown. Only 30% of PGNMID cases have a detectable circulating monoclonal immunoglobulin (Ig) and a bone marrow corresponding clone.

Methods: We reviewed a French cohort of PGNMID with particular focus on hematological characteristics. A high-throughput sequencing assay from bone marrow and/or blood mRNA encoding immunoglobulins (RACE-RepSeq) was used to detect the underlying clone.

Results: Seventy-one patients (M/F ratio=1.6, median age 59 years) were included. At diagnosis, 73% had renal insufficiency (median serum creatinine=1.7 mg/dL). All patients had proteinuria, with nephrotic syndrome in 59% and microscopic hematuria in 85% of cases. No patient had extra-renal manifestations. By light microscopy, kidney biopsy revealed membranoproliferative glomerulonephritis (74%), mesangial glomerulonephritis (14%) or membranous glomerulonephritis (12%). By immunofluorescence (IF), deposits stained for IgG in 55 cases (mostly IgG3κ), IgM in 7 cases, IgA in 4 cases or light chain (LC) only in 5 cases. Serum and/or urine immunofixation was positive in 26 cases (37%). An underlying clone was found in 21 cases (30%) using bone marrow or blood flow cytometry analysis. The clonal detection rate was particularly low in IgG3κ-PGNMID (9%). The nature of the clone differed with PGNMID subtype: lymphoplasmacytic in IgM-PGNMID, and plasmacytic in IgA/LC-PGNMID. RACE-RepSeq analysis failed to detect a bone marrow or blood clone in 18/26 cases (IgG3κ-PGNMID, n=17; IgGAκ-PGNMID, n=1). IF analysis of kidney samples using anti-Vκ antibodies showed positive staining for Vκ1, Vκ2, Vκ3 and Vκ4 in 3/3 tested IgG3k-PGNMID patients without a detectable clone, whereas deposits stained only for Vκ2 in one IgG1k-PGNMID patient who had a bone marrow Vκ2 clone by RACE-RepSeq analysis.

Conclusions: These results suggest that PGNMID is a heterogeneous medical condition and that some cases might involve oligoclonal production of nephrotoxic Ig restricted to the IgG3k isotype. Such cases should no longer be classified as MGRS.

PO1891

Rituximab-Associated Flare of Cryoglobulinemic Vasculitis

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Background: Patients with cryoglobulinemic vasculitis (CV) can develop disease flare after rituximab administration. The pathogenesis is hypothesized to be from immune complex deposition in the microvasculature, wherein the immune complex consists of the involved cryoglobulin and an antigenic portion of rituximab. Our objective was to describe the prevalence, clinical characteristics, predisposing factors, and outcomes of rituximab-associated flare of CV.

Conclusions: Our study surprisingly highlights that both cisplatin/carboplatin-based CT and immunotherapy display a similar incidence of AKI and eGFR decay over time in NSLCL metastatic patients

PO1881

AKI with BRAF and MEK Inhibitors May Not Be a Class Effect

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Introduction: BRAF tyrosine kinase inhibitors are used in the treatment of BRAF mutant metastatic melanoma. Simultaneous MEK inhibition has been shown to have better response rates and fewer side effects. Renal toxicity has been reported with these agents which can include AIN, ATN and Fanconi syndrome. We report a case of AKI due to biopsy proven AIN from BRAF and MEK inhibitor vemurafenib and cobimetinib

Case Description: This is a 64-year-old woman with diabetes mellitus type 2, stage IV melanoma with BRAF V600E mutation and baseline serum creatinine (SCr) of 0.8 (0.6-1.1) mg/dL. She has been treated with multiple chemotherapy regimens and immunotherapy (last dose of immunotherapy 28 months prior to presentation). Patient received reduced dose dabrafenib and trametinib until 8 months prior to presentation but stopped due to development of fever and AKI (SCr 1.7mg/dL). She was started on vemurafenib 480 mg BID every other day and cobimetinib 40mg every other day 6 ½ months before presentation. Two months later the vemurafenib dose was increased to 960mg BID but patient was noted to have AKI with SCr of 4.5 mg/dl and vemurafenib and cobimetinib were stopped. Her blood pressure was elevated to 154/70 mmHg. Urinalysis showed protein of 100 mg/dL, 0-3 RBC/HPF and 0-6 WBC/HPF. SCr improved to 2.2 mg/dL but remained elevated and renal consult was obtained with subsequent kidney biopsy. It showed active, subacute, and chronic interstitial nephritis with extensive tubular atrophy. Patient was treated with prednisone 50 mg daily and was tapered down to 10 mg daily over two months. Repeat CT scan showed new peritoneal nodules and she was started on a new BRAF/ MEK combination of encorafenib and binimetinib. She is currently tolerating these medications with SCr stable at 1.5mg/dl.

Discussion: BRAF and MEK inhibitors are associated with AKI secondary to ATN and AIN. In the above case, the patient developed AIN with vemurafenib and cobimetinib which were discontinued resulting in significant improvement in kidney function. Due to progression of disease she was started on encorafenib and binimetinib which she is tolerating well. This case demonstrates that renal toxicity from BRAF and MEK inhibitor may not be a class effect and may also be dose dependent. It may be possible to consider a dose reduction or switch to another medication in the same class if renal toxicity is noted.

PO1882

Acute Proteinuric Renal Failure in a Lung Cancer Patient Treated with Poziotinib: First Case Described in the Literature

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Introduction: The therapeutic approach to non-small cell lung cancer (NSCLC) has changed significantly in recent years: genomic drivers have enabled the development of new molecularly targeted therapies. The improvements obtained in the survival of these patients, the adverse events related to these novel treatments should not be forgotten. Poziotinib is a new generation tyrosine kinase inhibitor which has been recently registered for the treatment of patients with EGFR/HER2 exon 20 insertion mutation.

Case Description: In 2017, a 58-year-old woman was diagnosed with a pT2, N2, M0, G2 NSCLC for which she was surgically treated with lobectomy and lymphadenectomy, followed by adjuvant CT; and after metastatic relapse, further CT until July 2020. Upon progression, she started Poziotinib. She was referred to us due to the occurrence of hypomagnesemia, hypokalemia and proteinuria (2.8 g/24 h), despite a normal renal function., The objective examination and blood tests were all normal, and the patient did not report any symptom. Due to a quick worsening of renal function (sCr 2 mg/dl), and in particular of proteinuria (3.3 g/24 h), Poziotinib was stopped and dexamethasone 4 mg/day was started. Examinations for glomerulopathies were not diriment; a renal biopsy was performed in order to guide therapeutic decisions. The histological picture showed incomplete glomerular sclerosis (5/15 glomeruli), outbreaks of tubulointerstitial sclero-atrophy, as well as interstitial inflammatory lymphoplasmacytic infiltrate; immunofluorescence was negative for all antisera, while electron microscopy is presently still in progress. Following the discontinuation of Poziotinib, a progressive improvement of AKI and a reduction of proteinuria (1.3 g/24 h) was observed, allowing to hold the drug accountable, in the absence of any other risk factor, for the renal AE observed. From a histological viewpoint, nephroangiosclerosis was documented, but steroidal therapy may have hidden peculiar glomerular lesions. Poziotinib wasn't resumed.

Discussion: This is the very first case of renal toxicity from Poziotinib treatment reported so far. Cases like this highlight the need for both a nephro-oncological evaluation as well as for dedicated paths to perform rapid renal biopsies in order to characterize these events and improve their management.

PO1883

Enfortumab Vedotin-Induced Diabetic Ketoacidosis and AKI: A Case Report

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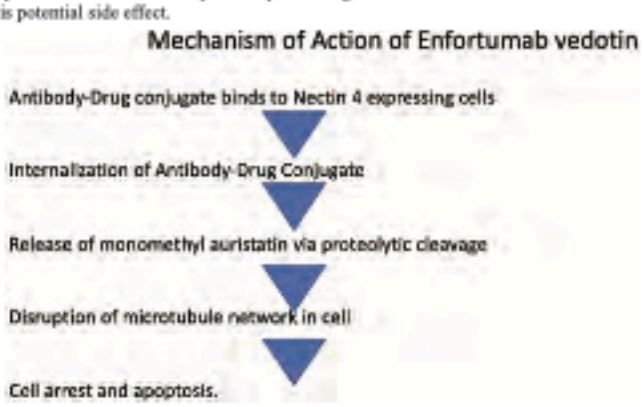
Introduction: Enfortumab vedotin is a novel antineoplastic agent in the management of advanced urothelial cancers. While hyperglycemia has been reported, diabetic ketoacidosis and AKI are rare.

Case Description: A 69-year-old male with history of metastatic urothelial cancer (treated with carboplatin/gemcitabine and Nivolumab) and CKD who presented to hospital one week after receiving Enfortumab with Diabetic Ketoacidosis (DKA) and AKI with Cr of 3.6mg/dL (Baseline 1.8mg/dL). Urine microscopy revealed granular casts consistent with tubular injury. Patient remained hyperglycemic despite titrating dose of IV regular insulin and subsequently developed shock, toxic epidermal necrolysis, and worsening renal failure with anuria requiring continuous renal replacement therapy. Despite maximal support, patient passed away.

Discussion: Enfortumab vedotin comprises antinectin-4 antibody and a microtubule-disrupting agent monomethyl auristatin E (MMAE). The drug binds to Nectin-4, expressed on tumor cells, with high affinity, which induces the internalization of MMAE and leads to subsequent cell apoptosis through impaired cell division. Dermatologic toxicity occurs from drug binding to Nectin-4 expressed on normal skin cells. AKI was reported in 1% of patients of the phase 2 trial but not in the phase 3 trial. Nectin-4 protein is expressed and can be stained in renal tubular epithelial cells. While DKA may have contributed to our patient's tubular injury, direct tubular toxicity may be possible and requires further research. Physicians prescribing Enfortumab vedotin should be aware of this potential side effect.



PO1884

An Elevated Serum Creatinine in a Patient Receiving Palbociclib

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Introduction: Serum Creatinine (SCr) is the most widely used parameter in clinical practice to estimate glomerular filtration rate (GFR). Various drugs have been reported to cause a reversible and transient elevation in SCr without a true reduction in overall kidney function

Case Description: A 66-year-old woman with a past medical history of metastatic right breast poorly differentiated invasive ductal carcinoma, hormone receptor-positive, and HER2 negative. Who received treatment with fulvestrant and palbociclib, the dose of Palbociclibwas was 100mg orally a day. Presented for evaluation of elevated serum creatinine with decreased eGFR. On initial evaluation sCr was 1.6mg/dl, blood urea nitrogen of 21mg/dl, eGFR of 33ml/min/1.73m^2, her baseline eGFR was ranging from 42 to 52 ml/min/1.73m^2 in the past one year. An estimated glomerular filtration rate by cystatin C was performed and showed a value of 47ml/min with a cystatin-C level of 1.36mg/dl, which was at her baseline kidney function for the past year.

Discussion: Creatinine is freely filtered by the glomerulus and actively secreted by the proximal tubule from the peritubular capillaries, which accounts for 10-40% of creatinine clearance. The organic cation transporter 2 (OTC2), multidrug and toxin extrusion protein (MATE) 1 and MATE2-K, are the solute carrier transporters in the kidney that mediate this active tubular secretion. Clinical studies of abemaciclib, another selective inhibitor of CDK 4/6, have shown a reversible increase in creatinine of about 15-40% over baseline of patients with cancer and healthy subjects. This effect has been seen in about 25% of patients treated with abemaciclib however none of the clinical trials on palbociclib have