BOOK OF ABSTRACTS

All abstracts listed in C-KIN 2015 Book of Abstracts have been assigned a prefix for the type of presentation, and a sequential abstract number. The authors' whose names are in bold are the presenting authors.

Poster abstracts have been divided in 8 topics as follows:

1. Case reports
2. Epidemiology
3. Complications Cancer/ CKD
4. Complications Treatments
5. Treatment in Cancer & CKD patients
6. Transplantation & Urology
7. eGFR, equations and measurements
8. Genomics and genetics

Hanging and removal of paper board posters

Poster boards will be marked with the final abstract numbers.

**Poster mounting time:** Tuesday, 14 April as of 07:30. Posters need to be mounted prior to Tuesday, 14 April at 12:00.

**Poster removal time:** Wednesday, 15 April, as of 14:00. Posters that have not been removed by 16:00 will be disposed of by the organisers.

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**OC 001 - Outcomes of Late Relapse Metastatic Renal Cell Carcinoma Patients Treated with Targeted Therapies**

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**Background**

Approximately 20-30% of patients with renal cell carcinoma (RCC) develop recurrence after treatment of localized disease. Of these patients, the great majority recur within the first few years following surgery. Rarely, late recurrences are seen after 5 years of disease-free survival. The outcome of metastatic Renal Cell Carcinoma has improved markedly with targeted therapies (TT). Little data is available about outcomes of patients with metastatic Renal Cell Carcinoma from late recurrences who are treated with TT.

**Method**

We retrospectively reviewed records of consecutive patients with metastatic Renal Cell Carcinoma who had late recurrence > 5 years and were treated with TT between 11/1/2006 and 11/1/2013. All the patients had prior nephrectomies. Outcomes were tabulated using basic statistical techniques. Adverse Events (AEs) were graded using CTCAE v4.0.

**Results**

25 patients (100% clear-cell, all with prior nephrectomies) met inclusion criteria with late recurrence > 5 years. 76% of patients had favourable risk and 24% had intermediate risk on MSKCC criteria. 11 pts died. Estimated median overall survival time for all patients was 60.5 months. The 3-year overall survival rate was 71.78%. The median number of sequential TT received was 2 (range 1-4). Median time on first line TT was 20.7 months. 41% of pts received pazopanib in the frontline setting, 26% received sunitinib, and 26% received sorafenib, and 7% received other TT. 68% received TT in the second-line and subsequent settings. Common adverse events of TT included fatigue (52%), diarrhea (36%), hypertension (36%), anorexia (28%), hair and skin changes (24%), increased liver function tests (20%), nausea/vomiting (16%), and 95% of adverse events were grade 1/2.

**Conclusion**

In this retrospective study, patients who were diagnosed with metastatic disease from RCC after disease free interval >5yrs have prolonged survival when treated with TT. Overall survival and 3-year survival rates were better than historical controls. Adverse events were mild/moderate and manageable.

**References**

1. Survival Outcome and Treatment Response of Patients with Late Relapse from Renal Cell Carcinoma in the Era of Targeted Therapy, Kroeger N. et al, Eur Urol. 2013 Jul 30

**OC 002 - Everolimus-Associated Acute Kidney Injury in Cancer Patients with Impaired Kidney Function**

**Ji Hyeon Park, Hye Ryoun Jang, Wooseon Huh, Yoon-Goo Kim, Dae Joong Kim, Ha Young Oh, Jung Eun Lee**

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**Background**

Everolimus was recently introduced as a second-line treatment for renal cell carcinoma (RCC) and many other cancers. Several prospective studies have shown that serum creatinine levels are increased in a significant proportion of patients receiving everolimus. However, data on the occurrence of acute kidney injury (AKI) during everolimus treatment in clinical practice are sparse. Here, we report the incidence, risk factors, and clinical significance of AKI associated with everolimus treatment in patients with cancer.
Method
We analyzed patients who received everolimus for more than 4 weeks as an anticancer therapy. AKI was defined as increase in creatinine levels from baseline levels greater than 1.5-fold.

Results
The majority of the 110 patients enrolled in this analysis had RCC (N = 93, 84.5%). AKI developed in 21 (23%) RCC patients; none of the patients (N = 17) with other cancers had AKI. Fourteen of 21 cases were considered to be everolimus-associated AKI, in which there were no other nephrotoxic insults other than everolimus at the onset of AKI. The incidence of AKI increased progressively as baseline estimated glomerular filtration rate (eGFR) decreased (10% in subjects with eGFR >90 mL/min/1.73 m², 17% in subjects with eGFR 60–90 mL/min/1.73 m², 28% in subjects with eGFR 30–60 mL/min/1.73 m², and 100% in subjects with eGFR 15–30 mL/min/1.73 m²; P = 0.029 for trend). Baseline eGFR was an independent risk factor for the development of everolimus-associated AKI (hazard ratio per 10 mL/min/1.73 m² increase, 0.70; 95% confidential interval, 0.49–1.00; P = 0.047). Nine of 14 patients with everolimus-associated AKI continued receiving the drug at a reduced dose or after a short-term off period. Administration of the drug was discontinued in four of 14 patients because of progression of an underlying malignancy. Only one patient stopped taking the drug because of AKI.

Conclusion
Our study suggests that AKI is a common adverse effect of everolimus treatment, especially in subjects with impaired renal function. However, the occurrence of AKI did not require the discontinuation of the drug, and the treatment decision should be made via a multidisciplinary approach, including the assessment of the oncological benefits of everolimus and other therapeutic options.

OC 003 - Management of Cancer PTS with (or at Risk of) CKD. Experience of an Ambulatory of Onco-Nephrology
Laura Cosmai1,5, Camillo Porta2,5, Wanda Liguigli3, Marina Foramitti1, Fabio Malberti1, Maurizio Gallieni4
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Background
Onco-Nephrology is a novel subspecialty dealing with 1) renal toxicity from chemotherapy (CT), targeted agents (TA) or contrast medium (CM), 2) active cancer treatment (aTx)-related electrolyte disturbances, alterations of the calcium/phosphorus metabolism and hypertension, 3) management of pts nephrectomized for a malignancy. Here we report the preliminary results of 3 years’ experience of a dedicated ambulatory of Onco-Nephrology.

Method
This ambulatory, run by a Nephrologist, takes place once a week within an Oncology outpatient ward, in order to allow closer interaction between specialists and easier access to pts’ data.

Results
Until now, we have followed 349 cancer pts with CKD on aTx, and 92 untreated cancer pts with CKD; 127 pts were nephrectomized for a localized or metastatic renal cell carcinoma (RCC); beyond RCC, patients had also lung (48 cases), gastric (50), prostate (34), bladder (38), or other cancers (52). Among 47 pts nephrectomized for metastatic RCC under aTx, we had only 4 aTx interruptions, while among the 80 previously nephrectomized pts for a localized RCC (not on aTx), at a median follow-up of 12 months, we did not observe any CKD progression (vs an expected percentage of 63% at 3 years). Only one patient (out of 15) treated with cisplatin had to discontinue CT because of renal toxicity. Only 10 pts have developed an episode of acute kidney injury (AKI), but all were able to resume aTx; 6 pts with advanced CKD began dialysis while on aTx. Furthermore, no cases of AKI from CM were observed (vs an expected rate of 50% in high-risk pts, and of 5% in low-risk pts).
thanks to the implementation of specific protocols of CM nephropathy prevention. Finally, previously some cases of previously unreported renal toxicities were observed.

Conclusion
Our experience shows that an Onco-Nephrological assessment may improve pts’ outcome. Further development of Onco-Nephrology (e.g. dedicated ambulatories and specific trials) is warranted.

OC 004 - New Insights in Renal Toxicity of BRAF Inhibitor Vemurafenib in Patients with Metastatic Melanoma
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Background
Vemurafenib is a selective B-RAF inhibitor used in treatment of BRAF-V600-mutant metastatic melanoma. It improves patients’ survival as compared to the standard chemotherapy. Side effects that are more common are cutaneous and hepatic, leading regularly to discontinuation or diminution of the treatment. Acute kidney injury (AKI) has recently been reported, but his incidence, mechanism and impact in daily practice are unknown.

Method
We conducted a retrospective study including 74 patients with metastatic melanoma treated by vemurafenib in a single institution. Serum creatinine was collected before treatment, monthly during targeted therapy and one month after treatment disruption. AKI was defined as an increase of at least 25% of creatinine from baseline value according to RIFLE criteria. Patients were defined in two groups with or without AKI (defined as AKI+ and AKI – respectively). Kidney biopsies were performed on three patients with AKI.

Results
The mean duration of treatment was 10 months (from 2 months to 39 months). 78% of patients (n=58) experimented AKI. The AKI occurred mainly during the first trimester of treatment (51 patients; 69%): 39 patients (53%) during the first month; 8 (11 %) during the second and 4 (5%) during the third month. The median time of onset was at 2.2 months.

In the AKI+ group, the severity of the renal failure was variable: an increase of 25 to 50% of the baseline creatinine was observed in 67% of AKI+ patients (n=39), between 50 and 75% in 24% (n=14) and above 75% in 9% (n=5).

When compared AKI + to the AKI- group (n=16; 21.6%), no difference was shown in blood pressure, diabetes, cardiovascular diseases, history of nephropathy or nephrotoxic treatment. In contrast, men were more exposed to AKI that women (39/45 men (87%) vs 19/29 women (66%); p= 0.031). The two groups were similar by age (61 and 60 years old).

9% of patients had Chronic Kidney Disease (CKD) before Vemurafenib. There was no more AKI in CKD population (5/7 (71%) vs 53/67 normal renal function (79 %); p=0.64). Kidney biopsies showed tubular toxicity and interstitial fibrosis. One biopsy showed focal, non-inflammatory and discrete lesions of interstitial fibrosis seven month after the first observation of AKI. The two others performed less than three months after AKI showed marked a specific chronic tubular and interstitial lesions in the one hand, and acute and focal lesions of epithelial damage, compatible with acute tubular necrosis in the other hand.

We collected creatinine evolution after treatment discontinuation for 27 patients in AKI + group. Every patient returned to creatinine basal rate with margin of 25%.

Conclusion
Our study, which includes so far the largest cohort on this topic in the literature, found frequent renal toxicity of Brat inhibition by vemurafenib, highlighting the necessity of monitoring renal function, with particular attention during the first trimester. Histological evidence has been made for the first time with three biopsy showing consistent tubular and interstitial lesions.

AKI is most of the time moderate and do not justify the discontinuation of treatment. Creatinine
elevation is also tolerated, especially because response to vemurafenib is might increase the overall survival of the patients, allowing temporarily stabilization or regression of metastatic lesions. We show for the first time that AKI is secondary to tubular injury, suggesting the possibility of renal recovery. Moreover, when vemurafenib is stopped for any reason, creatinine level usually returns to baseline value.

References

OC 005 - eGFR Equations as Predictors of Outcomes after Cisplatin Chemotherapy in Cancer Patients

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Background
Estimation of renal function is essential in patients (pts) treated with cisplatin (DDP). We aimed to compare the estimated glomerular filtration rate (eGFR) according to Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), Modification of Diet in Renal Disease (MDRD) and Cockcroft-Gault (CG) equations to investigate if a decrease in eGFR using these equations could predict negative outcomes, as death, need of dialysis or acute renal failure (ARF).

Method
Uni-institutional, retrospective and exploratory study
All pts were >18y, diagnosed with head & neck (H&N) or thoracic cancers and had been treated with DDP, for at least for one cycle. DDP was administered in NS 500mL in 60 min, following NS 1000 mL, KCl 25 mEq, MgSO4 100 mg and manitol 20 g. Baseline eGFR was calculated using CKD-EPI, MDRD and CG equations and ARF was defined as an elevation of serum creatinine ≥ 0.3 md/dL or more than 50% in comparison to baseline. We defined treatment-related deaths if they occurred in the first 28 days after DDP dose.

Results
157 pts were included: median age 58y (26–78), 68% male. Lung (61%), larynx (13%), oral cavity (8%) and oropharynx (8%) were the most common primary sites. First DDP cycle was administered to all 157 pts, the second to 154 pts, the third to 127 pts and 91 pts received the fourth one. Median DDP dose was 80mg/m2 for all cycles. Median baseline pre-DDP serum creatinine was 0.75mg/dL (0.46–1.76) and it increased to 0.78 (0.40–1.51, p=0.044, t-test), 0.80 (0.42–1.68; p=0.005) and 0.77 (0.41–1.69, p=0.075) after each DDP dose.

At baseline, median eGFR (ml/min/1.73 m2) was 86 (34–175) (CG), 107 (44–226) (MDRD) and 100 (45–145) (CKD-EPI). Considering normal eGFR as >90 (CG), >125 (MDRD) and >100 (CKD-EPI), according to ROC analysis, the agreement between MDRD and CG was fair (k=0.291) and between MDRD and CKD-EPI was moderate (k=0.553). Bland-Altman analysis revealed that CG underestimated eGFR in comparison to MDRD (-19) and to CKD-EPI (-7). Furthermore, MDRD overestimated eGFR in comparison to CKD-EPI (+11). After first DDP dose, according to ROC analysis, cut-off values of eGFR reductions were calculated as follows (ml/min/1.73m2): 10 (CG; sensitivity 78%, specificity 72%, AUC 0.816, 95%CI 0.74–0.88, p=0.0001), 8 (CKD-EPI; 72%, 76%, 0.75, 0.67–0.82, 0.0003) and 20 (MDRD; 78%, 89%, 0.83, 0.76– 0.90, 0.0001). Decreased renal
function estimated by any equations was able to predict negative outcomes, with OR 9.0 (CG, 95%CI 2.8–29.2, p<0.0001), OR 33.0 (MDRD, 95%CI 9.3–116.3, p<0.0001) and OR 8.5 (CKD-EPI, 95%CI 2.8–25.6, p<0.0001). Overall, four treatment-related deaths were observed and the incidence of ARF was low: 9 pts (6%), 11 pts (8%) and 1 pt (1%) after first, second and third DDP cycles, respectively.

Conclusion
Decrease in renal function estimated by all three equations seemed to predict negative outcomes (ARF, dialysis and 28-day mortality) after one cycle of DDP-based chemotherapy in patients with H&N and thoracic cancers. The agreement between these equations is not good and CG should be used with caution as the reference eGFR in these pts.

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**OC 006 - A Case of Acute Kidney Injury from Crystal Nephropathy Secondary to Pomalidomide Use**

Sam Leung¹, Phyllicia Baird¹, Olawumi Babalola¹, Craig Devoe¹, Rimda Wanche³, Kenar D. Jhaveri³
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**Background**
Pomalidomide is an analogue of thalidomide indicated for treatment of refractory Multiple Myeloma. The reported incidence of renal failure is less than 5%. We report a case suggesting crystal nephropathy as the mechanism for acute kidney injury (AKI) in pomalidomide use.

**Method & Results**
A 76 year-old female with a history of refractory IgG Kappa multiple myeloma presented with a two-day history of fevers, productive cough and weakness. Prior to admission, she had taken four days of a planned 21-day course of pomalidomide. Upon admission, she was noted to have a fever of 102.2 degrees Fahrenheit and a white cell count of 2.6 K/ul with absolute neutrophil count of 1.6 K/ul and 17% bands. Respiratory viral panel was positive for respiratory syncytial virus. In the setting of neutropenic fever, she was started on vancomycin, piperacillin/tazobactam and levofloxacin for multifocal pneumonia, seen on computed tomography of the chest without contrast. Additionally, pamidronate was held. On hospital day 2, her creatinine was noted to increase to 1.65 mg/dl from 1.10mg/dl on admission. Her creatinine continued to trend upwards despite adequate hydration and avoidance of nephrotoxins. Urinalysis was significant for pH of 5, and protein of 25 mg/dl with no granular casts. Microscopic analysis of urine sediment collected on second day of admission was significant for long, spindle shaped crystals. A diagnosis of pomalidomide induced crystal associated tubular necrosis was made. Levofloxacin was discontinued on day 2 and the other antibiotics were continued. Vancomycin levels ranged between 10-27 µg/ml. Urine culture grew out 30,000 CFU E. coli, but blood cultures were negative. Over the following 3 weeks, her serum creatinine peaked at 3.99mg/dl, but returned to a baseline of 0.9mg/dl after three months. Due to thrombocytopenia, a kidney biopsy could not be performed.

**Conclusions**
This patient’s urine microscopy showed long, spindle-shaped crystals, which strongly supports a diagnosis of drug induced crystal nephropathy. Given the time course of chemotherapy, urine microscopy findings and lack of use of other medications that are known to cause crystal nephropathy, pomalidomide is the most likely cause of her crystal nephropathy in an acidic urine environment. This rare case of acute kidney injury due to crystal nephropathy after treatment with pomalidamide illustrates an unreported and potentially serious side effect of pomalidomide.

**References**
2. Pomalidomide package insert


OC 007 - An Unusual Case of Renal Carcinomatous Embolus with Rapid Renal Failure during Axitinib Treatment

Mayeur D.1, Fournier P.1, Silmonaggio A.1, Rouvier P.1

1Hôpital Mignot

Background

Anti-angiogenic treatment with Anti-VEGF or RTKI in metastatic cancer is expected to prolong PFS, even if often not increasing overall survival. Renal complications of these treatments are common, blood hypertension, proteinuria, de novo renal failure or progression of a known chronic renal failure, which do not lead, most often, to document the renal underlying process by a renal biopsy. Renal biopsy may be indicated in case of a rapidly progressive renal failure, and if information afforded may have an impact on treatment. Our observation shows that, in such cases, renal biopsy may not always reveal thrombotic microangiopathy as the main cause of renal failure, but sometimes complex lesions, and unexpected findings, here carcinomatous embolus.

Method & Results

A 64-years-old man, type 2 diabetes since he was 10, treated by Metformin and Vildagliptin, without retinopathy, without microalbuminuria, and with normal renal function (eGFR 76 ml/mn), presents with lumbar pain and anorexia. Diagnosis of left kidney tumour, with locoregional metastatic lymph nodes is made. The patient undergoes an extended nephrectomy in May 2013. Pathological examination shows clear cell renal carcinoma with a component of eosinophilic cells, Führman 3 to 4, with lymphatic and vascular embolus, two metastatic lymph nodes and classified pT3apN1. Treatment with SUNITINIB has then started. Toxicity is moderate: nausea grade 2, asthenia grade 2, leukopenia and thrombocytopenia grade 2; eGFR (MDRD) is 39.7 ml/mn/1.73m² at the beginning of SUNITINIB treatment and 37 ml/mn/1.73m² when SUNITINIB is stopped on October 2013, due to lymph node progression.

Second line AXITINIB has started on mid-November 2013. Blood pressure increased, but was controlled by introduction of AMLODIPIN. In the following three weeks, eGFR decreased to 25 ml/mn/1.73m² and 18 ml/mn/1.73m² on mid-December, proteinuria was 0.7 g/24 H, Haptoglobin and LDH were normal, schistocytosis was less than 1%. The patient had unfortunately taken NSAID. Diagnostic discussion was AKI secondary to NSAID and/or thrombotic microangiopathy. Oncologists faced a dilemma: should one stop AXITINIB and deprive the patient of any chance to stop progression, or take opportunity to exonerate AXITINIB of any renal toxicity and pursue the treatment. Transjugular renal biopsy was performed. The main picture was acute tubular necrosis, with glomerular ischemia. Mesangial matrix was slightly increased, and there were several images of double contour, but no intra-capillary thrombi. Surprisingly, there were two distinct pictures of intra-vascular carcinoma embolus. There was soon after a progression of disease, leading to stop AXITINIB, and palliative care was provided to the patient who died two months later.

Conclusion

The underlying process behind a renal failure in a context of treatment with RTKI might be complex, as illustrates our observation, cumulating toxicity of NSAID, microangiopathy, and here, a very
unusual carcinomatous embolus, of undefined significance. Carcinomatous embolus of the pulmonary vessels is a well-known clinical entity, even if rare, with a dramatic evolution in some weeks and a frequent post-mortem diagnosis. To our knowledge, carcinomatous embolus of the renal vessels has not been described, but in our observation, seems to share the same catastrophic prognosis as its pulmonary counterpart.

OC 008 - Thrombotic Microangiopathy Associated with the Use of Bortezomib in a Patient with Multiple Myeloma

Jan Van Keer, Michel Delforge, Evelyne Lerut, Ben Sprangers, Daan Dierickx, MD, PhD, Kathelijne Peerlinck, MD, PhD

1UZ Leuven

Background

Bortezomib is a first generation proteasome inhibitor that is extensively used in the treatment of patients with multiple myeloma (MM). Several reports have linked bortezomib exposure with the development of thrombotic microangiopathy (TMA). Here we report a case of biopsy-proven renal TMA associated with the use of bortezomib in a patient with MM, in whom re-exposure to bortezomib 18 months later was associated with recurrence of TMA.

Method & Results

A 51-year-old Caucasian male is treated with bortezomib - thalidomide - dexamethasone (VTD) after diagnosis of IgG lambda MM. 9 years earlier he was diagnosed with severe MGUS related acral ulcers, for which he had received treatment with rituximab (7 doses) and therapeutic plasma exchange prior to diagnosis of MM. Therapeutic plasma exchange was continued afterwards on an approximately bi-weekly basis throughout the course of his illness. After completion of the first cycle of VTD therapy, the patient developed acute kidney failure (creatinine elevation from 1.3 mg/dL at baseline to 2.7 mg/dL), dysmorphic hematuria, subnephrotic range proteinuria and peripheral blood schistocytosis. Kidney biopsy findings were consistent with TMA. Creatinine slowly returned to a new baseline value of 2.1 mg/dL. Therapy was subsequently changed to VCD (cyclophosphamide instead of thalidomide) and lenalidomide - dexamethasone, mainly because of worsening acral ulcers. 18 months later, he was rechallenged with bortezomib and dexamethasone because of disease progression under lenalidomide. After completion of the first cycle he developed acute on chronic kidney failure with nephrotic range proteinuria, macroscopic hematuria, high peripheral blood schistocytes and end stage renal failure (creatinine 7.5 mg/dL) necessitating hemodialysis.

Conclusion

We describe a case of TMA associated with exposure to bortezomib in MM. To our knowledge, this is the first biopsy-proven case to be reported. The recurrence of TMA after rechallenge supports a causal role of bortezomib. The exact mechanisms remain to be elucidated.

References

OC 009 - Cancer and Dialysis: Practical Issues in the Daily Practice
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Background
Kidney failure is most often an exclusion criterion in the clinical studies. Few data are available in dialysis patients receiving cancer drugs. A response to two situations that may be encountered is proposed here.

Method
Patient A: a 79 years old with a history of colon adenocarcinoma, acute renal failure in peri-prosthetic inflammation requiring 3 weekly dialysis sessions. Discovery of an urothelial carcinoma to be treated with chemotherapy according to the following regimen: gemcitabine 1000 mg / m² on day 1 and carboplatin AUC 4 on day 1

Patient B: 55 years old presenting with a history of squamous cell carcinoma of the mandible treated with surgery and adjuvant radiation therapy, chronic renal failure dialyzed 3 weekly sessions. He is taken in charge for a metastatic esophageal adenocarcinoma. The following chemotherapy regimen is prescribed: 5-FU = 1000 mg / m² D1 to D5 continuously and carboplatin AUC 5 at D1. A literature search was conducted as well as a request for information from the ICAR-Service (Pitié-Salpêtrière, Paris).

Results
- Carboplatin is mainly eliminated by the kidney (95%) in the form of platinum and derivatives. It is significantly dialyzed during a hemodialysis session.
- Fluorouracil is mainly metabolized by the liver in 3 metabolites: DHFU, FUPA, and BET. Urinary excretion is the main elimination mode: 10% unchanged, 60 to 90% as metabolites, mainly BET (pharmacologically active in animal and in vitro). It is dialyzable.
- The pharmacokinetics of gemcitabine is not altered in patients with renal failure. It is not necessary to adjust the dose in these patients. An increase by a factor of 5 to 10 of the elimination half-life and of the AUC of an inactive metabolite of gemcitabine (dFdU) is observed.

Conclusion
Based on pharmacokinetic data, the following dosing regimens can be recommended:
- Carboplatin and 5FU (both dialyzable) should be administered after the session, the days of hemodialysis. Carboplatin dosage is adapted to the patient considering a glomerular filtration rate of 0 mL / min. The prescribed dose is thus 25 x AUC
- The lack of data on the clearance of gemcitabine leads to advise the administration after the session, the days of hemodialysis.
- The patient A’s chemotherapy regimen is administered after hemodialysis. Patient B to receive chemotherapy during hemodialysis session, dose adjusted carboplatin should be administered after the session. 5FU, usually diluted in a 1L bag of NaCl 0.9%, should be prepared pure in a cassette to limit fluid intake. Moreover, the use of pump will allow stopping the administration during dialysis sessions and then resuming later.
- These cases illustrate the difficulties encountered in the medical management of kidney failure patients due to the lack of available information. The physician-pharmacist dialogue is essential. This kind of clinical situation demonstrates the importance of studying the “kidney failure - drugs” relationship on significant cohorts of patients.
OC 010 - Tumor-Induced Osteomalacia (TIO) with Elevated FGF23 Causing Hypophosphatemia in Ovarian Malignancy
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Background
Tumour-induced osteomalacia (TIO) is a rare paraneoplastic syndrome characterized by elevated phosphatonin (FGF 23), renal phosphate wasting and abnormal Vitamin D metabolism. It has been reported in benign mesenchymal tumors and head and neck cancers. Serum or plasma FGF23 concentrations are known to be elevated in patients with advanced-stage epithelial ovarian cancer; however reductions in serum phosphate concentrations are not commonly seen. We report a case of resistant hypophosphatemia secondary to elevated FGF23 in the setting of ovarian malignancy.

Method & Results
A 63-year-old female was diagnosed with ovarian cancer (unknown type) with lung and liver metastases after presenting with abdominal distention and decreased appetite. She had persistent severe hypophosphatemia that was difficult to replete, for which a nephrology consultation was requested. Laboratory findings revealed an inappropriately elevated urine phosphorous (Fe Phos of 35.7%), a low serum 1,25-OH vitamin D3 with a moderately low serum 25-OH vitamin D3, normal PTHrP, low normal intact PTH and eventually a strikingly elevated FGF23 level (238 RU/mL, normal < 180). Given her significant phosphaturia with elevated FGF23 levels, a diagnosis of paraneoplastic FGF 23 production from ovarian cancer was made. Imaging findings confirmed metastatic ovarian malignancy with CDX2 positive pulmonary metastases. No additional pathology was available as the patient subsequently elected for hospice care. Despite repletion with high doses of intravenous and oral phosphate, intravenous and oral vitamin D, normalizing her phosphate continued to be challenging as her underlying malignancy was progressive and untreated.

Conclusion
Serum or plasma FGF23 concentrations are elevated in patients with advanced-stage epithelial ovarian cancer without reductions in serum phosphate concentrations. Our patient was unique in that there was significant reduction in the serum phosphorus level. We could find only one case similar to ours in the literature. TIO and ovarian neoplasm (if not already diagnosed) should be considered in patients presenting with weakness, bone pain, hypophosphatemia and fractures.

References

OC 011 - A Biopsy-Confirmed Case of Native Kidney-BK Nephropathy in Patient Receiving Ibrutinib or CLL
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Background
BK polyoma virus nephropathy (PVN) is a well-described cause of renal allograft dysfunction; however, its occurrence in native kidneys is rare. We report a case of BK PVN involving the native kidneys in a patient receiving ibrutinib for chronic lymphocytic leukemia (CLL). Case description: A 48-year-old male was diagnosed with complex karyotype CLL two years prior to presentation with poor responses to multiple standards of care regimens (FCR, RICE, ofatumumab, steroids). There were no documented episodes of acute kidney injury (AKI) for the duration of these treatments. He was referred to our institution for consideration for a clinical trial, and at that time his
serum creatinine was 1.28 mg/dL. He was enrolled in a trial to receive ibrutinib, a novel inhibitor of Bruton’s tyrosine kinase. The patient achieved a sustained response to this single agent at 420 mg daily. However, serum creatinine rose to 1.6 mg/dl approximately after 7 months of therapy, which was accompanied by microscopic hematuria and subnephrotic proteinuria of 600 mg per day. The patient’s renal function continued to decline and he was referred to nephrology for further evaluation. After fourteen months of ibrutinib treatment, the patient underwent kidney biopsy for evaluation of progressive acute kidney injury of unknown etiology. Creatinine was 2.1 mg/dl at the time of biopsy. Light microscopy revealed zonal renal cortical scarring with an associated interstitial inflammatory infiltrate comprised primarily of small, mature lymphocytes. The cortical scarring involved approximately 25% of the renal cortex overall. Immunohistochemical staining was negative for kidney involvement by CLL; however, a BK polyoma virus immunostain was positive in a few tubular epithelial cells in the scarred areas, consistent with BK PVN. Plasma and urine BK viral loads were 2.9x10^5 c/ml and 6.8x10^9 c/ml, respectively. Given the decline in renal function, ibrutinib was stopped for one month, during which time the plasma BK viral load decreased to 1.7x10^5 c/ml. Unfortunately, his CLL progressed and ibrutinib was resumed in combination with leflunomide with the intention of reducing BK viremia. Despite leflunomide, serum creatinine has since continued to rise and is most recently 2.2 mg/dl.

Method & Conclusion
BK PVN is a well described cause of kidney allograft dysfunction as a consequence of longterm immunosuppression. However, BK PVN is becoming more appreciated in native kidneys in the setting of an immunocompromised state. In a recent case series 1, BK PVN in native kidneys was seen in hematologic malignancies, all of which were either bone marrow transplant recipients on immunosuppression or on immunosuppressive agents as treatment for the underlying malignancy. This case series also noted BK PVN in native kidneys of immunosuppressed non-kidney solid-organ recipients. Our patient had stable renal function while suffering from refractory CLL and then developed BK PVN while clinically improving with ibrutinib. While this does not imply a direct causal relationship between BK PVN and ibrutinib, it does suggest that the immunosuppression resulting from ibrutinib is related to BK PVN as opposed to the immunosuppression associated with advanced CLL. Ibrutinib has shown considerable promise in relapsed and refractory CLL as well as other B cell malignancies 2, 3. Thus, we suggest including BK PVN in the differential diagnosis for patients who develop unexplained AKI while receiving ibrutinib, especially when the underlying B cell malignancy is clinically responding to treatment.

References
PO 1-1 - Liposarcoma Complicated by Paraneoplastic Renal Failure Due to Acute Crystal Induced Nephropathy

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Background
Dedifferentiated liposarcoma complicated with paraneoplastic syndrome is rare and often fatal even when localized with a high peri-surgery mortality.

Patient and treatment - We report the case of a 74 years-old patient initially hospitalized in nephrology department for progressively severe impairment of renal function, hypercalcæmia with normal PTH and PTHrp, leukocytosis. Examination showed irregular fever, loss weight and a right retroperitoneal mass corresponding to a poorly differentiated liposarcoma at biopsy. Renal biopsy showed an extensive tubular epithelial necrosis with phosphate pentahydrate octacalcium (OCP) deposits in the tubular lumens. Medical treatment of hypercalcemia stabilized renal impairment but only temporarily control hypercalcemia. Given the localized nature of this liposarcoma an “en bloc resection” preceded by chemotherapy in order to control the paraneoplastic syndrome were performed. Three courses of doxorubicin were scheduled. Efficiency was attested by a reduced incidence of hyperthermia spikes and by a decreased and more heterogeneous hypermetabolism on PET-CT scan. Renal failure, serum calcium and neutrophils were almost normalized after first course chemotherapy but quickly recurring leading to a last course one week before surgery. Cephalic pancreaticoduodenectomy and right hemicolectomy lead to recovery of normal neutrophil count and calcemia. After two years of follow-up, the patient shows no sign of relapsed and has a stabilized renal function.

Method & Results
To the best of our knowledge, it is the first description of a paraneoplastic syndrome involving hypercalcæmia, leukemoid reaction and acute crystal induced nephropathy (ACIN with phosphate pentahydrate octacalcium deposits (OCP)) in the setting of a solid tumor. ACIN caused by calcium metabolites are mostly described in cases of intoxication or hyperparathyroidism, but can also occur in case of high cellular turnover. However, acute tubular necrosis is exceptionally found in the evolution of solid tumors. Our case is original because it is the first case where a renal biopsy demonstrates the presence of tubular necrosis with OCP in the framework of a solid tumor. OCP correspond to a rare lithogenic stone component in common conditions, and are found in a relatively higher proportion in carbapatite stones of pregnant women, suggesting an original physiopathological pathway in its formation. Unfortunately after common causes (hyperparathyroidism, bone metastases, secretion of PTHrp, myeloma) have been eliminated, we failed to explain this hypercalcæmia. Indeed, even if in previously described HCG producing liposarcoma, no hypercalcæmia was reported, findings of OCP in pregnant women suggested a potential role for HCG in this tumor but pathological analysis of the surgical specimen showed no production of HCG. In our observation, the severity of renal disease had initially challenged the patient to a radical surgery, standard treatment of localized resectable liposarcoma.

Conclusion
To conclude, this case shows that neoadjuvant doxorubicin is feasible and efficient in undifferentiated liposarcoma to control paraneoplastic syndrome such as hypercalcæmia, or leukemoid reaction and to allow surgery in a curative intent.

References

PO 1-2 – Light Chain Fanconi Syndrome in a Patient with Acute Myeloid Leukemia and MGUS
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Background
When monoclonal gammopathy of uncertain significance (MGUS) has renal dysfunction with paraprotein injury, it is termed monoclonal gammopathy of renal significance (MGRS). MGRS can manifest as cast nephropathy, Light Chain Fanconi Syndrome (LCFS), amyloidosis or other glomerular diseases seen with paraproteinemias. We report the first case of AML with MGUS leading to MGRS.

Method & Results
A 61 years old Filipino male with stage 2 chronic kidney disease and a recent diagnosis of myelodysplastic syndrome presented with fever, headache and transformation to AML. Physical examination was unremarkable. Urinalysis demonstrated proteinuria and glucosuria. Lab data revealed >20 gm proteinuria/24 hours, hypokalemia, hypophosphatemia and hypouricemia with increase in the fractional excretion of potassium, phosphorous and uric acid. A repeat bone marrow biopsy confirmed acute myeloid leukemia with 3% plasma cells noted, an increase from 1% previously. Serum protein immunoelectrophoresis showed an IgG lambda migratory protein. Within a week of his admission, on no medications, his serum creatinine rose from 1.4 mg/dl to 1.99 mg/dl. A diagnosis of LCFS was considered in the setting of MGUS. His renal function worsened and serum creatinine peaked at 2.65 mg/dl. After the initiation of chemotherapy for the AML, the serum creatinine rapidly declined and returned to his baseline of 1.3 mg/dl with resolution of proteinuria, hypokalemia, and glucosuria.

Conclusion
The patient’s presentation was consistent with LCFS. This entity is typically seen in multiple myeloma and rarely in chronic lymphocytic leukemia. To our knowledge this represents the first case of LCFS to be reported in a patient with AML and MGRS.

References
PO 1-3 - Radiation Recall Dermatitis: New Case Report with Targeted Therapy
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Background
Radiation Recall Dermatitis (RRD) represents an acute inflammatory reaction in a previously irradiated anatomic area, which has been incited by a pharmacologic agent. This phenomenon is rare and often discarded by oncologists. A multiple anti-cancer cytotoxic drugs and thyrosine kinase-inhibitors were associated with this reaction, but to our knowledge a single case has been reported with pazopanib treatment. Our patient is a 64-year-old man with stage IV clear cell kidney denocarcinoma presenting a multiple bone metastasis.
In April 2013, the patient received a surgical treatment followed by 20 Gy palliative radiotherapy on the right humerus as primary oncological treatment, without any skin reaction. In March 2014, three weeks after starting the first line TKI treatment by Pazopanib at the dosage of 400 mg twice daily, the patient developed an erythematous patch and edema that strictly corresponded with the previously irradiated area. A one-week pazopanib interruption and per os steroids was sufficient to obtain a complete regression of symptoms. This reaction is a non-severe skin toxicity, very rare and unpredictable. It is, obviously, underreported in literature.

References

PO 1-4 - Oncogeriatrics: Kidney Failure Is Not the Sole Issue
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Background
The population of elderly patients increased in the past years in cancer centers. They frequently present with renal impairment (physiological decrease of glomerular filtration rate of 1 ml/min/1.73 m² each year) and drugs dosage adjustment is compulsory. They also present with other comorbidities, making the pharmacist’s advisory and education role essential. We report the case of an oncogeriatrics patient whose treatment required a pharmacist consultation to prevent iatrogenic accidents.

Method
The patient was an 82 years-old woman, presenting with an endometrial cancer treated by a cisplatin-based regimen. She presented with several comorbidities, among which hypertension and hypercholesterolemia. The cardiologist had prescribed beta-blockers and furosemide for hypertension and pravastatin for cholesterol disorders. Besides, the onco-geriatrician detected certain fragility and recommended a pharmaceutical consultation to focus on the different treatments, looking forward to reducing the number of drugs prescribed and to preventing iatrogenic events.
Results
A one-hour pharmaceutical consultation took place.
First, the purpose of the consultation was:
- To explain the treatments and make sure the patient was familiar with the different drugs
- To help the patient with her treatment management, establishing a medication schedule
- To make an update on all treatments in search of potentially harmful drug interactions
- To suggest to the oncologist to suspend furosemide time of chemotherapy to prevent acute tubular necrosis
- To prevent renal effects of cisplatin, advising the patient to drink a lot, after returning home

Besides cisplatin toxicity prevention, which the patient had clearly understood, the consultation highlighted a possible drug-food interaction that the physician had not detected. When the patient was told to “drink a lot to prevent kidney damages due to chemotherapy”, she answered she used “to have 1 L of grapefruit juice / day and no one should worry for her kidneys”.

Conclusion
The pharmacist was able to identify a potential harmful situation; cisplatin renal toxicity was prevented but CYP3A4 interactions were not. Grapefruit juice is known to be a strong CYP3A4 inhibitor dramatically increasing drugs exposure for those that are metabolized by CYP3A4. For instance, statins bioavailability can be raised to 1500% when associated to grapefruit juice, leading to possible lethal rhabdomyolyses.

This case illustrates the role of the clinical pharmacists in the management of elderly cancer patients. The “drugs professional” can give precious advice and have a valuable input, allowing preventing renal failure aggravation but also other deleterious iatrogenic events.

PO 1-5 - Esophageal Cancer-Associated Pauci-Immune Glomerulonephritis: A Case Report
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Background
In general, ANCA-associated vasculitis is idiopathic. However, few cases have been reported in the context of cancer suggesting ANCA-associated vasculitis can be paraneoplastic.

Method
We report a case of p-ANCA positive vasculitis with glomerulonephritis and peripheral nerve involvement associated with esophageal cancer.

Results
A 64-year old woman was admitted to the hospital with a 2-month history of anorexia, intermittent fever, fatigue, nighty cough, staggered myalgia and paresthesia in her fingers. Physical examination was unremarkable.
EMG demonstrated a sensorymotoric peripheral neuropathy. Laboratory findings showed an acute kidney insufficiency stage 3 (failure) according to the RIFLE classification with a plasma creatinine level of 4.39 mg/dL (eGFR of 10 ml/min/ 1.73 m2 (CKD-EPI)). Urinalysis showed microscopic dysmorphic hematuria and limited proteinuria (0.42g/L). The patient required intermittent hemodialysis. P-ANCA (1/1280) were positive against MPO with a titer more than 134 U/mL. A kidney biopsy was performed and showed glomerulonephritis with vasculitis and crescents with negative immunohistochemic stains confirming the diagnosis of p-ANCA associated pauci-immune vasculitis/glomerulonephritis. Because of anorexia and fatigue, gastroscopy was performed, which showed a polypoid lesion with a maximal diameter of 2.5 cm at the height of the gastro-esophageal junction. Histopathology revealed an adenocarcinoma, staged pT2N1M0.
The patient underwent a curative partial esophagectomy. There was a marked improvement of her condition following the operation; attenuation of paresthesia and better gait, improvement of kidney function with no further need for dialysis and decrease of ANCA titers (1/320). Because of incomplete
clinical response, in addition immunosuppressive therapy with high dose steroids and rituximab weekly (during 4 weeks) was administered six weeks post-operatively, leading to further clinical and biochemical recuperation.

Conclusion
ANCA-associated vasculitis can possibly be paraneoplastic in nature; with remission obtained with the curative treatment of the underlying malignancy. Here we report on a case of MPO-associated chemotheraphy.3 Life prognosis of the recipient depends on the cancer stage at diagnosis, on cancer brain or metastatic tumour) could help to target the donors at risk.2,6,7 The recommendation for donation.5 These data underline the importance of the autopsy of the donor. Identification of risk origin of the tumour.3,4 According to the literature, about 7% of deceased donors present with an 1-5/10,000 grafts.1,2 Molecular biology techniques associated to selected clinical criteria (e.g. same histological tumour types in donor and recipient or in two recipients from the same donor; acute resection of the tumour after withdrawal of immunosuppressive therapy) allow to confirm the allogenic origin of the tumour.3,4 According to the literature, about 7% of deceased donors present with an unknown cancer at the time of organ removal and 60% of them have no contraindication to organ donation.5 These data underline the importance of the autopsy of the donor. Identification of risk factors for cancer transmission such as age, non-traumatic cerebral haemorrhage (that could mask brain or metastatic tumour) could help to target the donors at risk.2,6,7 The recommendation for treatment of donor-transmitted tumours is cessation of immunosuppression in order to enhance rejection of the allograft and transplanted cancer cells, followed by graft removal, radio and/or chemotherapy.3 Life prognosis of the recipient depends on the cancer stage at diagnosis, on cancer

PO 1-6 - Donor Cancer Transmission in Kidney Transplantation: Case Report and Literature Review
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Background
Despite a selection of donors, the inadvertent transmission of tumour remains a rare but dramatic complication in organ transplantation. We report such a case and propose some careful guidelines from literature survey.

Method
Thirty-four months after hemodialysis initiation for unspecified end-stage glomerulopathy, our 53-yr old patient received a kidney graft from a deceased donor without any complication. Initial immunosuppression at the time of transplantation consisted of anti-IL2R, mycophenolate mofetil, tacrolimus and steroids. He was discharged on the 8th postoperative day (the nadir of plasma creatinine reached 1.5 mg/dL during the follow-up). After 100 days, the patient was admitted in the emergency department for abdominal discomfort. Initial work-up revealed multiple opacities on the chest radiography suggestive of metastases and an increase of plasma creatinine level (2.2 mg/dl). An extensive work-up was then performed including a graft biopsy, resulting in the diagnosis of a metastatic low differentiated adenocarcinoma from unknown origin. We were later informed that 2 additional recipients from the same donor (kidney and liver) had also developed cancer. Finally, a caryotype and a PCR of the microsatellite DNA region were done on the tumoral part of the biopsy and confirmed the donor origin of the tumour (PCR amplification: 79% of cells of donor origin; caryotypes of the tumour and the recipient were XX and XY, respectively). The patient was explanted and returned to hemodialysis. A chemotherapy consisting of cisplatin and 5-Fluorouracil was started. After 5 cures of this regimen, pet-scan demonstrated a spectacular improvement of the metastatic lesions. As the evolution was even better than expected, we considered the fact that the patient’s own immunity was able to control the disease. Therefore we decided to stop chemotherapy and to plan a close regular follow-up. One year later, patient remained stable without any sign of cancer progression.

Results
Frequency of tumour transmission from deceased donor with no known tumour has been estimated at 15/10,000 grafts.1,2 Molecular biology techniques associated to selected clinical criteria (e.g. same histological tumour types in donor and recipient or in two recipients from the same donor; acute resection of the tumour after withdrawal of immunosuppressive therapy) allow to confirm the allogenic origin of the tumour.3,4 According to the literature, about 7% of deceased donors present with an unknown cancer at the time of organ removal and 60% of them have no contraindication to organ donation.5 These data underline the importance of the autopsy of the donor. Identification of risk factors for cancer transmission such as age, non-traumatic cerebral haemorrhage (that could mask brain or metastatic tumour) could help to target the donors at risk.2,6,7 The recommendation for treatment of donor-transmitted tumours is cessation of immunosuppression in order to enhance rejection of the allograft and transplanted cancer cells, followed by graft removal, radio and/or chemotherapy.3 Life prognosis of the recipient depends on the cancer stage at diagnosis, on cancer
differentiation and on tumour type (e.g. 5-year survival rate is less than 30% for a melanoma and more than 70% for a renal carcinoma, respectively).

**Conclusion**
Donor transmitted cancers are a rare but dramatic complication of renal transplantation and the prognosis remains poor despite aggressive management. Targeted autopsies could help in reducing the risk of transmission.

**References**

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**PO 1-7 - Chronic Lymphocytic Leukemia: Eligible or Non-Eligible for Kidney Transplantation?**
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**Background**
An important issue in transplantation medicine is the eligibility of patients who have been treated for malignancies to undergo organ transplantation. Chronic Lymphocytic Leukemia (CLL) is a chronic hematological disorder characterized by accumulation and proliferation of small B-lymphocytes. Although a malignant disorder, a substantial proportion of patients have a life expectancy of more than 10-15 years. In addition, given a median age of about 70 years at diagnosis, many patients will show chronic kidney disease during the course of the disease. Whether CLL patients with end stage renal disease (ESRD) can be offered a kidney transplantation remains an open question. When looking into the literature we were able to identify only nine cases. Seven of these cases experienced a dismal outcome. Here we present the clinical, biochemical and molecular features and the outcome of a tenth patient.

**Method**
A 59-years-old woman, with ESRD due to familial hepatorenal polycystic disease, was diagnosed with CLL 13 years ago. During this period the disorder remained stable with no treatment need except for two short courses of chlorambucil. Both clinical staging and new prognostic markers (normal karyotype/isolated del13q14 on FISH/mutated variable region immunoglobulin heavy chain/no CD38 expression) predicted a slowly progressive disease. During the last months her general condition deteriorated quickly due to severely handicapping polycystic hepatomegaly with ascites, a very low performance status, and a dramatic loss of quality of life (QOL). Pro’s (curative treatment, no QOL, good prognosis of CLL) and contra’s (infectious/malignant complications, possible progression of CLL) of combined liver/kidney transplantation were discussed and the decision for combined transplantation was finally taken. The first weeks postTx were uncomplicated with spectacular amelioration of her general condition. However, one month postTx, she was admitted because of fever and pancytopenia. Bacterial and viral infections, drug fever, postTx lymphoproliferative disorder and graft-versus-host-disease were excluded. Bone marrow examination showed infiltration with CLL.
cells with no residual hematopoiesis. She finally expired due to persistent pancytopenia and fatal invasive pulmonary aspergillosis.

**Conclusion**

This case illustrates the ethically difficult question as to whether hematological disorders -apparently stable and of good prognosis- should be considered as a contra indication to transplantation. This case indicates that, even though classical and new prognostic markers are predictive of a slow progressive disease, complications and recurrence can still develop and are very difficult to manage. Whether new prognostic markers can help in selecting ESRD patients with CLL for transplantation is not clear. We previously reported a patient with early CLL and good prognostic features with a favorable long term outcome. On the other hand this case clearly demonstrates the dramatic outcome, which was also observed in both the French and Cincinnati Transplant Registry.

**References**


**PO 1-8 - Paraneoplastic Focal Segmental Glomerulosclerosis in a Patient With Metastatic Renal Cell Carcinoma**

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**Background**

Paraneoplastic glomerulonephritides are glomerular lesions, induced by secreted factors from tumor cells and are not directly related to tumor burden, invasion, or metastasis. Solid tumor-associated membranous nephropathy and Hodgkin lymphoma-associated minimal change disease have become recognized as ‘classical’ paraneoplastic glomerulonephritides. Other glomerulopathies, such as focal segmental glomerulosclerosis, can also be associated with malignancies, but are very rare.

**Method & Results**

A 55-year-old man is referred to our emergency department because of acute kidney injury and hyperkalemia. Two weeks before admission, the patient was diagnosed with a metastatic clear cell renal cell carcinoma. Because of cervical adenopathies, a CT scan was performed and revealed multiple adenopathies mediastinal, cervical and retroperitoneal. The scan showed no solid tumors in the kidney, only a small cystic lesion with calcifications in the left kidney was detected. At admission, blood tests show impaired renal function parameters with increased serum creatinine (3.24 mg/dL), defective creatinine clearance (20 mL/min), hyperkalemia (6.38 mmol/L) and reduced plasma albumin (18 g/L). Urinalysis reveals a daily proteinuria of 11 g and dysmorphic hematuria. The clinical presentation is suggestive of severe nephrotic syndrome with weight gain and bilateral edema of the lower extremities. Immunological tests and protein electrophoresis are negative. Potassium lowering therapy and albumin with furosemide are started and two weeks later, an ACE inhibitor is associated. Kidney biopsy reveals a focal glomerulosclerosis lesion with also discrete interstitial inflammation. In addition, high doses of methylprednisolone (64 mg a day) and sunitinib, a receptor tyrosine kinase inhibitor, are introduced. Normalization of the kidney function in combination with resolution of proteinuria is seen from two weeks after the introduction of sunitinib. Two months later, a PET/CT scan shows partial resolution of the adenopathies. Six months after the diagnosis of renal cell carcinoma, progression is detected on CT and sunitinib is switched to cabozantinib. The steroids are tapered over a period of ten months to 4 mg a day. One year later, the patient presents with deep vein thrombosis in the left lower extremity and increased serum creatinine (1.8 mg/dL), reduced plasma albumin (23.6 g/L) and proteinuria of 7 g a day. New CT scanning shows tumor progression in the
considered if glomerulonephritis occurs in the presence of malignancy and when it remits after focal segmental glomerulosclerosis, in association with clear cell renal cell carcinoma is very rare, just disease with a normal kidney function, without proteinuria.


PO 1-9 - Histone Deacetylase Inhibition as a Cause of FSGS in a Patient with Multiple Myeloma
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Background
Histone deacetylase (HDAC) inhibitors represent a novel class of antineoplastic agents found to be efficacious in the treatment multiple myeloma (MM). We report a case of proteinuria and kidney injury in a patient with MM after initiating therapy with the HDAC inhibitor suberoylanilide hydroxamic acid (SAHA). We postulate a mechanism for injury and describe the drugs effect on the renal parenchyma.

Method and Results
A 54-year-old African American male with IgG lambda MM was referred to the Nephrology clinic after developing proteinuria and kidney injury. Two months prior to presentation, he was started on maintenance therapy for MM with Revlimid and Vorinostat (SAHA). At baseline, he had normal renal function (serum creatinine: 0.92 mg/dl) and low level proteinuria at 347 mg/dl. At presentation his serum creatinine increased to 1.5 mg/dl and proteinuria increased to 3572 mg/dl. Serum and urine immunofixation along with 24-hour urine light chains showed no evidence of myeloma recurrence. A renal biopsy was performed and revealed a focal segmental glomerulosclerosis (FSGS) pattern. There was no evidence of myeloma kidney and no alternative cause for FSGS was identified. The patient was started on an ACE inhibitor and SAHA was discontinued. Over the next 3 months renal parameters improved with serum creatinine improving to 0.86mg/dl and proteinuria reduced to 342 mg/day on 24-hour collection. The patient was diagnosed with drug-induced FSGS caused by SAHA. This case illustrates a new cause for kidney injury and proteinuria in patients with multiple myeloma. HDAC inhibitors cause damage to the proximal renal tubule through apoptosis by both caspase dependent and independent mechanisms. The mechanism of FSGS and proteinuria in this case is likely mediated through caspase dependent apoptosis induced by the HDAC inhibitor SAHA. As this therapy becomes a part of standard myeloma treatment, Nephrologists will need to be aware of the potential harm to the kidney that can be caused by these novel agents.
PO 1-10 - Interstitial Nephritis after Anti-PD1 Therapy with Pembrolizumab in Disease Refractory to Ipilimumab

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Introduction
The number of chemotherapeutic agents available in our arsenal for treatment of metastatic melanoma has been on the rise. There have been recent successes in the use of anti-CTLA4 and anti-PD1 therapies, and the side effect profile for those agents is evolving. We report a case of interstitial nephritis in a patient that received Pembrolizumab for disease refractory to Ipilimumab.

Method
A 58 year old male with metastatic melanoma that was refractory to Ipilimumab, dabrafenib, trametinib, carboplatin, taxol, bevacizumab, paclitaxel and was receiving Pembrolizumab (2mg/kg q21 days, 2 cycles received) and denosumab (120mg po qd) was admitted to the hospital for investigation of a creatinine of 4.0mg/dl that was incidentally discovered on routine outpatient labs (baseline 0.7mg/dl). His urine analysis showed numerous leukocytes, and his urine protein-to-creatinine ratio was 0.7g/g. Imaging of his kidneys was unremarkable. Patient was not subjected to any nephrotoxins except for a combination naproxen-esomeprazole pill. Conservative management with hydration and cessation of all potential nephrotoxins failed. He underwent a kidney biopsy which on the H&E stain showed prominent, diffuse, active interstitial inflammatory infiltrate comprised primarily of mononuclear cells suggestive of acute drug-related interstitial nephritis. Patient was started on prednisone 60mg/d and his creatinine improved to 1.17.

Results & Conclusion
Acute interstitial nephritis is a relatively common side effect for many medications in use today. With the development of new therapies, the number of known culprits for this complication will be on the rise.

Ipilimumab has been described to have many immunologic side effects such as rashes, colitis, hypophysitis, hepatitis, pancreatitis, iridocyclitis, lymphadenopathy, neuropathies, and nephritis, collectively known as “immune-related adverse events” (irAEs), those are thought to be unique side effect of immune check point inhibitors and are thought to be related to general immune system enhancement. Those side effects have been primarily described with CTLA4 inhibitors, but more cases have been recently reported with other check point inhibitors such as Programed Cell Death-1 receptor inhibitors. Interstitial nephritis due to Ipilimumab has reported in 6 cases previously, 5 of which showed granulomatous interstitial nephritis. All patients were treated with steroids and five of them responded favorably (no data on the 6th patient).

On the other hand, biopsy-proven acute interstitial nephritis with Pembrolizumab was only reported twice before. Patients also received high dose steroids with full recovery.

In our patient, causality cannot be firmly established, as the patient was taking a PPI and an NSAID, both of which are known to cause AIN, but the time-frame of his injury is highly suggestive of Pembrolizumab-induced acute interstitial nephritis.

We suggest keeping a high index of suspicion for AIN in any patient who presents with AKI in the setting of anti-CTLA4 or PD-1 therapy, and having a low threshold for a kidney biopsy to confirm the diagnosis as this process has been shown to be mostly reversible with high dose prednisone therapy.”

References
PO 2-1 - Renal Cancer: Prevalence, Risk Factors and our Prevention in the Great Lakes Region
Jean Safari1
1Great Lakes Regional Hospital

Background
The renal cancer occurs sporadically but the etiology factors leading to its occurrence are quite different. We need to provide the prevalence and the risk factors of the renal cancer in the Great Lakes Region and to propose our prevention.

Method
We selected adult patients (>18 years) from January 2013 to January 214, interviewed to sociodemographic status, classical triad of Kidney cancer (gross hematuria, flank pain, palpable mass); metastatic symptoms (dyspnea or cough, seizure or headache, bone pain); paraneoplastic syndromes (erythrocytosis, hypercalcemia, hypertension); anemia or ESR.

Results
We included 581 patients [age median: 31.5 (30 – 40); OR=3.8; 95% CI: 1.4 – 3.3], men: 229 (43.9); women: 352 (60.6), p<10-4. In multivariate analysis adjusted on age and sex; the risk factors of Kidney cancer were tobacco smoking (128; 22, 3%), obesity (119; 20, 5); aspirin use (97; 16, 7), acquired polycystic kidney disease (78; 13, 4%).

Conclusion
The kidney cancer is strongly associated with certain risk factors. A significant association is now reported between tobacco smoking; aspirin use and acquired polycystic kidney disease. We apologize for screening to each patient who presents gross hematuria, flank pain, palpable mass; bone pain, hypercalcemia, hypertension or anemia by MRI or Pelvis X-ray to exclude to confirm kidney cancer.

References

PO 2-2 - Renal Cancer: Prevalence and Risk Factors in the Great Lakes Region
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Background
Prevalence of cancer is unknown as well as the Kidney disease in the Great Lakes Region. Although the earliest is the diagnosis, the more benefit will be the treatment. Our aim is to know the vulnerable people profile of cancer in our Region.

Method
We conducted a cross-sectional study from June 2012 to May 2014. Each patient with obesity, HTA or tobacco smoking was interviewed for microalbuminuria and hematuria. We used the Fagerstom test to evaluate the physical dependence. SPSS 13.0 software was used for data entry and data processing. The bilateral paired t test was used for continuous data. Multivariate logistic regression was used to estimate the odds ratio. P <0.05 was considered significant.

Results
Among 1500 with abnormal renal biomarkers and high tobacco smoking dependence, 103 patients (6, 9%) had a terminal hematuria and Hb < 10 mg/dl (sex ratio 1.3 for men; age 21 ± 5 years) which signed a renal cancer. Our anti-tobacco program used Varenicline (Champix) 0.5 mg and our patients stopped tobacco completely after 14 days.
Conclusion
The renal cancer is more common among men than women and it’s the third urological cancer behind the Prostatic and the bladder cancers. Tobacco is one of the risk factors. At the stage of renal failure, medical interventions should slow the progression of renal failure and avoid nephrotoxins such as tobacco. Tobacco toxicity is due to the hemodynamic and non-hemodynamic effects. The hemodynamic effect is an elevated peripheral vascular resistance which occurs an elevated blood pressure. Smoking People have 3 or 12mmHg and high myocardia Infarctus and cerebral hemorrhagy hemodynamic effect is an elevated peripheral vascular resistance which occurs an elevated blood pressure. Smoking People have 3 or 12mmHg and high myocardia Infarctus and cerebral hemorrhagy.

References

PO 2-3 - Incidence of Chronic Kidney Disease in Patients with Kidney Cancer after Surgical Treatment
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1Scientific Centre of Urology named after B. U. Dzharbussynov

Background
Kidney cancer is the 13th most common malignancy worldwide [1]. Renal cell carcinoma (RCC) accounts for approximately 90% of all renal malignancies [2]. CKD is increasingly being recognized as a significant public health problem worldwide. The incidence and prevalence have been steadily and continuously rising, followed by an increase in associated complications and deteriorations in general health conditions [3]. Patients with RCC are at increased risk of CKD development and progression, especially after surgical treatment [4]. Aim of the study was to determine the incidence of chronic kidney disease (CKD) at patients with kidney cancer after surgical treatment.

Method
This is single-center study. 163 patients with kidney cancer were under observation from 2010 till 2014 years. There were performed 116 nephrectomy (71.2%), 4 cryodestruction of renal mass (26.4%). 4 patients had bilateral kidney cancer and end-stage renal disease (ESRD), so they were inoperable. For control group we also examined 120 patients after nephrectomy due to other reasons such as hydronephrosis, staghorn nephrolithiasis and cystic disease. All patients underwent clinical, laboratory examination, ultrasound, and multispiral computer tomography with angiography. Control
examination was performed after 12-24-36 months. GFR was estimated by Cockroft-Gault formula. Statistical analysis was performed on Statgraphics Centurion XVI.

Results
The mean age of patients with kidney cancer was 55.8 ± 6.6 years. 52 patients (31.9%) had no clinical symptoms of kidney tumor, so it was diagnostic finding. 86 patients (52.8%) were hypertensive and 38 (23.3%) had diabetes mellitus. Before surgery, only 13 patients (7.9%) had decreased GFR lower than 60 ml/min/1.73 m², 4 patients had ESRD. Of 159 operated patients, there were 7 cases (6%) of internal bleeding during nephrectomy and 1 case during cryodestruction. After operation, 4 patients had infectious complications (2.5%). After 12 months of observation, signs of CKD were determined in 38 patients (28.9%). 24 months later, after operation CKD was diagnosed in 57 patients (35.8%), and after 3 years of follow-up in 71 patients (44.6%) had stable CKD. Of 71 patients with CKD, 38 patients (53.5%) had nephrectomy, 59 patients had nephrectomy, 1 – cryodestruction of renal mass. Compared to patients who underwent cryodestruction, patients after nephrectomy had significantly high risk of CKD (OR = 2.67; 95% CI: 1.25, 5.57, P=0.01).

In control group of 120 patients, 44 (36.6%) had CKD after 3 years follow-up. Compared to control group, patients who had surgery due to kidney cancer had a moderate, statistically significant, increase in risk of CKD (OR = 1.78; 95% CI: 1.06, 3.00, P=0.02).

Conclusion
Nephrectomy can be considered as a serious condition since more than a half of operated patients after 3 years of follow-up have CKD. Diagnosed on early stage, kidney cancer can be operated by partial nephrectomy or cryodestruction, and the risk of CKD will be significantly lower. The incidence of CKD at patients after nephrectomy due to kidney cancer is significantly higher than at patients who had nephrectomy due to other reasons.

References

PO 3-1 - Prevalence of Anemia and Chronic Kidney Disease in Cancer Patients. Potential Inter-Relationships
Scotté F., 1 Janus N., 1 Ray-Coquard I., 1 Beuzeboc P., 1 Daniel C., 1 Gligorov J., 1 Selle F., 1 Goldwasser F., 1 Mir O., 1 Spano JP., 1 Thery JC., 1 Rey JB., 1 Jouannaud C., 1 Morere JF., 1 Oudard S., 1 Deray G., 1 Launay-Vacher V. 1
1 Pitié-Salpêtrière Hospital

Background
Anemia in cancer patients is often, if not only, considered as chemotherapy-induced anemia (CIA). However, CKD which may induce renal anemia, is also highly prevalent in solid-tumour patients. The results of 3 clinical studies we conducted (IRMA-1, IRMA-2 and MARS) were pooled. In all 3, the methods and staff were the same to define anemia and CKD and determine their prevalence.

Method
Anemia was defined as Hb <10 g/dL. Patients were classified according to the ESMO definition. CKD was defined according to the KDIGO and the glomerular filtration rate estimated with the MDRD formula, as recommended.

Results
10'753 patients were included in total. Mean/median age was 58.8/59.0 years. Female: 63.9%. Main cancers were breast (4'123), colorectal (1'520), lung (1’013), ovarian (649), and prostate (525). 12.2%
of the patients had a Hb<10 g/dL and 11.6% had CKD (MDRD<60). The mean Hb was slightly but significantly lower in CKD patients: 11.5 vs 12.0 g/dL, p=0.0001) and the prevalence of Hb<10 was nearly twice and significantly higher in CKD patients: 21.3% vs 11.1%, p=0.0001.

Conclusion
The prevalence of anemia in our patients was higher in cancer patients with CKD, suggesting that renal anemia may be present in addition to other cancer-related causes. This observation is of importance since, although the treatments are the same (IV iron and erythropoiesis-stimulating agents), the doses and schedules may vary between CIA and renal anemia.

PO 3-2 - Multiple Myeloma and High Cut-Off Hemodialysis: On the Right Track for Better Outcomes?
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Background
Acute kidney injury (AKI) is commonly associated with Multiple Myeloma (MM). It is essentially a consequence of direct exposure of renal tubules to the large amounts of free light chains (FLC) in circulation and confers a poor prognosis. Hence, limiting FLC exposure is one the main therapeutic goals. Chemotherapy (CT) has evolved in the last years, with bortezomib among the first-line regimens in patients with renal impairment at the present days. Studies have related improved prognosis, but little is known about outcomes in patients with dialysis-dependent AKI. Removal of serum FLC by high cut-off hemodialysis (HCOH) has recently been described as an adjuvant to further increase renal outcomes. However, it remains unclear whether HCOH effectively provides a clinical benefit over CT alone.

With this in view, we aimed to analyse the clinical progress and outcomes of a group of patients with MM dependent AKI by assessing the prognostic impact of HCOH and bortezomib-based CT in renal function recovery (RFR) and overall survival in comparison with other conventional risk factors.

Method
We retrospectively reviewed the medical records of patients presenting to our center between 1st January 1999 and 31st March 2013 with MM and dialysis dependent AKI.

Results
A total of 46 patients were admitted to our center during the study period. The median age at the beginning of dialysis was 68 (56-73) years old and 57.4% were male. Nine patients were treated with HCOH. All of them were also treated with bortezomib regimens.

Eleven patients (23.9%) recovered renal function and 63.6% of these were treated with HCOH. Three potential factors significantly increased the probability of RFR according to univariate analysis: CT regime with bortezomib (p<0.001), HCOH (p<0.001) and the presence of hypercalcemia (p=0.037). In multiple logistic regression, the only consistent and significant predictor factor was HCOH. Patients submitted to HCOH had a significantly higher probability of recovering renal function than patients who underwent conventional hemodiafiltration (OR=11.491; 95% CI: 1.044-126.488).

After a median follow-up of 18 months (range, 0 to 62), 33 (71.7%) patients died, 1(2.2%) was lost to follow-up and 13 (28.3%) were still alive at the time of this report. The median survival rate was 20 months. The overall 1-year survival rate was 58.3%.

In univariate analysis, RFR (p<0.001) and gender (p=0.012) had a significant impact on overall survival. Age, type of light chain, HCOH, bortezomib, hematopoietic stem cell transplantation (HSCT) and hypercalcemia were not associated with overall survival.

Multivariate analysis confirmed the influence of gender and RFR. Male sex was associated with worse overall survival, presenting an increased hazard ratio (HR) of death due to MM (HR=4.920; 95% CI: 1.971-12.284). In turn, RFR (HR=0.244; 95% CI: 0.074-0.802) was a significant predictor for prolonged survival compared with those who remained on dialysis.
Conclusion
Our study shows that, even though the novel anti-myeloma agents have been associated to improved disease control, adding HCOH is independently associated to better outcomes in patients with MM and dialysis-dependent AKI.

PO 3-3 - Tumor Lysis Syndrome: Monocentric Evaluation of a Predictive Tool
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Background
Tumor lysis syndrome (TLS) is an oncological and metabolic emergency caused by massive lysis of malignant cells. Despite the beneficial effect of preventive administration of rasburicase, the decision to start this therapy largely depends on subjective evaluation of the treating physician. Recently, Sanofi-Aventis developed a software tool aiming to evaluate the individual risk for TSL development, based on recent guidelines (Collier B, et al. 2008). Aim. We undertook a monocentric retrospective analysis of patients with hematological malignancies aiming to determine the correlation between the subjective and the effective TLS risk.

Method
Adult patients treated with induction chemotherapy and rasburicase in our center between 2003 and 2010 were included. For all these patients the predictive TLS tool was calculated.

Results
116 patients were included (57.5% males, median age 55.5 years) in this analysis, all diagnosed with acute leukemia or aggressive lymphoma subtype. Fourteen patients developed acute renal failure requiring hemodialysis. Four weeks following start of therapy, 64 patients were alive. Based on the TLS tool a risk analysis was calculated: 46 patients were considered high, 24 intermediate and 18 low risk for TLS, whereas 28 patients only had features of laboratory TLS at diagnosis.

Conclusion
There seems to be a huge discrepancy between the subjective feeling of high TLS risk and the risk determined by a recently developed tool. Such types of tool may help clinicians in more correct estimation of the real TLS risk, which also has economic impact given the high cost associated with rasburicase treatment.

References

PO 4-1 - Hypertension, Proteinuria and Overall Survival in Elderly Cancer Patients Treated with Bevacizumab
Spano JP¹, Janus N.¹, Ray-Coquard I.¹, Gligorov J.¹, Selle F.¹, Beuzeboc P.¹, Daniel C.¹, Thery JC.¹, Goldwasser F.¹, Mir O.¹, Rey JB.¹, Jouannaud C.¹, Morere JF.¹, Oudard S.¹, Scotté F.¹, Azzi JM.¹, Dorent R.¹, Deray G.¹, Launay-Vacher V.¹
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Background
MARS is a multicentric, non-interventional, prospective study which first reported the high prevalence of both baseline and de novo hypertension (HTN) and proteinuria (Pu) in several sub group of cancer patients [Gligorov J et al. SABCS 2013; Ray-Coquard I et al. ASCO GI 2014; Ray-Coquard I et al. ASCO GU 2014; Goldwasser F et al. ECC 2013; Launay-Vacher V et al. ASCO 2013]. In this subgroup analysis, we focused on elderly cancer (EC) patients treated with bevacizumab.

Method
MARS included 1'124 patients, all naïve of any previous anti-VEGF treatment. A First Renal
Assessment was performed at baseline before the anti-VEGF was started with periodic follow-up for 1 year. Elderly was defined as age ≥65 years at inclusion. Univariate (UA) and multivariate analyses (MA) tested the associations of HTN and Pu, at baseline or de novo, with overall survival (OS) (pre-planned) in EC patients.

Results
845 patients treated with bevacizumab were included. Among them 226 were EC patients (colorectal 81, breast 78, ovarian 26, lung 22...). At inclusion, HTA was statistically higher in EC patients, mean aMDRD was 79.6 ml/min/1.73m² and 15.1% had aMDRD<60. De novo HTA; de novo Pu and Scr increase were not statistically more frequent in EC patients than in non-EC patients. In addition, renal function decreased by -4.1 ml/min/1.73m²/year and 16.2% had aMDRD<60 at the end of follow-up. Baseline and de novo HTN and Pu were not associated with reduced OS in EC patients in both UA and MA analyses.

PO 4-2 - Management of Antiangiogenics’ Renovascular Safety (MARS Study) in Renal Cell Carcinoma
Oudard S.1, Janus N.1, Ray-Coquard I.1, Goldwasser F.1, Mir O.1, Scotté F.1, Spano JP.1, Thery JC.1, Beuzeboc P.1, Daniel C.1, Rey JB.1, Jouannaud C.1, Gligorov J.1, Morere JF.1, Azizi M.1, Dorent R.1, Deray G.1, Launay-Vacher V.1.
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Background
MARS is a prospective multicentric study conducted to assess the renovascular tolerance of anti-VEGF drugs (AVD) in the clinical setting in France, in a number of different tumor types.

Methods
Patients (pts) from 8 centres were included when they were 1) naïve of any AVD and 2) about to start treatment with an AVD, from 2009 to 2012, with a follow-up (f/u) of 1 year. Data collected included: gender, age, serum creatinine (Scr), HTN, hematuria (Hu) and dipstick Pu, at baseline and at each visit during f/u. This sub-group analysis presents the results for metastatic renal cell carcinoma (mRCC) pts receiving sunitinib.

Results
1124 pts were included. 137 had mRCC and 112 received sunitinib. Median age: 61.0 years. Visceral, bone and cerebral metastasis frequencies were 71.4, 42.0 and 12.5%, respectively. All except 3 pts, had at least one kind of metastasis. At inclusion, HTN prevalence was 43.8%. Baseline renal assessment retrieved: Pu 15.6%, Hu 8.1%, mean aMDRD 69.4 ml/min/1.73m². The incidence of de novo Pu and HTN during f/u was 75.0 and 21.4%. All pts with Pu at inclusion improved or remained stable. Among pts with de novo Pu, 75.8% afterwards improved/normalized. Mean aMDRD was 72.2 at the end of f/u. 0.7% had grade 3 Scr increase (no grade 4). No thrombotic micro-angiopathy (TMA) was reported.

Conclusion
These results on the renovascular safety of AVD in RCC patients showed that 1) TMA is rare, 2) Pu develops in 75.0% of the pts, 3) 21.4% developed HTN. Furthermore, in case of a renovascular effect, investigators followed the recommendations from the French Society of Nephrology (Halimi JM. Nephrol Ther 2008) and no treatment withdrawal for unmanageable renovascular toxicity occurred.

PO 4-3 - Management of Antiangiogenics’ Renovascular Safety (MARS Study) in Colorectal Cancer
Janus N.1, Ray-Coquard I.1, Spano JP.1, Thery T.1, Goldwasser F.1, Mir O1, Beuzeboc P.1, Daniel C.1, Morere JF.1, Rey JB.1, Jouannaud C.1, Oudard S.1, Scotté F.1, Gligorov J.1, Selle F.1, Azizi M.1, Dorent R.1, Deray G.1, Launay-Vacher V.1.
1GH Pitié-Salpêtrière
Background
MARS is a prospective multicentric study conducted to assess the renovascular tolerance of anti-VEGF drugs (AVD) in the clinical setting in France, in a number of different tumor types.

Method
Patients (pts) from 8 centres were included when they were 1) naïve of any AVD and 2) about to start treatment with an AVD, from 2009 to 2012, with a follow-up (f/u) of 1 year. Data collected included: gender, age, serum creatinine (SCr), HTN, hematuria (Hu) and dipstick Pu, at baseline and at each visit during f/u. This sub-group analysis presents the results for colorectal cancer (CRC) pts receiving bevacizumab (BVZ).

Results
1124 pts were included. 200 had CRC and all but 5 received BVZ. Median age: 63.2 years. Visceral, bone and cerebral metastasis frequencies were 91.3, 10.8 and 0.5%, respectively. All pts presented metastasis. At inclusion, HTN prevalence was 26.2%. Baseline renal assessment retrieved: Pu bevacizumab (BVZ).

Conclusion
These results on the renovascular safety of BVZ in CC patients showed that 1) TMA is rare, 2) Pu develops in 78.2% of the pts, (no Grade 4), 3) 16.1% developed HTN. Furthermore, in case of a renovascular effect, investigators followed the recommendations from the French Society of Nephrology (Halimi JM. Nephrol Ther 2008) and no treatment withdrawal for unmanageable renovascular toxicity occurred.

PO 4-5 - In Vitro Study for the Identification of Drugs Able to Prevent Cisplatin-Induced Acute Kidney Injury
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Background
Acute kidney injury (AKI) is a severe adverse effect of cisplatin (CisPt) -based chemotherapy in cancer patients, affecting proximal tubular epithelial cells (RPTECs). Injuries are associated with an increased oxidative stress and can trigger cell death, contributing to the rapid loss of the renal function, for which severity and duration depend on the regeneration capacities of tubular cells. Other processes occurring in CisPt-induced AKI involve the loss of phenotypic characteristics of RPTECs leading to their dedifferentiation in mesenchymal cells (the so-called epithelial-to-mesenchymal transition (EMT)), eventually evolving in fibroblasts. The subsequent deposition of extracellular matrix (ECM) results in interstitial fibrosis and chronic renal failure.

The current clinical procedure aiming to prevent CisPt tubulotoxicity (hyperhydration) is only partially effective: about one third of patients experience acute tubular necrosis and AKI. Nephroprotective strategies including pharmacological approaches remain to be developed. In this in vitro study, we aimed at identifying tubuloprotective compounds isolated from herbs reported to be useful against nephrotoxic drugs: Angelicae sinensis radix, Eleutherococci radix, Ginseng radix, Schisandrace chinensis fructus and Silybi mariani fructus.

Method
HK-2 cell line, originating from human RPTECs, was used as an in vitro nephrotoxicity model. Herbal extracts were produced and tested for possible protection along 5 phenomena involved in the pathophysiology of CisPt-induced AKI:
- Cell death and apoptosis, respectively measured with the resazurin (cell survival) assay and flow cytometry detection after annexin V/PI staining;
Conclusions

- Oxidative stress elevation, evaluated by assessing the antioxidant potential of the herbal products (radical scavenging capacity) and by quantification of oxidative stress mediators in cellulo (fluorescent probe oxidation);
- ECM deposition, assessed by means of collagen quantification (picrosirius red staining and spectrophotometric determination);
- β-catenin delocalization, used as a marker for epithelial or EMT phenotypes, respectively investigated by (i) the determination of its membranous form; and (ii) the quantification of the cytoplasmic/nuclear isoform by flow cytometry;
- Modulation of regeneration capacities, assessed by possible enhancement of cellular proliferation (Ki-67 index and cell cycle phase distribution) and motility (scratch assay for migration rate). The most promising extract was further tested to link its activity to one (or several) of its compound(s) along the same methodology.

Results

Among the 5 tested herbs, Angelicae sinensis radix exhibited the most promising potential to reduce CisPt tubulotoxicity (particularly in improving cell survival, reducing ECM deposition and enhancing regeneration capacities). Its putative active compounds, ferulic acid, Z-ligustilide and E-ligustilide were further tested. Ferulic acid emerged as the most potent drug for improving cell survival and for alleviating CisPt-induced apoptosis. It also allowed to restrain the collagen production, enhanced the regeneration capacities of healthy cells and partially inhibited the activation of the β-catenin pathway. However, it was ineffective in reducing oxidative stress.

Conclusion

By exhibiting a protective activity on RPTECs exposed to CisPt in vitro, ferulic acid appears as a promising drug candidate deserving further preclinical investigations (e.g. in vivo studies) for the prevention of AKI and chronic complications.

PO 4-6 - Membranous Nephropathy is Significantly Increased after Hematopoietic Stem Cell Transplantation

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Background

Chronic kidney disease (CKD) occurs in 10 to 30% of subjects after hematopoietic stem cell transplantation (HSCT). In addition to medication toxicities and radiation, graft versus host disease (GVHD) and membranous nephropathy (MN) are specific causes of CKD in these subjects. Nephrotic range proteinuria (NRP, which is 3 or more grams urine protein per day) is a sign of MN.

Method & results

We evaluated all 271 adults who underwent allogeneic HSCT at our center from 2005 to 2011, by reviewing their record for the presence of nephrotic range proteinuria (NRP). Nine of these 271 had NRP. At kidney biopsy four (4) had MN, two had focal glomerulosclerosis, one had minimal change nephrosis, and two had only tubulointerstitial injury. The onset of NRP in our cohort was a late event, occurring at a median of 812 days after transplantation (range 342–2555 days). The amount of proteinuria ranged from 3.3 to 10.2 g in 24 h urine specimens. Serum albumin level ranged from 2.2 to 3.7 g/dL with a median value of 3 g/dL. Seven patients had a preceding history of cGVHD. Among these seven patients, three were off immunosuppression, one was being tapered off immunosuppression and the remaining two patients were on active immunosuppression for cGVHD. In the remaining two patients NRP was the sole (potential) manifestation of cGVHD. We estimated the incidence of membranous nephropathy compared to that of the general population. For 271 patients, there is ~1500 person year follow-up. Four cases out of 1500 is an estimated incidence of 267/100,000; the 95% confidence interval for that estimate is 72 to 638 / 100,000. The incidence of MN in the general population is one (1) per 100,000. The much higher incidence of MN in our series is very significantly higher than that of the general population (p<0.01). Further studies are underway to define its pathogenesis in subjects who have undergone HSCT.
PO 4-7 - Hemato-Oncological Diseases and Acute Kidney Injury requiring Nephrology: The Dark Side of the Moon?

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Background
Acute kidney injury (AKI) is a common complication in hemato-oncological diseases (HOD). The great majority of these patients is managed by the attending physician. Yet, a small group, most often coincident with the worst presentation and prognosis, requires nephrology consultation and follow-up, challenging the clinician with ethical issues regarding the type and level of investment, namely the indication for renal support therapy (RST). Unfortunately, the literature available in the area is scarce. The purpose of this work is to characterize the epidemiology of AKI in HOD and to identify the prognostic determinants for in-hospital mortality in this population.

Method
We retrospectively reviewed the medical records of in-hospital patients with AKI and HOD between 1st January 1995 and 31st December 2014, who met the RIFLE classification of I or higher and were followed by a nephrologist. Patients considered with terminal disease / on palliative care were excluded.

Results
A total of 345 patients were included in the study. The median age was 51 (34-63) years and 60% were male. 148 patients (43%) died.

The tumors had the following proportion: 31% non-hodgkin lymphoma (NHL), 19% acute lymphoid leukemia (ALL), 18.5% multiple myeloma (MM), 18.5% acute myeloid leukemia (AML), 13% other hematologic neoplasms. 40% were submitted to stem-cell transplantation (SCT) (87% of them allo and 13% auto transplant). 13% had graft versus host disease and 9.2% tumoral lysis syndrome (TLS).

51.4% were admitted to the Intensive Care Unit (ICU). 41.3% met criteria for septic shock and 43.4% needed invasive mechanical ventilation (IMV). AKI, was, mostly, a multifactorial syndrome: obstruction was identified in 8.7%, nephrotoxicity in 35.3% (essentially calcineurin inhibitors, aminoglycosides, antiviral and antifungal drugs), prerenal in 27% (exclusive prerenal failure in only 6.1%). Hypercalcemia was found in 6.4%.

50% of the patients required RST: 33% of them underwent hemodialysis (HD), 54% continuous venovenous hemofiltration (CVVH) and 13% did both.

In univariate analysis, the following provided protection against death: Prerenal AKI (p<0.01), obstruction (p<0.05), TLS (p<0.05) e hypercalcemia (p<0.05), MM (p=0.01) 7 factors were associated with an increased risk of death: age > 19 < 54 (p<0.05), SCT (p<0.01), admission to ICU (p<0.01), IMV (p<0.01), septic shock (p<0.01), nephrotoxicity (p<0.01), TSFR (p<0.01).

Variables that independently predicted the risk of death were: septic shock (OR 4.29; 95% CI: 2.06-8.94); IMV (OR 4.31 95% CI: 2.08-8.93) and allo SCT (OR 2.23; 95% CI: 1.26-3.95). The addition of these conditions was used to estimate the probability of dying. The C-statistics was 0.83 (95% CI 0.78-0.88), indicating that the model including the 3 variables had great discriminatory power. The sensitivity and specificity values were 76.2% and 82.5%, respectively, with an overall accuracy of 79.8%. The Hosmer-Lemeshow test confirmed the goodness of fit of the model (p=0.505)

Conclusion
Our work reveals a usually hidden dark side of clinical practice. Patients with HOD and AKI who are submitted to allo-SCT, suffer from septic shock and need IMV are associated to such a high mortality that this is often kept an untold story.

PO 4-8 - Active Malignancy is a Novel Risk Factor of Community-Acquired Acute Kidney Injury in Outpatients

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Background
Compared with hospital-acquired AKI, little is known about community-acquired AKI (CA-AKI). The definition of AKI is a small increase in Cre from baseline within 2-7 days, and extending this duration could cause an increase of false positives such as the patients with Cre fluctuation or chronic kidney disease (CKD). Therefore, the aim of study is to clarify the prevalence, risk factors, and outcome of CA-AKI in outpatients.

Method
Firstly, we enrolled the patients whose Cre is increased by 50% or +0.3mg/dl in electric health record from baseline Cre, defined as the most recent Cre during preceding 12 months between Sep 2011 and Mar 2012 in our hospital. Next, the enrolled patients were divided into “False positive” and “CA-AKI” group. False positive group consisted of two subgroups; one is a group of patients with Cre fluctuation, who did not fulfill the criteria when baseline Cre was redefined as the mean value of Cre obtained one year before the enrolled date, and the other is a group of patients with CKD, whose slope of the reciprocal Cre curves was constant during 6 months before and after the enrolled date. The rest of above patients were all classified into CA-AKI group. Finally, the prevalence rates of comorbidities and the outcome (AKI stage 2 and 3, or death within one year) determined from chart review were compared between CA-AKI and False positive group by multivariate analysis.

Results
Among 85172 outpatients in the analysis, 1298 patients (1.5%) were enrolled, and classified into False positive (457 patients: 0.51%), and CA-AKI (841 patients: 0.99%) group. CA-AKI group had higher prevalence of active malignancy (OR 2.98; CI 1.91-4.76), cardiovascular disease (OR 1.88: 1.36-2.62), age>65 (OR 1.71: 1.23-2.36), NSAIDs (OR 2.22-6.63), Calcineurin Inhibitor (OR 3.74: 2.22-6.63), and ACEi/ARB (OR 1.68: 1.23-2.30) compared with False positive group. The proportion of AKI stage 2 and 3, or death within a year was higher in CA-AKI group (OR 6.81 p<0.001).

Conclusion
CA-AKI could occur in approximately 1% of outpatients and showed poor outcome. Active malignancy could be candidates of the risk factors for CA-AKI, along with several comorbidities and nephrotoxic agents.

PO 5-1 - Intermittent Dosing of Aromatase Inhibitors (AI) to Improve Tolerance in Post-Menopausal Women
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Background
Clinical rationale
A significant proportion of post-menopausal, patients treated with AI reports side-effects, especially bone pain. In such patients, the difficulties to treat pain and to clearly identify its causes may lead to treatment discontinuation. Individual cases reported an improvement in AI tolerance when dosage is reduced. The aim of this work was thus to analyse pharmacological data in order to validate this concept i.e. ensuring that intermittent dosing would not result in a possibly deleterious under-dosing of AI.

Pharmacological rationale
Ageing is associated with physiological modifications that may impair drug pharmacokinetics (PKs). The elimination can be altered, with decreased drug clearance (CL), resulting in an increased exposure to the drug, reflected by increased AUCs. Drugs benefit-risk balance can thus be modified. The major sources of PKs alterations in the elderly are hepatic and/or renal impairments (HI/RI).

Results
It has been shown that AI PKs are altered in the elderly and/or in case of HI or RI. Exemestane AUC is increased 3-fold in the elderly and in case of RI [1,2]. Letrozole AUC can double in case of HI [3].
and a 42%-increase has been reported in the elderly [4]. The renal CL of anastrozole is reduced by 50% in RI, resulting in a 10% decrease in total body CL. In HI, total body CL is 30% lower as compared to normal [5].

These data demonstrate that elderly patients may be overexposed to AI when treated with the usual dosage, resulting in safety issues occurring in some patients. As a result, a dosage adjustment approach could help prevent over-exposure and reduce side-effects incidence/severity.

**Conclusion**

**Proof-of-Concept studies:** The reported increases in AI exposure being around 50%, an intermittent dosing schedule of 1 administration every other day could result in a similar drug exposure as compared to the usual daily schedule. AI elimination half-lives in the absence of any alteration also are consistent with this dosing schedule (24, 48, and 50 hours for exemestane, letrozole, and anastrozole, respectively). In order not to impair plasma concentrations, such a schedule is preferably suggested as compared to a half-dose daily schedule. Prospective studies are needed, in which the PKs, efficacy, and safety of this intermittent dosing schedule should be conducted.

**References**

1. Aromasin® FDA Labeling Information; 2013 labeling revision; http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020753s014lbl.pdf; accessed 04/29/2014
5. Arimidex® FDA Labeling Information; 2013 labeling revision; http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020541s027lbl.pdf; accessed 04/29/2014

**PO 5-2 - Chronic Kidney Disease, Anticancer Drug Adjustment and SiteGPR®**

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**Background**

Chronic kidney disease (CKD) is highly frequent in cancer patients and has already been assessed in several studies. The IRMAs studies [1-3], for example, reported that 50 to 60% of cancer patients had abnormal glomerular filtration rate. As a result, the question of anticancer drug handling, and more specifically dosage adjustment, rises to prevent dose-related toxicities. However, the main difficulty is to find adequate recommendations in this population. Service ICAR created the website SiteGPR® (www.sitegpr.com) to provide drug dosage recommendations in CKD patients, based on the international literature. Service ICAR performed an analysis of the SiteGPR® database in order to analyze the usage of the website.

**Method**

Extraction from the SiteGPR® was performed for all consultations of the recommendations from January 2012 to October 2014. Anticancer drugs were classified as “yes” when dosage adjustment was required, “no” when dosage adjustment was not necessary, and “ND” when no data were available in the international literature. The recommendations were analyzed from SiteGPR® and compared to summary of product characteristics (SmPC) 1) for each anticancer drug International Nonproprietary Names (INN) and 2) for all the recommendation seen by physicians/pharmacists concerning anticancer drugs.

**Results**

SiteGPR® provided recommendations for 821 different INN, including 136 anticancer drugs (chemotherapy, targeted therapy…). Among these 136 anticancer drugs INN, SiteGPR® provided a
recommendation for 73.5% (INN labelled “yes” for 31.6% or “no” for 41.9%). For the remaining 26.5% (INN labelled ND), it was possible to ask the website team for a specific recommendation. Consequently, SiteGPR® was able to propose a drug dosage recommendation for 100% of cases (after asking for specific recommendations). On the contrary, in 77.2% of these 136 anticancer drugs’ SmPCs, no usable recommendations were provided (INN labelled ND). Physicians/Pharmacists consulted 13 098 anticancer drug dosage recommendations on the SiteGPR®. Among these, SiteGPR® provided a recommendation for 85.2% (recommendation labelled “yes” for 46.6% and labelled “no” for 38.6%). For the remaining 14.8%, the Service ICAR team could provide a specific recommendation if required. However, SmPCs were not able to provide a recommendation in 71.0% of cases for the corresponding consultations. SmPCs were usable in only 29.0% of cases.

Conclusion
This analysis of the SiteGPR® database underlined that
1) many anticancer drugs need a drug dosage adjustment in CKD patients;
2) SmPCs are not an adequate and useful source of information for prescribing anticancer drugs in CKD patients
3) SiteGPR® provide in most INN and cases a drug dosage recommendations in CKD patients.
Finally, if SiteGPR® does not provide a recommendation for drug dosage, physicians/pharmacists can ask Service ICAR on SiteGPR®.

References

PO 5-3 - Retrospective Survey on the Use of Two TKIs in Metastatic RCC Patients Receiving Haemodialysis (HD)
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Background
Patients requiring HD are usually excluded from randomized controlled trials of anticancer agents. Thus, safety and efficacy of oncological treatments are almost unknown in this setting. The aim of this retrospective, real-world, study was to investigate the safety and efficacy of two first-generation TKIs (i.e. sunitinib and sorafenib) in patients with metastatic renal cell carcinoma (mRCC) and end-stage renal disease requiring HD. Patients — Between July 2006 and December 2010, 24 mRCC patients (16 males and 8 females, median age: 65 years) undergoing HD were treated with sunitinib and/or
sorafenib in 14 Italian institutions. We retrospectively reviewed the medical records of these patients with the aim of evaluating the administered doses of TKIs, their treatment-related adverse events, as well as the clinical efficacy of the oncological treatment.

Results
Sunitinib was administered at the dose of 50 mg daily in 6 patients, at 37.5 mg daily in 7 patients (one of them subsequently increased the dose to 50 mg daily), at 25 mg daily in 2 patients, and at 12.5 mg daily in 1 patient; for all these patients, irrespective of the dose used, the schedule was the classical one, consisting of 4 weeks of treatment and 2 weeks of pause. Among the 8 patients treated with sorafenib, 4 received the standard dose of 800 mg daily (400 mg b.i.d.), 3 patients received 400 mg daily, and 1 patient 200 mg daily, all within a continuous dosing schedule. The estimated median PFS of the whole cohort were 10.3 months and 22.6 months, respectively. With regards to safety profile, notably, no unexpected adverse events were registered and no grade 4 haematological or non-haematological toxicities were reported. No patient had to change the number of dialysis sessions (three times a week) during the oncological treatment, while sunitinib and sorafenib were administered at any time regardless of the timing of HD.

Conclusion
Despite all the biases of a retrospective study, sunitinib and sorafenib appear to be not contraindicated in patients with mRCC undergoing HD. Indeed, the outcome of these patients was similar to that observed in patients with normal renal function treated with TKIs.

PO 5-4 - Management of Nephrectomized Cancer Patients Receiving or Not Active Oncological Treatment
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Background
Nephrectomized cancer pts have an increased risk of developing chronic kidney disease (CKD); such a risk is higher in those under aTx due to its possible renal toxicity. Furthermore, when a nephrectomized patient receives aTx, his/her risk of developing aTX-related adverse events increases. Therefore, we started to follow, within a dedicated outpatient Onco-Nephrology Ambulatory, nephrectomized cancer pts with normal kidney function but with concomitant risk factors (e.g. diabetes, hypertension, etc ...), as well as nephrectomized cancer pts with CKD; all pts were either under aTx, or just followed-up. Patients – To date, 127 pts have been referred to us; 51 had stage I-III CKD, 32 stage IV CKD (17 being under aTx) and 23 stage V CKD (13 being on aTx). Pts were evaluated every 3 months for 1 year after nephrectomy if renal function was normal or in case of stage I-III CKD, and then every 6 months (for both followed-up and treated pts); pts with stage IV and V CKD were seen every 30-60 days.

Results
In stage I-III CKD pts, no cases of CKD progression were recorded, but 1 case of reversible AKI was observed, together with 2 cases of proteinuria from aTx (which was stopped). Of stage IV CKD pts, 1 developed acute kidney injury (AKI) after heart failure induced by cancer therapy (which was stopped), while 2 others had a worsening of their CKD with the need for aTx dose adjustment. Finally, among stage IV CKD pts, 2 started dialysis treatment, but continued aTx, and 2 more had a reversible episode of AKI due to dehydration.

Conclusion
The role of the Nephrologist in the management of nephrectomized cancer pts, either under aTx or not, is key, potentially leading to relevant benefits: reduced progression of pre-existing CKD, reduced risk of developing de novo CKD, continuation of life-prolonging aTx even in pts with severe CKD or receiving dialysis. Further development of Onco-Nephrology (including dedicated ambulatoires) is warranted.
PO 5-5 - Full-Dose Everolimus in Advanced RCC Patients with Different Degrees of Renal Impairment
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Background
The oral mTOR inhibitor Everolimus is well known by Nephrologist, being commonly used as an immunosuppressant for kidney transplant recipients; more recently, it has been registered also for the treatment of aRCC patients already pre-treated with tyrosine kinase inhibitors. However, the two uses of this agent are completely different the one from the other, especially in terms of the doses used in the two indications. Experience with Everolimus in aRCC patients (who are usually nephrectomized) is almost limited to patients with normal or just slightly compromised renal impairment, due to the strict selection criteria used for the registgtive placebo-controlled, randomized phase III, RECORD-1 trial. Consequently, almost no safety and efficacy data are available in patients with more pronounced kidney impairment. Patients – Thus, we retrospectively stratified 20 advanced kidney cancer patients from everyday’s clinical practice who received Everolimus, according to the degree of their kidney impairment, comparing Everolimus safety and efficacy. Since Everolimus do mainly act as a cytostatic (and not a pure cytotoxic) drug, the efficacy variables considered were Disease Control Rate (DCR), i.e., objective responses + disease stabilizations, and Progression Free Survival (PFS). As far as toxicity, adverse events were graded according to NCI-CTC; particular attention was obviously given to variations of the degree of kidney impairment.

Stage eGFR (mL/min/1.73 m2) Number of pts.
2 Mild decrease in kidney function 60-89 9
3 Moderate decrease in kidney function 30-59 6
4 Severe decrease in kidney function 15-29 5

Results
DCR and PFS were super-impossible in the three subgroups (and consistent with that expected on the basis of the RECORD-1 trial data), as it was the safety profile, with no unexpected or exaggerated AEs. Two patients, both form stage 3 (those with the lower GFR at the baseline), presented a progressive worsening of their renal function during treatment, which we did not considered to be drug-related; indeed, neither a reduction of Everolimus dosage (from 10 to 5 mg daily) in one patient, nor treatment interruption (in the other patient), nor the ultimate treatment withdrawal (due to disease progression) lead to an improvement of their renal function.

Conclusion
Everolimus treatment is safe and effective in aRCC patients with various degrees of renal impairment.

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PO 5-6 - Safety and Efficacy of Everolimus in Metastatic MRCC Patients Receiving Hemodialysis (HD)
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Background
Patients requiring HD are usually excluded from randomized controlled trials of anticancer agents. Thus, safety and efficacy of oncological treatments are almost unknown in this setting. The aim of this retrospective, real-world, study was to investigate the safety and efficacy of the oral mTOR inhibitor Everolimus administered in patients with metastatic Renal Cell Carcinoma (mRCC) and end-stage renal disease (ESRD) requiring HD.

Method
Between November 2009 and December 2012, 9 mRCC patients with end-stage renal disease undergoing HD were treated with Everolimus at 8 Italian Institutions. We retrospectively reviewed the medical records of these patients with the aim of evaluating the administered doses of Everolimus, its treatment-related adverse events, as well as its clinical efficacy. Progression-free survival (PFS) and overall survival (OS) (determined using the Kaplan-Meier method) were the main efficacy endpoints considered.

Results
Everolimus was initiated at a dose of 10 mg daily in 8 patients, and at 5 mg daily in one patient. No unexpected adverse events (AEs) or grade 4 AEs (non-hematological or hematological) were reported. The majority of treatment-related AEs were grade 1 or 2 in severity; these included fatigue, dyslipidemia, anemia, cutaneous rash, oral mucositis, and hyperglycemia. The estimated median PFS and OS for the patients of this cohort were 9.01 and 14.36 months, respectively. Notably enough, the PFS value here reported, although biased, is higher than the PFS observed in the registrative Everolimus RECORD-1 trial (i.e. 4.9 months), while OS is similar between the large phase III study (14.8 months) and our retrospective series.

Conclusion
Despite all the biases of a retrospective study, Everolimus appeared to be safe in mRCC patients with ESRD requiring HD. However, larger prospective studies are required to confirm these findings.

PO 5-7 - Pharmaceutical Analysis of Anticancer Drug Doses: Relevance
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Background
Cancers trend to become chronic diseases since new efficient treatments and diagnosis have been available. Both renal failure and nephrotoxicity induced by anticancer medication (ACM) are frequently observed in cancer patients. Close attention is required for prescriptions including ACM in order to provide adapted dosage and avoid treatment discontinuation. Pharmacists of our hospital decided to implement a new method in order to check an efficient adjustment of ACM dose to the renal function of the patient. The improving target consisted in providing to the pharmacist the serum creatinine value of each patient using the software Chimo®. The aim of this study is to evaluate the relevance of the validation of ACM doses by pharmacists, in prevention of renal and systemic toxicities in cancer patients.

Method
All patients treated by ACM in our hospital between September 2013 and September 2014 were included. For each prescription of ACM, computer calculated the glomerular filtration flow (GFF) estimated using the Modification of Diet in Renal Disease shorthand (aMDRD). The pharmacists checked the ACM dose prescribed taking into account the calculated GFF; in case of non-compliance or missing serum creatinine value, pharmacist advised prescribers and/or proposed the appropriate dose. Evaluation criteria were the number and the different kinds of pharmaceutical interventions (PI) and the reasons of potential refusal.

Results
During the study, 1508 patients were included. Twenty-seven prescriptions were concerned by a PI. Seventy-eight percent of these interventions (n=21) concerned dose adjustments and 22% of them (n=6) required an evaluation of the renal function. The most (95%) of dose adjustments (n=20)
proposed by the pharmacist were dose reductions while only one (5%) was a dose increase. The ACM concerned were principally Cisplatin (26%), Etoposide (26%) and Oxaliplatin (22%). Fifty-two per cent of the pharmacist opinions issued (n=14) have been accepted by the respective prescribers, 18% of them have been refused while the others 30% remained unanswered and were considered as refusals. After discussion with prescribers, the most frequent ground for refusal is principally based on a difference observed between the real value of the serum creatinine of the patient and the value recorded in the computer (69%; n=9). The other ground for refusal concerned 3 patients with a Body Mass Index (BMI) less than 18.5 kg/m2 and corresponded to 4 prescriptions of ACM (31%).

Conclusion
Dose adjustment by monitoring the renal function in case of nephrotoxic ACM and/or in case of prescription of ACM in patients with renal failure avoided renal and systemic toxicities and thus treatment continuations in 14 patients. Nevertheless, only one part of the pharmaceutical interventions have been accepted. First, this study points out that serum creatinine value are not always mentioned or updated in the computer, thus preventing the pharmacist from a pertinent analysis of the prescription and exposing patient to risks. Secondly, consensus is not achieved for patient with extreme BMI. In order to harmonise practices and secure prescriptions of ACM, it was decided to constitute a multidisciplinary working group. Results and decisions of this working group will be presented in a further study.

PO 5-8 - Securing the Prescription of Anticancer Drugs According to Renal Function
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Background
Cancers tend to become chronic diseases since the improvement in healthcare management and the development of new treatments. Renal function impairment and nephrotoxicity of some anticancer drugs (ACD) are frequent in cancer patients. The challenge is to secure the prescription of ACD for patients with cancer according to the renal function, thus avoiding renal and systemic toxicities. A first approach implemented between 2013 and 2014 in a French Hospital consisted in providing to the pharmacist the serum creatinine value of the patient in order to assess the preparation of appropriate doses of ACD. This approach is interesting as far as validation of the doses of ACD lead currently to dose adjustments. Nevertheless, this first approach pointed out different difficulties preventing the pharmacist from a complete and relevant analysis, thus exposing cancer patients to potential toxicities. The aim of this study is to secure the prescription of ACD according to renal function.

Method
A multidisciplinary working group composed of at least an onco-hematologist, a pharmacist and a nephrologist was constituted. Several meetings occurred between May 2014 and October 2014. The working areas concerned the evaluation of the renal function, the lack of recommendation for prescription in patients with extreme Body Mass Index (BMI) (<18.5 kg/m2 or >30 kg/m2), discorances between glomerular filtration flow (GFF) calculated by the software and the result provided by analytical laboratories.

Results
The working group provided different tools and guidelines in order to harmonize medical practices and secure the use of ACD. Firstly, it concerned the evaluation of the renal function. It was decided to use the CKD –EPI or aMDRD equations at each chemotherapy course or at least monthly; and for patients with extreme BMI, GFF currently expressed in ml/min/1.73m2 is now adjusted to the real body surface area of the patient. Secondly, a table precision the dose adjustments according to the renal function and the nephrotoxicity of all ACD was developed to support the prescription and the pharmaceutical validation of ACD. The relevant information source selected was the database “Guide de Prescription & Rein”. The third working area concerned the optimization of the software Chimio®. In order to avoid approximations and to access the same renal data, it was decided to enter the estimated GFF provided by the analytical laboratories rather than the serum creatinine value. Finally, reasons for dose reductions have to be mentioned; this allows the pharmacist to take into account if
the dose adjustment is correlated to a systemic toxicity or a renal impairment; thus, providing a relevant pharmaceutical analysis.

**Conclusion**
This work permitted to harmonize medical practices and give guidelines to help prescribers in the prescription of ACD according to the renal function. The use of reliable renal data shared between health professionals improved the relevance of the pharmaceutical analysis. These guidelines contribute to secure the use of ACD in our hospital thus limiting renal and systemic toxicities in cancer patients.

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**PO 6-1 - BCG Therapy in Bladder Cancer after Renal Transplantation for Aristolochic Acid Nephropathy**

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**Background**
Aristolochic acids (AA) are nitrophenanthrene derivatives with nephrotoxic and carcinogenic properties. Human environmental exposure to AA as well as the regular use of AA containing traditional herbal remedies are now recognized as a worldwide public health problem (1, 2). Indeed, AA nephropathy (AAN) is frequently associated with upper tract urothelial carcinoma (3). An unusually high 52% incidence of bladder cancer (BC), mostly early stage, has been found in our cohort of kidney transplant recipients for end-stage AAN (4). A very long persistence of deoxyadenosine aristolactam I-DNA adducts in renal tissue (>20 years) was also reported, appearing as a critical determinant for the AA mutational fingerprint found in oncogenes and tumor suppressor genes recently identified (5).

Our patients receiving a kidney transplant for end-stage AAN benefit from a bilateral nephroureterectomy as well as regular cystoscopic examination in order to detect BC at an early stage. From 1998 to 2007, the therapeutic approach to high-grade non-muscle-invasive bladder cancer (NMIBC) (CIS and high Grade Ta/T1) consisted of transurethral resection of the bladder tumor (TURBT) followed by intravesical mitomycin C for 1 year. Local immunotherapy using bacillus Calmette-Guerin (BCG) had been considered to be contraindicated in immunosuppressed patients. However, faced with recurrent CIS lesions and following results from reported cases (6), we decided to offer the same therapeutic option to our AAN renal transplanted patients with NMIBC at high risk of tumor progression (pT1high grade or CIS). We present here our experience of the efficacy and tolerance of BCG therapy in such patients.

**Method**
Our screening program consists of bi-annual cystoscopy, including cytological analysis and pathological examination of biopsied tissues or resected tumors. With application of guidelines for BCG usage, namely NMIBC of high grade (pT1G3) and/or carcinoma in situ (CIS), 8 patients were treated. Precautions have been applied to reduce risks of graft rejection and infection: doubling of calcineurin or mTOR inhibitors and prophylactic antituberculous treatment (isoniazid 150mg/d and rifampicin 300mg/d) at day -1, 0 and +1 of BCG instillation (Oncotice®) under ciprofloxacin prophylaxis. The tolerance to BCG was recorded clinically (pain, hematuria, fever). Regular follow-up with fluorescence cystoscopy (Hexvix®) was performed along with renal graft function monitoring after 6 weekly cures, 3 maintenance cures and then every 3-6 months.

**Results**
BCG has been used as rescue therapy in 5 patients initially treated with mitomycin C instillations, and as first-line therapy in 3 additional patients. Seven of the 8 patients (54-72 years) are cancer-free after a mean follow-up of 50 months (25-80 months). The patient who relapsed with CIS was considered as having failed therapy after 36 months and was proposed for radical cystectomy with a trans-ileal cutaneous ureterostomy. Tolerance was good, except for one episode of fever and one early
discontinuation because of subjective discomfort. No systemic tuberculous infection was observed. Renal graft function parameters remained stable, as evidenced by individual values of serum creatinine before and after BCG instillations.

Conclusion
This is the first clinical observation of successful BCG therapy for NMIBC in patients given transplant for end-stage AAN. Under standardized conditions, immunotherapy based on intravesical BCG is feasible, effective and well tolerated in renal transplantation.

References

PO 6-2 - Renal Function and Ureteroenteric Strictures following Radical Cystectomy with Ileal Conduit

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UZLeuven

Background
An extensive, single tertiary center study was performed to investigate the different risk factors and treatment options for ureteroenteric strictures following radical cystectomy with ileal conduit.

Method
We reviewed the datasheet of 304 consecutive patients who were treated with a radical (RC) and ileal conduit (IC) between January 2001 and May 2011 in our tertiary center and who followed a strict follow-up protocol. Multivariable analysis was performed to determine which factors were independently associated with UES and long-term treatment outcome was retrospectively analyzed. Renal function (eGFR) was measured every 3 months during the first 2 years, every 6-months during the third, fourth and fifth year and annually after 5 years. No nuclear imaging was performed due to institutional habits.

Results
27 UES were diagnosed in 22/304 (7.2 %) patients, when a new-onset hydrouretero-nephrosis (HUN) or increase of the pre-existing HUN was imaged by ultrasound or CT-scan. A retrograde loopogram was performed next to confirm the UES. The mean follow-up time was 33 months. No risk factors for UES could be found. Symptoms like flank pain and UTI’s were indications for active therapy. 7 Patients underwent DJ stent placement, 2 patients received percutaneous nephrostomy tubes (PCN)
as a definitive treatment and 2 patients underwent uretero-intestinal re-implantation. 10 Asymptomatic patients with an UES and a favourable renal function (RF) were conservatively managed. All conservatively managed patients remained asymptomatic during follow-up and no active treatment was performed. The conservatively managed group had a reduction of 13 ml per minute/1.73 m², the PCN/DJ group a reduction of 14.8 ml per minute/1.73 m² and the group without an UES had a RF reduction of 10.4 ml per minute/1.73 m² during follow-up of up to 60 months. The PCN/DJ group had an initial RF improvement after dealing with the UES. Later there is a small decline with a stable moderately reduced RF (CKD stage 3A). The conservatively treated group maintains a good RF but no statistical significant result could be obtained because of the small number of patients in this group.

Conclusion
According to our long term data, a good RF is preserved in a selected population of asymptomatic patients with a favourable RF at time of UES diagnosis. We recommend a conservative approach for these patients because it’s safe and preserves maximal patient comfort.

PO 6-6 - PTLD Following Kidney Transplantation: A Single Center Retrospective Analysis
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Background
Post-transplant lymphoproliferative disorder (PTLD) is a rare but life threatening disorder following both solid organ and hematopoietic stem cell transplantation. Information on PTLD is mainly derived from large transplant registries, providing information on a large population, but with little detail.

Method
This retrospective monocentric study aims to better define incidence, clinico-pathological characteristics, risk factors, management and outcome results of PTLD following kidney transplantation (KT). All biopsy-confirmed PTLD after KT at the University Hospitals Leuven in the period 1989-2010 were identified. Patient-, transplantation- and disease related characteristics, prognostic factors and outcome were collected and analyzed from the clinical database.

Results
Forty-five biopsy-proven PTLD cases were included, corresponding with an incidence rate of 1.5%. The median time between transplantation and PTLD diagnosis was 9.3 years (range 0.36-35.38), whereas the median age at diagnosis was 57.5 years (range 13-83). There was a male predominance (75%). According to the International Prognostic Index (IPI) patients were categorized as low (n=17), low-intermediate (n=12), high-intermediate (n=13) en high risk (n=12). Besides the IPI a new score, called the Caillard score, was also calculated. One-, 3- and 5-year overall survival were 70.4, 59 and 47.7%, respectively. Both the IPI and Caillard score were independent predictors in KT patients with biopsy-confirmed PTLD.

Conclusion
In this study we obtained single center data on incidence, clinic-pathological characteristics and prognosis of PTLD following KT. We were able to validate the new prognostic scoring system of Caillard in an independent cohort of 54 KT patients. However, in our cohort this new score was not superior to the classical IPI score.

References

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**PO 7-1 - Prospective Study of Renal Function using CystatinC and Functional MRI in Children with Renal Tumors**

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*The Children's Hospital of Philadelphia*

**Background**

Serum creatinine (sCr) is an imprecise measure of renal function in children. Improved methods to estimate glomerular filtration rate (GFR) are needed. Serum cystatin C (cysC) is more sensitive than sCr and functional MRI (fMRI) can discriminate contribution of each kidney to overall renal function.

**Method**

Renal function was serially evaluated in children with newly diagnosed renal tumors. sCr, cysC and fMRI were obtained at presentation and during treatment in children (n=11, 5 males) median (range) 3y (0.5-7.8y). Three children had a tumor predisposition syndrome and one had a horseshoe kidney. Diagnoses were Wilms tumor [unilateral (n=5), multifocal/bilateral (n=4)] metanephric stromal tumor (n=1) and no renal mass (n=1). Therapy included unilateral total nephrectomy (n=5), partial nephrectomy (n=3), bilateral partial nephrectomy (n=2), chemotherapy (n=9), and flank/whole abdomen radiation (n=4). GFR was calculated using the Schwartz formula (GFRCr) or cysC (GFRcycC).

**Results**

At baseline, median (range) GFRCr was 138 (81-198) mL/min/1.73m2 and GFRcycC was 108 (77-136) mL/min/1.73m2 (R=0.9). Three patients had GFRCr < 100 mL/min/1.73m2 at diagnosis, one had family history of Wilms tumor and progressive acute kidney injury during therapy. Pre vs post surgery (n=8), median GFRCr was 142 vs 104 mL/min/1.73 m2 (p=0.04) and GFRcycC was 114 vs 88 mL/min/1.73 m2 (p=0.01). At the completion of therapy, median (range) percent change from baseline in GFRCr was -23% (-64 to +23%), GFRcycC was -25% (-60 to +24%). MRI was adequate for functional analysis in 26/27 scans. The median (range) percent change in total parenchymal volume evaluated pre and post-op by IMRI was -50% (-17 to +63%) after unilateral nephrectomy (n=3) and -9% (-40 to +5%) after partial nephrectomy (n=4).

**Conclusion**

Some children with Wilms tumor have decreased GFR at diagnosis. At completion of therapy, the median decrease in GFR is 25%. GFRcysC may be more sensitive to changes in renal function. fMRI is feasible and MRI may detect bilateral or multifocal Wilms tumor. Partial nephrectomy spared 90% of renal parenchymal volume in this small cohort of children.

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**PO 7-2 - GFR by Iohexol Plasma versus the Updated Schwartz Equation and 24-Hour Urine**

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*University of New Mexico*

**Background**

The accurate determination of glomerular filtration rate (GFR) is important to screen for acute kidney injury, to dose chemotherapy, and to identify risk for chronic kidney disease. Being correlated with inulin clearance, measured glomerular filtration rate by iohexol plasma disappearance (iGFR) is seen as the new gold standard for measurement of kidney function in pediatric cohort studies (1,2). iGFR is based on the clearance of an exogenous marker and is unaffected by endogenous compounds or a patient’s muscle mass. We sought to compare measured iGFR with 24-hour urinary of creatinine clearance (24urccl) and urea clearance (24urea). With these measures, we also determined the adequacy of, the modified Schwartz GFR estimating equation (GFR=0.413X height/ Serum creatinine).
Method
From an on-ongoing study, we present preliminary data from 4 subjects, ages 3-18 years, continent of
urine and diagnosed with a malignancy in the past 5 years. Eligible subjects should have stable
kidney function for at least two weeks prior to planned study. Consented subjects had baseline
assessments including height, weight and vital signs. Blood samples were obtained for serum
chemistry, and time zero iohexol. iGFR determined by 5mL iohexol solution infused over 1-2 minutes
followed by 10mL of sterile saline. Blood was drawn at 10, 30, 120 and 300 minutes. Plasma
disappearance of iohexol was calculated using a two-compartment model and area under the curve.
Plasma iohexol concentration is determined by HPLC. On the day of iGFR, 24h urine collection is also
initiated.

Results

<table>
<thead>
<tr>
<th>Subject</th>
<th>1</th>
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<tr>
<td>Gender</td>
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<td>F</td>
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<td>Age (yr)</td>
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<td>24 urea Cl (mL/min/m2)</td>
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<td>Mean(24hr Cr and UCL)</td>
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<td>iGFR (mL/min/m2)</td>
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<td>Schwartz equation* (mL/min/m2)</td>
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<td>199</td>
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</tbody>
</table>

*GFR=0.413 X height/Serum creatinine

Conclusion
Compared to a measured iGFR the modified Schwartz equation and the combined mean 24-urea and
24ucrcl appear to perform better than 24ucrcl alone. The significant variability between 24ucrcl and
iGFR might be due to an unexpectedly low serum creatinine. As illustrated by subject 2, the 24ucrcl
alone and Schwartz equation overestimate GFR compared to the iGFR. We speculate that this might
be related to decreased muscle and sub-acute malnutrition. Therefore, creatinine-based
determinations of GFR alone may not be accurate in this population. If a 24-hour urine is used for
determination of GFR, we suggest that the mean of 24-urea and 24ucrcl is a more precise measure
than 24ucrcl alone.

References
1. Schwartz GJ, Muñoz A, Schneider MF, Mak RH, Kaskel F, Warady BA, Furth SL. New equations
Background
Aristolochic acid (AA) causes aristolochic acid nephropathy (AAN), first described in Belgian women accidentally prescribed Aristolochia fangchi in a slimming treatment, and also Balkan endemic nephropathy (BEN), through probable dietary contamination with Aristolochia clematitis seeds (1). Both nephropathies have a high risk of urinary upper tract and bladder urothelial cancer, justifying the prophylactic surgical removal of native kidneys and ureters in dialysed patients and kidney transplant recipients for end-stage AAN (2, 3). In renal tissues, a distinct DNA adduct, 7-(deoxyadenosin-N6-yl)-aristolactam I (dA-AAI), has been detected (2, 4, 5). It is a premutagenic lesion inducing a mutational signature of AT to TA transversions in critical genes involved in carcinogenesis such as the H-ras protooncogene (in rodents) and the TP53 tumour suppressor gene (in humans) (6, 7). The same molecular epidemiology approach has also been applied to DNA isolated from renal tissue of patients with upper tract urothelial cancer (UUC) from Taiwan, indicating that exposure to AA contributes significantly to the high incidence of UUC in Taiwan (8).

Method
Eleven AAN patients from the Belgian cohort were selected on the basis of a long time period (110 to 240 months) between exposure and the prophylactic surgical removal of their native kidneys and ureters. Except for 1 case, all prescriptions given to them from 1990 to 1992 were obtained from the pharmacists and for each patient the cumulative dose was calculated. Histopathological diagnoses were reviewed by the same uropathologist. Urothelial carcinomas were graded and staged according to the 2004 World Health Organization Classification of Tumors and the 2010 Union of International Cancer Classification, the TNM Classification, respectively. The detection of AA-DNA adducts was performed by using 32P-postlabelling analysis and online column-switching liquid chromatography coupled to electrospray ionisation tandem mass spectrometry, with isotopic dilution of a 15N-labelled internal standard (10, 11).

Results
Six out of 11 AAN patients were chronically dialysed at the time of surgery, and 4 had received a kidney transplant. They were estimated to have been exposed to a total dose ranging between 66 to 226 grams; this cumulative dose of A. fangchi was a significant risk factor in developing urothelial cancer (2). Histopathological findings reported 3 cases of low to moderate urothelial dysplasia of the renal pelvis and 1 case of carcinoma in situ of the ureter. The most abundant AA-DNA adduct in the renal tissue samples was dA-AAI (relative adduct labelling ranging from 3 to 22/ 108 nucleotides). The chemical structure of this adduct was confirmed in 2 cases where sufficient amount of DNA (50-100 µg) was available for analysis.

Conclusion
As Aristolochia species are still used in traditional herbal remedies in Asia and other countries (12), the potential for exposure to AA worldwide is high. This study demonstrates that premutagenic AA-DNA adducts, specifically dA-AAI, have an exceptionally long-term persistence in the renal DNA of AAN patients and thus can serve as mechanistically relevant biomarkers to assess AA exposure, even decades later. Our data also attest to the role of AA in human urothelial malignancy.

References


