Aprire un Ambulatorio di Onco-Nefrologia

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Italian Association of Medical Oncology (A.I.O.M.)
Working Group on Onco-Nephrology

Why, when, and how a Nephrologist should be involved in the management of a cancer patient

The relationship between kidney and cancer could be regarded as 'circular'[1], indeed, if on one hand the presence of the tumor or of an oncological treatment may … deteriorate renal function, … the presence of renal disease in cancer patients may worsen prognosis, increase mortality and have impact on the … safety profile of oncological drugs

In patient with CKD, the doses of a number of oncological drugs need to be reduced, not to take into account the fact that potentially active treatments are too often omitted in patients with renal impairment

Some very effective anticancer agents may be avoided as a potential option in CKD patients due to the lack of specific information on their pharmacokinetic properties in this setting

Drug-induced nephrotoxicity remains a significant complication that can potentially impair treatment efficacy

AVOID UNNECESSARY ONCOLOGICAL TREATMENT INTERRUPTIONS AND DOSE REDUCTIONS

1. Porta C, et al. *Nat Rev Nephrol* 2015

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Too often cancer patients with CDK or on dialysis are UNDERTREATED

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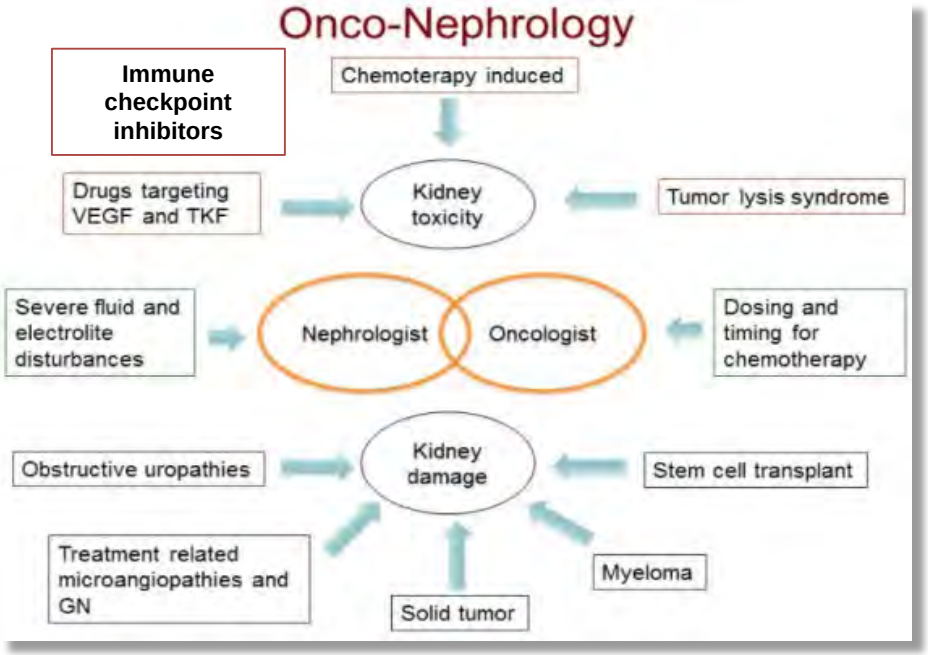
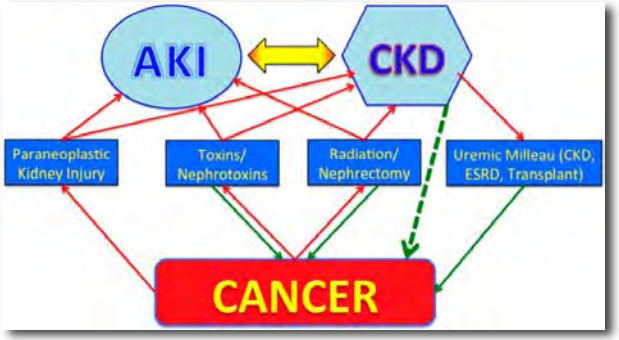
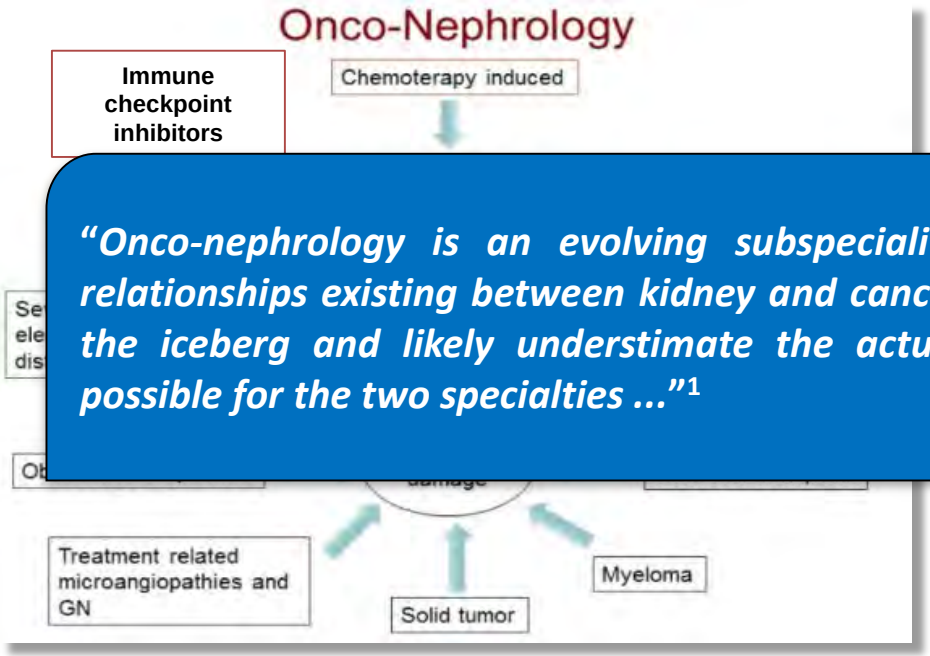


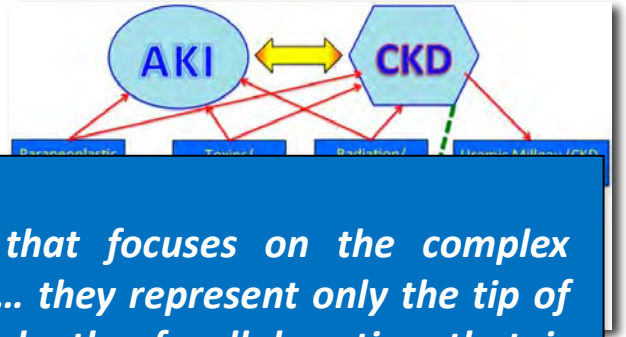


- **CKD impacts on overall survival**
- **CKD increases the risk of cancer**
- **CKD increases cancer-related mortality**
- **CKD impact on oncological treatments**
- **Interruption or dose reduction of oncological treatments reduces survival in cancer patients**

Perazella MA, et al. *ASN Core Curriculum* 2015

Why, when, and how a Nephrologist should be involved in the management of a cancer patient





"Onco-nephrology is an evolving subspeciality that focuses on the complex relationships existing between kidney and cancer … they represent only the tip of the iceberg and likely understimate the actual depth of collaboration that is possible for the two specialties ..."[1]

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- **CKD impact on oncological treatments**
- **Interruption or dose reduction of oncological treatments reduces survival in cancer patients**

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Onco-Nephrology: a decalogue

Nephrol Dial Transplant (2016) 31: 515–519
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Advance Access publication 3 September 2015

ndt
Nephrology Dialysis Transplantation

NDT Perspectives

Onco-nephrology: a decalogue

Laura Cosmai[1,2], Camillo Porta[2,3], Maurizio Gallieni[2,4] and Mark A. Perazella[5]

[1]Division of Nephrology and Dialysis, Outpatient Clinic of Nephro-Oncology, Istituti Ospitalieri, Cremona, Italy, [2]Joint Italian Association of Medical Oncology (AIOM)/Italian Society of Nephrology (SIN) Working Group on Onco-Nephrology, Rome, Italy, [3]Division of Medical Oncology, I.R.C.C.S. San Matteo University Hospital Foundation, Pavia, Italy, [4]Nephrology and Dialysis Unit, San Carlo Borromeo Hospital, University of Milano, Milano, Italy and [5]Department of Internal Medicine, Section of Nephrology, Yale University School of Medicine, New Haven, CT, USA

1) acute kidney injury and chronic kidney disease in cancer patients
2) nephrotoxic effects of anti-cancer therapy, either traditional chemotherapeutics or novel
3) paraneoplastic renal manifestations

4) management of patients nephrectomized for a kidney cancer
5) renal replacement therapy and active oncological treatments
6) kidney transplantation in cancer survivors and cancer risk in ESRD patients
7) oncological treatment in kidney transplant patients
8) pain management in patients with cancer and kidney disease
9) development of integrated guidelines for onco-nephrology patients
10) clinical trials designed specifically for onco-nephrology

Cosmai L, et al. *Nephrol Dial Transplant* 2015

… beyond the decalogue

1. Anemia and ESAS in cancer patients with CKD;
2. Contrast medium in oncological patients;
3. Electrolytes and acid-base disorders in malignancy;
4. Interstitial nephritis from Immune Checkpoint Inhibitors;
5. Nutritional consultation for cancer patients with CKD;
6. Hematologic disorders and kidney disease;
7. Cancer and anticancer drugs - related TMA;
8. Tumor Lysis Syndrome;
9. MGRS in cancer patients;
10. Phosphorus and novel FGFRs inhibitors;
11. Urological cancers, not only RCC …;
12. Bone, kidney and cancer;
13. Radiation-associated kidney injury

"*The Ten Commandments*", by C. B. DeMille (1956)

Prevalence of CKD and cancer patients…

Incidenza	Maschi				Femmine			
	Nord	Centro	Sud-Isole	ITALIA	Nord	Centro	Sud-Isole	ITALIA
Vie aerodigestive superiori*	29,0	23,0	23,5	27,0	7,4	5,7	4,9	6,5
Esofago	7,8	4,1	3,4	6,3	2,0	1,4	0,8	1,6
Stomaco	32,6	36,9	24,5	30,7	16,1	19,1	12,9	15,5
Colon-retto	93,0	95,7	85,0	91,0	58,6	62,1	55,1	57,9
Fegato	32,1	21,6	30,9	30,8	10,3	7,4	12,4	10,6
Colecisti vie biliari	7,4	7,0	8,6	7,7	6,5	6,2	8,0	6,9
Pancreas	24,0	19,6	17,2	21,6	18,4	15,8	13,2	16,7
Polmone	105,2	102,9	102,9	104,3	34,7	32,8	21,1	30,6
Osso	1,4	1,6	1,4	1,4	1,1	1,2	0,9	1,0
Melanomi	23,5	26,6	12,4	20,4	19,0	20,8	10,4	16,5
Mesotelioma	5,2	2,8	3,2	4,4	1,6	0,6	0,7	1,3
Sarcoma di Kaposi	1,9	1,1	2,8	2,1	0,5	0,3	1,0	0,6
Tessuti molli	4,3	4,3	3,6	4,1	2,7	2,6	2,2	2,5
Mammella	1,9	1,5	1,5	1,7	162,6	145,2	123,6	149,7
Ovaio					15,4	15,7	14,5	15,2
Utero cervice					7,6	8,0	6,9	7,4
Utero (corpo)					24,4	25,3	22,8	24,1
Prostata	147,3	139,6	108,3	135,7				
Testicolo	7,3	6,7	6,6	7,0				
Rene e vie urinarie**	31,8	31,8	19,1	28,1	13,3	13,3	8,2	11,8
Vescica***	67,4	73,4	70,6	68,9	13,0	13,8	10,8	12,4
S.N.C.^	11,4	12,1	10,3	11,2	7,7	8,1	7,2	7,6
Tiroide	9,2	11,0	9,5	9,4	24,9	29,6	27,2	26,0
L. Hodgkin	4,2	4,7	3,9	4,1	3,5	3,6	3,3	3,4
L. non Hodgkin	26,2	23,7	20,2	24,2	18,3	16,0	13,9	16,8
Mieloma	11,1	12,2	10,6	11,1	7,8	8,3	7,3	7,7
Leucemie, tutte	17,2	18,2	17,8	17,5	10,2	10,7	10,9	10,5
Totale	**735,5**	**708,5**	**635,7**	**704,4**	**512,0**	**493,9**	**423,0**	**484,7**

TABELLA 8. Tasso medio annuale di incidenza dei tumori in Italia, per sede/tipo, sesso, e area geografica[1]

1. Periodo 2008-2014, standardizzazione sulla popolazione nuova europea 2013 per 100.000 abitanti
* Vie Aero Digestive Superiori comprende lingua, bocca, orofaringe, rinofaringe, ipofaringe, faringe NAS, laringe
** Comprende rene, pelvi e ureteri
*** Comprende sia tumori infiltranti che non infiltranti
^ S.N.C. comprende cervello e sistema nervoso centrale

Sede	Maschi	Femmine	Totale
	N. (%)	N. (%)	N. (%)
Vie Aero Digestive Superiori -VADS*	7.276 (3,7)	2.580 (1,4)	9.856 (2,6)
Esofago	1.710 (0,9)	684 (0,4)	2.394 (0,6)
Stomaco	8.458 (4,3)	6.098 (3,4)	14.556 (3,9)
Colon-Retto	23.420 (12,0)	20.282 (11,2)	43.702 (11,6)
Fegato	8.978 (4,6)	4.034 (2,2)	13.012 (3,5)
Pancreas	6.847 (3,5)	7.416 (4,1)	14.263 (3,8)
Colecisti e vie biliari	2400 (1,2)	3.000 (1,7)	5.400 (1,4)
Polmone	27.554 (14,1)	13.328 (7,3)	40.882 (10,9)
Melanomi	8.147 (4,2)	6.716 (3,7)	14.863 (4,0)
Mesotelioma	1.523 (0,8)	463 (0,3)	1.986 (0,5)
Mammella		54.976 (30,3)	54.976 (14,6)
Ovaio		5.179 (2,8)	5.179 (1,4)
Utero (cervice)		2.365 (1,3)	2.365 (0,6)
Utero (corpo)		8.335 (4,6)	8.335 (2,2)
Prostata	36.074 (18,5)		36.074 (9,6)
Testicolo	2.289 (1,2)		2.289 (0,6)
Rene, vie urinarie**	9.049 (4,6)	4.472 (2,5)	13.521 (3,6)
Vescica***	20.477 (10,5)	5.015 (2,8)	25.492 (6,8)
Sistema Nervoso Centrale	3.533 (1,8)	2.589 (1,4)	6.122 (1,6)
Tiroide	3.333 (1,7)	9.850 (5,4)	13.183 (3,5)
Linfomi di Hodgkin	1.222 (0,6)	929 (0,5)	2.151 (0,6)
Linfomi non Hodgkin	7.011 (3,6)	6.171 (3,4)	13.182 (3,5)
Mieloma multiplo	3.019 (1,6)	2.740 (1,5)	5.759 (1,5)
Leucemie, tutte	4.738 (2,4)	3.229 (1,8)	7.967 (2,1)
Totale	**194.754 ******	**181.857**	**376.611**

TABELLA 6. Numero di nuovi casi di tumore (e percentuali sul totale) stimati per il 2020 in base al sesso e per le sedi più frequenti[§]. Sono esclusi i carcinomi della cute non melanomi

§ Il numero totale dei casi stimati per il 2020 è stato calcolato applicando un modello statistico indipendente da quello usato per ciascuna singola sede

*VADS (Vie Aero Digestive Superiori) comprendono lingua, bocca, orofaringe, rinofaringe, ipofaringe, faringe NAS, laringe
** Sono inclusi: rene, pelvi e ureteri
*** Sono inclusi tumori infiltranti e non infiltranti
**** Sono inclusi 589 casi di tumori della mammella maschili

2.1 Quanti nuovi tumori maligni saranno diagnosticati in Italia nel 2020?

AIRTUM Working Group

Sulla base dei dati di popolazione raccolti dai Registri Tumori Italiani si stima che, nel 2020, in Italia saranno diagnosticati circa 377.000 nuovi casi di neoplasie maligne (esclusi i tumori della cute non melanomi): 195.000 negli uomini e 182.000 nelle donne

I Numeri del Cancro in Italia. *AIOM* 2020

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	3.533 (1,8)	2.589 (1,4)	6.122 (1,6)
	3.333 (1,7)	9.850 (5,4)	13.183 (3,5)
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	4.738 (2,4)	3.229 (1,8)	7.967 (2,1)
	194.754 ****	**181.857**	**376.611**

Prevalence of CKD in cancer patients ranges from 12% to 25%

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I Numeri del Cancro in Italia. *AIOM* 2020

Onco-Nephrology… What does it really mean?

MANAGEMENT OF

- Renal involvement in cancer
- Renal toxicities of classic CT
- Renal toxcities of novel immune and targeted therapies
- Electrolyte disorders
- Acute kidney injury
- Tumor Lysis syndrome
- Thrombotic microangiopathies
- AKI or worsening pre-existing CKD
- Paraneoplastic glomerulopathies
- Interstitial nephritis
- Contrast medium

SPECIAL SITUATIONS

Patients with CKD

Patients on hemodialysis

Transplant patients

Patients with disimmune glomerulonephritis

Patients with RCC or nephrectomized for RCC

Urothelial cancer patients

Patients with risk factors for CKD

Improvements or emerging problems…

Cytotoxic chemotherapy

Antimetaboliti
- 5- Fluoruracile
- Metotrexate
- Capecitabina
- Gemcitabina
- Pemetrexed

Derivati/Sali del platino
- Cisplatino
- Carboplatino
- Oxaliplatino

Antracicline/Antracenedioni
- Adriamicina
- Epirubicina
- Idarubicina
- Mitoxantrone
- Antracicline liposomiali

Alcaloidi della vinca
- Vincristina
- Vindesina
- Vinorelbina
- Vinflunina

Alchilanti
- Ciclofosfamide
- Carmustina
- Ifosfamide
- Temozolomide
- Fotemustina

Camptotecine/Inibitori delle Topoisomerasi
- Irinotecan
- Topotecan
- Etoposide

Antibiotici
- Mitomicina C
- Bleomicina

Taxani
- Paclitaxel
- Docetaxel
- Cabazitaxel
- Nab-Paclitaxel

Bifosfonati
- Zolendronato
- Pamidronato

Altri chemioterapici
- Mitotane
- Trabectedina

Target Therapies

Agents targeting VEGF/VEGFRs
- Bevacizumab
- ziv-Aflibercept
- Sunitinib
- Pazopanib
- Axitinib
- Ramucirumab

B-RAF inhibitors ± MEK inhibitors
- Vemurafenib
- Dabrafenib
- Trametinib
- Cobimetinib
- Binimetinib

EGFR inhibitors
- Gefitinib
- Erlotinib
- Afatinib
- Cetuximab
- Necitumumab
- Panitumumab
- Dacomitinib
- Osimertinib

mTOR inhibitors
- Temsirolimus
- Everolimus

HER2-targeting agents
- Trastuzumab
- Lapatinib
- Neratinib
- Pertuzumab
- T-DM1

Other multikinase inhibitors
- Sorafenib
- Imatinib
- Regorafenib
- Vandetanib
- Lenvatinib
- Cabozantinib
- Apatinib

CDK4/6 inhibitors
- Palbociclib
- Ribociclib
- Abemaciclib

FGFRs inhibitors
- Pemigatinib
- Erdafitinib

Bone targeting agents
- Denosumab

Novel ormonal agents
- Abiraterone
- Enzalutamide
- Apalutamide

ALK inhibitors
- Crizotinib
- Ceritinib

Novel cytotoxics
- Nab-Paclitaxel
- Olaparib
- Trabectidine

PARP Inhibitors
- Rucaparib
- Nirapanib

Other agents
- Catumaxomab
- Olaratumab
- Sonidegib
- Dinotuximab

Immune Checkpoints inhibitors

ANTI- PD-1
- Nivolumab
- Pembrolizumab

ANTI- PD-L1
- Atezolizumab
- Durvalumab
- Avelumab

ANTI-CTLA-4
- Ipilimumab
- Tremelimumab

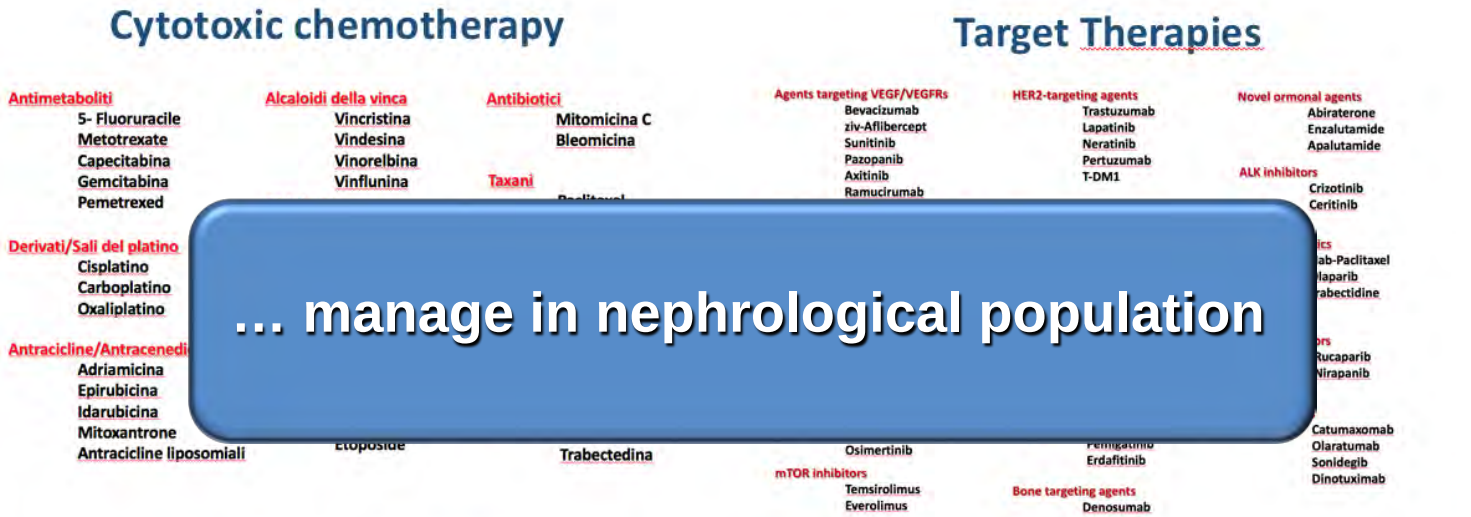
CAR-T cells and upcoming CAR-NK cells

- Tisagenlecleucel
- Axicabtagene

avoid unnecessary treatment interruptions and dose reductions

deal with anticancer drugs and their renal toxicities in our nephrological patients

Improvements or emerging problems…



avoid unnecessary treatment interruptions and dose reductions

deal with anticancer drugs and their renal toxicities in our nephrological patients

New drugs, new toxicities …

A number of anticancer agents may directly or indirectly affect the kidneys.While the nephrotoxicity associated with traditional cytotoxic agents is well characterized, the recent development of a large number of molecularly targeted agents and immune checkpoint inhibitors and their release into clinical practice has dramatically widened the spectrum of adverse renal events. Indeed, like opening Pandora's box, a wide array of previously unrecognized and ill-defined abnormalities of kidney function … are increasingly being observed with these targeted agents. This highlights the need for specially trained clinicians with specific knowledge of these complications who can treat patients receiving these drugs

… toxicities that we must recognise and learn to manage[1]

John William Waterhouse, "Pandora", 1896

1. Porta C, et al. *Clin Exp Med* 2007

A daily problem

TO DECIDE HOW AND WHEN CONTINUE, DISCONTINUE, OR CHANGE A TREATMENT GUIDELINES DOES NOT EXIST;
LACK OF DATA IN THE LITERATURE

THE DECISION DEPENDS STRONGLY ON THE EFFECTIVENESS OF THERAPY

EFFECTIVE TREATMENT

WHEN STOP, DISCONTINUE, OR CHANGE AN EFFECTIVE TREATMENT DUE TO ITS RENAL AEs?

NOT EFFECTIVE TREATMENT

STOP TREATMENT

The risks of a suboptimal use of anticancer agents

If CKD is not recognized
or
if CKD is recognized, but treatment is not adjusted accordingly

↓

OVER TREATMENT

↓

Increased toxicity

If CKD is recognized
but dose adjustment is:
- excessive and/or
- empiric

↓

UNDER TREATMENT

↓

Decreased efficacy

CKD patients are at risk for suboptimal management:

Over-dosage ➔ Toxicity ➔ Survival reduction

Under-dosage ➔ Loss of efficacy ➔ Survival reduction

Prescription of the right dosage
(i.e. adequate to kidney function) is key

The risks of a suboptimal use of anticancer agents

If CKD is not recognized
or
if CKD is recognized, but treatment
is

If CKD is recognized
but dose adjustment is:
- excessive and/or

CKD, by itself, is not a reason to reduce or even to deny targeted therapies, at least in the absence of others comorbidities

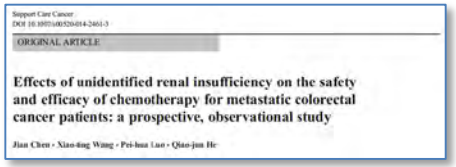
ENT

CKD patients are at risk for suboptimal management:

Over-dosage ➔ Toxicity ➔ Survival reduction

Under-dosage ➔ Loss of efficacy ➔ Survival reduction

Prescription of the right dosage
(i.e. adequate to kidney function) is key


Support Care Cancer
DOI 10.1007/s00520-014-2461-3

ORIGINAL ARTICLE

Effects of unidentified renal insufficiency on the safety and efficacy of chemotherapy for metastatic colorectal cancer patients: a prospective, observational study

Jian Chen · Xiao-ling Wang · Pei-hua Luo · Qiao-jun He

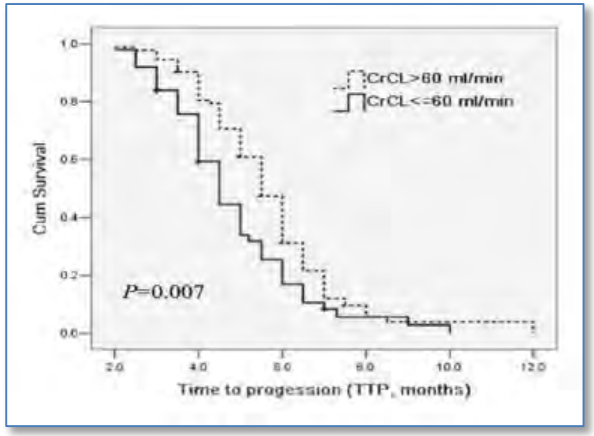
Suboptimal use of anticancer agents

It is not just theory!

Modifications or interruptions of Tx schedule

Table 3 Toxicity-associated adverse events and response rate

Characteristic	CrCL<60 ml/min (*N*=50)	CrCL>60 ml/min (*N*=93)	Univariate OR (95 % CI)	Adjusted OR (95 % CI)
Dose interruption, %	52 (95 % CI 38–68)	26 (95 % CI 20–33)	1.86 (1.13–2.14) *P*<0.001	1.72 (1.21–2.05) *P*<0.001
Dose modification, %	34 (95 % CI 26–41)	14 (95 % CI 9–18)	2.13 (1.23–2.87) *P*<0.001	1.98 (1.14–2.23) *P*<0.001
Hospitalization, %	14 (95 % CI 9–18)	5 (95 % CI 3–12)	1.31 (0.83–1.78) *P*=0.16	1.12 (0.89–1.31) *P*=0.25



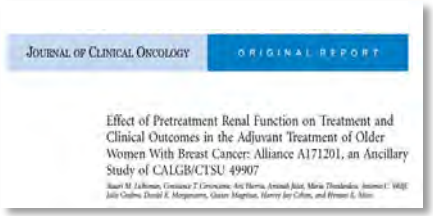
Reduced survival

Table 2 Toxicities

Toxicities	CrCL<60 ml/min (*N*=50)	CrCL>60 ml/min (*N*=93)	Univariate OR (95 % CI, *P* value)	Adjusted OR (95 % CI, *P* value)
Cytopenia, % (95 % CI)				
Grades 1 to 2	76.0 (57–89)	61 (48–76)	2.13 (0.97–2.97, 0.008)	1.85 (1.39–2.53, <0.001)
Grades 3 to 4	22 (11–28)	19 (11–26)	1.87 (0.78–3.17, 0.08)	1.02 (0.51–2.78, 0.96)
Diarrhea, % (95 % CI)				
Grades 1 to 2	34 (25–43)	29 (20–35)	3.97 (1.47–5.89, <0.001)	3.76 (0.95–6.53, 0.007)
Grades 3 to 4	20 (14–23)	11 (8–15)	2.16 (1.14–3.21, 0.003)	1.53 (0.45–4.89, 0.014)
Nausea or vomit, % (95 % CI)				
Grades 1 to 2	22 (16–28)	17 (12–31)	1.47 (0.87–2.47, 0.15)	1.31 (0.93–5.24, 0.16)
Grades 3 to 4	6 (3–11)	5 (3–13)	1.17 (0.34–4.17, 0.81)	1.09 (0.47–2.86, 0.85)
Stomatitis, % (95 % CI)				
Grades 1 to 2	10 (7–15)	6 (4–9)	2.47 (1.47–3.89, <0.001)	2.81 (1.10–4.28, 0.002)
Grades 3 to 4	6 (3–9)	3 (1–6)	2.57 (0.97–3.79, 0.006)	2.14 (0.89–3.26, 0.022)
H-F syndrome, % (95 % CI)				
Grades 1 to 2	18 (14–26)	11 (7–15)	2.87 (1.47–4.23, <0.001)	2.56 (0.86–5.41, 0.045)
Grades 3 to 4	16 (11–24)	12 (8–18)	1.24 (0.87–2.45, 0.41)	1.58 (0.27–3.61, 0.084)
Neurovirulence, % (95 % CI)				
Grades 1 to 2	30 (23–41)	29 (21–36)	1.24 (0.23–3.87, 0.76)	0.91 (0.12–3.36, 0.414)
Grades 3 to 4	12 (7–16)	9 (6–12)	1.57 (0.53–4.27, 0.39)	1.23 (0.72–5.24, 0.68)

Increased toxicities

Chen J, et al. *Support Care Cancer* 2015.

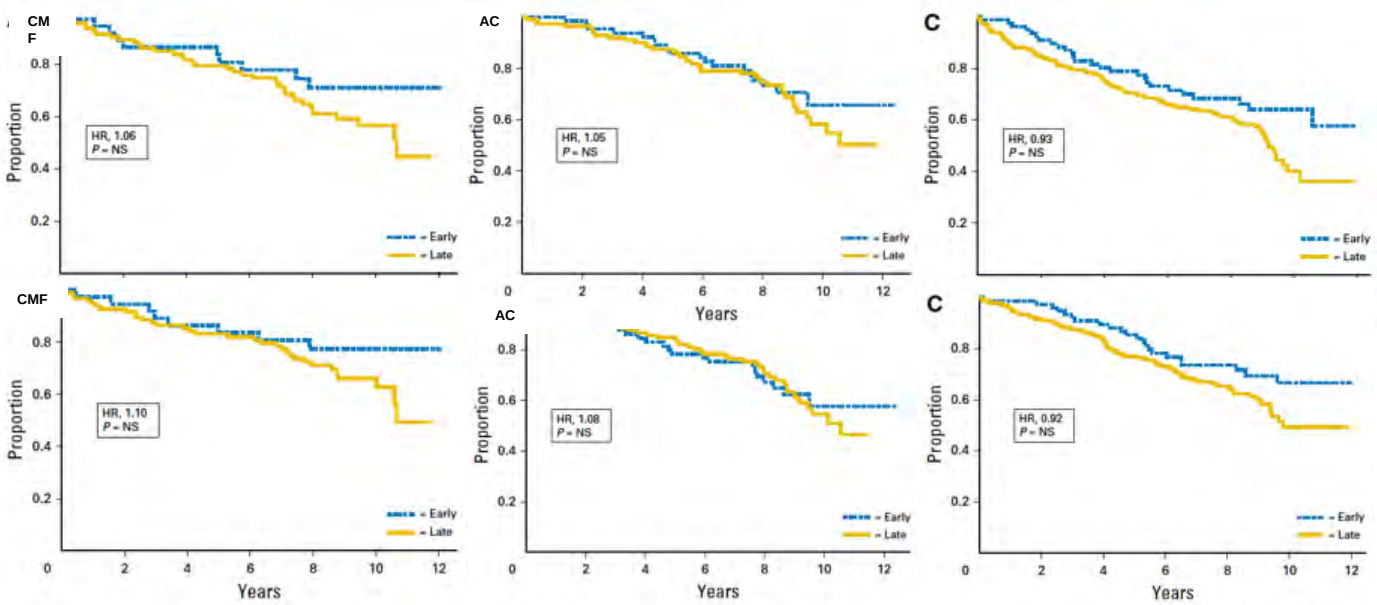


Suboptimal use of anticancer agents

Relapse-Free Survival and Overall Survival

Early: dose adjusted to renal function at treatment start

Late: dose adjusted to renal function during treatment



Phase III prospective study
CMF: Cyclophosphamide – Methotrexate – Fluoruracil;
AC: Cyclophosphamide – Doxorubicine;
C: Capecitabine

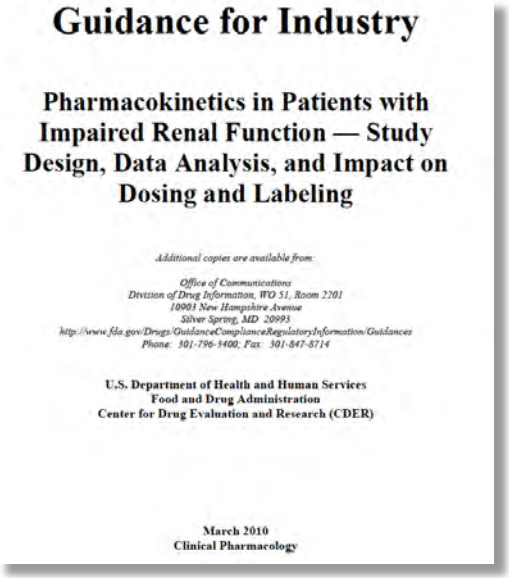
Lichtman SM, et al. *J Clin Oncol* 2016.

Cancer patients with CKD

IN PATIENT WITH WITH CKD, THE DOSES OF MANY DRUGS NEED TO BE REDUCED; FURTHEMORE, SOME PROMISING AGENTS MAY BE OMITTED IN PATIENTS WITH RENAL CKD[1]

- **Frequently oncologists ask to assess the degree of kidney function impairment for dosage adjustment of anticancer therapy**
- **A thoroughly knowledge of the specific metabolism of anticancer agents and of their pharmacokinetic and pharmacodynamic properties is thus mandatory to decide if, when, and at what extent to reduce treatment doses**
- **…taking into account that evidence is lacking for the majority of these patients, usually excluded from registrative clinical trials …**

1 Darmon M, et al. *Crit Care* 2006



Guidance for Industry

Pharmacokinetics in Patients with Impaired Renal Function — Study Design, Data Analysis, and Impact on Dosing and Labeling

Additional copies are available from:

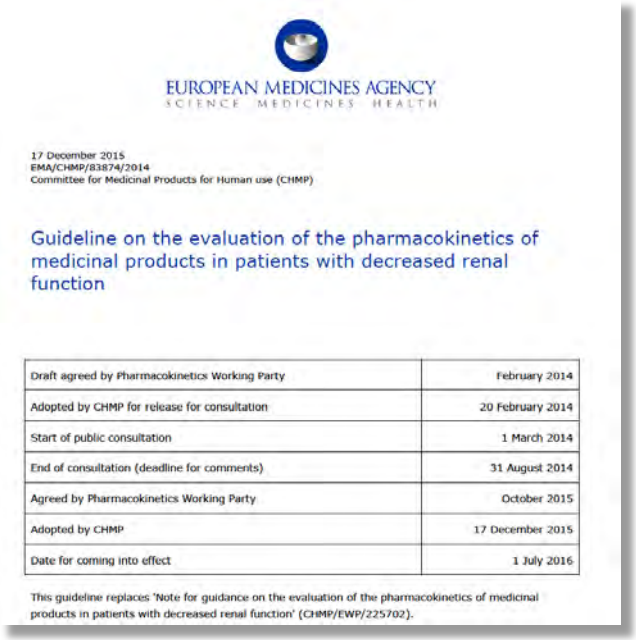
Office of Communications
Division of Drug Information, WO 51, Room 2201
10903 New Hampshire Avenue
Silver Spring, MD 20993
http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances
Phone: 301-796-3400; Fax: 301-847-8714

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

March 2010
Clinical Pharmacology

FDA

EMA



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

17 December 2015
EMA/CHMP/83874/2014
Committee for Medicinal Products for Human use (CHMP)

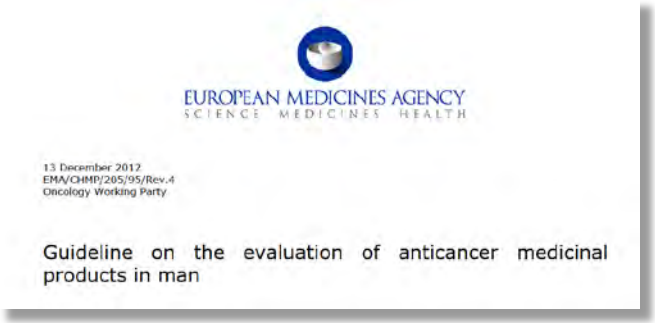
Guideline on the evaluation of the pharmacokinetics of medicinal products in patients with decreased renal function

Draft agreed by Pharmacokinetics Working Party	February 2014
Adopted by CHMP for release for consultation	20 February 2014
Start of public consultation	1 March 2014
End of consultation (deadline for comments)	31 August 2014
Agreed by Pharmacokinetics Working Party	October 2015
Adopted by CHMP	17 December 2015
Date for coming into effect	1 July 2016

This guideline replaces 'Note for guidance on the evaluation of the pharmacokinetics of medicinal products in patients with decreased renal function' (CHMP/EWP/225702).

5 major recommendations

1. To conduct renal impairment studies for drugs that are eliminated via a nonrenal route and for drugs eliminated via the renal route
2. To categorize renal function either by estimated GFR (estimated using the MDRD equation) or by creatinine clearance (CLcr) (estimated using the C-G equation)
3. To conduct studies in HD patients (during- and off-dialysis periods), when appropriate
4. To study PK of therapeutic proteins in renally impaired patients, when appropriate
5. To describe the results of the renal impairment studies in the label under the new Physician Labeling Rule

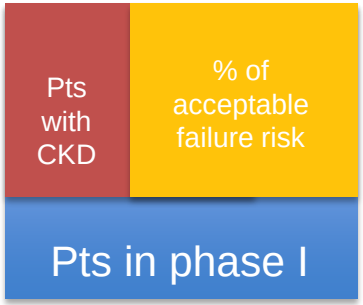


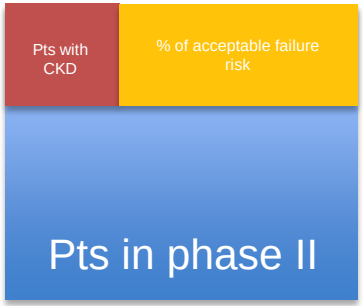
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

13 December 2012
EMA/CHMP/205/95/Rev.4
Oncology Working Party

Guideline on the evaluation of anticancer medicinal products in man

Today's reality



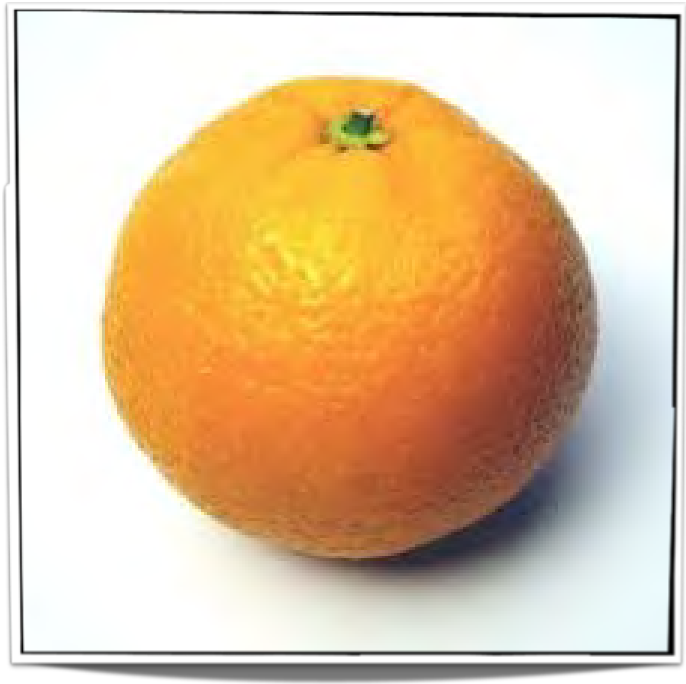


A number of phase I studies do accept the enrolment of patients with kidney impairment

In phase II, and expecially phase III, studies this patients' population is almost completely lost

What is known (and thus reported on SPCs) comes from population studies, usually conducted on a limited number of patients, often lacking key data

As I always say …



Clinical trial participant

Typical patient with cancer … and CKD

The real problem in the present day

I'm Oncologist…
I do not see

I'm Company…
I do not hear

I'm Nephrologist…
I do not speak

Summary of Product Characteristics Dilemma in CKD Patients

«An integrated analysis of all clinical trials showed that the pharmacokinetic characteristics of … are not influenced by … renal function. To date, have been studied only patients with adequate renal function (serum creatinine ≤ 1.5 times the upper limit of normal) …

The results of a population pharmacokinetic model (data from subjects with baseline ClCr ranging from 30 ml/min and 150 ml/min) indicated that it is unlikely that renal insufficiency has a clinically relevant effect on the pharmacokinetics of … No dosage adjustment is required in patients with creatinine clearance greater than 30 ml/min.

Caution **is advised in patients with creatinine clearance less than 30 ml/min as there is no experience in this population»**

You can not find what you do not look for

Terminology issue

Table 2. Adverse Events and Selected Laboratory Abnormalities.*

Variable	Sunitinib (N=375)			Interferon Alfa (N=360)		
	All Grades	Grade 3	Grade 4	All Grades	Grade 3	Grade 4
	percent					
Adverse event						
Diarrhea†	53	5	0	12	0	0
Fatigue†	51	7	0	51	11	1
Nausea	44	3	0	33	1	0
Stomatitis	25	1	0	2	1	0
Vomiting†	24	4	0	10	1	0
Hypertension†	24	8	0	1	1	0
Hand–foot syndrome†	20	5	0	1	0	0
Mucosal inflammation	20	2	0	1	1	0
Rash	19	1	1	6	1	0
Asthenia	17	4	0	20	4	0
Dry skin	16	1	0	5	0	0
Skin discoloration	16	0	0	0	0	0
Changes in hair color	14	0	0	1	0	0
Epistaxis	12	1	0	1	0	0
Pain in a limb	11	1	0	3	0	0
Headache	11	1	0	14	0	0
Dry mouth	11	0	0	6	1	0
Decline in ejection fraction	10	2	0	3	1	0
Pyrexia	7	1	0	34	0	0
Chills	6	1	0	29	0	0
Myalgia	5	1	0	16	1	0
Influenza-like illness	1	0	0	7	1	0
Laboratory abnormality						
Leukopenia†	78	5	0	56	2	0
Neutropenia†	72	11	1	46	7	0
Anemia	[illegible]	[illegible]	[illegible]	[illegible]	4	1
Increased creatinine	66	1	0	49	1	0
Thrombocytopenia†	[illegible]	[illegible]	[illegible]	[illegible]	0	0
Lymphopenia†	60	12	0	63	22	0
Increased lipase†	52	13	3	42	5	1
Increased aspartate aminotransferase	52	2	0	34	2	0
Increased alanine aminotransferase	46	2	1	39	2	0
Increased alkaline phosphatase	42	2	0	35	2	0
Increased uric acid	41	0	12	31	0	8
Hypophosphatemia	36	4	1	32	6	0
Increased amylase†	32	4	1	28	2	1
Increased total bilirubin	19	1	0	2	0	0

Table 3
Incidences of immune-related, select adverse reactions reported for nivolumab 3 mg/kg q2w, representing "adverse events of specific interest (AESI)".

Standard organ class	CA209017-003 [19] sq NSCLC 3 mg/kg q2w N=248 (100%)		CA209037-066 [18] adv Melanoma 3 mg/kg q2w N=474 (100%)	
	Any	≥3	Any	≥3
Skin events	nr	nr	**171 (36.1%)**	**4 (0.8%)**
Pruritus	nr	nr	86 (18.1%)	1 (0.2%)
Rash	30 (12.1%)	2 (0.8%)	65 (13.7%)	2 (0.4%)
Rash maculo-papular	nr	nr	22 (4.6%)	1 (0.2%)
Gastrointestinal events	nr	nr	**78 (16.5%)**	**6 (1.3%)**
Diarrhea	} 23 (9.3%)	} 4 (1.6%)	75 (15.8%)	3 (0.6%)
Colitis			5 (1.1%)	3 (0.6%)
Pulmonary events	**13 (5.2%)**	**4 (1.6%)**	**11 (2.3%)**	**0**
Pneumonitis incl. ILD	13 (5.2%)	4 (1.6%)	**11 (2.3%)**	0
Endocrine events	**12 (4.8%)**	**1 (0.4%)**	**40 (8.4%)**	**3 (0.6%)**
Hypothyroidism	0	0	27 (5.7%)	0
Hyperthyroidism	0	0	12 (2.5%)	1 (0.2%)
Hypophysitis	0	0	1 (0.2%)	1 (0.2%)
Adrenal insufficiency	1 (0.4%)	1 (0.4%)	1 (0.2%)	0
Diabetes mellitus	0	0	1 (0.2%)	0
Diabetic ketoacidosis	0	0	1 (0.2%)	1 (0.2%)
Renal events	**8 (3.2%)**	**1 (0.4%)**	**9 (1.9%)**	**3 (0.6%)**
Renal failure	nr	0	2 (0.4%)	0
Renal failure acute	nr	0	2 (0.4%)	2 (0.4%)
Tubulointerstitial nephritis	1 (0.4%)	1 (0.4%)	1 (0.2%)	1 (0.2%)
Hepatic events	**3 (1.2%)**	**0**	**29 (6.1%)**	**9 (1.9%)**
ALAT increase	nr	0	17 (3.6%)	5 (1.1%)
ASAT increase	nr	0	17 (3.6%)	3 (0.6%)
GGT increase	nr	0	3 (0.6%)	1 (0.2%)
Hepatic enzyme increased	nr	0	2 (0.4%)	1 (0.2%)
Liver function test abnormal	nr	0	2 (0.4%)	2 (0.2%)
Hypersensitivity/infusion reaction events	**4 (1.6%)**	**2 (0.8%)**	**25 (5.3%)**	**1 (0.2%)**
Infusion related reaction	nr	1 (0.4%)	13 (2.7%)	1 (0.2%)
Hypersensitivity	nr	1 (0.4%)	12 (2.5%)	0

* Event terms included blood creatinine increased, blood urea increased, blood urea increased, creatinine renal clearance decreased, hypercreatinemia, nephritis, nephritis allergic, nephritis autoimmune, renal failure, acute renal failure, renal tubular necrosis, tubulointerstitial nephritis, and urine output decreased.

Motzer RJ, et al. *NEJM* 2007

Eigentler TK, et al. *Cancer Treat Rev* 2016

You can not find what you do not look for

"Torre di Babele" Brueghel Pieter il Vecchio, 1563

Motzer RJ, et al. *NEJM* 2007

Eigentler TK, et al. *Cancer Treat Rev* 2016

why, when and how a nephrologist should be involved in the management of a cancer patient

DEDICATED NEPHRO-ONCOLOGICAL OUTPATIENT AMBULATORY
(IN STRICT COOPERATION WITH ONCOLOGISTS)

- **the prevalance of both cancer and CKD are growing up, patients with cancer can survival longer, so there is an increasing demand for physician who can provide long-term management**

- **the increasing number of therapies require an expertise of onco-nephrologists who must be aware of the array of new anticancer agents and their potential impact on kidney function**

Started in Cremona since May 2011

DEDICATED ONCO-NEPHROLOGICAL AMBULATORY

FAST ACCESS TO

- Biopsy in patients with proteinuria
- Acid-base status for electrolyte disturbances
- Renal Artery Doppler Ultrasound and Renal US
- Hypertension Ambulatory with ABPM
- Dedicated Nutritional Ambulatory for cancer patients with CKD
- Protocols for contrast medium

UNITS INVOLVED

- Oncology
- Radiotherapy
- Urology
- Breast Unit
- Surgery
- Hematology

Nephrol Dial Transplant (2018) 33: 1503–1510
doi: 10.1093/ndt/gfy188
Advance Access publication 5 July 2018

ndt
Nephrology Dialysis Transplantation

Opening an onconephrology clinic: recommendations and basic requirements

Laura Cosmai[1,*], Camillo Porta[2,*], Mark A. Perazella[3], Vincent Launay-Vacher[4], Mitchell H. Rosner[5], Kenar D. Jhaveri[6], Matteo Floris[7], Antonello Pani[7], Cécile Teuma[8], Cèzary A. Szczylik[9] and Maurizio Gallieni[1,10]

- **Critical mass of patients**
- **Proximity to the haematology and oncology ward**
- **Availability of medical records across clinics**
- **Shared (electronic) database**
- **Referral to the Onconephrologist**

- **Multidiciplinary team**
- **Core team**
- **Involvement of other health professionals**
- **Availability of certain diagnostic tests**
- **Which patients**
- **Diseases managed**
- **Performance indicators and obstacles**

Cosmai L, et al. *Nephrol Dial Transplant* 2018

Wich patients are appropriate for Onconephrology clinic?

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Table 1. Patients for whom referral to the onconephrology clinic is suggested

Type of patient(s)	Main issue(s)
Cancer patients with kidney impairment before, during or after active cancer treatment	To guarantee the best cancer treatment possible, without unnecessary dose reduction and/or treatment interruptions, which could hamper the possibility of success of the oncological treatment
Cancer patients at risk of kidney impairment	To prevent the development of kidney impairment, possibly leading to dose reduction or treatment interruption
• due to concomitant illnesses (e.g. hypertension, diabetes, etc.)	Education of oncologists and patients about classic kidney failure risks
• due to the potential nephrotoxicity of the planned treatment	
Cancer patients developing adverse renal events from antineoplastic treatment	AKI Worsening of CKD Hypertension Proteinuria Electrolyte disturbances TMA
Cancer patients at significant risk of CIN	Prevention of AKI or worsening of CKD through implementation of prophylactic measures
Kidney cancer patients at risk for postsurgical (or postablative) AKI or progressive CKD	Prevention of AKI or worsening of CKD Management of treatment-related AEs
Patients with urothelial cancer (all)	Prevention of AKI or worsening of CKD Prevention/management of obstructions Prevention/management of chronic infections Management of treatment-related AEs
Patients with suspected or *de facto* paraneoplastic glomerulopathies	Screening for an occult cancer (if any) Diagnosis Management strategies (e.g. use of immunosuppressive agents in the cancer patient)
Transplantation patients:	When to allow transplantation or donation in a patient with previous or active cancer
• donors	Management strategies (e.g. use of immunosuppressive agents in the cancer patient)
• recipients	
• transplanted patient who develops cancer	
Cancer patients on dialysis	Management of drug dosing, toxicity Use of erythropoietin-stimulating agents Shared decision making
Haematological cancer patients	Management of renal involvement in myeloma and lymphomas Management of secondary amyloidosis
Bone metastases in cancer patients with CKD	Management of bone-targeted therapies (bisphosphonates or denosumab) Management of bone-targeted therapies-induced hypocalcaemia

Outpatients but also inpatient during therapy or during recovery

- **treated or untreated cancer patients with pre-existing CKD;**
- **patients with glomerulopathies;**
- **patients who develope renal AEs (any);**
- **cancer patients that should start a potentially nephrotoxic Tx;**
- **RCC patients, undergoing or not active oncological Tx;**
- **patients with urothelial cancer and CKD;**
- **transplanted patients who develop cancer;**
- **patients on dialysis who develop cancer;**
- **patients with haematological malignancy**

Cosmai L, et al. *Nephrol Dial Transplant* 2018

Minimum workup for the Onconephrology patient

Table 2. Clinical evaluation of the patient with cancer and kidney disease

Physical examination
Evaluation of comorbidities and preexisting kidney impairment (clinical and subclinical)
Evaluation of ongoing (and previous) therapies, both oncological and not oncological
Renal function tests
eGFR with a CKD-EPI formula
When needed, directly measure eGFR (creatinine clearance, nuclear medicine GFR evaluation, etc.)
Basic haematology, including differential white blood cell count
Urinalysis and examination of urinary sediment examination; quantification of proteinuria
Electrolytes and serum enzymes (including serum calcium, phosphorus, uric acid and magnesium, LDH and uric acid).
Obtain trends of all pertinent labs including SCr, LDH, CBC and urine protein:creatinine ratio
Acid–base balance and abnormalities
Blood pressure (including ABPM whenever necessary)
Basic imaging: renal/abdominal US
Basic imaging: oncological disease status evaluation, as appropriate (CT, MRI, etc.)

CBC, complete blood count; SCr, serum creatinine; LDH, lactate dehydrogenase; US, ultrasound; CT, computed tomography; MRI, magnetic resonance imaging.

Patient History
- **Risk factors**
- **Comorbities**
- **Previous oncological and non-oncologicale treatments**

Clinical Assessment
- **Vital signs**
- **Performace Status**
- **Hydratation**
- **Edema**
- **Fever**
- **ECG**
- **Blood pressure**
- **Other Sympotms**

Laboratory Findings
- **Kidney Function (MDRD; CKD-EPI; ClCr)**
- **URINALYSIS !!!**
- **Complete blood count**
- **Serum Electrolytes**
- **Glicemia**

Radiologic Finding
- **CT Scans**
- **US**
- **MRI**

RENAL BIOPSY !!!

Cosmai L, et al. *Nephrol Dial Transplant* 2018

Development of protocols for the Onconephrology clinic

What we should do …

Table 4. Onconephrology protocols

Screening and follow-up protocols to prevent kidney damage for each given antineoplastic agent
Screening and follow-up protocols to prevent kidney damage from radiology contrast media
Developing indications for kidney biopsy and implementing their use in cancer patients
Screening and follow-up protocols for cancer patients in dialysis and with ESRD
Screening and follow-up protocols for transplantation patients (evaluation and possibly prevention of the risk of malignancy)
Screening and follow-up protocols for transplantation candidates
if and when to transplant a patient who previously had cancer
if and when to allow donation from a patient who previously had a cancer

ONCO-NEPHROLOGICAL REFERRAL:

- **Nephrologist reference for cancer patients (consultant)**
- **Management of these patients within a *Multisciplinary Team***
- **Protocols for the screening and follow-up of cancer patients, according to different class of anticancer drugs**
- **Protocols for screening and follow-up of patients exposed to contrast medium and oncological drugs-induced nephrotoxicity (e.g. Cisplatin)**
- **Protocol for management of RCC an urothelial cancer patients**
- **Protocols for the management and follow-up of cancer patients who developed renal Adverse Events**
- **Protocols for management therapy in our CKD patients**

Cosmai L, et al. *Nephrol Dial Transplant* 2018

Audits and (proposed) indicators of performance

Table 5. Performance indicators for an onconephrology clinic

Indicator of performance	Reason(s)	Value to be achieved (in Year 1)
Percentage of patients discussed by the core team	To ensure that (ideally) all patients presenting with onconephrology issues are adequately evaluated at least by the core team	100%
Percentage of patients brought to the attention of the MDT	To ensure that all complex patients presenting are brought to the attention of and discussed within each given MDT	100%
Number of episodes of AKI from anticancer treatment	AKI episodes lead to worsening of cancer patients' prognosis (especially in terms of reduced overall survival); also increase CKD	Reduction of at least 25% as compared to the previous year
Number of episodes of CIN	CIN episodes lead to both AKI and worsening of CKD	Reduction of at least 25% as compared to the previous year
Number of visits to emergency ward due to kidney toxicity from oncological treatments	Increase of costs and hospitalization rates	Reduction of at least 25% as compared to the previous year
Number of hospital admissions due to kidney toxicity	Increase of costs	Reduction of at least 25% as compared to the previous year
Number of treatment interruptions due to kidney toxicity	Potentially hampers treatment efficacy	Reduction of at least 25% as compared to the previous year
Number of treatment withdrawals due to kidney toxicity	Hampers treatment efficacy precluding the continuation of potentially life-extending treatments	Reduction of at least 25% as compared to the previous year
Number of drug-related adverse reactions due to kidney disease	Increases morbidity and (potentially) also mortality, as well as hospitalization rates; increases treatment interruptions and withdrawals	Reduction of at least 25% as compared to the previous year
Patients' satisfaction	Linked to improved QoL	100%
Health care workers' satisfaction	Linked to improved medical service quality and patients' satisfaction	100%

CIN, contrast-induced nephropathy; QoL, quality of life.

Cosmai L, et al. *Nephrol Dial Transplant* 2018

Obstacles in the development of an Onconphrology outpatient clinic

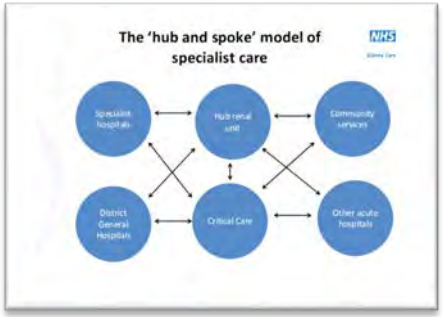
Table 6. Foreseen obstacles in establishing an outpatient onconephrology clinic

Specific requirement	Obstacle(s)
Critical mass of patients	Presence of a small oncology/haematology service
	Nihilistic approach to patients with both kidney diseases and cancer
Proximity to the haematology/oncology ward	Structural difficulties (especially in hospitals not built to favor multidisciplinarity)
Availability of medical records across clinics	Not an issue
Shared (electronic) database	Not an issue
Referral to the onconephrologist	Clear-cut identification of the onconephrology referral specialist within the hospital
	Clear-cut definition of the patients to refer for consultation
	Information/education of physicians who should know when an onconephrological referral is needed
MDT and core team	Time
	Bringing together and motivating different specialists towards a real multidisciplinary consultation
	Nihilistic approach to patients with both kidney diseases and cancer
	Need for specific training and for maintaining proficiency in onconephrology
Involvement of other health professionals	Bringing together and motivating different health professionals and caregivers
Availability of certain diagnostic tests	Not an issue
Appropriateness of patients	Clear-cut definition of the patients to refer for consultation
	Nihilistic approach to patients with both kidney diseases and cancer
Minimal workup	Sharing minimal requirements among different specialists
	Sharing a common language
	Clear-cut evaluation of kidney function
Disease management	Nihilistic approach to patients with both kidney diseases and cancer
Development of specific protocols	Identification of topics and objectives
Audits and indicators of performance	Time and personnel
	Variability of indicators over time
Hub and spoke model	Costs
	Bringing together and motivating different structures and health professionals
Education and training	Identification of educational needs
	Standardization of trainees' curriculum

We should not forget the costs …

Maybe, we should allocate economic resources in the right way (i.e. where it is worth-while …)

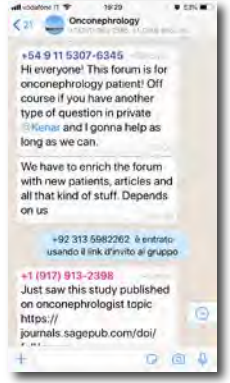
Cosmai L, et al. *Nephrol Dial Transplant* 2018

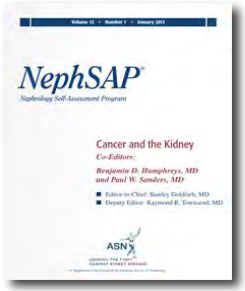


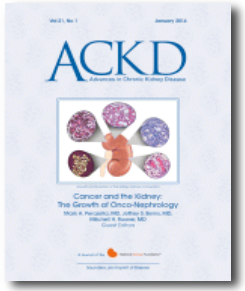
- **The «HUB- and- SPOKE» model for Onconephrology;**
- **Education and training to create the Onconephrologist**

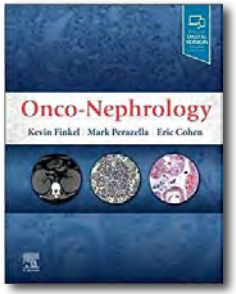
ASN
American Society of Nephrology

Onconephrology Core Curriculum









Main issues in our dedicated outpatient clinic…

- **Hypertension**
- **Proteinuria**
- **Cancer treatments elegibility**
- **Management of anticancer Tx in CKD, ESRD, or on dialysis**
- **Use of contrast medium in CKD**
- **RCC patients**
- **Urothelial cancer patients with CKD**
- **Acute Kidney Injury**
- **Electrolyte disturbances**
- **Management of cancer patients with glomerulopathies**
- **Anemia in patients with CKD and cancer**
- **Thrombotic Microangiopathies**
- **Tumor Lysis Syndrome**
- **Hematological malignancy (Mieloma/Limphoma)**

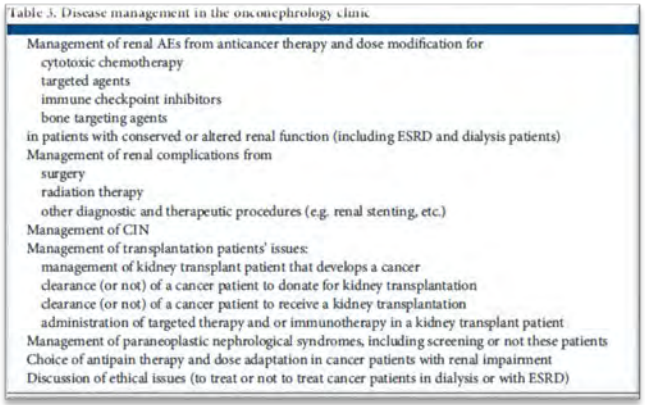


Table 3. Disease management in the onconephrology clinic

Management of renal AEs from anticancer therapy and dose modification for
cytotoxic chemotherapy
targeted agents
immune checkpoint inhibitors
bone targeting agents
in patients with conserved or altered renal function (including ESRD and dialysis patients)
Management of renal complications from
surgery
radiation therapy
other diagnostic and therapeutic procedures (e.g. renal stenting, etc.)
Management of CIN
Management of transplantation patients' issues:
management of kidney transplant patient that develops a cancer
clearance (or not) of a cancer patient to donate for kidney transplantation
clearance (or not) of a cancer patient to receive a kidney transplantation
administration of targeted therapy and or immunotherapy in a kidney transplant patient
Management of paraneoplastic nephrological syndromes, including screening or not these patients
Choice of antipain therapy and dose adaptation in cancer patients with renal impairment
Discussion of ethical issues (to treat or not to treat cancer patients in dialysis or with ESRD)

Cosmai L, et al. *Nephrol Dial Transplant* 2018

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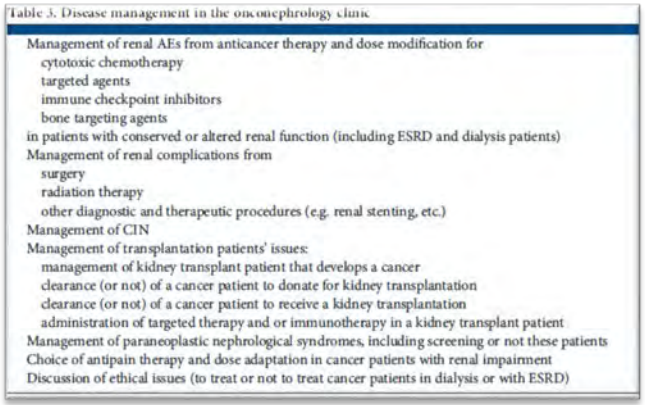

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Prestazioni Ambulatorio Onco-Nefrologia Anno 2018			
MESE	Prime viste	Controlli	TOTALE
gennaio	27	50	77
febbraio	11	41	52
marzo	39	37	76
aprile	23	41	64
maggio	25	60	85
giugno	33	73	106
luglio	27	51	78
agosto	9	36	45
settembre	19	62	81
ottobre	26	75	101
novembre	22	102	124
dicembre	14	83	97
TOTALE	275	711	986

Prestazioni Ambulatorio Onco-Nefrologia Anno 2019			
MESE	Prime viste	Controlli	TOTALE
gennaio	11	64	75
febbraio	10	45	55
marzo	10	87	97
aprile	21	69	90
maggio	23	61	84
giugno	21	71	92
luglio	20	45	65
agosto	10	34	44
settembre	17	55	72
ottobre	29	65	94
novembre	21	82	103
dicembre	15	64	79
TOTALE	208	742	950

Data from “Ospedale San Carlo Borromeo”, Milan”

Cosmai L, et al. *Nephrol Dial Transplant* 2018

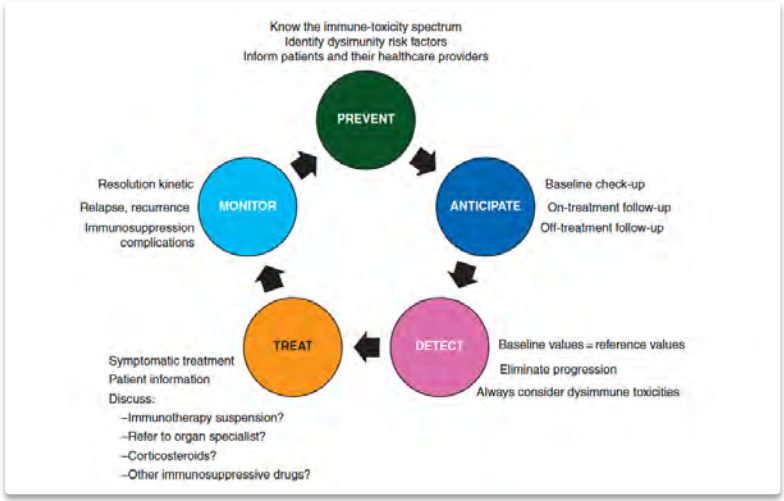
special article

Annals of Oncology 27: 559–574, 2016
doi:10.1093/annonc/mdv623
Published online 28 December 2015

Management of immune checkpoint blockade dysimmune toxicities: a collaborative position paper

S. Champiat[1,2], O. Lambotte[3,4,5,6], E. Barreau[7], R. Belkhir[8], A. Berdelou[9], F. Carbonnel[10], C. Cauquil[11], P. Chanson[12,13,14], M. Collins[10], A. Durrbach[15], S. Ederhy[16], S. Feuillet[17,18], H. François[15], J. Lazarovici[19], J. Le Pavec[17,18,20], E. De Martin[21,22], C. Mateus[23], J.-M. Michot[1], D. Samuel[21,22], J.-C. Soria[1,2], C. Robert[2,23], A. Eggermont[24] & A. Marabelle[1,24,25*]

This is true not only for immune checkpoint inhibitors



Champiat S, et al. *Ann Oncol* 2016.

immunotherapy permanent discontinuation

Apart from certain exceptions, the causing immunotherapy should be definitively discontinued in case of adverse immune dysfunction:

- life-threatening (grade 4)
- severe (grade 3) and recurring
- moderate (grade 2) but not resolutive in 3 months despite appropriate treatment

Endocrinopathies that are controlled by hormone replacement therapy, even grade 4, do not require the termination of immunotherapy.

temporary suspension

After suspension, resumption of immunotherapy can only be envisaged:

- if the side-effect is stabilized ≤ grade 1 (returned to baseline) and
- if the steroid dose is reduced to ≤10 mg/day prednisone or equivalent and
- in the absence of other immunosuppressive drugs.

Immunotherapy dose reduction is currently not recommended for the three EMA approved ICBs [18–20]. Phase I studies have indeed shown not dose/toxicity correlation for anti-PD1 or PD-L1. However, anti-CTLA4 trials have revealed that the 10 mg/kg regimen has a higher rate of toxicity.

organ specialist referral: why, when and how?

The current experience of managing immunotherapy toxicities is low and requires expertise. Organ specialist or internist referral is needed for mainly two reasons: for oncologists to learn proper management of specific dysimmune toxicities but also for organ specialists to increase their knowledge about these new drug-mediated toxicities and therefore creating a virtuous circle for patients management. For this purpose, oncologists should define their local organ specialist team based on their interest and expertise on the topic but also availability and responsiveness to sollicitation.

Oncologists should seek for organ specialist support as soon as the diagnosis and treatment of dysimmune toxicities become difficult. Some toxicities such as asymptomatic hypothyroidism or grade 1–2 rash can be easily managed but for most other toxicities, especially if grade >1, specialist expertise is often needed for proper monitoring over time.

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S. Champiat[1,2], O. Lambotte[3,4,5,6], E. Barr…
C. Cauquil[11], P. Chanson[12,13,14], M. …
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D. Samuel[21,22], J.-C. Soria[1…

This …

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STRONGLY IN COLLABORATION!!!

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Champiat S, et al. *Ann Oncol* 2016.

Something achieved in these years

Now we are discussing about onconephrology both among nephrologists and oncologists ... finally we became aware of this important issue!

- National (AIOM, SIN) and International Scientific Society Congresses (EDTA, ASN, ISN) with dedicated sessions and Educational courses
- National Oncological and Urological congresses
- Epidemiological studies in Italy
- Books and Papers published on Intenational Journals
- Urological Guideline on kidney cancer (AURO 2012)
- AIOM Guideline on kidney cancer (2015-2016-2017-2018-2019-2020)
- TMD Project (Italian Multidisciplinary Group on GU cancer)
- Dedicated Onco-Nephrological Ambulatories
- Collaboration between Nefrological e Oncological International Society
- Interdisciplinary Working Group on Onco-Nephrology (AIOM-SIN) dedicatet to specific projects (i.e. contrast medium in cancer patients)

The very first Ambulatory in a Italian Cancer Centre

… the future

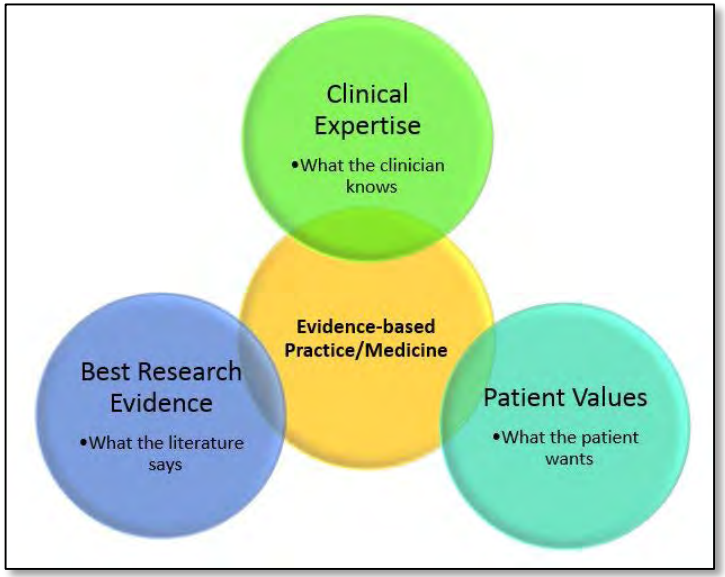
Onco-Nephrology Service, i.e.

- **Onco-Nephrological Ambulatory**
- **Multidisciplinary consultation for GU cancers**
- **The presence of a Nephrologist in every Comprehensive Cancer Centers in Italy as a structured part of their multidisciplinary team**
- **Onco-Nephrological Referral in every Nephrologic departement**
- **The Kidney Unit or better GU Cancer Unit**

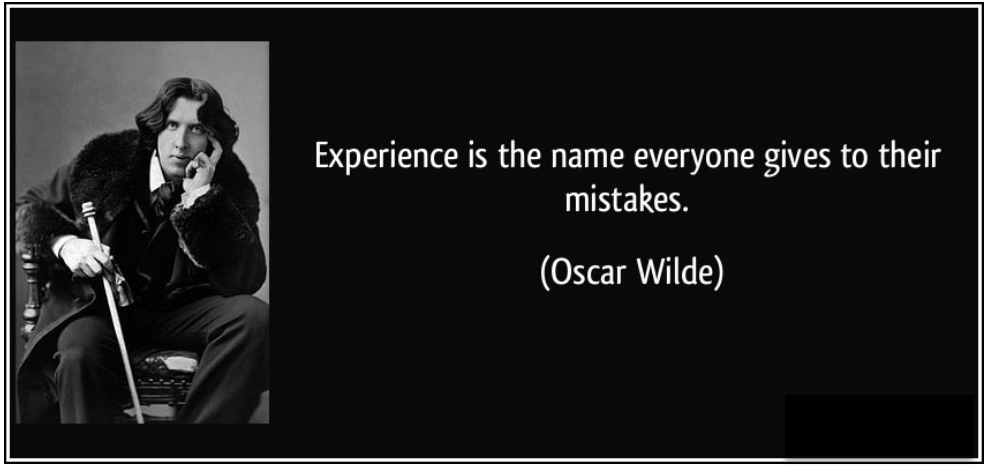
In the US, the "Comprehensive Cancer Centers" have already adopted Nephrologists as a structured part of their multidisciplinary team

FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI

What does ‘EBM? Really mean?



Evidence-Based Medicine



Experience-Based Medicine

… and what we must do …
mainly research

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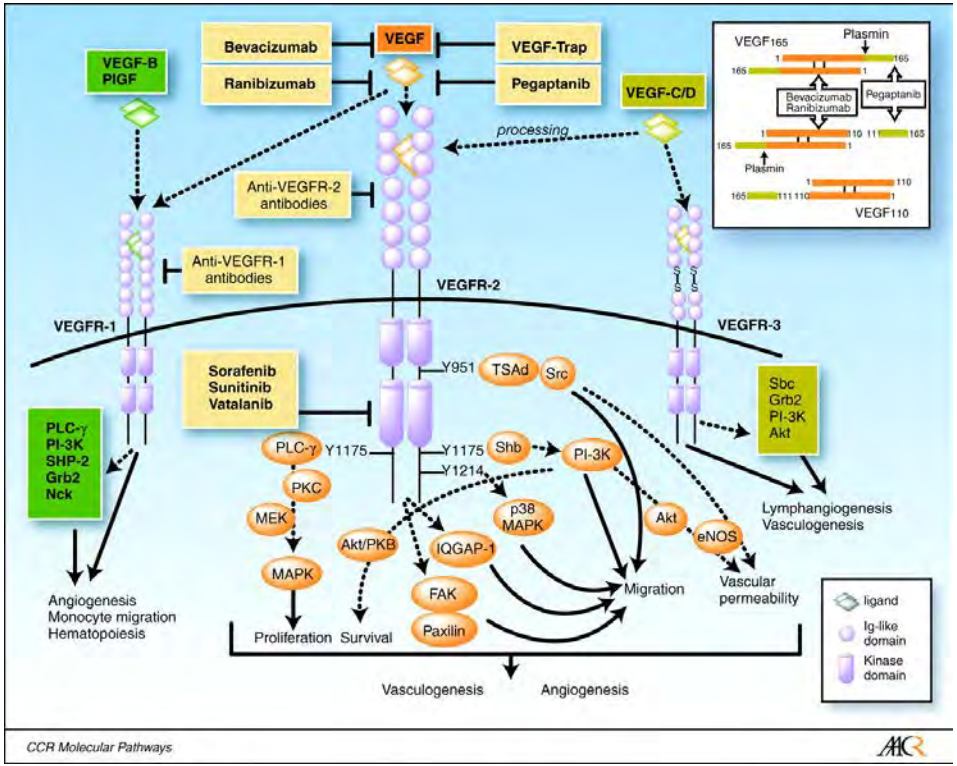

… do not forget ‘the elephant in the room’

Thank You for Your kind attention!!!

laura.cosmai@asst-fbf-sacco.it