I SIMPOSIO GETHI

17 DE NOVIEMBRE DE 2015

SEDE: HOSPITAL UNIVERSITARIO LA PAZ · AULA JASO · MADRID

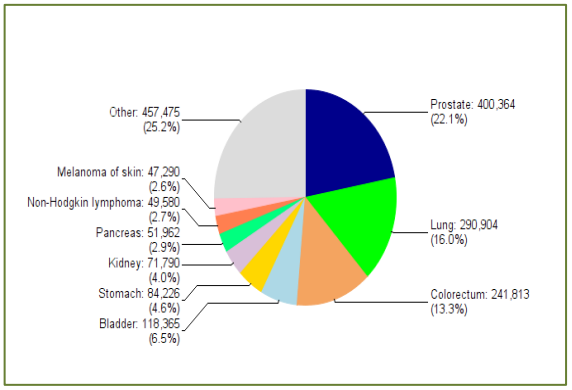
TUMORES UROLÓGICOS INFRECUENTES

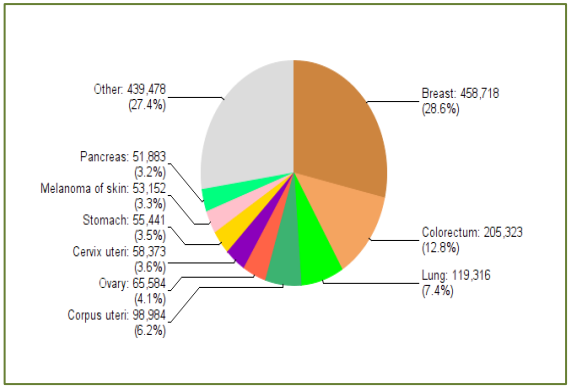
Carmen Beato Zambrano. Hospital NISA Sevilla-Aljarafe

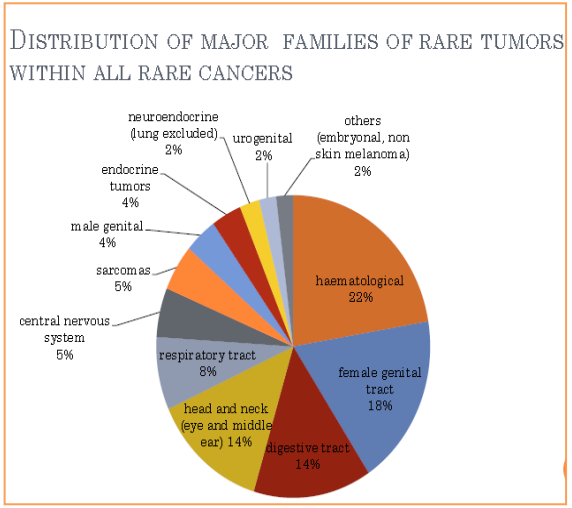
Los tumores urológicos son, per se, un grupo infrecuente de tumores…

Estimated New Cases*

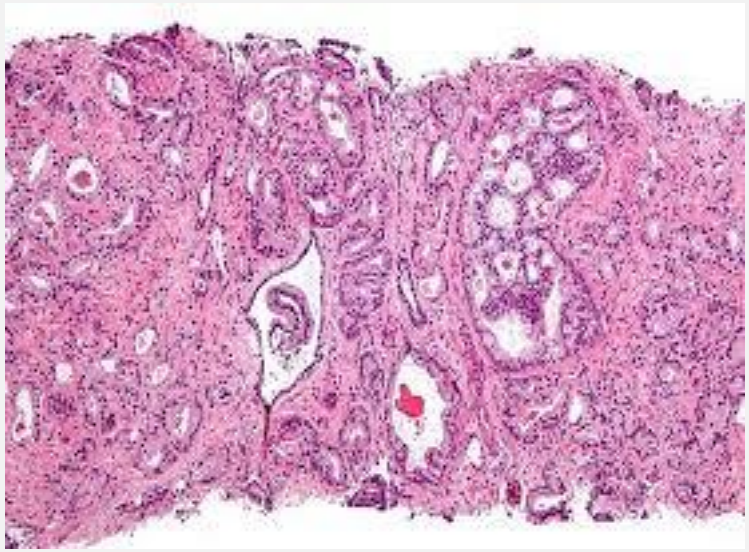
Males			Females		
Prostate	238,590	28%	Breast	232,340	29%
Lung & bronchus	118,080	14%	Lung & bronchus	110,110	14%
Colorectum	73,680	9%	Colorectum	69,140	9%
Urinary bladder	54,610	6%	Uterine corpus	49,560	6%
Melanoma of the skin	45,060	5%	Thyroid	45,310	6%
Kidney & renal pelvis	40,430	5%	Non-Hodgkin lymphoma	32,140	4%
Non-Hodgkin lymphoma	37,600	4%	Melanoma of the skin	31,630	4%
Oral cavity & pharynx	29,620	3%	Kidney & renal pelvis	24,720	3%
Leukemia	27,880	3%	Pancreas	22,480	3%
Pancreas	22,740	3%	Ovary	22,240	3%
All Sites	**854,790**	**100%**	**All Sites**	**805,500**	**100%**







NEOPLASIAS INFRECUENTES DE LA PRÓSTATA



TUMORES EPITELIALES DE LA PRÓSTATA

Tumour	Rate	Patients
EPITELIAL TUMOURS OF PROSTATE	47,89	385.278
Adenocarcinoma with variants of prostate	40,51	325.916
Adenocarcinoma NOS	39,70	319.386
Acinic cell adenocarcinoma	0,41	3.302
Mucinous adenocarcinoma	0,03	208
Signet ring cell carcinoma	0,01	82
Adenocarcinoma with neuroendocrine differentiation	<0.01	2
Oxyphilic adenocarcinoma	<0.01	1
Spindle cell adenocarcinoma	<0.01	2
Lymphoepithelial carcinoma	NE	0
Squamous cell carcinoma with variants of prostate	0,11	909
Squamous carcinoma	0,01	121
Adenosquamous carcinoma	<0.01	14
Infiltrating duct carcinoma of prostate	0,47	3.777
Cribriform carcinoma	0,35	2.777
Solid carcinoma, NOS	0,02	185
Papillary adenocarcinoma, NOS	0,01	112
Transitional cell carcinoma of prostate	0,06	518
Salivary gland type tumours of prostate	<0.01	13
Adenoid cystic carcinoma	<0.01	12
Basaloid carcinoma	<0.01	1
Basal cell adenocarcinoma	NE	0

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GUIDELINES

NCCN Comprehensive Cancer Network®

NCCN Guidelines Version 1.2015
Prostate Cancer

NCCN Guidelines Index
Prostate Table of Contents
Discussion

Progression to CRPC

Patients who progress during primary ADT to CRPC should receive a laboratory assessment to assure a castrate level of testosterone. In addition, imaging tests may be indicated to monitor for signs of distant metastases. Factors affecting the frequency of imaging include individual risk, age, PSA velocity, Gleason grade, and overall patient health.

A number of options for systemic therapy should be considered based on metastasis status, as discussed in the following sections.

CRPC without Signs of Metastasis

rare tumors are typically associated with low PSA levels despite large metastatic burden and visceral disease.[320] Thus, a biopsy of accessible lesions should be considered to identify patients with small cell histomorphologic features.[321] These cases may be managed by cytotoxic chemotherapy, such as cisplatin/etoposide, carboplatin/etoposide, or a docetaxel-based regimen.[322,323] Participation in a clinical trial is another option. Physicians should consult the NCCN Guidelines for Small Cell Lung Cancer since the behavior of small cell carcinoma of the prostate is similar to that of small cell carcinoma of the lung. Small cell carcinomas of the prostate differ from neuroendocrine prostate cancers; the latter histology may be more common and should not alter treatment.

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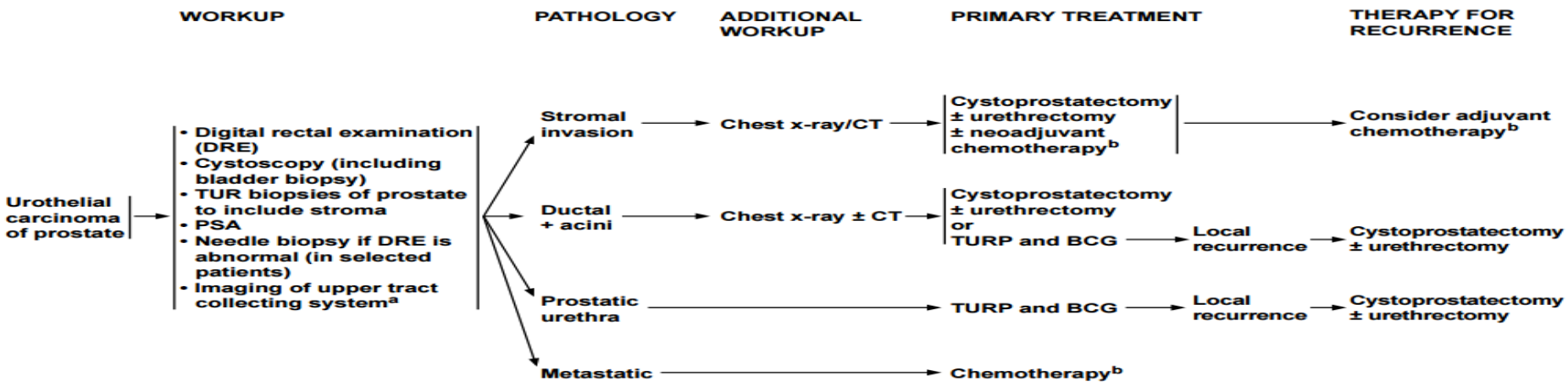
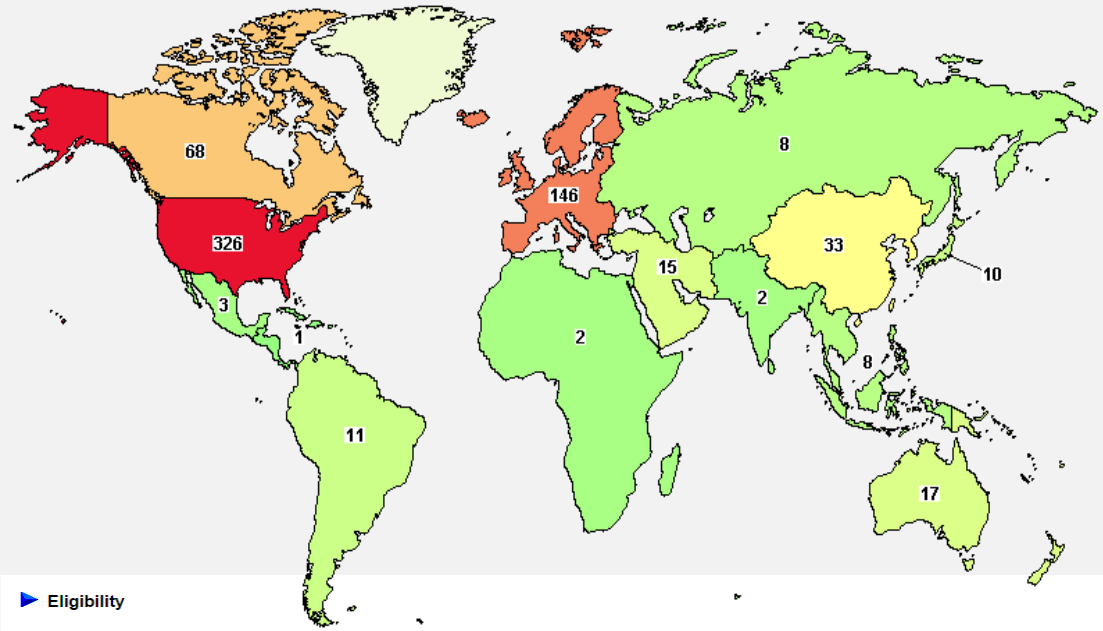
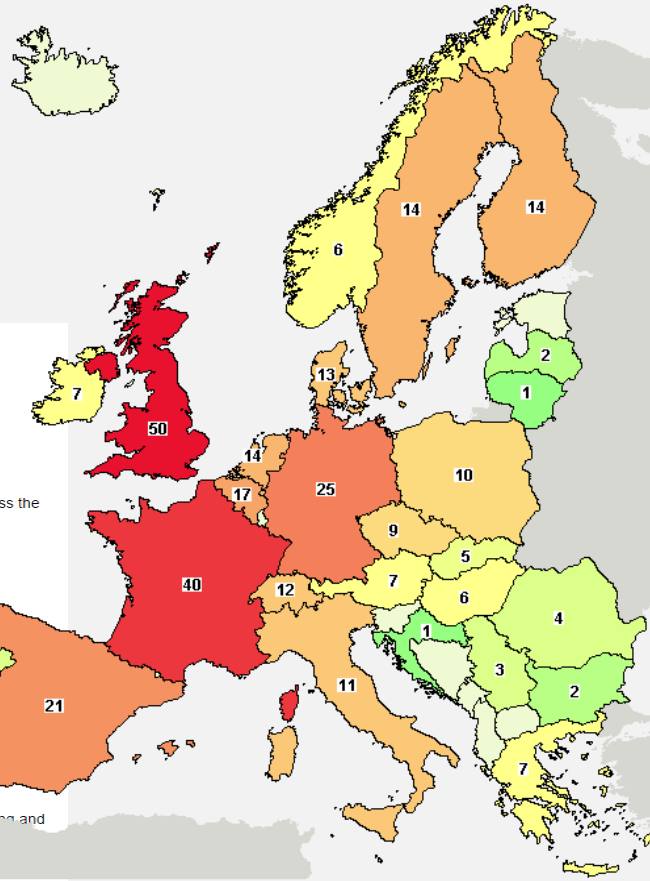
NCCN Guidelines Version 2.2015
Urothelial Carcinoma of the Prostate

NCCN Guidelines Index
Bladder Cancer TOC
Discussion



An Open Label, Multi-center Pasireotide Roll-over Protocol for Patients Who Have Completed a Previous Novartis-sponsored Pasireotide Study and Are Judged by the Investigator to Benefit From Continued Pasireotide treatment.





Eligibility

Ages Eligible for Study:	18 Years and older
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

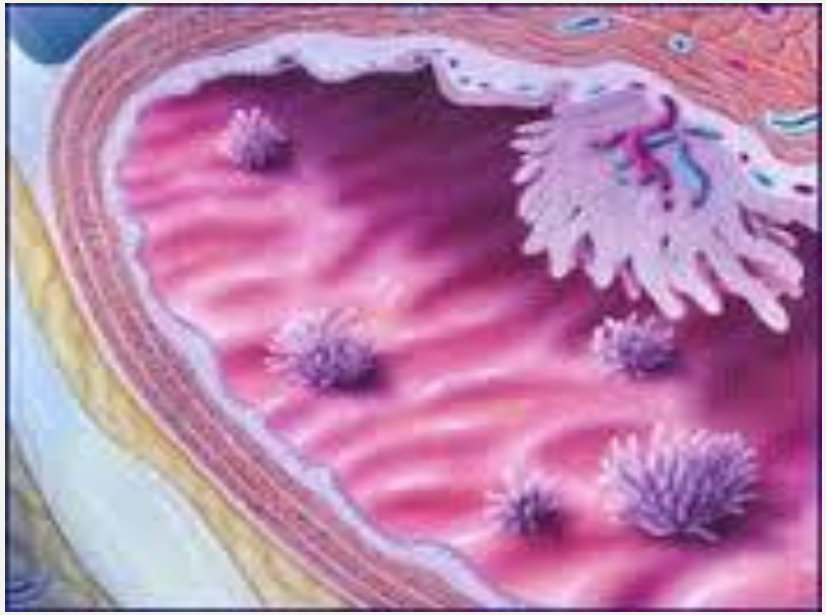
Inclusion Criteria:

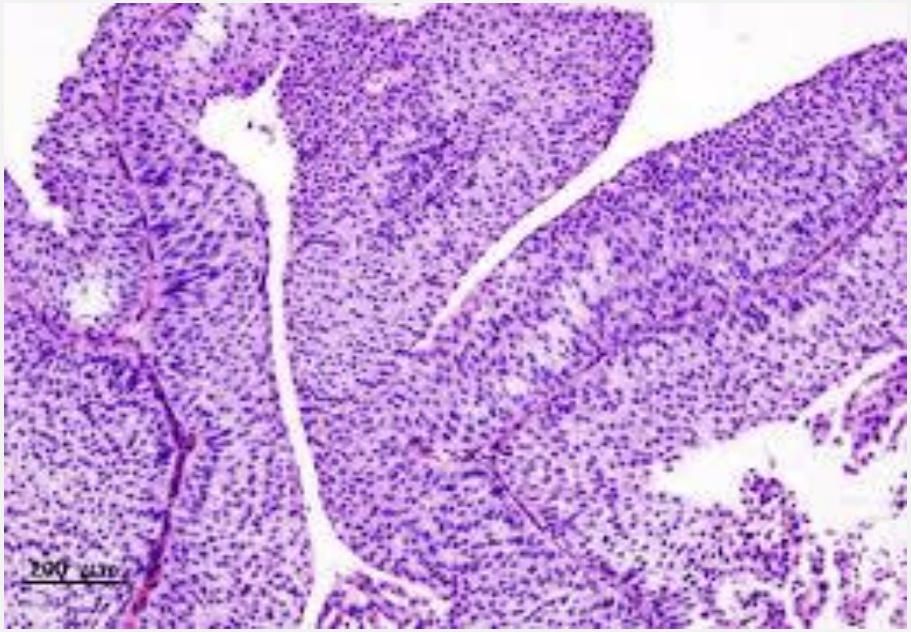
- Patient is currently participating in a Novartis Oncology sponsored study receiving pasireotide (LAR and/or s.c.) and has fulfilled all required assessments in the parent study (unless the study is being terminated) and patients that are benefiting from the study drug have no other alternatives
- Patient is currently benefiting from the treatment with pasireotide, as determined by the investigator
- Patient has demonstrated compliance, as assessed by the investigator, with the parent study requirements
- Willingness and ability to comply with scheduled visits, treatment plans and any other study procedures
- Written informed consent obtained prior to enrolling in roll-over study and receiving study medication • If consent cannot be expressed in writing, it must be formally documente witnessed, ideally via an independent trusted witness

Exclusion Criteria:

- Patient has been permanently discontinued from pasireotide study treatment in the parent study due to unacceptable toxicity, non-compliance to study procedures, withdra or any other reason
- Patient has participated in a Novartis sponsored combination trial where pasireotide was dispensed in combination with another study medication and is still receiving co therapy. (only patients receiving pasireotide monotherapy can be included)
- Pregnant or nursing (lactating) women, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test
- Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using highly effective methods of contraception during and for 1 months after pasireotide s.c. last dose and 3 months after pasireotide LAR last dose Highly effective contraception methods include:
  - Total abstinence (when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulatic withdrawal are not acceptable methods of contraception

TUMORES INFRECUENTES DE VEJIGA





TUMORES EPITELIALES DE VEJIGA

Tumour	Rate	Patients
EPITHELIAL TUMOURS OF BLADDER	**20,11**	**161.780**
Transitional cell carcinoma of bladder	**17,41**	**140.075**
Undifferentiated carcinoma	0,08	666
Transitional cell carcinoma spindle cell	0,01	68
Transitional cell carcinoma with squamous differentiation		
Lymphoepithelial carcinoma	<0.01	7
Giant cell carcinoma	<0.01	8
Transitional cell carcinoma micropapillary	<0.01	3
Squamous cell carcinoma with variants of bladder	**0,43**	**3.428**
Verrucous carcinoma	<0.01	29
Adenocarcinoma with variants of bladder	**0,29**	**2.305**
Mucinous adenocarcinoma	0,01	121
Clear cell adenocarcinoma, NOS	0,01	117
Signet ring cell carcinoma	0.01	99
Salivary gland type tumours of bladder	**<0.01**	**9**
Basaloid carcinoma	<0.01	3
Adenoid cystic carcinoma	<0.01	5
Mucoepidermoid carcinoma	<0.01	1

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GUIDELINES

Initial treatment options for female patients with T2 tumors include chemoradiation or urethrectomy with or without cystectomy. Partial urethrectomy was associated with a high urethral recurrence rate.[124] At recurrence, the patient may receive chemotherapy or chemoradiotherapy (both category 2A) or pelvic exenteration (category 2B).

A multimodal treatment approach (ie, surgery, chemotherapy, radiation) is common for advanced disease. If chemotherapy is used, the choice

Non-Urothelial Carcinomas of the Bladder

Approximately 10% of bladder tumors are non-urothelial (non-transitional cell) carcinoma. These pathologic entities include mixed histology, pure squamous, adenocarcinoma, small cell tumors, urachal carcinoma, or primary bladder sarcoma. Depending on the pathologic findings, adjuvant chemotherapy may or may not be recommended. Patients with non-urothelial invasive disease are generally treated with cystectomy, although those with certain urachal tumors require complete urachal resection (en bloc resection of the urachal ligament

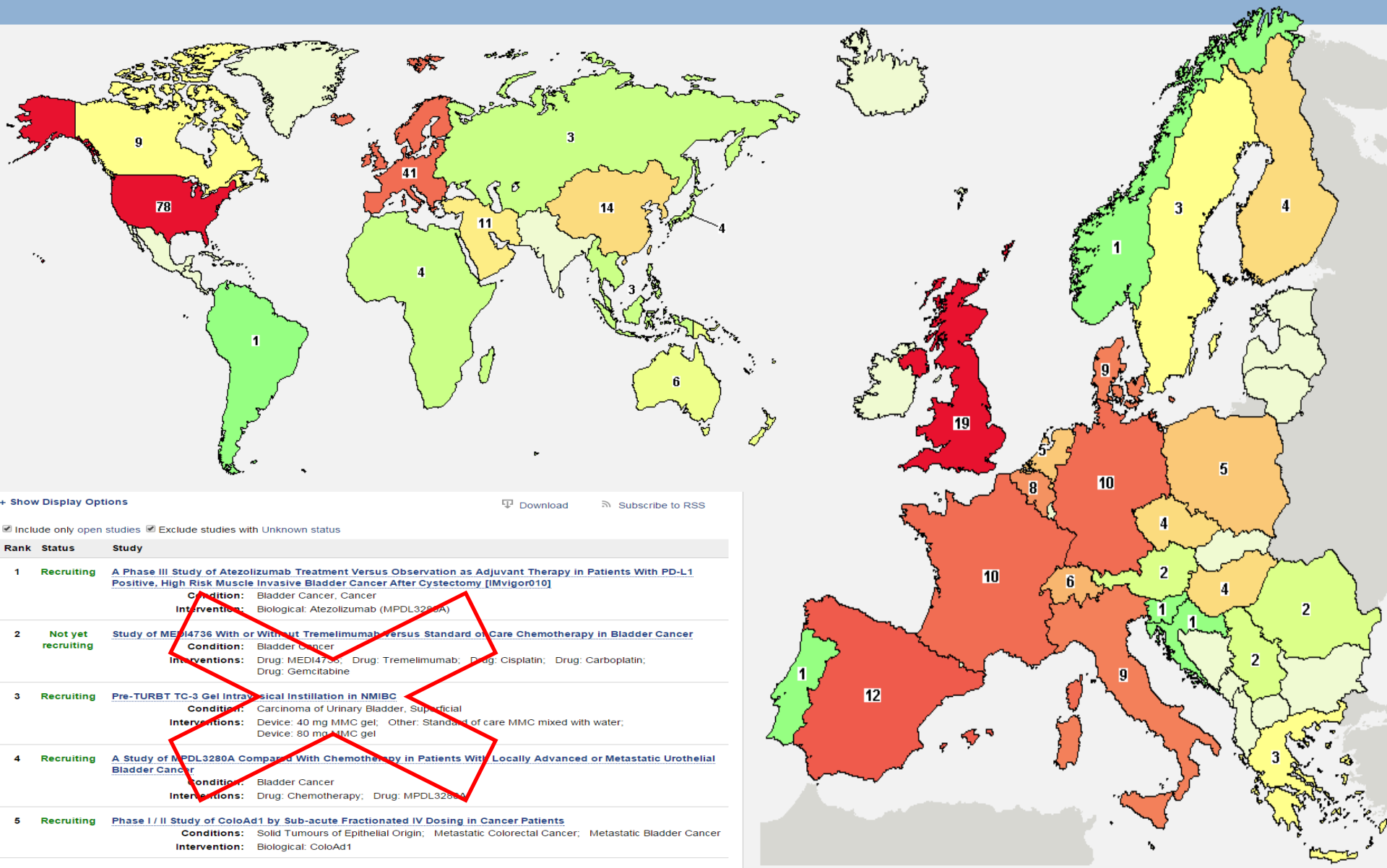
 MS-23

with the umbilicus) or may be appropriately treated with partial cystectomy. In patients with non-urothelial carcinomas of any stage, no data support the use of adjuvant chemotherapy, although the risk for relapse may be high. Some of the general principles of management applicable to urothelial carcinomas are appropriate with minor variations. These variations are documented in the algorithm.

Patients with small cell carcinoma of the bladder are best treated with initial chemotherapy (see NCCN Guidelines for Small Cell Lung Cancer) followed by either radiation therapy or cystectomy as consolidation, if there is no metastatic disease. Primary bladder sarcomas are treated as per the NCCN Guidelines for Soft Tissue Sarcoma.

Finally, within the category of metastatic disease, several new agents have been identified that seem superior to those currently considered standard therapies. Experts surmise that the treatment of urothelial tumors will evolve rapidly over the next few years, with improved outcomes for patients at all stages of disease.

12 EC ABIERTOS EN ESPAÑA, EN TODOS ES CRITERIO DE INCLUSIÓN “CARCINOMA UROTELIAL DE VEJIGA”

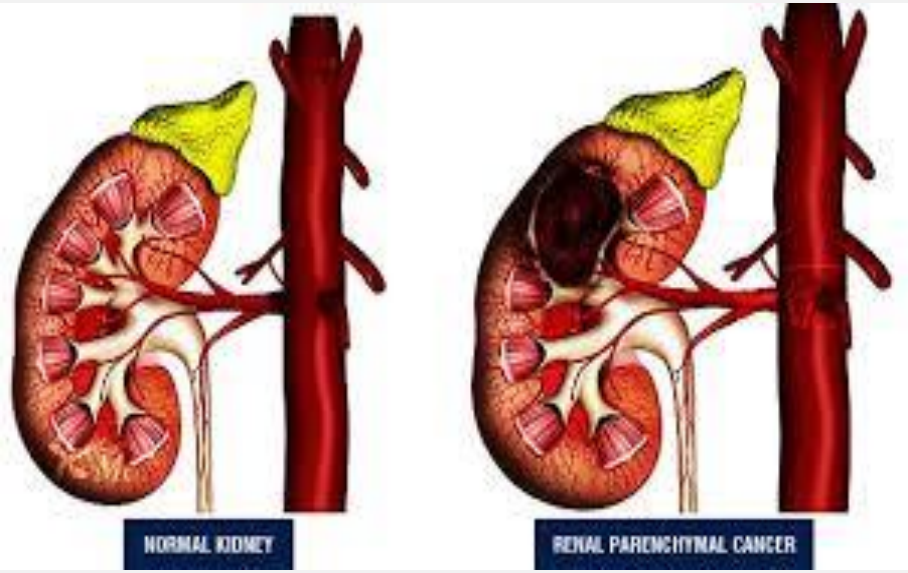


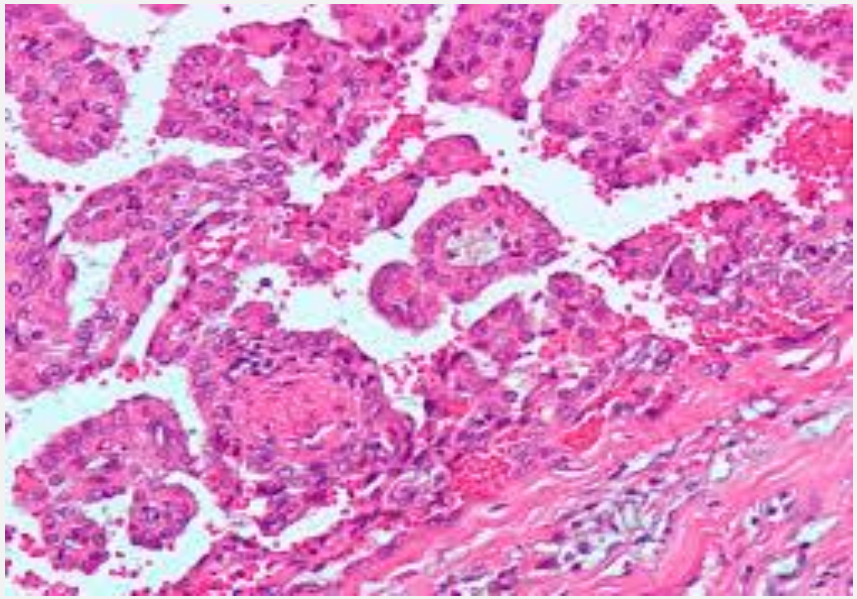
+ Show Display Options Download Subscribe to RSS

Include only open studies Exclude studies with Unknown status

Rank	Status	Study
1	Recruiting	A Phase III Study of Atezolizumab Treatment Versus Observation as Adjuvant Therapy in Patients With PD-L1 Positive, High Risk Muscle Invasive Bladder Cancer After Cystectomy [IMvigor010] Condition: Bladder Cancer, Cancer Intervention: Biological: Atezolizumab (MPDL3280A)
2	Not yet recruiting	Study of MEDI4736 With or Without Tremelimumab Versus Standard of Care Chemotherapy in Bladder Cancer Condition: Bladder Cancer Interventions: Drug: MEDI4736; Drug: Tremelimumab; Drug: Cisplatin; Drug: Carboplatin; Drug: Gemcitabine
3	Recruiting	Pre-TURBT TC-3 Gel Intravesical Instillation in NMIBC Condition: Carcinoma of Urinary Bladder, Superficial Interventions: Device: 40 mg MMC gel; Other: Standard of care MMC mixed with water; Device: 80 mg MMC gel
4	Recruiting	A Study of MPDL3280A Compared With Chemotherapy in Patients With Locally Advanced or Metastatic Urothelial Bladder Cancer Condition: Bladder Cancer Interventions: Drug: Chemotherapy; Drug: MPDL3280A
5	Recruiting	Phase I / II Study of ColoAd1 by Sub-acute Fractionated IV Dosing in Cancer Patients Conditions: Solid Tumours of Epithelial Origin; Metastatic Colorectal Cancer; Metastatic Bladder Cancer Intervention: Biological: ColoAd1
6	Recruiting	A Dose Escalation Study in Adult Patients With Advanced Solid Malignancies

TUMORES INFRECUENTES DE RIÑÓN





TUMORES EPITELIALES DE RIÑÓN

Tumour	Rate	Patients
EPITELIAL TUMOURS OF KIDNEY	**10,55**	**84.863**
Renal cell carcinoma with variants	**8,35**	**67.152**
Adenocarcinoma NOS	0,51	4.071
Renal cell adenocarcinoma	5,55	44.638
Clear cell adenocarcinoma, NOS	1,99	15.994
Papillary adenocarcinoma, NOS	0,14	1.135
Renal cell carcinoma chromophobe type	0,01	107
Collecting duct carcinoma	<0.01	15
Xp translocation carcinoma		
Carcinoma associated with neuroblastoma		
Renal medullary carcinoma	<0.01	4
Mucinous tubular and spindle cell carcinoma		
Squamous cell carcinoma spindle cell type of kidney	**0,01**	**56**
Squamous cell carcinoma with variants of kidney	**0,04**	**283**

GUIDELINES

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2016
Kidney Cancer

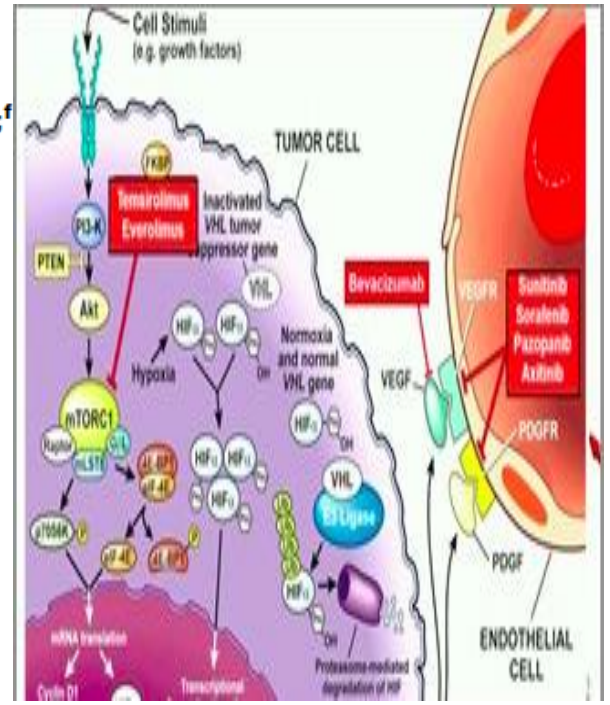
NCCN Guidelines Index
Kidney Cancer TOC
Discussion

SYSTEMIC THERAPY[i,k]

Relapse or Stage IV and surgically unresectable → **Non-clear cell histology** →

Clinical trial (preferred)
or
Temsirolimus (category 1 for poor-prognosis patients;[f] category 2A for other risk groups)
or
Sorafenib
or
Sunitinib
or
Pazopanib
or
Axitinib
or
Everolimus
or
Bevacizumab
or
Erlotinib

and
Best supportive care:[h]
See NCCN Guidelines for Palliative Care



For patients with advanced RCC we administer molecularly-targeted therapy rather than immunotherapy or chemotherapy because the limited data suggest that immunotherapy or chemotherapy has little impact on the outcomes of these patients

GUIDELINES

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NCCN Guidelines Version 1.2016
Kidney Cancer

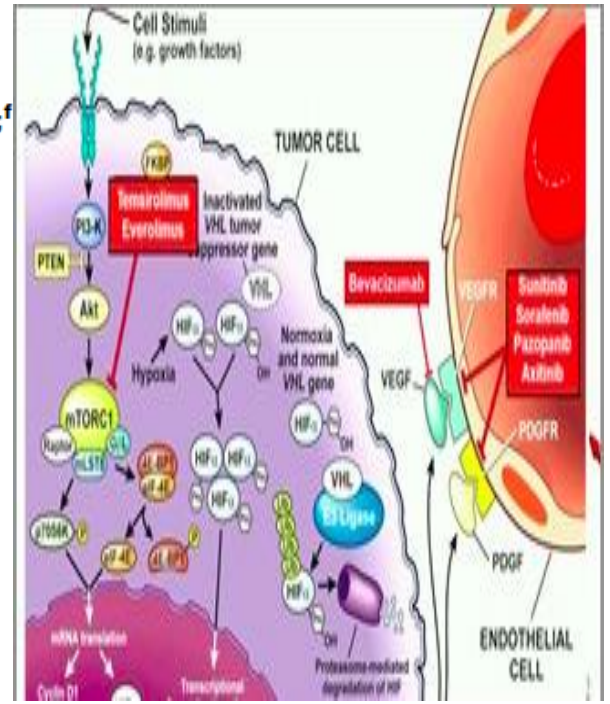
NCCN Guidelines Index
Kidney Cancer TOC
Discussion

SYSTEMIC THERAPY[i,k]

Relapse or Stage IV and surgically unresectable → Non-clear cell histology →

Clinical trial (preferred)
or
Temsirolimus (category 1 for poor-prognosis patients;[f] category 2A for other risk groups)
or
Sorafenib
or
Sunitinib
or
Pazopanib
or
Axitinib
or
Everolimus
or
Bevacizumab
or
Erlotinib

and
Best supportive care:[h]
See NCCN Guidelines for Palliative Care



For patients with advanced RCC we administer molecularly-targeted therapy rather than immunotherapy or chemotherapy because the limited data suggest that immunotherapy or chemotherapy has little impact on the outcomes of these patients

1 **Recruiting** **A Phase II Study of Axitinib in Metastatic Non-clear Cell Renal Cell Carcinoma Patients Previously Treated With Temsirolimus**

Conditions: Renal Cell Carcinoma; Nonclear Cell; Temsirolimus Resistance

Intervention: Drug: Axitinib

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2 **Recruiting** **Everolimus and Bevacizumab in Advanced Non-Clear Cell Renal Cell Carcinoma (RCC)**

Condition: Renal Cell Carcinoma

Intervention: Drug: everolimus and bevacizumab

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3 **Recruiting** **Pazopanib Hydrochloride in Treating Patients With Metastatic Kidney Cancer**

Conditions: Carcinoma of the Collecting Ducts of Bellini; Papillary Renal Cell Carcinoma; Recurrent Renal Cell Carcinoma; Sarcomatoid Renal Cell Carcinoma; Stage IV Renal Cell Cancer; Type 1 Papillary Renal Cell Carcinoma; Type 2 Papillary Renal Cell Carcinoma

Intervention: Drug: Pazopanib Hydrochloride

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4 **Recruiting** **pazopanib_NCRCC,Ph2 STUDY**

Condition: Locally Advanced or Metastatic Non-clear Cell Type Renal Cell Carcinoma

Intervention: Drug: pazopanib

GUIDELINES

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NCCN Guidelines Version 1.2016
Kidney Cancer

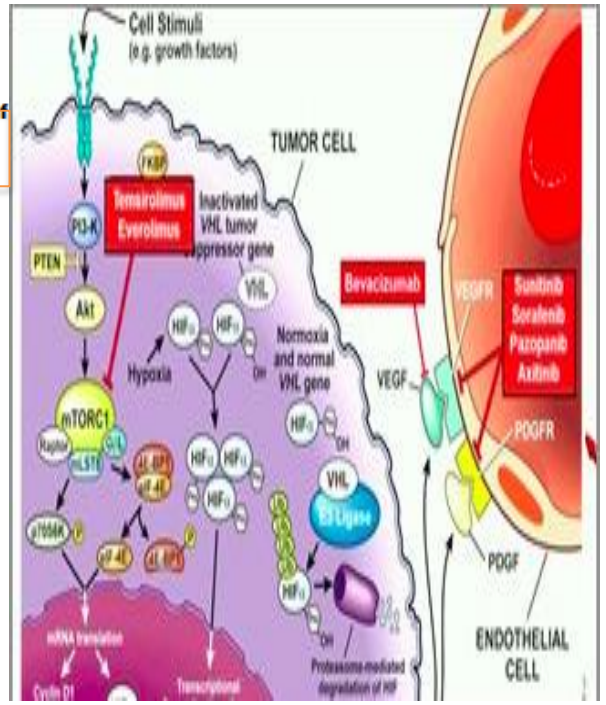
NCCN Guidelines Index
Kidney Cancer TOC
Discussion

SYSTEMIC THERAPY[i,k]

Relapse or Stage IV and surgically unresectable → **Non-clear cell histology** →

Clinical trial (preferred)
or
Temsirolimus (category 1 for poor-prognosis patients;[f] category 2A for other risk groups)
or
Sorafenib
or
Sunitinib
or
Pazopanib
or
Axitinib
or
Everolimus
or
Bevacizumab
or
Erlotinib

and
Best supportive care:[h]
See NCCN Guidelines for Palliative Care



For patients with advanced RCC we administer molecularly-targeted therapy rather than immunotherapy or chemotherapy because the limited data suggest that immunotherapy or chemotherapy has little impact on the outcomes of these patients

NON-CLEAR CELL HISTOLOGY HAS A WORSE PROGNISTIC…?

European Urology

Volume 67, Issue 4, April 2015, Pages 740–749

Review – Kidney Cancer

Systemic Therapy for Non–clear Cell Renal Cell Carcinomas: A Systematic Review and Meta-analysis

Francisco E. Vera-Badillo[a], Arnoud J. Templeton[a], Ignacio Duran[b], Alberto Ocana[c], Paulo de Gouveia[a], Priya Aneja[a], Jennifer J. Knox[a], Ian F. Tannock[a], Bernard Escudier[d], Eitan Amir[a].

A total of 49 studies comprising 7771 patients were included in the analysis. Of these, 1244 patients (16.0%) had non-ccRCC, 6300 (83.1%) had ccRCC, and 227 (2.9%) had sarcomatoid tumours. The overall response rate for non-ccRCC with targeted agents was 10.5%. In studies directly comparing non-ccRCC and ccRCC, **there were significantly lower response rates for non-ccRCC (odds ratio for response: 0.52; 95% confidence interval, 0.40–0.68; $p < 0.001$). For non-ccRCC treated with targeted agents, median PFS and OS were 7.4 and 13.4 mo, respectively; for patients with ccRCC, these were 10.5 mo and 15.7 mo, respectively** (p value for difference <0.001 for both parameters).

SHOULD I TREAT IT LIKE A POOR-RISK CC RENAL CANCER…??

A Randomized Trial of Everolimus vs. Sunitinib in Patients with Metastatic Non-Clear Cell Renal Cell Carcinoma (ASPEN)

Andrew J. Armstrong[1], Susan Halabi[2], Samuel Broderick[3], Timothy Eisen[4], Robert Jones[5], Walter M. Stadler[6], Christine Lusk[7], Ulka Vaishampayan[8], Jorge Garcia[9], Robert Hawkins[10], Christian Kollmansberger[11], and Daniel J. George[1]

[1]Duke Cancer Institute, Durham NC USA, [2]Department of Biostatistics, Duke University, [3]Duke Clinical Research Institute, [4]Addenbrooke's Hospital, Cambridge, England, [5]Beatson West Scotland Cancer Center, Glasgow UK, [6]University of Chicago, Chicago IL, [7]inVentiv Health Clinical, [8]Karmanos Cancer Center, Wayne State University, Detroit MI, [9]Cleveland Clinic, Cleveland OH, [10]The Christie Hospital NHS Foundation Trust, Manchester UK, [11]BC Cancer Agency, Vancouver BC.

DUKE CANCER INSTITUTE

Background

- Current evidence to support a front-line standard of care in patients with metastatic non-clear cell RCC is weak and based on single arm trials or case series without control groups.
- Heterogeneity in patient populations (front-second line, histologic type, risk group) limit the interpretations of these trials across trials.
- Evidence to support a VEGF-targeted strategy or an mTOR-targeted strategy each exist for specific RCC non-clear cell subtypes (papillary, chromophobe, undifferentiated).
- ASPEN is a randomized, controlled clinical trial inclusive of patients with metastatic non-clear cell RCC specifically designed to address this unmet clinical need.
- This is a Duke Cancer Institute investigator initiated, global trial of an mTOR based (everolimus) vs. a VEGF TKI-based (sunitinib) front line strategy.

Objectives

Primary Objective:

The primary endpoint is a comparison of the **progression-free survival (PFS)** between the treatment arms following therapy initiation. Disease progression is defined by documentation of progressive disease (RECIST), a new primary malignancy, or death (whichever occurs first).

Secondary Objectives:

- PFS, OS, overall response rates, safety, quality of life (FKSI), time to new metastatic disease

Exploratory Objectives

- To evaluate expression of baseline genomic, genetic, and protein-based aberrations associated with non-clear cell RCC with outcome overall and in each treatment arm
- To evaluate associations of baseline and longitudinal serum and urine angiokine biomarkers with outcome and during development of treatment resistance

Selection of Subjects

- Full eligibility and protocol details are available on clinicaltrial.gov; NCT01189643

Brief Eligibility Criteria

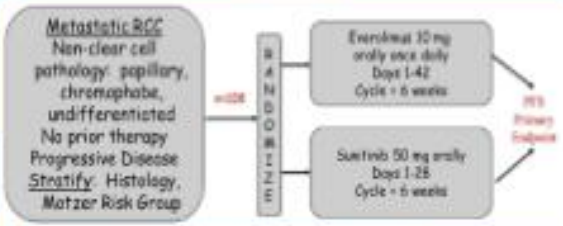
1. Histologically confirmed advanced RCC, with non-clear cell pathology. Mixtures of these non-clear cell variants are allowed as long as pathology consists predominantly of papillary or chromophobe or undifferentiated histology. Translocation carcinoma (if known) is allowed regardless of the histologic mixture.
2. RCC tumor tissue available for correlative sciences, from either primary or metastatic site.
3. Subject must have radiographic evidence of metastatic disease with at least 1 measurable per RECIST 1.1 criteria.
4. KPS ≥60
5. No prior systemic therapy
6. No active CNS metastases
7. No collecting duct or medullary histology. Sarcomatoid is permitted if non-clear cell component is >50% predominant.
8. Adequate hepatic, renal, and bone marrow function
9. Informed consent

Methods

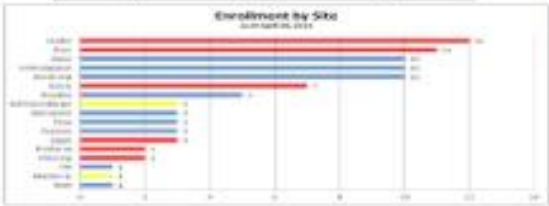
- After randomization, open label with everolimus 10 mg once daily or sunitinib at standard dosing (50 mg on 4/2 schedule) begins and continues until progression/ unacceptable toxicity (**see schema. Drug is provided by the study.**
- 1:1 randomization (34 per arm) stratified by Memorial Sloan Kettering Cancer Center (MSKCC) risk and histology
- Sample size based on a two sided hypothesized relative improvement of 50% in the rate of PFS over time for one treatment arm, power of 85%, alpha error of 0.20 (randomized phase 2 design)

Design and Trial Progress to Date

Trial Schema



Accrual and Geographic Distribution of Patients



Summary of Trial Progress to Date (May 1, 2013)

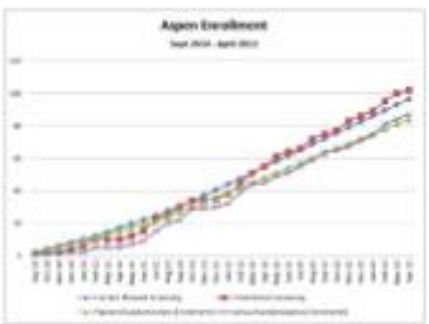
- Accrual of 87 patients with metastatic non-clear cell RCC according to the following strata:
  - **34 chromophobe/poorly differentiated histology**
  - **53 papillary histology**
- 17 sites are open and actively accruing at a rate of ~ 3 per month
- Targeted completion of accrual estimate to be by **December of 2013 (n=108)**
- DSMB initial meeting concluded at the end of 2012 after 40 subjects had completed at least 6 months of therapy or progressed and revealed no unexpected safety signals that would compromise the conduct of the study
- A second DSMB meeting will occur Fall of 2013 after 70 subjects have completed 6 months of therapy
- All subjects are contributing correlative samples for planned and future research on biomarkers of prognosis and prediction for VEGF vs mTOR-based therapies and novel markers for drug development
- All subjects are followed until death, and subsequent treatments are captured
- Initial publication of safety and efficacy results is anticipated in mid 2014.

Summary of Correlative Studies

Available for 100% of patients (tissue requirement for eligibility)
Goal is prediction of PFS benefit with specific therapy
Samples banked at the Duke Center for Human Genetics and Quintiles for the following planned analyses:
Protein biomarkers (IHC):
- **HIF-1/2, VEGFR1-3, CAIX expression**
- **Akt/mTOR pathway interrogation (p-S6K, p-4EBP1, p-Akt)**
- **PTEN and VHL status**
- **c-kit and c-met (phospho-met and total) expression levels**

Genetic: mutational screen (BHD, FH, c-met), SNP/CGH analysis, germline DNA on primary/metastases
Plasma/serum: LDH, multiplexed angiokines (baseline, cycle 3, at progression)
Urine: Multiplexed angiokines (baseline, cycle 3, at progression)
Biorepository established at Duke for future correlative and hypothesis-driven research, collaboration (FFPE and frozen tissues)

ASPEN: A Randomized Phase 2 Study of Afinitor (Everolimus) vs. Sutent (Sunitinib) in Patients with MEtastatic Non-Clear Cell RCC

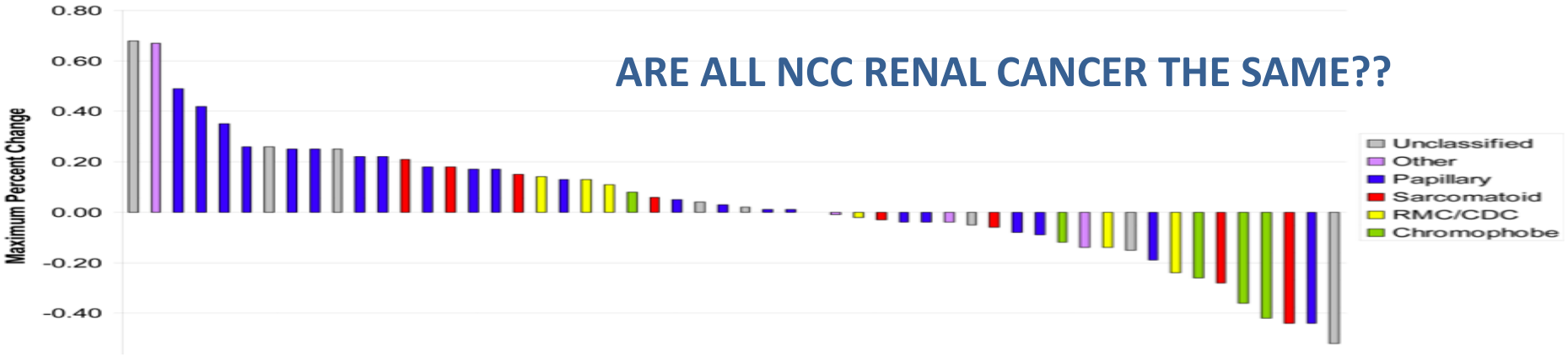


Acknowledgements: We wish to thank Pfizer and Novartis for funding this investigator initiated global trial, and to thank the patients and their families for their support of this trial and participation.

A Randomized Trial of Everolimus vs. Sunitinib in Patients with Metastatic Non-Clear Cell Renal Cell Carcinoma (ASPEN)

Andrew J. Armstrong[1], Susan Halabi[2], Samuel Broderick[3], Timothy Eisen[4], Robert Jones[5], Walter M. Stadler[6], Christine Lusk[7], Ulka Vaishampayan[8], Jorge Garcia[9], Robert Hawkins[10], Christian Kollmansberger[11], and Daniel J. George[1]

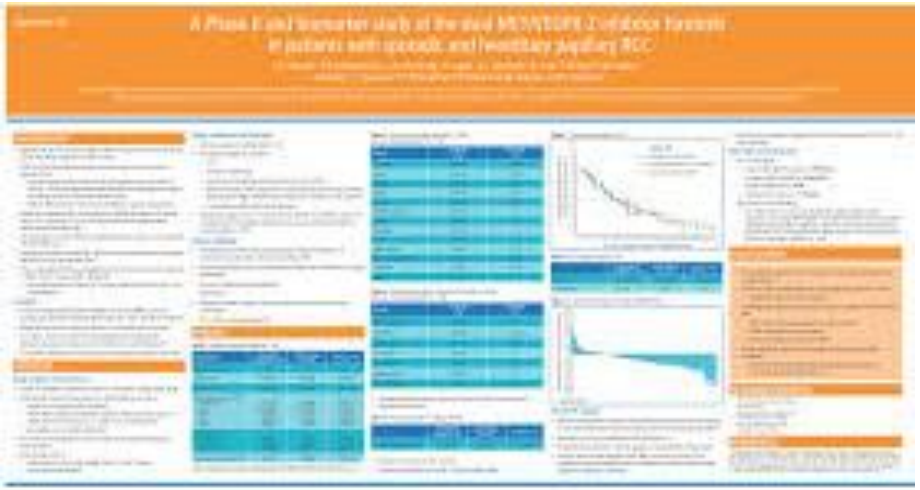
[1]Duke Cancer Institute, Durham NC USA, [2]Department of Biostatistics, Duke University, [3]Duke Clinical Research Institute, [4]Addenbrooke's Hospital, Cambridge, England, [5]Beatson West Scotland Cancer Center, Glasgow UK, [6]University of Chicago, Chicago IL, [7]inVentiv Health Clinical, [8]Karmanos Cancer Center, Wayne State University, Detroit MI, [9]Cleveland Clinic, Cleveland OH, [10]The Christie Hospital NHS Foundation Trust, Manchester UK, [11]BC Cancer Agency, Vancouver BC.



ARE ALL NCC RENAL CANCER THE SAME??

A phase 2 trial of sunitinib in patients with advanced non-clear cell renal cell carcinoma

Nizar M. Tannir[1], Elizabeth Plimack[6], Chaan Ng[2], Pheroze Tamboli[3], Neby Bekele[7], Lianchun Xiao[4], Lisa Smith[1], Zita Lim[1], Lance Pagliaro[1], John Araujo[1], Ana Aparicio[1], Surena Matin[5], Christopher G Wood[5], and Eric Jonasch[1]



Stamatakis L, Singer EA, Siddiqui MM, et al. Phase II trial of bevacizumab and erlotinib in patients with advanced hereditary leiomyomatosis and renal cell cancer (HLRCC) or sporadic papillary renal cell carcinoma. Eur J Cancer 2011:Abstr 2753

Srinivasan R, et al. Mechanism based targeted therapy for hereditary leimyomatosis and renal cell cancer and sporadic papillary renal cell carcinoma: interim results from a phase 2 study of bevacizumab and erlotinib (abstract 5). EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics (2014)

ARE ALL NCC RENAL CANCER THE SAME??

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JOURNAL OF CLINICAL ONCOLOGY

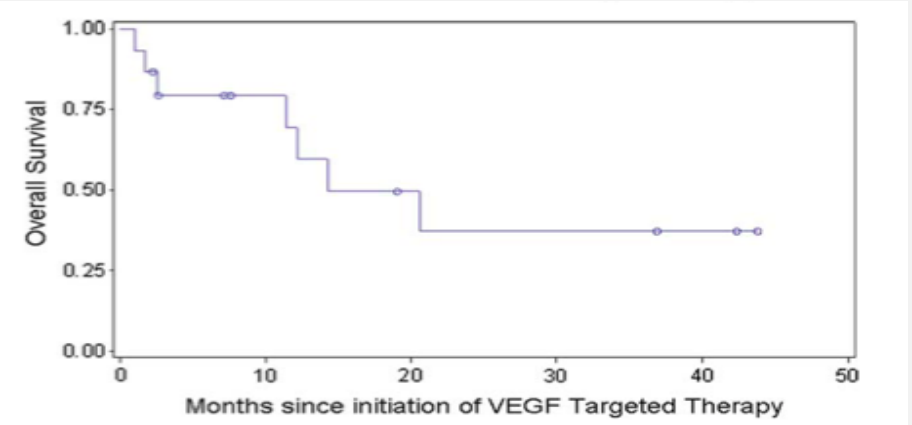
ORIGINAL REPORT

Metastatic Sarcomatoid Renal Cell Carcinoma Treated With Vascular Endothelial Growth Factor–Targeted Therapy

Ali Reza Golshayan, Saby George, Daniel Y. Heng, Paul Elson, Laura S. Wood, Tarek M. Mekhail, Jorge A. Garcia, Hakan Aydin, Ming Zhou, Ronald M. Bukowski, and Brian I. Rini

Chittoria N, Zhu H, Choueiri TK, et al. Outcome of metastatic sarcomatoid renal cell carcinoma (sRCC): Results from the International mRCC Database Consortium. ASCO Meeting Abstracts 2013; 31:4565

Michaelson MD, McDermott DF, Atkins MB, et al. Combination of antiangiogenic therapy and cytotoxic chemotherapy for sarcomatoid renal cell carcinoma. ASCO Meeting Abstracts 2013; 31:4512



Prospective Multicenter Phase II Study of Gemcitabine Plus Platinum Salt for Metastatic Collecting Duct Carcinoma: Results of a GETUG (Groupe d'Etudes des Tumeurs Uro-Génitales) Study

Stéphane Oudard, Eugeniu Banu, Annick Vieillefond, Laure Fournier, Franck Priou, Jacques Medioni, Adela Banu, Brigitte Duclos, Fréderic Rolland, Bernard Escudier, Nina Arake[illegible] Culine

javascript:void(0);

Triple combination of bevacizumab, gemcitabine and platinum salt in metastatic collecting duct carcinoma

N. Pécuchet[1,2*], F. Bigot[1,2], J. Gachet[1,2], C. Massard[3], L. Albiges[3], C. Teghom[1], Y. Allory[4], A. Méjean[2,5], B. Escudier[3] & S. Oudard[1,2]

Table 3. Studies of targeted therapy in mCDC patients

	Drug	Study type (No. of CDC patients)	Outcomes
Kinase inhibitors			
Mego et al. [28]	Sunitinib	Case report ($n = 1$) tubulocystic carcinoma*	PR > 5 months
Miyake et al. [29]	Sunitinib	Case report ($n = 1$)	PR = 7 months
Staehler et al. [30]	Sunitinib	Case report ($n = 2$)	No response
Molina et al. [31]	Sunitinib	Phase II trial of non-cc RCC ($n = 4/15$)	SD: 3/4 patients
Tannir et al. [32]	Sunitinib	Phase II trial of non-cc RCC ($n = 6^{b}/57$)	SD: 4/6 (median PFS, 3.1 months)
Ansari et al. [33]	Sorafenib	Case report ($n = 1$)	PR > 13 months
Procopio et al. [34]	4 sorafenib 1 sunitinib 2 temsirolimus	Case report ($n = 7$)	Long-lasting disease control: 1 patient sorafenib (33 months) followed by sunitinib (10 months) 1 patient temsirolimus (6 months) followed by sunitinib (9 months)
Monoclonal antibodies			
Bronchud et al. [35]	Trastuzumab + lapatinib[c] + capecitabine	Case report ($n = 1^{c}$)	Good response
Barrascout et al. [9]	Bevacizumab + gemcitabine + platinum salt	Case report ($n = 1$)	Disease control 24 months after diagnosis of lung metastases
This study	Bevacizumab + gemcitabine + platinum salt	Case reports ($n = 5$ including patient in [9])	3 PR, 2 SD > 16 months, Median PFS: 15.1 months (95% CI 5.6–20.4) Median OS: 27.8 months (95% CI 12.4–unreached)

COMPLETED

Prospective Randomized Phase-II Trial With Temsirolimus Versus Sunitinib in Previously Untreated Patients With Advanced or Metastatic Non-Clear Cell Renal Carcinoma

A Randomized Phase II Study of Afinitor (RAD001) vs. Sutent (Sunitinib) in Patients With Metastatic Non-Clear Cell Renal Cell Carcinoma (ASPEN)

Phase II Trial of Sunitinib Malate (Sutent) Therapy in Patients With Advanced Non-Clear Cell Renal Cell Carcinoma

Everolimus Versus Sunitinib Therapy in Patients With Advanced Non-clear Cell Renal Cell Carcinoma

To assess the efficacy and safety of RAD001 (everolimus) in non-clear cell renal cell carcinoma

RAPTOR: RAD001 as Monotherapy in the Treatment of Advanced Papillary Renal Cell Tumors Program in Europe (MACS0460)

COMPLETED

A Study to Assess the Safety, Pharmacokinetics and Effectiveness of AGS-16C3F Monotherapy in Subjects With Renal Cell Carcinoma(RCC) of Clear Cell or Papillary Histology

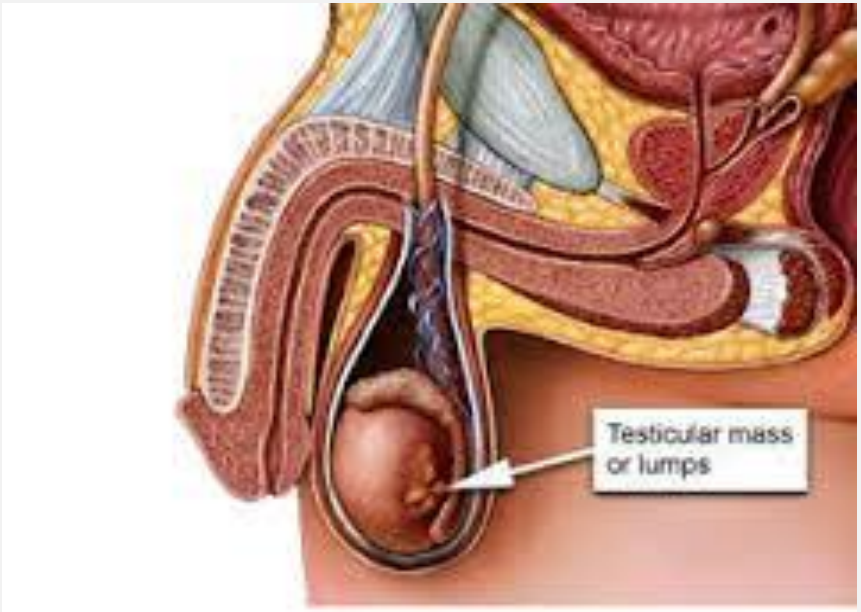
Study of Capecitabine in Metastatic Non-clear Cell Renal Cell Carcinoma (RCC) Patients

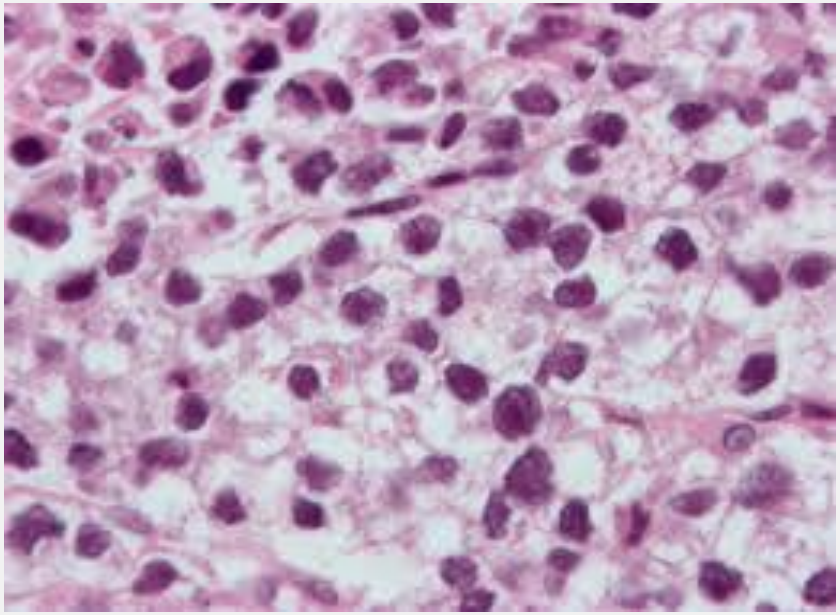
Pemetrexed Plus Gemcitabine in Renal Cell Cancer CLOSED POOR RECRUITMENT

A Phase II Study of Bortezomib (Velcade) Administered as a Single Agent in Metastatic Non-Clear Cell Renal Cell Carcinoma (RCC) Patients

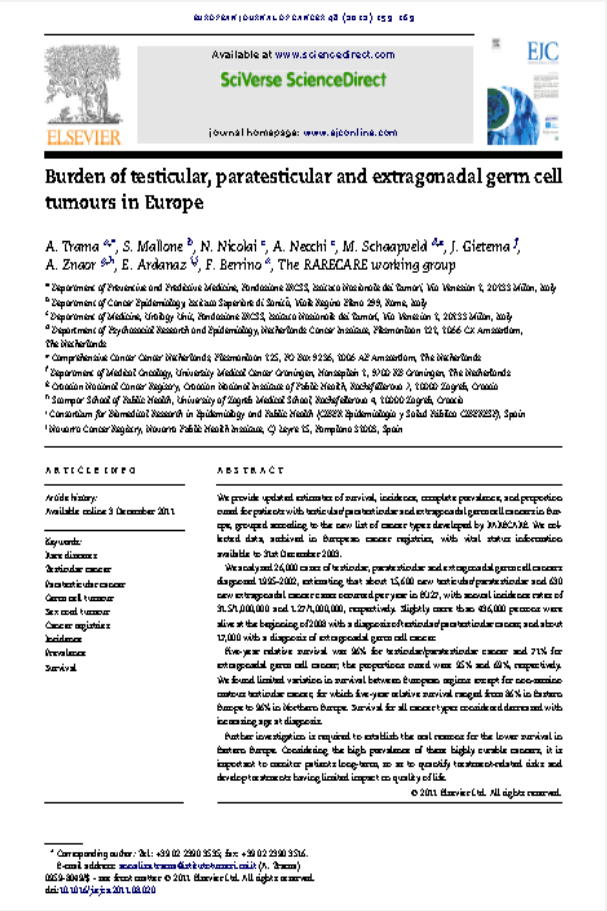
Phase II Study of Sunitinib in Metastatic Renal Cancer With Non-clear Cell Histology

TUMORES INFRECUENTES DE TESTÍCULO





TUMORES DE TESTIS Y PARATESTIS



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Burden of testicular, paratesticular and extragonadal germ cell tumours in Europe

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Sex cord tumour
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Incidence
Prevalence
Survival

ABSTRACT

We provide updated estimates of survival, incidence, complete prevalence, and prospective count for patients with testicular/paratesticular and extragonadal germ cell cancers in Europe, grouped according to the new list of cancer types developed by RARECARE. We collected data, archived in European cancer registries, with vital status information available to 31st December 2003.

We analysed 24,000 cases of testicular, paratesticular and extragonadal germ cell cancers diagnosed 1995–2002, estimating that about 15,600 new testicular/paratesticular and 630 new extragonadal cancers are occurred per year in 2022, with annual incidence rates of 31.5/1,000,000 and 1.2/1,000,000, respectively. Slightly more than 436,000 persons were alive at the beginning of 2003 with a diagnosis of testicular/paratesticular cancer, and about 17,000 with a diagnosis of extragonadal germ cell cancer.

Five-year relative survival was 96% for testicular/paratesticular cancer and 71% for extragonadal germ cell cancer; the proportions cured were 95% and 69%, respectively. We found limited variation in survival between European regions except for non-seminoma testicular cancer, for which five-year relative survival ranged from 86% in Eastern Europe to 96% in Northern Europe. Survival for all cancer types considered decreased with increasing age at diagnosis.

Further investigation is required to establish the real reasons for the lower survival in Eastern Europe. Considering the high prevalence of these highly curable cancers, it is important to monitor patients long-term, so as to quantify treatment-related risks and develop treatments having limited impact on quality of life.

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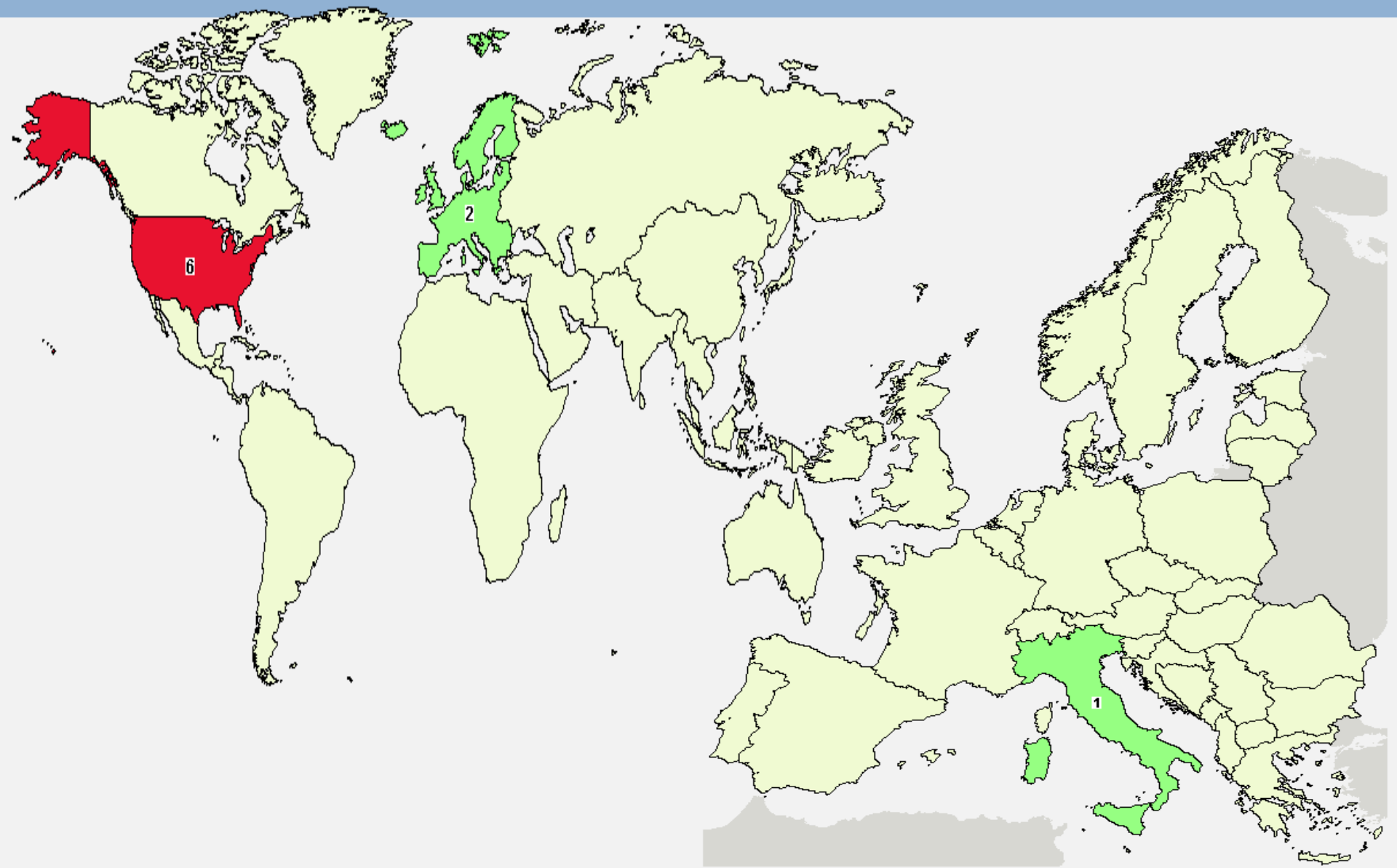
doi:10.1016/j.ejca.2011.08.020

TUMOURS OF TESTIS AND PARATESTIS	3,15	25.357
Tumour	Rate	Patients
Adenocarcinoma with variants of paratestis	<0.01	12
Endometrioid adenocarcinoma, NOS	<0.01	12
Clear cell adenocarcinoma, NOS	NE	0
Serous cystadenocarcinoma, NOS	NE	0
Mucinous cystadenocarcinoma, NOS	NE	0
Collecting duct and rete testis carcinoma	NE	0
Transitional cell carcinoma, NOS	NE	0
Germ cell non seminomatous tumours of testis	1,21	9.754
Mixed germ cell tumour	0,22	1.791
Teratocarcinoma	0,12	981
Choriocarcinoma combined with other germ cell elements	0,04	316
Embryonal adenocarcinoma, NOS	0,29	2.371
Yolk sac tumour	0,06	459
Choriocarcinoma, NOS	0,02	139
Germ cell seminomatous tumours of testis	1,71	13.777
Seminoma, NOS	1,66	13.391
Spermatocytic seminoma	0,03	221
Teratoma with malignant transformation	<0.01	11
Sex cord tumours of testis	0,02	177
Leydig cell tumour malignant	0,02	131
Sertoli cell carcinoma	<0.01	38
Malignant sex cord/gonadal stromal tumours	<0.01	2

ENSAYOS ABIERTOS EN EL MUNDO



1 **Recruiting** **CC-486 (Oral Azacitidine) Bioequivalence Study in Patients With Solid Tumor or Hematologic Malignancies**

Conditions: Hematological Neoplasms; Non-Hodgkin's Lymphoma; Hodgkin's Lymphoma; Lymphoma; Multiple Myeloma; Acute Myeloid Leukemia; Leukemia; Myelodysplastic Syndromes; Neoplasms; Melanoma; Breast Cancer; Metastatic Breast Cancer; Non-Small Cell Lung Cancer; Small Cell Lung Cancer; Renal Cell Carcinoma; Glioblastoma Multiforme; Osteosarcoma; Sarcoma; Thyroid Cancer; Genitourinary

Interventions: Drug: CC-486; Drug: Vidaza

2 **Recruiting** **Phase I/II Study to Assess the Safety and Activity of Enhanced TCR Transduced Autologous T Cells in Metastatic Melanoma**

Condition: Melanoma

Intervention: Biological: NY-ESO-1

3 **Recruiting** **Brentuximab Vedotin (SGN-35) as Salvage Treatment for CD30-positive Germ Cell Tumors**

Condition: Germ Cell Cancer

Intervention: Drug: Brentuximab Vedotin

4 **Recruiting** **Sirolimus, Cyclosporine, and Mycophenolate Mofetil In Preventing Graft-Versus-Host Disease in Treating Patients With Hematologic Malignancies Undergoing Donor Peripheral Blood Stem Cell Transplant**

Conditions: Accelerated Phase Chronic Myelogenous Leukemia; A

https://clinicaltrials.gov/ct2/show/

5 **Recruiting** **Veliparib, Paclitaxel, and Carboplatin in Treating Patients With Solid Tumors That Are Metastatic or Cannot Be Removed by Surgery and Liver or Kidney Dysfunction**

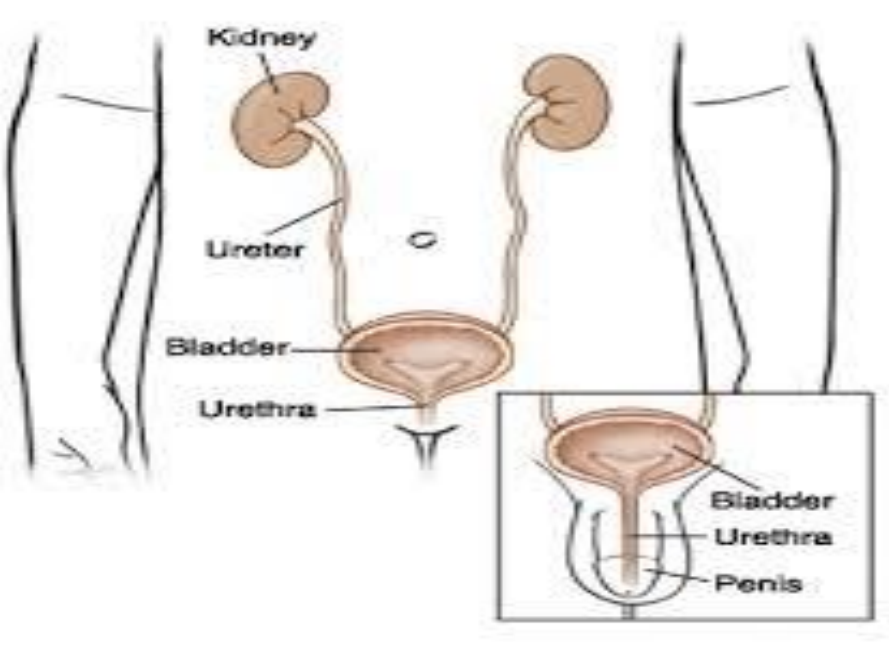
Conditions: Adult Solid Neoplasm; Bladder Carcinoma; Breast Carcinoma; Endometrial Carcinoma; Esophageal Carcinoma; Lung Carcinoma; Malignant Head and Neck Neoplasm; Melanoma; Ovarian Neoplasm; Renal Pelvis and Ureter Urothelial Carcinoma; Testicular Lymphoma; Ureter Carcinoma; Urethral Carcinoma

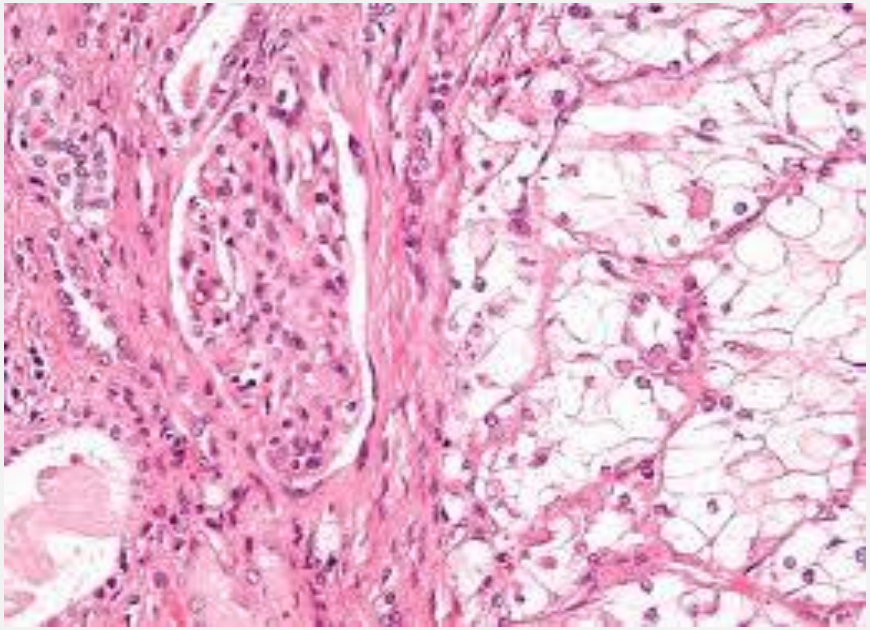
Interventions: Drug: Carboplatin; Other: Laboratory Biomarker Analysis; Drug: Paclitaxel; Other: Pharmacological Study; Drug: Veliparib

6 **Recruiting** **Donor T Cells After Donor Stem Cell Transplant in Treating Patients With Hematologic Malignancies**

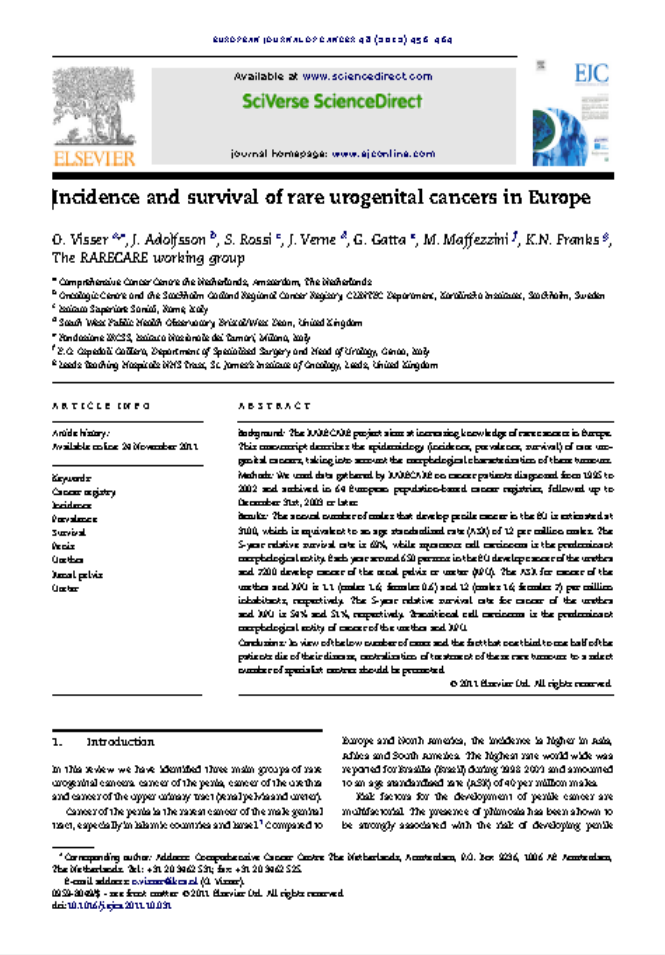
Conditions: Accelerated Phase Chronic Myelogenous Leukemia; Adult Acute Myeloid Leukemia With 11q23 (MLL) Abnormalities; Adult Acute Myeloid Leukemia With Del(5q); Adult Acute Myeloid Leukemia With Inv(16)(p13;q22); Adult Acute Myeloid Leukemia With t(15;17)(q22;q12); Adult

URETHRA, URETERAL AND RENAL PELVIS CANCER





TUMORES EPITELIALES DE PELVIS, URETER Y URETRA



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Incidence and survival of rare urogenital cancers in Europe

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Penis
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Ureter

ABSTRACT

Background: The RARECARE project aims at increasing knowledge of rare cancers in Europe. This manuscript describes the epidemiology (incidence, prevalence, survival) of rare urogenital cancers, taking into account the morphological characterisation of these tumours.

Methods: We used data gathered by RARECARE on cancer patients diagnosed from 1995 to 2002 and archived in 64 European population-based cancer registries, followed-up to December 31st, 2003 or later.

Results: The annual number of males that develop penile cancer in the EU is estimated at 3100, which is equivalent to an age standardised rate (ASR) of 12 per million males. The 5-year relative survival rate is 63%, while squamous cell carcinoma is the predominant morphological entity. Each year around 650 persons in the EU develop cancer of the urethra and 2200 develop cancer of the renal pelvis or ureter (KPU). The ASR for cancer of the urethra and KPU is 1.1 (males 1.4, females 0.8) and 1.2 (males 1.6, females 0.7) per million inhabitants, respectively. The 5-year relative survival rate for cancer of the urethra and KPU is 54% and 51%, respectively. Transitional cell carcinoma is the predominant morphological entity of cancer of the urethra and KPU.

Conclusions: In view of the low number of cases and the fact that more than one half of the patients die of their disease, centralisation of treatment of these rare tumours to a select number of specialist centres should be promoted.

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1. Introduction

In this review we have identified three main groups of rare urogenital cancers: cancer of the penis, cancer of the urethra and cancer of the upper urinary tract (renal pelvis and ureter).

Cancer of the penis is the rarest cancer of the male genital tract, especially in Islamic countries and Israel.[1] Compared to Europe and North America, the incidence is higher in Asia, Africa and South America. The highest rate world wide was reported for Israelis (Israel) during 1998–2002 and amounted to an age standardised rate (ASR) of 40 per million males.

Risk factors for the development of penile cancer are multifactorial. The presence of phimosis has been shown to be strongly associated with the risk of developing penile

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EPITHELIAL TUMOURS OF PELVIS, URETER AND URETHRA	1,58	12.728
Tumour	**Rate**	**Patients**
Transitional cell carcinoma of pelvis, ureter and urethra	**1,37**	**11.005**
Undifferentiated carcinoma	0,01	44
Transitional cell carcinoma spindle cell	<0.01	9
Lymphoepithelioma-like carcinoma	NE	0
Transitional cell carcinoma, giant cell	NE	0
Transitional cell carcinoma, micropapillary	NE	0
Squamous cell carcinoma with variants of pelvis, ureter and urethra	**0,05**	**41**
Verrucous carcinoma	<0.01	2
Adenocarcinoma with variants of pelvis, ureter and urethra	**0,04**	**299**
Mucinous adenocarcinoma	<0.01	8
Clear cell adenocarcinoma, NOS	0,01	83
Signet ring cell carcinoma	<0.01	3
Salivary gland-type tumours of pelvis, ureter and urethra	**<0.01**	**2**
Basaloid carcinoma	<0.01	1
Adenoid cystic carcinoma	NE	0
Mucoepidermoid carcinoma	NE	0

1 **Recruiting** **A Study of Ramucirumab Plus Pembrolizumab in Participants With Gastric or GEJ Adenocarcinoma, NSCLC or Transitional Cell Carcinoma of the Urothelium**

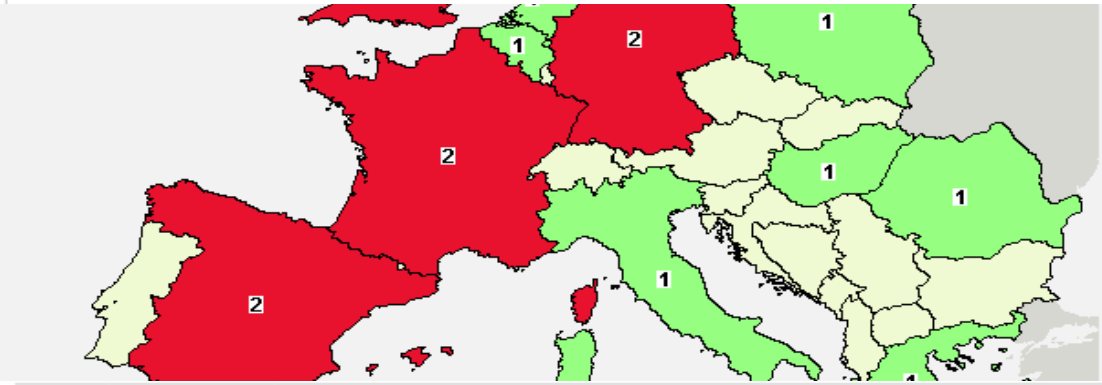
Conditions: Gastric Adenocarcinoma; Adenocarcinoma of the Gastroesophageal Junction; Non-small Cell Lung Cancer; Carcinoma, Transitional Cell

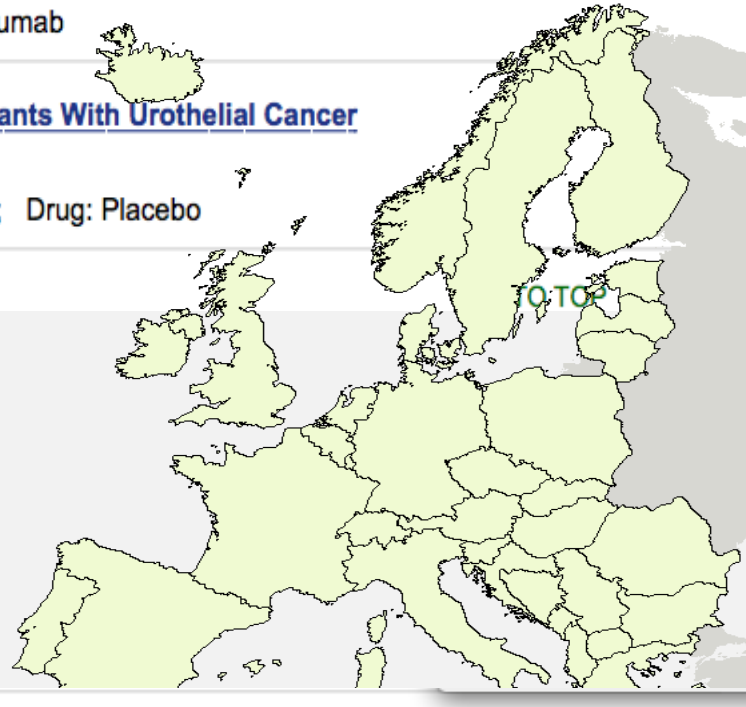
Interventions: Drug: Ramucirumab; Drug: Pembrolizumab

2 **Recruiting** **A Study of Ramucirumab (LY3009806) Plus Docetaxel in Participants With Urothelial Cancer**

Condition: Urothelial Carcinoma

Interventions: Drug: Ramucirumab; Drug: Docetaxel; Drug: Placebo





2 **Recruiting** **Eribulin Mesylate in Treating Patients With Locally Advanced or Metastatic Cancer of the Urothelium and Kidney Dysfunction**

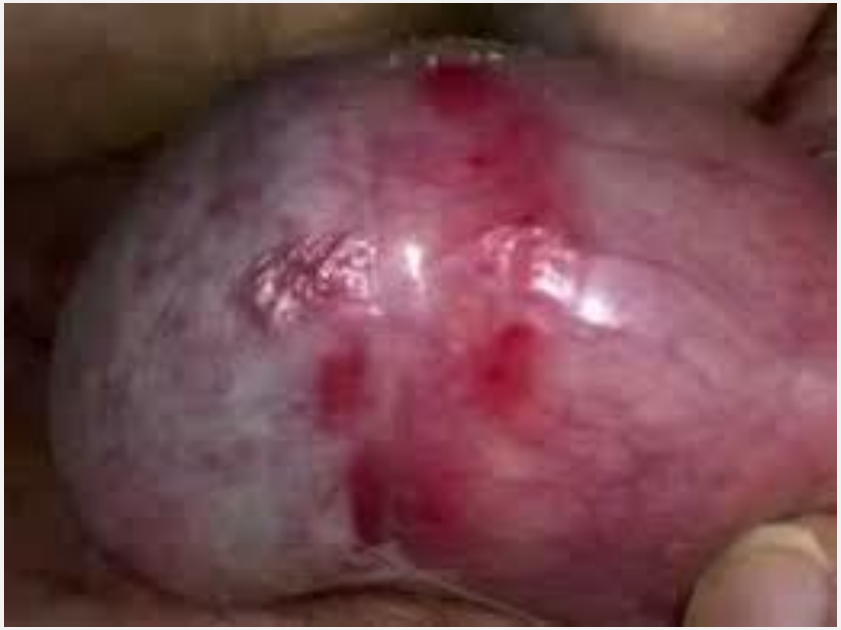
3 **Recruiting** **Pembrolizumab and Docetaxel or Gemcitabine Hydrochloride in Treating Patients Urothelial Cancer**

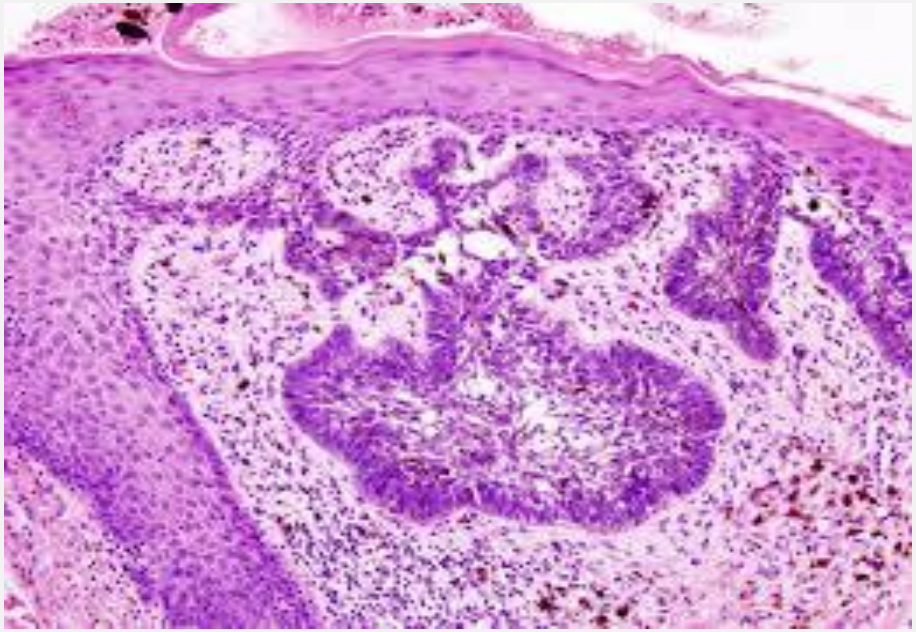
Conditions: Metastatic Urothelial Carcinoma of the Renal Pelvis and Ureter; Recurrent Bladder Carcinoma; Recurrent Urothelial Carcinoma of the Renal Pelvis and Ureter; Regional Urothelial Carcinoma of the Renal Pelvis and Ureter; Stage III Bladder Urothelial Carcinoma; Stage III Urethral Cancer; Stage IV Bladder Urothelial Carcinoma; Stage IV Urethral Cancer; Urethral Urothelial Carcinoma

Interventions: Drug: Pembrolizumab; Drug: Docetaxel; Drug: Gemcitabine Hydrochloride

4 **Recruiting** **Veliparib, Paclitaxel, and Carboplatin in Treating Patients With Solid Tumors That Are Metastatic or Cannot Be Removed by Surgery and Liver or Kidney Dysfunction**

CÁNCER DE PENE





TUMORES EPITELIALES DEL PENE, INCIDENCIA 0.62/100.000/AÑO

C = common R = rare	Layer	Tumour	Rate	Patients
	1	**EPITHELIAL TUMOURS OF PENIS**	**0,62**	**5.016**
R	2	**Squamous cell carcinoma with variants of penis**	**0,57**	**4.611**
	3	Squamous carcinoma	0,42	3.418
	3	Verrocous carcinoma	0,04	288
	3	Squamous cell carcinoma, sarcomatoid	<0.01	8
	3	Adenosquamous carcinoma	<0.01	2
	3	Basaloid carcinoma	NE	0
R	2	**Adenocarcinoma with variants of penis**	**<0.01**	**40**
	3	Extramammary Paget's disease	<0.01	20
	3	Sebaceous adenocarcinoma	NE	0
	3	Papillary adenocarcinoma, NOS	NE	0
	3	Mixed tumour malignant, NOS	NE	0
	3	Clear cell adenocarcinoma, NOS	NE	0
	3	Basal cell adenocarcinoma	NE	0

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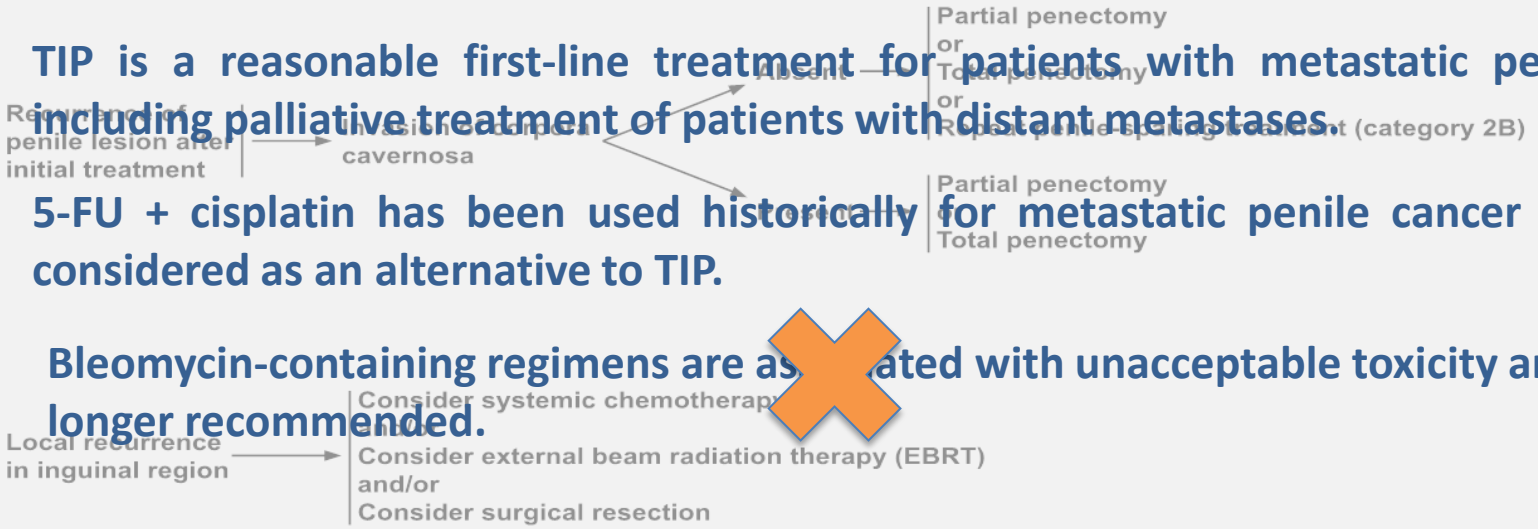
MANAGEMENT OF RECURRENT DISEASE

TIP is a reasonable first-line treatment for patients with metastatic penile cancer, including palliative treatment of patients with distant metastases.

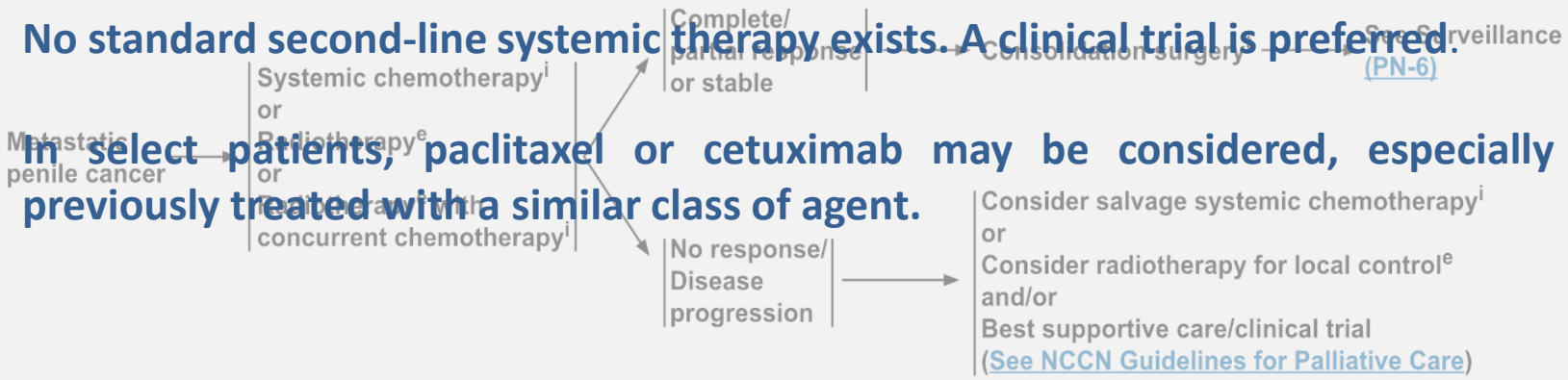
5-FU + cisplatin has been used historically for metastatic penile cancer and can be considered as an alternative to TIP.

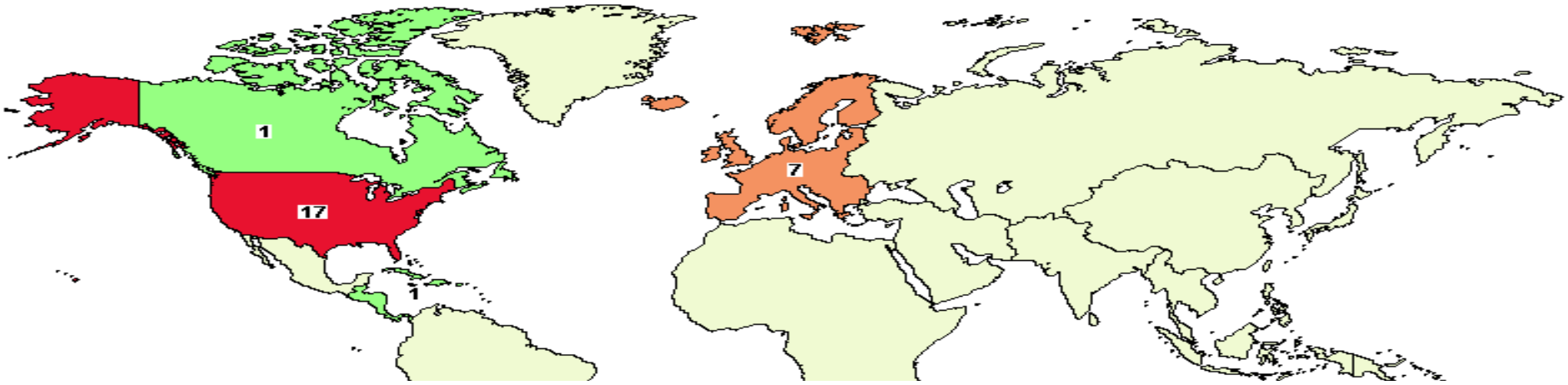
Bleomycin-containing regimens are associated with unacceptable toxicity and are no longer recommended.



No standard second-line systemic therapy exists. A clinical trial is preferred.

In select patients, paclitaxel or cetuximab may be considered, especially if not previously treated with a similar class of agent.





13 **Recruiting** **T Cell Receptor Immunotherapy Targeting HPV-16 E6 for HPV-Associated Cancers**

Conditions: Vaginal Cancer; Cervical Cancer; Anal Cancer; Penile Cancer; Oropharyngeal Cancer

Interventions: Drug: Fludarabine; Drug: Cyclophosphamide; Biological: E6 TCR; Drug: Aldesleukin

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14 **Recruiting** **Vaccine Therapy in Preventing Human Papillomavirus Infection in Young HIV-Positive Male Patients Who Have Sex With Males**

Conditions: Anal Cancer; Nonneoplastic Condition; Penile Cancer; Precancerous Condition

Interventions: Biological: quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine; Other: laboratory biomarker analysis

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15 **Recruiting** **HPV-16/18 E6/E7-Specific T Lymphocytes, Relapsed HPV-Associated Cancers, HESTIA**

Conditions: Human Papillomavirus-Related Carcinoma; Human Papillomavirus Positive Oropharyngeal Carcinoma; Human Papillomavirus Positive Cervical Carcinoma; Human Papillomavirus Positive Anal Carcinoma; Human Papillomavirus Positive Vulvar Carcinoma; Human Papillomavirus Positive Penile Carcinoma

Intervention: Genetic: HPV Specific T Cells

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16 **Recruiting** **Cisplatin-based Chemotherapy Combined With P16_37-63 Peptide Vaccination in Patients With HPV-positive Cancers**

Condition: HPV-induced Cancers

Interventions: Biological: P16_37-63 peptide combined with Montanide® ISA-51 VG; Biological: P16_37-63 peptide without Montanide® ISA-51 VG

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17 **Recruiting** **A Phase II Trial of Vinflunine Chemotherapy in Locally-advanced and Metastatic Carcinoma of the Penis (VinCaP)**

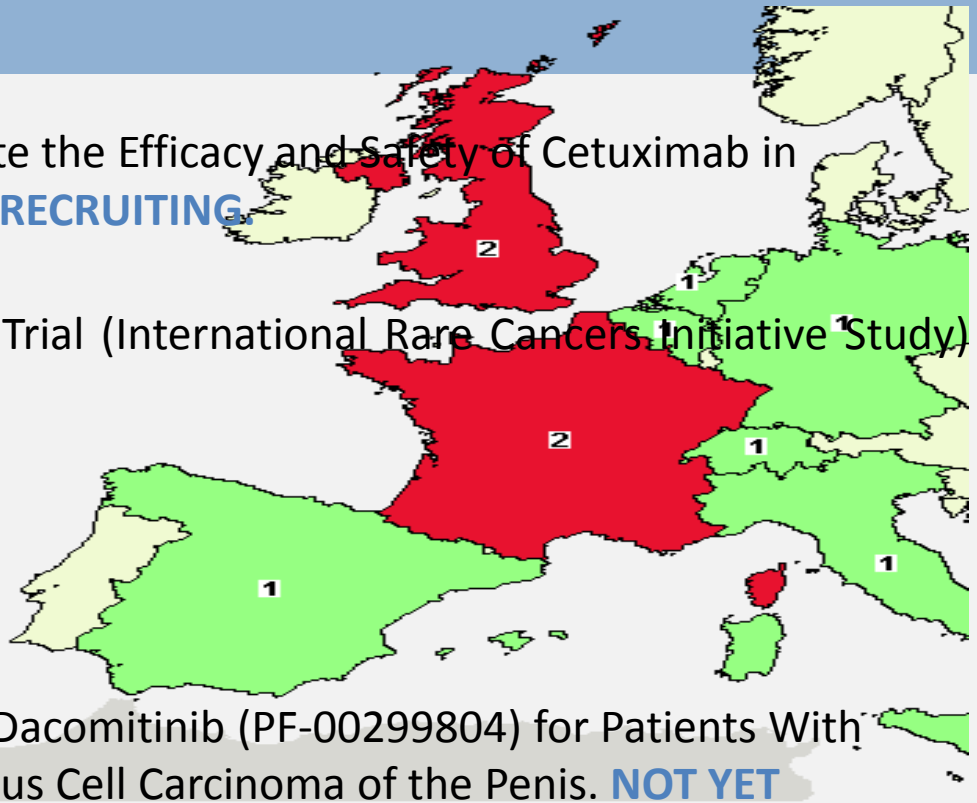
Condition: Locally-advanced or Metastatic Penile Neoplasms

Intervention: Drug: Vinflunine

NOT YET RECRUITING CLINICAL TRIALS

A Randomized Phase II Study to Evaluate the Efficacy and Safety of Cetuximab in Metastatic Penile Carcinoma. **NOT YET RECRUITING.**

International Penile Advanced Cancer Trial (International Rare Cancers Initiative Study) (InPACT). **NOT YET RECRUITING**



Phase II Study of the Pan-HER Inhibitor Dacomitinib (PF-00299804) for Patients With Locally Advanced or Metastatic Squamous Cell Carcinoma of the Penis. **NOT YET RECRUITING.**

Phase II Study With Pazopanib and Weekly Paclitaxel in Metastatic or Locally Advanced Squamous Penile Carcinoma Patients Previously Treated With Cisplatin Based Chemotherapy. **NOT YET RECRUITING**

COMPLETED CLINICAL TRIALS

Phase II Study of Irinotecan (CPT 11) and Cisplatin (CDDP) in Metastatic or Locally Advanced Penile Carcinoma**. COMPLETED.**

Phase II trial to study the effectiveness of docetaxel in treating patients who have locally advanced or metastatic penile cancer. **COMPLETED.**

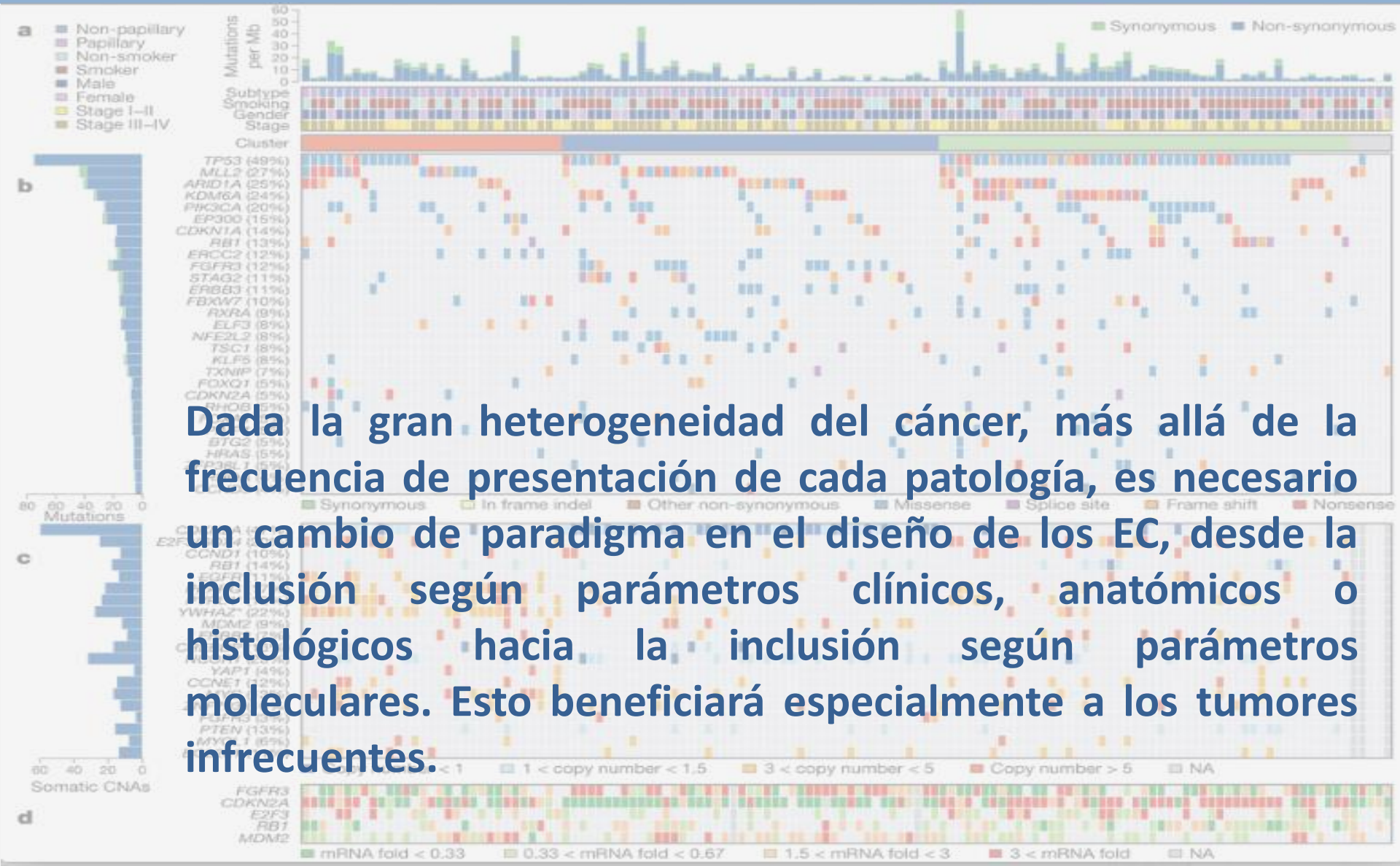
Phase II trial to study the effectiveness of interferon alfa plus isotretinoin in treating patients with recurrent cancer. **COMPLETED.**

Vaccine **therapy** and detection of immunologic responses with human papillomavirus 16 e6 and e7 peptides in patients with metastatic or locally advanced cervical cancer. **COMPLETED.**

Phase I trial is studying the side effects and best dose of MS-275 in **treating** patients with advanced solid tumors or lymphoma. **COMPLETED**

A Phase II Study of (Neoadjuvant Chemotherapy Trial Prior to Extirpative Surgery) for Clinical Stage TanyN2-3M0 Squamous Cell Carcinoma of the Penis. **COMPLETED**

CONCLUSIONES: CANCER IS A MOLECULARLY HETEROGENEUS DISEASE



Dada la gran heterogeneidad del cáncer, más allá de la frecuencia de presentación de cada patología, es necesario un cambio de paradigma en el diseño de los EC, desde la inclusión según parámetros clínicos, anatómicos o histológicos hacia la inclusión según parámetros moleculares. Esto beneficiará especialmente a los tumores infrecuentes.

DETERMINACIÓN DE VÍAS DE EXPRESIÓN EN TUMORES INFRECUENTES

Mientras tanto, inicidir en la necesidad de derivar a los pacientes a centros de referencia, donde se secuencie su ADN y se ofrezcan terapias dirigidas.

Table 1 Selected approved and experimental therapeutics agents currently in clinical evaluation in CRPC which do not target the AR (Source: clinicaltrials.gov)

	Stress response pathways	Proliferative signal transduction targets	Immune escape	Critical cellular proliferative components	Tumour microenvironment
Targets	Clusterin; Hsp90; Bcl-2; Hsp27	PI3K; Akt; mTOR; Mu-opoid receptor; eIF4E; IGF-IR; Her-2	Dendritic cells; CTLA-4; PD-1	Microtubules; PARP1; SERCA pump	Osteoclasts; IL-11Ra; RANK-L; FAP; Endoglin; alpha V integrin; VEGF/ FGFR; Neurotransmitters; Somatostatin receptor
Approved therapeutics			Sipuleucel-T	Docetaxel; Cabazitaxel	Denosumab; Radium-223
Experimental therapeutics	OGX-011; OGX-427	BEZ235; BKM120; AZD5363; MK2206; AZD8186; Naltrexone; ISIS 183750; Everolimus; Temsirolimus; Linsitinib; Lapatanib	Ipilimumab; BPX-201; BMS-936558; Pidilizumab	Tesetaxel; Patupilone; Ixabepilone; G-202	Sibrotuzumab; TRC-105; EMD 525797; BMTP-11; Dovitinib; Bevacizumab; Pazopanib; Phenelzine; Pasireotide

PI3K, phosphatidylinositol triphosphate kinase; CTLA4, cytotoxic T-lymphocyte antigen 4; PD1, programmed cell death protein 1; AMPK, adenosine monophosphate-activated protein kinase; VEGF, vascular endothelial growth factor; mTOR, mammalian target of rapamycin; PARP, poly-ADP ribose polymerase; IL-11Ra, interleukin-11 receptor alpha; SERCA, sarcoplasmic/endoplasmic

Y crear registros de tumores donde esta experiencia pueda quedar reflejada y ayude al tratamiento de casos similares.

GRACIAS