The LARCG-Latin American Renal Cancer Group: Creation, Aims, and Early Results

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Urology
Tutor at Graduate School
AC Camargo Cancer Center
Stênio de Cássio Zequi - Personal disclosures of any conflicts:

<table>
<thead>
<tr>
<th>Speaker</th>
<th>Preparation of scientific material</th>
<th>Economical Support for Scientific Meetings</th>
<th>Funded Clinical Trials</th>
<th>Advisory Board</th>
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<tbody>
<tr>
<td>Janssen</td>
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<td>Bayer</td>
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<td>Astellas</td>
<td>X</td>
<td>X</td>
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</tbody>
</table>
• Epidemiological & clinicopathological data- scarce in Latin America (LA)

• LA population: Singular ethnical composition

• LA Institutions: Not skilled in collaborative multicentric study groups

• Scientific Language Barriers

LARCG foundation – 2013 May
AC Camargo Center Center (Brazil) + Pasteur Hospital (Uruguay)
Regional urologic leaders were invited – Massive Adhesion!

Stênio de Cássio Zequi ACCC  Diego Abreu Clavijo – H Pasteur
LARCG - Background - Achievements

- LARCG Objectives
  - To improve RCC research in LA
  - To promote international scientific interchange in our sub continent
  - To produce High Level Scientific Information
  - To publish in peer reviewed journals
  - To start with Renal Cell Cancer... (Urologic/Other tumors)

www.larcg.org

“Non profit Organization”
LARCG Structure

LARCG

Coordinator Group

Member’s Council

Scientific Committee

Ethics Committee

Each Institution Urologist Leader

Each Institution Urologist Leader

LARCG Cell

Local Urologists

Uropathologists - LARCG Pathol Branch

Clinical Oncologists - LARCG Oncol Branch

LARCG Cell

Local Urologists

Uropathologists - LARCG Pathol Branch

Clinical Oncologists - LARCG Oncol Branch

Statute

Annual Assembly

Non Profit

Annual Fees/each LARCG cell

X...

LARCG Cells...
**Methods-January 2014**  
Deadline to return: (2014 -August)

- Excell databank: 150 codified variables (Individual ID blinded)
- Feb 2014- Questionnaire was sent for all centers (2014-Feb)
- IRB/inform consent docs.

Pilot - 1st Round: First Round: **N=4502** (24centers) Available: 3819

**LATAM Pathologists** are involved in **LARCG Pathol**

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**Central pathology review ISUP 2012**  
Brazil/Argentina/Uruguay/Chile

**Tissue microarray preparation N>4000 samples**  
Brazil (**2000 done! ~800 from LARCG**)

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Isabela W da Cunha – AC Camargo  
George Netto, MD  
Johns Hopkins
LARCG 2014 1st round

Initial: 4502 - Excluded: 683 cases:
378: Out of compliance/249: Partial nephrectomy series/57: Later

N: 3819
Follow-up (N=2062) 1 – 302 months
Mean: 33.6 months (SD: 33.25) - Median: 22 months

Presentation:
“Early results and Structural aspects of the LARCG”, at:

SPRING 2015 SWOG MEETING-
EMBARCADERO HYATT HOTEL SAN FRANCISCO, CA- APRIL 27-MAY 2ND
2014-2017- LARCG Members

N: 6032 = 30 active centers

Argentina
H. Italiano: 887
H. Clinicas: 348
C. Prof. Bengiò: 311
CEMIC: 261
H Britanico: 248
Policlinico Neuquen: 169
H. Austral: 107
CDU: 104
H. Aleman: 86
SEDESRL: 31
Ramos Mejia: 27

Brazil
AC Camargo Cancer Center: 842
PUC-RS: 120
Hospital Ipiranga: 84
UFMG-Belo Horizonte: 64
PUC Campinas: 50
IAVC-Sao Paulo: 61
Fac. Medicina ABC: 50
UNICAMP Campinas: None
UNESP Botucatu: None
H Cancer Barretos: None
FMUSP Rib. Preto: None

Peru
IN. Enf Neoplasicas: 302
H. Militar: 39
H NAAAE Chiclayo: 21
Centro Méd. Naval: None

Chile
Univ. Catolica: 582
Clinica Aleman: None
INDISA: None
Hospital San Borja: 71
Clínica Las Condes: None

Uruguay
H. Pasteur: 326
H. Militar: 46
H. Clinicas: 27
Coop M. Payssandu: 50

Bolivia
H. Obrero: 30
Clin. Los Olivos: 14
Caja Petrolera de Salud: None

Spain
H. Univ. Roy Juan Carlos+
H. Univ. Fund. Jimenez Diaz
Univ. Aut. Madrid: 300
Fundacion Puigvert: 911

Mexico
Int. NCMN Salvador Zubiran: 177
Hospital Militar Central DF: 95
Hope Urology Tijuana: None

USA-Collaborators
City of Hope CC
UC Davis
Lee Moffit CC

24 Centers /5 countries

Non profit work/No salary

1st Round (2014)
28 Centers /8 Countries
N:6032

2nd Round
(2015/2016/2017)
28 Centers /8 Countries

Inactive centers
**October 2016-SIU Congress -Buenos Ayres**


ASA ≥3 vs ASA 1/2

ASA ≥ 3:
- longer surgical time
- longer length of stay (p<0.001)

More metastases at diagnostic
ASA ≥ 3(17,7%) versus (5,1%) ASA1/2

ASA ≥ 3: twice more metastases after nephrectomy

Survival: Univariate Analysis
OS/CSS: Influenced by ASA Classification (p<0.001)

Survival: Univariate Analysis
necrosis, grade, pT stage, fat invasion, metastases and ASA Classification (p=0.003)
Presentations 2016

Cancer Renal Metastásico en América Latina: “Resultados Contemporáneos”
Latin American Renal Cancer Group (LARCG)

Grupos de Riesgo en Carcinoma de Celulas Renales metastásicos:
Resultados preliminares del LARCG
Outcomes in over 4,000 Patients with Renal Cell Carcinoma from the Latin American Renal Cancer Group (LARC)

A FOCUS ON METASTATIC DISEASE


INTRODUCTION

Over the past several years, a major international study collaboration has occurred among centers of excellence caring for kidney cancer termed the Latin American Renal Cancer Group (LARC).

OBJECTIVE

The aim of the present study is to assess the impact of clinical and pathologic variables on cancer specific survival (CSS) and overall survival (OS).

METHODS

Analysis of data from 28 centers from 8 countries, revealed 4,060 patients with renal cell carcinoma (RCC) who underwent nephrectomy from 1990 to 2015, 530 of which (14.5%) had metastases at clinical presentation. These are the focus of the present study. Median follow-up was six months (±1.24). Of 455 patients with survival data, 203 died (44.6%), 184 (90.6%) of RCC.

RESULTS

The median age of patients with metastatic RCC (mRCC) was 61 (52-74) years, 68% of patients were male and 32% female (21:1 ratio). The organs most frequently affected with metastases were lungs (45.5%), bone (21.5%), lymph nodes (16.4%), liver (8.7%), adrenal (4%) and brain (0.2%).

On univariate analysis, there were associations between 5-year OS and CSS and presence of ECOG PS ≥ 1 (p = 0.005 and p = 0.007, respectively), ASA 3 classification (p = 0.0001 for both), pt T4 (p = 0.019 and p = 0.009, respectively), pN1 (p = 0.001 and p = 0.0001, respectively), Fuhrman grade ≥ 3 (p = 0.002 and p = 0.008, respectively), NCC (p = 0.024 and p = 0.015), personal fat invasion (p = 0.0001), Hemoglobin <11 (p = 0.001 and p = 0.002), multiple metastases (p = 0.0001 and p = 0.001), two or more involved organs (p = 0.003 and p = 0.005, respectively), bone vs pulmonary metastases (p = 0.017 and p = 0.024), vertebra (0.035, for both), and more than five lung metastases (p = 0.003, for both).

It is possible, that the independent prognostic factor of 5-year OS was the ASA (p = 0.003), both OS and CSS were influenced by personal fat invasion (p = 0.001 for both), and two or more metastatic organ sites (p = 0.0001).

CONCLUSIONS

This study of the impact of clinical and pathologic variables on survival in mRCC in Latin America was possible thanks to the collaborative work done by the LARC. The presence of two or more sites of metastasis and the presence of personal fat invasion within the primary tumor predict shorter OS and CSS. ASA classification was an independent predictor of OS.

Worldwide Recognized Experts-2015 March

Before: Clear cell 64.6%
Unclassified 6.3%

After: Clear cell 59.7%
Unclassified 4.8%
AC Camargo+ Presidente Prudente : N: 756 (clear cell RCC)
Students Involved : PhD Thesis (2), MSc (6), Post DOC (3)
2016-17: Finished: RENIN (2017), NEW ISUP Grade, PBR-1, BAP-1, FOXP3
2018-19: Erithropoietin, STAT 3 , Beta Cathenin , Cadherin/Vimentin (EMT markers),NOS-3, FOXP3, KDM5C, SETD-2,CD 133

Lee Moffit Cancer Center
2017- **PD-1/PD-L1 (underway)**, CMET(papillary RCCs), VEGF, PDGF e TGF

**Hospital Pasteur: N:182**
Carbonic Anhidrase IX, (CAIX ), O Glicosilation Proteins , Tn antigens, (GalNAca-O-Ser/Thr); T6: Acetilgalactosaminiltransferasipolypeptides e-6 (ppGalNAc-T6) e T13: (ppGalNAc-T13).

- Tissue microarray
- Pathologic Review (ISUP 2012)
- Approved: our IRB and CONEP-Conselho Nacional de Ética em Pesquisa (Brazil)
- Funds- FAPESP, CNPq, Lee Moffit

**Markers expression**
Association with variables
Prognostic factors for:
- **Overall Survival**
- **Cancer Specific Survival**
- **Disease Free Survival**
Loss of Renin immunohistochemical expression in non metastatic Clear Cell RCC - N= 651

Associations:
- \( pT \) stage \((P < 0.001)\)
- \( pN+ \) \((P = 0.001)\)
- tumour size \((P < 0.001)\)
- ISUP grade \((P < 0.001)\)
- LVI \((P = 0.002)\)
- Necrosis \((P < 0.001)\)
- Sarcomatoid features \((P=0.011)\)

<table>
<thead>
<tr>
<th>Feature</th>
<th>10-year DSS</th>
<th>10-year RFS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariate</td>
<td>Multivariate</td>
</tr>
<tr>
<td>Tumor size (&gt; 7.0cm vs. 0-7.0cm)</td>
<td>&lt;0.001</td>
<td>4.186</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.626-10.779</td>
</tr>
<tr>
<td>Necrosis (Presence vs. Absence)</td>
<td>0.42</td>
<td>1.344</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.477-3.790</td>
</tr>
<tr>
<td>ISUP grade (High vs. Low)</td>
<td>0.002</td>
<td>0.901</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.473-4.031</td>
</tr>
<tr>
<td>LVI (Presence vs. Absence)</td>
<td>0.008</td>
<td>0.475</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.170-1.327</td>
</tr>
<tr>
<td>Stage (III/IV vs. I/II)</td>
<td>&lt;0.001</td>
<td>3.046</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.253-9.369</td>
</tr>
<tr>
<td>Renin (Negative vs. Positive)</td>
<td>0.001</td>
<td>2.551</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.025-6.346</td>
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</table>
Negative FOX-P3 expression in intra/or peritumoral inflammatory infiltrate

(Contesting the award for best work as resident physician at the 2017 Brazilian Congress of Pathology)

- The forkhead box protein (FOX P3) (at Xp11)
- Expressed by T reg cells
- FOX P3: immunomodulator (immunodeficiency syndromes)
### PBR-1 and BAP-1 Negative Expressions

**N:441 Non metastatic ccRCC**

**Associations (p<0.001)**
- **pT stage**
- **Tumour size**
- **ISUP grade**
- **LVI**
- **Type of nephrectomy**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Univariate</th>
<th>Multivariate</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p value</td>
<td>HR</td>
<td>95% CI</td>
<td>p value</td>
</tr>
<tr>
<td>pT Stage (pT2 vs. pT1)</td>
<td>&lt;0.001</td>
<td>2.447</td>
<td>1.084-5.524</td>
<td>0.031</td>
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<tr>
<td>Necrosis (Presence vs. Absence)</td>
<td>0.042</td>
<td>2.571</td>
<td>1.069-6.185</td>
<td>0.035</td>
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<tr>
<td>ISUP grade (High vs. Low)</td>
<td>0.002</td>
<td>1.633</td>
<td>0.734-3.631</td>
<td>0.229</td>
</tr>
<tr>
<td>LVI (Presence vs. Absence)</td>
<td>0.008</td>
<td>2.969</td>
<td>1.001-8.824</td>
<td>0.050</td>
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<td>PBRM1 (Negative vs. Positive)</td>
<td>&lt;0.001</td>
<td>0.850</td>
<td>0.193-3.736</td>
<td>0.830</td>
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<td>BAP1 (Negative vs. Positive)</td>
<td>0.001</td>
<td>0.873</td>
<td>0.271-2.815</td>
<td>0.820</td>
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<tr>
<td>PBRM1 and BAP1 (Both negative vs. one or both positive)</td>
<td>&lt;0.001</td>
<td>3.643</td>
<td>1.731-7.667</td>
<td>0.001</td>
</tr>
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</table>
LARCG 002/2015: “Metastatic Renal Cell Carcinoma: An epidemiological comparison between Latin American and Californian Populations.”  

Pls: Stênio de C Zequi ACCCC; Diego Abreu Clavijo H Pasteur-Uruguay  

Maria Nirvana C Formiga. Co PI, Clinical Oncologist ACCCC  

Milena S Tarik. Co PI, Clinical Oncologist ACCCC  

Aldo Abade Dettino Co PI, Clinical Oncologist ACCCC  

Paulo Bergerot. Co PI, Clinical Oncologist UNIFESP/Cityof Hope  

N:LARCG:530 Metastatic at presentation + 311 Metastatic after nephrectomy vs City of Hope: 280 “To merge both data banks”  

Agreement of Confidentiality:  
LARCG and UC City of Hope  
To be signed  
Approved by our IRB in August 2017  

No funds are required- Data collected
LARCG 002/2015: “Metastatic Renal Cell Carcinoma: An epidemiological comparison between Latin American and Californian Populations.”

AIMS

- To describe clinical, demographic and pathological features of populations with mRCCC (LATAM and US-California)
- To analyze solitary vs multiple metastasis, as well the employment of cytorreductive surgeries and metastasectomies.
- To described the first drugs used & sequential treatments
- To describe drug responses
- OS, CSS and PFS will be analyzed rates
- External Validation of internationally accepted prognostic scores, (like scores of Motzer, Heng, among others).
- To investigate a individualized score for this group of patients.
- It is believed that from this raw data, specific new research may be generated

N:LARCG: 530 vs City of Hope: 280
“To merge both data banks"

To be started!
<table>
<thead>
<tr>
<th>Date</th>
<th>City</th>
<th>LACG Meeting</th>
<th>Supporter Meeting</th>
<th>Supporter(s)</th>
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<tr>
<td>2014-Nov.-Punta Del Leste</td>
<td>1st. LARCG Annual Meeting</td>
<td>CAU- Confederacion Americana de Urologia Meeting</td>
<td>Special Thanks: Shlomo Raz, MD</td>
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<tr>
<td>2015- May -New Orleans</td>
<td>2nd. LARCG Annual Meeting</td>
<td>AUA- American Urological Association Annual Meeting</td>
<td>Special Thanks: Isabela Werneck Cunha</td>
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<tr>
<td>2015-March -São Paulo</td>
<td>XVII- International Pathologic Journey</td>
<td>AC Camargo Cancer Center+ EPOAHT</td>
<td>Special Thanks: Alejandro Nolazco, MD</td>
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<tr>
<td>2015-October-B. Ayres</td>
<td>Jornada Hospital Britânico</td>
<td>Hospital Britanico Buenos Aires</td>
<td>Special Thanks: Alejandro Nolazco, MD</td>
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<tr>
<td>2016 May-San Diego</td>
<td>3rd. LARCG Annual Meeting</td>
<td>AUA- American Urological Association Annual Meeting</td>
<td>Special Thanks: Shlomo Raz, MD</td>
<td></td>
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<tr>
<td>2017 May-Boston</td>
<td>4th. LARCG Annual Meeting</td>
<td>AUA- American Urological Association Annual Meeting</td>
<td>Special Thanks: Shlomo Raz, MD &amp; Manoj Monga, MD</td>
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</table>
Entirely endophytic: More necrosis (44.5% vs 19.1 – 31.5%); and Twice fat invasion (16.4% vs 8.0-9.1%) --p<0.05

>50% exophytic: Less renal capsular invasion (17.6% vs 30.6-31.8%), Less high grade Furhman (26% vs 35.7-36.5%)--p<0.05
Denutrition: Worst OS (p=0.03) & Fuhrman High Grade

Overweight/Obese/Morbidly obese: Higher CSS, less symptoms, (p<0.05), Smaller tumors 5.5cm x 5.0 cm (p=0.027)

BMI reported & BMI Calculated
**LARCG Survival analysis- 10 years Overall Survival and Cancer Specific Survial**

Log Rank Test  Cox Regression (Stepwise Backward)  P<0.005

For ≤ 50%  Missing Data:  **Multiple Imputation Method** (for inclusion on multivariate analysis)

N=6032  Non Metastatic RCC  N= 5670

Follow up (months): (0-421 [SD: 39.9])  Mean: 34  Median: 20.3

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<th>Country</th>
<th>N</th>
<th>%</th>
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<tr>
<td>Argentina</td>
<td>1878</td>
<td>33.1</td>
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<tr>
<td>Brasil</td>
<td>1073</td>
<td>18.9</td>
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<tr>
<td>Espanha</td>
<td>1050</td>
<td>18.5</td>
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<tr>
<td>Chile</td>
<td>558</td>
<td>9.8</td>
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<tr>
<td>Uruguay</td>
<td>458</td>
<td>8.1</td>
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<tr>
<td>Mexico</td>
<td>274</td>
<td>4.8</td>
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<tr>
<td>Peru</td>
<td>338</td>
<td>6.0</td>
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<tr>
<td>Bolívia</td>
<td>41</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>5670</td>
<td>100%</td>
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</table>

Survival information: N= 4508

All Deaths: 426 (7.51%)  -  Cancer Deaths: 292 (68.5% of all deaths)

Median OS:104 months (102.7 a 105.6)

Median CSS:109.8 months (107.8 a 110.3)

Survival Function

**OS: 90.6%**

**CSS: 93.5%**
<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>Frequency (N)</th>
<th>10yOS (%)</th>
<th>p</th>
<th>10y CSS (%)</th>
<th>p</th>
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<td></td>
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<tr>
<td>GENDER</td>
<td>Male</td>
<td>2935</td>
<td>282 (90.4)</td>
<td>0.282</td>
<td>192(93.5)</td>
<td>0.531</td>
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<tr>
<td></td>
<td>Female</td>
<td>1573</td>
<td>144 (90.8)</td>
<td></td>
<td>100 (93.6)</td>
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<tr>
<td>RACE*</td>
<td>White</td>
<td>2371</td>
<td>274(88.4)</td>
<td>&lt;0.001</td>
<td>171(92.8)</td>
<td>&lt;0.001</td>
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<tr>
<td></td>
<td>Black/mulatos</td>
<td>159</td>
<td>10 (93.7)</td>
<td></td>
<td>7(95.6)</td>
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<tr>
<td></td>
<td>Others/mestiços</td>
<td>354</td>
<td>56 (84.2)</td>
<td></td>
<td>53 (85)</td>
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<tr>
<td>GROUPED RACE*</td>
<td>White</td>
<td>2371</td>
<td>274 (88.4)</td>
<td>&lt;0.001</td>
<td>171(92.8)</td>
<td>&lt;0.001</td>
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<tr>
<td></td>
<td>Non whites</td>
<td>513</td>
<td>66 (87.1%)</td>
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<td>60 (88.3)</td>
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<tr>
<td>SYMPTOMS/SIGNALS</td>
<td>No</td>
<td>1854</td>
<td>135(92.7)</td>
<td>&lt;0.001</td>
<td>70(96.2)</td>
<td>&lt;0.001</td>
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<tr>
<td></td>
<td>yes</td>
<td>2656</td>
<td>326(87.7)</td>
<td></td>
<td>258 (90.3)</td>
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<tr>
<td>SMOKING</td>
<td>No</td>
<td>2771</td>
<td>256 (90.8)</td>
<td>0.454</td>
<td>184(93.4)</td>
<td>0.129</td>
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<tr>
<td></td>
<td>Smoker</td>
<td>547</td>
<td>127 (92.1)</td>
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<td>27 (95.1)</td>
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<tr>
<td></td>
<td>Ex-Smoker</td>
<td>1190</td>
<td>43 (89.3)</td>
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<td>81 (93.2)</td>
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<td>KPS</td>
<td>≤80</td>
<td>637</td>
<td>128 (79.9)</td>
<td>&lt;0.001</td>
<td>98 (84.6)</td>
<td>&lt;0.001</td>
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<tr>
<td></td>
<td>&gt;80</td>
<td>3871</td>
<td>298 (92.3)</td>
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<td>194 (95)</td>
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<td>ECOG</td>
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<td>4181</td>
<td>353 (91.6)</td>
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<td>231 (94.5)</td>
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<td>1+2</td>
<td>327</td>
<td>73 (77.7)</td>
<td>&lt;0.001</td>
<td>61 (81.3)</td>
<td>0.001</td>
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<tr>
<td>ASA</td>
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<td>3629</td>
<td>293 (80)</td>
<td></td>
<td>204 (94.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3-4</td>
<td>879</td>
<td>133(69.2)</td>
<td>0.024</td>
<td>88 (90.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anemia</td>
<td>HB≤10 G/dl</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>yes</td>
<td>1092</td>
<td>174(84.1)</td>
<td></td>
<td>129 (88.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>3416</td>
<td>252 (92.6)</td>
<td>&lt;0.001</td>
<td>163 (95.2)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Non imputed-excluded from multivariated analysis

Survival-Univariate analysis
Demographic and clinical features

Blacks vs others ſ ns
OS: p= 0,341
CSS: p= 0376

MSc Student
Eduardo Tanaka, MD starting in 2018

* Non imputed-excluded from multivariated analysis
## Survival-Univariate analysis-pathologic features

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>Frequency (N)</th>
<th>10y OS (%)</th>
<th>P</th>
<th>10y CSS (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>HISTOLOGIC TYPE*</td>
<td>Clear Cell</td>
<td>1993</td>
<td>147 (83.1)</td>
<td>0.020</td>
<td>201 (89.5)</td>
<td>0.020</td>
</tr>
<tr>
<td>*(N=2984)</td>
<td>Papillary Type 1</td>
<td>142</td>
<td>5 (83.3)</td>
<td>0.162</td>
<td>126 (88.7)</td>
<td>0.162</td>
</tr>
<tr>
<td></td>
<td>Papillary Type 2</td>
<td>18</td>
<td>13 (86.7)</td>
<td>0.174</td>
<td>17 (94.4)</td>
<td>0.174</td>
</tr>
<tr>
<td></td>
<td>Chromphobe</td>
<td>409</td>
<td>15 (93.8)</td>
<td>0.127</td>
<td>12 (97.1)</td>
<td>0.127</td>
</tr>
<tr>
<td></td>
<td>Inclassifiable</td>
<td>691</td>
<td>1 (25)</td>
<td>0.001</td>
<td>198 (98.6)</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>TTFE gene</td>
<td>7</td>
<td>0 (0)</td>
<td>0.001</td>
<td>0 (100)</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Collect Duct</td>
<td>34</td>
<td>2 (66.7)</td>
<td>0.607</td>
<td>0 (100)</td>
<td>0.607</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>412</td>
<td>0 (0)</td>
<td>0.955</td>
<td>25 (92)</td>
<td>0.955</td>
</tr>
</tbody>
</table>

| FUHRMAN'S GRADE | 1-2 | 2673 | 204 (92.4) | 0.088 | 118 (95.6) | <0.001 |
| | 3-4 | 1835 | 222 (97.9) | 0.174 | 174 (90.5) | 0.174 |

| NECROSIS | Yes | 1221 | 213 (82.6) | <0.001 | 160 (86.9) | <0.001 |
| No | 3287 | 213 (93.5) | 132 (96) | <0.001 |

| MICROVASCULAR INVASION (MVI) | Yes | 635 | 107 (83.1) | <0.001 | 88 (86.1) | <0.001 |
| No | 3873 | 319 (91.8) | 208 (94.7) | <0.001 |

| SARCOMATOID PATTERN* | Yes | 43 (69.8) | <0.001 | 10 (76.7) | <0.001 |
| *(N=2136) | No | 2093 | (89.1) | 136 (93.5) | <0.001 |

| PERIRRenal FATAL INVASION | yes | 554 | 142 (74.4) | <0.001 | 115 (79.2) | <0.001 |
| No | 3954 | 284 (92.8) | 177 (95.5) | <0.001 |

| RENAL VEIN INVASION | Yes | 348 | 68 (80.5) | <0.001 | 53 (84.8) | <0.001 |
| No | 4160 | 358 (91.4) | 239 (94.3) | <0.001 |

| INFERIOR VENA CAVA INVASION | Yes | 176 | 36 (78.4) | <0.001 | 29 (83.5) | <0.001 |
| No | 4332 | 388 (91) | 263 (93.9) | <0.001 |

| TUMOR SIZE | < 4.0 cm | 1569 | 98 (93.8) | 0.55 | 96.5 | <0.001 |
| > 4.1 to 7.0 cm | 1689 | 126 (92.5) | 0.79 | 95.3 | <0.001 |

| TUMOR SIZE (7.0 CM) | 0-7.0 cm | 3258 | 224 (93.1) | 0.134 | 95.9 | <0.001 |
| >7.0 cm | 1250 | 202 (83.8) | 0.158 | 87.4 | <0.001 |

| pT STAGE | pT0 | 277 | 8 (97.1) | 0.498 | 96.9 | <0.001 |
| pT1a | 1624 | 90 (94.5) | 0.51 | 96.9 |
| pT1b | 1081 | 76 (93.0) | 0.41 | 96.2 |
| pT2a | 500 | 57 (88.6) | 0.42 | 90 |
| pT2b | 227 | 52 (85.9) | 0.25 | 89 |
| pT3a | 555 | 87 (84.3) | 0.67 | 87.9 |
| pT3b | 134 | 34 (74.6) | 0.26 | 80.6 |
| pT4c | 29 | 10 (65.5) | 0.21 | 72.4 |
| pT4 | 57 | 29 (49.1) | 0.30 | 93.5 |

| GROUPED pT STAGE | T1-T2 | 3733 | (92.9) | 0.164 | 95.6 | <0.001 |
| T3-T4 | 775 | (79.4) | 0.128 | 83.5 |

| pN STAGE | pN0 | 2571 | 223 (91.3) | 0.206 | 157 (93.9) | 0.072 |
| pNx | 1806 | 168 (90.7) | 0.103 | 94.3 |
| pN+ | 131 | 35 (73.3) | 0.260 | 94.1 |

| GROUPED pN STAGE | pN0/pNx | 4377 | 391 (91.1%) | <0.001 | 260 (94.1) | <0.001 |
| pN+ | 131 | 35 (73.3%) | 0.32 | 75.6 |

* Non imputed-excluded from multivariated analysis
<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall Survival OR</th>
<th>95% CI</th>
<th>P</th>
<th>Cancer Specific Survival OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb&lt;10 g/dl</td>
<td>1.437</td>
<td>1.179-1.165</td>
<td>0.001</td>
<td>1.450</td>
<td>1.113-1.854</td>
<td>0.003</td>
</tr>
<tr>
<td>Symptoms/signals</td>
<td>1.257</td>
<td>0.999-1.581</td>
<td>0.051</td>
<td>1.665</td>
<td>1.226-2.261</td>
<td>0.001</td>
</tr>
<tr>
<td>ASA ≥ 3</td>
<td>1.486</td>
<td>1.187-1.861</td>
<td>0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KPS ≤ 80</td>
<td>2.122</td>
<td>1.1673-2.690</td>
<td>&lt;0.001</td>
<td>1.943</td>
<td>1.83-2.730</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ECOG≥ 2</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>1.643</td>
<td>1.115-2.421</td>
<td>0.012</td>
</tr>
<tr>
<td>Perirenal fat invasion</td>
<td>2.121</td>
<td>1.699-2647</td>
<td>&lt;0.001</td>
<td>2.107</td>
<td>1.609-2.760</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inferior vena cava invasion</td>
<td>1.614</td>
<td>1.146-2.273</td>
<td>0.006</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Necrosis</td>
<td>1.694</td>
<td>1.372-2.092</td>
<td>&lt;0.001</td>
<td>1.687</td>
<td>1.303-2.183</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MVI</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>1.398</td>
<td>1.069-1.829</td>
<td>0.014</td>
</tr>
<tr>
<td>Tumor Size (&gt;7.0 cm)</td>
<td>1.644</td>
<td>1.333-2.029</td>
<td>0.005</td>
<td>1.825</td>
<td>1.413-2.358</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>pN Stage</td>
<td>2.141</td>
<td>1.500-3.056</td>
<td>&lt;0.001</td>
<td>2.443</td>
<td>1.667-3.579</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fuhrman’s Grade</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>1.359</td>
<td>1.059-1.744</td>
<td>0.016</td>
</tr>
</tbody>
</table>

*Under Submission-Int Braz J Urol

Concomitant perirenal and sinus fat invasion
Specific mortality risks (HR 3.45)
Overall and local relapse risks (HR 3.06 and 8.18, respectively)

¿Es el diámetro tumoral um factor pronóstico importante em el cáncer renal estádio pT3a?
Argentina Córdoba- Bengió R, MD et al

N: 261 (1995-2013)
CSS: 7.0 cm- AUC (ROC Curve) 0.76 +/- 0.05
pT3a>7.0  HR: 4.90 (95% CI 1.17-13.9) p=0.002
Lower DFS

Perioperative Outcomes Following Surgical Treatment for Renal Cell Carcinoma In The Very Elderly (≥75 years): Data from LARC.

pT3-T4 and laparoscopic approach: more common in the very elderly (p=0.04 for both)
Surgical resection of RCC is a safe in patients 75 years or older.
Perioperative outcomes: similar to their younger counterparts
"RARE TUMORS"
Non Clear Cells RCC + Penile cancers

Tumor samples
Serum, blood, Demography, Clinical Information, proteomics, genomics, metabolomics etc...

Prognostic factors?
Treatments Resistance factors?
New drugs assays... etc

Funds By FAPESP got by “INCITO INOTE” Could Support LARCG Economic and hosting : “RED Cap Data Base”
To investigate human protein in exosomes
To test drugs in animal models- Samples from metastatic cases and or High risks cases
Phase II Study:
Sunitinib efficacy evaluation in the treatment of metastatic papillary renal carcinoma

"SWOG S1500-PAP MET Trial- Mirror Study"

A Standalone Common Arm-Control Arm- Sunitinib with Univ. California Davis

A Randomized, Phase II Efficacy assessment of Multiple MET Kinase Inhibitors (Cabozantinib [NCC#761968], Crizotinib [NSC#749005], Savolitinib [NSC#785348], and Sunitinib [NSC#736511]) in metastatic papillary renal cell carcinoma

SWOG Coordinators: Sumanta K Pal (Un. Califórnia-City of Hope + Primo N Lara (Un. of California- Davis)

Inclusion Criteria: Metastatic or Irrressecable Papillary I/II RCC

End Points
• Deaths or disease progression@3 years
• Posthoc common arm analyses of population related differences in toxicity and outcomes in the context of sunitinib therapy

Economical Support: None Ethics: Approved

2017 September: We have recruited: 02 (Two) patients
US/Canada: Arround 50-60
Aims (in 5 years) MOU- Memorandum of Understanding

- To reinforce and/or establish new International cooperations
- Host the LARCG’s DATA Bank in RED Cap System—(Password control & Hierarchical privileges)
- Economical support to our bilingual website (SPA/ENG)
- To promote/host two quinquennial international LARCG meetings
- Training
City of Hope /AC Camargo/LARCG- Residents & Young Doctors Rotation Program

2017-2019 – 4 colleagues/yearly

**Two Urologists** (LARCG/ACCCC)
**Two Clinical Oncologists** (LARCG/ACCCC)

City of Hope Support’s includes:
- A round trip coach airfare
- 2 months lodging
- No salary/Stipend

From: Sumanta K Pal’s & City Hope Budget

Thanks!!!!!
English:
Is not everything amazing that can fit inside a pencil?

¿NO ES INCREÍBLE TODO LO QUE PUEDE TENED ADENTRO UN LAPÍZ?

Larrey®