



Animal Model Workshop

ccRCC PDOX Models for 1st and 2nd Line Treatment and AVATAR Co-Clinical Trials

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Session 6: PDX Models



Kidney Cancer Association® IN PARTNERSHIP WITH

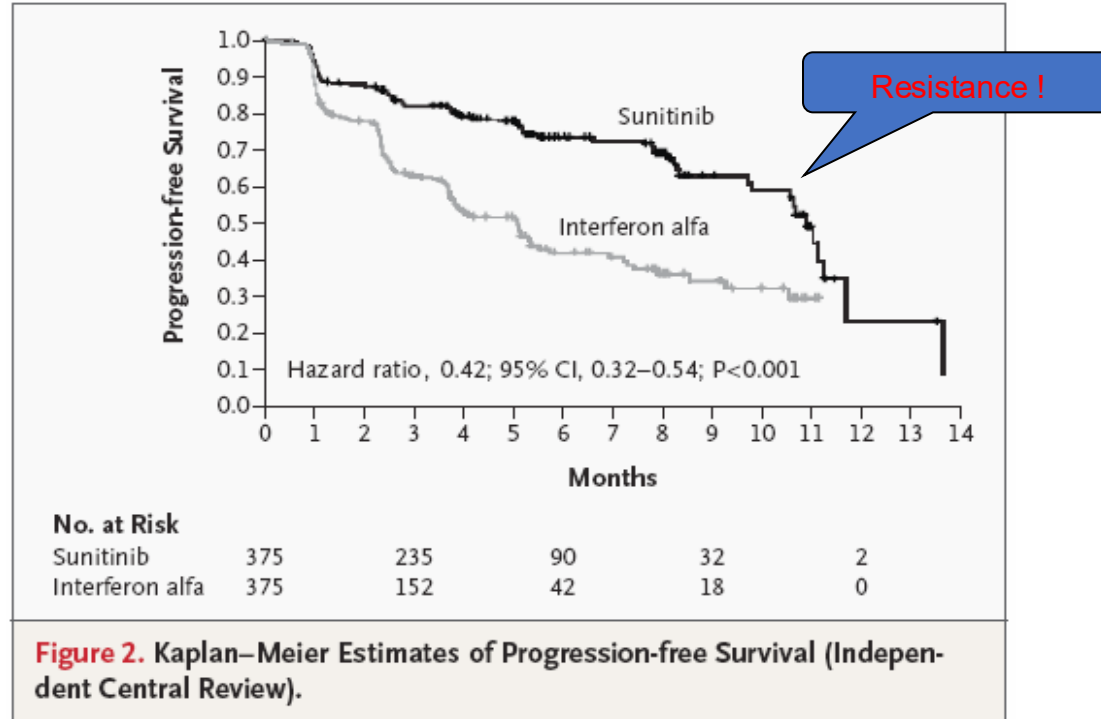
UT Southwestern
Medical Center
Kidney Cancer Program

Anti-Angiogenic Drugs Work in RCC, but...

Sunitinib versus Interferon Alfa in Metastatic Renal-Cell Carcinoma

N Engl J Med 2007;356:115-24.

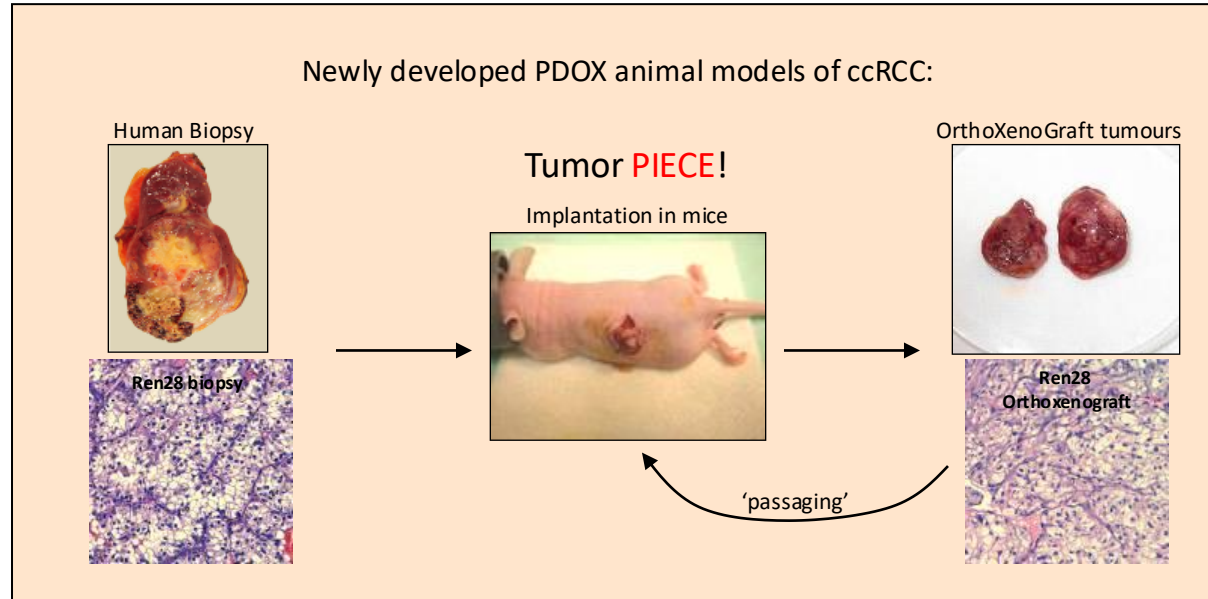
Ph3



Few animal models → Patient's Heterogeneous Responses ???

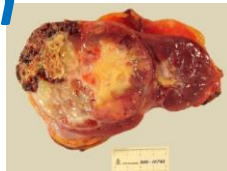


Patient-Derived OrthoXenograft animal model of Human RCC in mice



Implanted OT-piece	Tumorgraft generation		YES (%)
	NO	YES	
43	21	22	51.2

Human



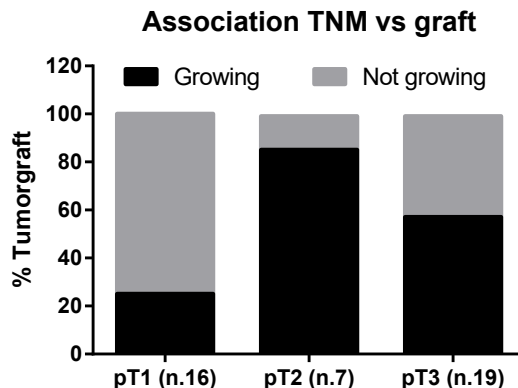
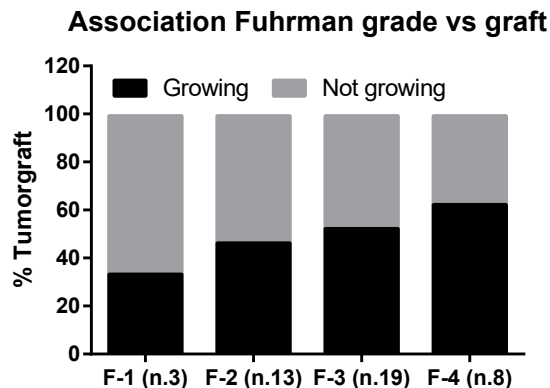
Grown in Mice



PATIENT CHARACTERISTICS		
ALL OT	n	% total
Total	43	
Female	unknown	
Male	unknown	
Age		
range	unknown	
median	unknown	
TNM	n*	% total
pT1	16	38.1
pT2	7	16.7
pT3	19	45.2
	*TNM only known in 42 patient	
Fuhrman	n	% total
1/4	3	7.0
2/4	13	30.2
3/4	19	44.2
4/4	8	18.6

PATIENT CHARACTERISTICS		
GROWING Tumorgraft	n	% total
Total	21	
Female	11	52.4
Male	10	47.6
Age	years	
range	39-89	
median	64	
TNM	n*	% total
pT1	4	20.0
pT2	6	30.0
pT3	11	55.0
	*TNM only known in 20 tumorgraft patient	
Fuhrman	n	% total
1/4	1	4.8
2/4	6	28.6
3/4	10	47.6
4/4	5	23.8

Ren-PDOX: best with high Furhman and Mets!

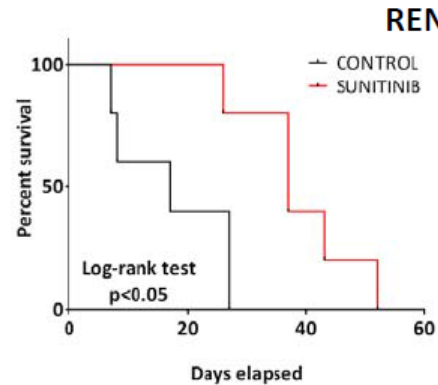
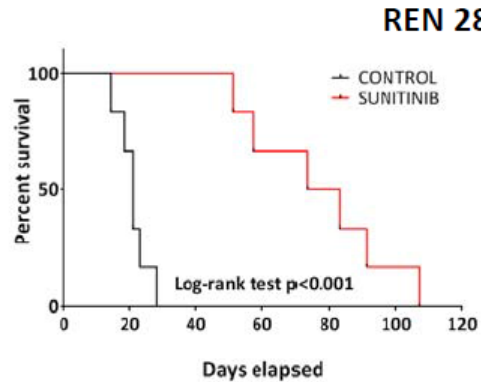
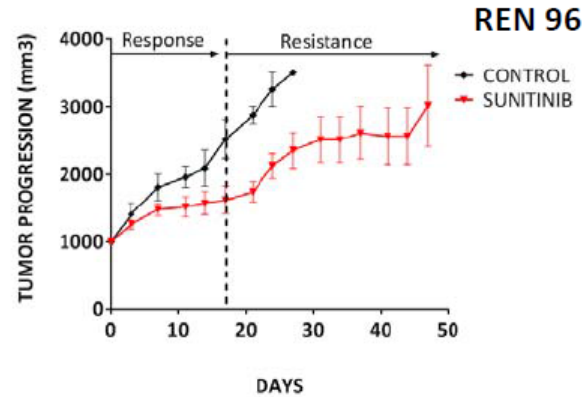
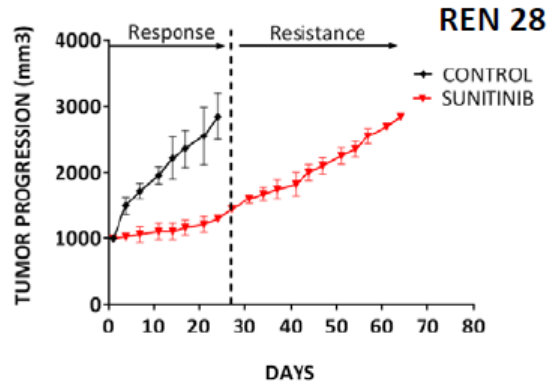


Association Met in patient Met in OrthoXenograft

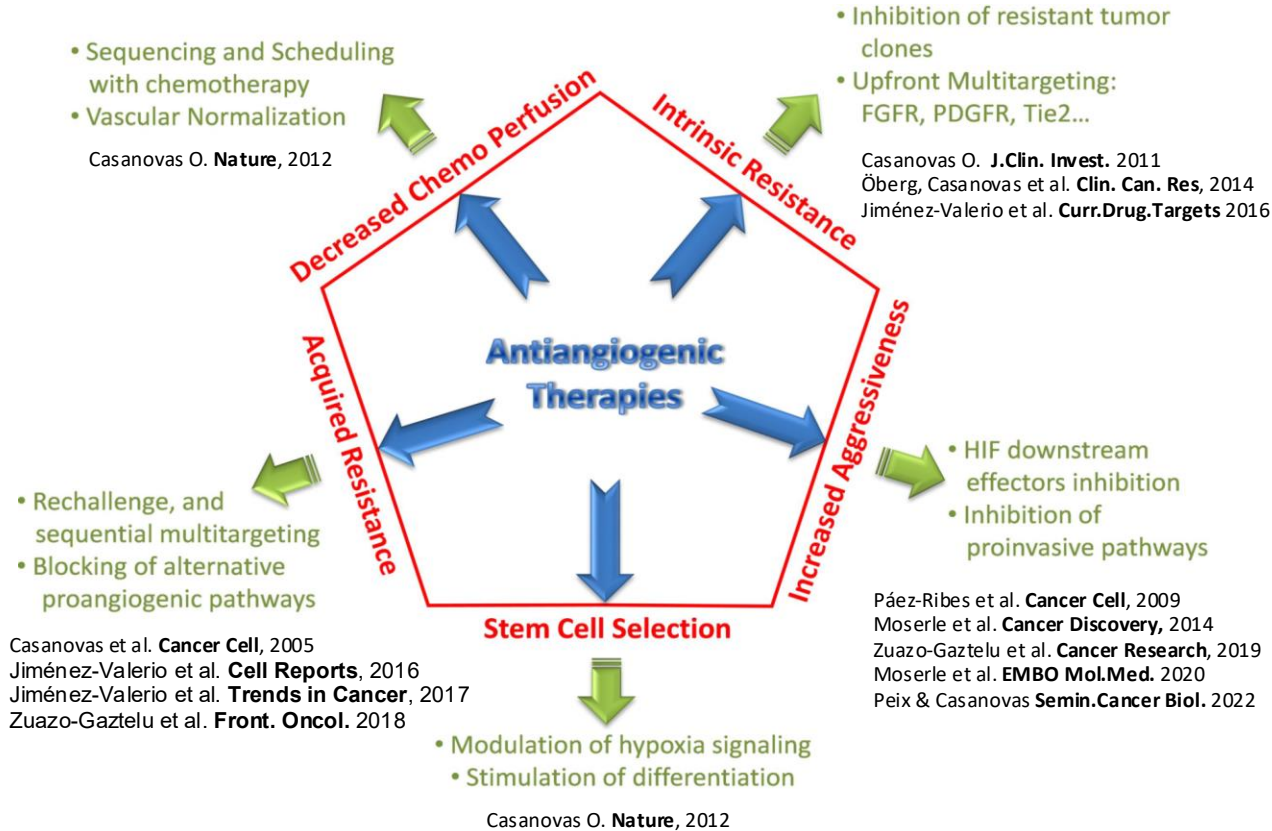
FOR GROWING TUMORGRAFTS ONLY			
	Patient mets at diagnosis or follow-up		
Mouse mets	NO	YES*	TOT
NO	10	5	15
YES	1	5	6
TOT	11	10	21*

*REN67 not evaluated for met

Tumor Responses to Antiangiogenic Therapies in RCC PDOX



Mechanisms of Resistance to Anti-Angiogenic Therapies

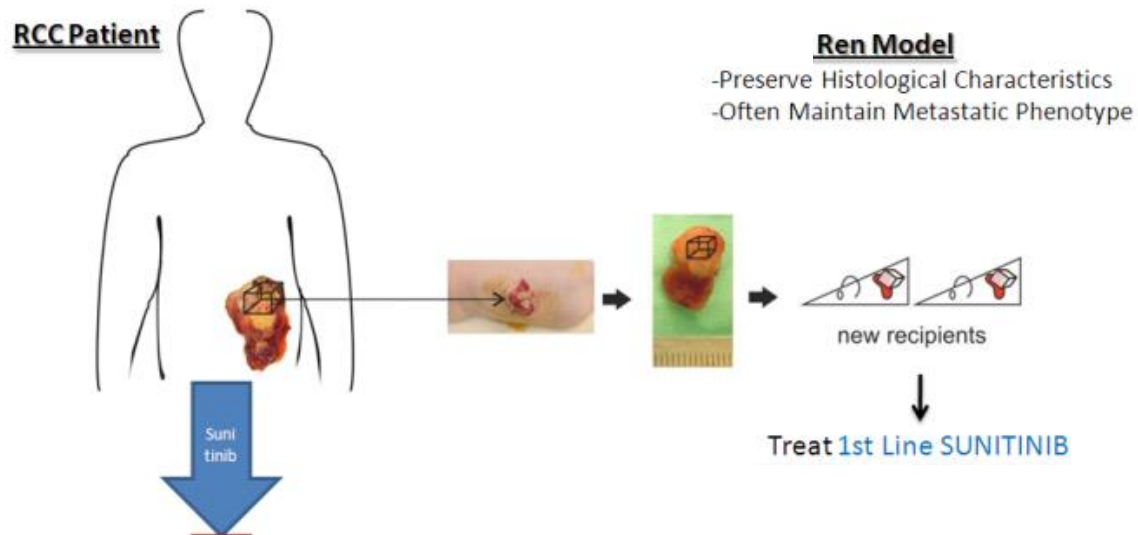


RCC Patient's PDOX in the MICE



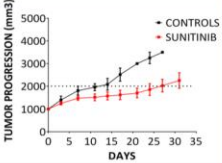
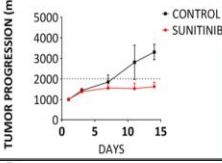
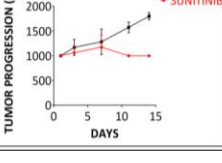
Can we use RCC PDOXs for Prediction of Response?

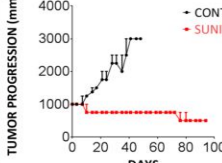
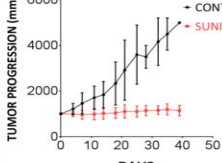
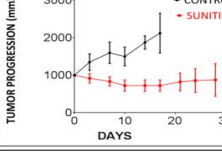
RCC Patient's PDOX in the MICE



RCC Patient's PDOX in the MICE

1st Line SUNITINIB

PATIENT. Tumor Description	Mouse AVATAR Model	1st Line Treatment in AVATAR	PATIENT Clinical Response
mRCC, Clear Cell, Stage pT3b, Führman G4	REN 96		POOR RESPONSE
mRCC, Clear Cell, Stage pT3b, Führman G4, BONE METASTASIS	REN 97		POOR RESPONSE
mRCC, Clear Cell, Stage pT4, Sarcomatoid	REN 108		POOR RESPONSE Progression at < 3 months

PATIENT. Tumor Description	Mouse AVATAR Model	1st Line Treatment in AVATAR	PATIENT Clinical Response
mRCC, Clear Cell, Stage pT2, Führman G3, INTERCOSTAL METASTASIS	REN100		GOOD RESPONSE 3 months with SUTENT & No progression
mRCC, Clear Cell, Stage pT3a, Führman G4, sunitinib-treated, Local Regrowth	REN 106		GOOD RESPONSE 12 months with SUTENT & No progression
mRCC, Clear Cell, Stage pT1b, Führman G2	REN 111		GOOD RESPONSE 8 months with SUTENT & No progression

RCC Patient's AVATARS in the MICE

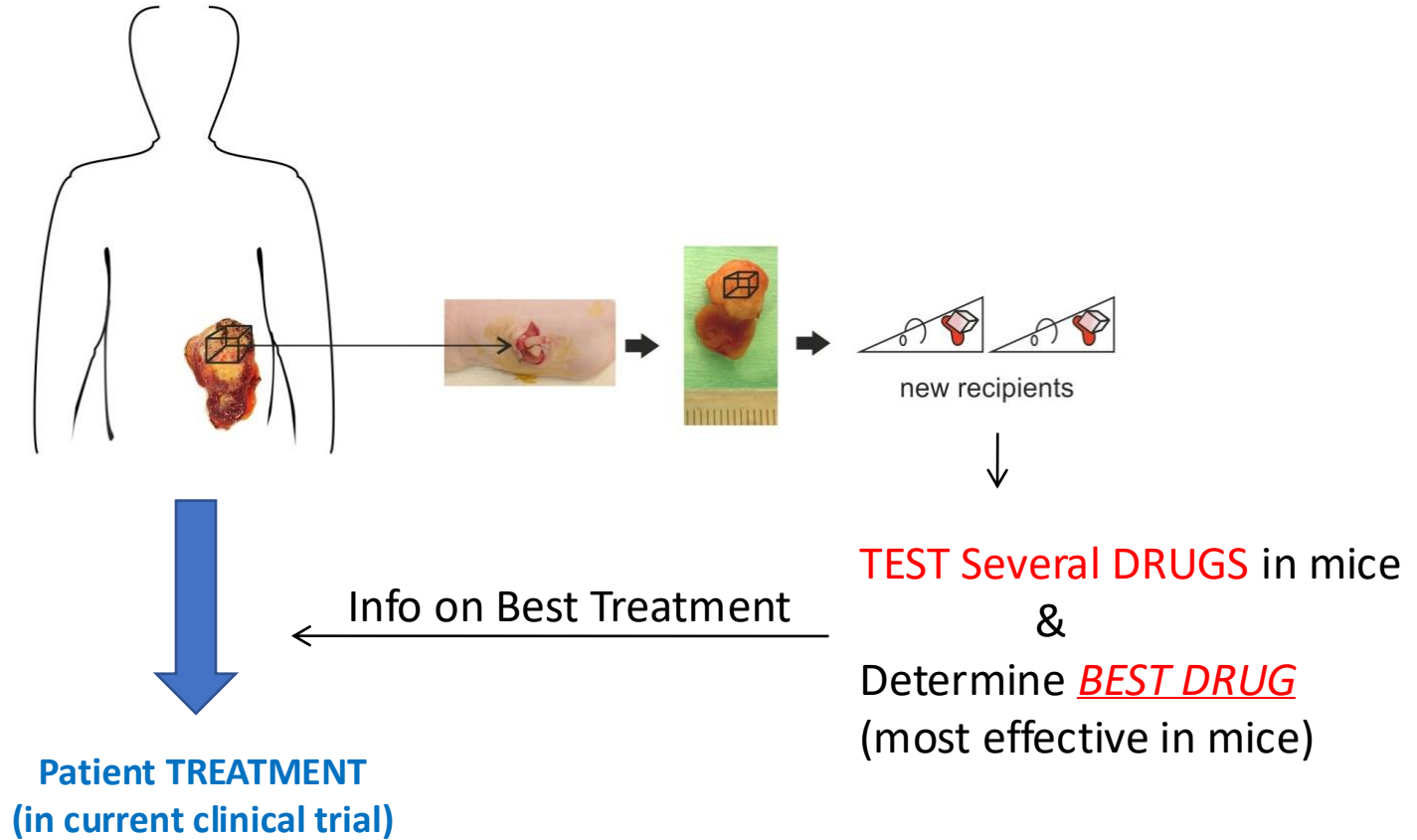


**-Can we develop RCC PDOXs from patients
to test treatments BEFORE the patient gets them?**

Patient AVATARS:



mRCC AVATAR Models:



mRCC AVATAR Models: Example

RCC Pt 2:

Male 64y

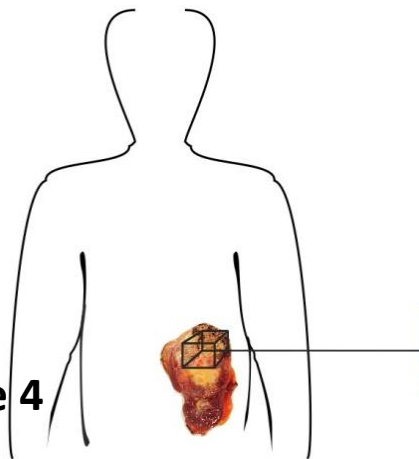
Stage IV

pT3bN0M1

(lung Mets)

Clear Cell

Fuhrman Grade 4



Nephrectomy (Dr. E.Trilla, Urology)

Tissue **piece** (Dra I. de Torres, AP
José Jiménez, OncMed-AP)



Dr J. Carles
Dra C. Suárez



mRCC AVATAR Models: Example

RCC Pt 2:

Male 64y

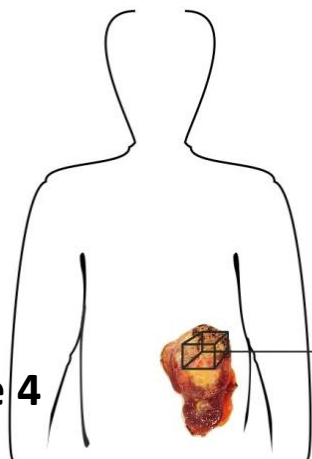
Stage IV

pT3bN0M1

(lung Mets)

Clear Cell

Fuhrman Grade 4



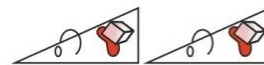
Ren96:

-High growth rate

-Clear Cell, Furhman 4

-Preserved histology

-Lung Metastasis!



new recipients

mRCC AVATAR Models: Example

RCC Pt 2:

Male 64y

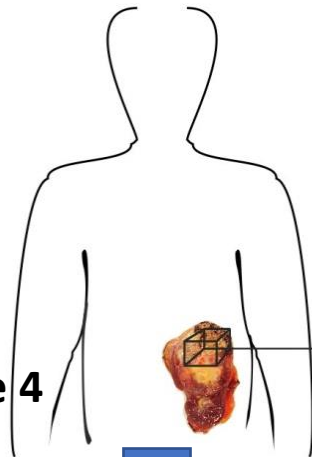
Stage IV

pT3bN0M1

(lung Mets)

Clear Cell

Fuhrman Grade 4



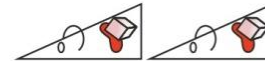
Ren96:

-High growth rate

-Clear Cell, Furhman 4

-Preserved histology

-Lung Metastasis!



new recipients



Treat 1st Line SUNITINIB &
TEST Several DRUGS 2nd line:

-Sunitinib

-Axitinib

-Cabozantinib

-Everolimus

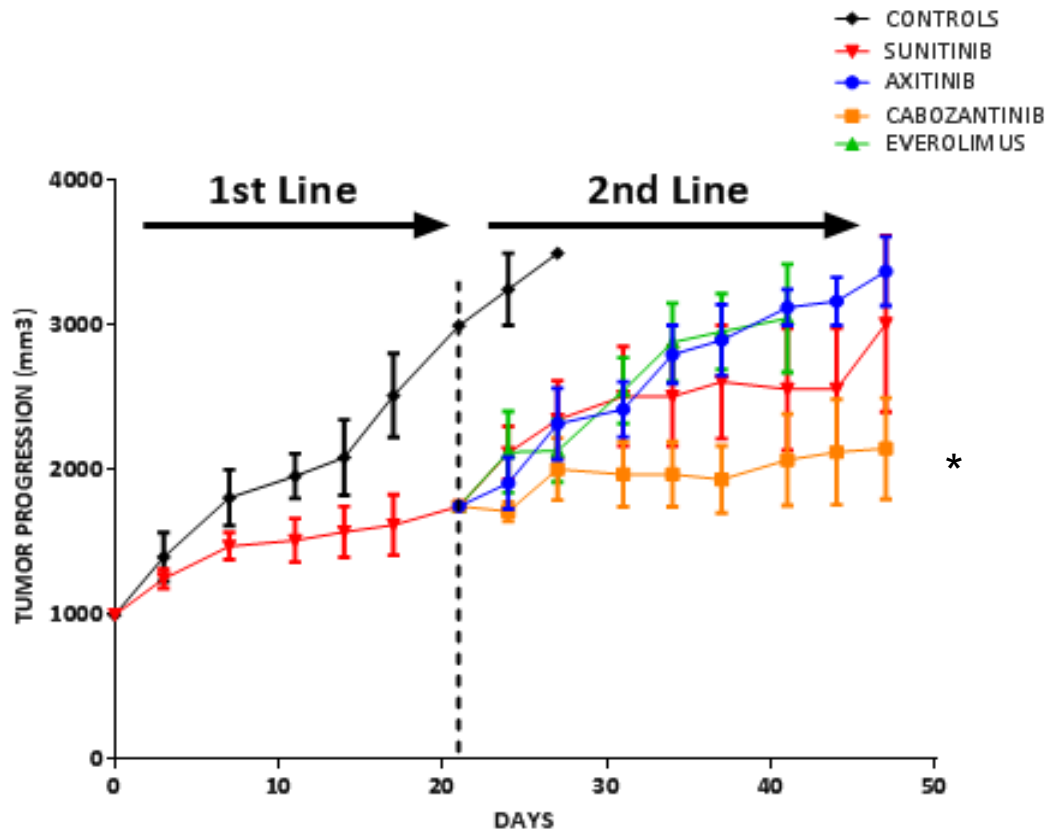
(*Clinical Use/Trials that were available
for that patient!)



Patient TREATMENT

AVATAR mouse model to test effectiveness of second-line treatment

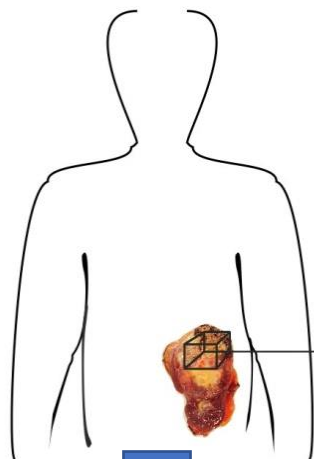
Ren96



Mar Martínez & "RCC team"

mRCC AVATAR Models: Example

Pt 2:
mRCC

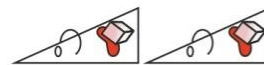


Patient could not
start 2nd line
DIED



Ren96:

- High growth rate
- Preserved histology



new recipients



CABOZANTINIB as Best Treatment

TEST Several DRUGS in mice
&
Determine **BEST DRUG**
(most effective in mice)

mRCC AVATAR Models: Example 2

Pt 3:

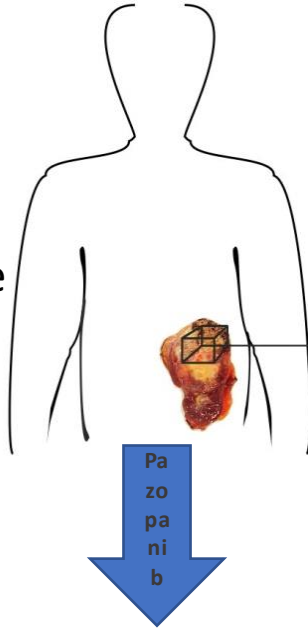
mRCC

Clear Cell

pT3a pNx

Nucleol. Grade

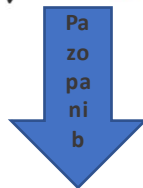
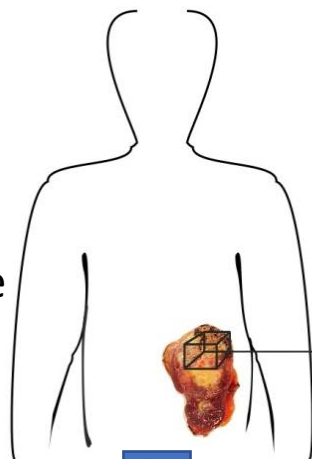
ISUP 3



mRCC AVATAR Models: Example 2

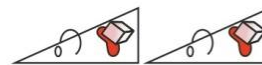
Pt 3:

mRCC
Clear Cell
pT3a pNx
Nucleol. Grade
ISUP 3



Ren122:

- High growth rate
- Preserved histology ccRCC
- Non metastatic

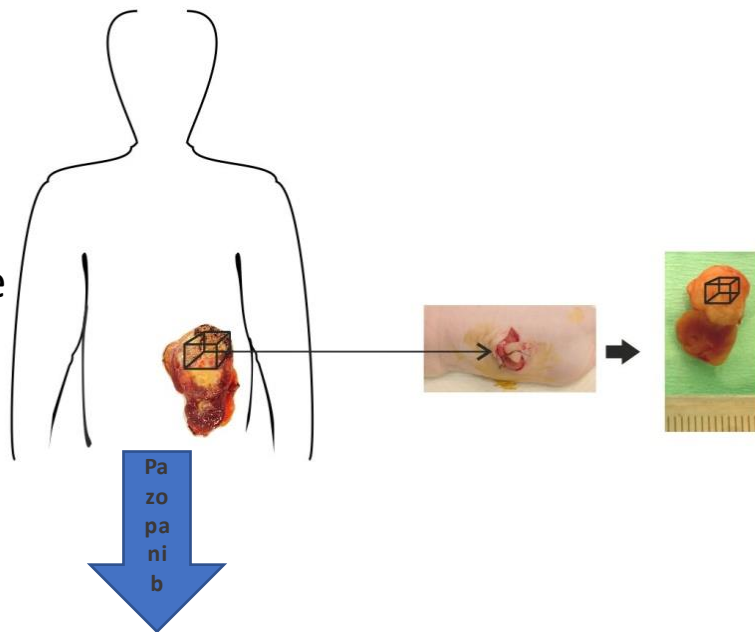


new recipients

mRCC AVATAR Models: Example 2

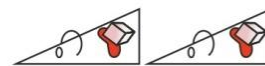
Pt 3:

mRCC
Clear Cell
pT3a pNx
Nucleol. Grade
ISUP 3



Ren122:

- High growth rate
- Preserved histology ccRCC
- Non metastatic



new recipients

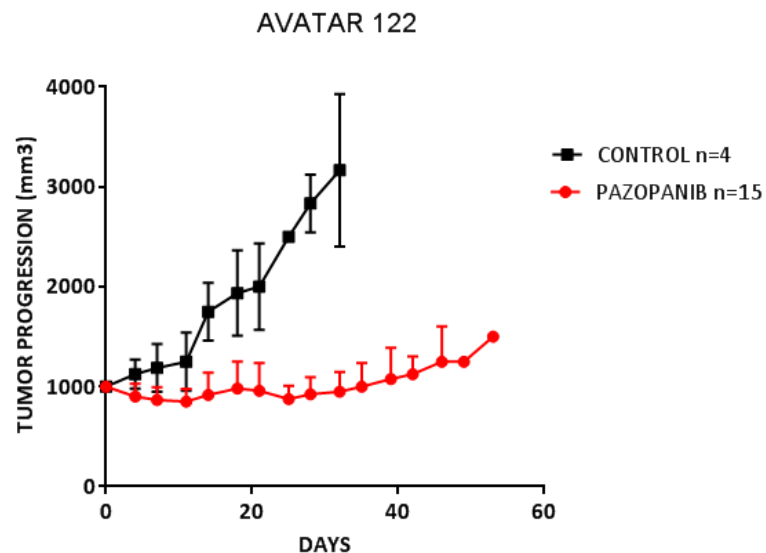
Treat **1st Line PAZOPANIB** &
TEST Several DRUGS 2nd line:

- Axitinib*
- Cabozantinib*
- Everolimus*

(*Clinical Trials were available
for the patient!)

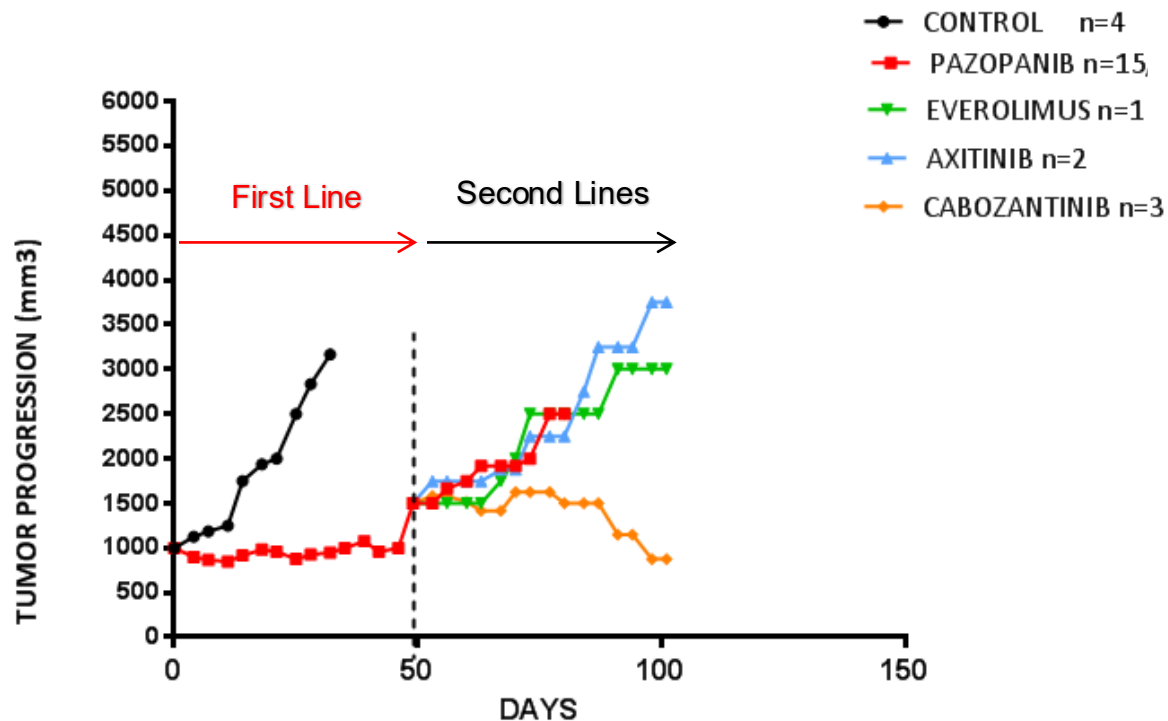
AVATAR mouse model to test effectiveness of second-line treatment

Ren122: High growth rate, ccRCC, Non metastatic.



AVATAR mouse model to test effectiveness of second-line treatment

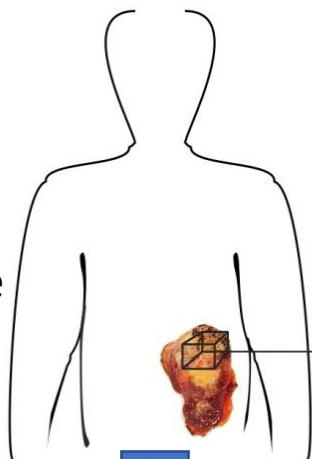
Ren122: High growth rate, ccRCC, Non metastatic.



mRCC AVATAR Models: Example 2

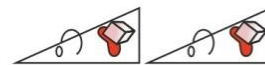
Pt 3:

mRCC
Clear Cell
pT3a pNx
Nucleol. Grade
ISUP 3



Ren122:

- High growth rate
- Preserved histology ccRCC
- Non metastatic

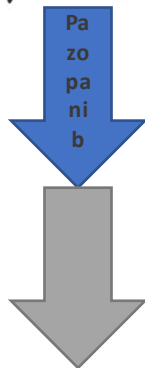


new recipients



TEST Several DRUGS in mice
&
Determine BEST DRUG
(most effective in mice)

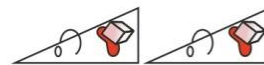
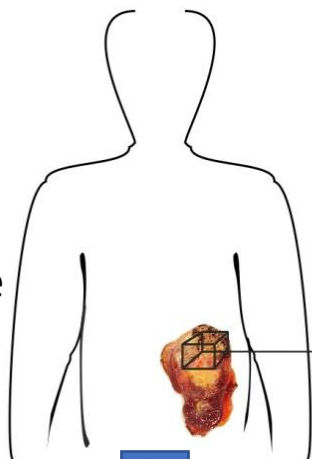
CABOZANTINIB as Best Treatment



mRCC AVATAR Models: Example 2

Pt 3:

mRCC
Clear Cell
pT3a pNx
Nucleol. Grade
ISUP 3



new recipients

Ren122:

- High growth rate
- Preserved histology ccRCC
- Non metastatic



TEST Several DRUGS in mice
&
Determine BEST DRUG
(most effective in mice)

CABOZANTINIB as Best Treatment

Pa
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Patient responded



Maria Ochoa, ICO
X García del Muro, ICO
August Vidal, AP HUB
Enric Condom, AP HUB
López-Costeá, Uro HUB



Joan Carles, VHIO
Cristina Suárez, VHIO
Enric Trilla, Uro HUVH
Inés de Torres, AP HUVH
José Jiménez, VHIO-AP



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