IX Congresso Internacional de Uro-Oncologia

IV SIMPÓSIO MULTIPROFISSIONAL DE URO-ONCOLOGIA

1 a 3 de Março de 2018

SHERATON SÃO PAULO WTC HOTEL

PÓS ASCO GU 2018

Testicular Câncer

ANA PAULA GARCIA CARDOSO
MD, HOSPITAL ISRAELITA ALBERT EINSTEIN

ALBERT EINSTEIN
HOSPITAL ISRAELITA
ONCOLOGIA E HEMATOLOGIA

ana.garcia@einstein.br

PÓS ASCO GU 2018
Testicular Cancer

ANA PAULA GARCIA CARDOSO
MD, HOSPITAL ISRAELITA ALBERT EINSTEIN

1- Keynote Letter: Manejo de Câncer de Testículo estadio II (A) com marcador tumoral negativo

2- General Session: Manejo de massas residuais pós quimioterapia
- Abstract 546- Serum miRNA to predict post-chemotherapy viable disease in testicular non-seminomatous germ cell tumor patients.

3- Rapid-Fire Abstract Session:
- Abstract 550- Sentinel node biopsy in clinical stage I testicular cancer;
- Abstract 549- Long-term sexual functioning in germ-cell tumor survivors;
- Abstract 551- Impact of medicaid expansion on diagnosis and management of patients with testicular cancer

4- Poster:
- Abstract 548- Collateral damage: Molecular aging and p16INK4a senescence protein in testicular cancer survivors treated with chemotherapy.
- Abstract 564- Effect of number of computed tomography (CT) scans during follow-up (FUP) of patients with clinical stage I (CSI) seminoma: A trial-level meta-analysis.
- Abstract 556 -Diagnostic radiation and testicular germ cell tumor risk.

ana.garcia@einstein.br

Serum miRNA to predict post-chemotherapy viable disease in testicular nonseminomatous germ cell tumor patients

Ricardo Leão MD
Dept. of Surgical Oncology, Princess Margaret Cancer Centre
Toronto, Canada

PIs: Robert J Hamilton MD MPH and Leendert Looijenga PhD

PRESENTED AT: 2018 Genitourinary Cancers Symposium | #GU18

Background

- **Post Chemotherapy Retroperitoneal Lymph Node Dissection (pcRPLND)** is part of multimodal treatment for patients with advanced nonseminoma testicular germ cell tumors
- Currently indicated in patients with ***normalized*** or ***plateaued*** serum tumor markers with residual disease (> 1 cm)
- **Rationale** to remove residual masses:
  - Teratoma (40-45%),
  - Viable chemorefractory germ cell tumor elements (10-15%)

Steyerberg EW. Prediction of residual retroperitoneal mass histology after chemotherapy for metastatic nonseminomatous germ cell tumor: multivariate analysis of individual patient data from six study groups.J Clinc Oncol. 1995 May; 13(5):1177-87
Fosså SD. Histology of tumor residuals following chemotherapy in patients with advanced nonseminomatous testicular cancer. J Urol. 1989 Nov;142(5):1239-42
Carver BS, Serio AM, Bajorin D, et al. Improved clinical outcome in recent years for men with metastatic nonseminomatous germ cell tumors. J Clin Oncol 2007;25:5603-5608.

ana.garcia@einstein.br

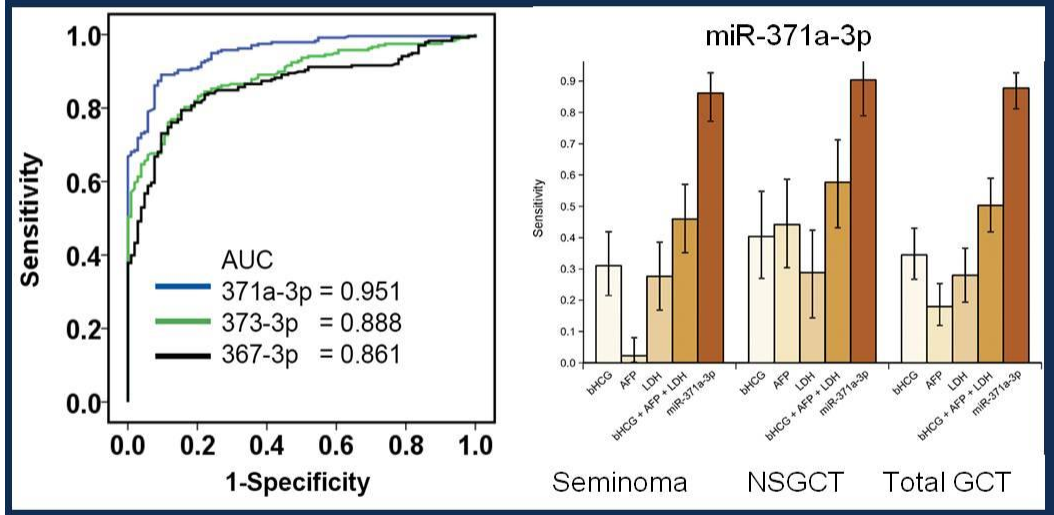
The problem...

Approximately 50% of patients are submitted to unnecessary surgery

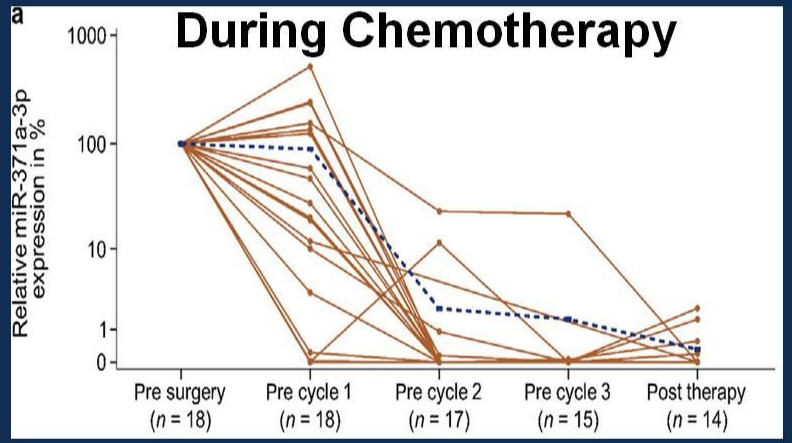
ana.garcia@einstein.br

miRNAs in Testicular Cancer

Diagnostic Properties



Prognostic Properties



Van Agthoven and Looijenga. Accurate primary germ cell cancer diagnosis unsing serum based miRNA detection (ampTSmiR test). Oncotarget. 2017 July 27; 8 (35):58037-58049
Dieckmann KP et al. Serum levels of MicroRNA miR-371a-3p: A sensitive and Specific New Biomarker for Germ Cell Tumours. Eur Urol. 2017 Feb;71 (2):213-220

ana.garcia@einstein.br

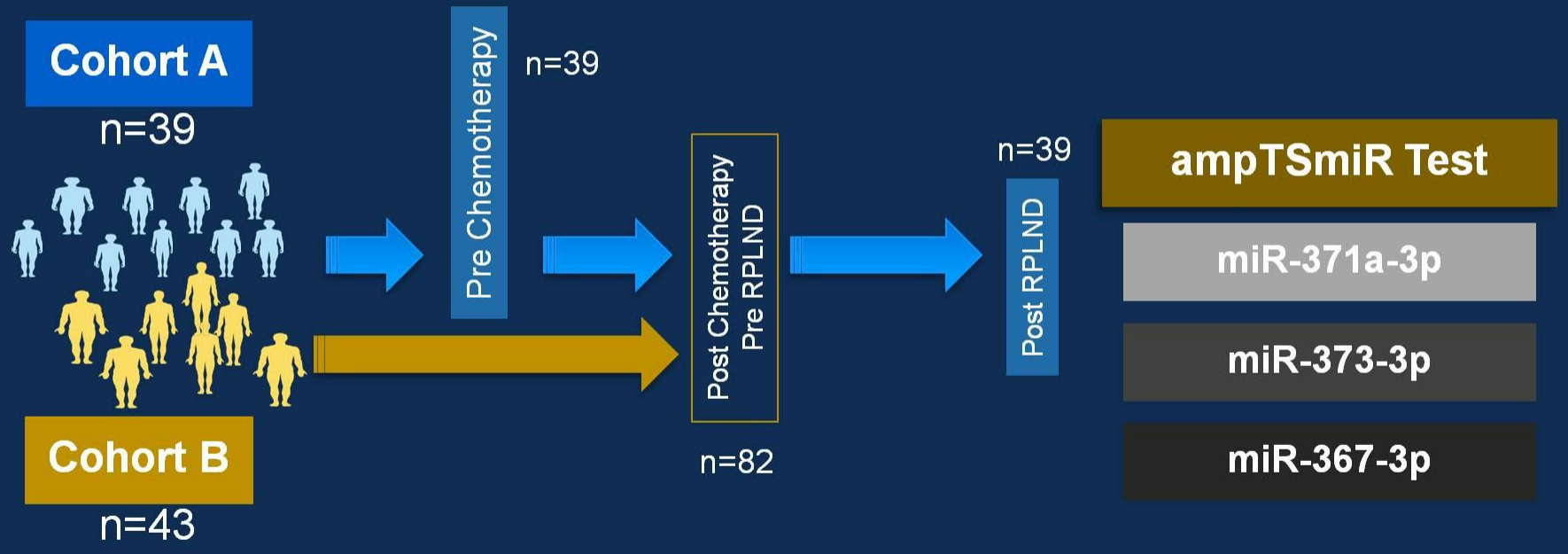
Hypothesis

Serum miRNAs are predictive markers for viable disease post-chemotherapy

ana.garcia@einstein.br

Patients and Methods

NSGCT patients submitted to orchiectomy, chemotherapy and pcRPLND



Van Agthoven and Looijenga. Accurate primary germ cell cancer diagnosis unsing serum based miRNA detection (ampTSmiR test). Oncotarget. 2017 July 27; 8 (35):58037-58049

ana.garcia@einstein.br

Patients and Methods

Post Chemotherapy Lesion Histology

Cohort A and B

n=82

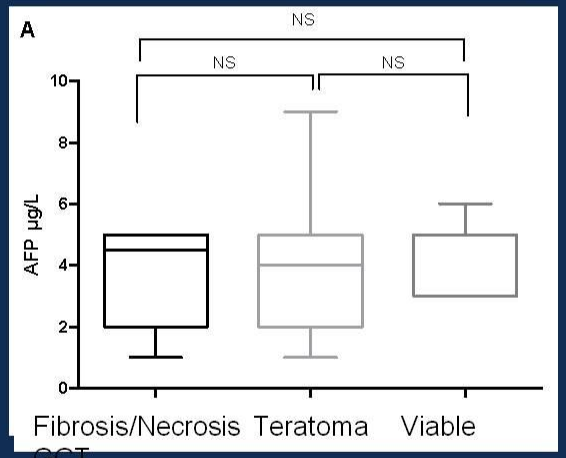
Necrosis/Fibrosis	36 (43.9%)
Teratoma	34 (41.5%)
Viable GCT	12 (14.6%)

ana.garcia@einstein.br

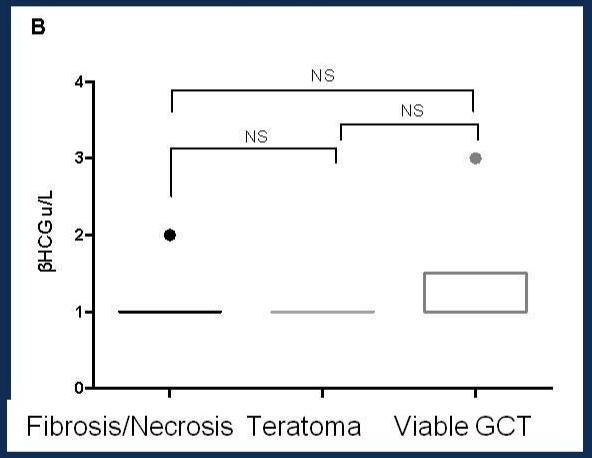
Results

Classical tumor markers do not predict post-chemotherapy residual masses histology

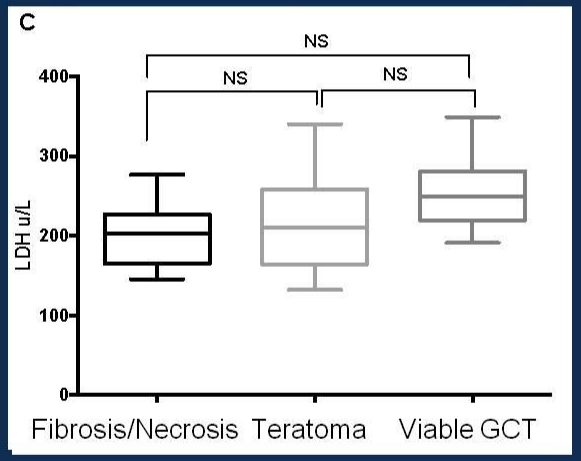
AFP



HCG



LDH



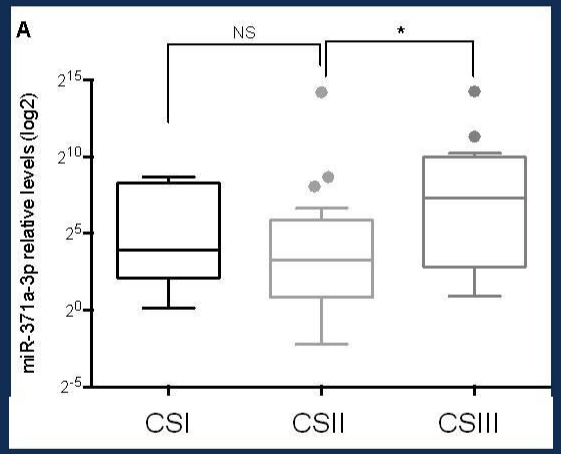
Presented by: Ricardo Leão et al

ana.garcia@einstein.br

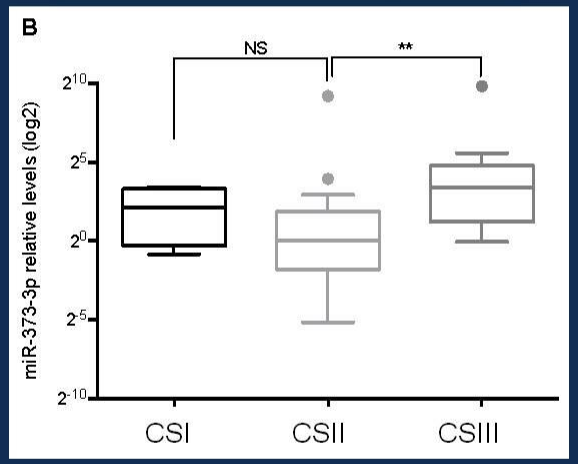
Results

Pre-chemotherapy serum miRNA levels are associated with clinical stage

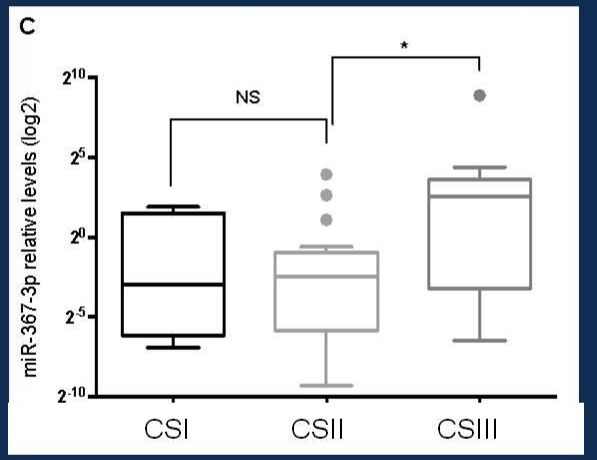
miR-371a-3p



miR-373a-3p



miR-367-3p



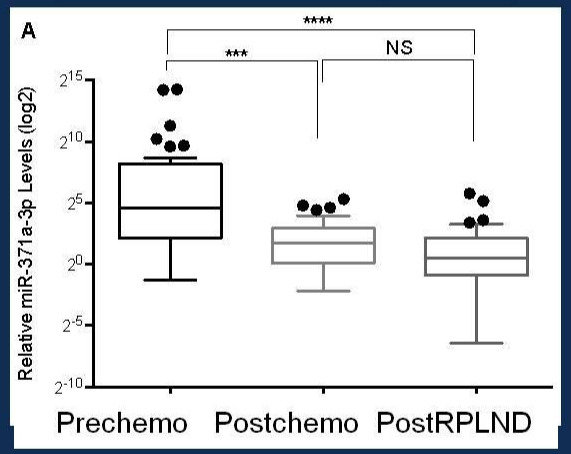
(Cohort A. n=39. **A**. *, p =0.046; **B**. **, p =0.003; **C**.*, p =0.038)

ana.garcia@einstein.br

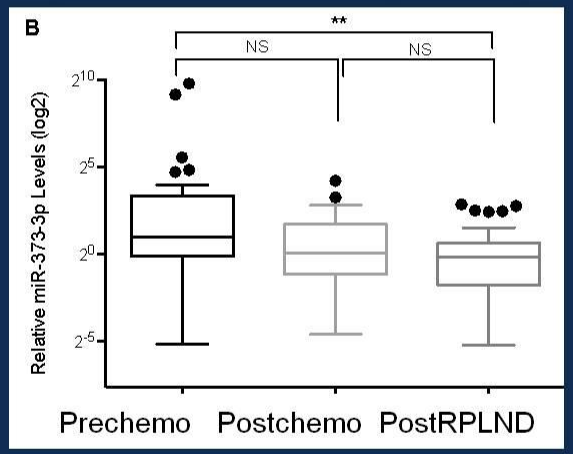
Results

Serum miRNA levels are associated with treatment response

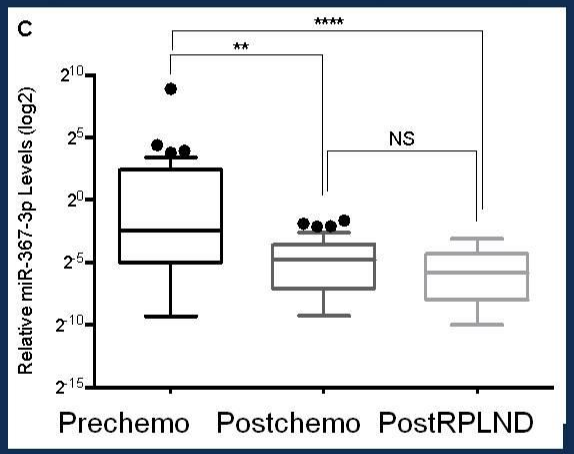
miR-371a-3p



miR-373a-3p



miR-367-3p



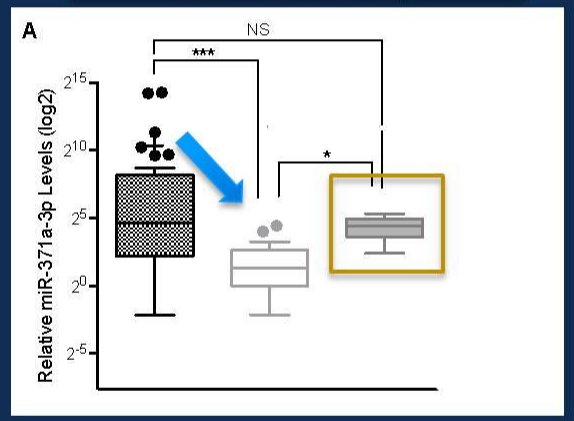
(Cohort A. n=39. A. miR-371, ****, p <0.0001, ***, p =0.0006; B. miR-373, **, p =0.0025; C. miR-367, **** p <0.0001, . **, p =0.005 .).

ana.garcia@einstein.br

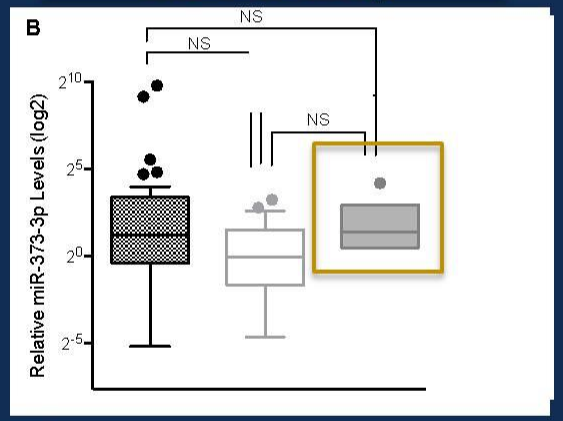
Results

Serum miRNA levels are higher in the presence of viable GCT post-chemotherapy

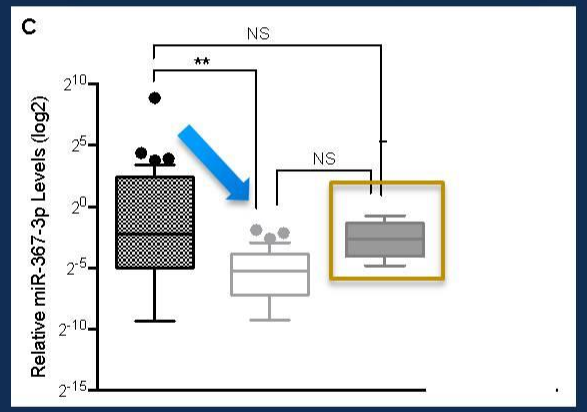
miR-371a-3p



miR-373a-3p



miR-367-3p



Pre-chemotherapy
Post-chemotherapy (Fibrosis/Necrosis + Teratoma)
Post-chemotherapy (Viable GCT)

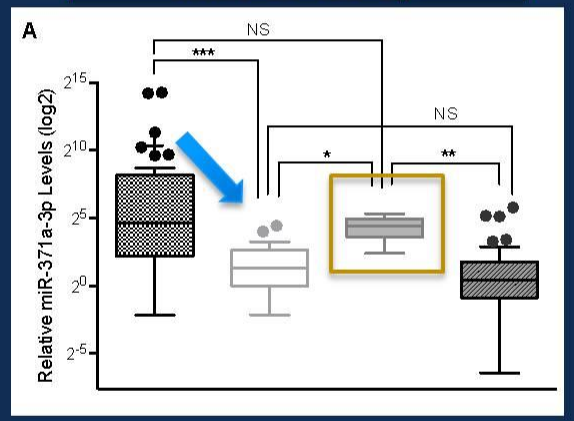
(Cohort A. n=39. A. ***, p=0.0002, .**, p=0.004; B. *, p=0.037; C. **, p=0.011, *, p=0.024)

ana.garcia@einstein.br

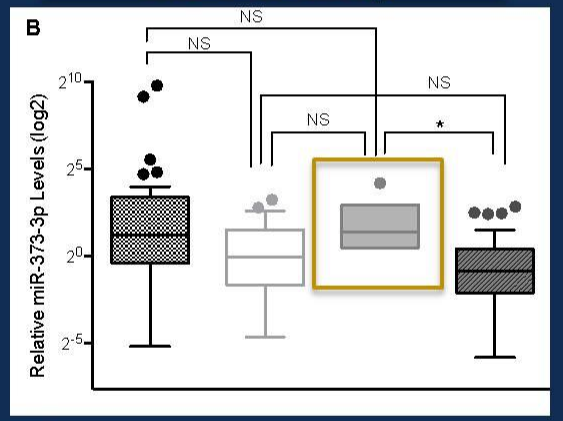
Results

Serum miRNA levels are higher in the presence of viable GCT post-chemotherapy

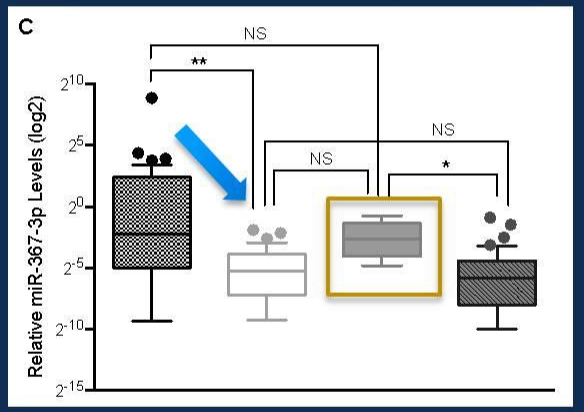
miR-371a-3p



miR-373a-3p



miR-367-3p



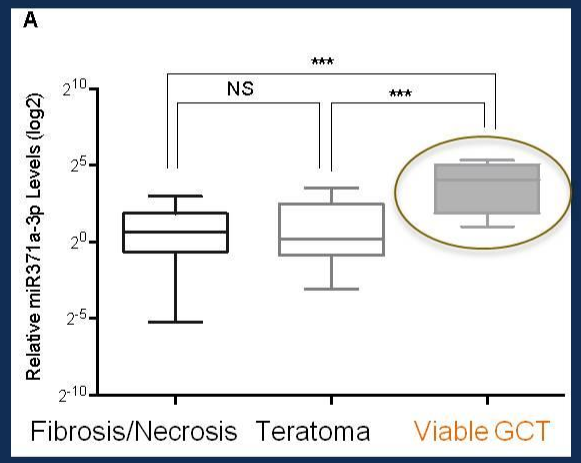
(Cohort A. n=39. A. ***, *p*=0.0002, .**, *p*=0.004; B. *, *p*=0.037; C. **, *p*=0.011, *, *p*=0.024)

ana.garcia@einstein.br

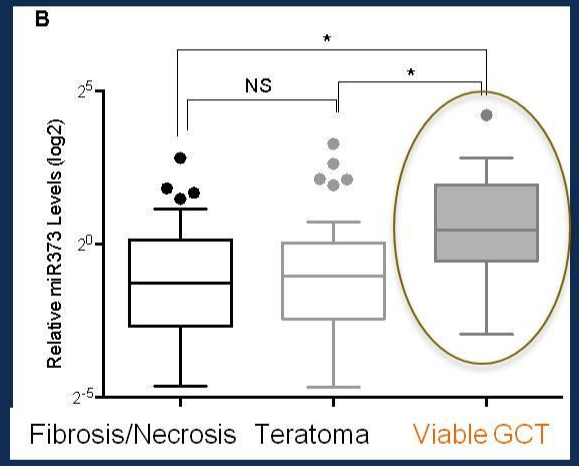
Results

Serum miRNA levels are higher in the presence of viable GCT post-chemotherapy

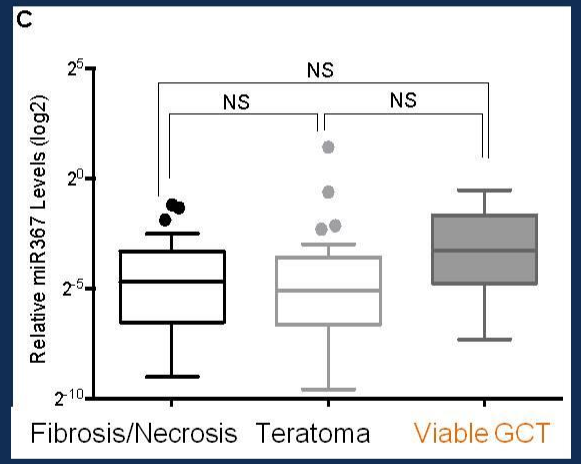
miR-371a-3p



miR-373a-3p



miR-367-3p

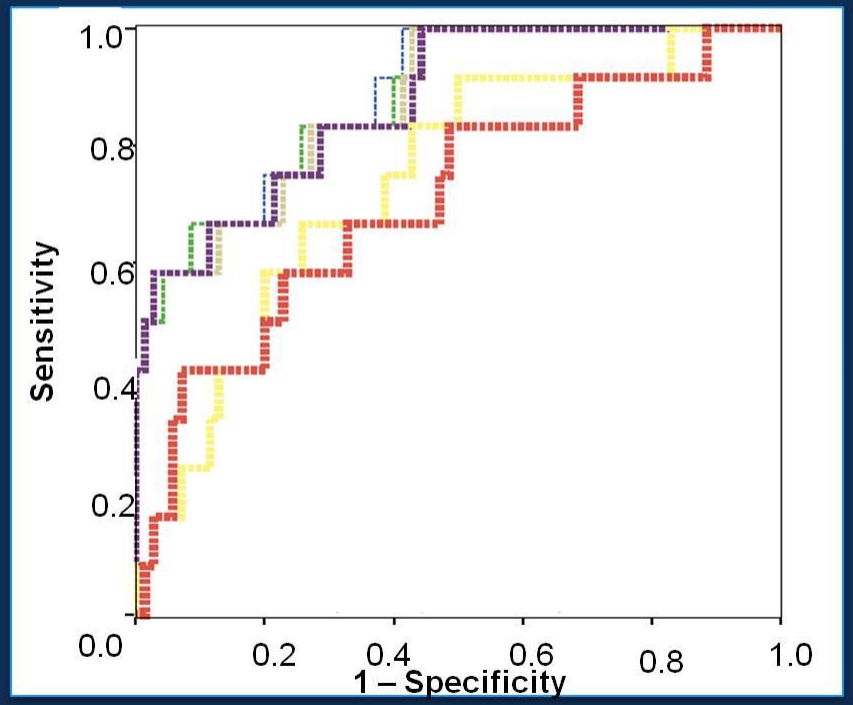


(Cohort A. n=82. A. ***, *p*=0.002; **B.***, *p*=0.032)

ana.garcia@einstein.br

Results

Serum miRNA accurately predict presence of viable GCT post-chemotherapy



Viable GCT vs. Fibrosis/Necrosis + Teratoma (n=82, post-chemotherapy)

- miR-371a-3p/miR-373-3p (AUC 0.885 95% CI 0.79-0.98)
- miR-371a-3p/miR-373-3p/miR-367 (AUC 0.880; 95% CI 0.79-0.99)
- miR-371a-3p (AUC 0.874; 95% CI 0.77-0.97)
- miR-371a-3p/miR-367 (AUC 0.873 95% CI 0.78-0.98)
- miR-373-3p (AUC 0.738; 95% CI 0.59-0.88)
- miR-367 (AUC 0.707; 95% CI 0.54-0.87)

ana.garcia@einstein.br

Results

Serum miR-371a-3p levels post-chemotherapy might support treatment decision in patients with residual retroperitoneal masses ≤ 3 cm

Residual Retroperitonal Masses ≤ 3 cm

n=39

miR-371a-3p Levels	Viable GCT (n =6)	Teratoma (n = 13)	Necrosis & Fibrosis (n = 20)
Negative (n=18)	0	8	10
Positive (n=21)	6	5	10

miR-371a-3p cut-off level 2.0 (Sensitivity 100%, Specificity 54%; NPV 100%, *p*=0.02)

Presented by: Ricardo Leão et al

ana.garcia@einstein.br

Conclusions/Take-Home Points

- Serum miRNA are associated with *clinical stage and treatment response*
- miR-371a-3p, as a single serum marker, accurately *predicts viable disease post-chemotherapy*
- In a sub-group of patients with retroperitoneal lesions measuring ≤ 3 cm, *miR-371a-3p profile might support treatment decision*
- *Promising* but *future studies are needed* to confirm our findings

ana.garcia@einstein.br

Limitations

- *Small cohort* of patients
- *Heterogeneous* population
- *Inability to distinguish teratoma* from necrosis & fibrosis
- Difficult to establish *correlation* with other studies using serum miRNAs (different assays and different population of testicular cancer patients)
- *Multi-institutional studies* with *standard miRNA quantification* assays are *needed* to establish miRNAs as clinical biomarkers

ana.garcia@einstein.br

Sentinel Node Biopsy in Clinical Stage I Testicular Cancer

Joost Blok, MD

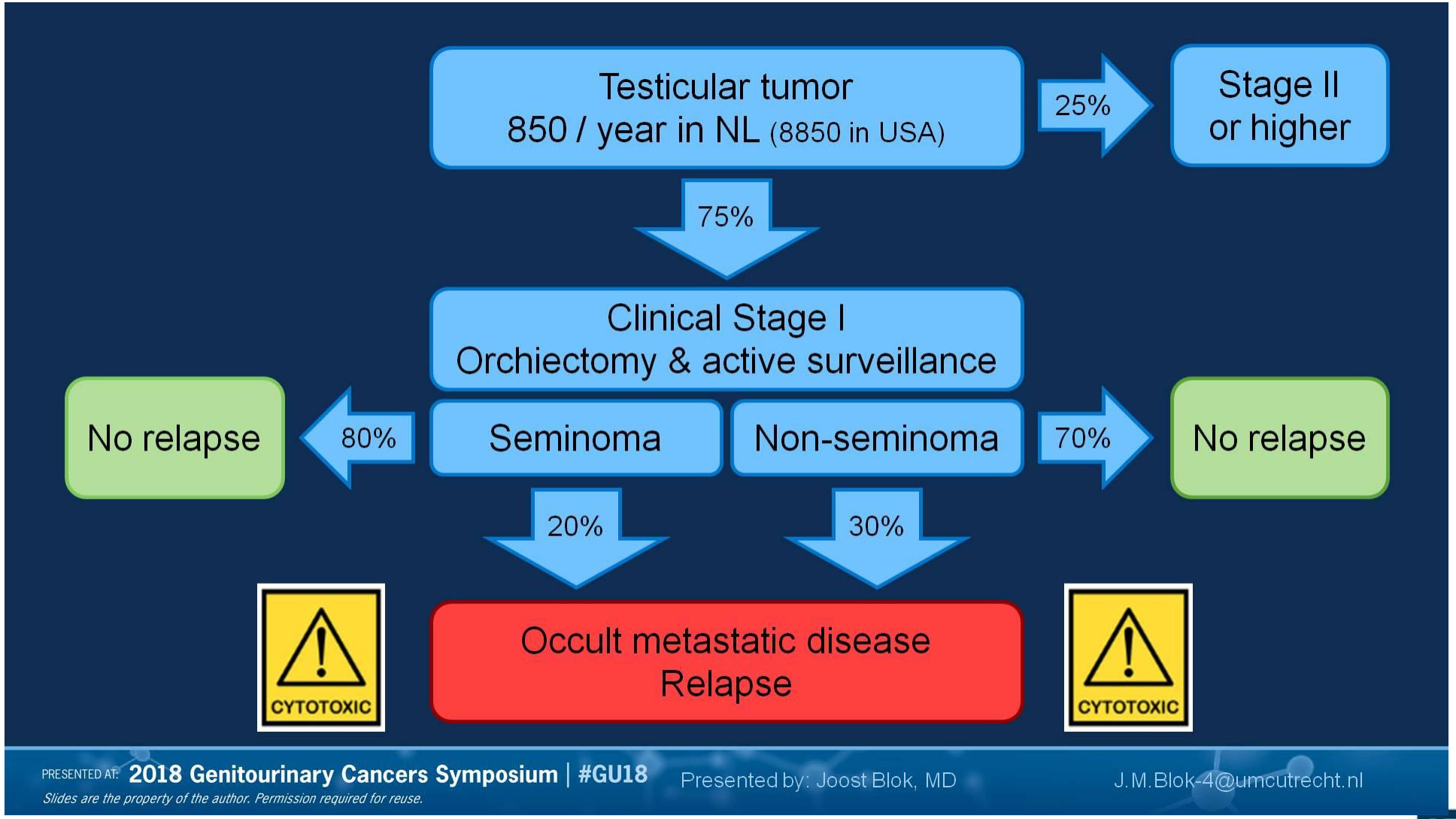
Physician-researcher / PhD Candidate

UMC Utrecht

NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

PRESENTED AT: 2018 Genitourinary Cancers Symposium | #GU18

ana.garcia@einstein.br



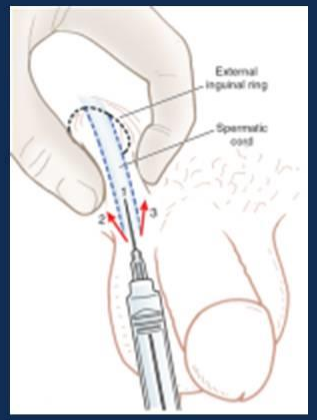
ana.garcia@einstein.br

Sentinel Lymph Node Biopsy

PRESENTED AT: 2018 Genitourinary Cancers Symposium | #GU18

Presented by: Joost Blok, MD

J.M.Blok-4@umcutrecht.nl



1.
Funicular block

2.
Intratesticular injection radiopharmaceutical

3.
Lymphoscintigraphy SPECT/CT

4.
Laparoscopic resection SN

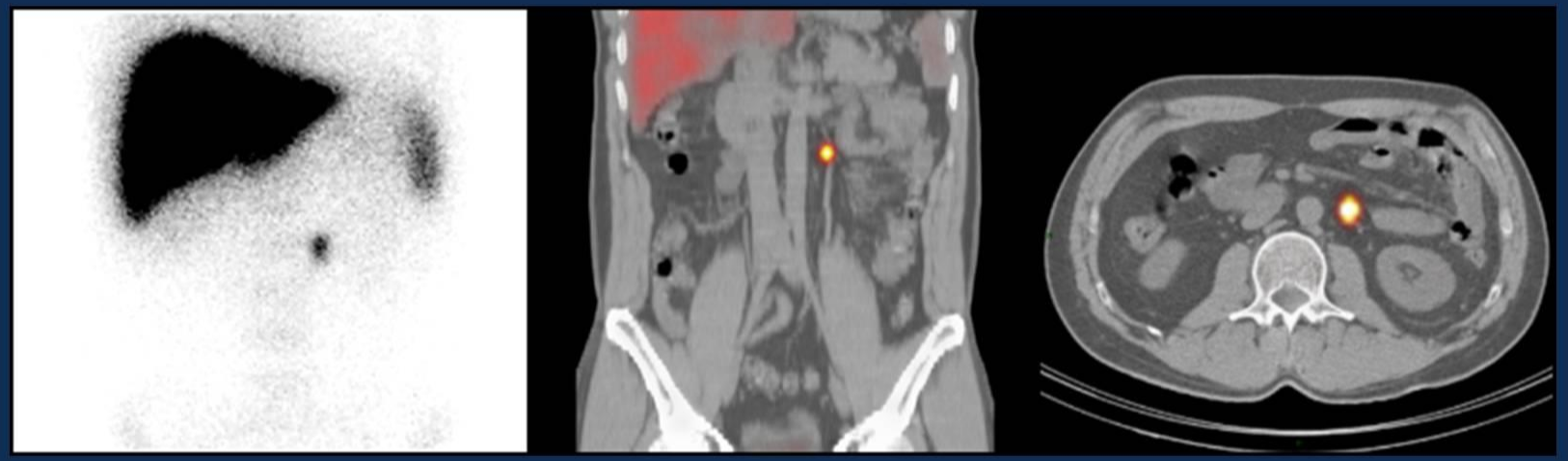
Gamma probe

5.
Radical orchiectomy

Presented by: Joost Blok, MD
J.M.Blok-4@umcutrecht.nl

ana.garcia@einstein.br

Lymphoscintigraphy & SPECT/CT



Presented by: Joost Blok, MD

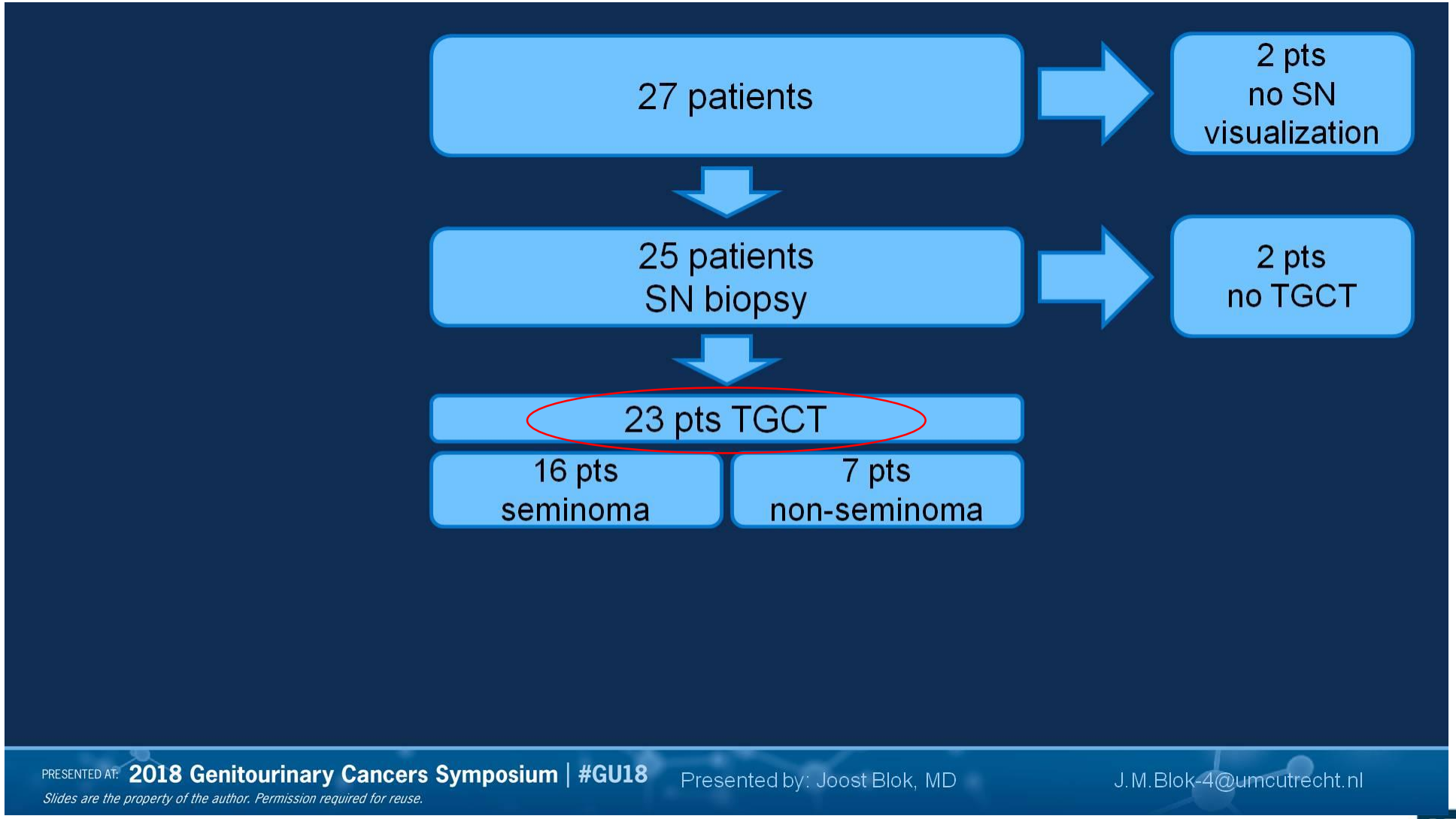
J.M.Blok-4@umcutrecht.nl

ana.garcia@einstein.br

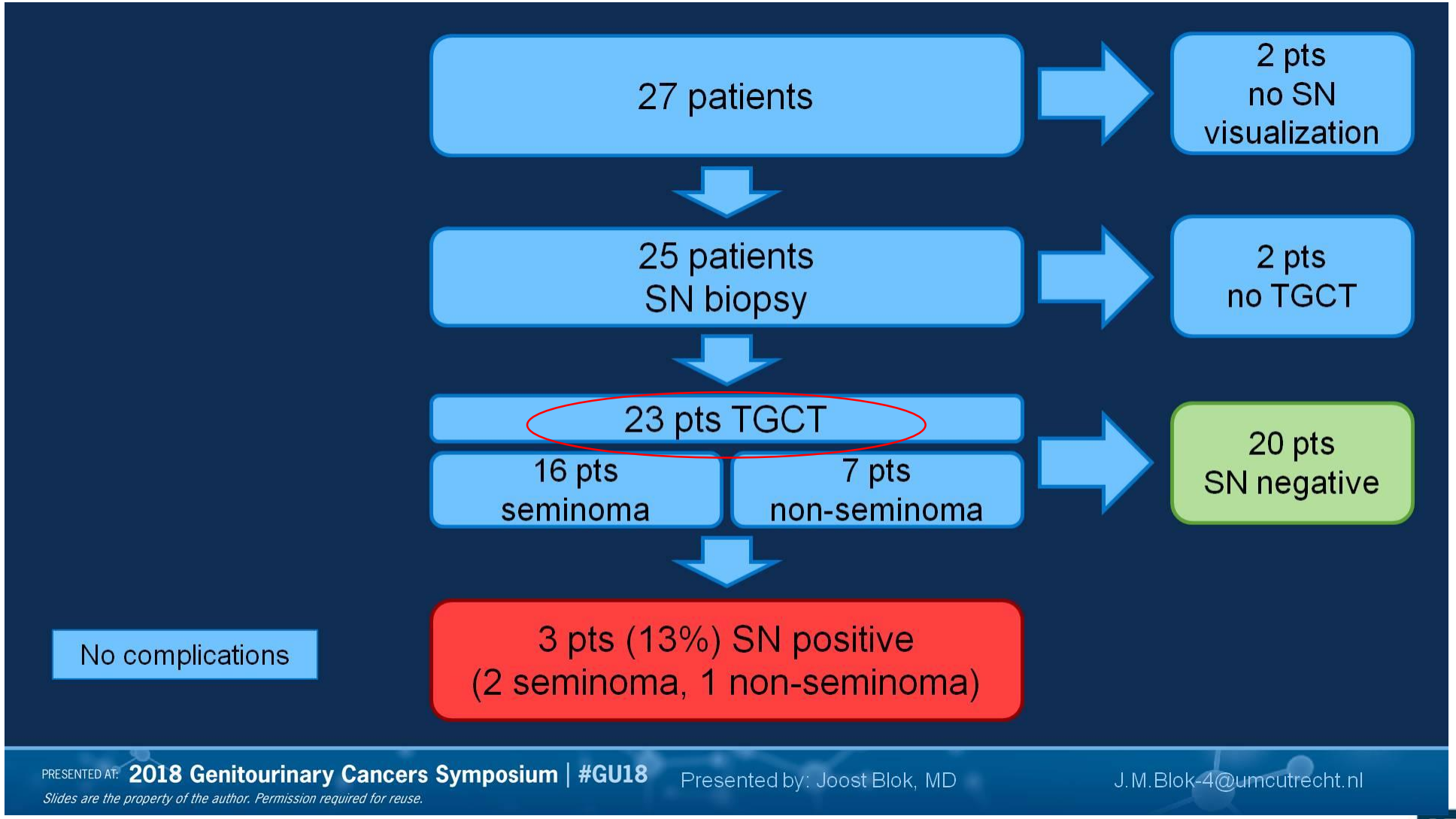
Results

Presented by: Joost Blok, MD J.M.Blok-4@umcutrecht.nl

ana.garcia@einstein.br



ana.garcia@einstein.br

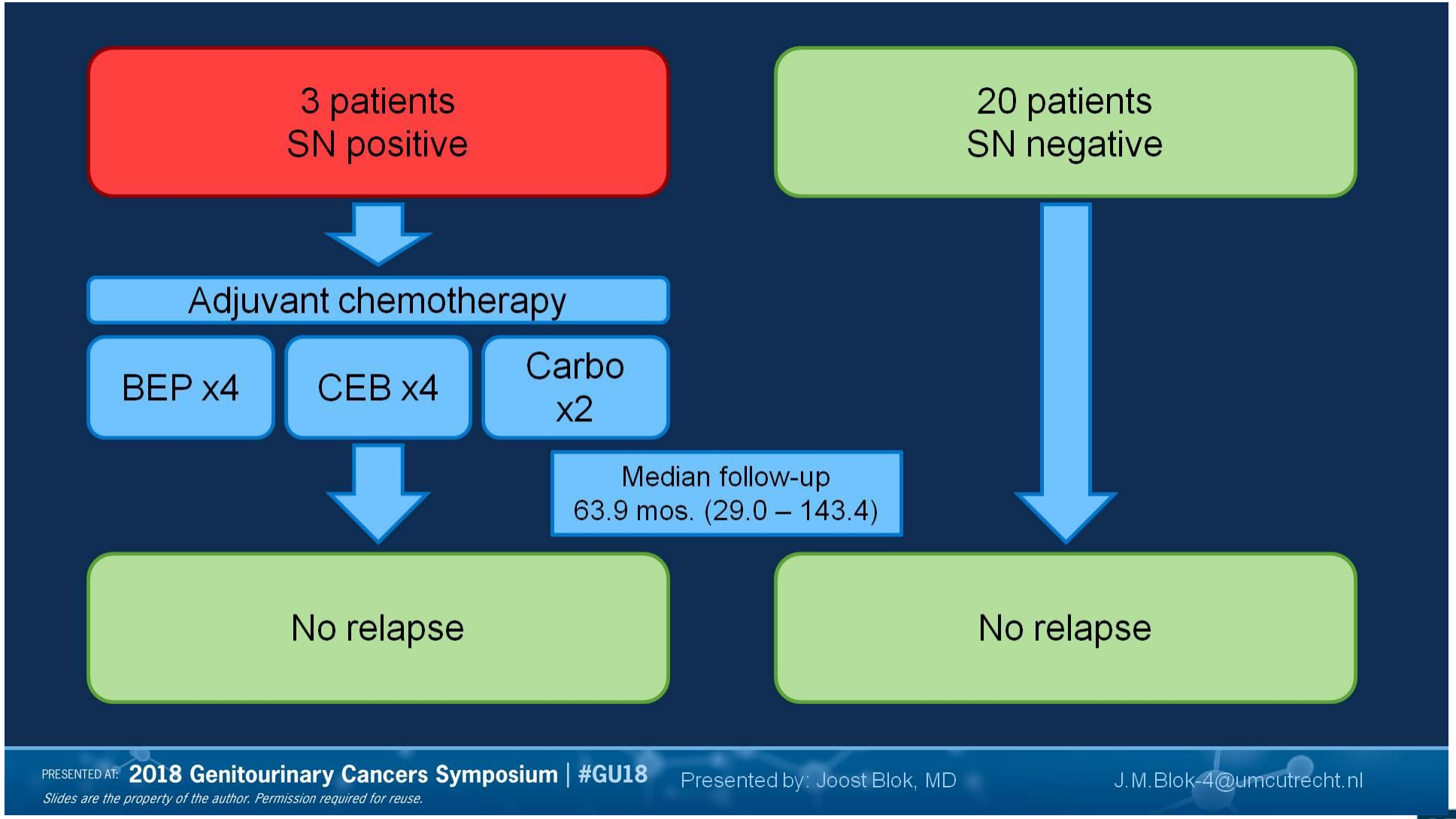


ana.garcia@einstein.br

Follow-up results

PRESENTED AT: 2018 Genitourinary Cancers Symposium | #GU18

Presented by: Joost Blok, MD J.M.Blok-4@umcutrecht.nl



ana.garcia@einstein.br

Take-home messages

- SN makes early identification of patients with occult metastatic disease possible
- Negative SN → no relapse (n=20)

Presented by: Joost Blok, MD J.M.Blok-4@umcutrecht.nl

ana.garcia@einstein.br

Adjusted treatment?

- SN negative: less intensive follow-up
- SN positive: less toxic treatment, at an early stage

Presented by: Joost Blok, MD J.M.Blok-4@umcutrecht.nl

However…

- Additional invasive procedure
  - Additional risk of complications
- ‘Unnecessary’ in some patients

Presented by: Joost Blok, MD J.M.Blok-4@umcutrecht.nl

SENATOR Study

- **SE**ntinal lymph **N**ode procedure in testicul**A**r germ cell **T**um**O**u**R**
- 76 patients
- Netherlands Cancer Institute and University Medical Center Utrecht
- Aim: investigate whether SN negative patients will experience relapse

Presented by: Joost Blok, MD J.M.Blok-4@umcutrecht.nl

ana.garcia@einstein.br

Long-term sexual functioning in germ-cell tumor survivors

Chovanec M, Vasilkova L, Setteyova L, Obertova J, Palacka P, Rejlekova K, Sycova-Mila Z, Kalavska K, Svetlovska D, Mladosievicova B, Mardiak J, Mego M

Faculty of Medicine, Comenius University in Bratislava
National Cancer Institute of Slovakia

PRESENTED AT: 2018 Genitourinary Cancers Symposium | #GU18

Presented by: Michal Chovanec

ana.garcia@einstein.br

Background

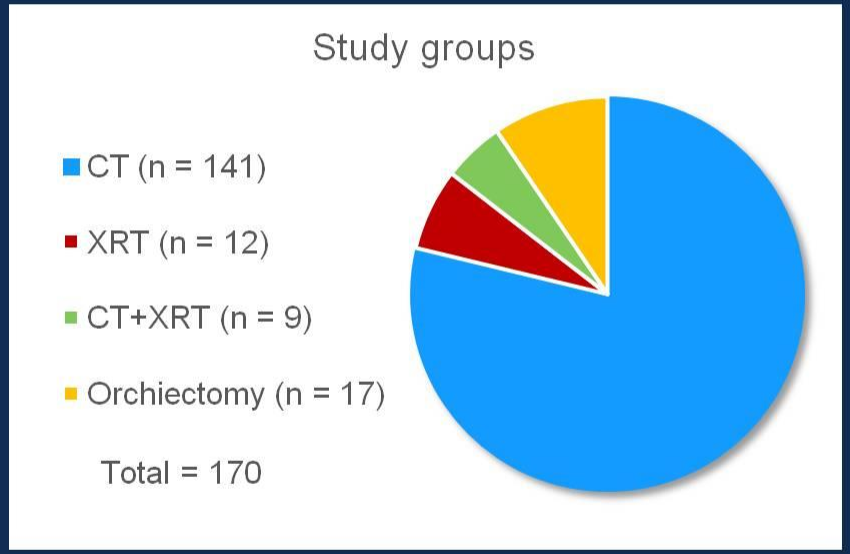
- Germ-cell tumors (GCTs) – curative Tx
- Late toxic treatment sequelae [1,2]
- Issues in quality of life
- Self reported outcomes – important in cancer care [3]

[1] Haugnes HS et al. J Clin Oncolo 2012, 30: 3752–3763
[2] Travis LB et al. J Natl Cancer Inst, 2010,102: 1114–1130
[3] Basch EM et al. J Clin Oncol, 2017, 35 (suppl; abstr LBA2)

ana.garcia@einstein.br

Study design and participants

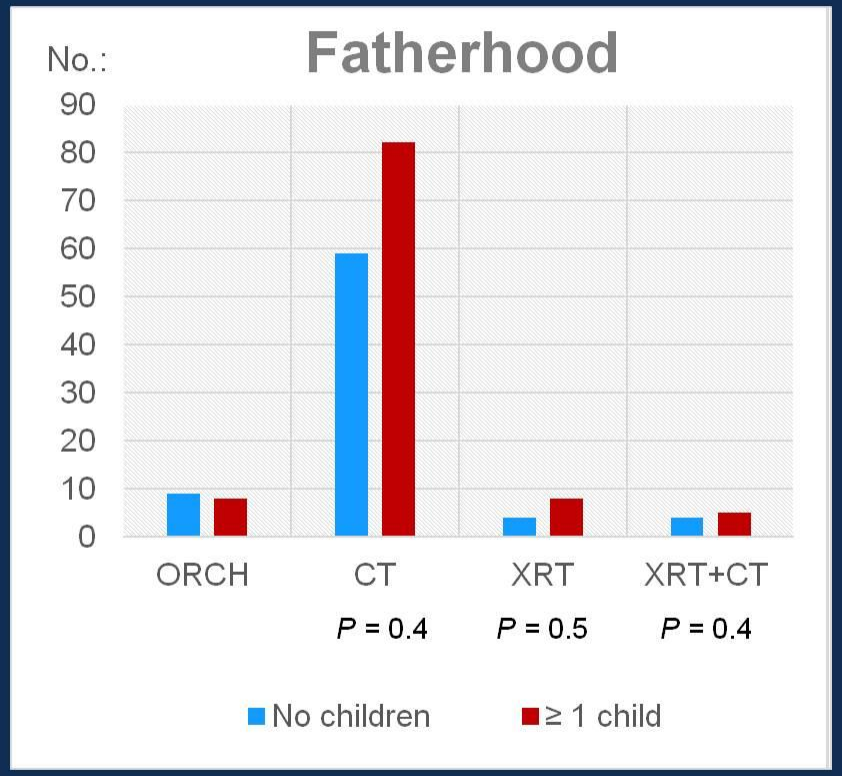
- Prospective study
- GCT survivors > 5 years after Tx (n=170)
- Median follow up – 10 yrs
- PROMIS modified sexual function questionnaire



ana.garcia@einstein.br

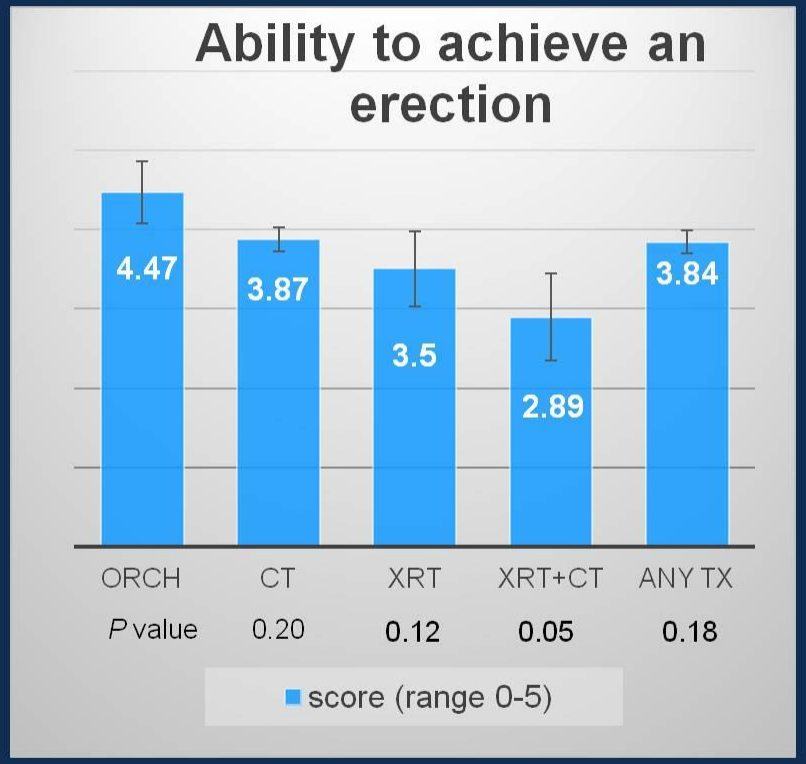
Education, job, marital status and fatherhood

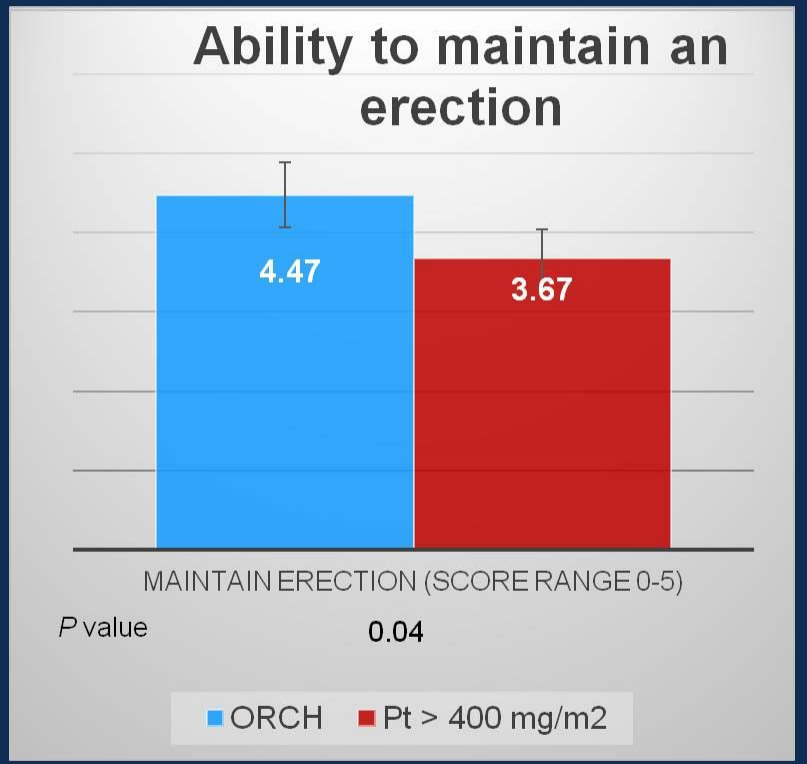
- No differences between study groups
- All $P > 0.05$



ana.garcia@einstein.br

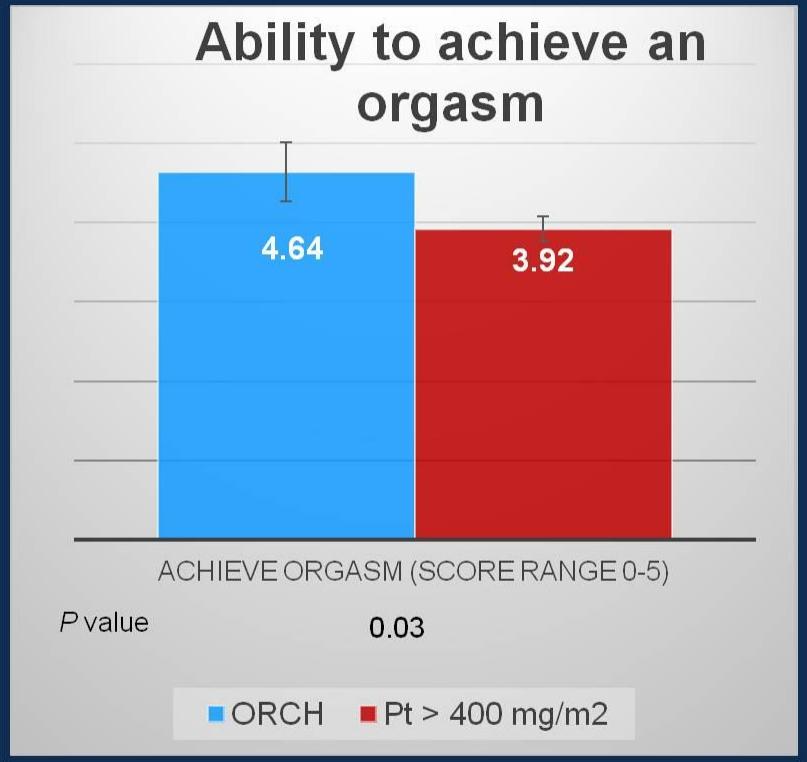
Results

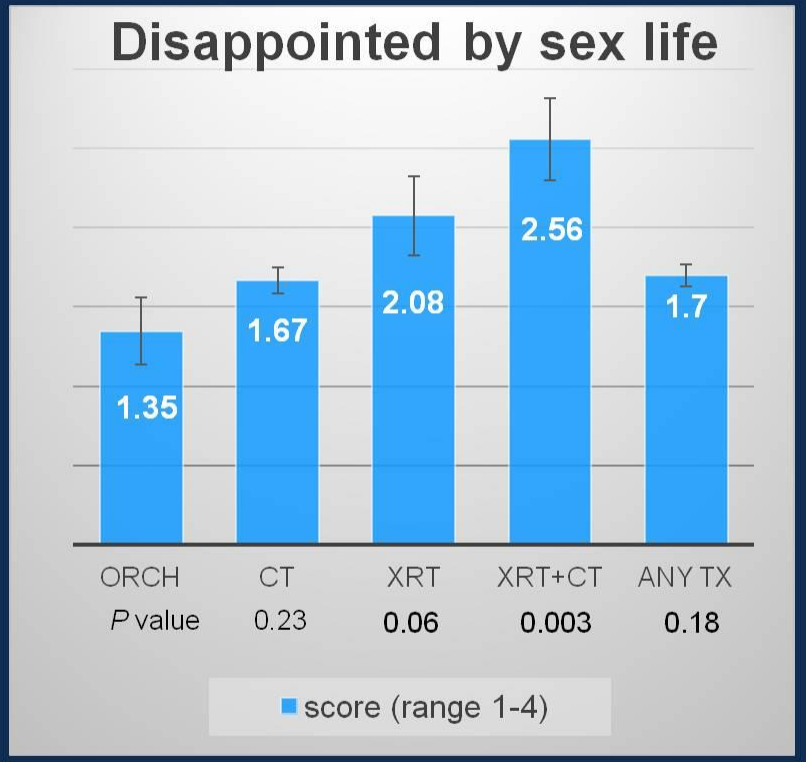




ana.garcia@einstein.br

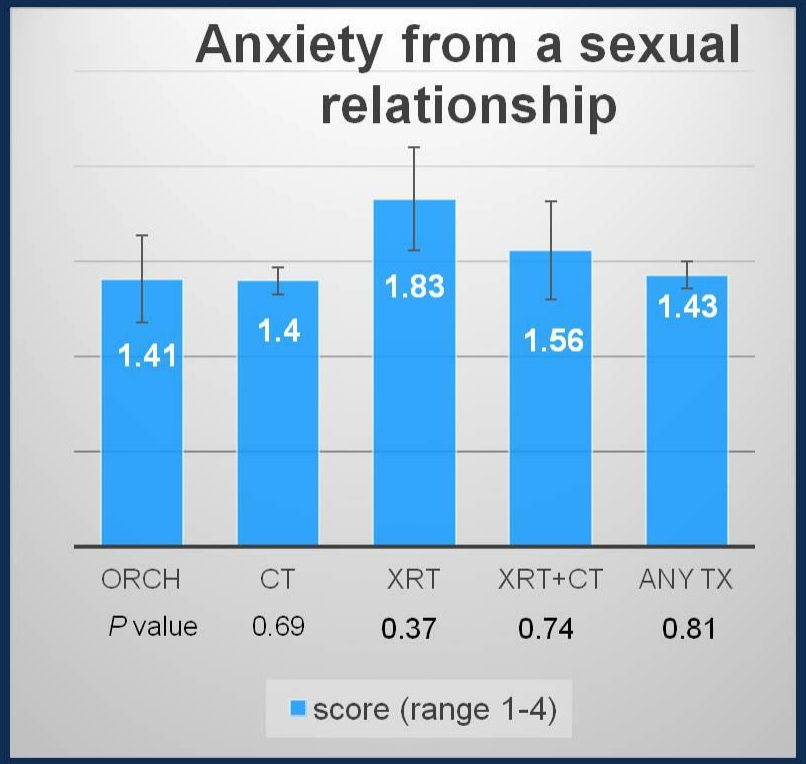
Results

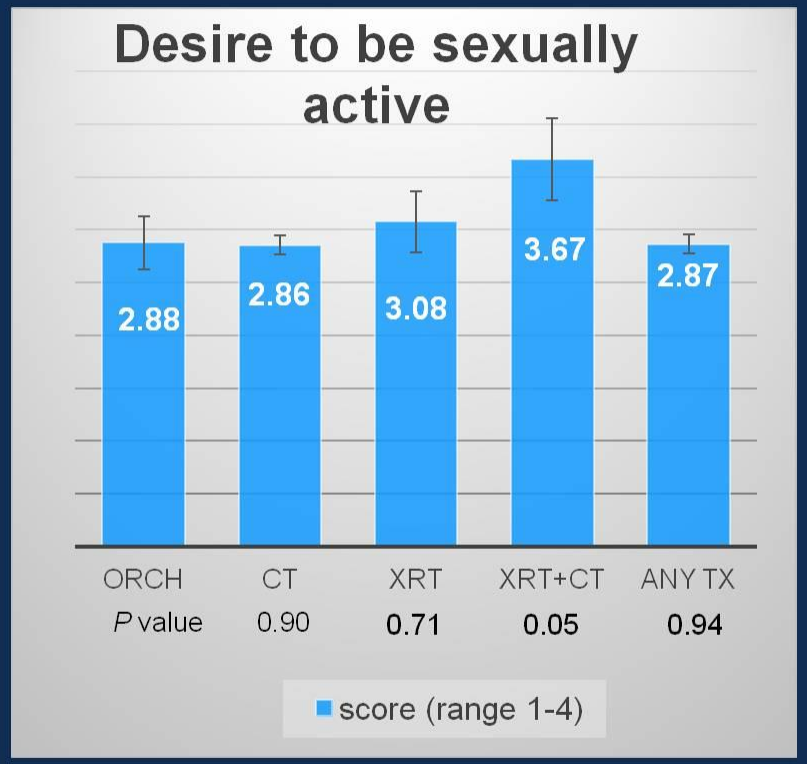




ana.garcia@einstein.br

Results





ana.garcia@einstein.br

Results

- Serious to severe impairment:
- 10 – 33 % of all survivors

ana.garcia@einstein.br

Variable	Testosterone (ng/mL)	N	Mean	SEM	Median	*P* value
Sexual desire	< 300	102	3.2	0.08	3	0.15
	> 300	22	2.9	0.19	3	
Attempts to initiate intercourse	< 300	102	2.4	0.15	2	0.41
	> 300	22	2.1	0.34	2	
Achieve erection	< 300	102	4.1	0.17	5	0.21
	> 300	22	3.5	0.36	5	
Maintain erection	< 300	102	4.0	0.16	5	**0.02**
	> 300	22	3.0	0.35	4	
Achieve orgasm	< 300	101	4.3	0.14	5	0.58
	> 300	21	4	0.31	5	
Disappointed with quality of sex life	< 300	101	1.7	0.09	1	0.88
	> 300	21	1.6	0.20	1	
Anxiety from sexual relationships	< 300	101	1.4	0.08	1	0.07
	> 300	21	1.8	0.18	1	

ana.garcia@einstein.br

Limitations

- Small numbers in some groups
- XRT and XRT+CT: need validation in a large cohort

ana.garcia@einstein.br

Conclusions

- Sexual functioning - serious issue in GCT srvs
- The highest risk
  - XRT
  - XRT+CT
  - cumulative Pt > 400 mg/m^2
- Sexual impairment – independent of low testosterone levels

ana.garcia@einstein.br

PÓS ASCO GU 2018
Testicular C^ncer
ANA PAULA GARCIA CARDOSO
HOSPITAL ISRAELITA ALBERT EINSTEIN

CONCLUSÃO

Estudos geradores de hipóteses, nenhum ”practice changing”:

1- Manejo de massas residuais pós quimioterapia

- Abstract 546- Serum miRNA to predict post-chemotherapy viable disease in testicular non-seminomatous germ cell tumor patients.

2- Biópsia de LN sentinela como ferramenta de seleção de pacientes ECI q vão receber tratamento adjuvante ou definir melhor o seguimento desses pacientes, inclusive sobre a frequência de exames de imagem que vão realizar

- Abstract 550- Sentinel node biopsy in clinical stage I testicular cancer;

3- Toxicidade a longo prazo – importância da disfunção sexual na qualidade de vida de pacientes sobreviventes ao pacientes sobreviventes ao tratamento de câncer de testículo

- Abstract 549- Long-term sexual functioning in germ-cell tumor survivors;

ana.garcia@einstein.br

IX Congresso Internacional de Uro-Oncologia
1 a 3 de Março de 2018


IX Congresso Internacional de
Uro-Oncologia
IV SIMPÓSIO MULTIPROFISSIONAL DE URO-ONCOLOGIA
1 a 3 de Março de 2018
SHERATON SÃO PAULO WTC HOTEL
OBRIGADA!
ALBERT EINSTEIN
HOSPITAL ISRAELITA
ONCOLOGIA E HEMATOLOGIA