SUM
Sociedad Urológica Madrileña

Hospital Universitario La Paz
Hospital de Cantoblanco
Hospital Carlos III
SaludMadrid
Comunidad de Madrid

CÁNCER DE PRÓSTATA LOCALIZADO DE ALTO RIESGO: CIRUGÍA VS RADIOTERAPIA

APALUTAMIDA NEOADYUVANTE

I REUNIÓN MULTIDISCIPLINAR EN URO – ONCOLOGÍA PARA RESIDENTES

21 de noviembre de 2023

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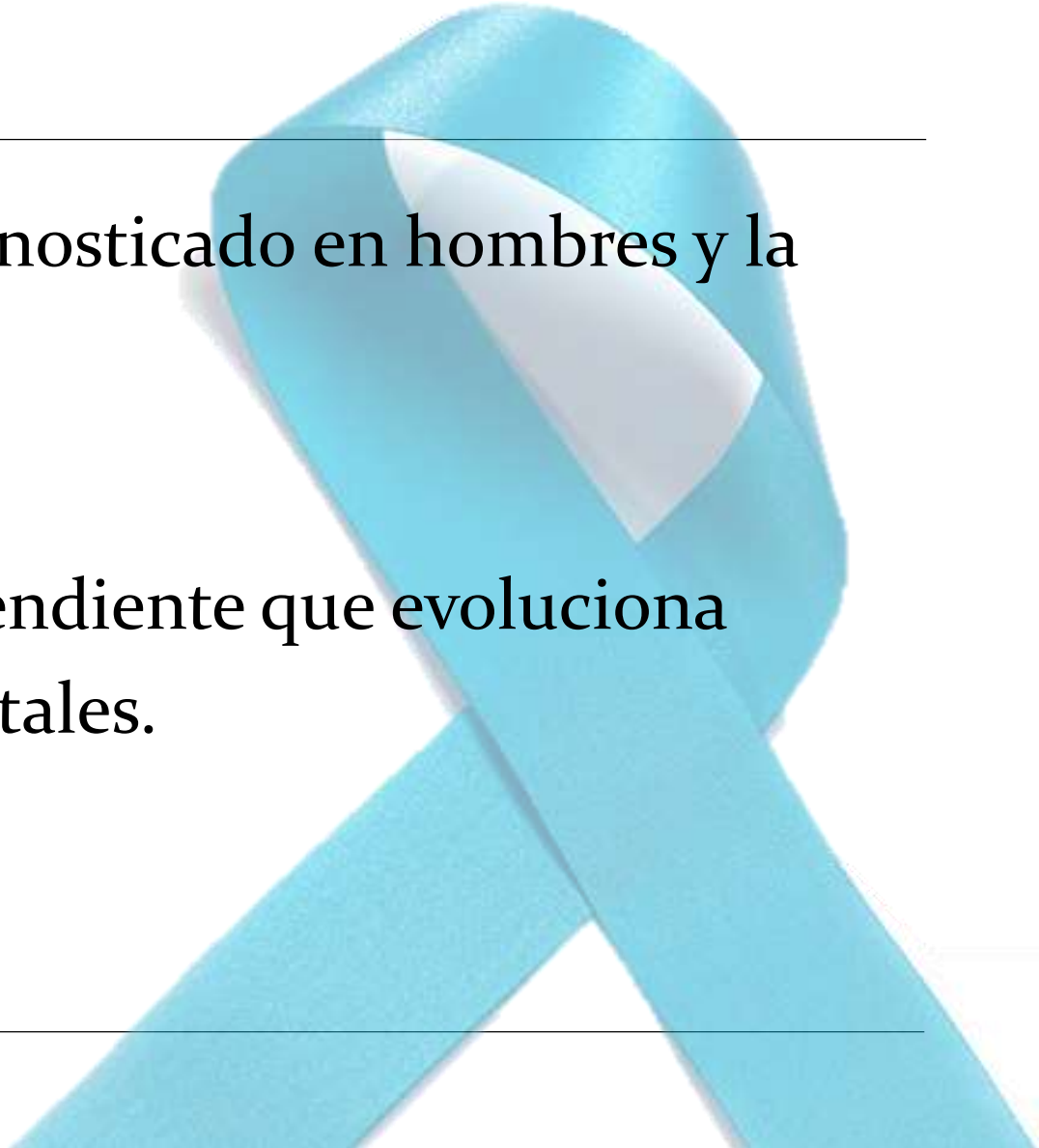
INTRODUCCIÓN

El cáncer de próstata es el tumor más diagnosticado en hombres y la segunda causa de muerte por cáncer.

Enfermedad heterogénea hormono – dependiente que evoluciona desde patrones indolentes hasta formas letales.



GRUPOS DE RIESGO

Definition			
Low-risk	**Intermediate-risk**	**High-risk**	
PSA < 10 ng/mL and GS < 7 (ISUP grade 1) and cT1-2a*	PSA 10–20 ng/mL or GS 7 (ISUP grade 2/3) or cT2b*	PSA > 20 ng/mL or GS > 7 (ISUP grade 4/5) or cT2c*	any PSA any GS (any ISUP grade)* cT3-4* or cN+**
Localised			**Locally advanced**

GS = Gleason score; ISUP = International Society of U… …specific antigen.

** Based on digital rectal examination.*

*** Based on CT/bone scan.*

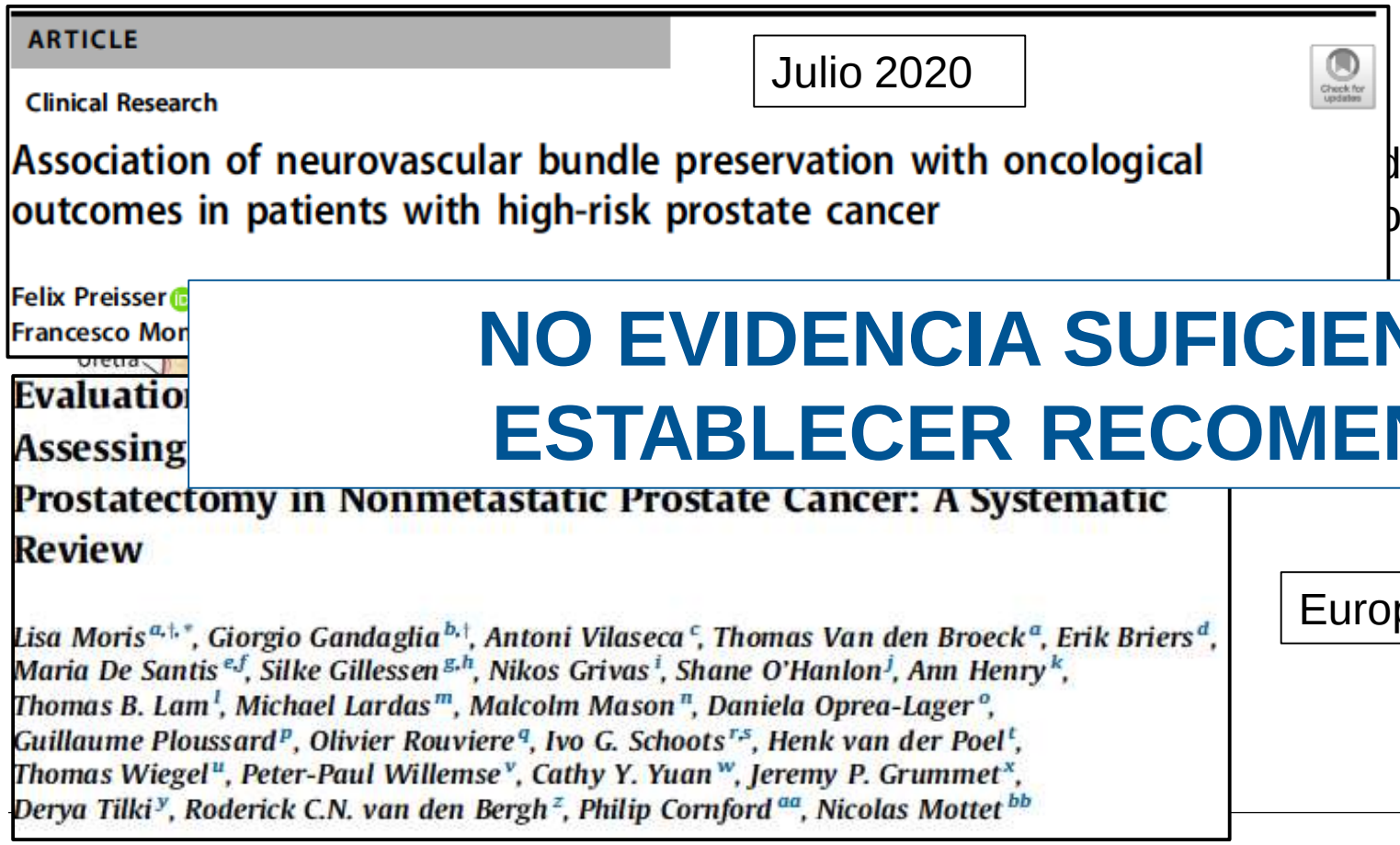
WW
RADIOTERAPIA + ADT$_{2-3\ a}$
PR + LDNe

CaP LOCALIZADO DE ALTO RIESGO: cirugía

Recommendations	Strength rating
Radical prostatectomy (RP)	
Radical prostatectomy can be safely delayed for at least 3 months.	Weak
Offer RP to selected patients as part of potential multi-modal therapy.	Strong
Extended pelvic lymph node dissection (ePLND)	
Perform an ePLND in high-risk PCa.	Strong
Do not perform a frozen section of nodes during RP to decide whether to proceed with, or abandon, the procedure (see Section 6.2.4.1).	Strong

Hasta 3 meses desde el diagnóstico.

CIRUGÍA: PROSTATECTOMÍA RADICAL



ARTICLE

Clinical Research

Julio 2020

Association of neurovascular bundle preservation with oncological outcomes in patients with high-risk prostate cancer

Felix Preisser
Francesco Mor

Evaluatio
Assessing
Prostatectomy in Nonmetastatic Prostate Cancer: A Systematic Review

Lisa Moris[a,†,*], Giorgio Gandaglia[b,†], Antoni Vilaseca[c], Thomas Van den Broeck[a], Erik Briers[d], Maria De Santis[e,f], Silke Gillessen[g,h], Nikos Grivas[i], Shane O'Hanlon[j], Ann Henry[k], Thomas B. Lam[l], Michael Lardas[m], Malcolm Mason[n], Daniela Oprea-Lager[o], Guillaume Ploussard[p], Olivier Rouviere[q], Ivo G. Schoots[r,s], Henk van der Poel[t], Thomas Wiegel[u], Peter-Paul Willemse[v], Cathy Y. Yuan[w], Jeremy P. Grummet[x], Derya Tilki[y], Roderick C.N. van den Bergh[z], Philip Cornford[aa], Nicolas Mottet[bb]

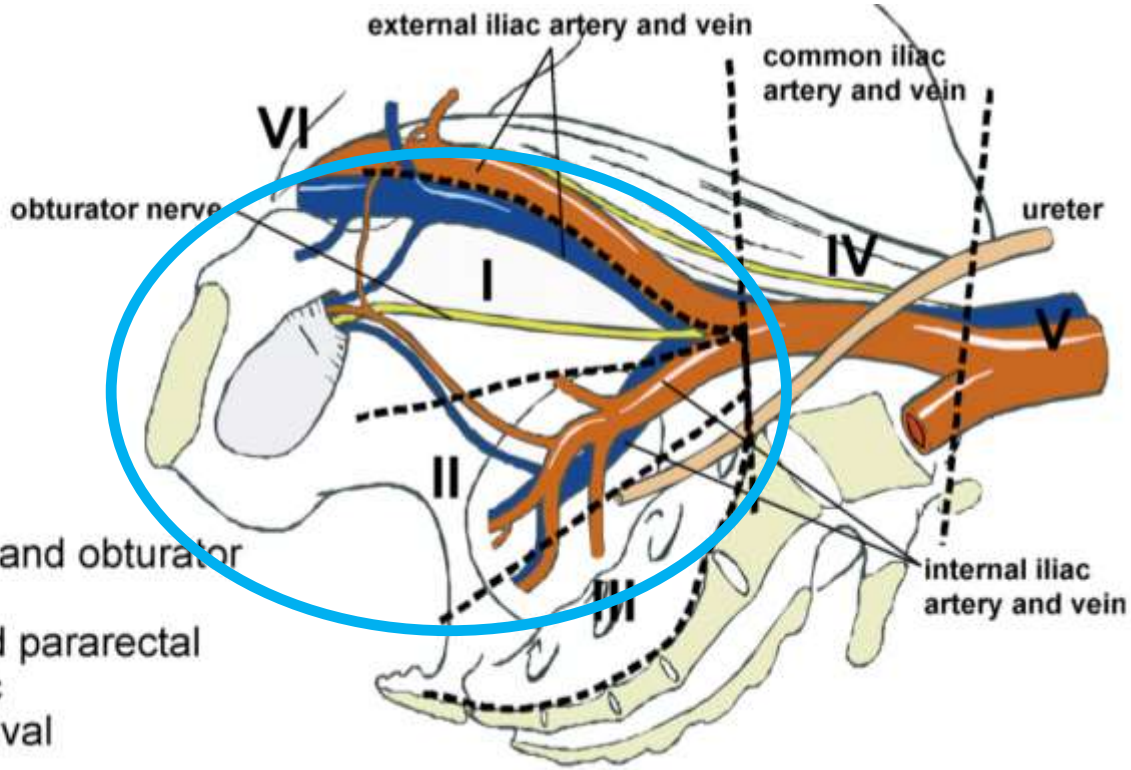
dajes: mismos resultados oncológicos y
onales.

NO EVIDENCIA SUFICIENTE PARA ESTABLECER RECOMENDACIÓN

European Urology Mayo 2021

CIRUGÍA: LINFADENECTOMÍA

La linfadenectomía es “gold estándar” para la estadificación, pero no influye en supervivencia global ni cáncer específica.



I = external iliac and obturator
II = internal iliac
III = presacral and pararectal
IV = common iliac
V = paraaortic/caval
VI = inguinal


¿CIRUGÍA O RADIOTERAPIA?

Survival after Radical Prostatectomy versus Radiation Therapy in High-Risk and Very High-Risk Prostate Cancer

Febrero 2022

Francesco Chierigo,[1,2,*] Mike Wenzel,[2,3] Christoph Würnschimmel,[2,4] Rocco Simone Flammia,[2,5] Benedikt Horlemann,[2] Zhe Tian,[2] Fred Saad,[2] Felix K. H. Chun,[3] Markus Graefen,[4] Michele Gallucci,[5] Shahrokh F. Shariat,[6-11] Guglielmo Mantica,[1] Marco Borghesi,[1] Nazareno Suardi,[1] Carlo Terrone[1] and Pierre I. Karakiewicz[2]

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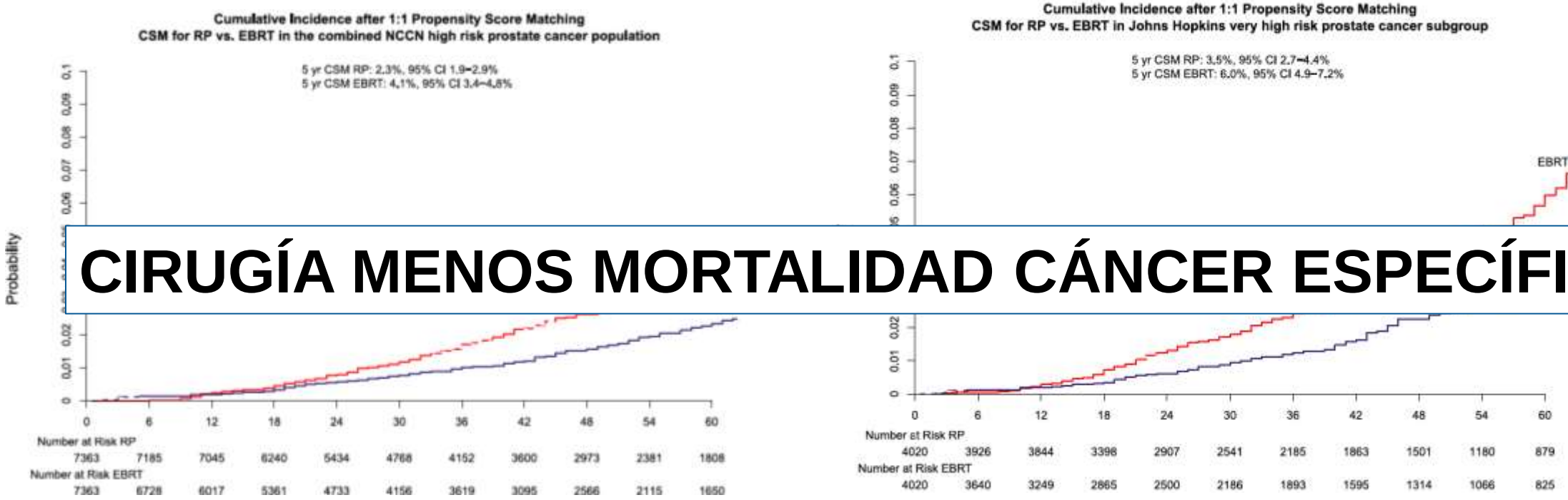
Revisión sistemática. n = 24 407 pacientes: 40% PR y 60% EBRT



CIRUGÍA MENOS MORTALIDAD CÁNCER ESPECÍFICA

International Urology and Nephrology (2022) 54:81–87
https://doi.org/10.1007/s11255-021-03055-7

UROLOGY - ORIGINAL PAPER

Cancer-specific mortality after radical prostatectomy vs external beam radiotherapy in high-risk Hispanic/Latino prostate cancer patients

Benedikt Hoeh[1,2] · Jan L. Hohenhorst[2,3] · Rocco Flammia[2,4] · Benedikt Horlemann[2] · Gabriele Sorce[2,5] · Francesco Chierigo[2,6] · Zhe Tian[2] · Fred Saad[2] · Markus Graefen[3] · Michele Gallucci[4] · Alberto Briganti[5] · Carlo Terrone[6] · Shahrokh F. Shariat[7,8,9,10,11,12] · Luis A. Kluth[1] · Andreas Becker[1] · Felix K. H. Chun[1] · Pierre I. Karakiewicz[2]

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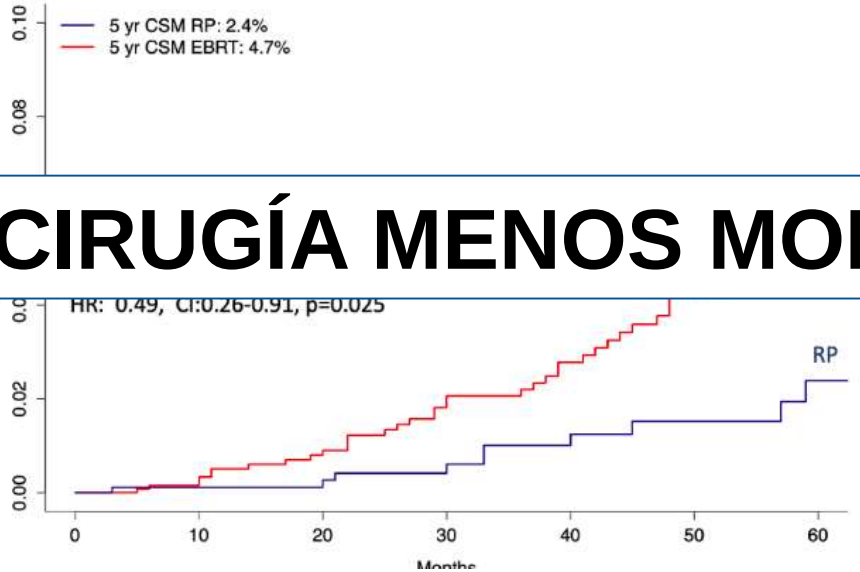
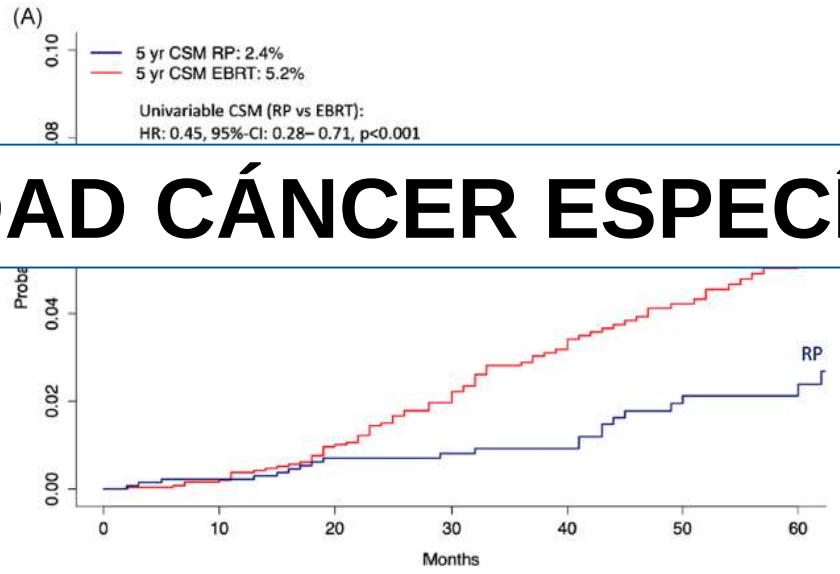


CIRUGÍA MENOS MORTALIDAD CÁNCER ESPECÍFICA

Cancer-specific survival after radical prostatectomy versus external beam radiotherapy in high-risk and very high-risk African American prostate cancer patients

Benedikt Hoeh MD[1,2] | Christoph Würnschimmel MD[2,3] | Rocco S. Flammia MD[2,4] | Benedikt Horlemann MD[2] | Gabriele Sorce MD[2,5] | Francesco Chierigo MD[2,6] | Zhe Tian MSc[2] | Fred Saad MD[2] | Markus Graefen MD[3] | Michele Gallucci MD[4] | Alberto Briganti MD[5] | Carlo Terrone MD[6] | Shahrokh F. Shariat MD[7,8,9,10,11,12] | Luis A. Kluth MD[1] | Philipp Mandel MD[1] | Felix K. H. Chun MD[1] | Pierre I. Karakiewicz MD[2]

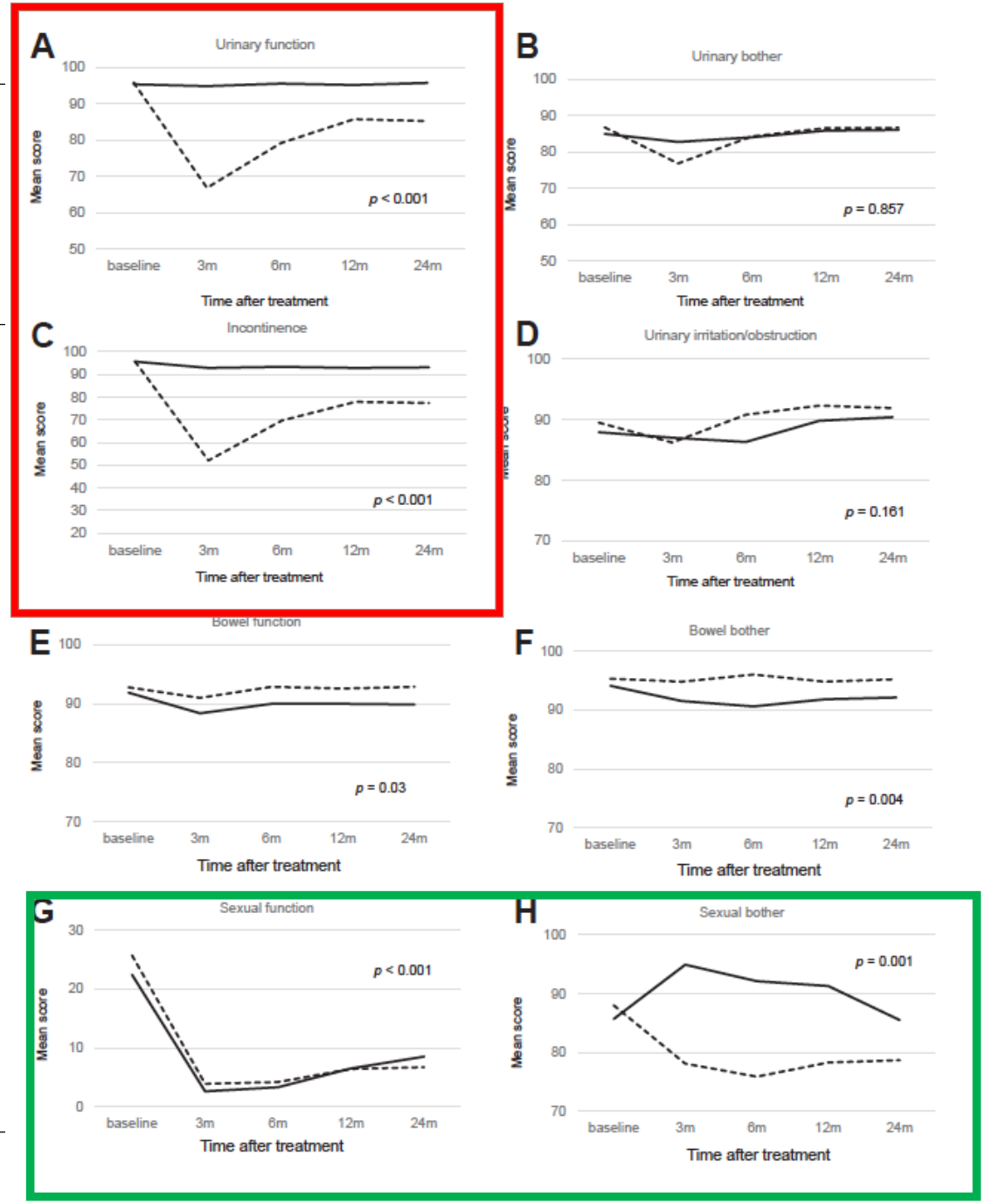


EFECTOS SECUNDARIOS

Oncology

Patient-perceived Satisfaction After Definitive Treatment for Men With High-risk Prostate Cancer: Radical Prostatectomy vs Intensity-modulated Radiotherapy With Androgen Deprivation Therapy

Shinya Yamamoto, Hitoshi Masuda, Shinji Urakami, Yasuhisa Fujii, Kimihiko Sakamoto, Takuyo Kozuka, Masahiko Oguchi, Iwao Fukui, and Junji Yonese



ELSEVIER

Urologic Oncology: Seminars and Original Investigations 37 (2019) 813.e11–813.e19

UROLOGIC ONCOLOGY

Clinical-Prostate cancer

Survival after radiotherapy vs. radical prostatectomy for unfavorable intermediate-risk prostate cancer

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Revisión sistemática. n = 10 439.

Compara CaP de riesgo intermedio tratado con PR, EBRT, BT y EBRT + BT.

No diferencias estadísticamente significativas entre grupos.

¿CIRUGÍA O RADIOTERAPIA?

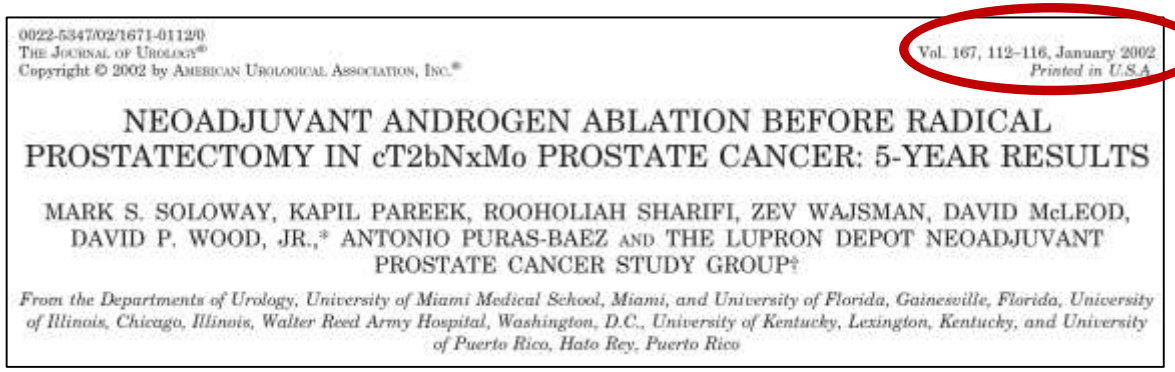
A DÍA DE HOY NO SE PUEDE ESTABLECER SUPERIORIDAD DE UNA SOBRE LA OTRA

NEOADYUVANCIA EN CÁNCER DE PRÓSTATA DE ALTO RIESGO

- 20 % de los cánceres de próstata localizados son de alto riesgo.
- ~ 50% tendrán recidiva bioquímica.
- 40 % de estos pacientes mueren de CaP (66% de las muertes en los primeros 10 años).

Neoadyuvancia ➡ OBJETIVO DUAL:

- Infraestadificación del tumor.
- Eliminar micrometástasis.



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NEOADJUVANT ANDROGEN ABLATION BEFORE RADICAL PROSTATECTOMY IN cT2bNxMo PROSTATE CANCER: 5-YEAR RESULTS

MARK S. SOLOWAY, KAPIL PAREEK, ROOHOLIAH SHARIFI, ZEV WAJSMAN, DAVID McLEOD, DAVID P. WOOD, JR.,* ANTONIO PURAS-BAEZ AND THE LUPRON DEPOT NEOADJUVANT PROSTATE CANCER STUDY GROUP†

From the Departments of Urology, University of Miami Medical School, Miami, and University of Florida, Gainesville, Florida, University of Illinois, Chicago, Illinois, Walter Reed Army Hospital, Washington, D.C., University of Kentucky, Lexington, Kentucky, and University of Puerto Rico, Hato Rey, Puerto Rico

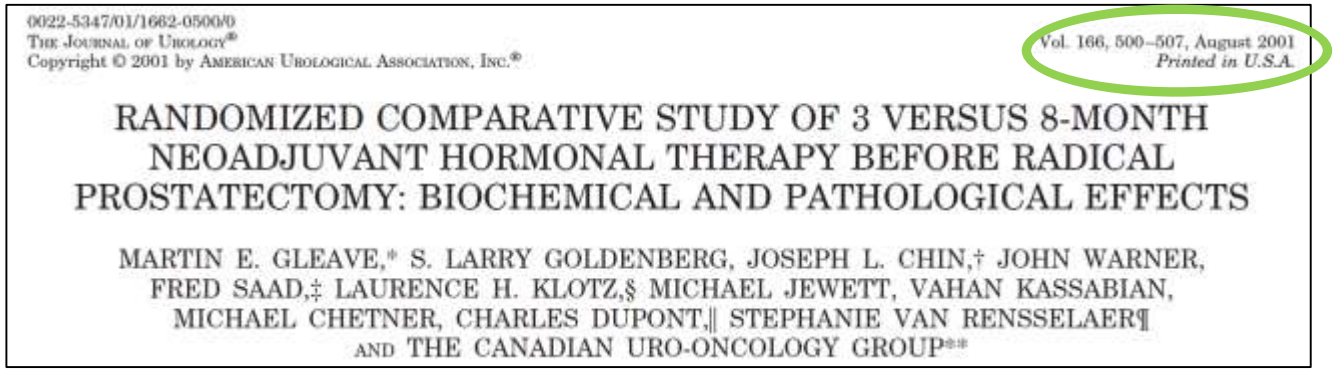
European Urology

Eur Urol 2000;38:706–713

Accepted after revision: June 2, 200

4-Year Follow-Up Results of a European Prospective Randomized Study on Neoadjuvant Hormonal Therapy prior to Radical Prostatectomy in T2–3N0M0 Prostate Cancer

Claude C. Schulman[a], Frans M.J. Debruyne[b], Gerhard Forster[c], Francesco P. Selvaggi[d], Alexandre R. Zlotta[a], Wim P.J. Witjes[b], for the European Study Group on Neoadjuvant Treatment of Prostate Cancer



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RANDOMIZED COMPARATIVE STUDY OF 3 VERSUS 8-MONTH NEOADJUVANT HORMONAL THERAPY BEFORE RADICAL PROSTATECTOMY: BIOCHEMICAL AND PATHOLOGICAL EFFECTS

MARTIN E. GLEAVE,* S. LARRY GOLDENBERG, JOSEPH L. CHIN,† JOHN WARNER, FRED SAAD,‡ LAURENCE H. KLOTZ,§ MICHAEL JEWETT, VAHAN KASSABIAN, MICHAEL CHETNER, CHARLES DUPONT,‖ STEPHANIE VAN RENSSELAER¶ AND THE CANADIAN URO-ONCOLOGY GROUP**

Agonistas LHRH/GnRH +/- Antiandrógenos 1ªG
3 – 8 meses

- Mejoría resultados quirúrgicos: ↓ R1, N+, pT3.
- No aumento de SUPERVIVENCIA.

¿Papel actual de la neoadyuvancia en la cirugía del cáncer de próstata de alto riesgo?

GUÍAS EUROPEAS 2023:

Surgical treatment	
Radical prostatectomy (RP) can be safely delayed for at least 3 months from diagnosis in any risk category.	Weak
Inform patients that no surgical approach (open-, laparoscopic- or robotic RP) has clearly shown superiority in terms of functional or oncological results.	Weak
When a lymph node dissection (LND) is deemed necessary based on a nomogram, perform an extended LND template for optimal staging.	Strong
Consider avoiding nerve-sparing surgery when there is a risk of ipsilateral extra-capsular extension (based on cT stage, ISUP grade, magnetic resonance imaging, or with this information combined in a nomogram).	Weak
Do not offer neoadjuvant androgen deprivation therapy before surgery.	Strong

EVIDENCIA: ENSAYOS CLÍNICOS CLÁSICOS VS ACTUALES

CLÁSICOS

- Periodos de seguimiento cortos.

- No evaluación sistémica de la respuesta patológica.

ACTUALES

Antiandrógenos 2ªG +/- Agonistas LHRH/GnRH

- Periodos de seguimiento largos.

- Evaluación sistémica de la respuesta patológica.

¿PODEMOS CURAR A ESTOS PACIENTES

NEAR

ARTICLE OPEN Prostate Cancer and Prostatic Diseases

Clinical Research

Enero 2022

NEAR trial: A single-arm phase II trial of neoadjuvant apalutamide monotherapy and radical prostatectomy in intermediate- and high-risk prostate cancer

Lui Shiong Lee[1,2,9,10]✉, Adelene Y. L. Sim[2,3,9], Chee Wee Ong[4,9], Xinyan Yang[4,9], Cedric C. Y. Ng[3], Wei Liu[3], Vikneswari Rajasegaran[3], Abner M. S. Lim[3], Edwin Jonathan Aslim[4], Nye-Thane Ngo[2,5], Li-Yan Khor[2,5], Ravindran Kanesvaran[2,6], John Carson Jr Allen[7], Kae Jack Tay[2,4], John Shyi Peng Yuen[2,4], Tsung Wen Chong[2,4], Sun Sien Henry Ho[2,4], Bin Tean Teh[2,3,10] and Melvin L. K. Chua[2,3,8,10]

Apalutamida oral 240 mg/día durante 12 semanas seguido de PRR +LDN.

n = 30 pacientes (20 alto riesgo y 10 intermedio).

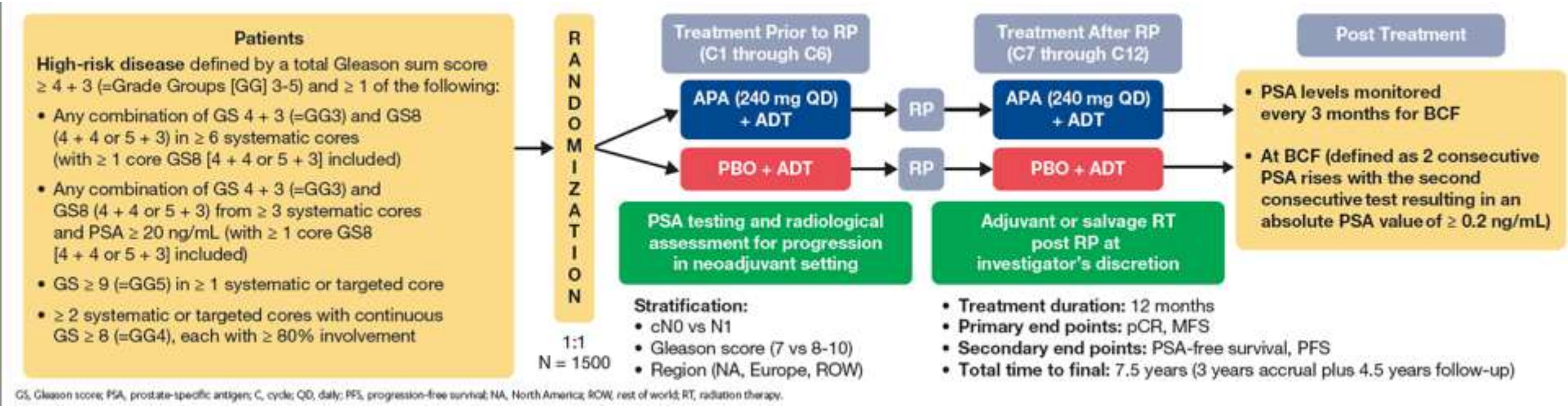
Objetivo principal: Respuesta patológica completa (↓ márgenes, N, pT) y respuesta bioquímica (PSA < 0,03 ng/mL).

Resultados:

25 pacientes cumplieron el tratamiento:

- **Ningún** paciente presentó respuesta patológica.
- 72% presentaron respuesta bioquímica.

PROTEUS


Patients
High-risk disease defined by a total Gleason sum score ≥ 4 + 3 (=Grade Groups [GG] 3-5) and ≥ 1 of the following:
• Any combination of GS 4 + 3 (=GG3) and GS8 (4 + 4 or 5 + 3) in ≥ 6 systematic cores (with ≥ 1 core GS8 [4 + 4 or 5 + 3] included)
• Any combination of GS 4 + 3 (=GG3) and GS8 (4 + 4 or 5 + 3) from ≥ 3 systematic cores and PSA ≥ 20 ng/mL (with ≥ 1 core GS8 [4 + 4 or 5 + 3] included)
• GS ≥ 9 (=GG5) in ≥ 1 systematic or targeted core
• ≥ 2 systematic or targeted cores with continuous GS ≥ 8 (=GG4), each with ≥ 80% involvement
RANDOMIZATION
1:1
N = 1500
Treatment Prior to RP (C1 through C6)
Treatment After RP (C7 through C12)
Post Treatment
APA (240 mg QD) + ADT
RP
APA (240 mg QD) + ADT
PBO + ADT
RP
PBO + ADT
• PSA levels monitored every 3 months for BCF
• At BCF (defined as 2 consecutive PSA rises with the second consecutive test resulting in an absolute PSA value of ≥ 0.2 ng/mL)
PSA testing and radiological assessment for progression in neoadjuvant setting
Adjuvant or salvage RT post RP at investigator's discretion
Stratification:
• cN0 vs N1
• Gleason score (7 vs 8-10)
• Region (NA, Europe, ROW)
• Treatment duration: 12 months
• Primary end points: pCR, MFS
• Secondary end points: PSA-free survival, PFS
• Total time to final: 7.5 years (3 years accrual plus 4.5 years follow-up)
GS, Gleason score; PSA, prostate-specific antigen; C, cycle; QD, daily; PFS, progression-free survival; NA, North America; ROW, rest of world; RT, radiation therapy.

Results of a Randomized Phase II Trial of Intense Androgen Deprivation Therapy prior to Radical Prostatectomy in Men with High-Risk Localized Prostate Cancer

Rana R. McKay,* Wanling Xie, Huihui Ye,† Fiona M. Fennessy, Zhenwei Zhang, Rosina Lis,† Carla Calagua, Dana Rathkopf,‡ Vincent P. Laudone, Glenn J. Bubley, David J. Einstein,§ Peter K. Chang, Andrew A. Wagner, J. Kellogg Parsons,|| Mark A. Preston, Kerry Kilbridge, Steven L. Chang, Atish D. Choudhury,¶ Mark M. Pomerantz, Quoc-Dien Trinh,** Adam S. Kibel†† and Mary-Ellen Taplin§§,‡‡

From the University of California San Diego (RRM, JKP), La Jolla, California, Dana-Farber Cancer Institute (WX, FMF, ZZ, RL, MAP, KK, SLC, ADC, MMP, QDT, ASK, MET), Boston, Massachusetts, University of California Los Angeles (HY, CC), Los Angeles, California, Memorial Sloan Kettering Cancer Center (DR, VPL), New York, New York, and Beth Israel Deaconess Medical Center (CC, GJB, DJE, PKC, AAW), Boston, Massachusetts

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Julio 2021

EC Fase 2
n = 118. CaP alto riesgo

→ Apa + Abi + Leuprolide

→ Abi + Leuprolide

Objetivo principal: Respuesta patológica completa y enfermedad mínima residual (tumor <5mm).

Resultados EMR + RPC: 22% Apa+Abi y 20% Abi.

Marcadores de presencia de tumor residual :

- Pérdida de PTEN.
- ERG positivo.
- Carcinoma intraductal.

CONCLUSIONES

Actualmente no existen datos que justifiquen el tratamiento neoadyuvante a la cirugía en pacientes con cáncer de próstata localizado de alto riesgo.

Ensayos clínicos con nuevos antiandrógenos son prometedores.

- ✓ Nuevas combinaciones: iPARP, terapia dirigida.
- ✓ Estratificación por biomarcadores.
- ✓ PSMA-PET como marcador de respuesta.

MUCHAS GRACIAS