

“Novedades en el manejo del cáncer de próstata de alto riesgo”

Visión crítica y Experiencia Clínica

Álvaro Juárez

COI

Integrar ciencia con una visión crítica y experiencia clínica

Soy Urólogo

Soy IP EC PROTEUS

CaP Localizado Alto Riesgo: TPA en monoterapia

High or very high risk 60%

ORIGINAL PAPER

UROLOGICAL ONCOLOGY

Androgen deprivation monotherapy usage in non-metastatic prostate cancer: results from eight European countries

Dionysios Mitropoulos¹, Piotr Chlost², Michael Häggman³, Torbjorn Ström⁴, Vyrion Markussis⁵

¹National and Kapodistrian University of Athens Medical School, 1st Department of Urology, Athens, Greece

²Jagiellonian University, Department of Urology, Cracow, Poland

³Uppsala University Hospital, Department of Urology, Uppsala, Sweden

⁴Ipsen Sweden, Medical Department, Stockholm, Sweden

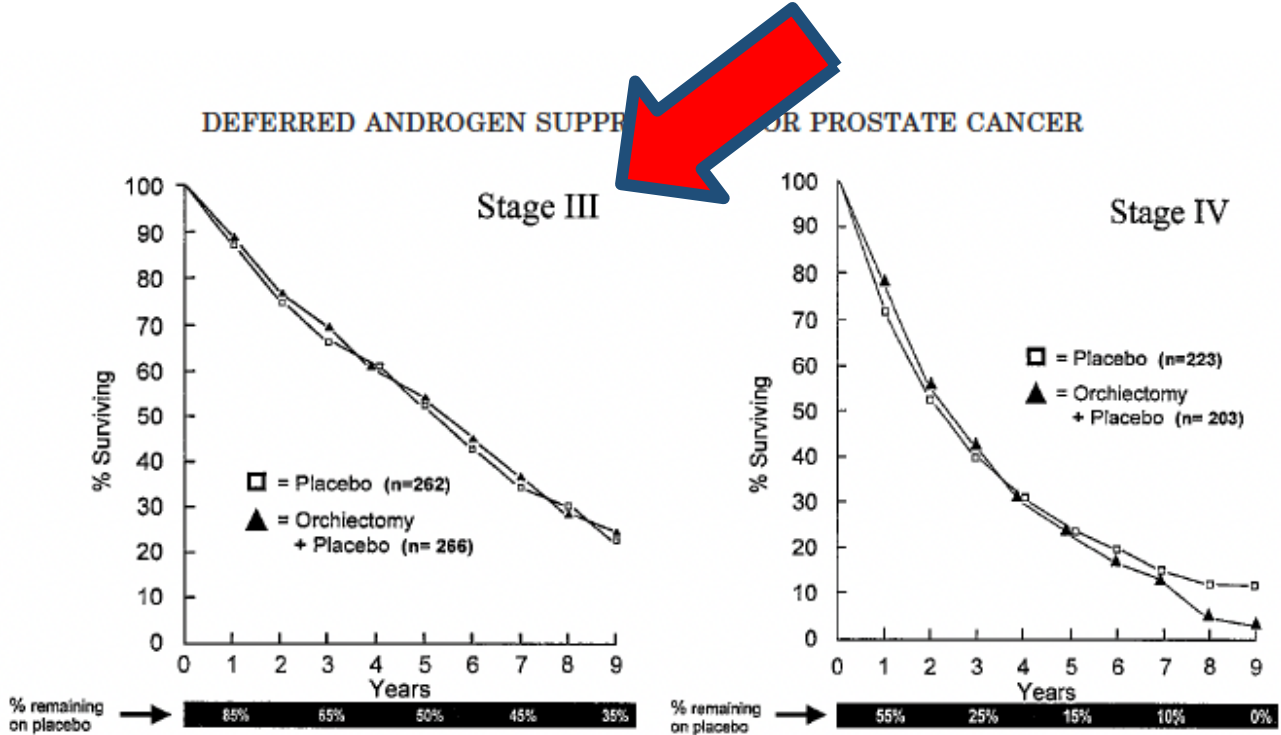
⁵Ipsen Greece, Medical Department, Athens, Greece

Citation: Mitropoulos D, Chlost P, Häggman M, Ström T, Markussis V. Androgen deprivation monotherapy usage in non-metastatic prostate cancer: results from eight European countries. Cent European J Urol. 2021; 74: 161-168.

THE VETERANS ADMINISTRATION
COOPERATIVE UROLOGICAL RESEARCH
GROUP'S STUDIES OF CANCER OF
THE PROSTATE

DAVID P. BYAR, MD*

510



TERAPIA
DE PRIVACIÓN
ANDROGÉNICA
SOLO?

FIG. 2. Overall survival of VACURG I patients with stages III (T3M0) and IV (M+) disease assigned to treatment with placebo or orchiectomy plus placebo.¹⁵ Reprinted with permission.

OBJETIVO DEL TRATAMIENTO

**“Reducir el riesgo de:
una progresión local y/o BCR y/o progresión M+”**

Control de la Enfermedad Local

Hindawi
Prostate Cancer
Volume 2018, Article ID 2654572, 7 pages
<https://doi.org/10.1155/2018/2654572>

Review Article

Local Treatment of Metastatic Prostate Cancer: What is the Evidence So Far?

Pedro Leonel Almeida and Bruno Jorge Pereira 

Faculdade de Ciências da Saúde, Universidade da Beira Interior (FCS-UBI), Covilhã, Portugal

La progresión local puede ocasionar invasión de estructuras adyacentes, produciendo dolor, invasión vejiga y recto, fístulas rectovesicales o rectouretrales e infiltración de los nervios pélvicos

MFS y OS

Systematic Review and Meta-analysis of the Survival Outcomes of First-line Treatment Options in High-risk Prostate Cancer

Jun H. Lei^{1*}, Liang R. Liu^{1*}, Qiang Wei¹, Shi B. Yan^{2*}, Tu R. Song¹, Fu S. Lin¹, Lu Yang¹, De H. Cao¹, Hai C. Yuan¹, Wen B. Xue¹, Xiao Lv¹, Ying C. Cai¹, Hao Zeng¹ & Ping Han¹

SCIENTIFIC REPORTS | 5 : 7713 | DOI: 10.1038/srep07713

El tratamiento del primario en el CaP localizado de alto riesgo tiene un impacto significativo en MFS y OS. PR resultó en mejores resultados en OS

BCR

“BCR por si misma no tiene significación clínica”

Lo relevante es su relación con la aparición de metástasis

Pacientes con BCR tienen una **biología diferente y más indolente** que los pacientes metastásicos (CPRC y CPHSm)

“RECIDIVA BIOQUÍMICA”

P.RADICAL ROBÓTICA

- CIRUGÍA MARZO 2022
- ADENOCA. DE PRÓSTATA G-7

EVOLUTIVO PSA:

- PSA POSTQUIRÚRGICO (mayo 22): $< 0,05$
- PSA 21-1-23: 0,2
- PSA 5-4-23: 0,18
- PSA 15-5-23: 0,21
- PSA 19-7-23: 0,27
- PSA 1-9-23: 0,31

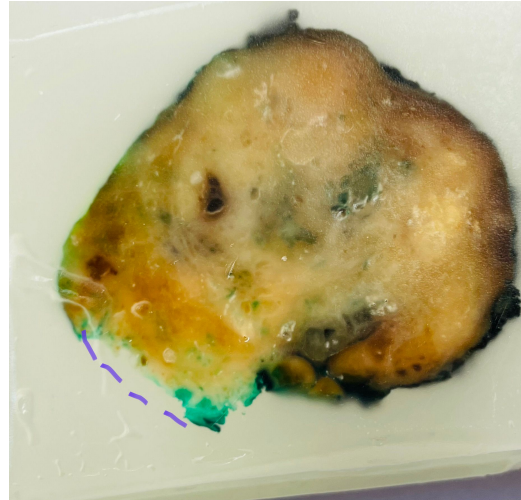
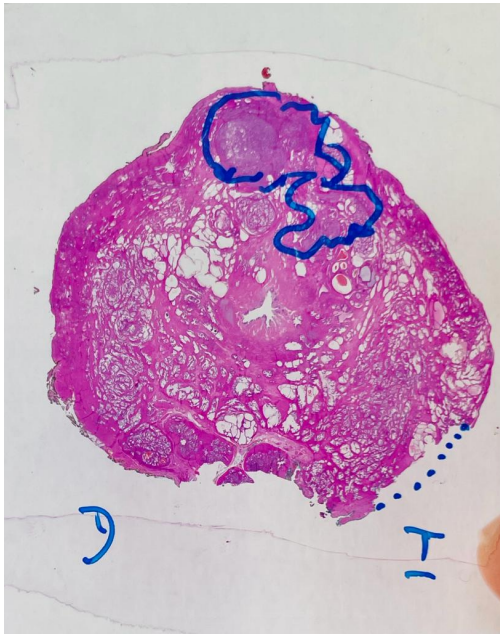
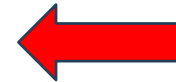
PSADT: 6,3 meses

BCR ALTO RIESGO

“FALSA RECIDIVA BIOQUÍMICA”

EVOLUTIVO PSA:

- PSA POSTQUIRÚRGICO (mayo 22): $< 0,05$
 - PSA 21-1-23: 0,2
 - PSA 5-4-23: 0,18
 - PSA 15-5-23: 0,21
 - PSA 19-7-23: 0,27
 - PSA 1-9-23: 0,31
 - **PSA 10-11-23 0,30**
- PSADT: 6,3 meses
- PSA 08-10-24 0,311
 - PSA 23-05-25 0,30



¿En que pacientes se ha estudiado la BCR?

Hasta el 53% de los pacientes que se les trata el primario tienen “RECIDIVA BIOQUÍMICA” (EAU Guidelines 2023)

La información disponible se basa en estudios retrospectivos y algún metaanálisis en los que:

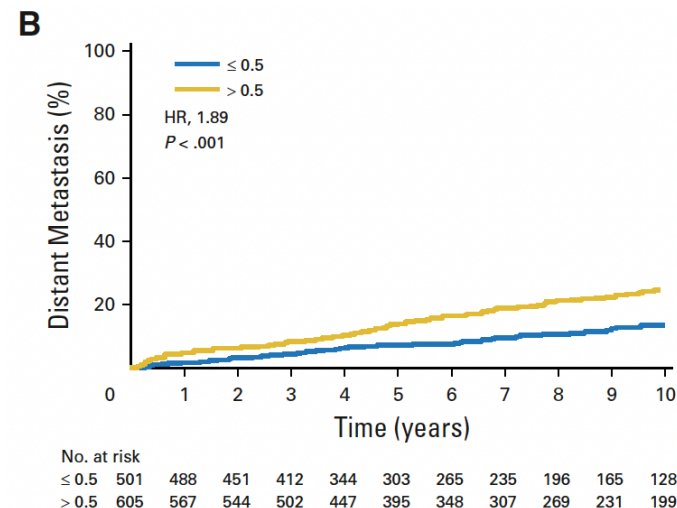
- **“pT” INEXACTA:** El diagnóstico de Cáncer de Próstata se sustenta en biopsias aleatorias (mala interpretación de la realidad oncológica de esa próstata)
- **“pN” AUSENTE O INEXACTA:** Linfadenectomías no “realizadas o limitadas”. NI TIPO DE LINFA, NI N° GANGLIOS, NI SI SE HACE O NO LINFA
- **“M” ausente o INEXACTA:** Pruebas de imágenes para el diagnóstico o seguimiento no realizadas o convencionales.

Linfadenectomía y BRC

Gleason score		
≤ 6	330	29.8
7	550	49.7
8	82	7.4
9-10	97	8.8
Missing	47	4.3

Pathologic nodal stage		
0	1,087	98.3
1	11	1.0
Missing	8	0.7

**1106 pacientes.
“node samples”**



**6% pN1 de los
pacientes con
Gleason 8-10**

VOLUME 34 • NUMBER 32 • NOVEMBER 10, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Improved Metastasis-Free and Survival Outcomes With Early Salvage Radiotherapy in Men With Detectable Prostate-Specific Antigen After Prostatectomy for Prostate Cancer

Bradley J. Stish, Thomas M. Pisansky, William S. Harmsen, Brian J. Davis, Katherine S. Tzou, Richard Choo, and Steven J. Buskirk



Hospitales Universitarios de Jerez y Punta de Europa

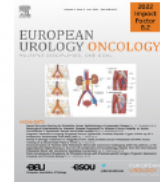
N=26	Edad media	PSA medio	cN1	Mediana N	pN1	<pISUP	RT adyuvante
	66 años (53-80)	18,34 (3,95-69,4)	4 Sólo 1=pN1	16 (9-42)	7 (26%) (+: 1-9)	N=11 (42%)	50%

Pacientes incluidos en sub-estudio PROTEUS

TERAPIA LOCAL EN cN1

EUROPEAN UROLOGY ONCOLOGY 7 (2024) 355–364

available at www.sciencedirect.com
journal homepage: eunoncology.europeanurology.com

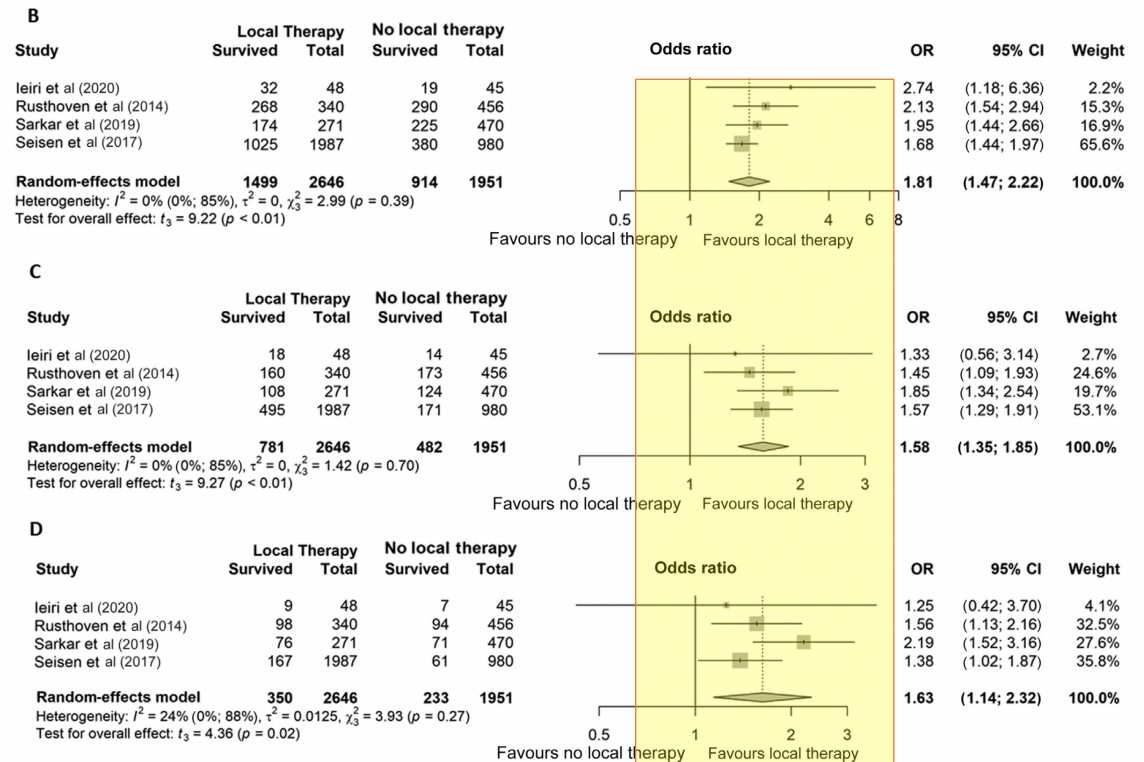


Local Therapy on Clinically Lymph Node–positive Prostate Cancer: A Systematic Review and Meta-analysis

Clyve Yu Leon Yaow^{a,†}, Han Jie Lee^{b,†}, Seth En Teoh^a, Ryan Ian Houe Chong^a, Tze Kiat Ng^b,
Kae Jack Tay^b, Henry Ho^b, Yan Mee Law^c, Jeffrey Tuan^d, John Yuen^b, Kenneth Chen^{b,*}

^aYong Loo Lin School of Medicine, National University of Singapore, Singapore; ^bDepartment of Urology, Singapore General Hospital, Singapore; ^cDepartment of Diagnostic Radiology, Singapore General Hospital, Singapore; ^dDepartment of Radiation Oncology, National Cancer Centre Singapore, Singapore

OS RATES AT 4,6 AND 8 YEARS



“The use of Local Therapy in Pca patients with cN1 disease leads to improved oncological outcomes compared with observation or ADT alone”

TERAPIA LOCAL EN cN1: PR vs RT

EUROPEAN UROLOGY ONCOLOGY 7 (2024) 355–364

available at www.sciencedirect.com
journal homepage: euoncology.europeanurology.com



Local Therapy on Clinically Lymph Node–positive Prostate Cancer: A Systematic Review and Meta-analysis

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^aYong Loo Lin School of Medicine, National University of Singapore, Singapore; ^bDepartment of Urology, Singapore General Hospital, Singapore; ^cDepartment of Diagnostic Radiology, Singapore General Hospital, Singapore; ^dDepartment of Radiation Oncology, National Cancer Centre Singapore, Singapore



OS RATES AT 4 AND 6 YEARS

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EUROPEAN UROLOGY ONCOLOGY 7 (2024) 355–364

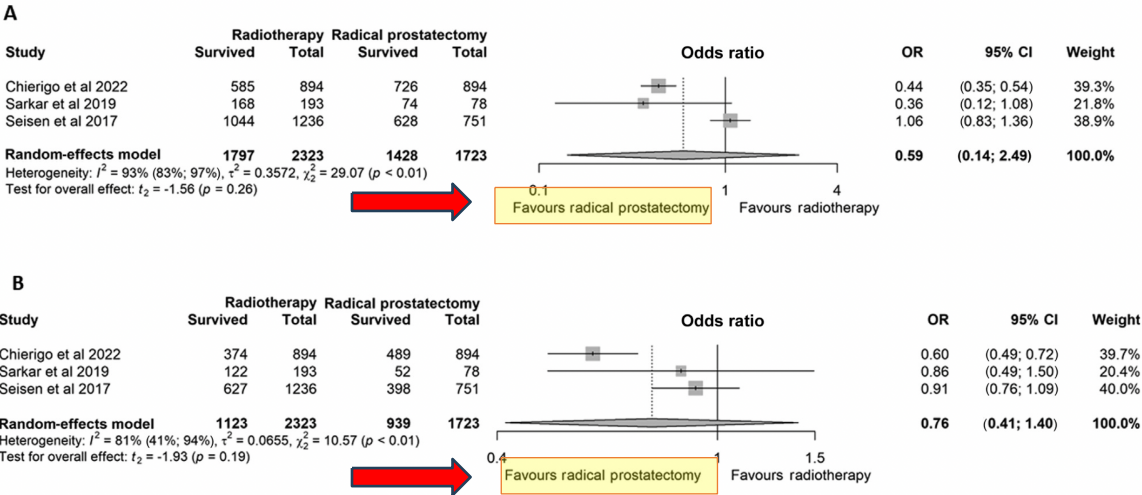


Fig. 4 – Radiotherapy versus radical prostatectomy; overall survival rates at (A) 2-yr and (B) 4-yr time points. CI = confidence interval; OR = odds ratio.

“no significant difference in OS between patients treated with RP ± ADT and RT ± ADT”

Linfadenectomía Extendida (LE) y BCR

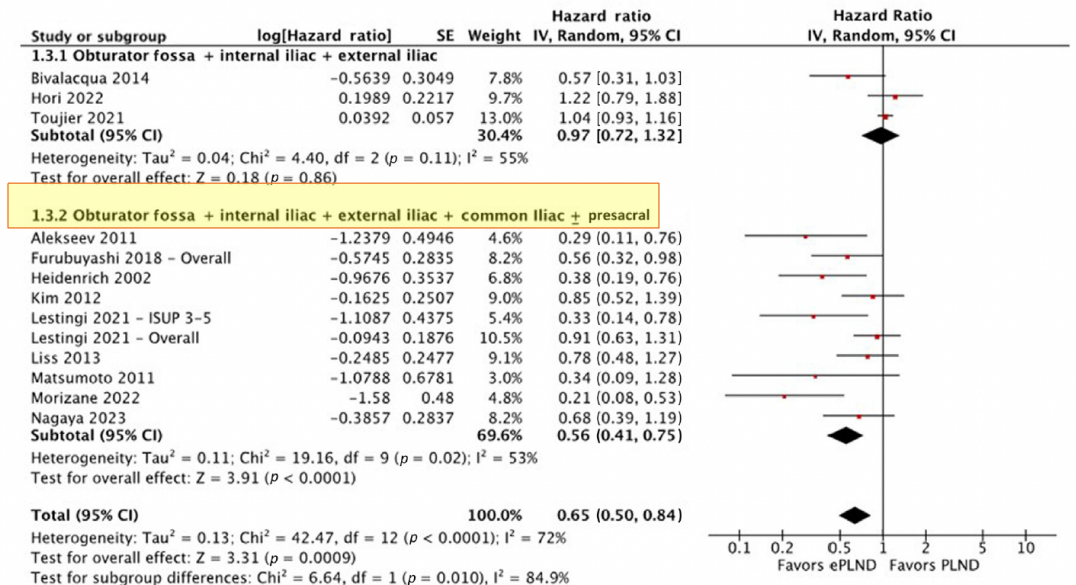


Fig. 3 – Forest plot for biochemical recurrence stratified by the extension of the extended dissection template. CI = confidence interval; ePLND = extended PLND; IV = inverse variance; PLND = pelvic lymph node dissection; SE = standard error.

- La LE tiene un 35% menos de riesgo de recidiva bioquímica que la estándar
- La probabilidad de N1 es mayor en los pacientes con LE (OR 3,44)

¿Cómo reducir el riesgo de una BCR Y/O progresión M+?

**Existe relación* entre linfadenectomía extendida y MFS,
pero no con BCR**

EAU24 | PARIS, FRANCE
5-8 April 2024

Pelvic Lymph Node Dissection in Prostate Cancer: Update of the Limited vs. Extended Randomized Clinical Trial.

Karim A. Touijer; Emily A. Vertosick; Daniel D. Sjoberg; Nicole Liso; Sunny Nalavenkata;
Barbara Melao; Vincent P. Laudone; Behfar Ehdaie; Brett Carver; James A. Eastham;

Peter T. Scardino; Andrew J. Vickers.

Memorial Sloan Kettering Cancer Center

*Tendencia, sin significación estadística

www.eau24.org

EAU European
Association
of Urology

Linfadenectomía Extendida (> 12 ganglios)

Received: 24 January 2023 | Revised: 6 June 2023 | Accepted: 15 June 2023
DOI: 10.1002/cam4.6292

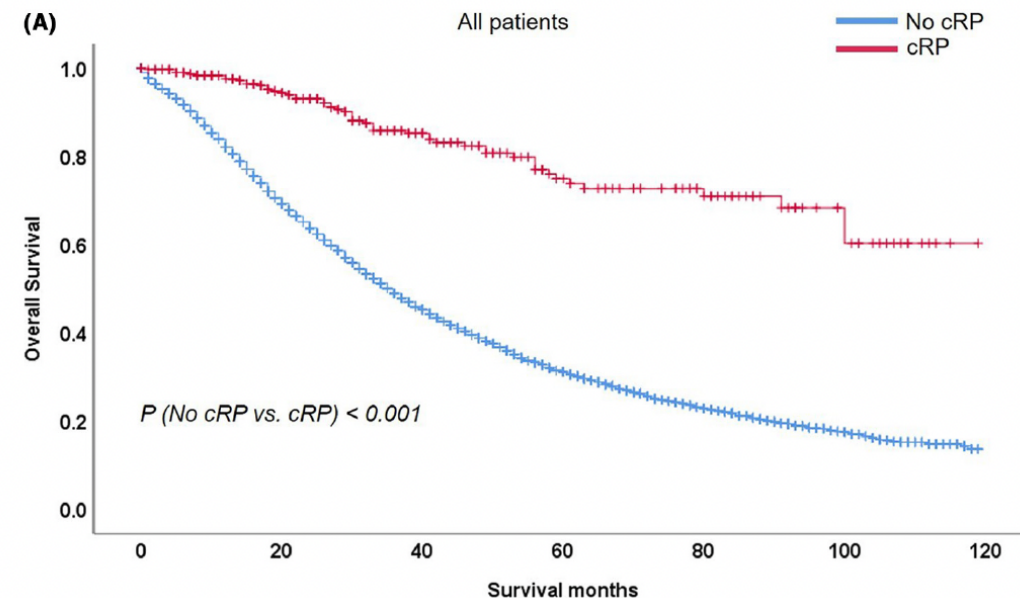
RESEARCH ARTICLE

Cancer Medicine WILEY

The role of cytoreductive radical prostatectomy and lymph node dissection in bone-metastatic prostate cancer: A population-based study

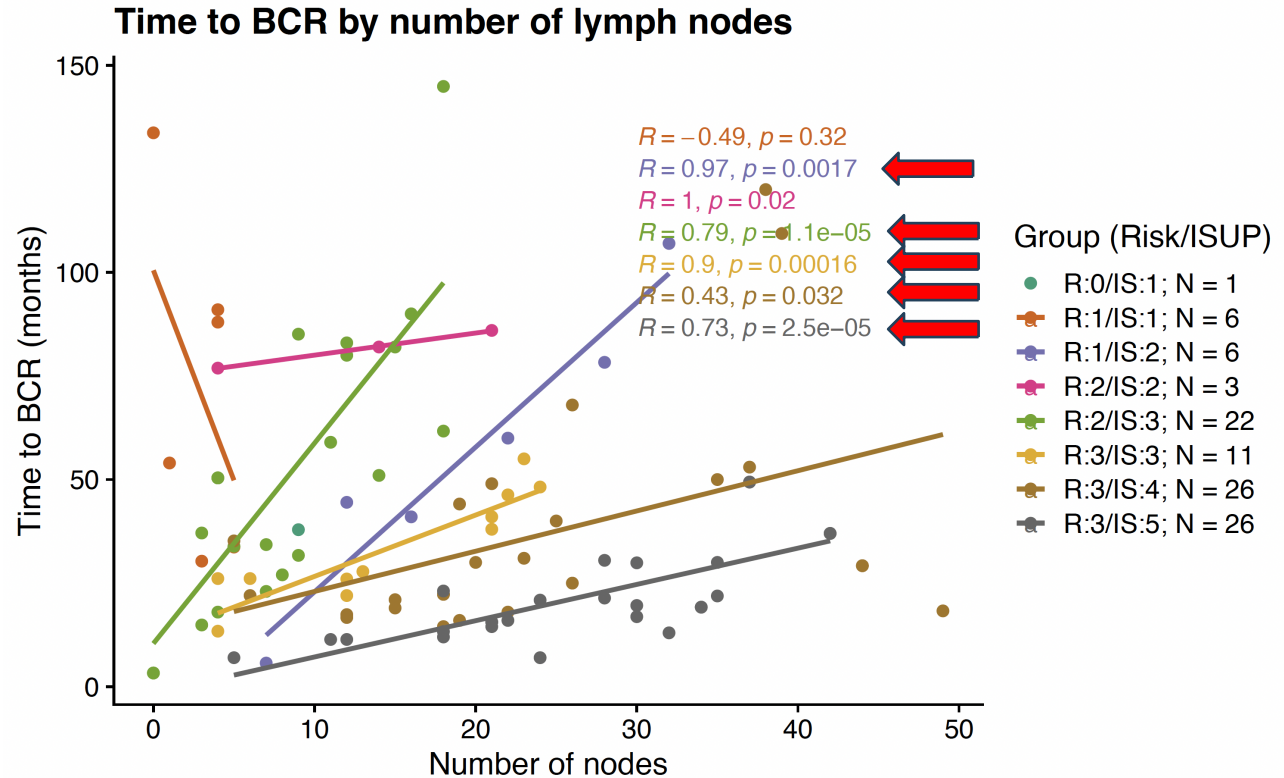
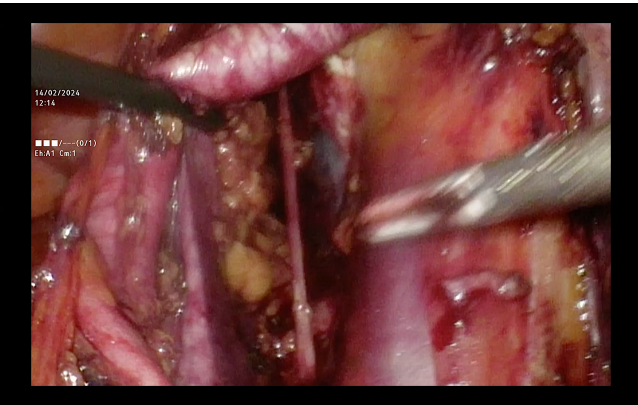
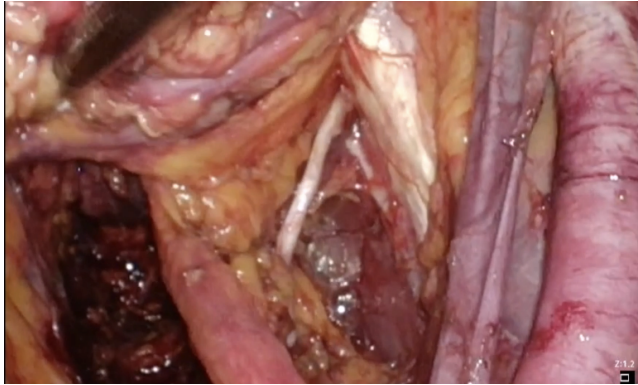
Tingshuai Zhai  | Jinliang Ma | Yi Liu | Haitao Li | Yanli Peng | Wenmin Guo | Jiedong Jia | Xiaolin Wu | Huanrong Jiang | Jun Tian | Dongwen Wang

ZHAI ET AL.



La linfadenectomía extendida incrementa la OS y la CSS en pacientes sometidos a Prostatectomía Radical citorreductora

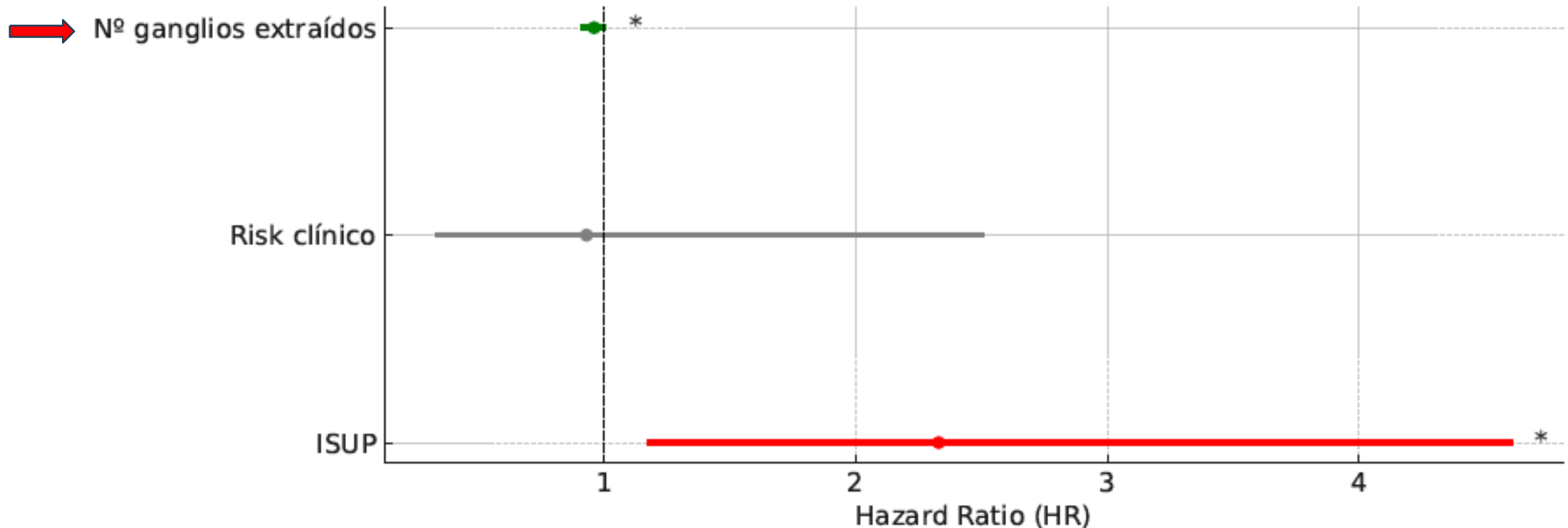
Servicio de Urología H.U Jerez y PE: BCR y número de ganglios



N: 105

Hay correlación entre el tiempo a la BCR y el número de ganglios extraídos por linfadenectomía.

Servicio de Urología H.U Jerez y PE: Tiempo a PET-PSMA+



Una mayor extensión de la linfadenectomía se asocia a menor riesgo de PET PSMA +, sugiriendo un posible impacto terapéutico

¿ Por qué tiene sentido clínico la P. Radical + Linfa extendida?

☒ **Control local inmediato**

- Extirpación completa del tumor y tejidos periprostáticos.
- Elimina el foco de progresión local y origen potencial de metástasis.

☒ **Diagnóstico patológico completo**

- Márgenes, invasión extracapsular, vesículas seminales y ganglios, FALSAS BCR



☒ **Detección precoz de recaída**

- PSA postoperatorio debe ser indetectable.
- Cualquier elevación orienta a tratamiento precoz.

☒ **Plataforma para tratamiento escalonado**

- Cirugía curativa → RT adyuvante → ADT si necesario.
- Doble/triple oportunidad con intención curativa.

Control de la Enfermedad Local: P.Radical vs RT+/- TPA

Ensayo Clínico SPCG-15

(Fase III, abierto, multicéntrico, randomizado)

**Brazo experimental:
P.Radical con linfa
extendida +/- RT**

**Brazo control: RT +
TPA Neoady/adyuv**

**Objetivo Primario:
supervivencia cáncer
específica**

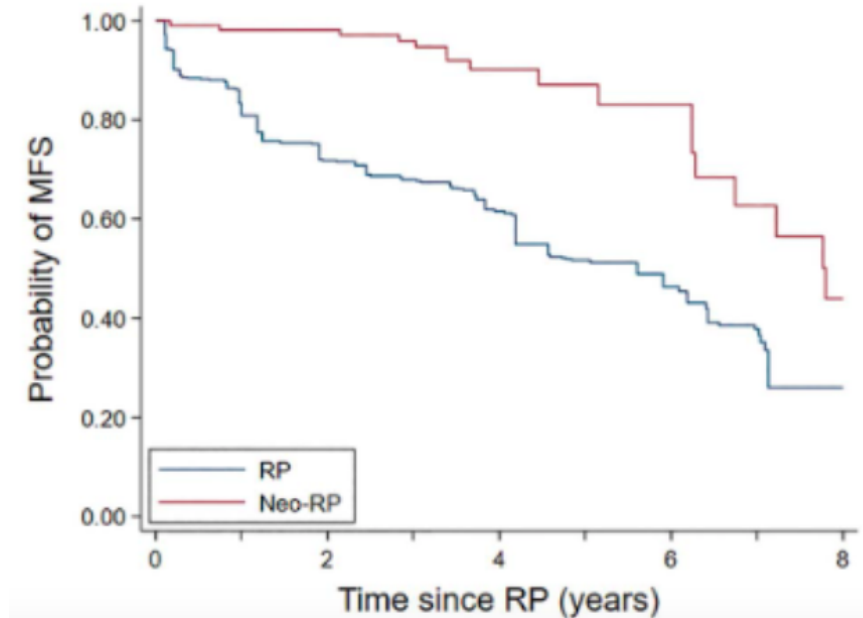
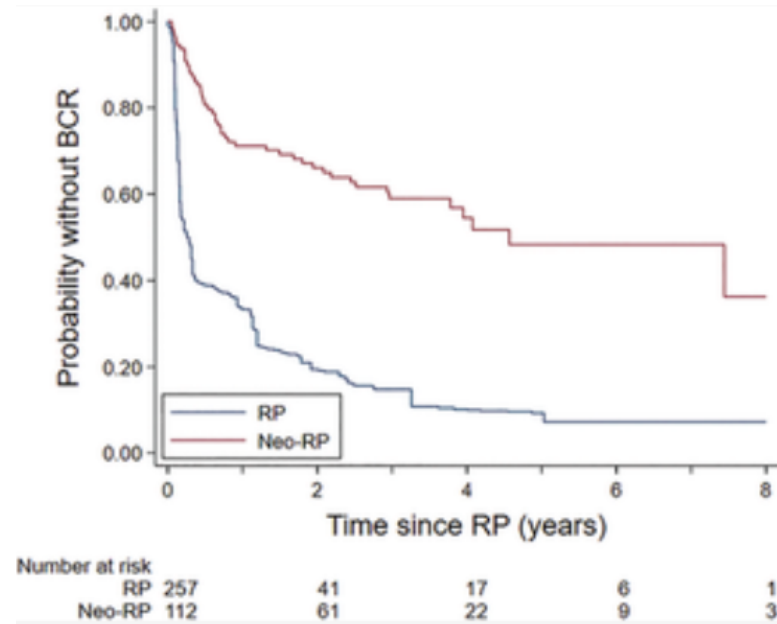
NEOADYUVANCIA

THE JOURNAL
of UROLOGY[®]
www.auajournals.org/journal/juro

JU Insight

Neoadjuvant Novel Hormonal Therapy Followed by Prostatectomy versus Up-Front Prostatectomy for High-Risk Prostate Cancer: A Comparative Analysis

Praful Ravi, Lucia Kwak, Wanling Xie, et al.



PROTEUS

R4

PROTEUS: a randomized, double-blind, placebo-controlled, phase 3 trial of apalutamide plus androgen deprivation therapy (ADT) vs placebo plus ADT prior to and after radical prostatectomy in patients with localized or locally advanced high-risk prostate cancer

Adam S. Kibel,¹ Martin Gleave,² Sabine D. Brookman-May,¹⁴ Won Kim,³ Christopher P. Evans,⁶ Eleni Efstathiou,¹ Philip W. Kantoff,¹⁴ Ashley Ross,¹⁴ Neal D. Shore,¹¹ Alberto Briganti,¹² Boris A. Hadaschik,¹³ Axel Heidenreich,¹³ Brendan Rooney,¹³ Shaozhou Ken Tian,¹⁵ Lisa Wetherhold,¹⁵ Weichun Xu,¹⁶ J. Kellogg Parsons,¹⁷ Kesav Yerru,³ Mary-Ellen Taplin¹⁸

¹Brigham & Women's Hospital, Boston, MA; ²University of British Columbia, Vancouver, BC, Canada; ³Janssen Research & Development, Los Angeles, CA; ⁴Ludwig-Maximilians-University, Munich, Germany; ⁵Janssen Research & Development, San Francisco, CA; ⁶University of California Davis, Sacramento, CA; ⁷Houston Methodist Cancer Center, Houston, TX; ⁸Memorial Sloan Kettering Cancer Center, New York, NY; ⁹Convergent Therapeutics, Inc, Cambridge, MA; ¹⁰Northwestern University, Chicago, IL; ¹¹Carolina Urologic Research Center, Myrtle Beach, SC; ¹²Vita-Salute San Raffaele University, Milan, Italy; ¹³University of Duisburg-Essen, Essen, Germany; ¹⁴University Hospital of Cologne, Cologne, Germany; ¹⁵Janssen Research & Development, High Wycombe, UK; ¹⁶Janssen Research & Development, Spring House, PA; ¹⁷Janssen Research & Development, La Jolla, CA; ¹⁸Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute, Boston, MA

INTRODUCTION

- Rates of disease recurrence following radical prostatectomy (RP) in patients with localized high-risk prostate cancer (PC) remain high (around 50%).¹⁻⁴
- Phase 2 studies have shown that treatment with androgen blockade before RP may reduce tumor burden post RP and potentially improve clinical outcomes in patients with high-risk disease.²⁻⁴
- Apalutamide (APA) is an androgen receptor inhibitor approved for treatment of metastatic castration-sensitive PC (mCSPC) and nonmetastatic castration-resistant PC (nmCRPC) with ongoing treatment with a gonadotropin-releasing hormone analog.⁵

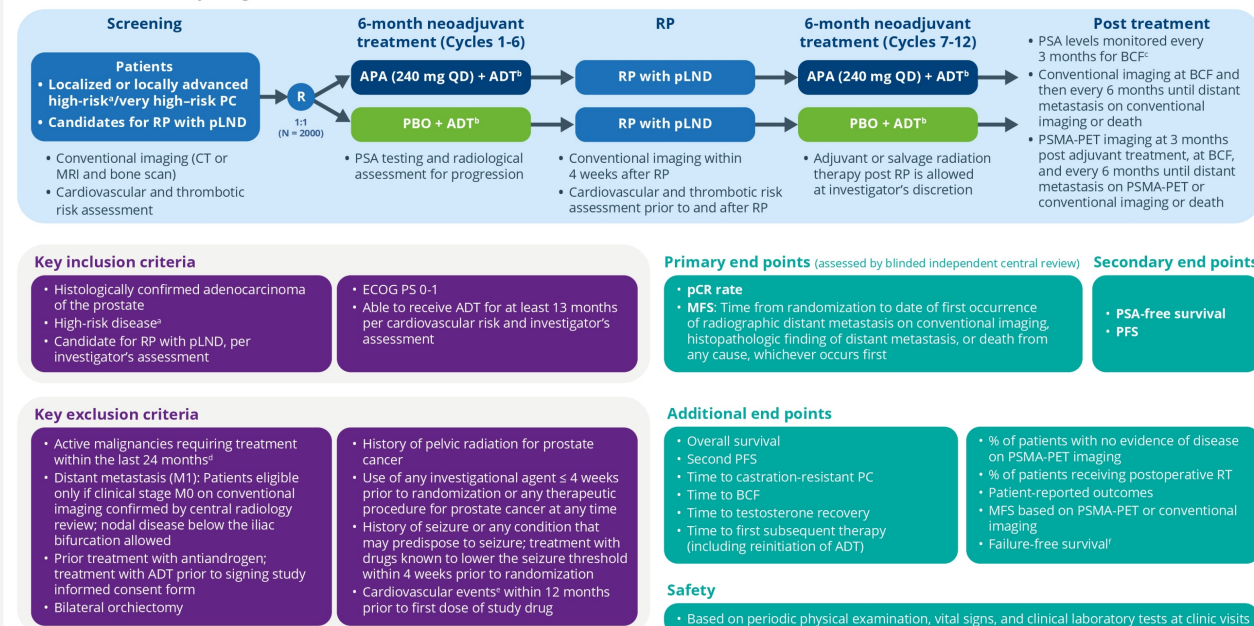
OBJECTIVE

- We are investigating whether treatment with perioperative androgen blockade (APA + ADT before and after RP) would improve clinical outcomes (pathologic complete response [pCR] rate and metastasis-free survival [MFS]) in patients with localized or locally advanced high-risk PC versus placebo (PBO) + ADT.

METHODS

- PROTEUS is an international multicenter study (Figure 1).
- Approximately 2000 patients at > 203 sites in 18 countries will be enrolled, to receive treatment for up to 12 months.
- Stratification variables:
 - Gleason score (7 vs ≥ 8);
 - Pelvic node status (N0 vs N1);
 - Region (North America, Europe, rest of world).
- To reduce surgery-related risk of thromboembolic events, guidance for perioperative thrombotic prophylaxis is provided in the protocol.
- An independent data monitoring committee is reviewing trial data.

FIGURE 1: PROTEUS study design



^aDefined by a total Gleason sum score ≥ 4 + 3 (= grade groups [GG] 3-5) and ≥ 1 of the following: A) any combination of GS 4 + 3 (= GG 3) and GS 8 (4 + 4 or 5 + 3) in ≥ 6 systematic cores (with ≥ 1 core GS 8 [4 + 4 or 5 + 3] included); B) any combination of GS 4 + 3 (= GG 3) and GS 8 (4 + 4 or 5 + 3) from ≥ 3 systematic cores and PSA < 20 ng/mL (with ≥ 1 core GS 8 [4 + 4 or 5 + 3] included); C) GS > 9 (= GS 5) in ≥ 1 systematic or targeted core; D) ≥ 2 systematic or targeted cores with continuous GS ≥ 8 (= GG4), each with ≥ 80% involvement.

^bDuring the direct perioperative period, APA/PBO is stopped 2 weeks prior to planned RP and then resumed 4 weeks after RP. If post-RP imaging has been conducted to assess for lymph node and disease progression and resolution to grade ≤ 1, of any clinically significant adverse events considered related to RP.

^cDefined as 2 consecutive PSA rises, with the second consecutive test resulting in an absolute PSA value of ≥ 0.2 ng/mL.

^dExcept skin cancer considered completely cured, low-risk non-muscle-invasive urothelial cancer, and breast cancer adequately treated (lobular carcinoma in situ or ductal carcinoma in situ, or history of localized breast cancer and receiving antihormonal agents and considered to have a very low risk of recurrence).

^eSevere or unstable angina, myocardial infarction, symptomatic congestive heart failure, arterial or venous thromboembolic events, or clinically significant ventricular arrhythmias or New York Heart Association Class II to IV heart disease.

^fTime from randomization to failure of a cure.

BCF, biochemical failure; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; GS, Gleason score; MRI, magnetic resonance imaging; PFS, progression-free survival; pLND, pelvic lymph node dissection; PSA, prostate-specific antigen; PSMA-PET, prostate-specific membrane antigen positron emission tomography; QD, daily; R, randomization.

REFERENCES

1. Kane CJ, et al. *J Urol*. 2007;177:113-117. 2. Taplin ME, et al. *J Clin Oncol*. 2014;32:3705-3715. 3. McKay RR, et al. *Prostate Cancer Prostatic Dis*. 2018;21:364-372. 4. Efstathiou E, et al. *Eur Urol*. 2019;76:418-424. 5. ERLEADA (apalutamide) [prescribing information]. Horsham, PA: Janssen Pharmaceutical Companies; 2019.

Poster presented at ASCO Genitourinary Cancers Symposium, February 17-19, 2022, San Francisco, CA, and online. Supported by funding from Janssen Research & Development

STUDY STATUS

- The study start date was June 11, 2019.
- Approximately 2000 patients will be enrolled at > 203 sites in 18 countries to receive treatment for up to 12 months.
- Total time: 7.5 years (3 years accrual plus 4.5 years follow-up).

KEY STUDY CONSIDERATIONS

- The protocol was amended to include the following:
 - PSMA-PET imaging at 3 months post adjuvant treatment, at BCF, and every 6 months until distant metastasis or death;
 - Cardiovascular and thrombotic risk assessment at screening, prior to RP, and after RP;
 - Guidance for standard perioperative thrombotic prophylaxis;
 - In addition to MFS based on conventional imaging, MFS based on PSMA-PET or conventional imaging will be assessed as a separate end point.

Trial Registration

ClinicalTrials.gov identifier: NCT03767244

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Additional information can be viewed by accessing this link: <https://www.congresshub.com/oncology/gp2022/apalutamide/kibel>

ACKNOWLEDGMENTS

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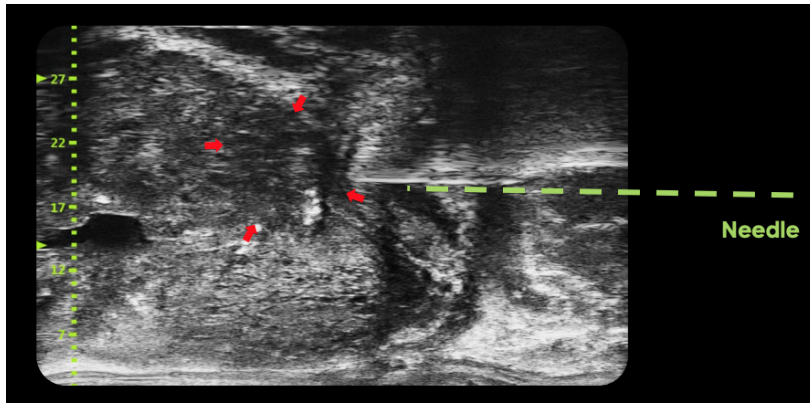
CONTACT INFORMATION

Adam S. Kibel: akibel@bwh.harvard.edu

PROSTATE CANCER



IDENTIFICAR PACIENTES CaP ALTO RIESGO



iCUA
INSTITUTO DE CIRUGIA
UROLOGICA AVANZADA

TARGETED 1

TARGETED 2

SYSTEMATIC LEFT LOBE

SYSTEMATIC RIGHT LOBE

MRI

Diagnóstico:
PRÓSTATA (biopsias-cilindros): ADENOCARCINOMA ACINAR.

LESIÓN A:

- muestra A: Gleason 6 (3+3) que afecta al 50%.
- muestra B: Gleason 7 (3+4) que afecta al 75%.
- muestra C: Gleason 7 (3+4) que afecta al 75%.
- muestra D: Gleason 7 (3+4) que afecta al 75%.
- muestra E: Gleason 7 (3+4) que afecta al 50%.

LESIÓN B:

- muestra F: Gleason 7 (4+3) que afecta al 60%.
- muestra G: Sin evidencia de neoplasia.
- muestra H: Gleason 8 (4+4) que afecta al 50%.

LÓBULO IZDO:

- muestra I: Gleason 8 (4+4) que afecta al 50%.
- muestra J: Gleason 7 (4+3) que afecta al 50%.
- muestra K: Gleason 8 (4+4) que afecta al 25%.
- muestra L: Gleason 8 (4+4) que afecta al 20%.

LÓBULO DCHO:

- muestra M: Sin evidencia de neoplasia.
- muestra N: Sin evidencia de neoplasia.
- muestra O: Gleason 6 (3+3) que afecta al 33%.
- muestra P: Sin evidencia de neoplasia.
- muestra Q: Sin evidencia de neoplasia.

*DESCRIPCIÓN RM MULTIPARAMÉTRICA:

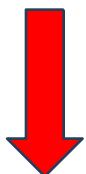
Lesiones PI-RADS 5, alta sospecha de malignidad, en zona transicional anterior izquierda, medio glandular y apical, y en lóbulo periférico izquierdo, medio glandular y apical, posterolateral y posteromedial (en esta última se observa abombamiento hacia la grasa y haz neurovascular, si se confirma proceso neoplásico lo valoramos como extensión hacia los mismos). *PSA AL DX : 12.87
*TNM: T1c

EVALUACIÓN CLÍNICA:

- Exploración dentro de la normalidad
- ECOG:0
- Peso: kg
- Altura: cms
- Temperatura: °C
- Frecuencia cardíaca: lpm
- Frecuencia respiratoria: rpm
- Tensión arterial:
- Se realiza ECG que está dentro de la normalidad

PROSTATECTOMÍA RADICAL EN ALTO RIESGO

Reducir el riesgo de una BCR Y/O Progresión M+. Control local



MEJORAR DX

MAPEO PRÓSTATA

Estadíaaje con PET-PSMA



MEJORAR TTO

- LINFADENECTOMÍA EXTENDIDA EN RIESGO INTERMEDIO Y ALTO(**)

****Incluir ganglios iliaca común y presacros en muy alto riesgo(Gleason 8 extenso, 9-10 o N1)**

PROTEUS??



MEJORAR SEGUIMIENTO

- Clasificación de Riesgo
- PET PSMA (PSA 0,2)
- SEGUIMIENTO PSA
- PRIMORDIUM?

¡Gracias!

