IX Congresso Internacional de Uro-Oncologia

IV SIMPÓSIO MULTIPROFISSIONAL DE URO-ONCOLOGIA

1 a 3 de Março de 2018

SHERATON SÃO PAULO WTC HOTEL

CURSO OS MELHORES RESUMOS DA ASCO-GU:
CÂNCER DE PRÓSTATA
LOCALIZADO E LOCALMENTE AVANÇADO (*ASCO*)

Osmar Barbosa Neto
Rádio-oncologista HIAE

ALBERT EINSTEIN
HOSPITAL ISRAELITA

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

2018 Genitourinary Cancers Symposium

TRANSLATING EVIDENCE TO MULTIDISCIPLINARY CARE

February 8-10, 2018 | Moscone West Building | San Francisco, CA | #GU18

IX Congresso Internacional de Uro-Oncologia

1 a 3 de Março de 2018

Daily versus weekly prostate cancer image-guided radiotherapy: A Phase 3 randomized trial

R. de Crevoisier, M.A. Bayar, P. Pommier, X. Muracciole, F. Pêne, P. Dudouet, I. Latorzeff, V. Beckendorf, J.M. Bachaud, A. Laplanche, S. Supiot, B. Chauvet, T.D. Nguyen, A. Bossi, G. Créhange, J.L. Lagrange

Funded by the French National Cancer Institute (INCa)

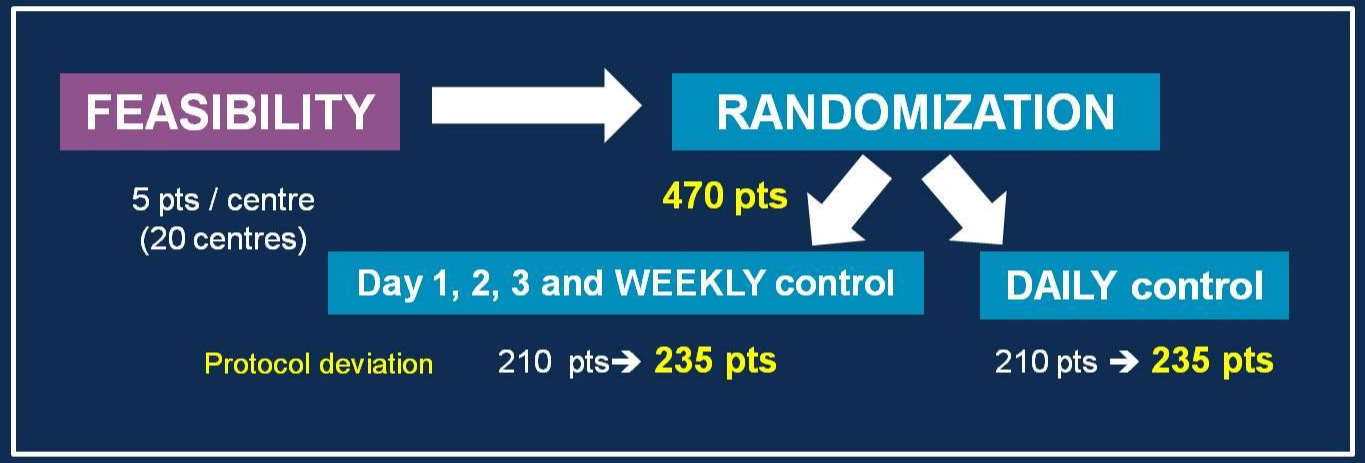
PRESENTED AT: 2018 Genitourinary Cancers Symposium | #GU18

Presented By Renaud de Crevoisier at 2018 Genitourinary Cancers Symposium: Translating Evidence to Multidisciplinary Care

Inclusion criteria

- Intermediate and high risk localized prostate cancer
- Total dose = 70-80 Gy (+ ADT for high risk)
- 3DCRT or IMRT
  PTV margins (1 cm / 5 mm post)
- Pelvic lymph node not irradiated
- IGRT modalities = by direct (CBCT) or indirect prostate visualization (fiducials + 2DkV imaging)

Study design and statistical hypothesis



- **HYPOTHESIS :** to detect a minimum 12% difference in 5-year DFS between the groups (power = 80% ; type-I error = 5%)
- **STRATIFICATION :** by centre, prognostic group, total dose and ADT

Characteristics of patients and Treatment

	Daily control group (N=236)	Weekly control group (N=234)
Prognostic group (D'Amico)		
1	3 (1%)	0 (0%)
2	**161 (68%)**	**164 (70%)**
3	72 (31%)	70 (30%)
Total dose to the prostate (Gy)	78 (44 – 80)	78 (62 – 80)
Radiation technique		
3DCRT	73 (31)	76 (32)
IMRT	**163 (69)**	**158 (68)**
Imaging modalities		
EPID + fiducials	24 (10%)	26 (11%)
2D kV images + fiducials	31 (13%)	24 (10%)
Cone beam CT	**180 (77%)**	**184 (79%)**
Ultrasounds	1 (<1%)	0 (0%)

→ **Follow-up = 4.1 years** (Q1–Q3 = 3.1–5.1)

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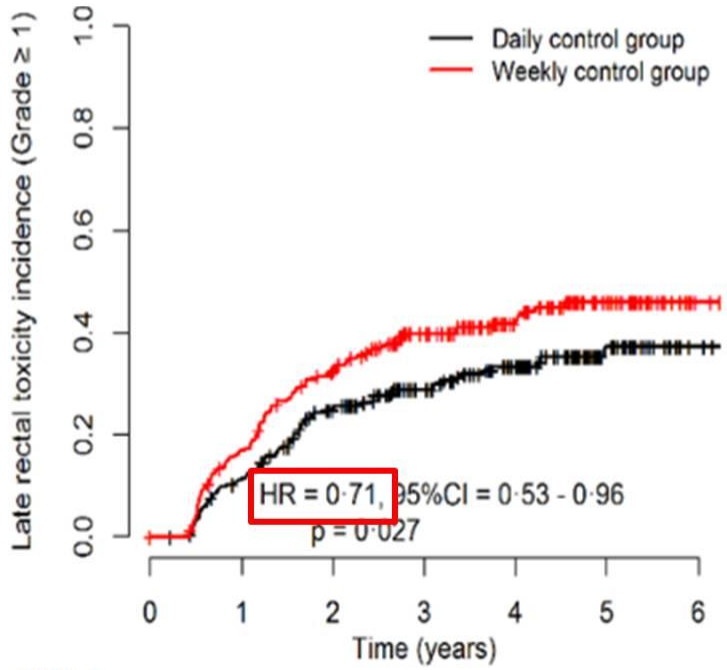
Toxicity (secondary endpoint)

Acute rectal bleeding (Grade ≥ 1)

Daily control group (N=236)	Weekly control group (N=234)	P value
14 (6%)	26 (11%)	0.014

→ **5-year rectal toxicity rate (Grade ≥ 2)** :
10 % in daily group vs.13 % in weekly group
(p = 0,261)

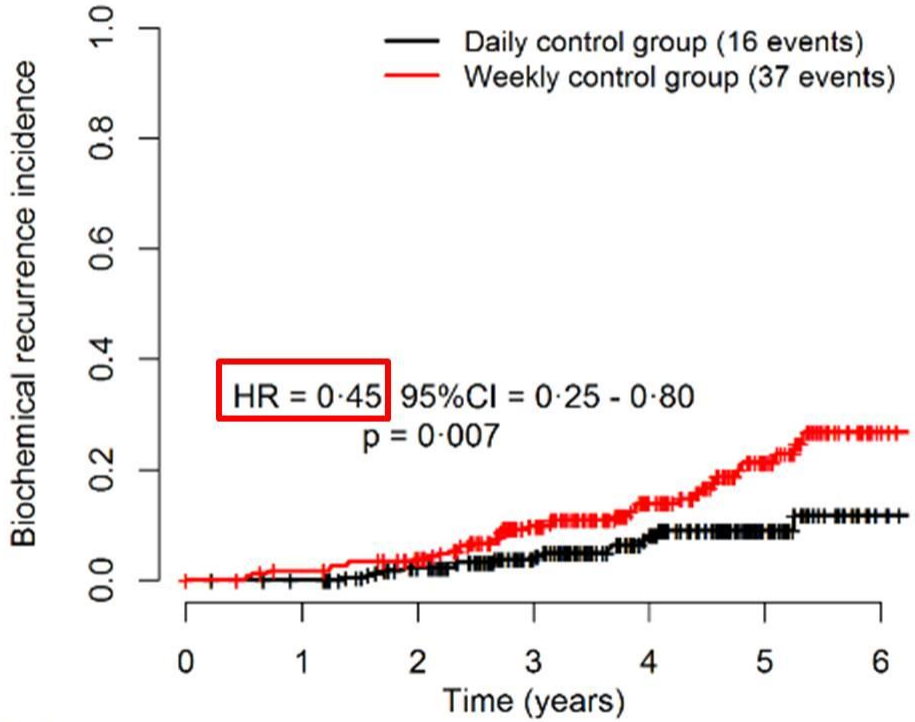
Late rectal toxicity (Grade ≥ 1)



No. At Risk

Daily control group	236	206	161	123	84	31	5
Weekly control group	234	191	150	108	73	39	5

Biochemical recurrence (secondary endpoint)



No. At Risk

Daily control group (16 events)	236	232	207	164	108	46	8
Weekly control group (37 events)	234	226	213	164	105	54	8

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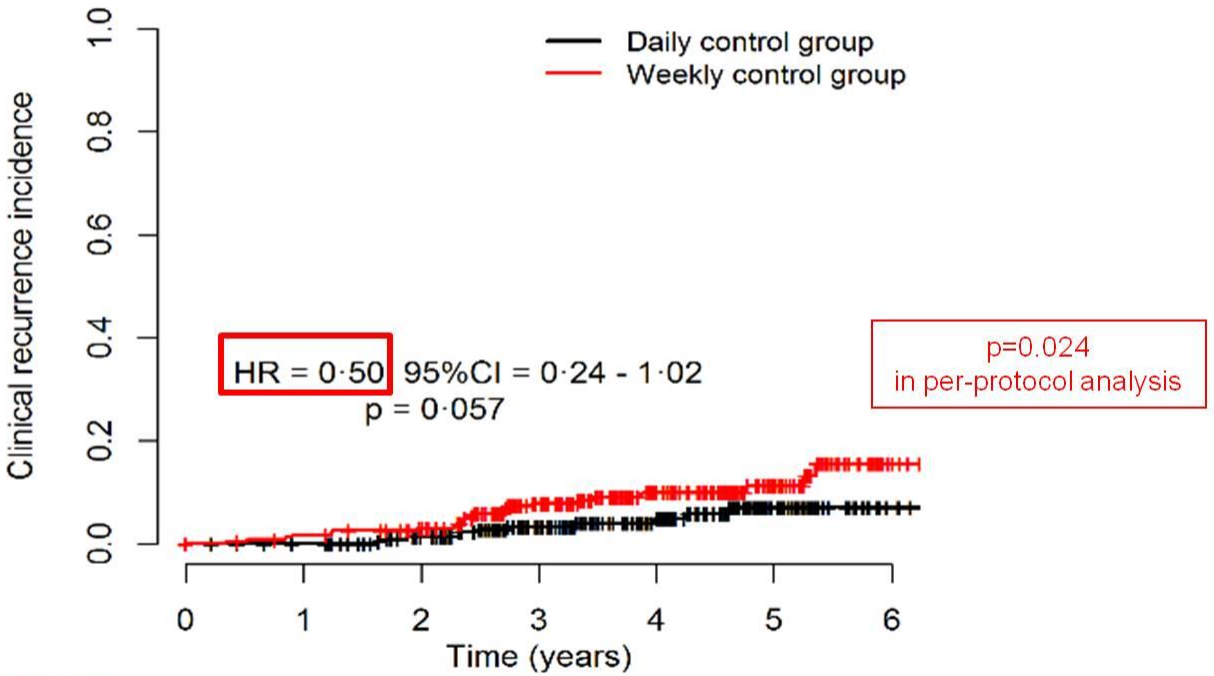
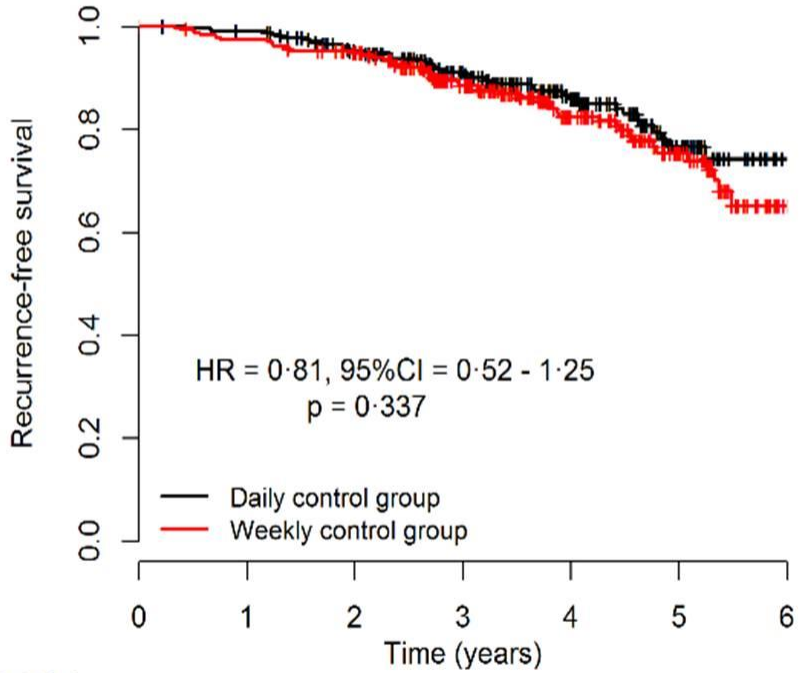
Clinical recurrence (secondary endpoint)



No. At Risk							
Daily control group	236	232	209	165	112	47	9
Weekly control group	234	227	216	167	108	57	9

Disease free survival (primary endpoint)



No. At Risk						
Daily control group 236	232	207	163	107	45	8
Weekly control group 234	226	213	164	104	54	8

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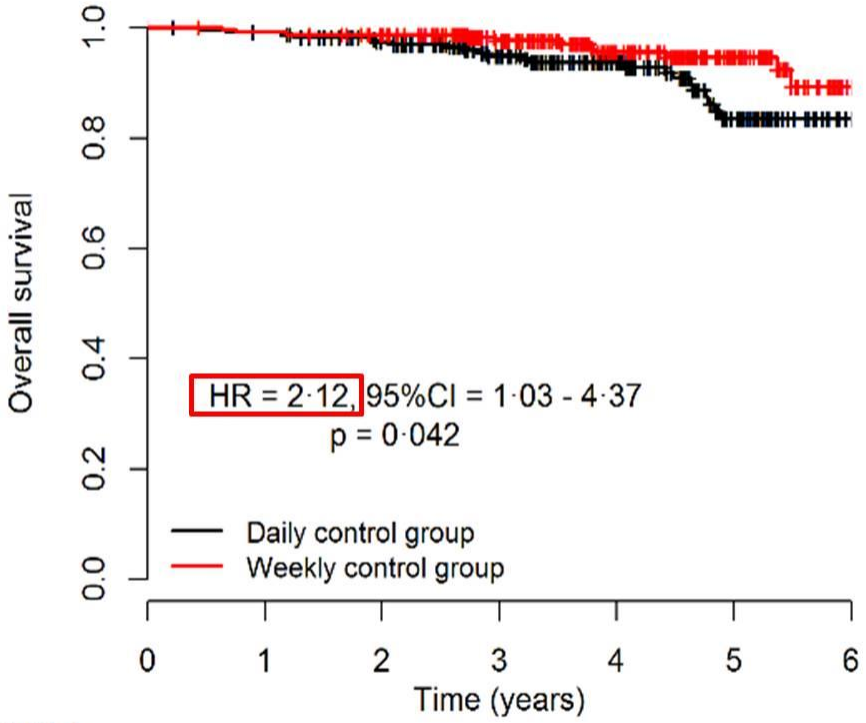
Overall survival (secondary endpoint)



No. At Risk						
Daily control group 236	232	212	171	119	53	11
Weekly control group 234	230	221	180	120	64	12

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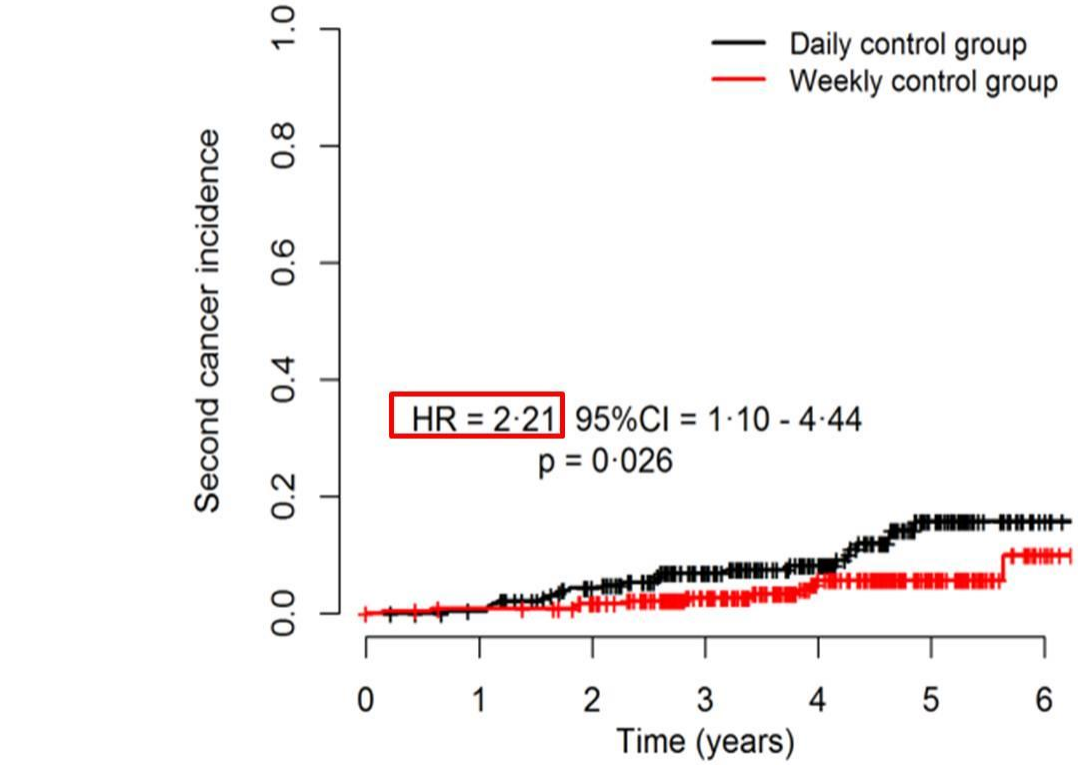
Second cancer incidence (post hoc analysis)



No. At Risk

Daily control group	236	231	205	164	114	46	10
Weekly control group	234	229	219	177	115	60	12

- **Time from randomization:**

  31 months (2-80 months)

- **Localization:**
  - **pelvis (18%)**
  - abdomen (33%), lung (13%)
  - head and neck and brain (10%), blood (13%), and skin (8%), unknown (5%)

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Conclusions

- Compared to weekly control, by improving targeting, daily control in prostate cancer IGRT significantly decreases the risks of recurrence and rectal toxicity but is associated with an increased risk of second cancer.

- Longer follow-up is however clearly needed to assess the rate of radiation-associated malignancies.

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HARVARD MEDICAL SCHOOL

Radiotherapy After Prostatectomy: Adjuvant vs. Early Salvage

Paul L. Nguyen, MD

Vice Chair for Clinical Research

Genito-Urinary Disease Center Co-Leader

Dana-Farber/Brigham and Women's

Associate Professor of Radiation Oncology

Harvard Medical School

Presented By Paul Nguyen at 2018 Genitourinary Cancers Symposium: Translating Evidence to Multidisciplinary Care

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The Contestants..

Observation and Early Salvage RT

Urologist

Christopher Amling, MD

Adjuvant RT

Radiation Oncologist

William Shipley, MD

DANA-FARBER CANCER INSTITUTE

BRIGHAM AND WOMEN'S HOSPITAL

HARVARD MEDICAL SCHOOL

Case

- 65 y/o M w cT1c, PSA 15, 6/12 cores with Gleason 4+3=7.
- Prostatectomy showed:
  - pT3a (ECE)
  - Gleason 4+3 involving 20% of the gland.
  - Positive Margin.
  - Lymph nodes were sampled and not involved.
  - Post-op PSA <0.1

Adjuvant versus early-salvage post-prostatectomy radiotherapy for prostate cancer with adverse pathologic features: a multi-institutional analysis

William L. Hwang[1], Rahul D. Tendulkar[2], Andrzej Niemierko[1], Shree Agrawal[3], Kevin L. Stephans[2], Daniel E. Spratt[4], Jason W. Hearn[4], Bridget F. Koontz[5], W. Robert Lee[5], Jeff M. Michalski[6], Thomas M. Pisansky[7], Stanley L. Liauw[8], Matthew C. Abramowitz[9], Alan Pollack[9], Drew Moghanaki[10], Mitchell S. Anscher[11], Robert B. Den[12], Anthony L. Zietman[1], Andrew J. Stephenson[2], Jason A. Efstathiou[1]

[1]Massachusetts General Hospital/Harvard Medical School; [2]Cleveland Clinic; [3]Case Western Reserve University; [4]University of Michigan; [5]Duke University; [6]Washington University; [7]Mayo Clinic; [8]University of Chicago; [9]University of Miami; [10]Hunter Holmes McGuire VA Medical Center; [11]Virginia Commonwealth University; [12]Thomas Jefferson University.

IMPORTANCE

Prostate cancer with adverse pathologic features (pT3 and/or positive margins) after prostatectomy may be managed with adjuvant radiotherapy (ART) or surveillance followed by early-salvage radiotherapy (ESRT) for recurrence. The optimal timing of post-operative radiotherapy is unclear.

PURPOSE

To compare clinical outcomes in prostate cancer patients with adverse pathologic features managed with post-operative ART versus ESRT.

METHODS

Propensity-score (PS) matched cohort study of 1566 consecutive prostate cancer patients with adverse pathologic features managed with post-operative ART (n = 371; PSA <0.1 ng/mL or undetectable) or ESRT (n = 1195; PSA 0.1-0.5 ng/mL) from ten U.S. academic medical centers (1987-2013). Propensity-score one-to-one matching was used to account for covariates potentially associated with treatment selection. Measured freedom from post-irradiation biochemical failure (FFBF), freedom from distant metastases (FFDM), prostate-cancer specific survival (PCSS), and overall survival (OS) from date of surgery to address lead-time bias.

RESULTS

Baseline Characteristics

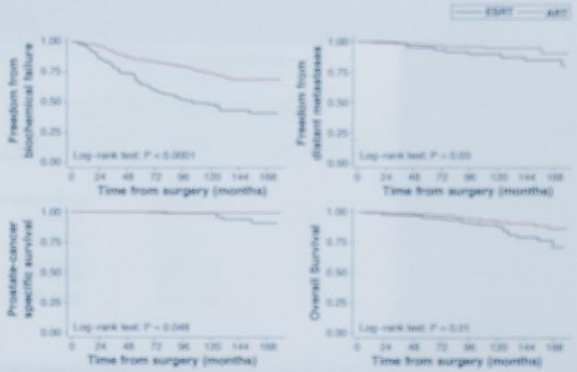
ESRT group had lower T-stage, Gleason score, rate of + margins, greater post-op ADT. PS matching yielded 366 well-balanced matched pairs.

	Before PS matching			After PS matching		
	ESRT (N = 1195)	ART (N = 371)	P	ESRT (N = 366)	ART (N= 366)	P
Age at surgery, yr (median, IQR)	60.0 (55.0, 64.7)	60.0 (55.2, 65.0)	0.44	61.0 (54.8, 65.3)	60.0 (55.0, 65.0)	0.90
Path T-stage (N, %): T2	553 (46.3%)	96 (26.4%)	<0.001	106 (29.8%)	98 (26.8%)	0.63
T3a	435 (35.4%)	183 (49.3%)		170 (46.4%)	181 (49.5%)	
T3b	207 (17.3%)	90 (24.3%)		87 (23.8%)	87 (23.8%)	
Surgical GS (N, %): 6	246 (20.8%)	50 (13.5%)	<0.001	33 (9.0%)	50 (13.7%)	0.18
7	722 (60.4%)	214 (57.7%)		208 (57.1%)	212 (57.4%)	
8-10	225 (18.8%)	107 (28.8%)		124 (33.9%)	106 (29.0%)	
Margins (N, %): Positive	721 (60.3%)	315 (84.9%)	<0.001	318 (86.9%)	313 (85.8%)	0.67
Negative	462 (38.7%)	53 (14.3%)		48 (13.1%)	53 (14.5%)	
Unknown	12 (1.0%)	3 (0.8%)				
Pre-RT PSA, ng/mL (median, IQR)	0.3 (0.2, 0.4)	<0.1	N/A	0.3 (0.2, 0.4)	<0.1	N/A
RT technique (N, %): 2D	245 (20.5%)	69 (18.6%)	<0.001	58 (15.9%)	69 (18.9%)	0.18
3D-CRT	311 (26.0%)	64 (17.3%)		70 (19.1%)	63 (17.2%)	
IMRT	436 (36.5%)	174 (46.9%)		192 (52.5%)	171 (46.7%)	
Nodal RT (N, %): Yes	141 (11.8%)	43 (11.6%)	1	47 (12.8%)	43 (11.7%)	0.74
No	1054 (88.2%)	328 (88.4%)		319 (87.2%)	323 (88.3%)	
RT dose to fossa, Gy (median, IQR)	64.8 (64.8, 68.1)	64.8 (61.2, 66.0)	<0.001	66.0 (64.8, 70.0)	64.8 (61.2, 66.0)	<0.001
Post-op ADT (N, %): Yes	135 (11.3%)	23 (6.2%)	0.004	19 (5.2%)	23 (6.3%)	0.63
No	1060 (88.7%)	348 (93.8%)		347 (94.8%)	343 (93.7%)	

RESULTS (continued)

Actuarial Analysis

ART was superior to ESRT for all outcomes. ART was associated with higher FFBF (12-yr: 69% vs. 43%; log-rank P <0.0001), FFDM (12-yr: 95% vs. 85%; log-rank P = 0.03), PCSS (12-yr: 99% vs. 94%; log-rank P = 0.048), and OS (12-yr: 91% vs. 79%; log-rank P = 0.01).



Multivariate Competing-Risks Regression

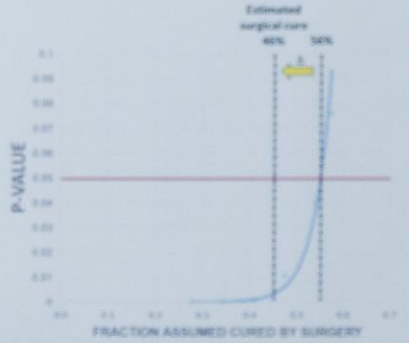
Multivariate competing-risks regression analysis of FFBF accounting for death as a competing risk. Favorable prognostic features for BF were ART, lower Gleason score and T-stage, nodal irradiation, and post-operative androgen deprivation therapy.

	PS-matched (competing-risks)	
	SHR (95% CI)	P
ART vs. ESRT	0.34 (0.24-0.48)	<0.0005
Age at surgery	1.00 (0.98-1.02)	0.65
Year of surgery	1.02 (0.99-1.05)	0.24
Pathologic T-stage: T2	Reference	
T3a	1.14 (0.78-1.67)	0.51
T3b	1.87 (1.20-2.92)	0.005
Surgical Gleason score	2.06 (1.75-2.41)	<0.0005
Surgical margin (-/+)	1.29 (0.82-2.04)	0.27
Omitting nodal RT	2.27 (1.33-3.87)	0.003
RT dose (Gy), prostate fossa	0.96 (0.91-1.01)	0.10
Post-operative ADT	0.30 (0.12-0.74)	0.009

RESULTS (continued)

Sensitivity Analysis

Unknown proportion of patients in the ART group who did not develop BF may have been cured by surgery. To address this limitation, we randomly removed patients in the ART cohort who did not develop BF by the last follow-up. ART benefit in FFBF only lost significance when more than 56% of patients were assumed to be cured by surgery. In comparison, the estimated 12-yr FFBF after surgery using MSKCC nomogram was 46%.



CONCLUSIONS & LIMITATIONS

- Largest multi-institutional retrospective study comparing ART vs. ESRT.
- After PS-matching, ART associated with ↑ post-irradiation FFBF, FFDM, PCSS, OS. Improvement in survival not previously demonstrated.
- National practice patterns indicate <10% ART use in high-risk patients despite AUA/ASTRO guidelines supporting consideration.
- Await results of prospective studies: RADICALS, GETUG-17, RAVES.
- ESRT had lower T3/+margins/GS but other unknown factors may have predisposed to worse outcomes.
- Half of ESRT group received <66 Gy, which is associated with increased risk of BF; higher salvage doses which may reduce ART advantage.
- Quality of life and economic data important for future studies.

Impact of Decipher Test

Jefferson
Philadelphia University + Thomas Jefferson University
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Can post-operative prostate fossa radiation be omitted in patients with high-risk features using a genomic classifier?

Joseph A. Marascio, Matthew D. Bloom, Mark D. Hurwitz, Leonard G. Gomella, Costas D. Lallas, Edouard J. Trabulsi, Mark J. Mann, J. Ryan Mark, Anne E. Calvaresi, W. Kevin Kelly, Jean H. Hoffman-Censits, J. Luke Godwin, Adam P. Dicker, Robert B. Den;
Thomas Jefferson University, Philadelphia, PA

PROSPECTIVE RANDOMIZED TRIAL OF GENOMIC CLASSIFIER IMPACT ON TREATMENT DECISIONS IN PATIENTS AT HIGH RISK OF RECURRENCE FOLLOWING RADICAL PROSTATECTOMY (G-MINOR)

Todd M. Morgan, David C. Miller, Rodney L. Dunn, Susan Linsell, Linda Okoth, Anna Johnson, Felix Y. Feng, Khurshid R. Ghani, Marguerite du Plessis, Elai Davicioni, James E. Montie, Michael L. Cher

MUSIC
Michigan Urological Surgery Improvement Collaborative

POSTER # 212

Validation of a genomic risk classifier to predict metastasis and prostate cancer specific-mortality (PCSM) in men with positive lymph nodes

JOHNS HOPKINS MEDICINE SCHOOL OF MEDICINE · MAYO CLINIC · KU LEUVEN · MD Anderson Cancer Center

Bruce J Trock[1], R Jeffrey Karnes[2], Frank Claessens[3], John Davis[4], Zaid Haddad[5], Kasra Yousefi[5], Elai Davicioni[5], Ashley Ross[6]

1. Johns Hopkins Dept of Urology 2. Mayo Clinic Dept of Urology 3. Leuven University Dept Cellular & Molecular Medicine
4. MD Anderson Cancer Center Dept of Urology 5. GenomeDx Biosciences Inc 6. Texas Urology Specialists

Decipher Test Impacts Adjuvant and Salvage Treatments Received following Radical Prostatectomy.

John L. Gore[1], Marguerite du Plessis[2], Darlene Dai[2], Kasra Yousefi[2], Darby J. S. Thompson[3], Lawrence Karsh[4], Brian Lane[5], Michael Franks[6], David Y.T. Chen[7], Mark Bandyk[8], Adam S. Kibel[9], Hyung Kim[10], William Lowrance[11], Paul Maroni[12], Scott Perrapato[13], Edouard J. Trabulsi[14], Robert Waterhouse[15], Elai Davicioni[2], Yair Lotan[16], Daniel W. Lin[1]

1 University of Washington, Seattle Cancer Care Alliance, Seattle, WA, 2 GenomeDx Biosciences Inc., Vancouver, BC, Canada, 3 EMMES Canada, Burnaby, BC, Canada, 4 The Urology Center of Colorado, Denver, CO, 5 Spectrum Health Medical Group, Grand Rapids, MI, 6 Virginia Urology, Richmond, VA, 7 Fox Chase Cancer Center, Philadelphia, PA, 8 Lakeland Regional Cancer Center, Lakeland, FL, 9 Brigham and Women's Hospital, Boston, MA, 10 Cedars-Sinai Medical Center, Los Angeles, CA, 11 Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, 12 University of Colorado, Anschutz Medical Campus, Aurora, CO, 13 University of Vermont Medical Center, Burlington, VT, 14 Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA, 15, Carolina Urology Partners, Gastonia, NC, 16 UT Southwestern Medical Center, Dallas, TX

SUO CTC

Decipher Predicts Adverse Pathology after Surgery in Men who are Candidates for Active Surveillance by Contemporary Practice Guidelines

Hyung Lae Kim[1], Brian R. Lane[2], Ping Li[1], Huei-Chung Huang[3], Samineh Deheshi[3], Tara Marti[3], Beatrice Knudsen[1], Hatem Abou Ouf[4], Lucia L.C. Lam[3], Marguerite du Plessis[3], Elai Davicioni[3], Jeffrey J. Tosoian[5], Ashley Ross[5], John W. Davis[6], James Mohler[7], M. Eric Hyndman[4], Eric A. Klein[8], Tarek A. Bismar[4]

[1]Cedars Sinai Medical Center, Los Angeles, CA; [2]Spectrum Health, Grand Rapids, MI; [3]GenomeDx Biosciences, Vancouver, BC; [4]University of Calgary, Calgary, AB; [5]Johns Hopkins Medical Institutions, Baltimore, MD; [6]The University of Texas MD Anderson Cancer Center, Houston, TX; [7]Roswell Park, Buffalo, NY [8]Cleveland Clinic Glickman Urology and Kidney Institute, Cleveland, OH

Genomic variations associated with prostate cancer in large cohort of African American men

Walter Rayford[1], Jennifer Jordan[2], Mandeep Takhar[2], Mohammed Alshalalfa[2], Darlene Dai[2], Nicholas Erho[2], Mark D. Greenberger[1], Randy Bradley[3], Elai Davicioni[2]

[1]The Urology Group LLC, Memphis, TN, USA, [2]GenomeDx Biosciences Inc., Vancouver, Canada, [3]University of Tennessee, Knoxville, TN

Prospective Analysis of 4,474 Prostate Biopsies to Evaluate Potential Treatment Management Impact of Combined Clinical-Genomic Risk Classification

Paul L. Nguyen[1], Jingbin Zhang[2], Kasra Yousefi[2], Elai Davicioni[2], Robert B. Den[3], Felix Y. Feng[4], Daniel E. Spratt[5]

Impact of Genomic Risk Scores on Treatment Decisions Following Radical Prostatectomy in a Prospective Medicare Registry

John L. Gore[1], Darlene Dai[2], Robert B. Den[3], Kasra Yousefi[2], Tiffany Le[2], Marguerite du Plessis[2], Roanna Padre[2], Worlanyo Sosu Sedzorme[2], Elai Davicioni[2], Paul L. Nguyen[4] and Ashley E. Ross[5]

[1]University of Washington, Seattle, WA, [2]GenomeDx Biosciences Inc, Vancouver, BC, Canada, [3]Sidney Kimmel Medical College at Thomas Jefferson University, Sidney Kimmel Cancer, Philadelphia, PA, [4]Department of Radiation Oncology, Dana-Farber/Brigham and Women's Cancer, Center and Harvard Medical School, Boston, MA, USA, [5]Texas Urology Specialists, Dallas, TX

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Decipher Test's Impact on the Postoperative Management of Prostate Cancer

Brian Calio[1], Matthew Murphy[1], Anne Calvaresi[1], James Ryan Mark[1], Mark Mann[1], Robert Den[2], Leonard Gomella[1], Edouard Trabulsi[1], Costas Lallas[1]

[1]Department of Urology; [2]Division of Radiation Oncology, Thomas Jefferson University Hospital, Philadelphia, PA, USA

The FALCON trial: Impact of ^{18}F-fluciclovine PET/CT on clinical management choices for men with biochemically recurrent prostate cancer

E. J. Teoh[1]

D. Bottomley[2], A. Scarsbrook[2], H. Payne[3], A. Afaq[3], J. Bomanji[3], N. van As[4], S. Chua[4], P. Hoskin[5], A. Chambers[5], G. Cook[6], V. S. Warbey[6], A. Chau[7], P. Ward[7], M. P. Miller[7], D. Stevens[7], L. Wilson[7], and F. V. Gleeson[1]

[1]Departments of Radiology and Nuclear Medicine, Oxford University Hospitals NHS Foundation Trust, Oxford, UK, [2]The Leeds Teaching Hospitals NHS Trust, Leeds, UK, [3]University College London, London, UK, [4]The Royal Marsden NHS Foundation Trust, London, UK, [5]Mount Vernon Cancer Centre, Northwood, UK, [6]Kings College London, London, UK, [7]Blue Earth Diagnostics Ltd, Oxford, UK.

The ROYAL MARSDEN NHS Foundation Trust | Mount Vernon NHS | University College London Hospitals NHS Foundation Trust | The Leeds Teaching Hospitals NHS Trust | Guy's and St Thomas' NHS Foundation Trust | Oxford University Hospitals NHS Foundation Trust

Presented By Eugene Teoh at 2018 Genitourinary Cancers Symposium: Translating Evidence to Multidisciplinary Care

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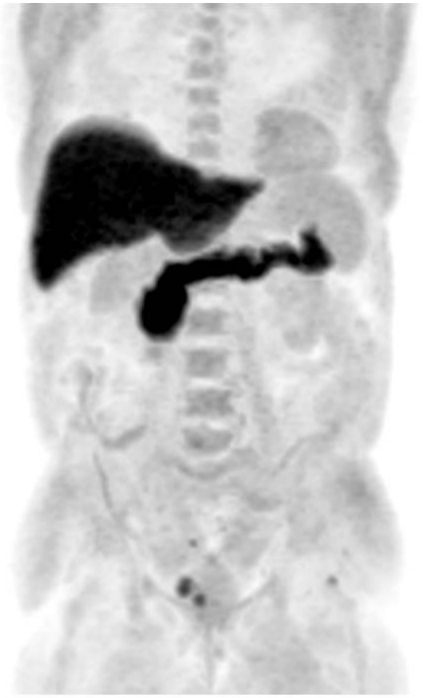
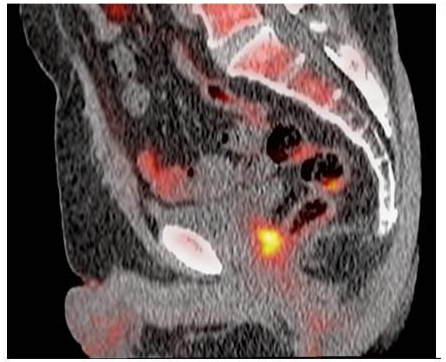
1 a 3 de Março de 2018

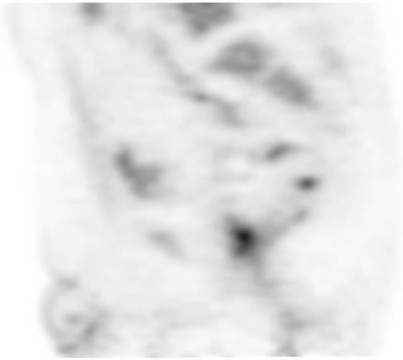
^{18}F-Fluciclovine

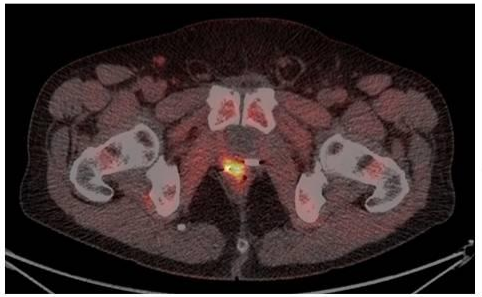
(*Anti*-1-amino-2-[^{18}F]fluorocyclobutane-1-carboxylic acid ([FACBC])

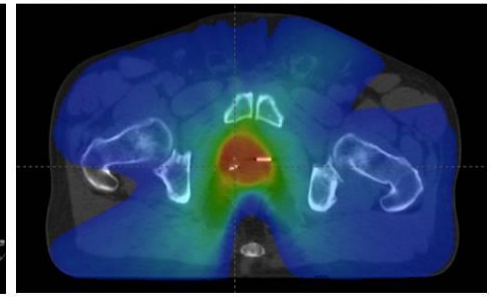
- A synthetic amino acid taken up by amino acid transporters[1] that are upregulated in many cancers, including prostate cancer.
- Well-established diagnostic performance in detecting sites of recurrent prostate cancer.[2,3]
  - ^{18}F-Fluciclovine is now approved in the US and Europe for PET imaging in BCR of prostate cancer.
  - Widely available and reimbursed by CMS in the US.







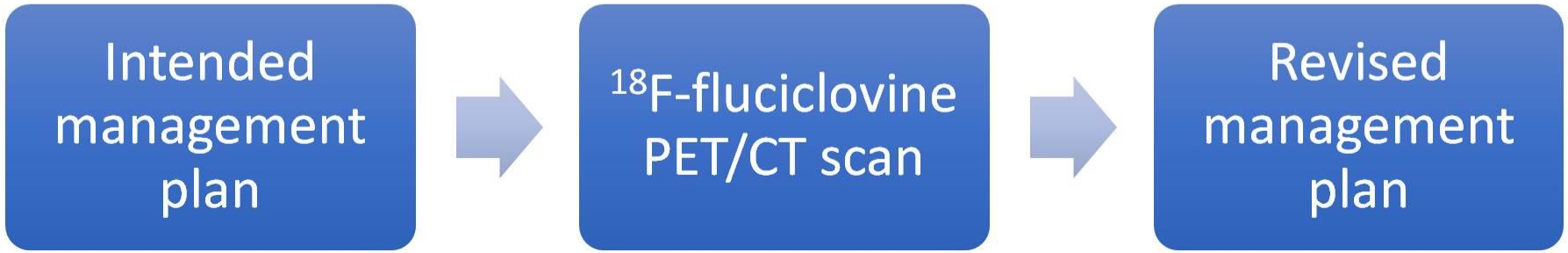




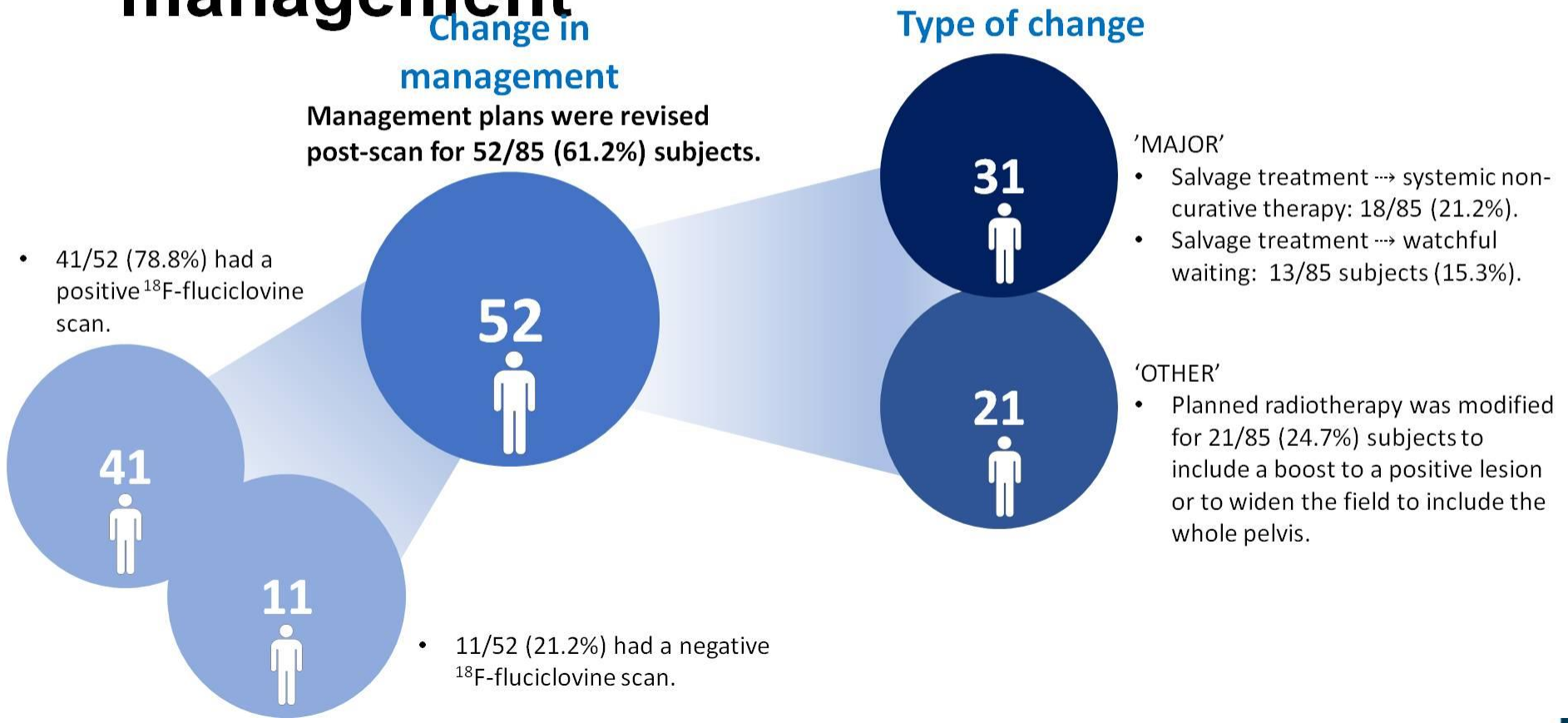
[1]Fuchs and Bode. *Semin Cancer Biol*. 2005;15(4):254-66. [2]Schuster et al. *J Urol*. 2014; 191: 1446. [3]Bach-Gansmo et al. *J Urol*. 2017; 197(3): 676-683.

The FALCON trial (NCT02578940)

Primary objective:	Endpoint:	Type of change:
To assess the clinical impact of a ^{18}F-fluciclovine PET/CT scan on patient management.	Record of a revised management plan following the ^{18}F-fluciclovine scan compared with the pre-scan intended management plan.	'MAJOR' e.g. change of treatment class such as salvage RT to ADT. 'OTHER' e.g. change within a class such as alterations to salvage radiotherapy fields.



Results – change in therapeutic management



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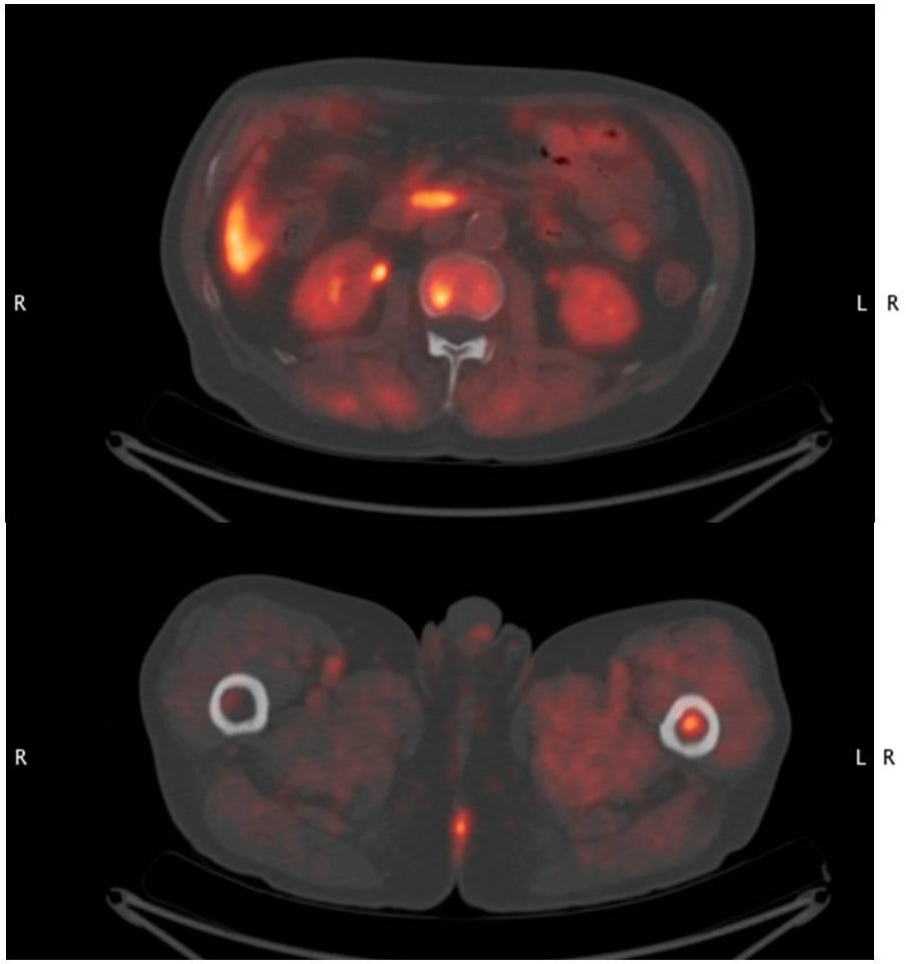
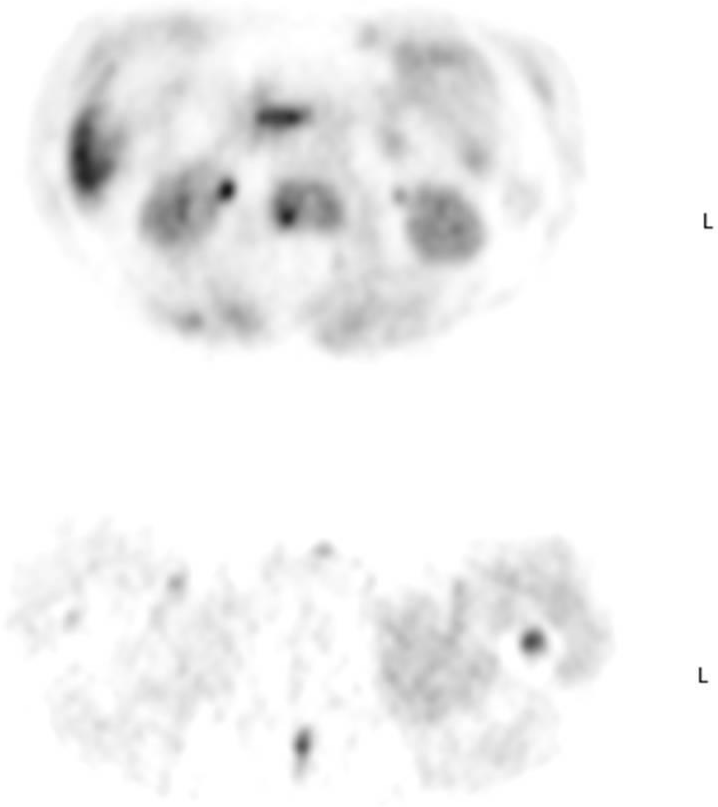
Case study 1

- 71 yr, 6 years post radical prostatectomy
- pT3b N0, GL 4+3
- **PSA 0.4 ng/mL**
- Intended management: salvage prostate bed RT





Bone metastases Revised management: ADT **PSA 0.4**

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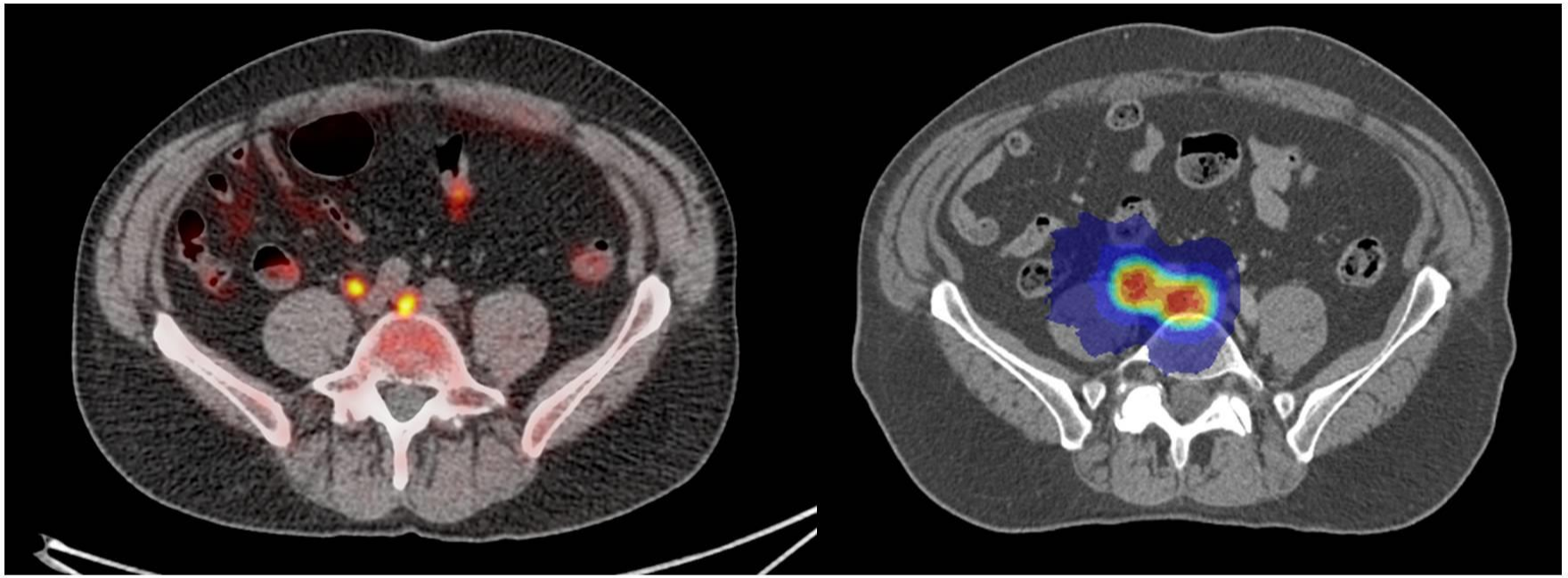
IX Congresso Internacional de Uro-Oncologia
1 a 3 de Março de 2018

Case study 2

- 64 yr, 5 years post primary prostate radiotherapy
- pT3a N0, GL 4+3
- PSA 6.9 ng/mL
- Intended management: salvage brachytherapy



- Sub-centimetre pelvic nodes
- Revised management: SABR to pelvic nodes and ADT
- PSA response (0.33 ng/mL at 7 months)

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Conclusions

- ^{18}F-fluciclovine PET/CT has a substantial impact on the clinical management of BCR.
  - Some subjects had treatment plans rationally modified to provide a better chance of cure or to avoid possibly futile salvage therapy.
- Further recruitment has been stopped due to the criterion of overwhelming efficacy having been met at this interim analysis.
- Follow-up underway to assess PSA response to treatment.
- Future studies to assess the long-term impact of ^{18}F-fluciclovine PET/CT-supported management changes on disease outcomes are warranted.

Ten year final results of the TROG 03.04 (RADAR) randomised phase 3 trial evaluating duration of androgen suppression ± zoledronic acid for locally advanced prostate cancer

David John Joseph[1,2*], David S Lamb[3], James William Denham[4], Christopher Oldmeadow[5], John Attia[5], Allison Steigler[4]

[1]Sir Charles Gairdner Hospital, Perth, Western Australia, Australia
[2]University of Western Australia, Perth, Australia
[3]University of Otago, Wellington, New Zealand
[4]University of Newcastle, Callaghan, Australia
[5]Hunter Medical Research Institute, Newcastle, Australia

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TROG 03.04 RADAR Phase 3 RCT

2x2 factorial design

Is 18 months AS plus radiotherapy (RT) ± 18 months Z more effective than 6 months of neoadjuvant AS plus RT ± Z for men with locally advanced PC ?

Presented by: David Joseph

Endpoints

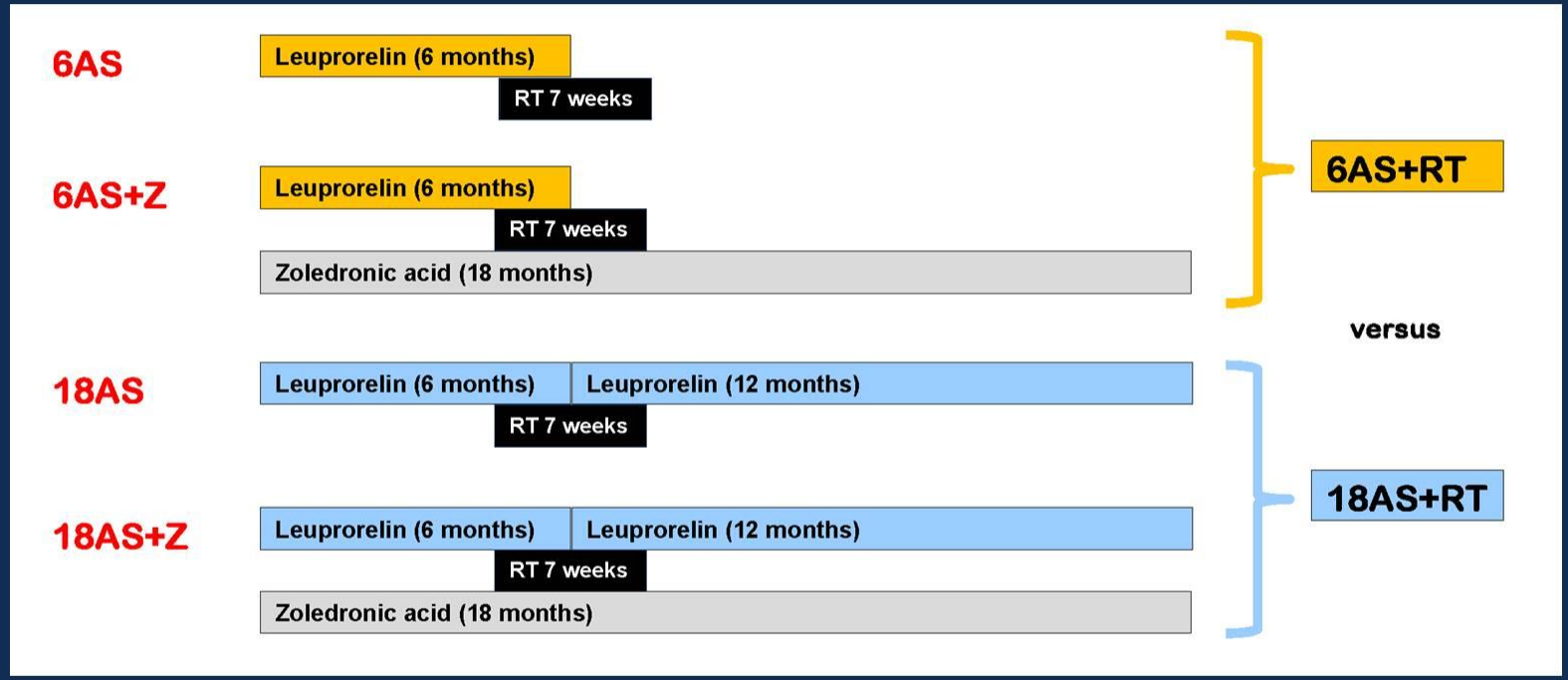
Main endpoint:

- Prostate cancer-specific mortality

Secondary Endpoints:

- Oncologic endpoints (PSA progression; sites of tumour progression; castration resistance; secondary therapeutic intervention; all-cause mortality)
- Quality of Life
- Adverse treatment effects

Factor 1: 12 months adjuvant AS



Leuprorelin = 22.5mg im every 3 months; **Zoledronic acid =** 4mg iv every 3 months; **RT** = dose escalated radiotherapy

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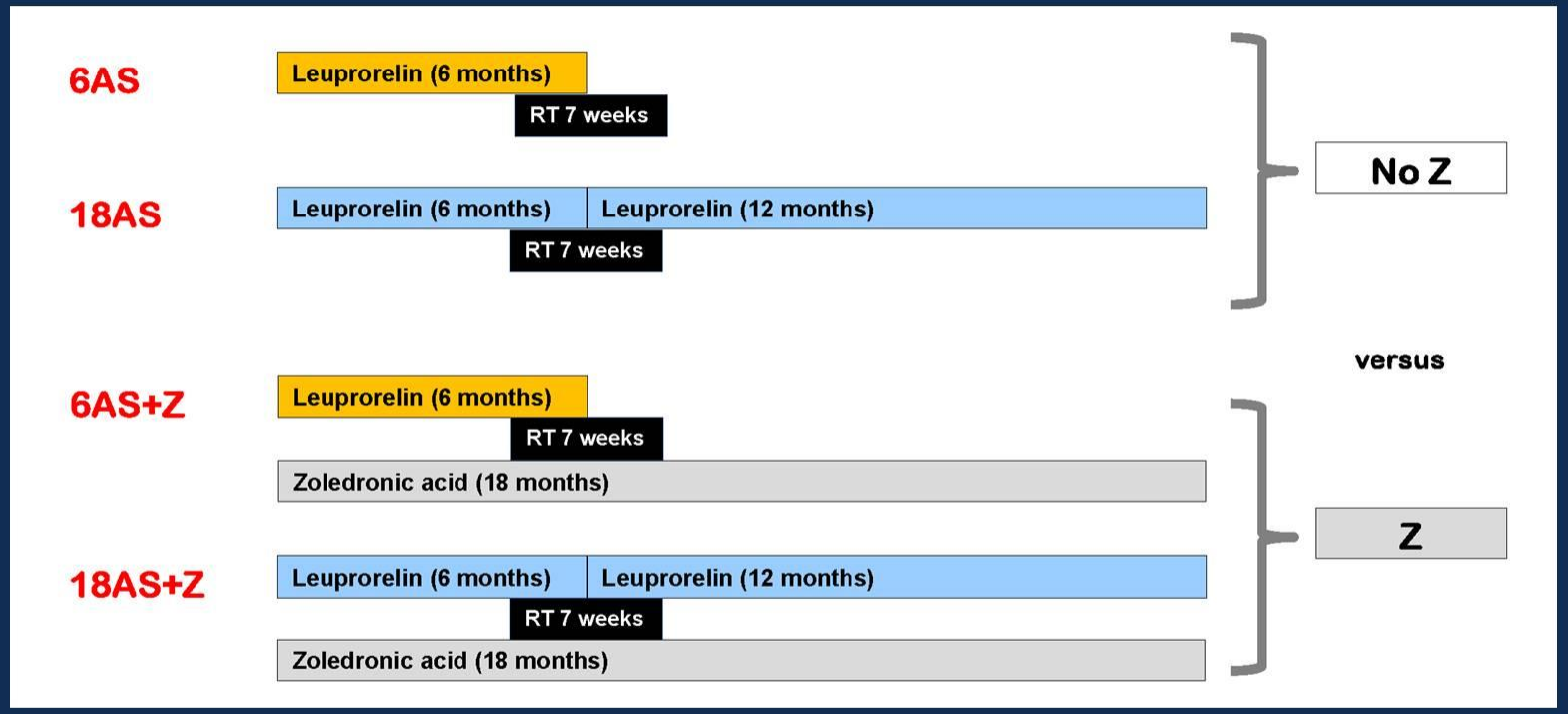
Factor 2: 18 months Z



Leuprorelin = 22.5mg im every 3 months; **Zoledronic acid =** 4mg iv every 3 months; **RT** = dose escalated radiotherapy

Trial demographics

Eligibility:

- T2-T4; N0, M0; ECOG<2 (T2a provided PSA ≥10 and Gleason score (GS) ≥7)

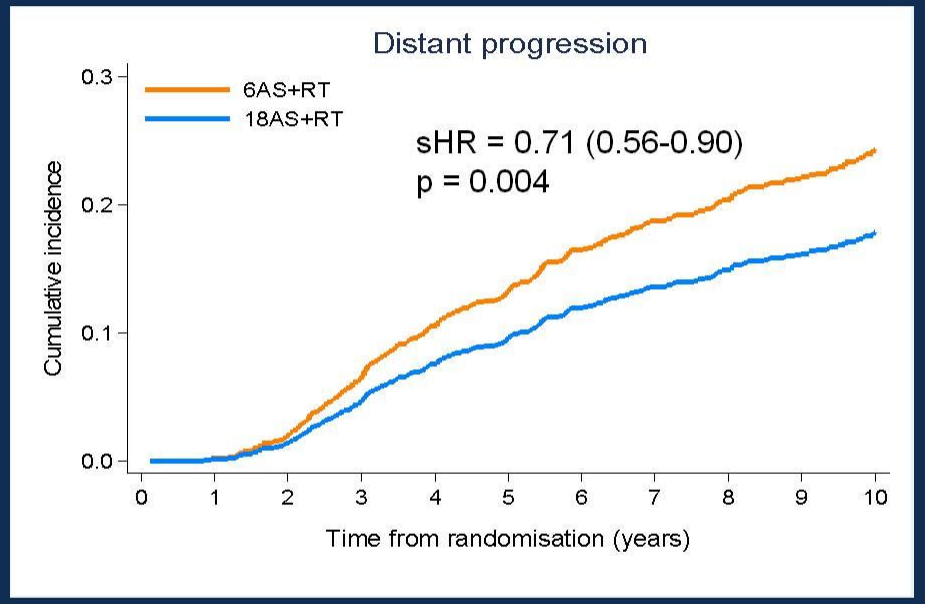
Enrolment:

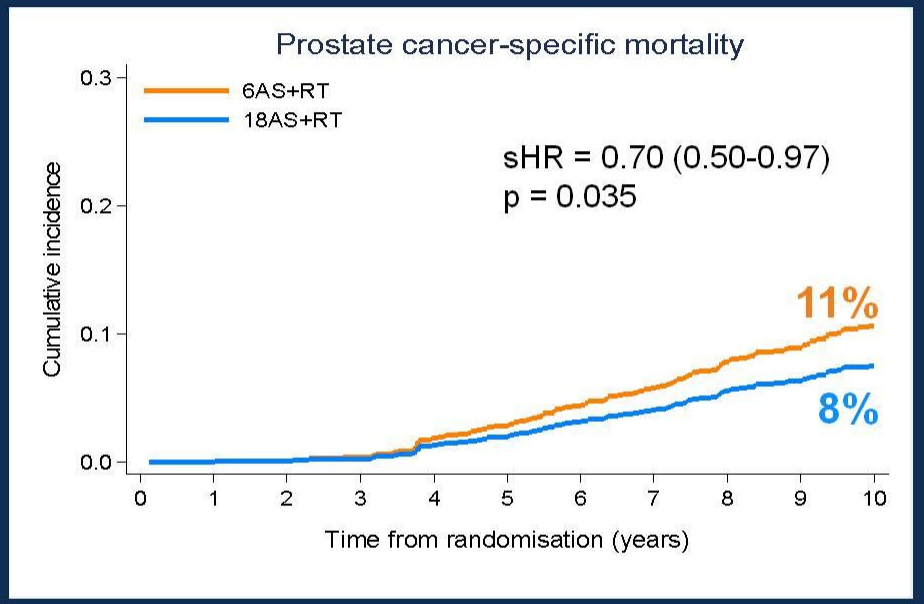
- 1071 men (randomised 2003-2007 from 23 centres around Australia and New Zealand)
- Median age 68.7 yrs
- Median follow-up 10.4 years (IQR: 7.9-11.7)
- Risk classification (MSK):
  high (66%), unfav. intermediate (31%), fav. intermediate (2%)

Cause of death by AS duration

	6AS+RT	18AS+RT	Total
	(n=536)	(n=535)	
Prostate cancer	**81**	**62**	**143 (38%)**
New primary cancer	43	47	90 (24%)
Cardiac	29	23	52 (14%)
CVA	8	7	15 (4%)
Respiratory	20	15	35 (9%)
Renal	1	5	6 (2%)
Trauma	2	2	4 (1%)
Dementia	6	4	10 (3%)
Other known	5	8	13 (3%)
Other unknown	5	2	7 (2%)
Total deaths	200	175	375 (100%)

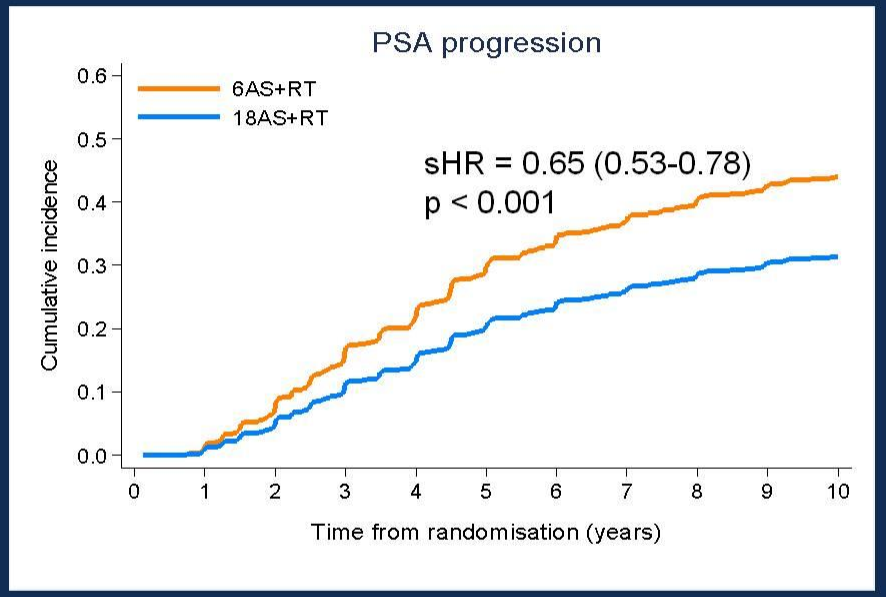
Primary endpoint: PCSM

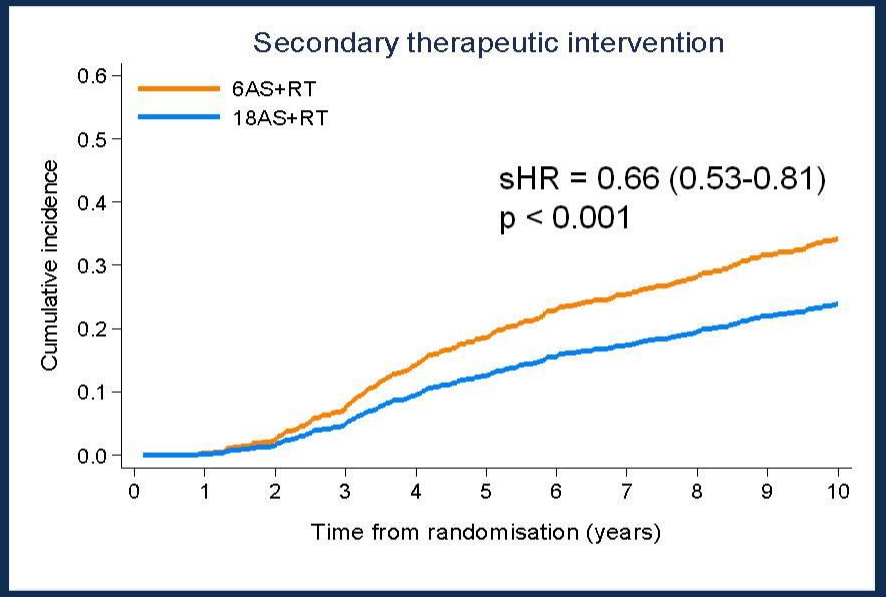




A 29% reduction in distant progression was the main driver of the 30% reduction in PCSM

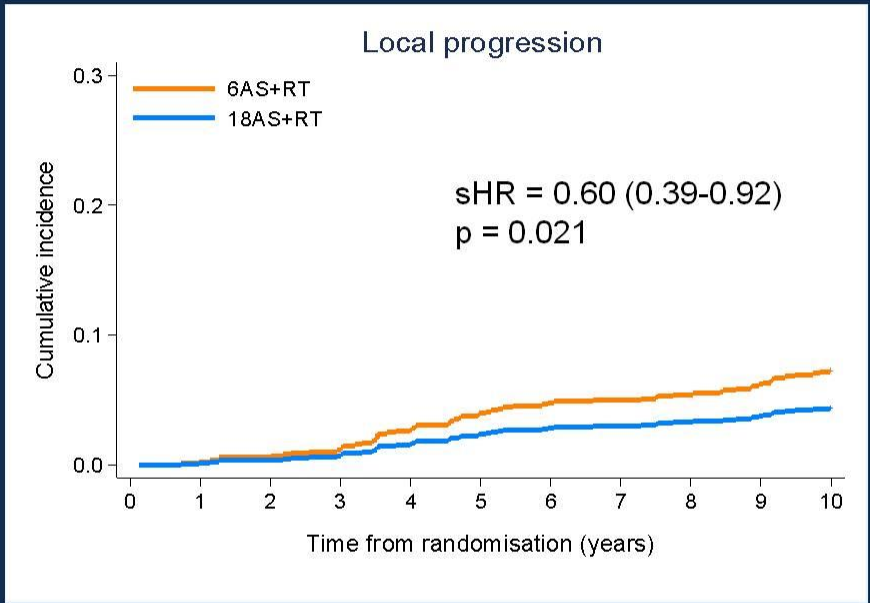
Secondary endpoints (cont.)

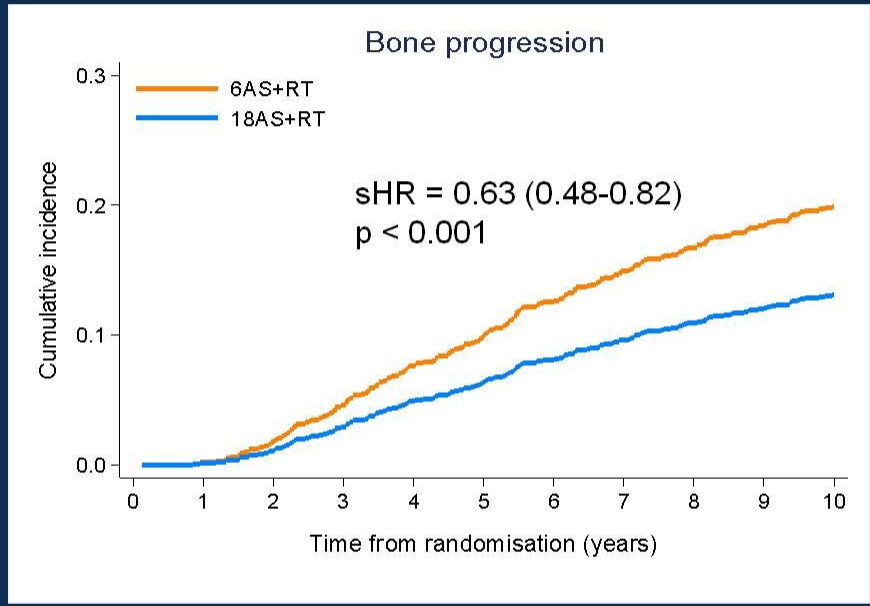




A 35% reduction in PSA progression also contributed to a reduction in secondary therapeutic intervention of 34%

Secondary endpoints



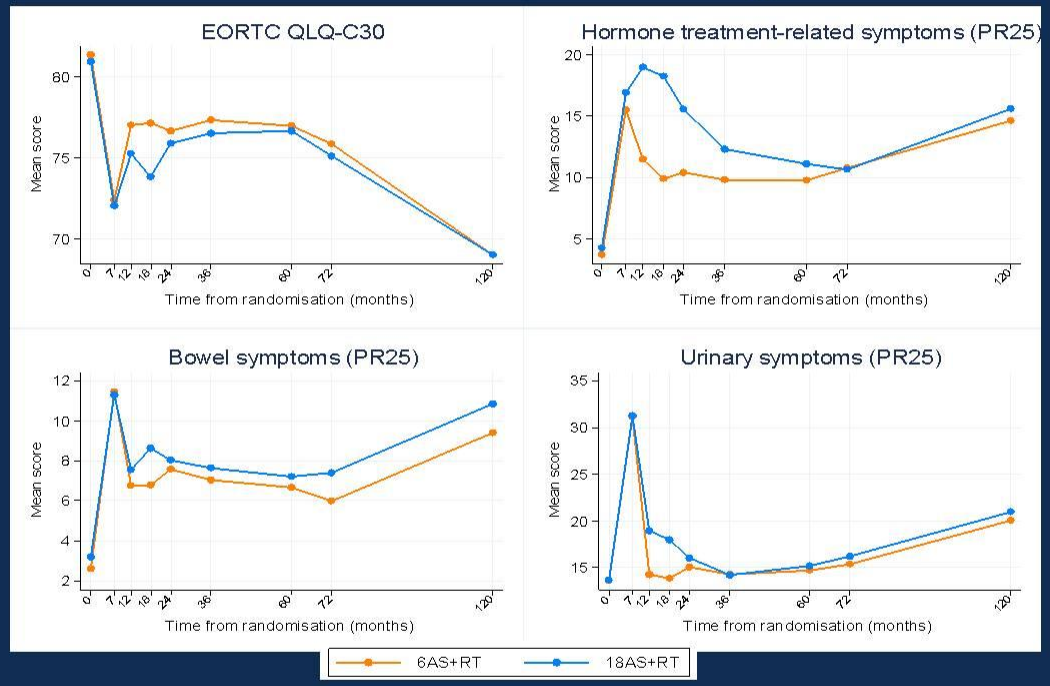


Similar reductions (40%) were observed in both local and bone progressions

18 vs 6 months AS: oncological endpoints

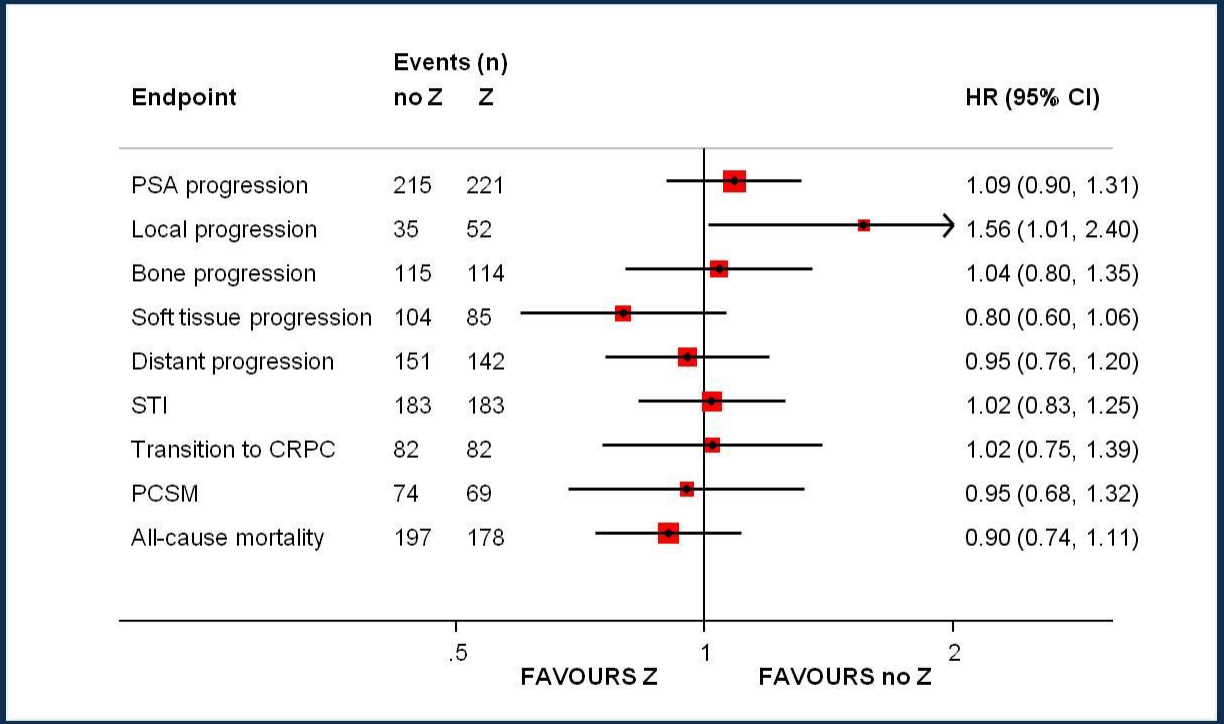
- **Significant reductions**
  - Primary endpoint: PCSM (relative effect size 30%)
  - Secondary endpoints: PSA, local, bone, distant progressions; secondary therapeutic intervention; transition to castration resistance (relative effect sizes 29-41%)
- **Non-significant reductions**
  - Soft tissue progression; all-cause mortality

18 vs 6 months AS: Quality of Life



The oncological benefits of the additional 12 months of AS in the 18 AS+RT group were bought at the cost of modest temporary increases in adverse PRO's and dysfunctional bowel and urinary symptoms

Z v no Z: Oncological endpoints



STI, secondary therapeutic intervention; CRPC, castrate-resistant prostate cancer; PCSM, prostate cancer-specific mortality

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Conclusions

In men with locally advanced PC:

- 18 months of AS is more effective than 6 months of AS
- The addition of 18 months of zoledronic acid provides no benefit


OBRIGADO
osmarbneto@gmail.com