IL TEAM INTERDISCIPLINARE NEL CARCINOMA DELLA PROSTATA

LA MALATTIA ORGANO-CONFINATA: IL CARCINOMA PROSTATICO AD ALTO RISCHIO

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CLASSE DI RISCHIO ALTO-MOLTO ALTO

RISCHIO ALTO (se presente uno dei tre parametri):

- Valori di PSA superiori a 20 ng/ml,
- *Gleason Score* sul prelievo bioptico maggiore di 7,
- Stadio clinico T3a-cT3b-T4.

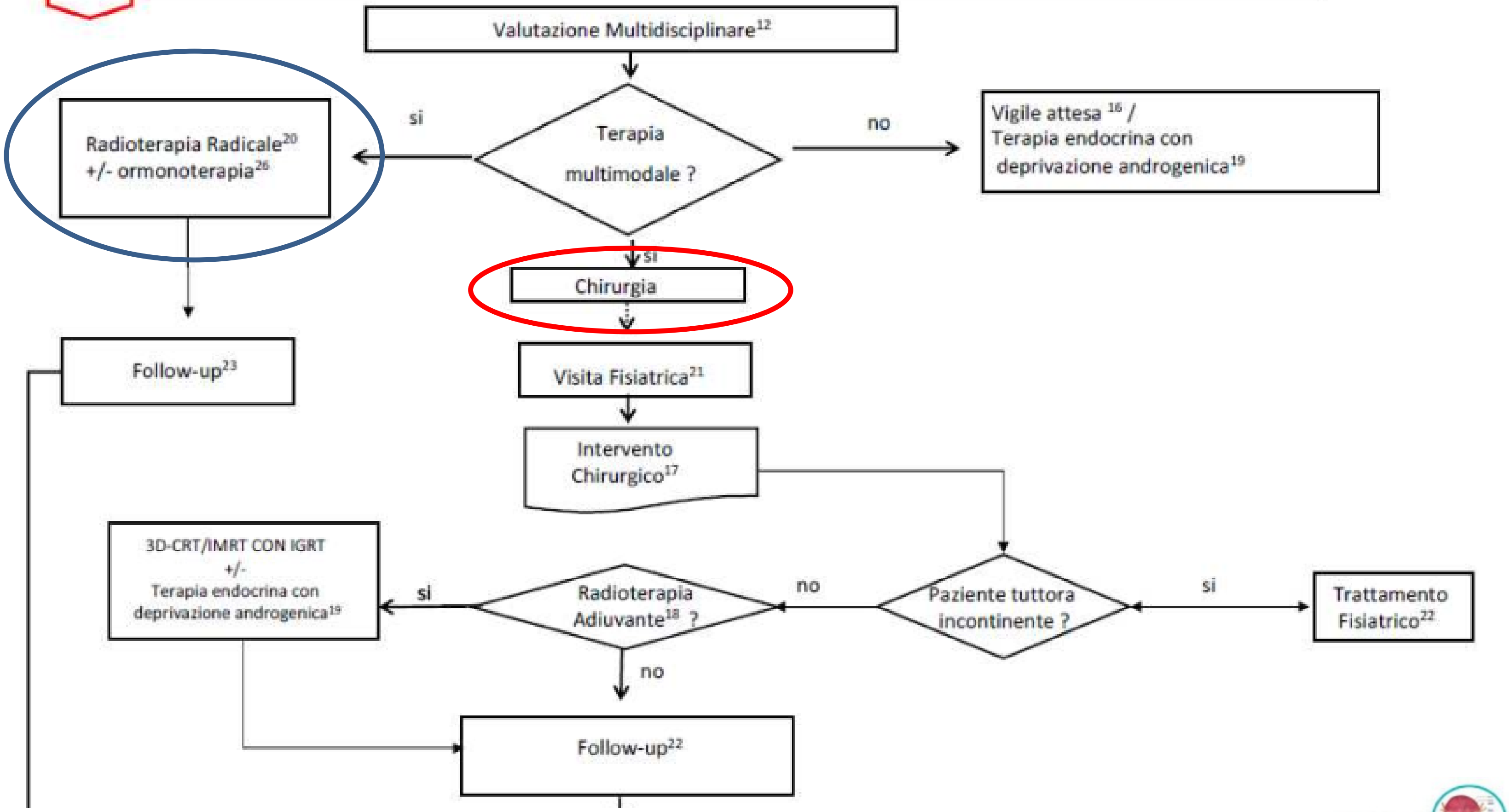
PDTA
per i pazienti
affetti
da tumore
prostatico

DIMENSIONI DEL PROBLEMA

- 37000 nuovi casi di carcinoma prostatico stimati in Italia nel 2019
- Alla diagnosi 80% sono localizzati
- Il 15% sono ad alto rischio (4000-5000 casi)
- La recidiva biochimica a 5 anni è circa 50%
- La mortalità cancro specifica a 15 anni è pari a 20-50%

- ‘I numeri del cancro in Italia 2019’ AIRTum, Shevack Clin Adv Hem Onc 2019, Kellokumpu-Lehtinen Eur Urol 2019, Fizazi Lancet Oncol 2015, Pietzak Curr Urol Rep 2016

Classe di Rischio Alto



Valutazione Multidisciplinare[12]

Terapia multimodale ?

si

Radioterapia Radicale[20] +/- ormonoterapia[26]

Follow-up[23]

no

Vigile attesa [16] / Terapia endocrina con deprivazione androgenica[19]

si

Chirurgia

Visita Fisiatrica[21]

Intervento Chirurgico[17]

Paziente tuttora incontinente ?

si

Trattamento Fisiatrico[22]

no

Radioterapia Adiuvante[18] ?

si

3D-CRT/IMRT CON IGRT +/- Terapia endocrina con deprivazione androgenica[19]

no

Follow-up[22]

PDTA per i pazienti affetti da tumore prostatico

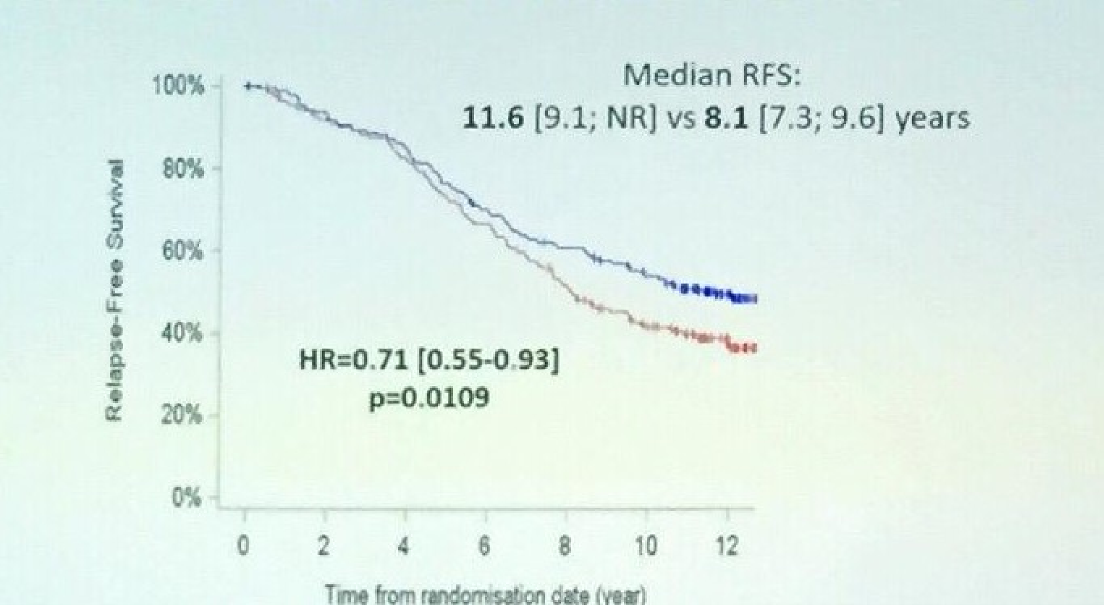
- CHEMIOTERAPIA NEOADIUVANTE
- CHEMIOTERAPIA ADIUVANTE

- CHEMIOTERAPIA NEOADIUVANTE
- CHEMIOTERAPIA ADIUVANTE

Androgen deprivation therapy plus docetaxel and estramustine versus androgen deprivation therapy alone for high-risk localised prostate cancer (GETUG 12): a phase 3 randomised controlled trial

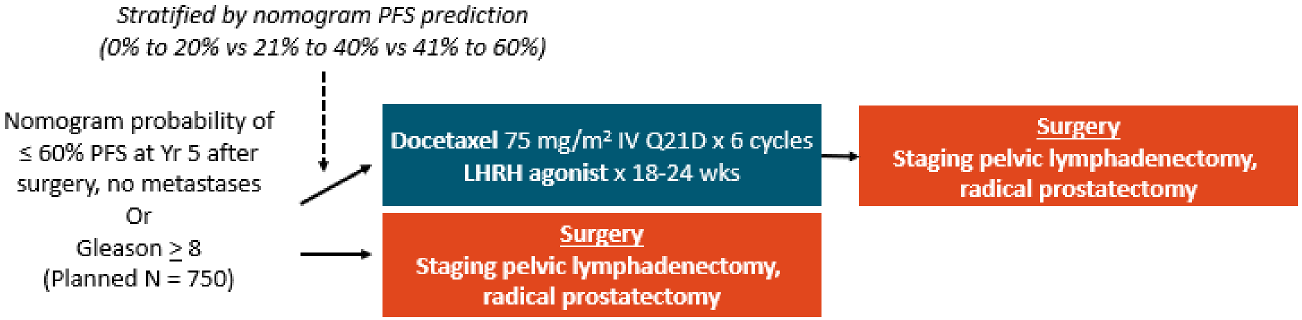
Karim Fizazi, Laura Faivre, François Lesaunier, Remy Delva, Gwenaëlle Gravis, Frédéric Rolland, Frank Priou, Jean-Marc Ferrero, Nadine Houede, Loïc Mourey, Christine Theodore, Ivan Krakowski, Jean-François Berdah, Marjorie Baciuchka, Brigitte Laguerre, Aude Fléchon, Alain Ravaud, Isabelle Cojean-Zelek, Stéphane Oudard, Jean-Luc Labourey, Paule Chinet-Charrot, Eric Legouffe, Jean-Léon Lagrange, Claude Linassier, Gaël Deplanque, Philippe Beuzeboc, Jean-Louis Davin, Anne-Laure Martin, Muriel Habibian, Agnès Laplanche, Stéphane Culine

- T3-T4
- Gleason score 8-10
- PSA > 20
- N+



- Goserelin 10.8 per 3 anni
- Goserelin + Docetaxel/Estramustine per 4 cicli

Can We Improve on Surgery for Very High–Risk Patients? Phase III CALGB 90203



Stratified by nomogram PFS prediction (0% to 20% vs 21% to 40% vs 41% to 60%)

Nomogram probability of ≤ 60% PFS at Yr 5 after surgery, no metastases
Or
Gleason $\geq$ 8
(Planned N = 750)

Docetaxel 75 mg/m² IV Q21D x 6 cycles
LHRH agonist x 18-24 wks

Surgery
Staging pelvic lymphadenectomy, radical prostatectomy

Surgery
Staging pelvic lymphadenectomy, radical prostatectomy

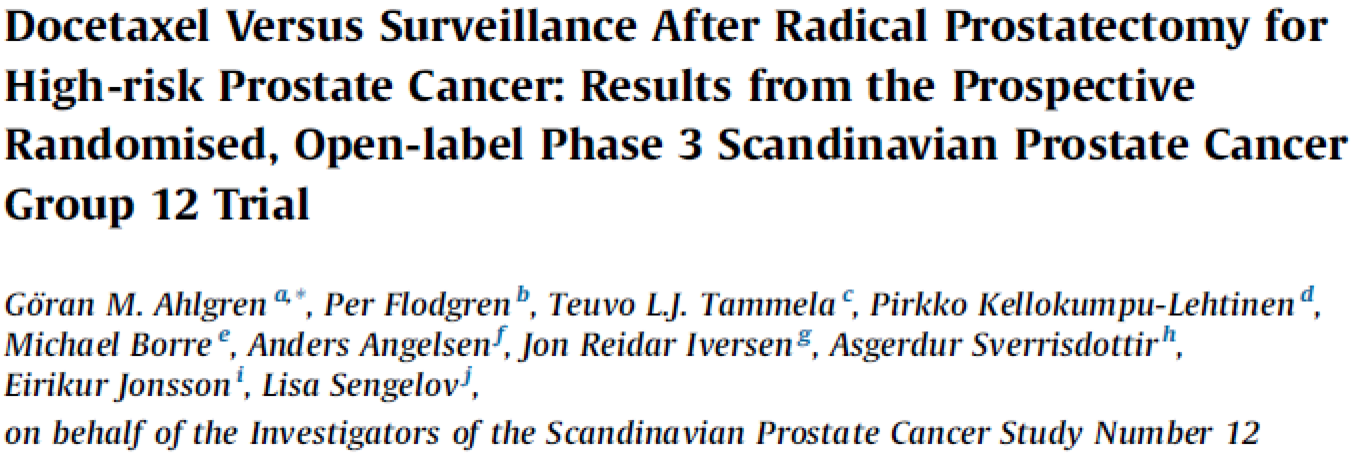
- Primary outcome: 5-yr biochemical PFS (45 vs 60 mos; HR: 1.35)
- Secondary outcomes: safety/tolerability of LHRH agonist, effect on pathologic tumor stage, time to clinically apparent progression, OS

Eastham JA, et al. Urology. 2003;62(suppl):55-62.

Slide credit: clinicaloptions.com

- CHEMIOTERAPIA NEOADIUVANTE

- CHEMIOTERAPIA ADIUVANTE



Docetaxel Versus Surveillance After Radical Prostatectomy for High-risk Prostate Cancer: Results from the Prospective Randomised, Open-label Phase 3 Scandinavian Prostate Cancer Group 12 Trial

Göran M. Ahlgren [a,], Per Flodgren [b], Teuvo L.J. Tammela [c], Pirkko Kellokumpu-Lehtinen [d], Michael Borre [e], Anders Angelsen [f], Jon Reidar Iversen [g], Asgerdur Sverrisdottir [h], Eirikur Jonsson [i], Lisa Sengelov [j],*

on behalf of the Investigators of the Scandinavian Prostate Cancer Study Number 12

- pT2 margini positivi
- pT3a GS 4+3, 8-10
- pT3b
- N+

- Docetaxel per 6 cicli
- Sorveglianza

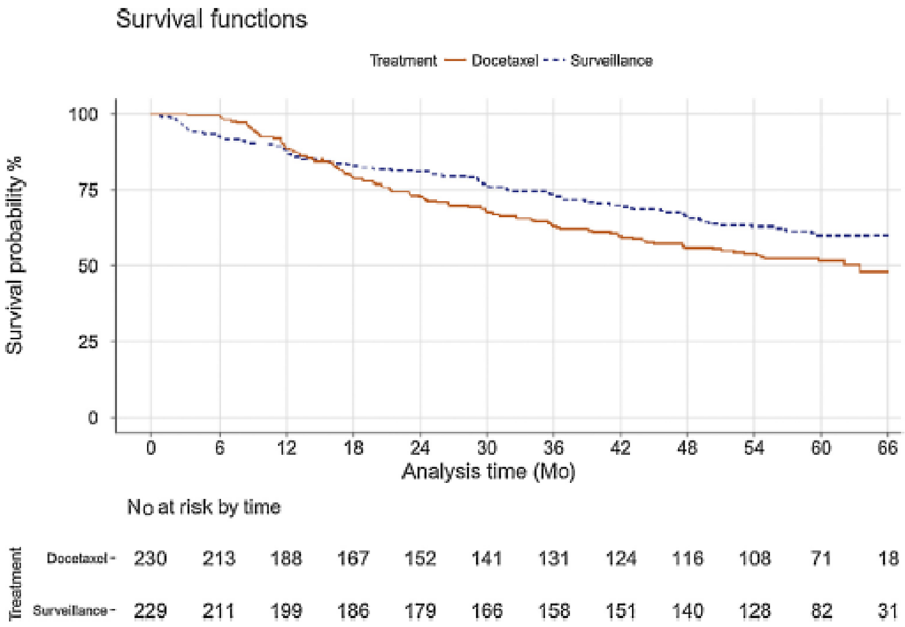


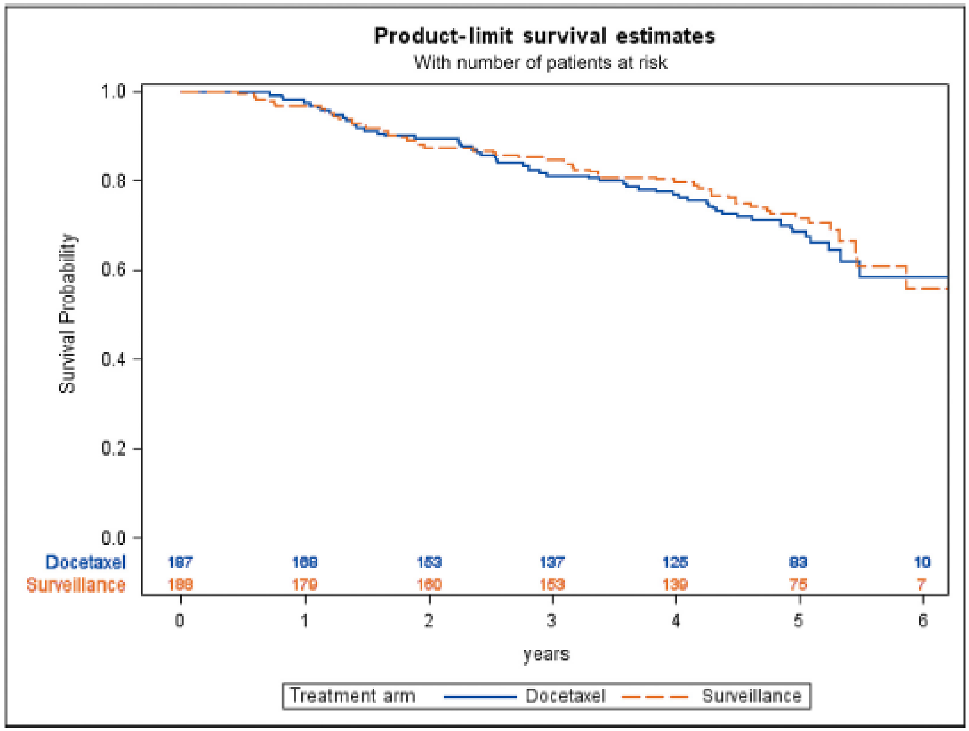
Fig. 2 – Kaplan-Meier curves of survival free of progression (prostate-specific antigen > 0.5 ng/ml) by intention to treat in Arm A (docetaxel) and Arm B (surveillance; p = 0.06).

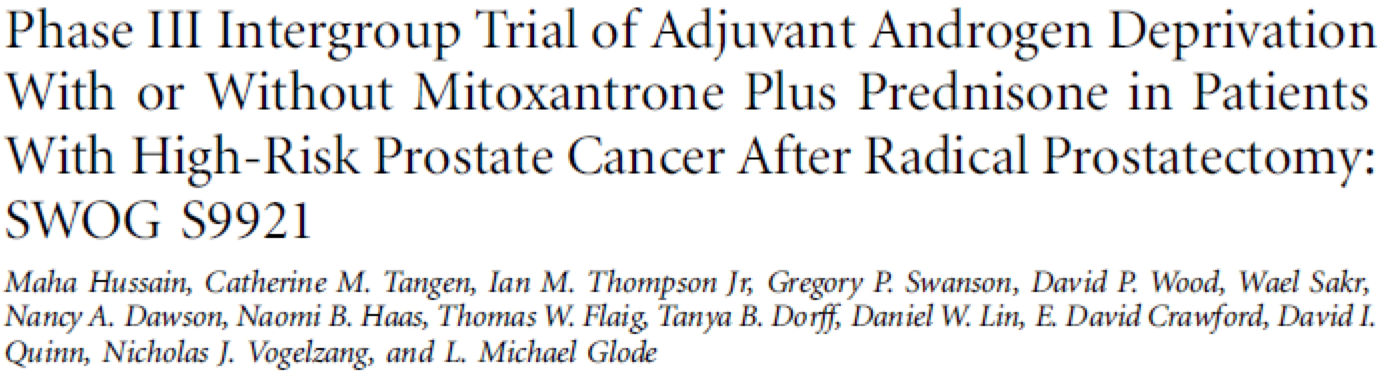
Docetaxel Versus Surveillance After Radical Radiotherapy for Intermediate- or High-risk Prostate Cancer—Results from the Prospective, Randomised, Open-label Phase III SPCG-13 Trial

Pirkko-Liisa Kellokumpu-Lehtinen [a,], Marie Hjälm-Eriksson [b,c], Camilla Thellenberg-Karlsson [d],*
Lennart Åström [e], Lars Franzen [f], Ann-Sofie Fransson [g], Markku J. Leskinen [h], Mihalj Zeke [i],
Teppo Huttunen [j], Claes Ginman [k],
on behalf of the Investigators of the Scandinavian Prostate Cancer Study No. 13

- T2 GS 4+3 PSA > 10
- T2 GS 8-10 PSA < 70
- T3

- LH-RH analogo per 9 mesi
- LH-RH + docetaxel per 6 cicli





Phase III Intergroup Trial of Adjuvant Androgen Deprivation With or Without Mitoxantrone Plus Prednisone in Patients With High-Risk Prostate Cancer After Radical Prostatectomy: SWOG S9921

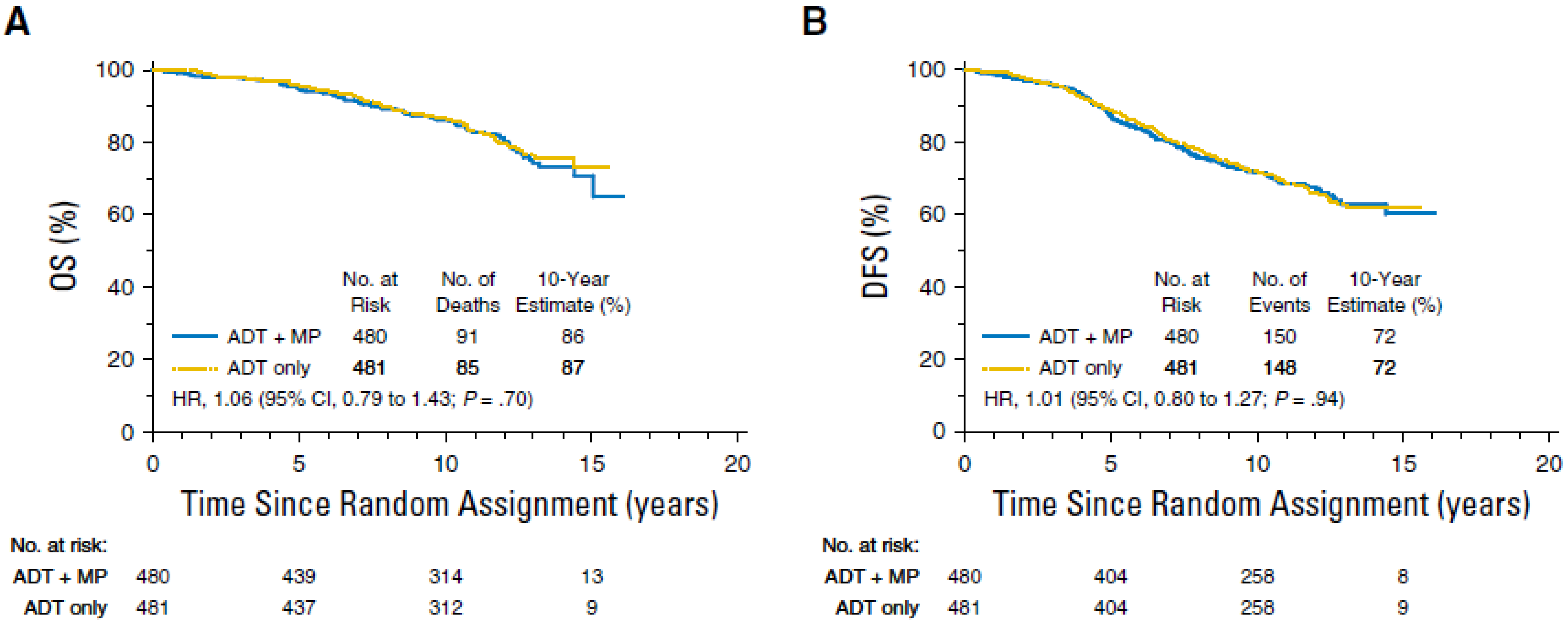
Maha Hussain, Catherine M. Tangen, Ian M. Thompson Jr, Gregory P. Swanson, David P. Wood, Wael Sakr, Nancy A. Dawson, Naomi B. Haas, Thomas W. Flaig, Tanya B. Dorff, Daniel W. Lin, E. David Crawford, David I. Quinn, Nicholas J. Vogelzang, and L. Michael Glode

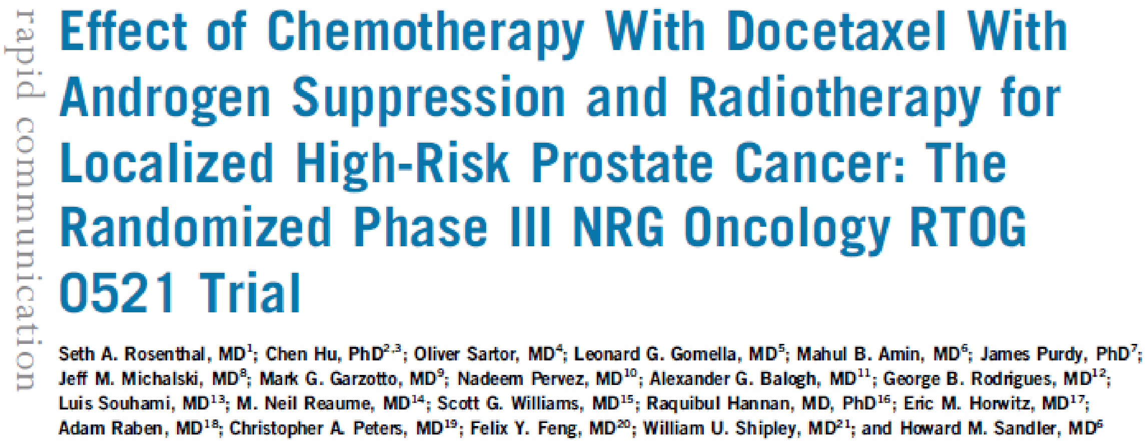
- pT3b, pT4, pN+
- GS 7 e margini positivi
- GS 8-10
- PSA preoper. > 15
- GS bioptico > 7
- GS bioptico > 6 e PSA > 10

- Goserelin 10,8 + Bicalutamide 50 per 2 anni
- Goserelin/Bicalutamide + Mitoxantrone per 6 cicli

Phase III Intergroup Trial of Adjuvant Androgen Deprivation With or Without Mitoxantrone Plus Prednisone in Patients With High-Risk Prostate Cancer After Radical Prostatectomy: SWOG S9921

Maha Hussain, Catherine M. Tangen, Ian M. Thompson Jr, Gregory P. Swanson, David P. Wood, Wael Sakr, Nancy A. Dawson, Naomi B. Haas, Thomas W. Flaig, Tanya B. Dorff, Daniel W. Lin, E. David Crawford, David I. Quinn, Nicholas J. Vogelzang, and L. Michael Glode





rapid communication

Effect of Chemotherapy With Docetaxel With Androgen Suppression and Radiotherapy for Localized High-Risk Prostate Cancer: The Randomized Phase III NRG Oncology RTOG 0521 Trial

Seth A. Rosenthal, MD[1]; Chen Hu, PhD[2,3]; Oliver Sartor, MD[4]; Leonard G. Gomella, MD[5]; Mahul B. Amin, MD[6]; James Purdy, PhD[7];
Jeff M. Michalski, MD[8]; Mark G. Garzotto, MD[9]; Nadeem Pervez, MD[10]; Alexander G. Balogh, MD[11]; George B. Rodrigues, MD[12];
Luis Souhami, MD[13]; M. Neil Reaume, MD[14]; Scott G. Williams, MD[15]; Raquibul Hannan, MD, PhD[16]; Eric M. Horwitz, MD[17];
Adam Raben, MD[18]; Christopher A. Peters, MD[19]; Felix Y. Feng, MD[20]; William U. Shipley, MD[21]; and Howard M. Sandler, MD[6]

- GS 9-10
- GS 7-8 e PSA > 20
- GS 8 e cT2-4

- LH-RH analogo + Antiandrogeno orale per 24 mesi + RT
- LH-RH/Antiandrogeno/RT + Docetaxel per 6 cicli

Effect of Chemotherapy With Docetaxel With Androgen Suppression and Radiotherapy for Localized High-Risk Prostate Cancer: The Randomized Phase III NRG Oncology RTOG 0521 Trial

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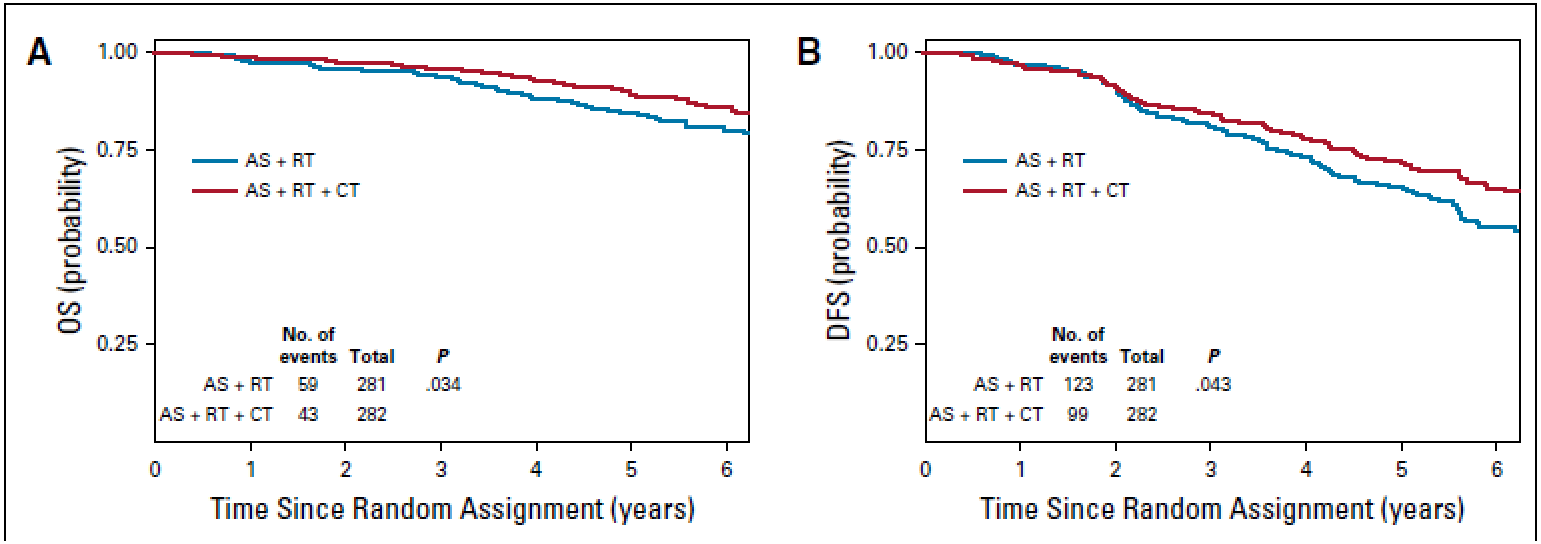
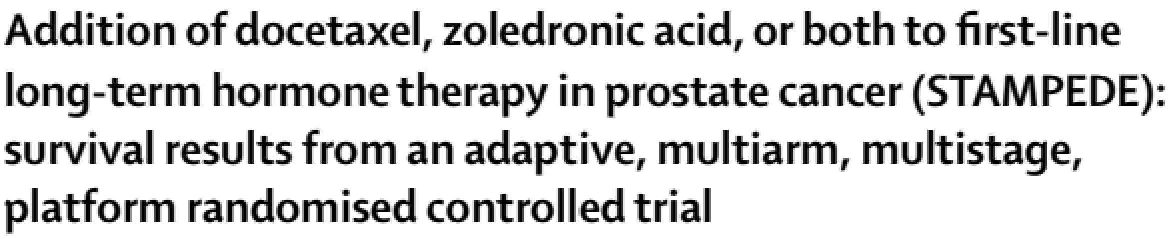
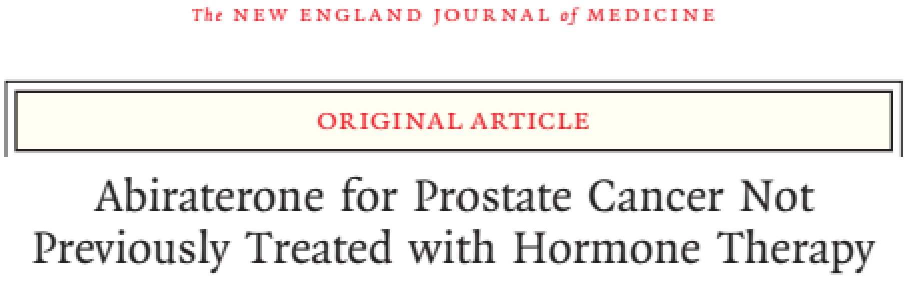


TABLE 3. RTOG 0521: Summary of Efficacy Results, ITT Analysis

End Point (years)	% (95% CI) AS + RT (n = 281)	% (95% CI) AS + RT + CT (n = 282)	HR (95% CI)	*P**
OS			0.69 (0.49 to 0.97)†	.034
4	88.7 (84.3 to 91.9)	93.3 (89.6 to 95.7)		
6	80.6 (75.2 to 85.0)	86.0 (80.8 to 89.9)		
Median	Not reached	Not reached		



Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy

- Attualmente non c’è un vantaggio di OS nei pazienti non metastatici e senza interessamento linfonodale

Table. Ongoing Trials of Adjuvant Therapy in High-Risk Prostate Cancer

Trial Name	NCT Number	Inclusion Criteria for High-Risk Prostate Cancer	Comparison Arms		Primary Outcome(s)
			Control	Experimental	
Neoadjuvant and Adjuvant Abiraterone Acetate + Apalutamide Prostate Cancer Undergoing Prostatectomy	NCT02903368	GS ≥4 + 3 = 7 OR GS 3 + 4 = 7 AND at least 1 of the following: PSA >20 ng/dL or T3 disease (determined by MRI)	Prior to prostatectomy, 6 mo of neoadjuvant leuprolide, abiraterone acetate, and prednisone	Prior to prostatectomy, 6 mo of neoadjuvant leuprolide, abiraterone acetate, prednisone, and apalutamide	2-y minimal residual disease 2-y pathologic complete response
			Post-prostatectomy, observation	Post-prostatectomy, 12 mo of adjuvant leuprolide, abiraterone acetate, prednisone, and apalutamide	
ENZARAD	NCT02446444	GS 8-10 OR GS 4 + 3 AND clinical T2b-4 AND PSA >20 ng/mL OR N1 disease (involvement of lymph nodes at or below the bifurcation of the common iliac arteries)	RT plus traditional nonsteroidal antiandrogen for 6 mo and GnRH agonist for 24 mo from randomization	RT plus enzalutamide 160 mg daily and GnRH agonist for 24 mo from randomization	5-y overall survival
ATLAS	NCT02531516	GS ≥8 and ≤cT2c OR GS ≥7, PSA ≥20 ng/mL, and ≥cT2c	RT plus 30 mo of GnRH agonist and placebo	RT plus 30 mo of GnRH agonist and apalutamide	Metastasis-free survival
Abiraterone, Radiotherapy and Short-Term Androgen Deprivation in Unfavorable Localized Prostate Cancer	NCT01717053	GS 7 with PSA ≤20 ng/mL and clinical T1-2, OR GS 8-10, PSA ≤20 ng/mL and clinical T1-2a, OR PSA 10.1-40 ng/mL with GS <7 and clinical T1-2, OR Clinical T3 with GS <7 and PSA ≤10 ng/mL	None	RT plus 6 mo of abiraterone acetate/prednisone and GnRH agonist	Rate of undetectable PSA (<0.1 ng/mL) at 1 y
AASUR in High Risk Prostate Cancer	NCT02772588	GS 8-10 PSA ≥20 ng/mL within 2 mo prior to registration	None	Ultrafractionated stereotactic RT plus 6 mo of leuprolide, abiraterone, and apalutamide	Proportion of patients with biochemical failure
FORMULA-509	NCT03141671	GS 8-10 PSA >0.5 pN + pT3 or pT4	RP and salvage RT plus 6 mo of GnRH agonist and bicalutamide	RP and salvage RT plus 6 mo of GnRH agonist, abiraterone acetate/prednisone, and apalutamide	PSA PFS (up to 5 y)

GnRH, gonadotropin-releasing hormone; GS, Gleason score; mo, months; MRI, magnetic resonance imaging; PFS, progression-free survival; PSA, prostate-specific antigen; RP, radical prostatectomy; RT, radiation therapy; y, years.

CONCLUSIONI

- Chemioterapia neoadiuvante alla chirurgia o alla radioterapia: NO

- Chemioterapia adiuvante: NO (Docetaxel?)

- Aspettando Abiraterone, Enzalutamide, Apalutamide ecc.