Εικονικός ασθενής 6:

Διαχείριση της βιοχημικής υποτροπής μετά από ριζική προστατεκτομή και συνακόλουθη ακτινοθεραπεία

Διονύσιος Ν. Μητρόπουλος

Καθηγητής Ουρολογίας

ΙΑΤΡΙΚΗ ΣΧΟΛΗ

Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών

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Ανδρας ηλικίας 78 ετών, με ιστορικό ριζικής προστατεκτομής και ακτινοθεραπείας προσέρχεται με αυξανόμενο PSA (1,2 ng/ml έναντι 0,8 / 0,4 / 0,3 /0,3 προ 3,6,9 και 12 μηνών, αντίστοιχα

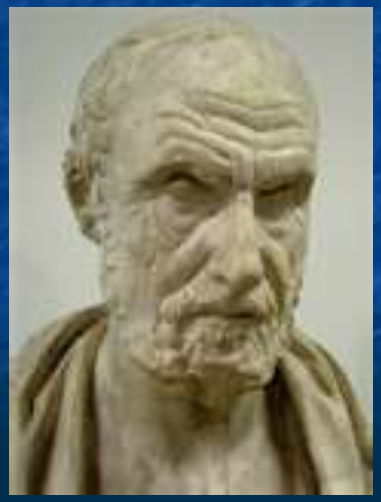
Α. Η θεραπευτική αντιμετώπιση, ανεξάρτητα από οτιδήποτε άλλο, θα είναι ο ανδρογονικός αποκλεισμός.
Επομένως, ο μόνος προβληματισμός αφορά τον τύπο του ανδρογονικού αποκλεισμού (πλήρης ή όχι, LHRH ανάλογο ή αντι-LHRH ή υποκάψιος ορχεκτομή)

Β. Τα δεδομένα είναι ανεπαρκή γιά την λήψη θεραπευτικής απόφασης. Χρειάζονται λεπτομέρειες από το ιστορικό και νέος απεικονιστικός έλεγχος


KEEP
CALM
AND
KNOW YOUR
ENEMY

"Δεν θα μπορείς πάντα να θεραπεύσεις την νόσο,
αλλά θα πρέπει πάντα να ανακουφίσεις τον ασθενή"

"Είναι πολύ πιό σπουδαίο να μάθεις ποιός έχει την
νόσο παρά ποιά νόσο έχει ο ασθενής"



Ιπποκράτης


PATIENT HEALTH HISTORY
DOB
PATIENT NAME
REASON FOR VISIT
SURGICAL HISTORY
What surgeries
Type?
Hospital?

Ανδρας ηλικίας 78 ετών, μέτρια υπέρβαρος, με ιστορικό ριζικής προστατεκτομής και ακτινοθεραπείας προσέρχεται με αυξανόμενο PSA (1,2 ng/ml έναντι 0,8 και 0,4 προ 3 και 6 μηνών, αντίστοιχα).

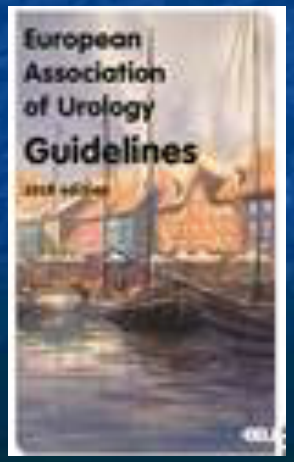
2011: Ριζική προστατεκτομή και μη εκτεταμένη λεμφαδενεκτομή (προεγχειρητικό PSA 6,8 ng/ml, $pT_{3\beta}N_0$, εστιακή διήθηση κάψας, Gleason score 4+3=7, μετεγχειρητικό PSA 0,05 ng/ml.

2011-2016: σταδιακή άνοδος του PSA μέχρι 0,8 ng/ml. Απόφαση γιά ακτινοθεραπεία με MRI κάτω κοιλίας χωρίς παθολογικά ευρήματα. PSA ναδίρ 0,2 ng/ml. Το 2013 διεπιστώθη σακχαρώδης διαβήτης τύπου 2 και το 2014 υπεβλήθη σε αγγειοπλαστική 2 αγγείων.

2016-2018: σταδιακή αύξηση του PSA σε 1,2 ng/ml έναντι 0,8/0,4/0,3/0,3 προ 3,6,9 και 12 μηνών, αντίστοιχα

Απεικονιστικός έλεγχος

- Ο συνήθης απεικονιστικός έλεγχος (bone scan, CT κοιλίας) είναι συνήθως αρνητικός σε ασυμπτωματικούς ασθενείς με BCR μετά από RP ή RT καθώς προηγείται των κλινικών μεταστάσεων κατά 7-8 έτη. Στους ασθενείς αυτούς η πιθανότητα θετικού bone scan σε ασθενείς με PSA < 7 ng/ml είναι < 5%.
- Οι περισσότεροι ασθενείς υποβάλλονται σε salvage RT χωρίς τοπική απεικόνιση
- Η mpMRI μπορεί να ανιχνεύσει τοπικές υποτροπές στη προστατική κοίτη αλλά η ευαισθησία της σε περιπτώσεις με PSA < 0.5 ng/mL παραμένει αντιφατική.
- Το Choline PET/CT είναι λιγότερο ευαίσθητο από την mpMRI όταν το PSA είναι <1 ng/mL
- Το PSMA-PET/CT είναι θετικό στο 15-58% των ασθενών με BCR και PSA < 0.5 ng/mL, αλλά οι δημοσιευμένες μελέτες είναι δύσκολο να ερμηνευθούν γιατί συνήθως αναμιγνύουν ασθενείς με υποτροπή μετά από τόσο RP όσο και RT και δεν εξειδικεύουν το ποσοστό των ασθενών με τοπικές μεταστάσεις έναντι απώτερων μεταστάσεων σε επίπεδα PSA < 0.5 ng/mL.
- Η ακριβής ανίχνευση και εντόπιση των τοπικών υποτροπών μετά από RP θα απαιτηθεί μόνον αν αποδειχθεί ότι η στερεοτακτική salvage RT στη θέση της υποτροπής βελτιώνει το θεραπευτικό αποτέλεσμα.



6.3.4.4. Guidelines for imaging in patients with biochemical recurrence

Prostate-specific antigen (PSA) recurrence after radical prostatectomy	LE	Strength rating
Perform imaging only if the outcome will influence subsequent treatment decisions.		Strong
If the PSA level is ≥ 1 ng/mL, perform a prostate-specific membrane antigen positron emission tomography computed tomography (PSMA PET/CT), if available, or a choline PET/CT imaging otherwise.	2b	Weak

Α. Η πορεία είναι η κλασσική που ακολουθεί κάθε ασθενής με τέτοια χαρακτηριστικά. Θα έπρεπε να είχε κάνει επικουρική ακτινοθεραπεία με ή χωρίς συνοδό ορμονοθεραπεία και θα είχε αντιμετωπίσει πλήρως το πρόβλημα

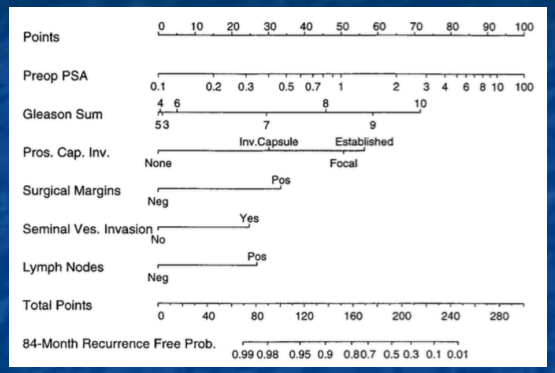
Β. Ο τρόπος αντιμετώπισης είναι αποδεκτός και η νόσος είναι απόλυτα αντιμετωπίσιμη και δεν αποτελεί δυνητική απειλή γιά την ζωή του, ειδικά μέσα στα πλαίσια της συνοδού νοσηρότητάς του

Memorial Sloan Kettering Cancer Center

Postoperative Nomogram for Disease Recurrence After Radical Prostatectomy for Prostate Cancer

J Clin Oncol 17:1499-1507. © 1999

Michael W. Kattan, Thomas M. Wheeler, and Peter T. Scardino



https://www.mskcc.org/nomograms/prostate/post_op

Post-Radical Prostatectomy

Your Results

Edit Information

Click the +/- to read more about your results

+ PROBABILITY OF REMAINING RECURRENCE-FREE AFTER SURGERY

2 YR 83% 5 YR 55%

7 YR 45% 10 YR 35%

+ 15-YEAR PROSTATE CANCER-SPECIFIC SURVIVAL

15 YR 97%

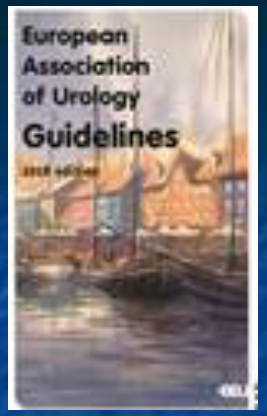
Με τα δεδομένα αυτά ο ασθενής θα είχε ωφεληθεί από:

Α. Adjuvant ακτινοθεραπεία

Β. Early salvage ακτινοθεραπεία

Γ. Salvage ακτινοθεραπεία

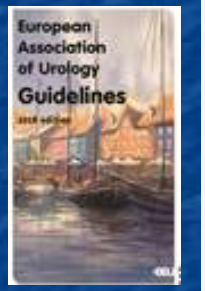
Δ. Παρατήρηση μέχρι την ανάπτυξη κλινικά εμφανών μεταστάσεων



6.3.8. ***Observation***

Observation until the development of clinically evident metastatic disease may represent a viable option for patients with low-risk features (PSA-DT > 12 months, time to BCR > 3 years, GS ≤ 7 and stage ≤ T3a) or unfit patients with a life expectancy less than ten years and/or are unwilling to undergo salvage treatment. In unselected relapsing patients, the median actuarial time to the development of metastasis will be eight years and the median time from metastasis to death will be a further five years [569].

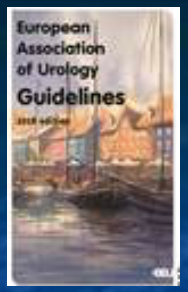
pT_{3b}, GS 7, time to BCR 5 χρόνια, PSA-DT > 12 μήνες, ικανοποιητικό (τότε) προσδόκιμο επιβίωσης



6.3.9. *Guidelines for second-line therapy after treatment with curative intent*

Local salvage treatment	Strength rating
Recommendations for biochemical recurrence after radical prostatectomy	
Offer active surveillance and possibly delayed salvage radiotherapy (SRT) to patients with biochemical recurrence and favourable prognostic factors (≤ pT3a, time to biochemical recurrence > three year, prostate-specific antigen doubling-time (PSA-DT) > twelve months, Gleason score ≤ 7), who may not benefit from intervention.	Strong
Treat patients with a PSA rise from the undetectable range with SRT. The total dose of SRT should be at least 66 Gy and should be given early (PSA < 0.5 ng/mL).	Strong
Recommendations for systemic salvage treatment	
Do not offer androgen deprivation therapy to M0 patients with a PSA-DT > twelve months.	Strong

pT_{3b}, GS 7, time to BCR 5 χρόνια, PSA-DT > 12 μήνες



6.3.5.1.2. Comparison of adjuvant radiotherapy (ART) and salvage radiotherapy (SRT)

In a large retrospective case-matching study to evaluate ART vs. early SRT including pT3N0 R0/R1 patients only (ADT was excluded), two and five years after surgery, biochemically no evidence of disease (bNED) rates were 91% and 78% for ART vs. 93% and 82% after salvage RT, respectively. Subgroup analyses did not yield significant differences for the two approaches. It was concluded that early salvage RT does not impair PCa control, but clearly helps to reduce over-treatment, which is a major issue in both ART and in SRT.

The results were confirmed for metastasis-free and OS. However, these retrospective studies are underpowered for high-risk cases such as pT3b/R1/GS 8-10.

Both approaches (ART and SRT) together with the efficacy of neoadjuvant ADT are currently being compared in three prospective RCTs: RADICALS, TROG, RAVES, and GETUG 17.

Decision-making on whether to proceed with adjuvant RT, for high-risk PCa, pT3-4 pN0 M0 with undetectable PSA after RP, or to postpone RT as an early salvage procedure in the event of biochemical relapse, remains difficult. In everyday practice, the urologist should explain to the patient before RP that adjuvant RT may be of benefit if the patient has negative prognostic risk factors. Ultimately, the decision on whether to treat requires a multidisciplinary approach that takes into account the optimal timing of RT when it is used, and provides justification when it is not, will best inform the discussion between the physician and the patient.

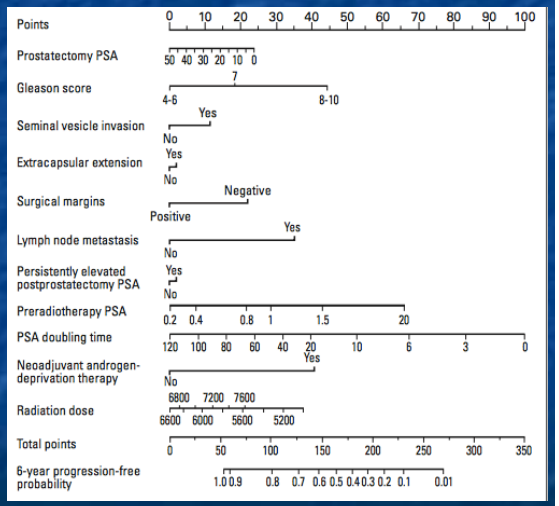
Memorial Sloan Kettering Cancer Center

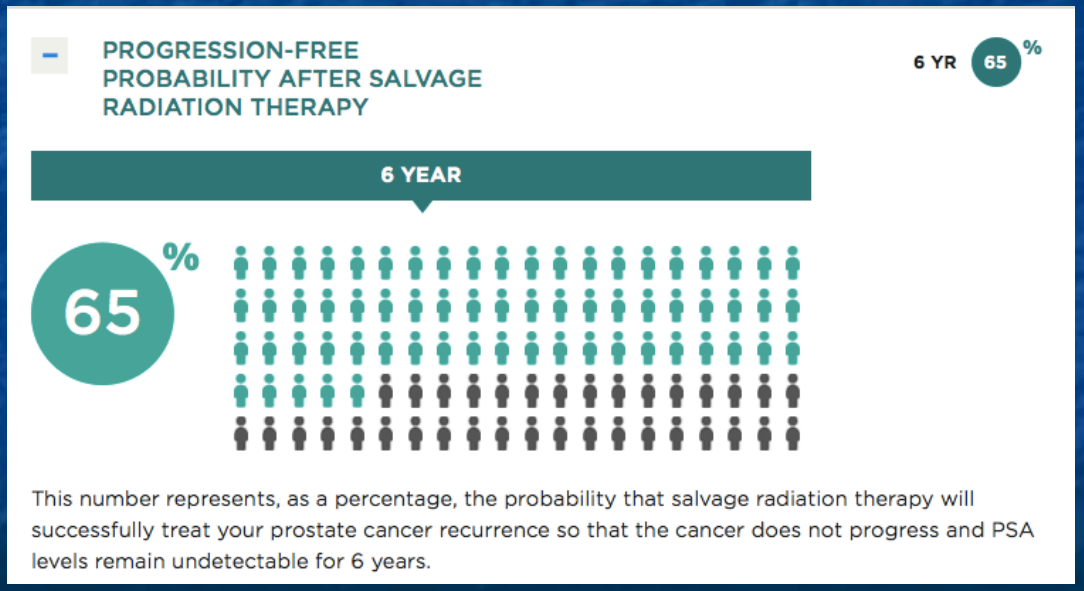
Predicting the Outcome of Salvage Radiation Therapy for Recurrent Prostate Cancer After Radical Prostatectomy

Andrew J. Stephenson, Peter T. Scardino, Michael W. Kattan, Thomas M. Pisansky, Kevin M. Slawin, Eric A. Klein, Mitchell S. Anscher, Jeff M. Michalski, Howard M. Sandler, Daniel W. Lin, Jeffrey D. Forman, Michael J. Zelefsky, Larry L. Kestin, Claus G. Roehrborn, Charles N. Catton, Theodore L. DeWeese, Stanley L. Liauw, Richard K. Valicenti, Deborah A. Kuban, and Alan Pollack

J Clin Oncol 25:2035-2041. © 2007

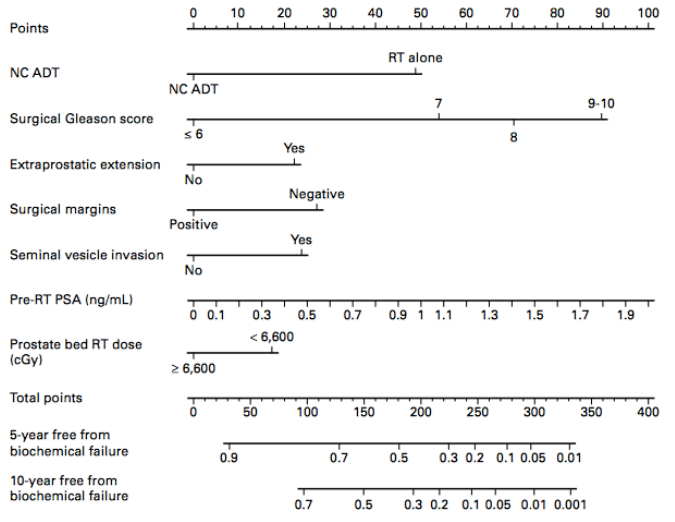
https://www.mskcc.org/nomograms/prostate/salvage_radiation_therapy





Cleveland Clinic

riskcalc.org/ProstateCancerAfterRadicalProstatectomyNew/



Contemporary Update of a Multi-Institutional Predictive Nomogram for Salvage Radiotherapy After Radical Prostatectomy

Rahul D. Tendulkar, Shree Agrawal, Tianming Gao, Jason A. Efstathiou, Thomas M. Pisansky, Jeff M. Michalski, Bridget F. Koontz, Daniel A. Hamstra, Felix Y. Feng, Stanley L. Liauw, Matthew C. Abramowitz, Alan Pollack, Mitchell S. Anscher, Drew Moghanaki, Robert B. Den, Kevin L. Stephans, Anthony L. Zietman, W. Robert Lee, Michael W. Kattan, and Andrew J. Stephenson

J Clin Oncol 34:3648-3654. © 2016

Result	Probability
5-year free from biochemical failure probability	65 %
10-year free from biochemical failure probability	53 %
5-year cumulative incidence of metastasis	6 %
10-year cumulative incidence of metastasis	12 %

Asian Journal of Andrology

(2017) 19, 493–499

Factors influencing biochemical recurrence in patients who have received salvage radiotherapy after radical prostatectomy: a systematic review and meta-analysis

CONCLUSIONS

Our meta-analysis suggests that GS ≥7, pT ≥3a, and SRT not combined with ADT and radiation dose <64 Gy are risk factors for BCR among patients who have received SRT for BCR following RP. However, preoperative PSA, surgical margin, perineural invasion, and SVI have no effect on BCR. Our predictive models might help clinicians to identify the best candidates who will benefit from SRT.

Μήπως έπρεπε να είχε υποβληθεί σε συνοδό ορμονοθεραπεία ;

Α. ΝΑΙ

Β. ΟΧΙ

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 2, 2017 VOL. 376 NO. 5

Radiation with or without Antiandrogen Therapy in Recurrent Prostate Cancer

W.U. Shipley, W. Seiferheld, H.R. Lukka, P.P. Major, N.M. Heney, D.J. Grignon, O. Sartor, M.P. Patel, J.-P. Bahary, A.L. Zietman, T.M. Pisansky, K.L. Zeitzer, C.A.F. Lawton, F.Y. Feng, R.D. Lovett, A.G. Balogh, L. Souhami, S.A. Rosenthal, K.J. Kerlin, J.J. Dignam, S.L. Pugh, and H.M. Sandler, for the NRG Oncology RTOG*

Subgroup	No. of Patients (%)	Bicalutamide Group	Placebo Group	Hazard Ratio (95% CI)	P Value
		12-yr overall survival rate (%)			
Overall	760 (100.0)	76.3	71.3	0.77 (0.59–0.99)	0.04
Gleason score					
2–6	214 (28.2)	79.5	79.2	0.95 (0.57–1.59)	0.84
7	413 (54.5)	78.5	70.9	0.69 (0.49–0.98)	0.04
8–10	131 (17.3)	63.9	58.4	0.76 (0.44–1.30)	0.32
PSA level at trial entry					
<0.7 ng/ml	405 (53.3)	76.8	80.7	1.13 (0.77–1.65)	0.53
0.7–1.5 ng/ml	237 (31.2)	77.0	67.5	0.61 (0.39–0.95)	0.03
>1.5 ngl/ml	118 (15.5)	73.5	48.9	0.45 (0.25–0.81)	0.007
Positive surgical margin					
No	191 (25.1)	73.5	72.9	0.87 (0.53–1.41)	0.56
Yes	569 (74.9)	77.3	70.7	0.73 (0.54–0.98)	0.04

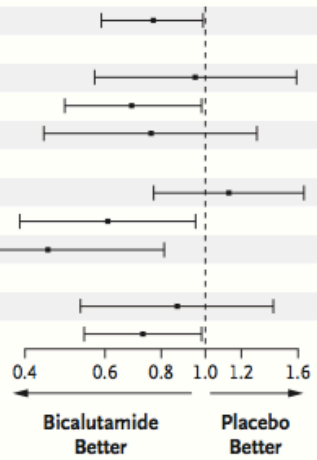


Figure 3. Effect of Antiandrogen Therapy with Bicalutamide on 12-Year Overall Survival.

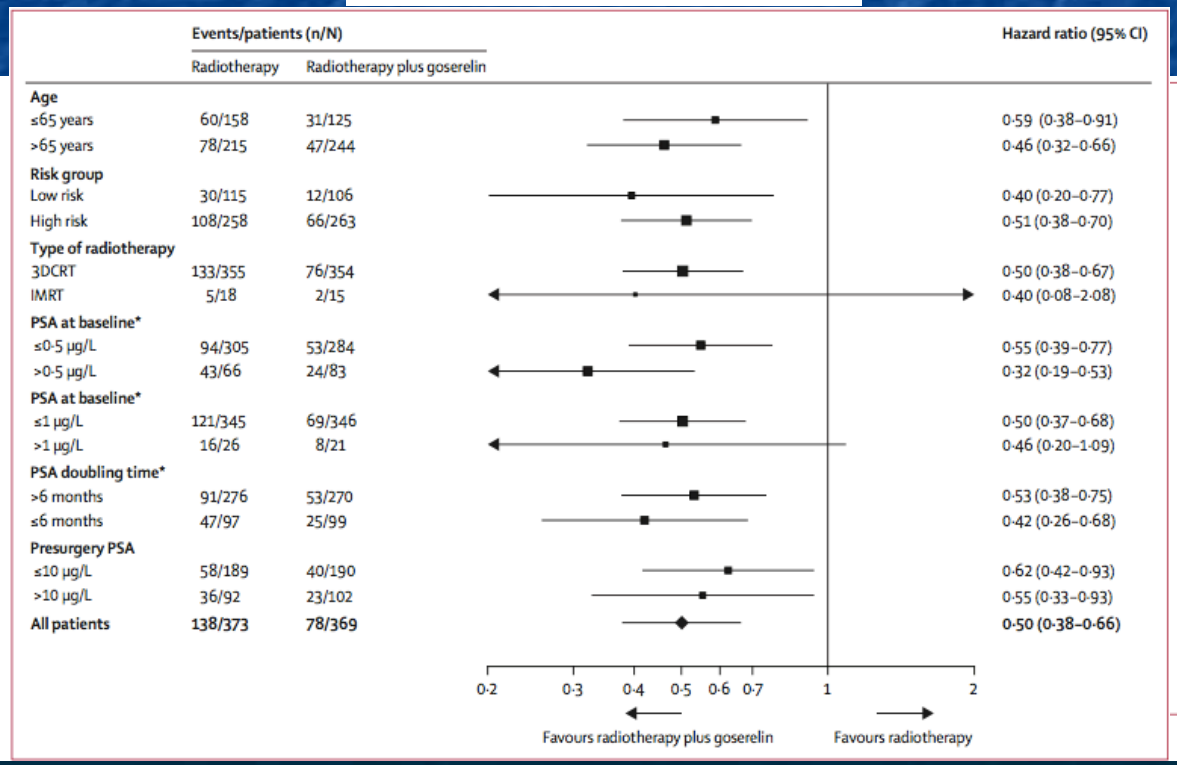
All patients underwent radiation therapy in addition to receiving either antiandrogen therapy with bicalutamide or placebo. The scale for the Gleason score ranges from 2 to 10, with higher scores indicating a worse prognosis. Data on the Gleason score were missing for one patient in each group. P values were calculated with the use of the log-rank test.

patients with active prostate cancer on the basis of central review.

Salvage radiotherapy with or without short-term hormone therapy for rising prostate-specific antigen concentration after radical prostatectomy (GETUG-AFU 16): a randomised, multicentre, open-label phase 3 trial

Christian Carrie, Ali Hasbini, Guy de Laroche, Pierre Richaud, Stéphane Guerif, Igor Latorzeff, Stéphane Supiot, Mathieu Bosset, Jean-Léon Lagrange, Véronique Beckendorf, François Lesaunier, Bernard Dubray, Jean-Philippe Wagner, Tan Dat N'Guyen, Jean-Philippe Suchaud, Gilles Créhange, Nicolas Barbier, Muriel Habibian, Céline Ferlay, Philippe Fourneret, Alain Ruffion, Sophie Dussart

Lancet Oncol 2016; 17: 747–56



	Events/patients (n/N)		Hazard ratio (95% CI)
	Radiotherapy	Radiotherapy plus goserelin	
Age			
≤65 years	60/158	31/125	0·59 (0·38–0·91)
>65 years	78/215	47/244	0·46 (0·32–0·66)
Risk group			
Low risk	30/115	12/106	0·40 (0·20–0·77)
High risk	108/258	66/263	0·51 (0·38–0·70)
Type of radiotherapy			
3DCRT	133/355	76/354	0·50 (0·38–0·67)
IMRT	5/18	2/15	0·40 (0·08–2·08)
PSA at baseline*			
≤0·5 µg/L	94/305	53/284	0·55 (0·39–0·77)
>0·5 µg/L	43/66	24/83	0·32 (0·19–0·53)
PSA at baseline*			
≤1 µg/L	121/345	69/346	0·50 (0·37–0·68)
>1 µg/L	16/26	8/21	0·46 (0·20–1·09)
PSA doubling time*			
>6 months	91/276	53/270	0·53 (0·38–0·75)
≤6 months	47/97	25/99	0·42 (0·26–0·68)
Presurgery PSA			
≤10 µg/L	58/189	40/190	0·62 (0·42–0·93)
>10 µg/L	36/92	23/102	0·55 (0·33–0·93)
All patients	**138/373**	**78/369**	**0·50 (0·38–0·66)**

73 (2018) 512–518

Use of Concomitant Androgen Deprivation Therapy in Patients Treated with Early Salvage Radiotherapy for Biochemical Recurrence After Radical Prostatectomy: Long-term Results from a Large, Multi-institutional Series

Giorgio Gandaglia[a,1], Nicola Fossati[a,1], R. Jeffrey Karnes[b], Stephen A. Boorjian[b], Michele Colicchia[b], Alberto Bossi[c], Thomas Seisen[c], Cesare Cozzarini[d], Nadia Di Muzio[d], Barbara Noris Chiorda[d], Emanuele Zaffuto[a], Thomas Wiegel[e], Shahrokh F. Shariat[f], Gregor Goldner[g], Steven Joniau[h], Antonino Battaglia[h], Karin Haustermans[i], Gert De Meerleer[i], Valérie Fonteyne[j], Piet Ost[j], Hendrick Van Poppel[e], Francesco Montorsi[a], Alberto Briganti[a,]*

Conclusions: The beneficial effect of ADT concomitant to eSRT varied significantly according to disease characteristics, such that only men with more aggressive PCa features benefit from ADT in the eSRT setting for BCR after RP.

Patient summary: The oncological benefits of concomitant androgen deprivation therapy (ADT) in patients undergoing salvage radiotherapy (SRT) vary according to pathological characteristics. Only patients with more aggressive disease characteristics seemed to benefit from the use of hormonal manipulation at the time of early SRT. Conversely, the potential side effects of ADT could be spared in patients with low prostate-specific antigen levels and favorable pathological features.

Androgen deprivation therapy during and after post-prostatectomy radiotherapy in patients with prostate cancer: a case control study

Kim *et al. BMC Cancer* (2018) 18:271

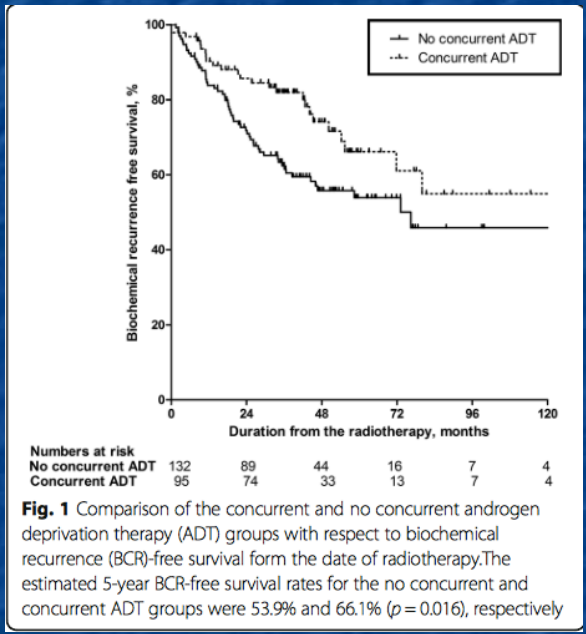


Fig. 1 Comparison of the concurrent and no concurrent androgen deprivation therapy (ADT) groups with respect to biochemical recurrence (BCR)-free survival form the date of radiotherapy.The estimated 5-year BCR-free survival rates for the no concurrent and concurrent ADT groups were 53.9% and 66.1% ($p = 0.016$), respectively

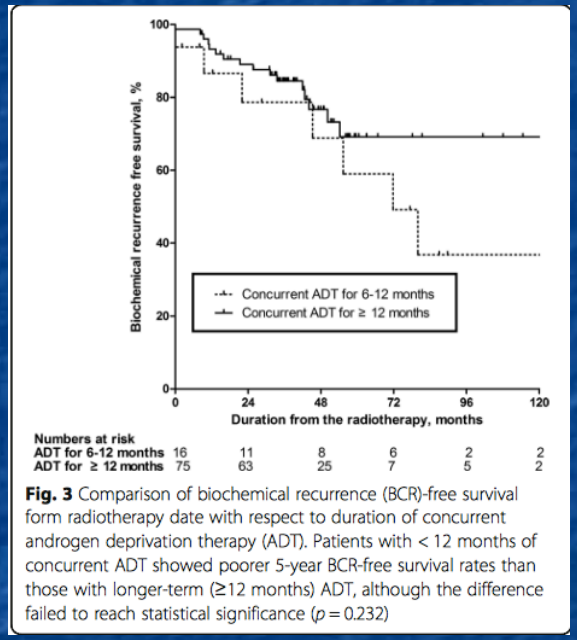
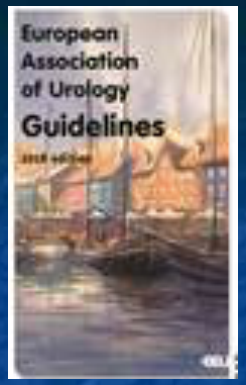


Fig. 3 Comparison of biochemical recurrence (BCR)-free survival form radiotherapy date with respect to duration of concurrent androgen deprivation therapy (ADT). Patients with < 12 months of concurrent ADT showed poorer 5-year BCR-free survival rates than those with longer-term (≥12 months) ADT, although the difference failed to reach statistical significance ($p = 0.232$)

Conclusions

Concurrent ADT during post-prostatectomy RT significantly improved BCR-free survival. Therefore, to maximize the oncological benefit, ADT of sufficient durations should be implemented. The results from ongoing RCTs are needed to confirm our results.

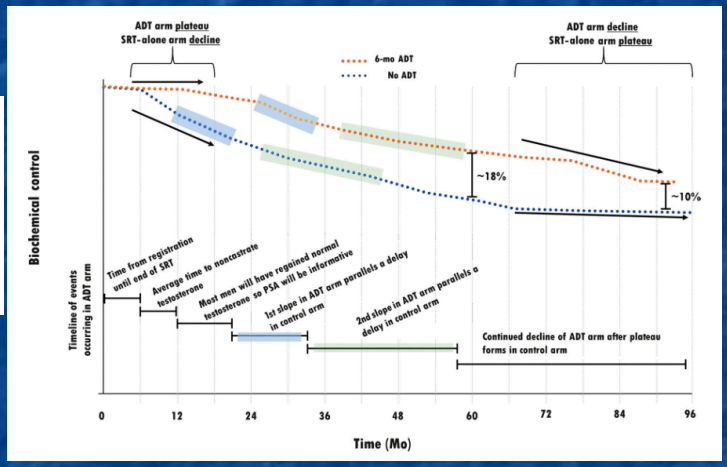


A recent literature review recommends risk stratification based on the pre-SRT PSA (> 0.7 ng/mL), margin status (positive), and high GS, to personalise the use of hormone therapy with SRT [643].

A Systematic Review and Framework for the Use of Hormone Therapy with Salvage Radiation Therapy for Recurrent Prostate Cancer

Daniel E. Spratt [a,†,], Robert T. Dess [a,†], Zachary S. Zumsteg [b], Daniel W. Lin [c], Phuoc T. Tran [d,e,f], Todd M. Morgan [g], Emmanuel S. Antonarakis [d], Paul L. Nguyen [h], Charles J. Ryan [i], Howard M. Sandler [b], Matthew R. Cooperberg [j], Edwin Posadas [k], Felix Y. Feng [l]*

EUROPEAN UROLOGY 73 (2018) 156–165



Conclusions: Similar to the selective use of HT with radiotherapy in localized prostate cancer, not all patients appear to derive a meaningful benefit from HT with SRT. Patient, tumor, and treatment factors must be considered when recommending the use of HT with SRT. Knowledge gaps exist in the level 1 data regarding the optimal duration and type of HT, as well as the ability to use predictive biomarkers to personalize the use of HT with SRT. Important clinical trials (RADICALS and NRG GU-006) are aimed to answer these questions.

Ο ασθενής, παρά την salvage ακτινοθεραπεία με 68 Gy το 2016, εμφανίζει σταδιακή αύξηση του PSA σε 1,2 ng/ml έναντι 0,8/0,4/0,3/0,3 προ 3,6,9 και 12 μηνών, αντίστοιχα (PSA-DT: 5,5 μήνες)

Α. Θα πρέπει να ξεκινήσει άμεσα ανδρογονικό αποκλεισμό

Β. Με προϋπόθεση ότι είναι απεικονιστικά M_0, μπορεί να περιμένει μέχρι την ακτινολογική επιδείνωση της νόσου με δεδομένη την σημαντική συνοδό νοσηρότητα

Γ. Με βάση τις τελευταίες ανακοινώσεις θα ωφεληθεί αν του χορηγηθεί ενζαλουταμίδη

Μέχρι στιγμής, οι διαθέσιμες πληροφορίες γιά την πορεία των ανδρών με βιοχημική υποτροπή μετά από μετεγχειρητική ακτινοθεραπεία περιορίζονται σε εκείνους που υπεβλήθησαν σε επικουρική (adjuvant) (ART) και όχι salvage (SRT) ακτινοθεραπεία.

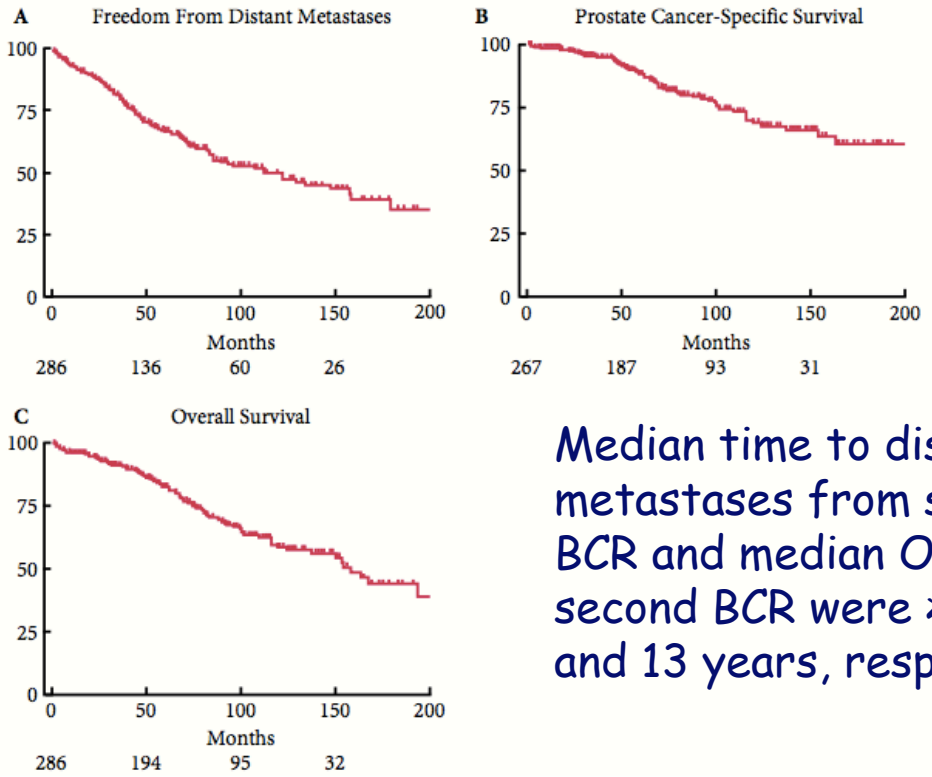
Οι παράμετροι που χρειάζεται να εκτιμηθούν είναι:

- τα ποσοστά ανάπτυξης απώτερων μεταστάσεων,
- ο χρόνος μέχρι την ανάπτυξη απώτερων μεταστάσεων (DMFS),
- τα ποσοστά ανάπτυξης ευνουχοάντοχου καρκίνου και
- ο χρόνος μέχρι την ανάπτυξή του (CRFS),
- η ειδική ως προς την νόσο επίβίωση (PCSS) και
- η συνολική επιβίωση (OS).

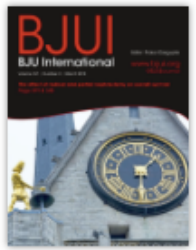
Volume 121, Issue 3
March 2018
Pages 365-372

Natural history of 'second' biochemical failure after salvage radiation therapy for prostate cancer: a multi-institution study

Fig. 1 Kaplan–Meier plots with numbers at risk for patients with biochemical failure after salvage radiotherapy for (**A**) freedom from distant metastasis, (**B**) prostate cancer-specific survival and (**C**) overall survival.



Median time to distant metastases from second BCR and median OS from second BCR were >9 years and 13 years, respectively.



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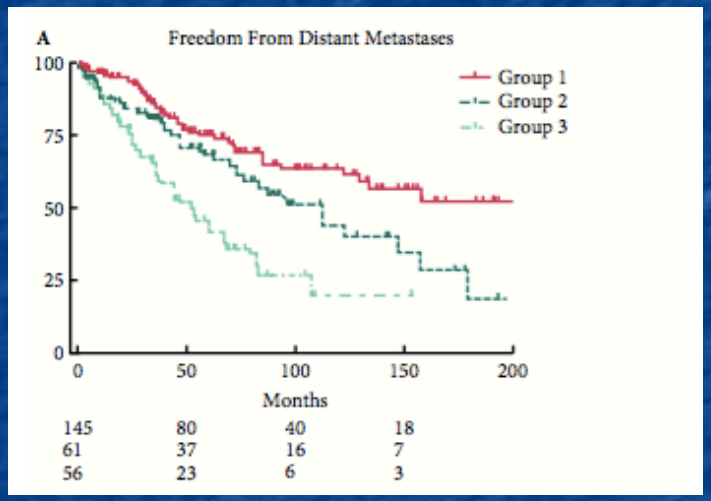

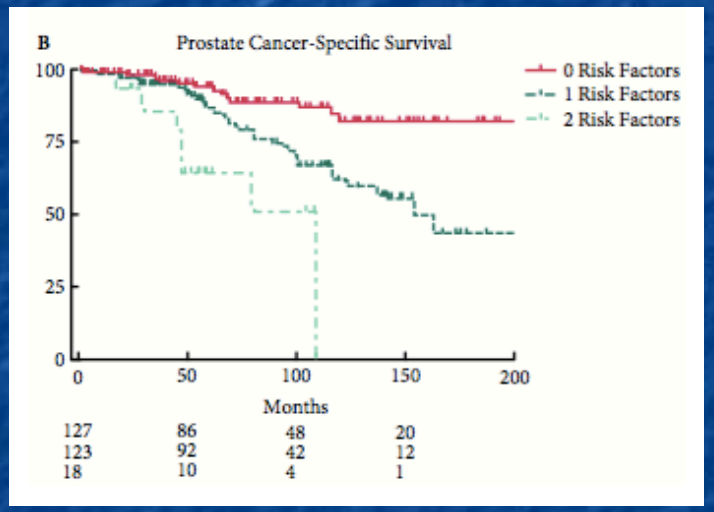

Risk groupings for patients with second biochemical failure after salvage radiotherapy (SRT) for (A) freedom from metastasis with stratification based on presence of Gleason 8–10 pathology, interval to second biochemical relapse <1 year, or failure despite concurrent androgen deprivation therapy (ADT) with SRT and (B) prostate cancer- specific survival with stratification based on presence of interval to second biochemical failure <1 year, and/or biochemical recurrence despite concurrent ADT with SRT.

Long-term Outcome of Prostate Cancer Patients Who Exhibit Biochemical Failure Despite Salvage Radiation Therapy After Radical Prostatectomy

American Journal of Clinical Oncology
Issue: Volume 40(6), December 2017, p 612–620

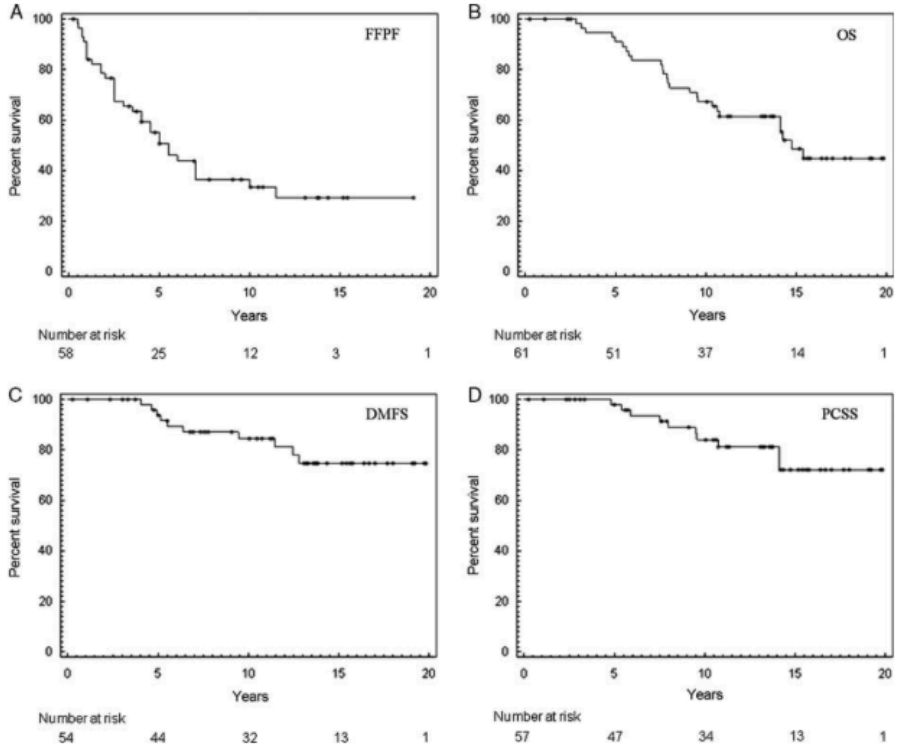

FIGURE 1. Kaplan-Meier survival curves after the start of salvage radiation therapy, n = 61. Freedom from prostate-specific antigen (PSA) failure (A); overall survival (B); distant metastasis-free survival (C); prostate cancer-specific survival (D). DMFS indicates distant metastases-free survival; FFPF, freedom from PSA failure; OS, overall survival; PCSS, prostate cancer-specific survival.

The median OS and freedom from PSA failure (FFPF) after SRT were 14.7 and 5.5 years, respectively. The OS were 91% and 67%, FFPF were 51% and 33%, prostate cancer specific survival (PCSS) were 98% and 84%, and distant metastases-free survival (DMFS) were 94% and 84% at 5 and 10 years, respectively

Long-term Outcome of Prostate Cancer Patients Who Exhibit Biochemical Failure Despite Salvage Radiation Therapy After Radical Prostatectomy

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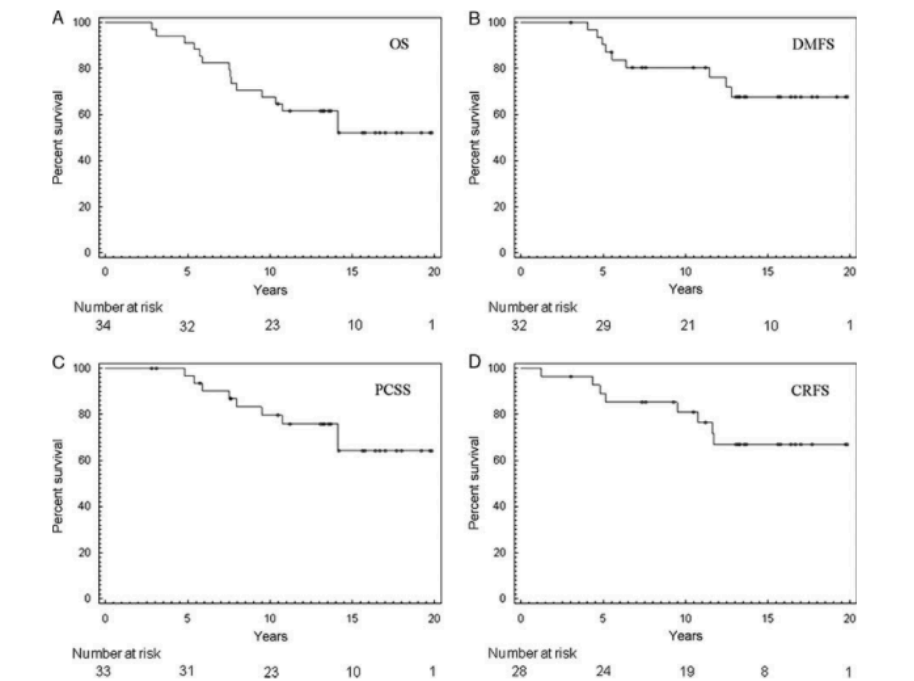

FIGURE 2. Kaplan-Meier survival curves after the start of salvage radiation therapy of patients who developed biochemical recurrence (BCR), n = 34. Overall survival (A); distant metastasis-free survival (B); prostate cancer-specific survival (C); castration-resistant-free survival (D). CRFS indicates castration-resistant-free survival; DMFS, distant metastases-free survival; OS, overall survival; PCSS, prostate cancer-specific survival.

Measuring from time of SRT initiation, OS of patients who developed BCR were 91% and 65%, PCSS were 97% and 80%, DMFS were 87% and 76%, and CRFS were 85% and 81% at 5 and 10 years, respectively

Long-term Outcome of Prostate Cancer Patients Who Exhibit Biochemical Failure Despite Salvage Radiation Therapy After Radical Prostatectomy

American Journal of Clinical Oncology
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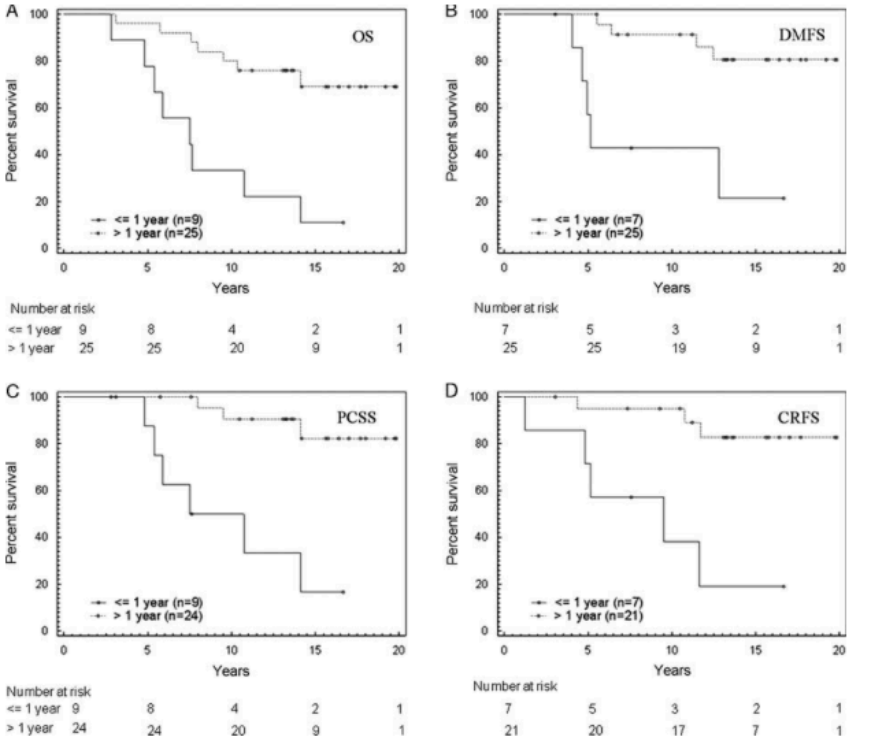


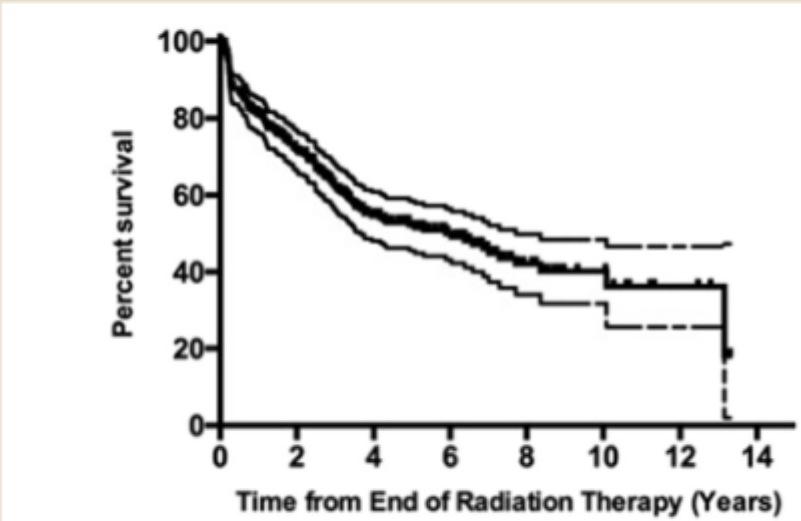
FIGURE 3. Kaplan-Meier survival curves after the start of salvage radiation therapy according to rapidity of failure (failure ≤ 1 y vs. failure > 1 y), n = 34. Overall survival (A); distant metastasis-free survival (B); prostate cancer-specific survival (C); castration-resistant-free survival (D). CRFS indicates castration-resistant-free survival; DMFS, distant metastases-free survival; OS, overall survival; PCSS, prostate cancer-specific survival.

When considering only those who failed SRT, time to BCR after SRT≤1 year correlated significantly with decreased OS (10y 33% vs. 80%, P = 0.001, hazard ratio [HR] 5.7, 2.0 to 15.9), DMFS (10 y 43% vs. 91%, P = 0.0027, HR 7.7, 2.0 to 28.9), PCSS (10 y 50% vs. 90.5%, P = 0.001, HR 10.6, 2.6 to 43.4), and CRFS (10 y 38% vs. 95%, P = 0.0037, HR 8.9, 2.0 to 39.0) on univariate analysis when measured from initiation of SRT

Risk Factors for Disease Progression After Postprostatectomy Salvage Radiation: Long-term Results of a Single-institution Experience

Clinical Genitourinary Cancer February 2018

Figure 1 Kaplan-Meier Curve for Interval to Disease Progression With 95% Confidence Intervals



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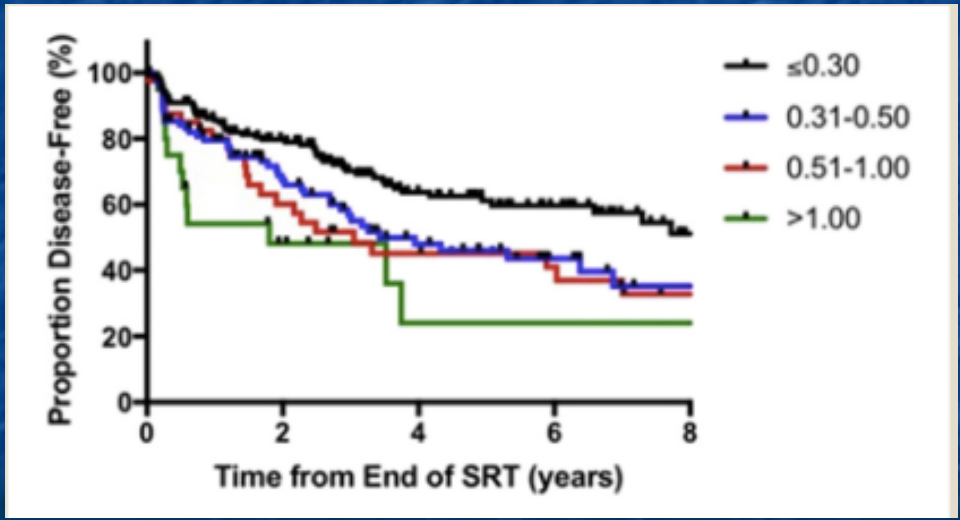


Kaplan-Meier Curves for Interval to Disease Progression Stratified by Presalvage Radiotherapy (Pre-SRT) PSA. Median Interval to Progression for Each Pre-SRT PSA Groups: ≤ 0.3 ng/mL, Not Available; 0.3 to 0.5 ng/mL, 3.95 Years; 0.5 to 1.0 ng/mL, 3.04 Years; and > 1.0 ng/mL, 1.80.

Androgen deprivation therapy during and after post-prostatectomy radiotherapy in patients with prostate cancer: a case control study

Kim *et al. BMC Cancer* (2018) 18:271

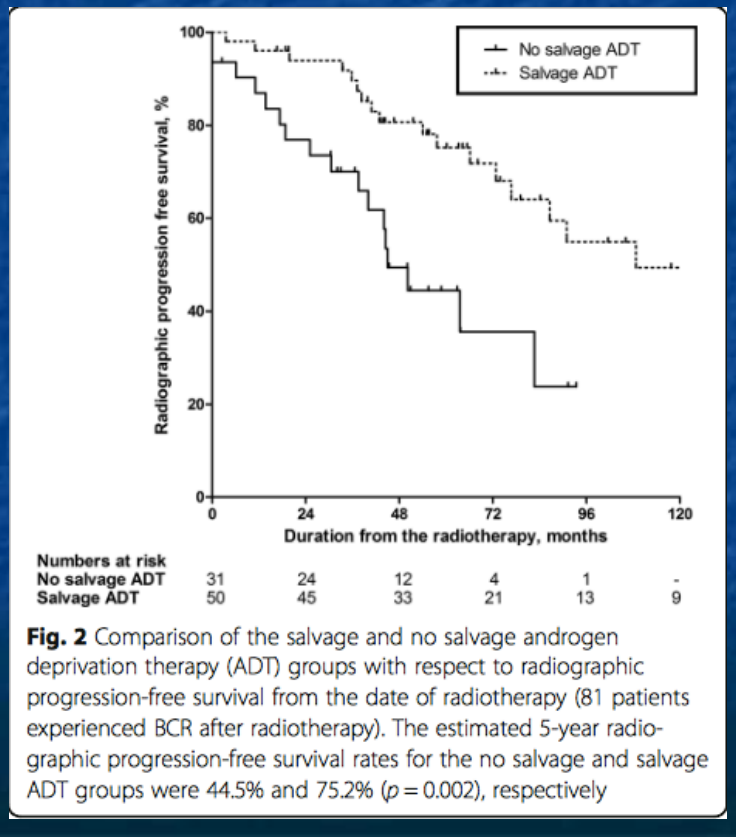
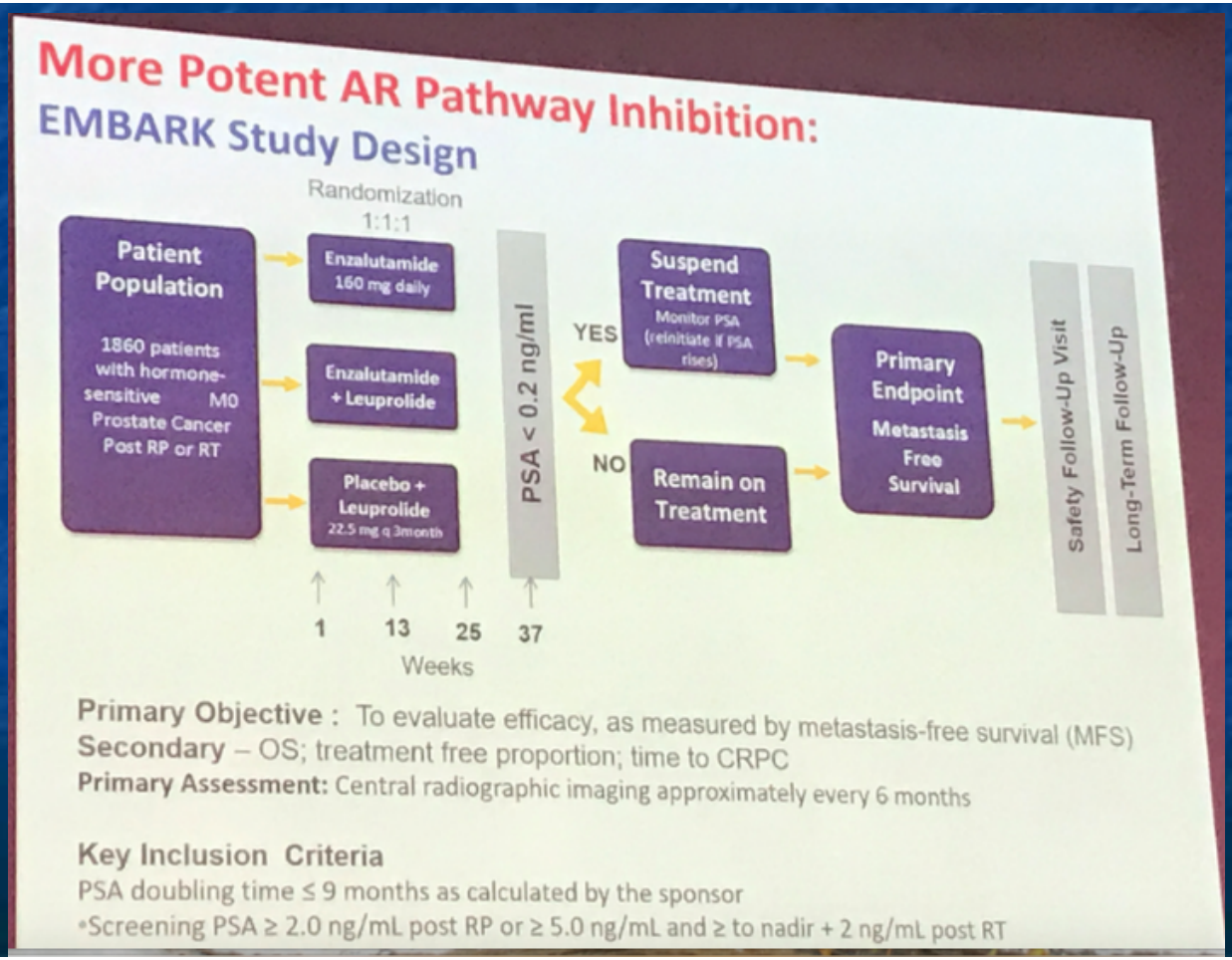


Fig. 2 Comparison of the salvage and no salvage androgen deprivation therapy (ADT) groups with respect to radiographic progression-free survival from the date of radiotherapy (81 patients experienced BCR after radiotherapy). The estimated 5-year radiographic progression-free survival rates for the no salvage and salvage ADT groups were 44.5% and 75.2% ($p = 0.002$), respectively

Conclusions

Salvage ADT after post-RT BCR improved radiographic progression-free survival.
Therefore, salvage ADT should be considered as a viable treatment option after post-RT BCR.
The results from ongoing RCTs are needed to confirm our results.

EMBARK: A phase 3, randomized, efficacy and safety study of enzalutamide plus leuprolide, enzalutamide monotherapy and placebo plus leuprolide in men with high-risk nonmetastatic prostate cancer progressing after definitive therapy FREE



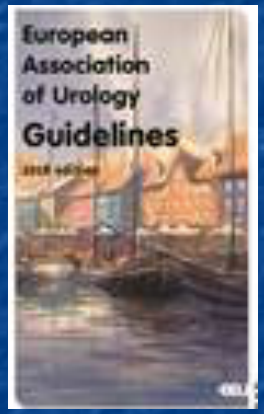
Ann Oncol. 2018 Feb 26. doi: 10.1093/annonc/mdy072. [Epub ahead of print]

Adding abiraterone or docetaxel to long-term hormone therapy for prostate cancer: directly randomised data from the STAMPEDE multi-arm, multi-stage platform protocol.

2.2 Patient selection

Eligible patients were those starting long-term ADT for the first time. This was defined as patients with metastatic disease, nodal involvement or node negative, non-metastatic disease with two or more of three high-risk features: T-category 3 or 4, Gleason sum score 8-10 or PSA>40ng/ml. Patients rapidly relapsing after previous local therapy were also permitted if they had PSA>20ng/ml or PSA>4ng/ml with a PSA doubling time <6 months or those who developed loco-regional or metastatic spread whilst not on hormone therapy.

CONCLUSIONS: This direct, randomised comparative analysis of two new treatment standards for hormone-naïve prostate cancer (HNPC) showed no evidence of a difference in overall or prostate cancer-specific survival, nor in other important outcomes such as symptomatic skeletal events, suggesting that Worst toxicity grade over entire time on trial was similar but comprised different toxicities in line with the known properties of the drugs.



8.2.4.Hormonal therapy side effects

8.2.4.1.Sexual function

Cessation of sexual activity is very common on men undergoing ADT, affecting up to 93% of men.

8.2.4.2.Hot flushes

Hot flushes are a common side-effect of ADT (prevalence estimated between 44-80% of men on ADT

8.2.4.3.Non-metastatic bone fractures

Due to increased bone turnover and decreased bone mineral density (BMD) in a time-dependent manner, ADT use is linked to an increased risk of fracture (up to 45% RR with long-term ADT)

8.2.4.4.Metabolic effects

Lipid alterations are common and may occur as early as the first 3 months of treatment. ADT also decreases insulin sensitivity and increases fasting plasma insulin levels, which is a marker of insulin resistance.

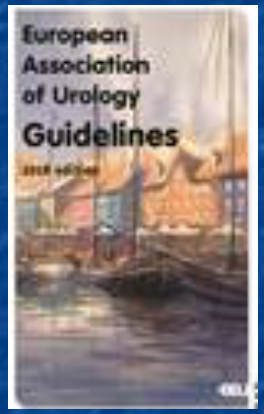
8.2.4.5.Cardiovascular morbidity

8.2.4.6.Fatigue

Fatigue often develops as a side-effect of ADT. Anaemia may be a cause of fatigue. Anaemia requires an etiological diagnosis (medullar invasion, mainly inflammatory, renal insufficiency, iron deficiency, chronic bleeding) and individualised treatment.

8.2.4.7.Neurological side-effects

Castration seems also to be associated with an increased risk of stroke, and is suspect to be associated with an increased risk for depression and cognitive decline such as Alzheimer disease



8.2.4.5. Cardiovascular morbidity

Cardiovascular mortality is now the most common cause of death in PCa patients, even exceeding PCa mortality [713,873,874]. Several studies showed that ADT, after only six months, was associated with an increased risk of diabetes mellitus, cardiovascular disease, and myocardial infarction [875]. The RTOG 92-02 [876] and 94-08 [381] trials confirmed an increased cardiovascular risk, unrelated to the duration of ADT and not accompanied by an overall increased cardiovascular mortality. No increase in cardiovascular mortality has been reported in a systematic meta-analysis of trials RTOG 8531, 8610, 9202, EORTC 30891 or EORTC 22863 [877]. However, serious concerns about the conclusions of this meta-analysis have been raised due to poor consideration of bias in the included studies [878,879]. Meta-analysis of observational data reports consistent links between ADT and the risk of CVD in men treated for PCa e.g. the associations between GnRH agonists and nonfatal or fatal myocardial infarction or stroke RR: 1.57 (95% CI, 1.26-1.94) and RR: 1.51 (95% CI, 1.24-1.84), respectively [880]. An increase in cardiovascular mortality has been reported in patients suffering from previous congestive heart failure or myocardial infarction in a retrospective database analysis [881] or presenting with a metabolic syndrome [882].

Role of Hormonal Treatment in Prostate Cancer Patients with Nonmetastatic Disease Recurrence After Local Curative Treatment: A Systematic Review

69 (2016) 802–820

Roderick C.N. van den Bergh[a], *Niels J. van Casteren*[b], *Thomas van den Broeck*[c], *Eve R. Fordyce*[d], *William K.M. Gietzmann*[e], *Fiona Stewart*[d], *Steven MacLennan*[d], *Saeed Dabestani*[f], *Joaquim Bellmunt*[g], *Michel Bolla*[h], *Erik Briers*[i], *Philip Cornford*[j], *Steven Joniau*[k], *Malcolm D. Mason*[l], *Vsevolod Matveev*[m], *Henk G. van der Poel*[n], *Theo H. van der Kwast*[o], *Olivier Rouvière*[p], *Thomas Wiegel*[q], *Thomas B. Lam*[d,e], *Nicolas Mottet*[r,*]

HT for recurrences after local curative treatment

The link between PSA relapse and survival is weak at best, and the management approach has to be individualised. Based on the lack of definitive efficacy and the undoubtedly associated significant side effects, not all patients with disease recurrence after primary curative therapy should receive standard HT at the outset. Only a minority of patients with disease recurrence progress to systemic progression or PCa-caused death. The objective of HT should be to improve OS, postpone distant metastasis, and improve QoL. QoL was reported as an outcome in only one of the included studies. Biochemical response to HT only holds no clinical benefit for a patient. For older patients and those with comorbidities, side effects of HT may even decrease life expectancy; in particular, cardiovascular risk factors need to be considered. However, high-risk patients with a long life expectancy may benefit from HT. Therefore, personalised risk stratification is warranted, taking patient (age, comorbidity, patient preferences) and disease-specific (Gleason score, PSA DT) factors into account in clinical decision making. No strong conclusions can be drawn on the preferable HT strategy in this setting.

Η αντιμετώπιση της βιοχημικής υποτροπής μετά από την αρχική, ριζική, αντιμετώπιση αλλά και την εφαρμογή Θεραπείας διάσωσης απαιτεί γνώση, σύνεση και στρατηγικό σχεδιασμό

Η σημαντική ετερογένεια της νόσου δημιουργεί σημαντικά προβλήματα στην επιλογή της καταλληλότερης θεραπευτικής προσέγγισης, γεγονός που επιβάλλει την εκτίμηση της επιθετικότητάς της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