Faculté de Médecine

Cancer de prostate : La radiothérapie

Avancées en 2019 et Futur

Université de Limoges

CHU

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« Liens » d'intérêt

- Astra Zeneca
- Ferring
- MSD
- Novartis
- Astellas
- Sanofi
- Ipsen
- Janssen

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THE ROAD TO RADIATION
Plan
1. Formes localisée : Revoir les stratégies thérapeutiques ?
2. Formes localisées : Revoir les modalités de l'irradiation ?
3. La radiothérapie post prostatectomie ! Quand ? Qui ?
4. Maladie oligométastatique

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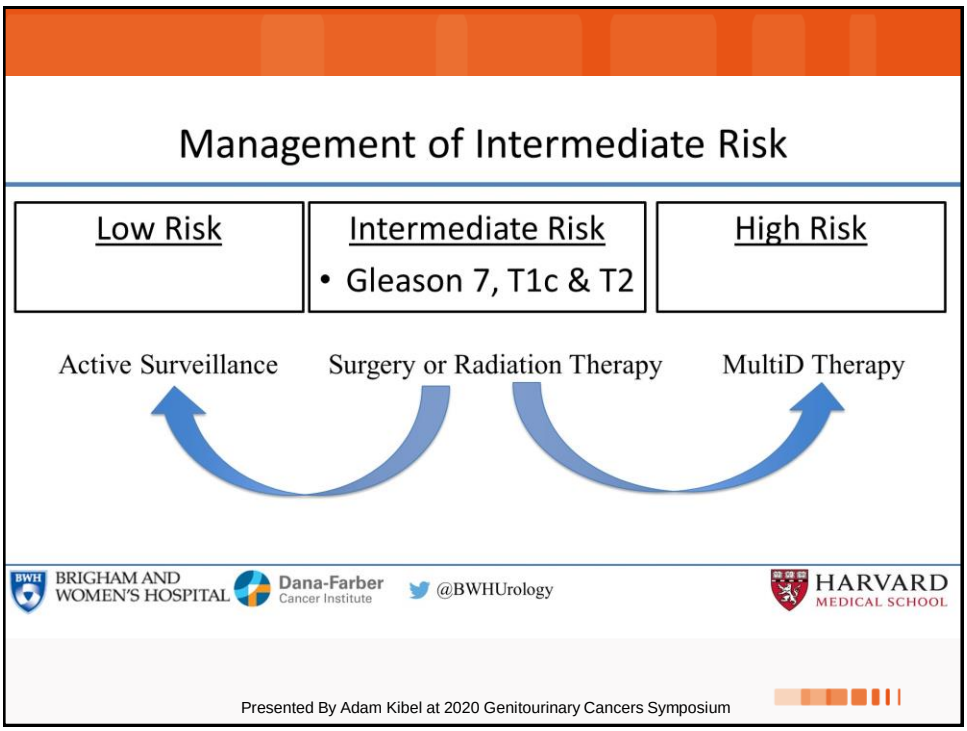
Management of Intermediate Risk
Low Risk
Intermediate Risk
• Gleason 7, T1c & T2
High Risk
Active Surveillance
Surgery or Radiation Therapy
MultiD Therapy
BRIGHAM AND WOMEN'S HOSPITAL
Dana-Farber Cancer Institute
@BWHUrology
HARVARD MEDICAL SCHOOL
Presented By Adam Kibel at 2020 Genitourinary Cancers Symposium

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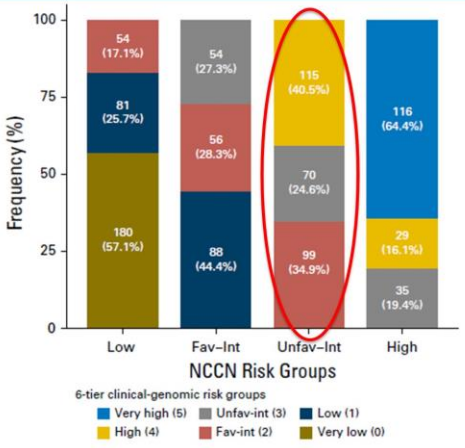
Apport de la génomique : Decipher

Risk Reclassification



- Favorable Intermediate Risk reclassified as low risk
  - Active Surveillance
- Favorable Intermediate Risk reclassified as Genomic Unfavorable Intermediate Risk
  - Treat (Rad or Surgery)
- Unfavorable Intermediate Risk did not reclassify as Low Risk
  - Treat (Rad or Surgery)

Spratt et al, JCO 2019

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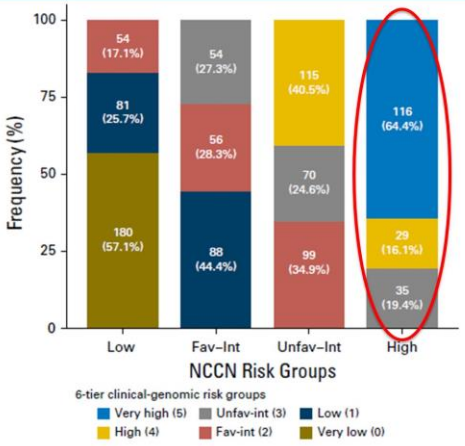
Apport de la génomique : Decipher

Risk Reclassification



- High risk disease
- None reclassified as
  - low risk
  - favorable int risk.
- No role for genomic testing
- MultiD treatment - all patients

Spratt et al, JCO 2019

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Development and Validation of a Novel Integrated Clinical-Genomic Risk Group Classification for Localized Prostate Cancer

Daniel E. Spratt, Jingbin Zhang, Maria Santiago-Jiménez, Robert T. Dess, John W. Davis, Robert B. Den, Adam P. Dicker, Christopher J. Kane, Alan Pollack, Radka Stoyanova, Firas Abdollah, Ashley E. Ross, Adam Cole, Edward Uchio, Josh M. Randall, Hao Nguyen, Shuang G. Zhao, Rohit Mehra, Andrew G. Glass, Lucia L.C. Lam, Jijumon Chelliserry, Marguerite du Plessis, Voleak Choeurng, Maria Aranes, Tyler Kolisnik, Jennifer Margrave, Jason Alter, Jennifer Jordan, Christine Buerki, Kasra Yousefi, Zaid Haddad, Elai Davicioni, Edouard J. Trabulsi, Stacy Loeb, Ashutosh Tewari, Peter R. Carroll, Sheila Weinmann, Edward M. Schaeffer, Eric A. Klein, R. Jeffrey Karnes, Felix Y. Feng, and Paul L. Nguyen

Grouping System		NCCN	Clinical-Genomic Risk Grouping System: Training		Validation	
10-year metastasis rate, % (95% CI)	Low	7.3 (1.9 to 12.8)	Low	3.5 (0.7 to 6.3)	Low	0.0 (0.0 to 0.0)
	Fav-int	9.2 (4.3 to 14.0)	Int	29.4 (23.8 to 35.0)	Int	25.9 (8.8 to 43.0)
	Unfav-int	38.0 (29.5 to 46.6)				
	High	39.5 (33.0 to 46.1)	High	54.6 (45.6 to 63.6)	High	55.2 (33.9 to 76.6)
C-index for 10-year metastasis (95% CI)		0.68 (0.64 to 0.73)		0.77 (0.72 to 0.81)		0.84 (0.61 to 0.93)
HR for metastasis (95% CI)	Low	Ref	Low	Ref	Low	Ref
	Fav-int	1.2 (0.5 to 3.0)	Int	9.3 (4.8 to 21.5)*	Int	21.3 (2.8 to 2,727.6)*
	Unfav-int	5.4 (2.8 to 12.0)*				
	High	6.0 (3.2 to 13.0)*	High	21.9 (11.1 to 50.4)*	High	62.5 (8.5 to 7,969.6)*

Spratt et al, JCO 2018

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PREDICT-RT (NRG-GU 009) Co-PI: Nguyen and Sartor

Screening/Eligibility
NCCN High Risk

Decipher Score Bottom 2/3
N=1692

Decipher Score Upper 1/3 (or N1)
N=786

De-Intensification Study

Stratify
1. Decipher Score
2. Boost type (EBRT vs. Brachy)
3. Pelvic Treatment (Y/N)
4. ACE-27 Comorbidity

Randomize

- RT+ 12 Mos ADT
- RT+ 24 Mos ADT

Intensification Study

Stratify
1. Boost type (EBRT vs. Brachy)
2. Pelvic Treatment (Y/N)
3. Node Status (pos/neg)

Randomize

- 24 Mos ADT + RT
- 24 Mos ADT + RT +24 Mos Abiraterone +24 Mos Apalutamide

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Traitement des « haut risque »
What have the large mature Phase 3 trials shown us?
• Radiation plus hormones is better than hormones alone (Warde et al, Lancet 2011: ↑OS@ 7 yrs and ↓PCSM)
• Radiation plus hormones is better than radiation alone
• Improved biochemical, cause specific and distant survival, reduced local and distant failure
• Higher radiation dose is better
• Improved biochemical and cause specific survival and reduced local and distant failure
Randomized Trials of hormones + radiation for High Risk
Study | n | F/up (yrs) | EBRT (Gy) | Randomization ADT duration | Results
Bolla EORTC 22863 | 415 | 9.1 | 70 | 0 vs. 3 yrs | ↑ 10 yr DFS (23 vs. 48%) ↑ OS 40 vs. 58% p=.0004
Denham TROG 9601 | 818 | 5.9 | 66 | 0 vs. 3 vs. 6 mo (15% intermed) | No Δ OS ↑ CSS 6 mo (HR 0.56, p=.04)
Pilepich RTOG 8531 | 977 | 7.6 | 65-70 | Adj. vs. @ fail | ↑ 10 yr OS (39 vs. 49%,p=.002) esp. GS 7-10
D'Amico | 206 | 4.5 | 70 | 0 vs. 6 mo (80% intermed) | ↑ 5 yr OS (78% vs. 88% p=.04)
Roach RTOG 8610 | 456 | 12.5 | 65-70 | 0 vs. 4 mo | ↑10 yr OS (34 vs. 43% p=.12)
Bolla EORTC 22961 | 970 | 6.4 | 70 | 6 vs. 36 mo | ↑ 5 yr OS (19% vs. 15%; non inferiority p=.65)
Horwich RTOG 9202 | 1554 | 11.3 | 65-70 | 4 vs. 28 mo | ↑10 yr OS (32 vs. 45%, p=.006) for GS 8-10
Randomized EBRT dose escalation studies
 | n | Arms Dose in Gy | Eligibility | Median followup | Std arm bNED | High dose bNED | Time Years
MDAnderson Kuban | 301 | 70/78 | T1-3 | 8.7 yrs | 59% | 78% | 8 p=0.004
GETUG Beckendorf | 306 | 70/80 | T1-3,PSA<50 | 5.1 yrs | 68% | 77% | 5 p=0.09
Dutch Multi center Peeters | 669 | 68/78 | T1-4 PSA<60 | 6.8 yrs | 45% | 56% | 7 p=0.03
Royal Marsden Dearnaley | 126 | 64/74 | T1-T3b | 6.2 yrs | 59% | 71% | 5 p=0.10
MGH Proton Zietman | 393 | 70.2/79.2 | T1-T2b PSA<15 | 5.5 yrs | 79% | 91% | 5 p<0.001
MRC Dearnaley | 843 | 64/74 | T1-3 PSA<50 | 5.3 yrs | 60% | 71% | 5 p=0.0007
A 10 Gy increase in EBRT dose is associated with ~10% increase in bDFS
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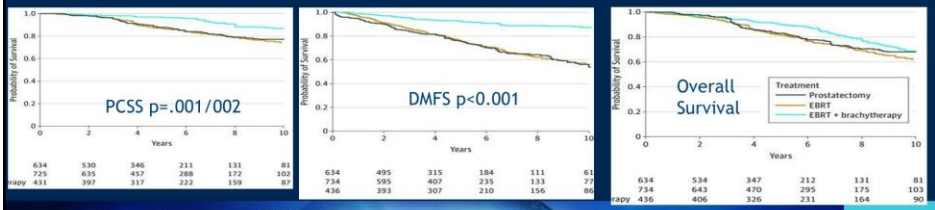
Que faire parmi toutes les options thérapeutiques locales ?

How are we doing?

Comparison of RP, EBRT or EBRT + BT for Gleason 9 and 10

Kishan et al JAMA 2018

- n =1809 Gleason 9-10: 12 tertiary referral centers
  - RP: 639, Follow up 4.2 years,
  - EBRT +ADT: 734, Follow up 5.1 years
  - EBRT + BT + ADT: 436, Follow up 6.3 years



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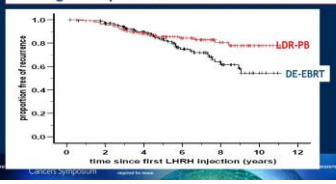
Apport du « boost » curiethérapie

Canadian ASCENDE-RT *WJ Morris et al, IJROBP 2017*

Level One Evidence for benefit of Brachytherapy

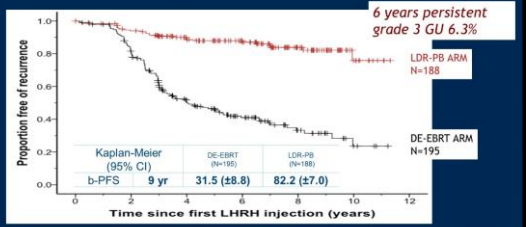
- Phase 3: 12 mos ADT +78 Gy vs. 46 Gy + LDR BT
- n=398: 69% high risk

276 high risk patients: nadir+2 definition for failure



9-year PSA RFS: 58% vs.78%; p=0.05

Biochemical-PFS using a PSA ≤0.2 ng/mL threshold
(by treatment received N= 383)



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ICR The Institute of Cancer Research

CANCER RESEARCH UK

CHHiP

Long term follow-up from a phase III randomised trial of conventional vs hypofractionated high dose intensity modulated radiotherapy for prostate cancer (CRUK/06/016): update from the CHHiP trial

Professor David Dearnaley
(on behalf of the CHHiP Investigators)

GU ASCO February 13th 2020

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Hormone treatment† (3-6 months)

Clinical T1b-T3a, N0, M0
Risk of seminal vesicle involvement* ≤ 30%
PSA ≤ 30ng/ml

Randomise 1:1:1

74Gy / 37f	60Gy / 20f	57Gy / 19f
7.4wks	4wks	3.8wks
N=1065	N=1074	N=1077

† optional for patients with low risk disease (T1c/T2a & Gleason score ≤6 & PSA ≤10ng/ml)

* PSA +([Gleason score-6] x10)

Non-inferiority design with a critical hazard ratio of 1.21 for each hypofractionated schedule compared to 74Gy/37f

Pas d'irradiation ganglionnaire pelvienne

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Baseline characteristics

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	Total N=3216	Central pathology review N=1875
	%	%
Age Median (IQR)	69 (64, 73)	69 (64, 73)
Risk group		
Low Risk	15	8↓
Intermediate Risk	73	73
High Risk	12	19↑
ISUP Grade Group		
1	35	22↓
2	43	55↑
3	19	16
4	3	4
5	0	3
Clinical T stage		
T1	36	35
T2	55	57
T3	9	8
Pre-hormone PSA (ng/ml) Median (IQR)	10 (7, 14)	10 (7, 14)

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CLASSIFICATION "ISUP"

- Groupe 1 : ancien Gleason 3+3
- Groupe 2 : ancien Gleason 3+4 (majorité de grade 3).
- Groupe 3 : ancien Gleason 4+3 (majorité de grade 4).
- Groupe 4 : ancien Gleason 4+4.
- Groupe 5 : anciens Gleason 9 ou 10.

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Time to biochemical failure/prostate cancer recurrence

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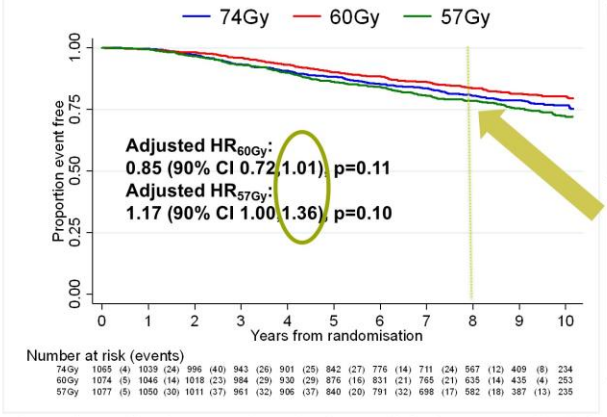

Lancet Oncology 2016*
- 5.2 years median follow-up
- 417 primary endpoint events

5 year event-free rates:
74Gy: 88.3% (95%CI 86.0-90.2)
60Gy: 90.6% (95%CI 88.5-92.3)
57Gy: 85.9% (95%CI 83.4-88.0)

Snapshot taken Oct 2019
- 9.3 years median follow-up
- 643 primary endpoint events

8 year event-free rates:
74Gy: 80.6% (95%CI 77.9-83.0)
60Gy: 83.7% (95%CI 81.2-85.9)
57Gy: 78.5% (95%CI 75.8-81.0)

* Dearnaley D, *et al* (2016). Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial. *Lancet Oncology*. 17(8):1047-60.

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Time to biochemical failure/prostate cancer recurrence: <75 and 75+ years

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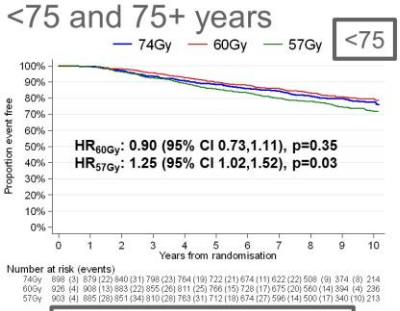

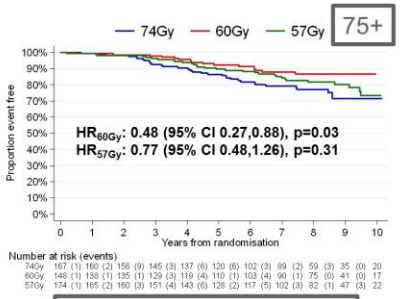

8 year event-free estimates
74Gy: 81.2% (95%CI 78.3-83.8)
60Gy: 83.2% (95%CI 80.5-85.6)
57Gy: 78.0% (95%CI 75.0-80.6)

8 year event-free estimates
74Gy: 77.1% (95%CI 68.9-83.3)
60Gy: 86.7% (95%CI 79.1-91.7)
57Gy: 81.6% (95%CI 74.0-87.1)

- With longer follow-up, hypofractionated RT continues to be effective in men ≥75 years

Wilson JM *et al* (2018). The Efficacy and Safety of Conventional and Hypofractionated High-Dose Radiation Therapy for Prostate Cancer in an Elderly Population: A Subgroup Analysis of the CHHiP Trial. *International Journal of Radiation Oncology*Biology*Physics.* 100(5):1179-89.

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Time to metastases and overall survival

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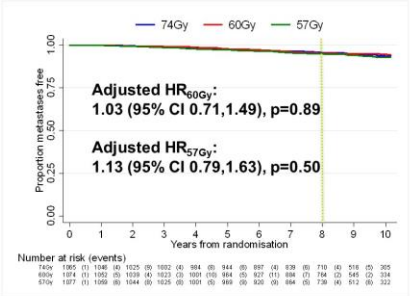
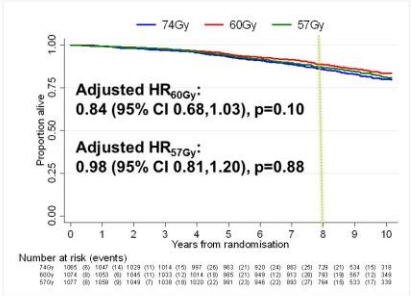
- 176 distant metastases

8 year metastases free rates:
74Gy: 95.6% (95%CI 94.0-96.7)
60Gy: 95.3% (95%CI 93.7-96.4)
57Gy: 94.8% (95%CI 93.2-96.0)



- 567 deaths

8 year overall survival rates:
74Gy: 85.9% (95%CI 83.6-87.9)
60Gy: 88.6% (95%CI 86.5-90.4)
57Gy: 86.7% (95%CI 84.5-88.7)



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Symptoms at 5 years

Clinician assessed RTOG toxicity

- No evidence of a difference between 74Gy and each hypofractionated schedule for grade≥2 bowel or bladder toxicity:

BOWEL	BLADDER
74Gy: 14/879 (1.6%)	74Gy: 17/879 (1.9%)
60Gy: 18/908 (2.0%)	60Gy: 14/908 (1.5%)
57Gy: 17/904 (1.9%)	57Gy: 17/904 (1.9%)

Patient reported toxicity

- No statistically significant differences in 'moderate or big' bowel or urinary bother

BOWEL BOTHER	URINARY BOTHER
74Gy: 19/349 (5.4%)	74Gy: 23/341 (6.7%)
60Gy: 29/381 (7.6%)	60Gy: 35/377 (9.3%)
57Gy: 21/393 (5.3%)	57Gy: 30/382 (7.9%)

- Bowel and urinary symptoms remains stable from 2 to 5 years for all schedules

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La radiothérapie de rattrapage

Eur Urol. 2017 Jun;71(6):886-893. doi: 10.1016/j.eururo.2016.07.028. Epub 2016 Jul 30.

Long-term Impact of Adjuvant Versus Early Salvage Radiation Therapy in pT3N0 Prostate Cancer Patients Treated with Radical Prostatectomy: Results from a Multi-institutional Series.

Fossati N[1], Karnes RJ[2], Boorjian SA[2], Moschini M[2], Moriacco A[3], Bossi A[3], Seisen T[3], Cozzarini C[4], Fiorino C[4], Noris Chiorda B[4], Gandaglia G[3], Dell'Oglio P[5], Joniau S[6], Tosco L[6], Shariat S[7], Goldner G[8], Hinkelbein W[9], Barthwalak D[10], Haustermans K[11], Tombal B[12], Montorsi F[3], Van Poppel H[6], Wiegel T[10], Briganti A[3].

CONCLUSIONS: At long-term follow-up, no significant differences between aRT and esRT were observed for MFS and OS. Our study, although based on retrospective data, suggests that esRT does not compromise cancer control and potentially reduces overtreatment associated with aRT.

Radiat Oncol. 2019 Nov 11;14(1):198. doi: 10.1186/s13014-019-1391-0.

Adjuvant versus early salvage radiotherapy: outcome of patients with prostate cancer treated with postoperative radiotherapy after radical prostatectomy.

Vogel MME[1,2], Kessel KA[1,2,3], Schiller K[1], Devecka M[1], Gschwend JE[4], Weichert W[3,5], Wilkens JJ[1], Combs SE[6,7,8].

CONCLUSION: For patients with PSA-triggered follow-up, close observation is essential and early initiation of local treatment at low PSA levels (<0.3 ng/mL) is beneficial. Our data suggest, that SRT administered at early PSA rise might be equieffective to postoperative ART in patients with locally advanced PC. However, the individual treatment decision must be based on any adverse risk factors and the patients' postoperative clinical condition.

*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 classified as EAU low-risk group at relapse who may not benefit from intervention.	Strong
Treat patients with a PSA rise from the undetectable range with SRT. Once the decision for SRT has been made, SRT (at least 66 Gy) should be given as soon as possible.	Strong
Offer pN0 patients undergoing SRT hormonal therapy (with bicalutamide 150 mg for two years, or LHRH agonists for up to two years).	Weak
Do not offer hormonal therapy to every pN0 patient treated with SRT.	Strong
Recommendations for biochemical recurrence after radiotherapy	
Treat highly selected patients with localised PCa and a histologically proven local recurrence with salvage radical prostatectomy.	Weak
Salvage RP should only be performed in experienced centres.	Strong
Do not offer high intensity focused ultrasound, cryosurgical ablation and salvage brachytherapy to patients with proven local recurrence since it is still experimental.	Strong
Recommendations for systemic salvage treatment	
Do not offer androgen deprivation therapy to M0 patients with a PSA-DT > twelve months.	Strong

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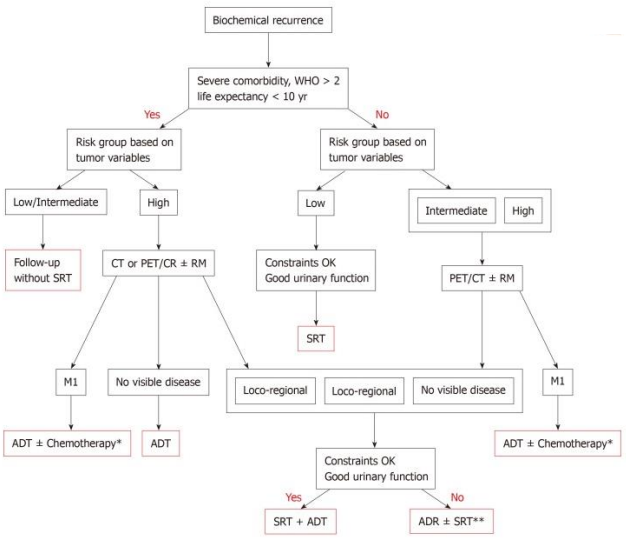
World J Clin Oncol. 2020 Jan 24;11(1):1-10. doi: 10.5306/wjco.v11.i1.1.

Are all prostate cancer patients "fit" for salvage radiotherapy?

González-San Segundo C[1], Gómez-Iturriaga A[2], Couñago F[3].



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A PHASE II RANDOMIZED, OPEN-LABEL STUDY COMPARING SALVAGE RADIOTHERAPY IN COMBINATION WITH 6 MONTHS OF ANDROGEN-DEPRIVATION THERAPY WITH LHRH AGONIST OR ANTAGONIST VERSUS ANTI-ANDROGEN THERAPY WITH APALUTAMIDE IN PATIENTS WITH BIOCHEMICAL PROGRESSION AFTER RADICAL PROSTATECTOMY
TRIAL IN PROGRESS (TIP)
BACKGROUND:
STUDY DESIGN:
OUTCOME MEASURES:
ACCRUAL:
PATIENT POPULATION:
PARTICIPATING CENTERS:
SCHEMATIC STUDY OVERVIEW:
(CONTACT) DETAILS:
ACKNOWLEDGEMENTS:

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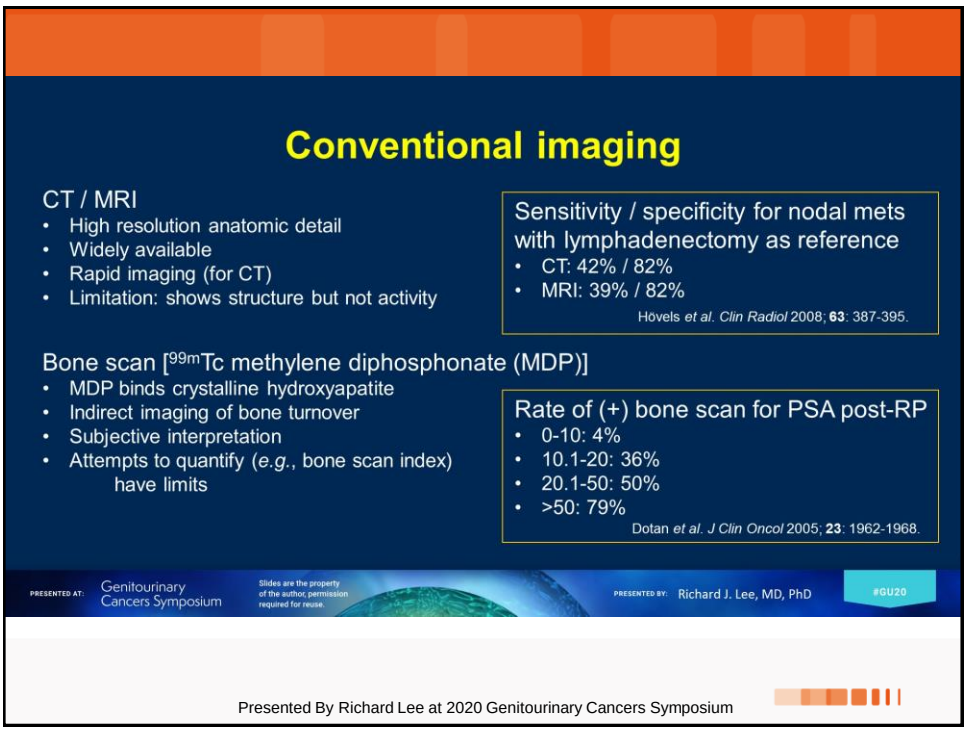
Conventional imaging
CT / MRI
• High resolution anatomic detail
• Widely available
• Rapid imaging (for CT)
• Limitation: shows structure but not activity
Sensitivity / specificity for nodal mets with lymphadenectomy as reference
• CT: 42% / 82%
• MRI: 39% / 82%
Hövels et al. Clin Radiol 2008; 63: 387-395.
Bone scan [99mTc methylene diphosphonate (MDP)]
• MDP binds crystalline hydroxyapatite
• Indirect imaging of bone turnover
• Subjective interpretation
• Attempts to quantify (e.g., bone scan index) have limits
Rate of (+) bone scan for PSA post-RP
• 0-10: 4%
• 10.1-20: 36%
• 20.1-50: 50%
• >50: 79%
Dotan et al. J Clin Oncol 2005; 23: 1962-1968.
PRESENTED AT: Genitourinary Cancers Symposium
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PRESENTED BY: Richard J. Lee, MD, PhD
#GU20
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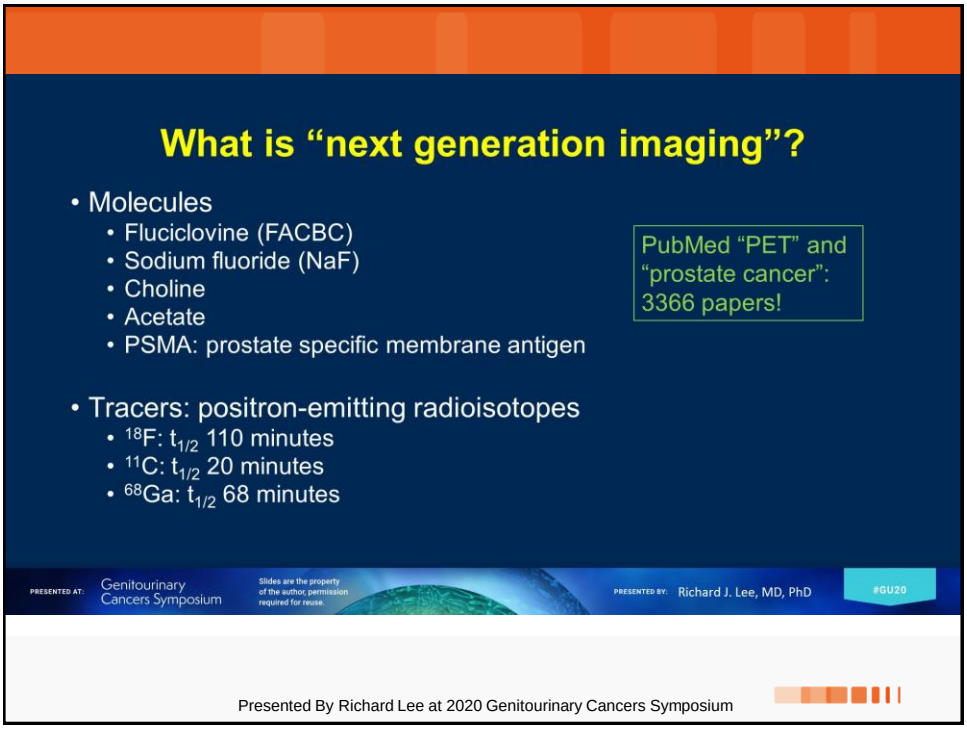

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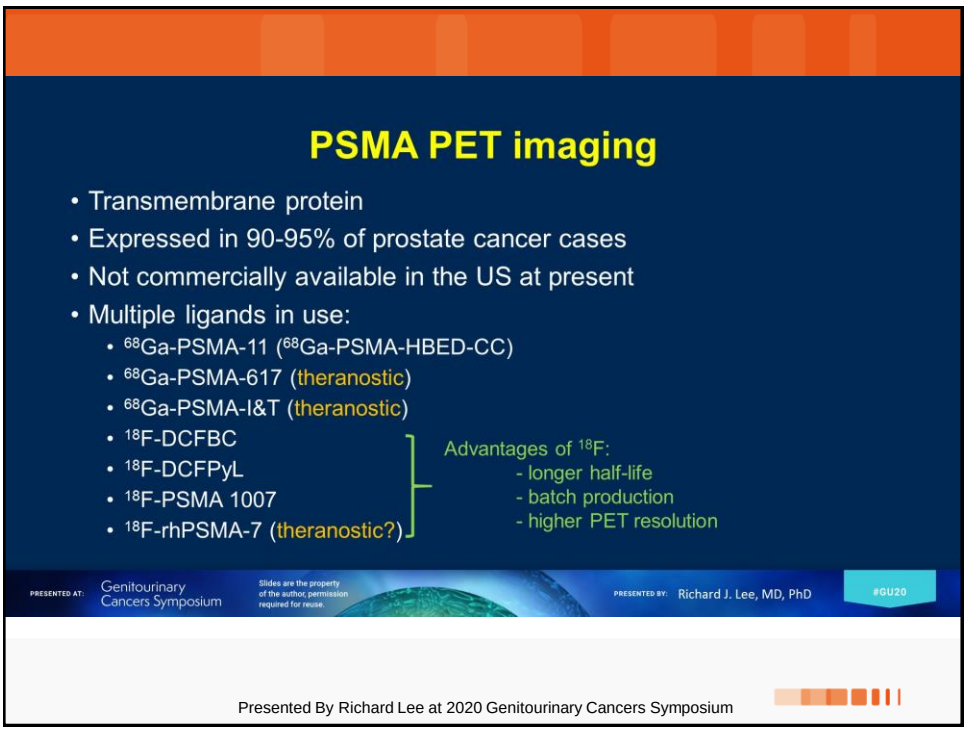

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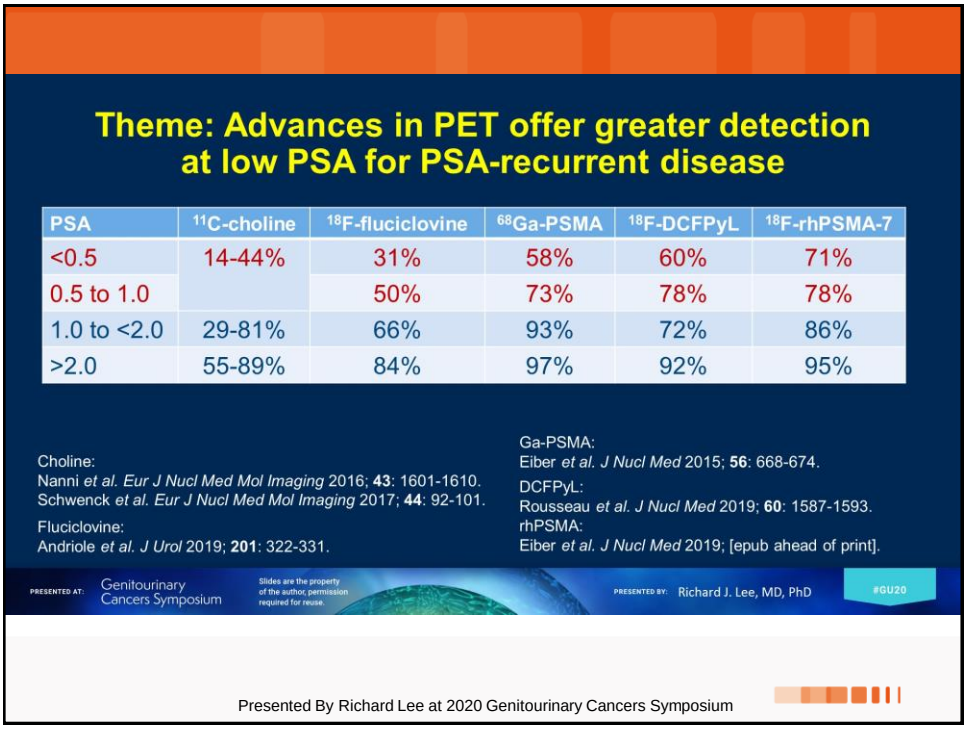

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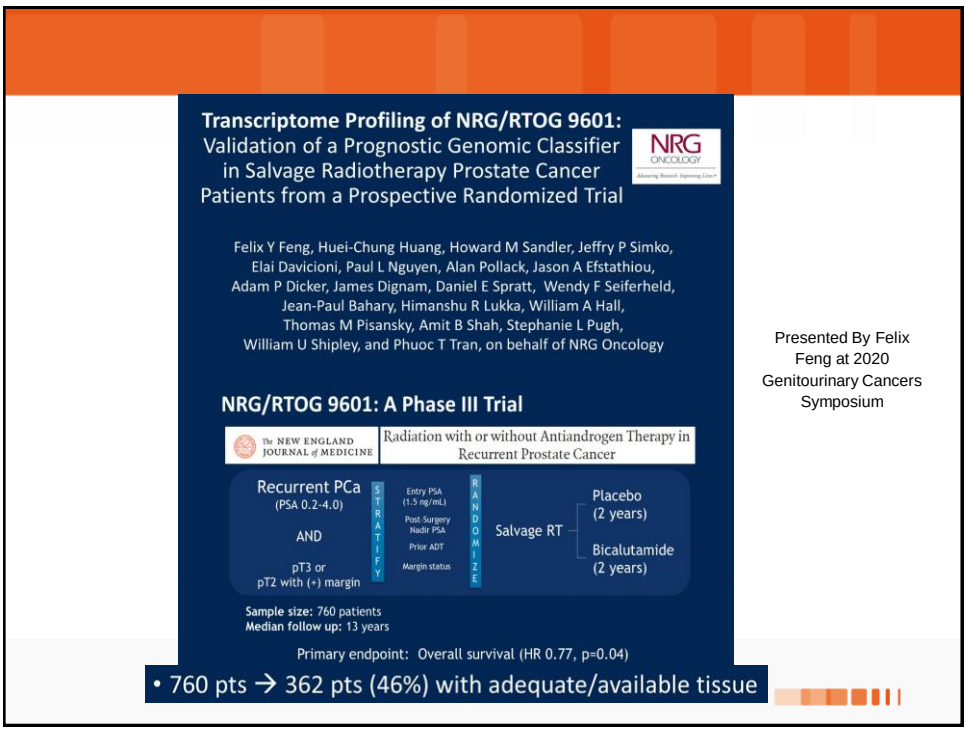

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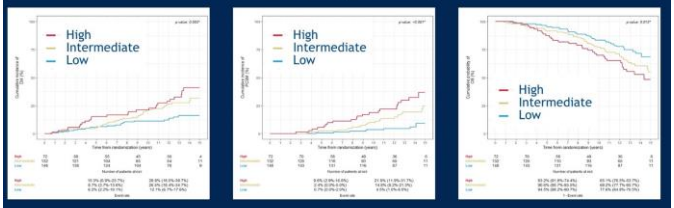
22-gene Decipher classifier risk stratifies all outcomes

Distant Metastases | Prostate Cancer Specific Mortality | Overall Survival



Decipher remains a significant predictor of outcome in a multivariable model

Variable	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value
	Distant Metastases		PCSM		OS	
Decipher score	1.17 (1.05 - 1.32)	0.006*	1.39 (1.20 - 1.63)	<0.001*	1.17 (1.06 - 1.29)	0.002*
Treatment vs. Placebo	0.62 (0.39 - 0.97)	0.037*	0.53 (0.30 - 0.92)	0.024*	0.82 (0.57 - 1.19)	0.293
Age 65+ vs. 65-	1.30 (0.83 - 2.06)	0.247	1.52 (0.88 - 2.66)	0.136	1.95 (1.33 - 2.91)	<0.001*
Black vs. non-Black	0.88 (0.28 - 2.13)	0.798	0.86 (0.17 - 2.73)	0.827	1.35 (0.57 - 2.77)	0.467
Gleason 8-10 vs. ≤7	2.11 (1.24 - 3.47)	0.007*	2.53 (1.38 - 4.49)	0.003*	1.87 (1.20 - 2.85)	0.007*
T3 vs. T2	1.42 (0.82 - 2.58)	0.220	2.01 (0.97 - 4.62)	0.061	1.24 (0.79 - 1.97)	0.350
Entry PSA	1.16 (0.88 - 1.49)	0.264	1.37 (1.01 - 1.80)	0.041*	1.08 (0.84 - 1.35)	0.530
Positive surgical margins	0.71 (0.44 - 1.16)	0.167	1.26 (0.68 - 2.44)	0.465	0.98 (0.64 - 1.53)	0.919
Non-nadir vs. nadir PSA (<0.5ng/ml)	1.31 (0.62 - 2.51)	0.456	2.10 (0.92 - 4.26)	0.074	1.98 (1.13 - 3.30)	0.019*

Hazard ratios of GC were per 0.1 unit increased.

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The *absolute* benefit from hormone therapy is smaller in the low Decipher risk groups

Entire cohort

The *absolute* benefit from hormone therapy is smaller in the low Decipher risk groups

Early salvage RT (PSA <0.7 ng/mL)

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En clinique avantage HT si psa > 1,5 ng/ml

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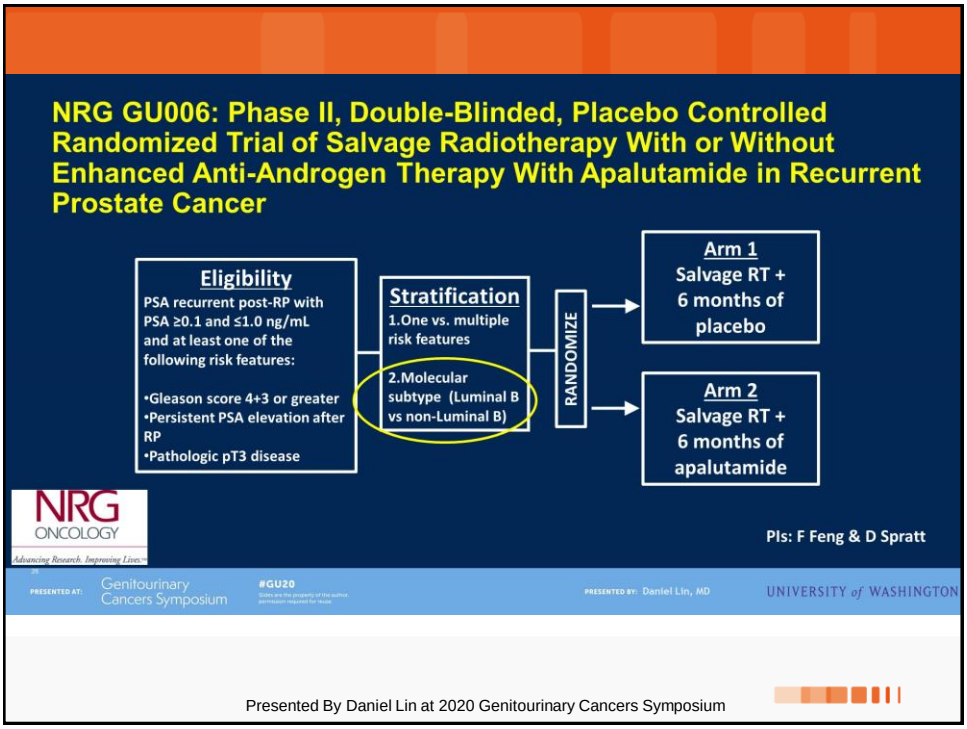

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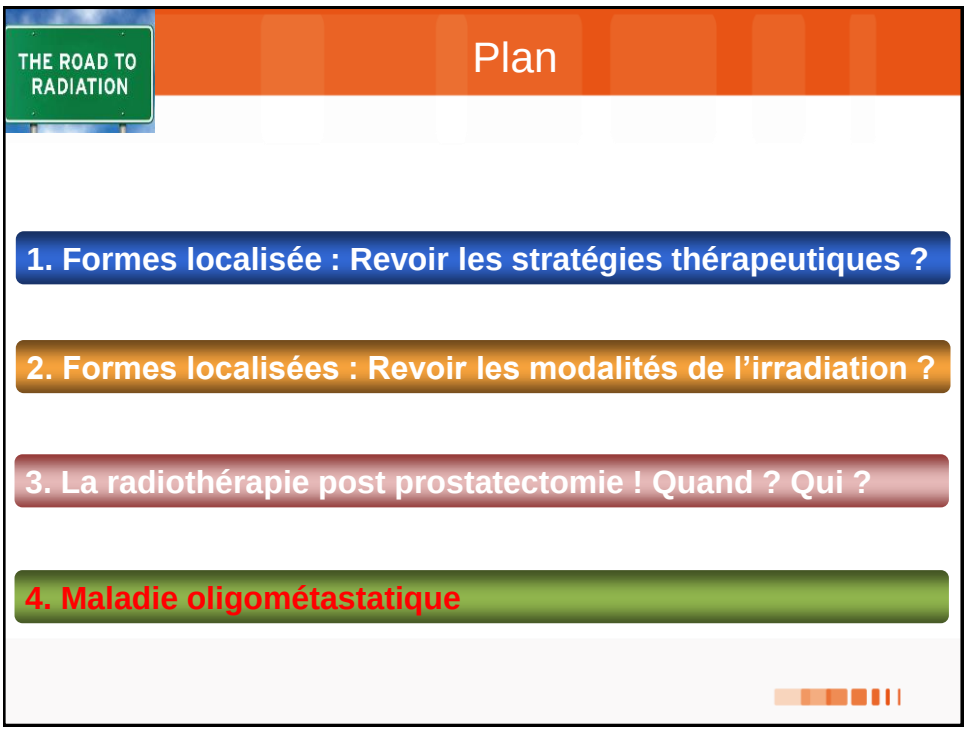

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Table 3 – Characteristics of patients at randomisation

	HORRAD [11]		STAMPEDE [12] [a]	
	ADT	RT + ADT	ADT	RT + ADT
Number of patients	216	216	845	849
Disease history				
Newly diagnosed M1	216 (100)	216 (100)	845 (100)	849 (100)
Type of ADT, n (%)				
Orchiectomy	4 (2)	1 (<1)	0	0
LHRH agonist	212 (98)	210 (97)	672 (80)	684 (81)
LHRH antagonist	0	0	165 (19)	159 (18)
Missing	0	5 (2)	8 (1)	6 (<1)
Time from initial diagnosis (mo), n (%)				
Median (IQR)	<1 (2–5 wk)	<1 (2–6 wk)	2.4 (1.8–3.3)	2.4 (1.8, 3.1)
Range	0–42	0–25	0–114.8	0–41.9
Missing	0	0	5	14
Time to ADT start (wk)				
Median (IQR)	−1 (−3, 0)	−1 (−3, 0)	−1.7 (−2.3, −1.1)	−1.7 (−2.3, −1.1)
Range	−17 to 2	−13 to 2	−2.8 to 1.1	−2.8 to 0.3
Missing	2	4	0	1
Age (yr)				
Median (IQR)	67 (61–71)	67 (62–71)	68 (63, 73)	68 (63, 73)
Range	47–85	47–79	37–84	45–87
WHO/ECOG performance status				
0	176 (82)	187 (87)	597 (71)	603 (71)
1+	40 (18)	29 (13)	248 (29)	246 (29)
PSA (ng/ml), n (%)				
Median (IQR)	149 (50–483)	125 (48–433)	100 (30, 311)	96 (33,299)
Range	4–4091	8–14,000	1–20,590	1–11,156
T category				
T0	0	0	0	2 (<1)
T1	5 (2)	7 (3)	11 (1)	11 (1)
T2	20 (10)	33 (15)	69 (8)	73 (9)
T3	128 (59)	125 (58)	474 (56)	500 (59)
T4	59 (27)	51 (24)	222 (26)	198 (23)
Tx	4 (2)	0	69 (9)	65 (7)
N category, n (%)				
N0	–	–	293 (35)	292 (34)
N+	–	–	500 (59)	498 (59)
Nx	216 (100)	216 (100)	52 (6)	59 (7)
Gleason sum score, n (%)				
<8	71 (33)	73 (34)	151 (18)	144 (17)
≥8	144 (66)	142 (65)	668 (79)	665 (78)
Unknown	1 (<1)	1 (<1)	26 (3)	40 (5)
Number of bone metastases, n (%)				
<5	71 (33)	89 (41)	404 (48)	399 (47)
≥5	145 (67)	127 (58)	397 (47)	393 (46)
Unknown	–	–	44 (5)	57 (7)
Metastatic burden (HORRAD definition[b]), n (%)				
Low burden	35 (16)	39 (18)	385 (46)	387 (46)
High burden	181 (84)	177 (82)	416 (49)	405 (48)
Unknown	–	–	44 (5)	57 (6)
Planned RT dose, n (%)				
36 Gy in 6 fr over 6 wk, n (%)	NA	NA	NA	416 (49)
55 Gy in 20 fr over 4 wk n (%)	NA	NA	NA	433 (51)
70 Gy in 35 fr over 7 wk, n (%)	NA	176 (82)	NA	NA
57.76 Gy in 19 fr over 4 wk, n (%)	NA	26 (12)	NA	NA
Unknown, n (%)		14 (6)		

ADT = androgen deprivation therapy; fr = fraction; IQR = interquartile range; LHRH = luteinising hormone-releasing hormone; NA = not available; RT = radiotherapy.
[a] Based on the participants who did not receive docetaxel as part of standard of care.
[b] low = Gleason sum score <9 and <5 bone lesions and PSA <142 (HORRAD median).

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Prostate Cancer

Prostate Radiotherapy for Metastatic Hormone-sensitive Prostate Cancer: A STOPCAP Systematic Review and Meta-analysis

Sarah Burdett[a,], Liselotte M. Boeve[b,c], Fiona C. Ingleby[d,], David J. Fisher[a], Larysa H. Rydzewska[a], Claire L. Vale[a], George van Andel[e], Noel W. Clarke[f], Maarten C. Hulshof[g], Nicholas D. James[d], Christopher C. Parker[h], Mahesh K. Parmar[a], Christopher J. Sweeney[i], Matthew R. Sydes[a], Bertrand Tombal[j], Paul C. Verhagen[b], Jayne F. Tierney[a], the STOPCAP M1 Radiotherapy Collaborators*

Trial	Years of accrual	Number of men randomised	De novo or relapsed M1?	Treatment	Control	Media follow (surviv
				Radiotherapy	ADT	
Radiotherapy + ADT vs ADT						
STAMPEDE A1 [10] (arm H vs arm A)	2013–2016	1694	De novo	36 Gy, 6 fractions over 6 wk or 55 Gy, 20 fractions over 4 wk	ADT (LHRH agonist or antagonist or orchiectomy)	41.9 mo
HORRAD [12]	2004–2014	432	De novo	70 Gy, 35 fractions over 7 wk or 57.76 Gy, 19 fractions over 6 wk	ADT (LHRH agonist or orchiectomy)	47 mo
PEACE-1A1 (NCT01957436)	2013–2018*	234	De novo	74 Gy, 37 fractions within 7–8 wk	ADT (LHRH agonist or antagonist or orchiectomy)	Not yet availab

ADT = androgen deprivation therapy; LHRH = luteinising hormone-releasing hormone. *PEACE-1 closed to accrual between submission and acceptance of manuscript

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STOPCAP méta-analyse

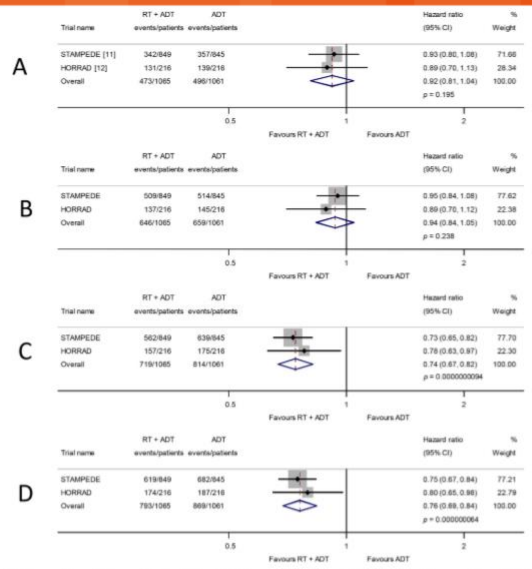

Fig. 1 – Effect of adding prostate radiotherapy to ADT on (A) survival, (B) progression-free survival, (C) biochemical progression, and (D) failure-free survival in men with mHSPC. Each filled square denotes the HR for that trial comparison, with the horizontal lines showing the 95% confidence interval (CI). The size of the square is directly proportional to the amount of information contributed by a trial. The diamond represents a (fixed-effect) meta-analysis of the trial HRs, with the centre of this diamond indicating the HR and the extremities the 95% CI. ADT = androgen deprivation therapy; HR = hazard ratio; RT = radiotherapy.

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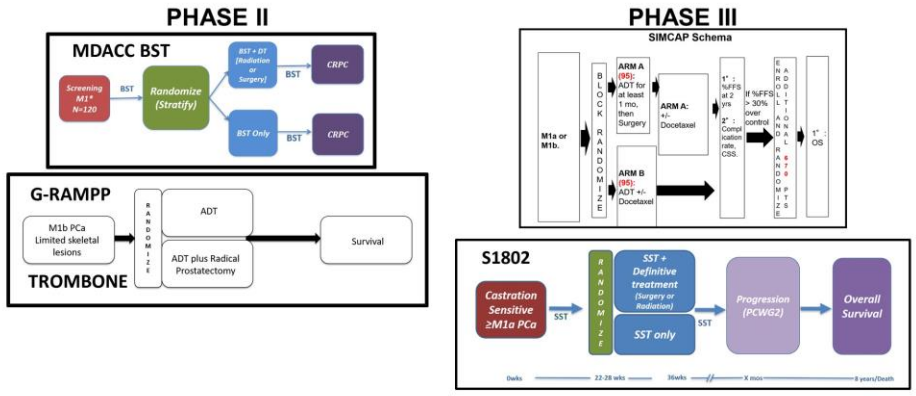
Prospective RANDOMIZED ADT +/- Surgery in M1 Disease



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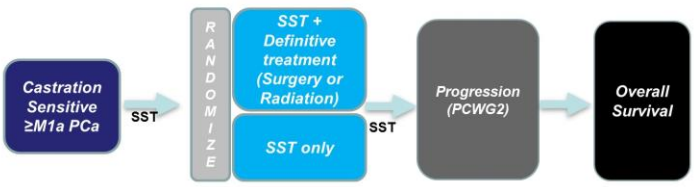
Randomized, Phase III Trial of Standard Systemic Therapy (SST) or SST Plus Definitive Treatment of the Primary Tumor in Metastatic Prostate Cancer (S1802)



PI: Brian F Chapin, MD
SWOG : Dan Lin, David Quinn, Ana Aparicio, Cathy Tangen, Nicholas Vogelzang, Ian Thompson

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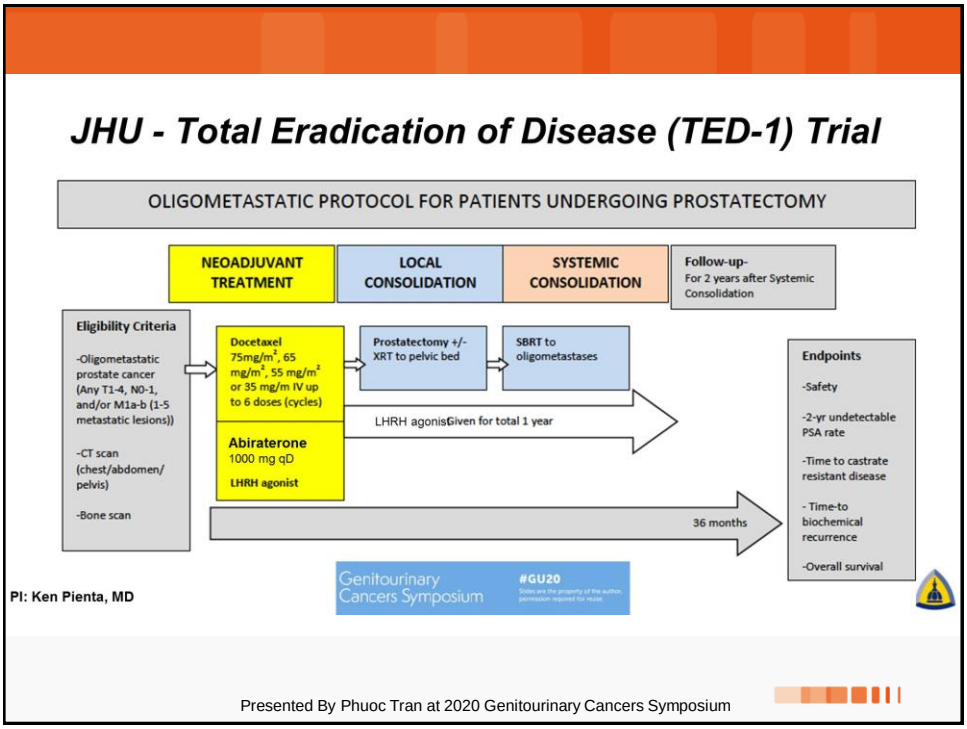

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