
XXXIII CONGRESSO NAZIONALE AIRO
AIRO2023
BOLOGNA,
27-29 OTTOBRE 2023
PALAZZO DEI CONGRESSI
Radioterapia Oncologica: l'evoluzione al servizio dei pazienti
Ciammella Patrizia
Reggio Emilia
Associazione Italiana
Radioterapia e Oncologia clinica

DISCLOSURE

None

STUDIO PROSPETTICO DI FASE 2 SULLA RADIOTERAPIA STEREOTASSICA ABLATIVA DOPO CHEMIOTERAPIA DI INDUZIONE NEI PAZIENTI CON TUMORE DEL PANCREAS LOCALMENTE AVANZATO NON RESECABILE: RISULTATI FINALI DELLO STUDIO LAPC02 (NCT03158779)

TIZIANA COMITO M.D.

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Unresectable LAPC (30-40%)

Chemotherapy or Radiotherapy alone

Chemo- radiation treatment

- Induction chemotherapy + chemoradiotherapy
- Induction chemotherapy + SBRT

→ improve systemic disease control
→ local control rates ranging from 70 to 100%
→ short treatment duration

SBRT in patients with unresectable LAPC

Authors, Year	Phase	Therapy	Gy/fx	n	mOS months	2yr OS %	Toxicity > Grade 3
Hoyer, 2005	II	SBRT	45/3	22	5.7	0	18%
Schellenberg, 2008	II	Gem SBRT --> Gem	25/1	16	11.9	18	19%
Schellenberg, 2011	II	Gem --> SBRT --> Gem	25/1	20	11.8	20	5%
Her							
Co							
He							
Te							
Ejl							
Mi							
Bo							

Metanalysis 2020: SBRT vs. Conventional RT → 2yrs OS 26.9% vs. 13.7%

→ BED ≥70 Gy

Ejlsmark MW, Schytte T, Bernchou U, Bahij R, Weber B, Mortensen MB, Pfeiffer P. Radiotherapy for Locally Advanced Pancreatic Adenocarcinoma-A Critical Review of Randomised Trials. Curr Oncol. 2023 Jul 18;30(7):6820-6837. doi: 10.3390/curroncol30070499. PMID: 37504359; PMCID: PMC10378124.

Ongoing Trial

Trial Number, Name	Stage	Phase	Therapy	RT Gy/fx	n	Primary Endpoint	Expected Completion
NCT04089150 MASTERPLAN	brPC LAPC	RII	GnP or mFFX GnP or mFFX ⟹ SBRT	 40/5	120	Local control	2025
NCT04331041	brPC LAPC	RII	Chemo ⟹ SBRT Chemo ⟹ SBRT + defactenib	50/5 50/5	42	PFS	2025
NCT04986930 SABER	LAPC	RII	mFFX mFFX ⟹ SBRT	 35/5	92	PFS	2024
NCT05083247 STEREOPAC	brPC	RII	GnP or mFFX GnP or mFFX ⟹ SBRT	 35/5	256	DFS	2030
NCT05585554 LAP-ABLATE	LAPC	-	Chemo Chemo ⟹ SBRT	 50/5	267	OS	2028
NCT04881487 ARCADE	Recur	RII	Chemo Chemo ⟹ SBRT	 40/5	174	OS	2028

Ejlsmark MW, Schytte T, Bernchou U, Bahij R, Weber B, Mortensen MB, Pfeiffer P. Radiotherapy for Locally Advanced Pancreatic Adenocarcinoma-A Critical Review of Randomised Trials. Curr Oncol. 2023 Jul 18;30(7):6820-6837. doi: 10.3390/curroncol30070499. PMID: 37504359; PMCID: PMC10378124.

Take Home Messages

SBRT in LAPC

- **Valid integration with systemic therapy**
- **Safe and well tolerated with adeguate IGRT**
- **Associated with improved local control (above all with dose escalation!).**
- **Time saving**
- **Lack of randomised studies to support its use in LAPC.**

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Radioterapia Oncologica: l'evoluzione al servizio dei pazienti

Radioterapia Oncologica:
l'evoluzione al servizio dei pazienti

Early salvage radiotherapy in patients with intermediate-risk prostate cancer: is it feasible? Preliminary results of a prospective study on 721 patients (EASY-1: EArly Salvage RadiotherapY-1).

Radioterapia di salvataggio precoce nei pazienti con carcinoma prostatico a rischio intermedio: è fattibile? Risultati preliminari di uno studio prospettico su 721 pazienti (EASY-1: EARly Salvage Radiotherapy-1).

Letizia Cavallini

Radiation Oncology, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum University of Bologna.

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Radioterapia Oncologica: l'evoluzione al servizio dei pazienti

Profiling PCa patients with BCR in the era of early imaging detection: an AIRO-URO group study

Dott.ssa Giulia Marvaso

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Università degli studi di Milano
giulia.marvaso@ieo.it

IEO Istituto Europeo di Oncologia

Marvaso et al.

- Retrospective multicentric study
- Inclusion criteria:
  - Pts who underwent RP and salvage RT
  - Pts who had detectable PSA at BCR
  - Pts with pN0 or pN1 at surgery
  - 2 years of follow-up
- 1625 pts (all underwent salvage RT)
- Median follow-up: 4.20 yrs (2.49, 6.28)
- Median time from surgery to salvage= 2,1 years
- Median PSA at BCR= 0.26 ng/ml
- HT = 23%
- LN RT= 38%

Cavallini et al.

- Prospective monocentric study
- Inclusion criteria:
  - PCa treated with RP
  - pT2 R1
  - pT3a, any R
  - pT3b R0
  - PSA<0.01ng/ml at 40 days
  - NO pN1
- 721 pts
- 64 (9.3%) with BCR; 60/64 pts (90%) treated with sRT
- Median follow up= 39 months (2-72)
- Median time from surgery to salvage= 15 months
- Median PSA at BCR= 0.21 ng/ml
- HT = 95% (median duration 12 months, range: 6-25)
- LN RT= 67%

Marvaso et al.

- High risk of BCR:
  - pT 3 or 4
  - ISUP 4 or 5

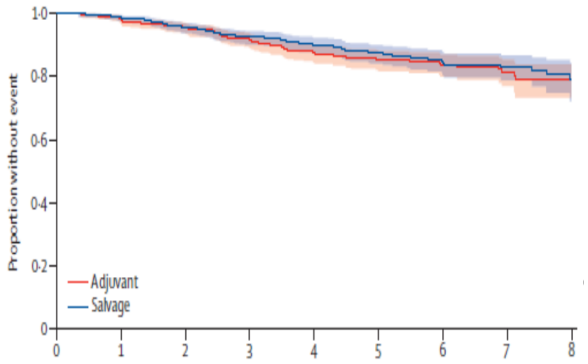
Cavallini et al.

- HIgh risk of BCR:
  - ISUP 4-5
  - pT3a R1

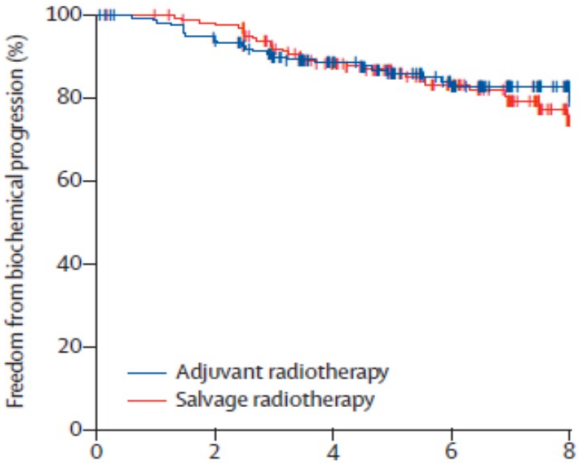
Characteristics	RADICALS-RT	GETUG-AFU 17	TROG 08.03/ANZUP RAVES
N° pts	1396	424	333
Accrual period	11/2007-12/2016	07/2008-06/2016	03/2009-12/2015
Key inclusion criteria	+ margins; pT3a/pT3b/pT4; GS 7-10	+ margins; pT3a/pT3b	+ margins; pT2/pT3a/pT3b
RT schedule	66/33 or 52.2/20	66/33	64/32
Randomization	ART vs. early SRT (identical at PSA >0.1 ng/ml)	ART vs. early SRT at PSA >0.1 ng/ml	ART (PSA <0.1 ng/ml) vs. early SRT (PSA >0.2 ng/ml)
ART timing	≤6 m of RP	≤6 m of RP	≤6 m of RP
eSRT timing	≤2 m of trigger PSA	As son as possible after PSA relapse and before PSA is 1 ng/ml	≤4 m of trigger PSA
Primary outcome	FFDM	EFS	FfBF
Trial design	Superiority	Superiority	Non-inferiority
Median FU (yr)	4.9	6.25	6.1
5 yr BPFS	85% vs. 88% (p=0.56)	92% vs. 90% (p=0.42)	86% vs. 87% (p>0.05)
OS or MFS	n.r.	n.r.	n.r.
Side effects	SR Urinary incontinence 1 yr: 4.8 vs. 4 (p=0.0023); urethral stricture grade ¾ 2 yr: 6% vs. 4% (p=0.02)	LT grade ≥2 GU 27% vs. 7% (p<0.001); ED 28% vs. 8% (p<0.001)	LT grade ≥ GU: 70% vs. 54% (p=0.002)

Comparison curves

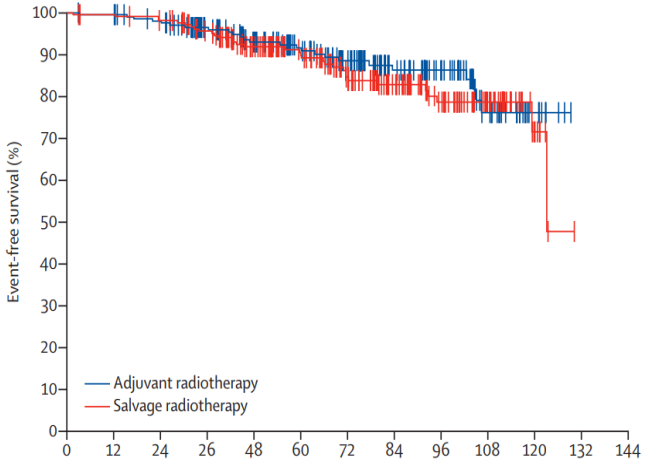
RADICALS-RT



TROG 08.03/ANZUP RAVES



GETUG-AFU 17



RADICALS-RT

	Early (<2 years)				Late (≥2 years)			
	All (n=1372)	Salvage radiotherapy (n=696)	Adjuvant radiotherapy (n=676)	p value	All (n=1220)	Salvage radiotherapy (n=621)	Adjuvant radiotherapy (n=599)	p value
Diarrhoea								
Grade 1 or 2	372 (27%)	112 (16%)	260 (38%)	<0·0001	153 (13%)	50 (8%)	103 (17%)	<0·0001
Grade 3	13 (1%)	3 (<1%)	10 (1%)	..	7 (1%)	2 (<1%)	5 (1%)	..
Grade 4	0	0	0	..	1 (<1%)	0	1 (<1%)	..
Proctitis								
Grade 1 or 2	196 (14%)	47 (7%)	149 (22%)	<0·0001	111 (9%)	34 (5%)	77 (13%)	<0·0001
Grade 3	11 (1%)	3 (<1%)	8 (1%)	..	7 (1%)	1 (<1%)	6 (1%)	..
Grade 4	0	0	0	..	0	0	0	..
Cystitis								
Grade 1 or 2	255 (19%)	84 (12%)	171 (25%)	<0·0001	122 (10%)	42 (7%)	80 (13%)	<0·0005
Grade 3	16 (1%)	5 (1%)	11 (2%)	..	10 (1%)	4 (1%)	6 (1%)	..
Grade 4	1 (<1%)	0	1 (<1%)	..	0	0	0	..
Haematuria								
Grade 1 or 2	96 (7%)	25 (4%)	71 (11%)	<0·0001	95 (8%)	25 (4%)	70 (12%)	<0·0001
Grade 3	22 (2%)	2 (<1%)	20 (3%)	..	26 (2%)	2 (<1%)	24 (4%)	..
Grade 4	0	0	0	..	0	0	0	..
Urethral stricture								
Grade 1 or 2	62 (5%)	21 (3%)	41 (6%)	0·020	55 (5%)	19 (3%)	36 (6%)	0·0025
Grade 3	64 (5%)	27 (4%)	37 (5%)	..	39 (3%)	13 (2%)	26 (4%)	..
Grade 4	5 (<1%)	3 (<1%)	2 (<1%)	..	3 (<1%)	3 (<1%)	0	..

TROG 08.03/ANZUP RAVES

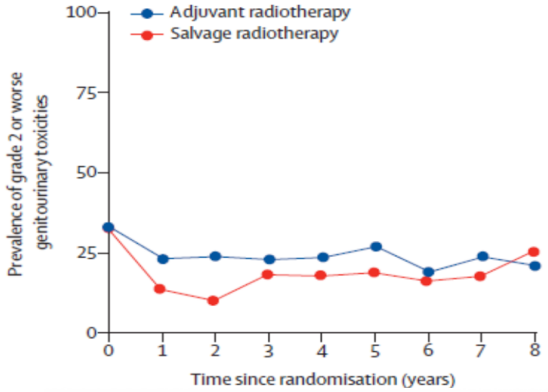


Table 2: Tabulation of adverse events

5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

GETUG-AFU 17

	Adjuvant radiotherapy group (n=212)			Salvage radiotherapy group (n=212)		
	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4
Gastrointestinal disorders	112 (53%)	0	0	42 (20%)	1 (<1%)	0
Diarrhoea	60 (28%)	0	0	17 (8%)	0	0
Proctitis	27 (13%)	0	0	6 (3%)	0	0
Anal inflammation	22 (10%)	0	0	5 (2%)	0	0
Intestinal obstruction	0	0	0	0	1 (<1%)	0
General disorders and administration site conditions	100 (47%)	2 (1%)	0	42 (20%)	1 (<1%)	0
Hot flush	81 (38%)	2 (1%)	0	35 (17%)	1 (<1%)	0
Asthenia	41 (19%)	0	0	19 (9%)	0	0
Metabolism and nutrition disorders	0	1 (<1%)	0	0	0	0
Type 2 diabetes	0	1 (<1%)	0	0	0	0
Renal and urinary disorders	143 (67%)	2 (1%)	1 (<1%)	53 (25%)	1 (<1%)	0
Increased urinary frequency	106 (50%)	1 (<1%)	0	37 (17%)	1 (<1%)	0
Urinary incontinence	47 (22%)	1 (<1%)	0	10 (5%)	0	0
Dysuria	32 (15%)	0	0	13 (6%)	0	0
Urinary retention	1 (<1%)	0	1 (<1%)	0	0	0
Reproductive system and breast disorders	16 (8%)	1 (<1%)	0	10 (5%)	1 (<1%)	0
Erectile dysfunction	10 (5%)	1 (<1%)	0	6 (3%)	1 (<1%)	0
Skin and subcutaneous tissue disorders	25 (12%)	0	0	16 (8%)	0	0

There were no deaths due to acute adverse events.

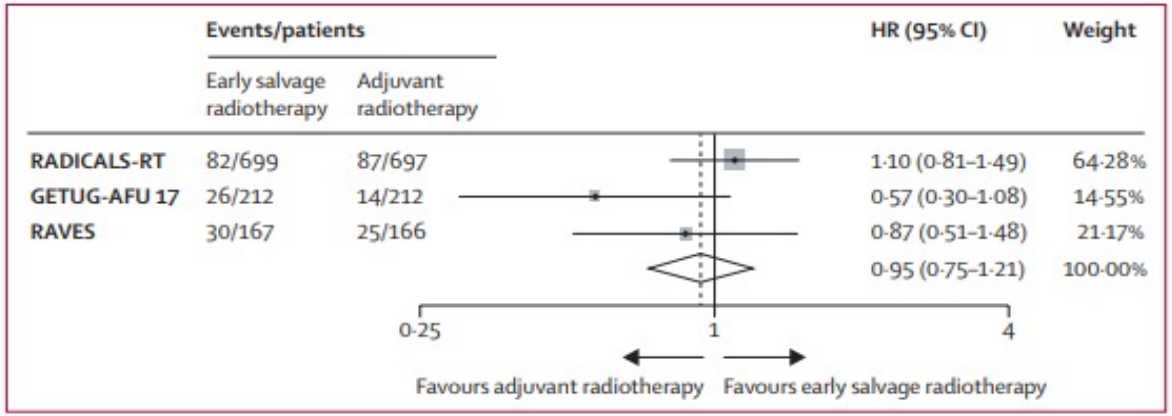
Higher rates of toxicity in the aRT arms

ARTISTIC meta-analysis

PRIMARY ENDPOINT →

Event-free survival: the time from randomisation until the first evidence of either biochemical progression (PSA ≥0·4 ng/mL and rising after completion of any postoperative RT), clinical or radiological progression, initiation of a nontrial treatment, death from prostate cancer, or a PSA ≥ 2.0 ng/mL at any time after randomisation.

THE LANCET Oncology 2020



No evidence that event-free survival was improved with ART compared with SRT **(HR 0.95, 95% CI 0.75–1.21; p=0.70)**
Only a 1 percentage point (95% CI −2 to 3) change in 5-year event-free survival: (89% vs 88%).
Results were consistent across trials **(heterogeneity p=0·18; I^2=42%)**

Conclusions

- eSRT and aRT offer **apparently** similar outcomes for event-free survival (even if studies are **formally negative**).
- eSRT spares many men from receiving radiotherapy and associated side-effects.
- Patients should be informed about the choice among immediate (adjuvant) or deferred (salvage) RT
- Incontinence to choice early salvage RT
- Pathological factors (pT3b, GS 8, pN+, some R1) for adjuvant RT

OPEN QUESTIONS:

- **HT?**
- **eSRT volumes?**

Radiotherapy and Oncology 183 (2023) 109544

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journal homepage: www.thegreenjournal.com

Original Article

ESTRO-ACROP recommendations for evidence-based use of androgen deprivation therapy in combination with external-beam radiotherapy in prostate cancer

Salvage EBRT in biochemically recurrent prostate cancer with pN0 at time of surgery

Salvage normo-fractionated EBRT with long-term ADT (24 months) is recommended in pN0 patients with high risk of further progression (PSA ≥ 0.7 ng/ml and ISUP grade group ≥ 4) and a life expectancy of over ten years.

Salvage normo-fractionated EBRT with short-term ADT (6 months) is recommended in pN0 patients with lower risk profile (PSA < 0.7 ng/ml and ISUP grade group 4).

RTOG 9601

GETUG-AFU 16

RTOG 0534 SPPORT

Marvaso et al.

HT = 23%

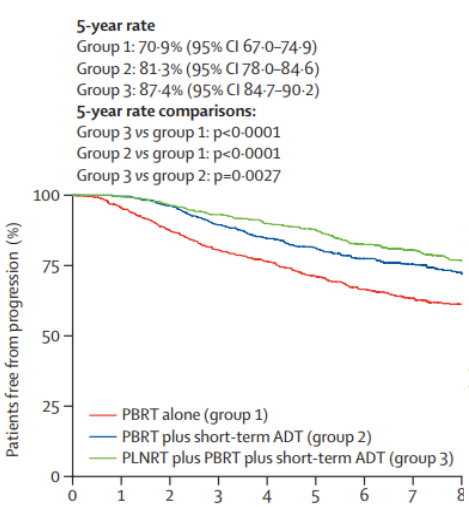
Median PSA at BCR= 0.26 ng/ml

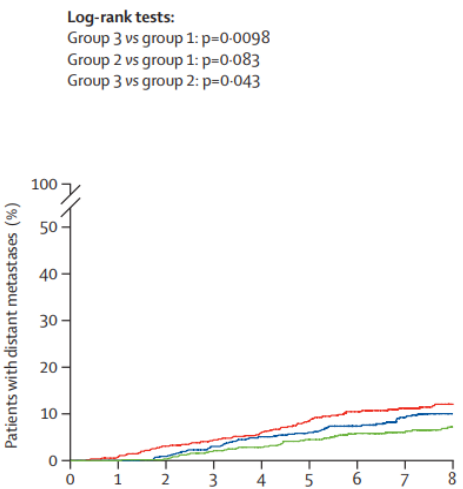
Cavallini et al.

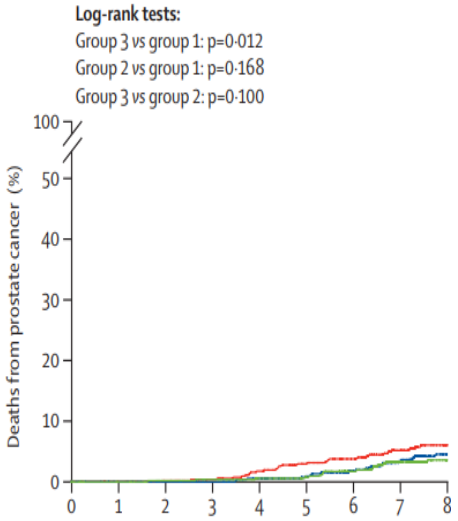
HT = 95% (median duration 12 months, range: 6-25)

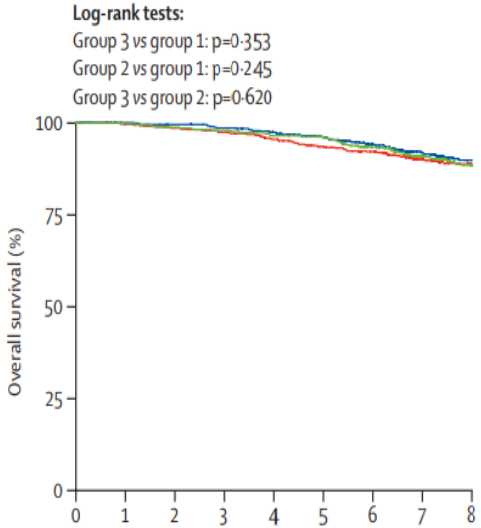
Median PSA at BCR= 0.21 ng/ml

The addition of androgen deprivation therapy and pelvic lymph node treatment to prostate bed salvage radiotherapy (NRG Oncology/RTOG 0534 SPPORT): an international, multicentre, randomised phase 3 trial



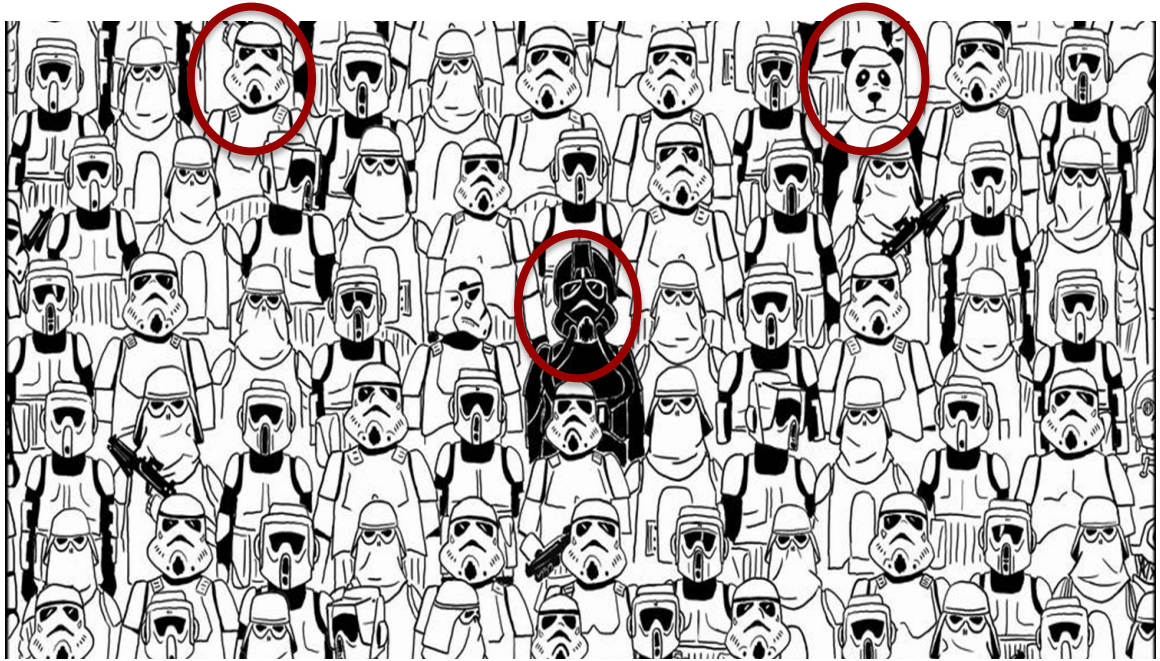






Pollack A et al,The Lancet 2022

esRT for all?



BCR Risk Stratification

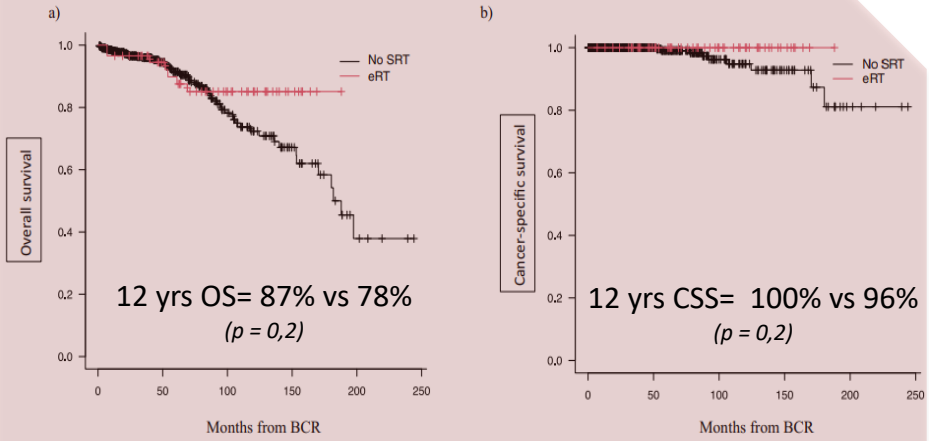
GS (or ISUP)

PSA DT

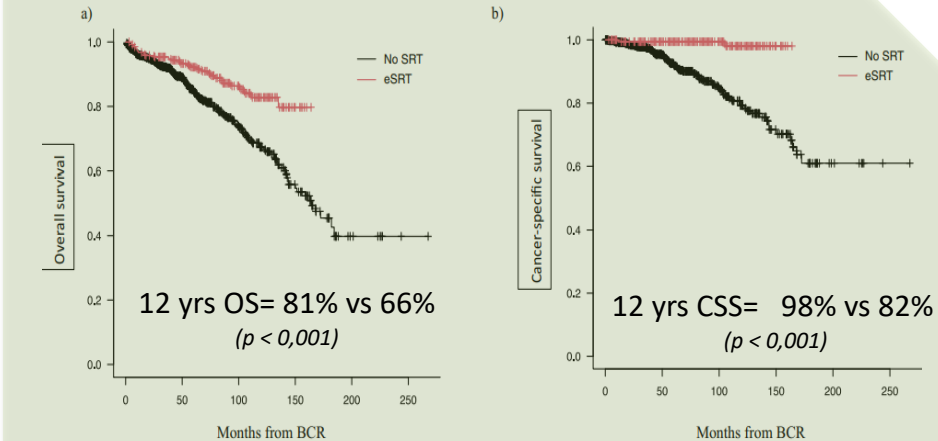
Prostate Cancer

European Association of Urology Biochemical Recurrence Risk Classification as a Decision Tool for Salvage Radiotherapy—A Multicenter Study

Objective: To assess whether this risk stratification helps in choosing patients for sRT



EAU low-risk BCR : GS<8 (or ISUP GG <4) and PSADT >12 mo



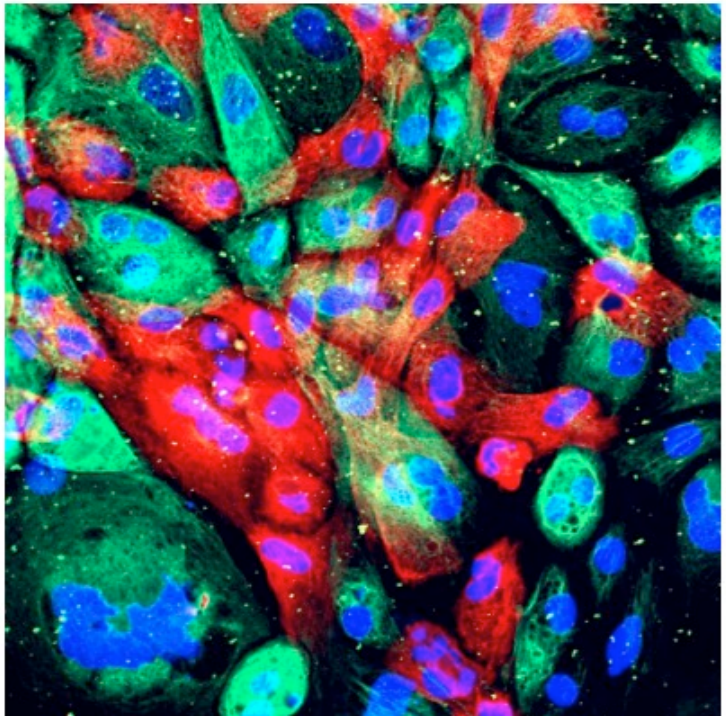
EAU high-risk BCR : GS≥8 (or ISUP GG 4-5) or PSADT ≤ 12 mo

Preisser F, EUROPEAN UROLOGY 2023

BCR Risk Stratification and Tailored therapy

- GS (or ISUP)
- PSA DT
- Molecular Targeted Imaging (MTI)
- Conventional Imaging
- Genomic Testing

https://www.deciphergenomics.org/



Decipher
PROSTATE BIOPSY GENOMIC CLASSIFIER

PATIENT REPORT
REPORT STATUS: FINAL
PAGE: 1 OF 3

SAMPLE REPORT: NOT A REAL PATIENT

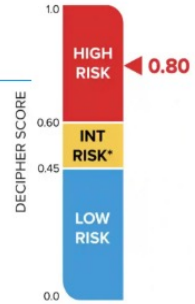
PATIENT	SPECIMEN INFORMATION	ORDERING PHYSICIAN
Name: **Sample Patient**	Order Date: --/--/----	Name: **Sample Physician, MD**
Date of Birth: --/--/----	Specimen ID: ----------	Clinic: **Sample Clinic**
Medical Record #: ----------	Specimen Received Date: --/--/----	Address: **123 Birch Avenue, Suite A, Anytown, CA 54321**
Date of Biopsy: --/--/----	Decipher Accession ID: **MC-123456**	Additional Physician: **Additional Sample Physician, MD**

CLINICAL AND PATHOLOGY DETAILS For reference only, not used in calculation of genomic risk

Specimen: **Needle Biopsy**	Most Recent PSA: **4.9 ng/mL**	NCCN Risk Category: **Intermediate**
Clinical Stage: **T1c**	Gleason Score: **3+4**	

DECIPHER GENOMIC RISK RESULTS

1



GENOMIC RISK IS: HIGH 2

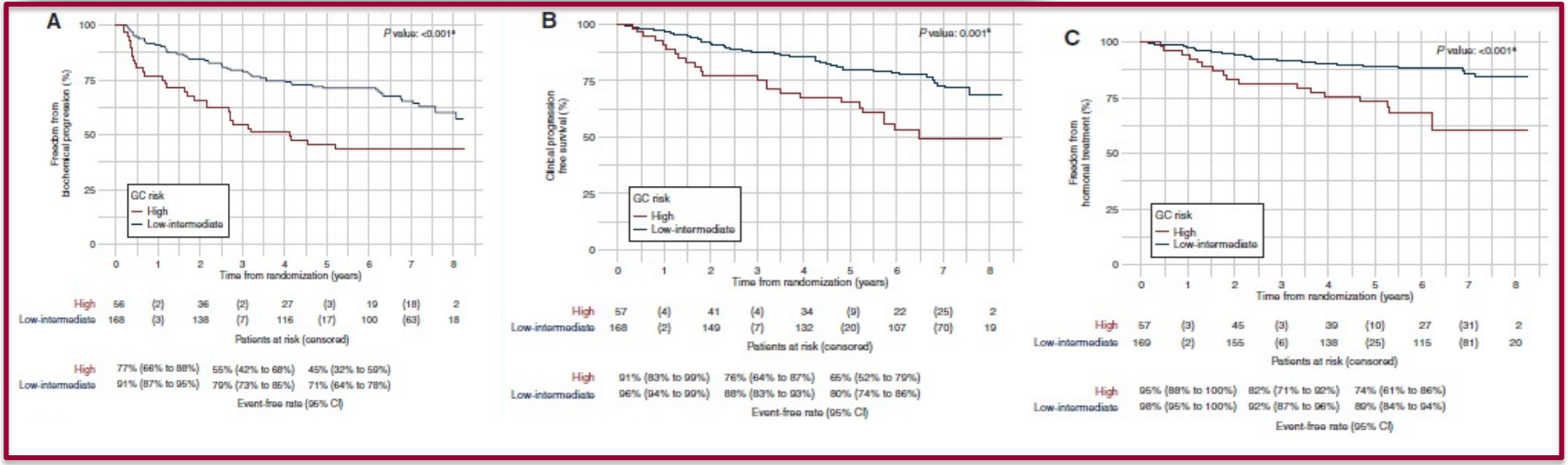
2.6%	6.5%	8.8%	48.1%
5-year	*10-year*	*15-year*	*At RP*
Risk of Metastasis with RT† or RP‡		**Risk of Prostate Cancer Mortality** with RT or RP	**Risk of Adverse Pathology**

Clinical studies have shown that Decipher high-risk patients have an unfavorable prognosis.

- These patients may benefit from treatment intensification with multimodal therapy.[2-5,9,10] 3
- These patients may not be ideal candidates for active surveillance.[1-3,8]

The Decipher score is determined solely by genomic characteristics of the tumor, independent of the NCCN risk category. No other clinical or pathologic parameters factor into the score.

Validation of the Decipher genomic classifier in patients receiving salvage radiotherapy without hormone therapy after radical prostatectomy – an ancillary study of the SAKK 09/10 randomized clinical trial☆



Ann Oncol. 2022 Sep;33(9):950-958

Risk-adapted Salvage Treatment in BCR after PR

After RP: PSA > 0.2 ng/ml

Salvage RT

- PSA level, < 0.7 ng/ml
- PSA DT, < 6 months

Salvage RT + ADT

- Genomic Classifier score, high
- GS, 8-10 (ISUP 4-5)
- Life expectancy > 10 years
- pre-RT PSA level, > 0.7 ng/ml
- Positive surgical margins

zienti

Grazie!