Moderately Hypo-RT using Tomo® for INT/ HR Pca: outcome and toxicities analysis in 123 consecutive pts treated at the Radiotherapy Unit of Modena

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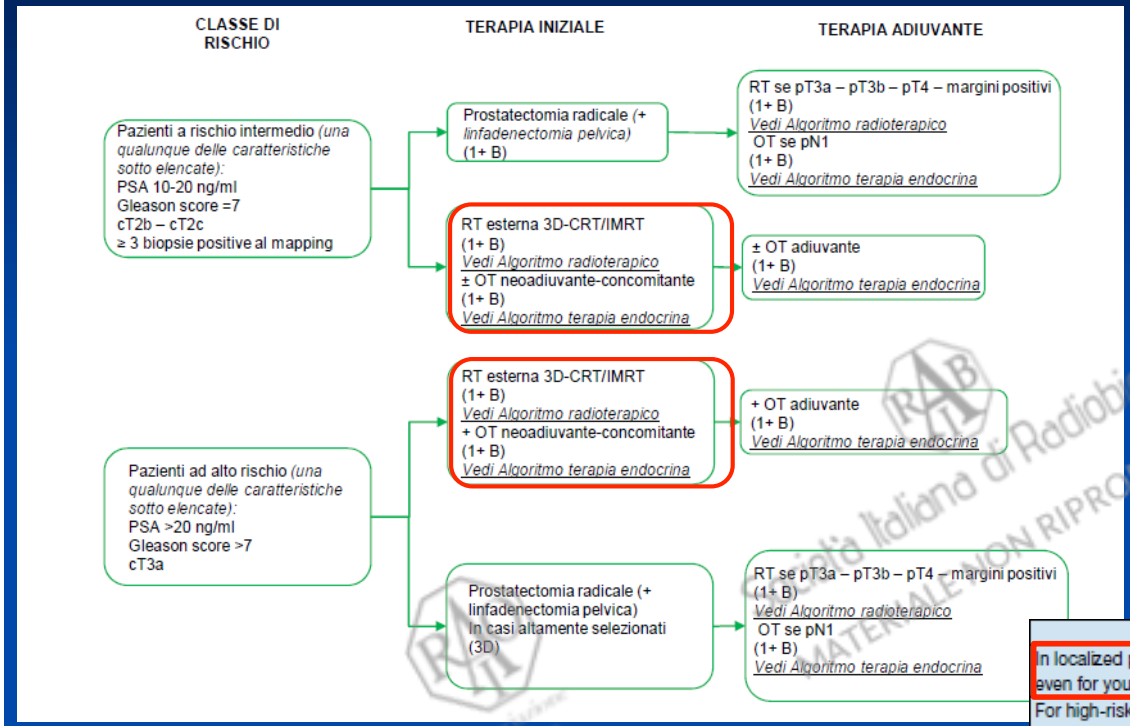
Background -1



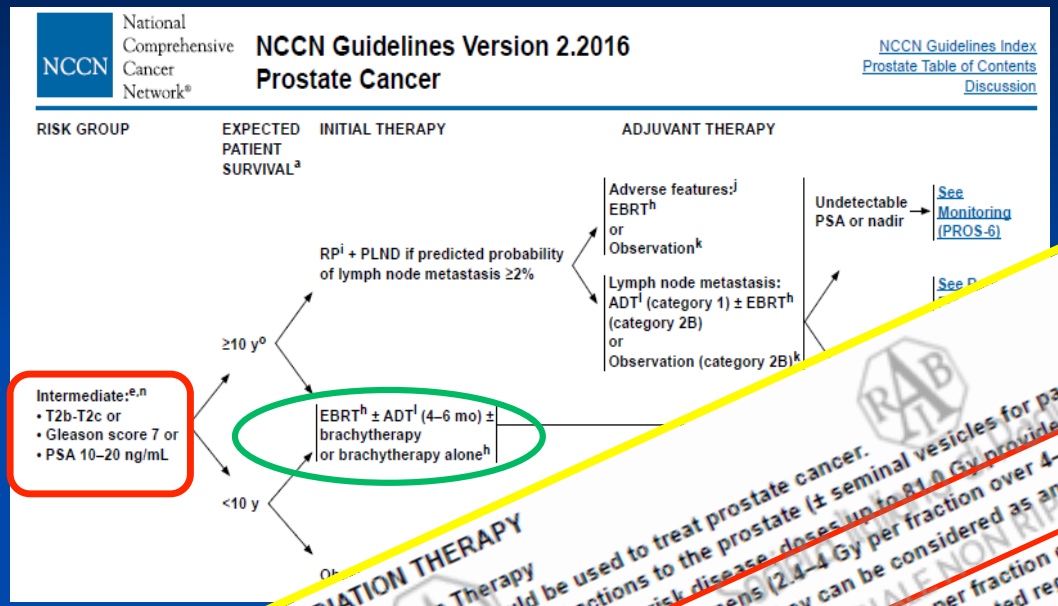
AIOM

European Association of Urology

EAU GUIDELINES 2014

	LE	GR
In localized prostate cancer, T1c-T2c N0 M0, 3D-CRT with or without IMRT, is recommended, even for young patients who decline surgical intervention.	1b	B
For high-risk patients, long-term ADT before and during radiotherapy is recommended, as it results in increased overall survival.	2a	B
In patients with locally advanced PCa (T3-4 N0 M0), who are fit enough to receive EBRT, the recommended treatment is EBRT plus long-term ADT and the use of ADT alone is inappropriate.	1b	A
In patients with cT1-T2a, Gleason score < 7 (or 3 + 4), PSA ≤ 10 ng/mL, prostate volume ≤ 50 mL, without a previous TURP and with a good IPSS, transperineal interstitial brachytherapy with permanent implants can be an alternative.	2a	B
In patients with pathological tumour stage T3 N0 M0, immediate post-operative external irradiation after RP may improve the biochemical and clinical disease-free survival, with the highest impact in cases of positive margins.	1b	A
In patients with locally advanced PCa T3-4 N0 M0, concomitant and adjuvant hormonal therapy for a total duration of 3 years, with external-beam irradiation for patients with WHO 0-2 performance status, is recommended, as it improves the overall survival.	1b	A
In a subset of patients with T2c-T3 N0-X and a Gleason score of 2-6, short-term ADT before and during radiotherapy can be recommended, as it may favourably influence the overall survival.	1b	A
In patients with very high-risk PCa c-pN1 M0, with no severe comorbidity, pelvic external irradiation and immediate long-term adjuvant hormonal treatment is recommended, as it may improve the overall survival, disease-specific failure rate, metastatic failure rate, and biochemical control.	2b	B

Background -2



NCCN 2016 V.2

Materials and Methods -1

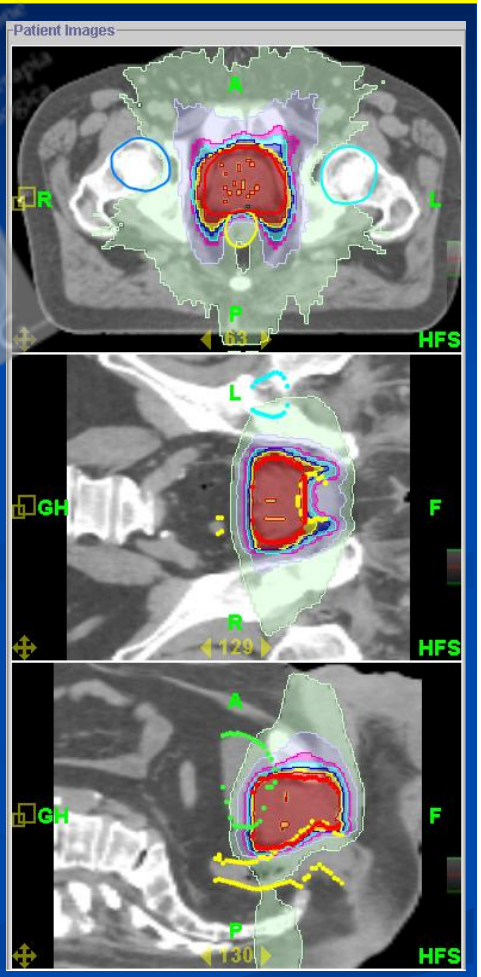
123 consecutive pts treated by Hypofractionated Radiotherapy with curative intent

July 2008 – September 2015

Median Age 73 Yrs
KPS 90-100 → 91,8%
Mean iPSA=19,5 ng/mL

GPS <7 in 32 pts
=7 in 50 pts
>7 in 41 pts

	T1	T2	T3a	T3b	T4	TOT
N0	18	45	29	20	0	112
N1	2	3	1	5	0	11
TOT	20	48	30	25	0	123



43/123 (**34,9%**) Intermediate

80/123 (**65,1%**) High/Very High Risk

Materials and Methods -2

- RT total treatment time: mean 42 ±5,9SD days
- Median total doses:

  PTV1 (Prostate): 70 Gy(range 57,3-75 Gy)

  PTV2 (Prostate+VS): 58,8Gy(range 54-70 Gy)

  PTV3 (P+VS+Pelvis): 50,4 Gy(range 50,4-58,8)

2,3 – 3,82 Gy/Die

SIB 83%

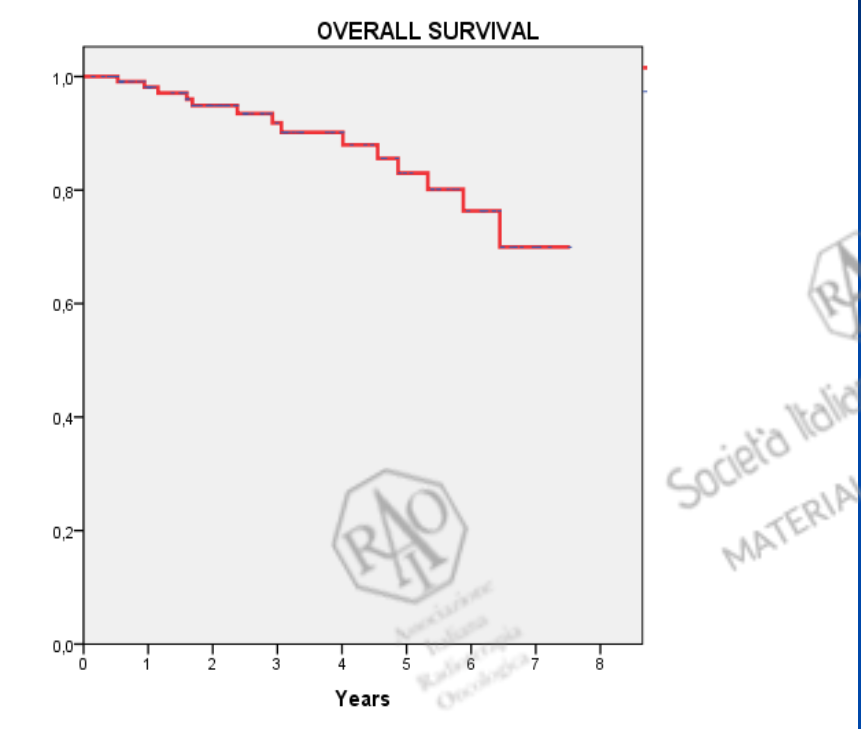
All pts completed the planned RT treatment ± ADT

Concomitant ADT in 71,5% of pts (88/123)
Prophilactic Pelvis RT in 61,7% of pts (76/123)

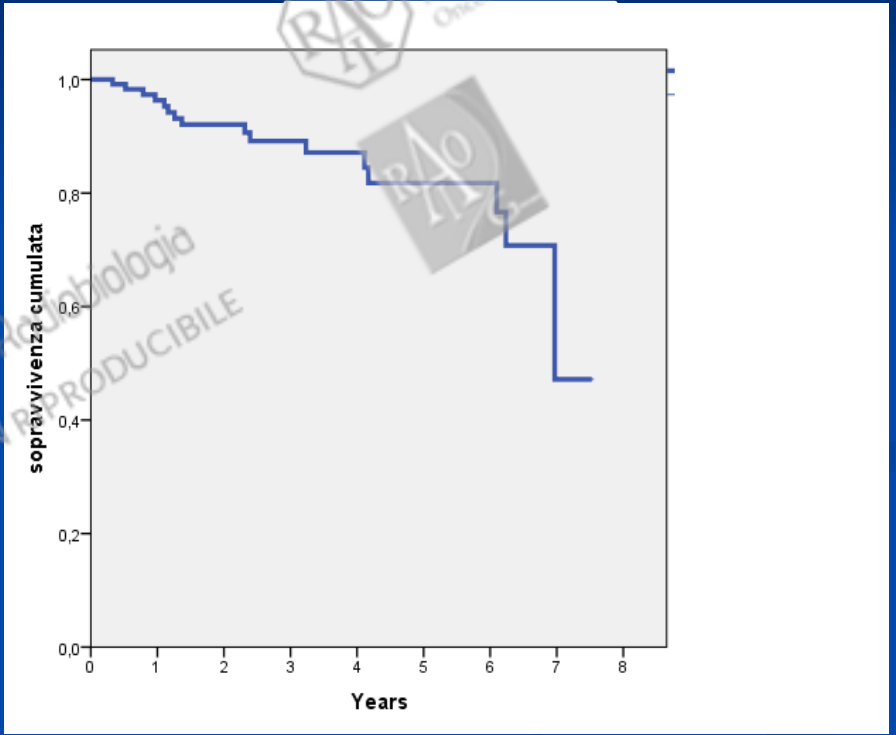
Mean FUP 39,6 mesi (range 4,0-84,7 mesi)

RESULTS -1

Overall Survival



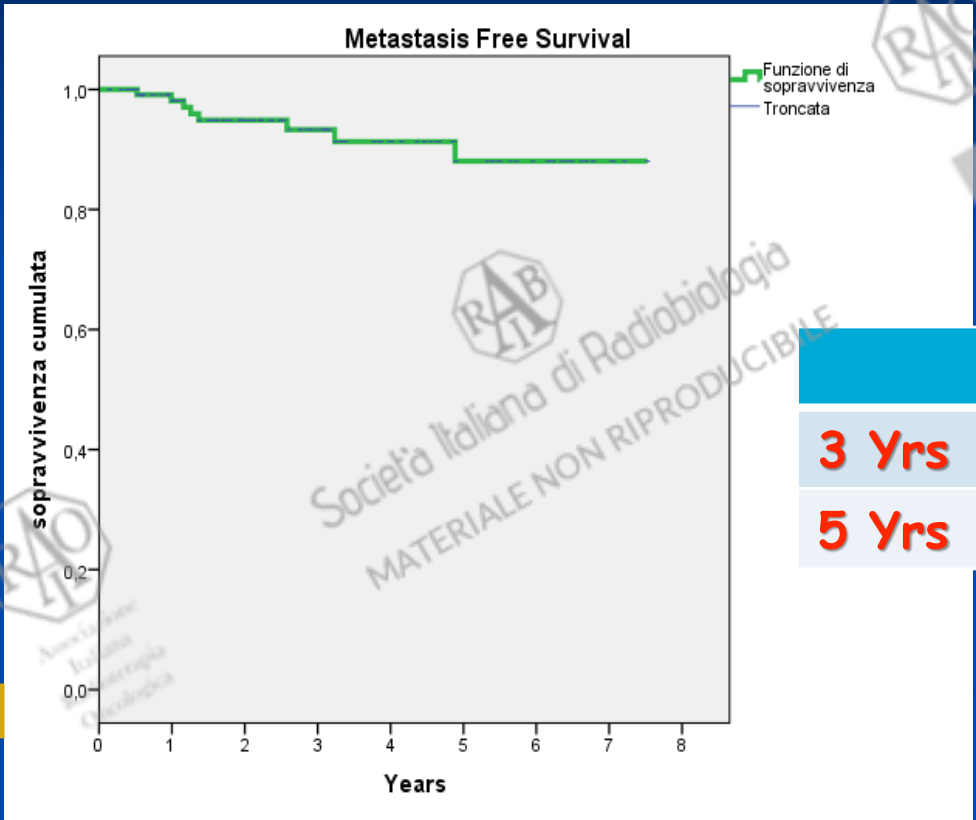
Disease Free Survival



	Overall Survival	Disease Free Survival
3 Yrs	91,0 +/- 3,0% ES	89,2 +/- 3,2%ES
5 Yrs	83,0 +/- 5,1% ES	81,8% +/- 5,1% ES

Results -2

Distant Metastasis Free Survival



	Mts Free Survival
3 Yrs	93,3 +/- 2,7% ES
5 Yrs	88,1 +/- 4,5% ES

Univariate Analysis

Multivariate Analysis

Results -3

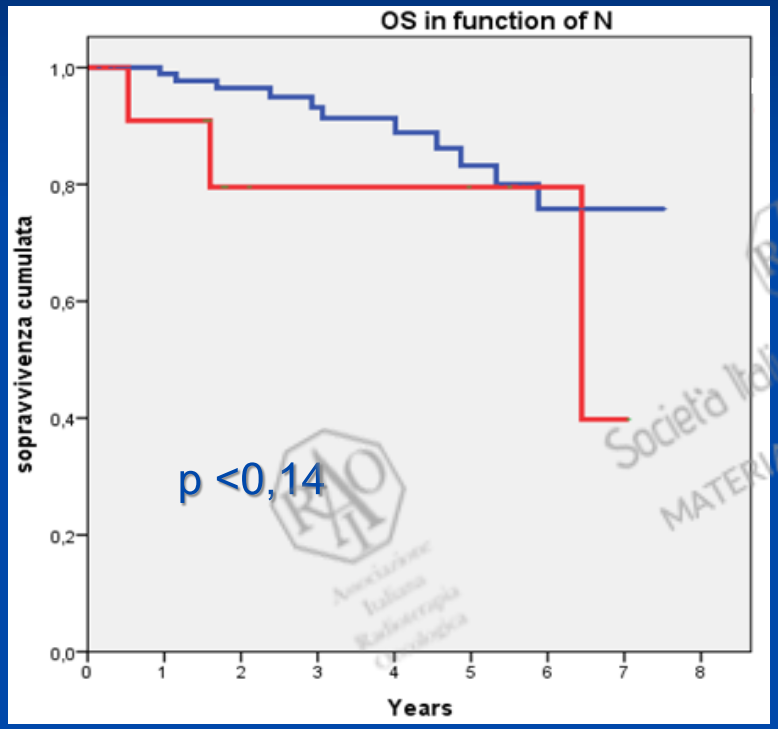
Univariate Analysis

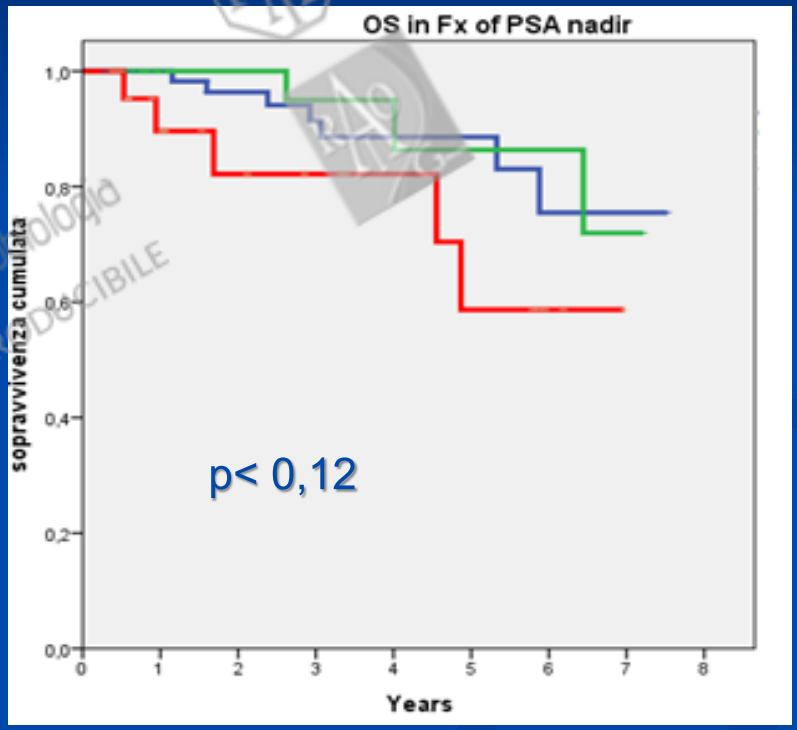
	OS	DMFS	DFS
Età	NS	NS	NS
KPS	NS	NS	NS
Gleason PS	NS	p <0,03	p < 0,0001
T	NS	NS	NS
N	p <0,14	p <0,10	p <0,0001
iPSA	NS	NS	NS
Risk Class	NS	NS	p <0,006
Dose RT	NS	NS	NS
WPRT	NS	p <0,08	p < 0,001
OT	NS	NS	p <0,005
Psa Nadir	p< 0,12	p <0,11	p <0,08

Results -4

Univariate Analysis

Overall Survival





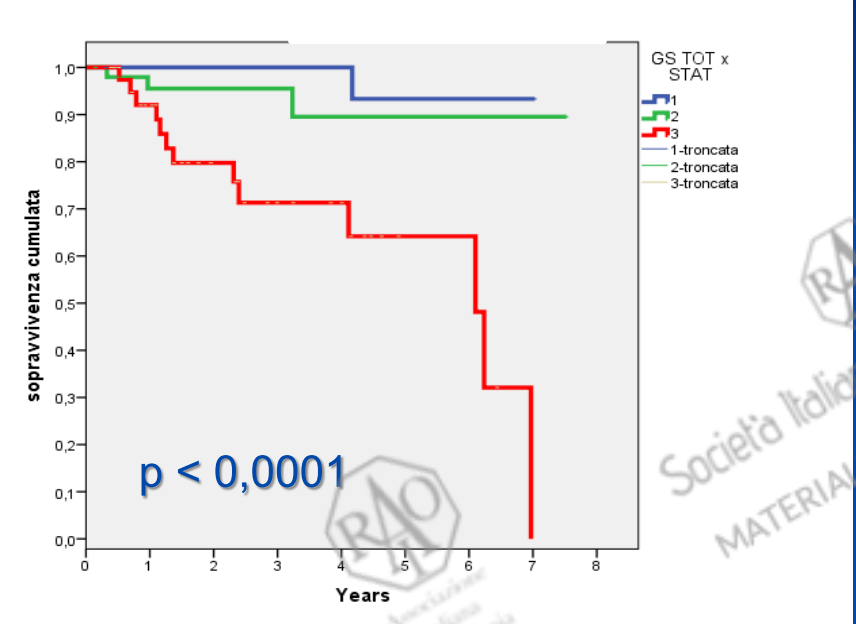
	3 YRS OS	5 YRS OS
N-	98,9 +/- 1,1 ES	83,2 +/- 5,5 ES
N+	90,9 +/- 8,7 ES	79,5 +/- 13,1 ES

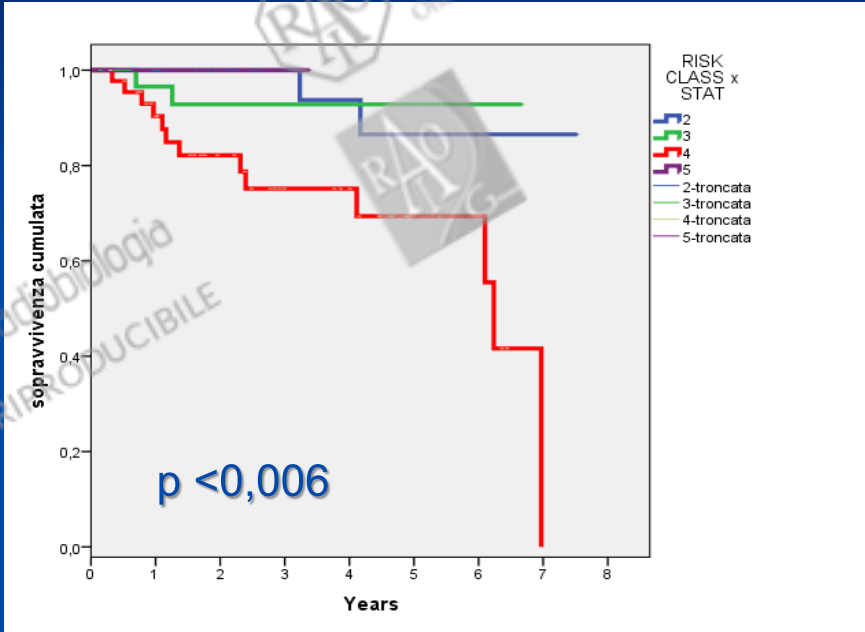
	3 YRS OS	5 YRS OS
PSAn <0,10	98,7+/- 1,2 ES	88,6 +/- 4,9 ES
PSAn >0,50	89,6 +/- 7,0 ES	58,7 +/- 15,6 ES

RESULTS-5

Univariate Analysis

Disease Free Survival





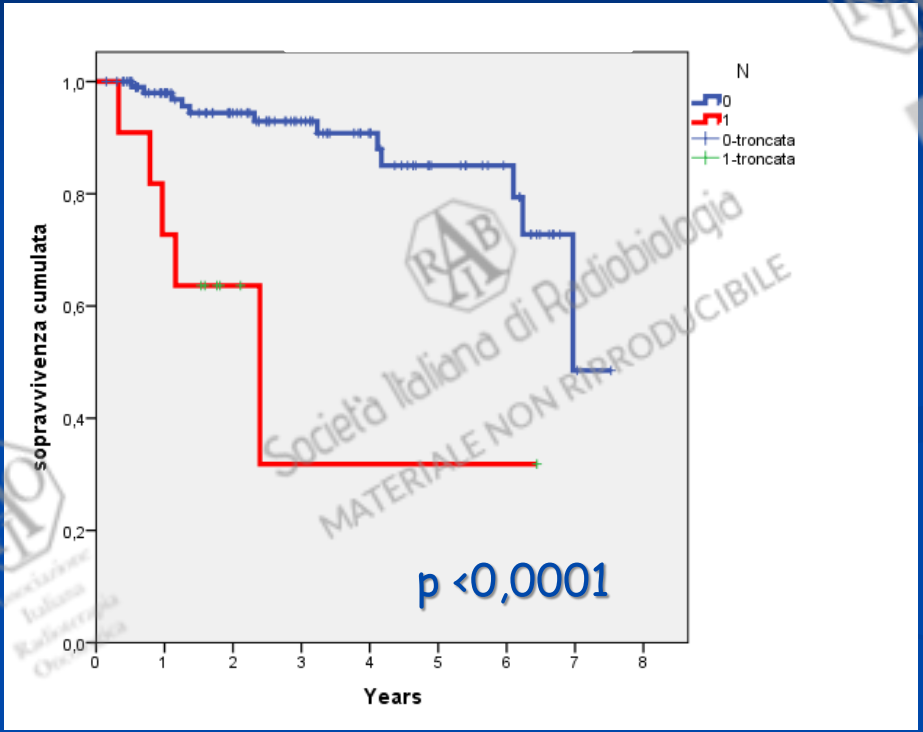
	3 YRS DFS	5 YRS DFS
GPS <7	100 +/- 0,0	93,3 +/- 6,4 ES
GPS = 7	95,5+/-3,1 ES	89,5 +/- 6,5 ES
GPS≥8	92,0 +/- 4,4	64,2 +/- 10,1 ES

	3 YRS DFS	5 YRS DFS
Low	100% +/- 0,0 ES	93,3% +/- 6,4ES
Interm	95,5% +/- 3,1 ES	89,5% +/- 6,5 ES
High	92,0% +/- 4,4 ES	64,2% +/- 10,1 ES

RESULTS-6

Univariate Analysis

Disease Free Survival

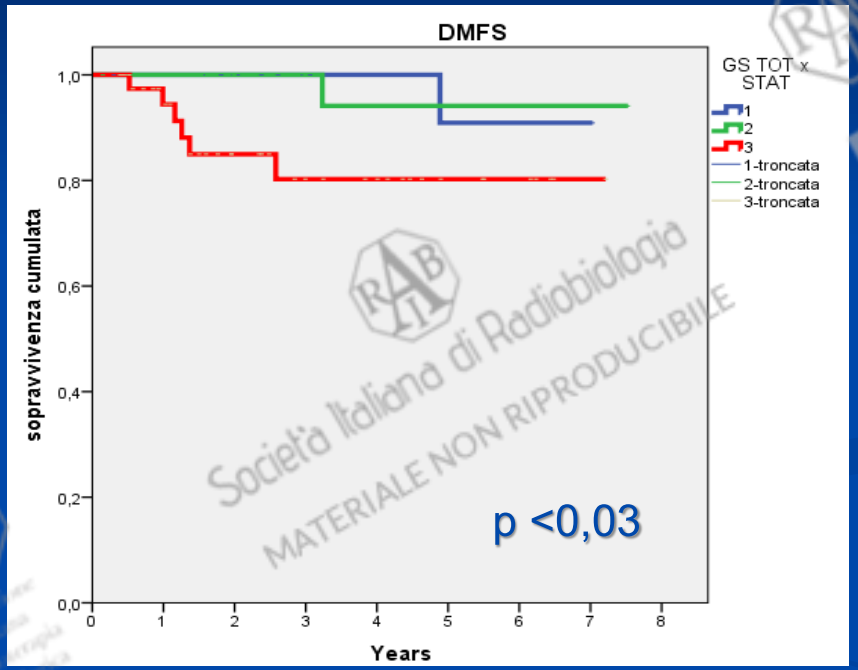


	3 YRS DFS	5 YRS DFS
N-	98,4% +/- 1,4 ES	85,0% +/- 5,1 ES
N +	72,7% +/- 13,4 ES	31,8% +/- 23,6 ES

RESULTS-7

Univariate Analysis

Distant Metastasis Free Survival



	3 YRS MFS	5 YRS MFS
GPS <7	100% +/- 0,0 ES	90,9% +/- 8,7 ES
GPS =7	100% +/- 0,0 ES	94,1% +/- 5,7 ES
GPS≥7	80,3% +/- 7,5 ES	80,3% +/- 7,5 ES

RESULTS-7

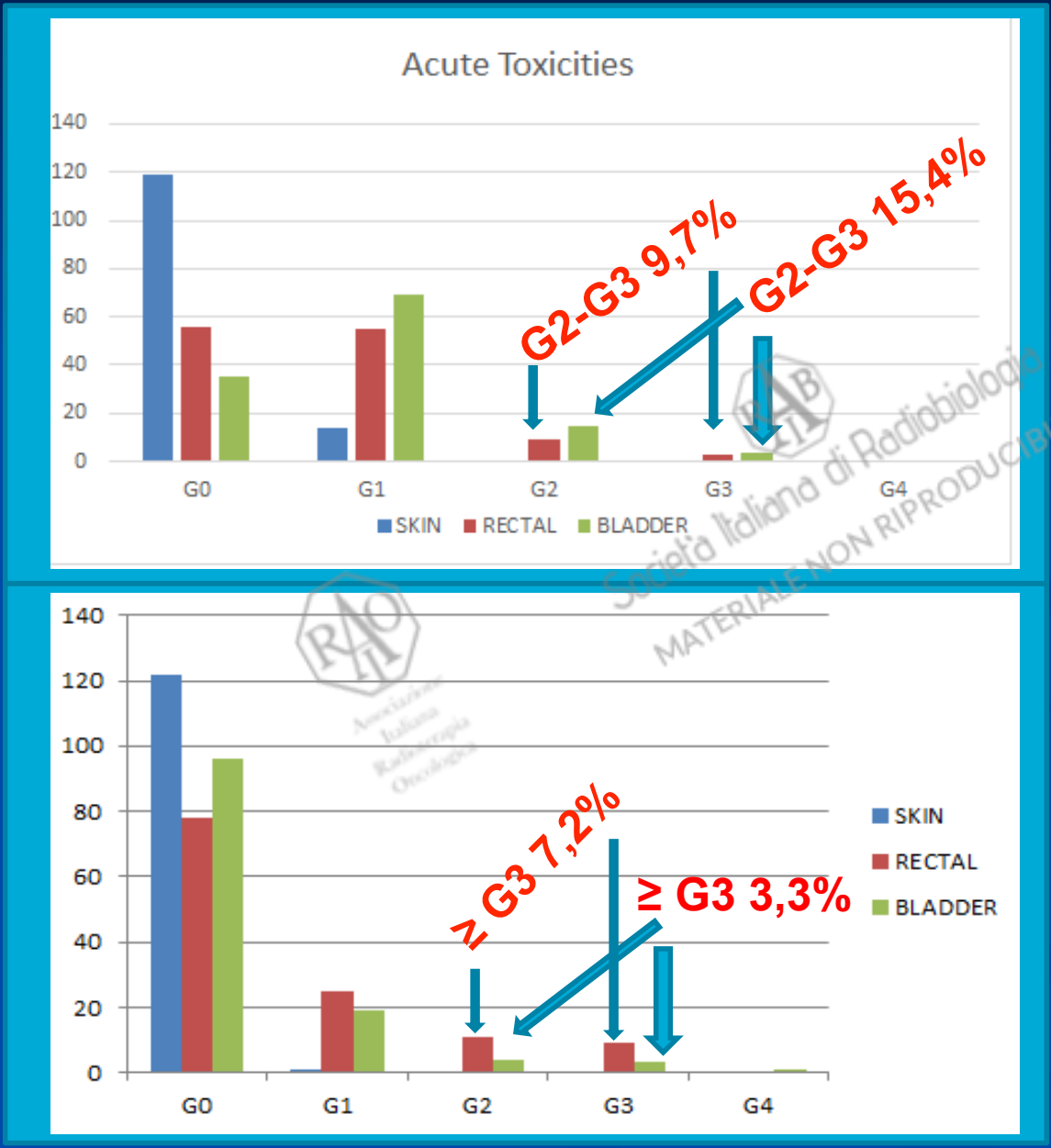
Multivariate Analysis

Multivariate analysis does not show any statistically significant prognostic factors in terms of OS and DMFS

BUT…

	DFS
Gleason PS	P<0,03
Nodal Involvement	P<0,006

RESULTS-8



Acute Toxicities

Three pts had G3 acute Rectal toxicities requiring short term RT interruption.
Four pts had G3 acute bladder toxicities with macrohematuria

Late Toxicities

Nine pts had G3 late Rectal bleeding requiring temporarily hospitalization.
Three pts had G3 late GU toxicities with persistent macrohematuria; 1 pt had G4 toxicity requiring cystectomy

DISCUSSION -1
RCTs

Study	Type of Study	End-point	#Pts	Risk Class	RTs	RT Hypo	
						Dose	BED1.5
US, Miami	Sup	BCDF 15%@5yr	303	All	76	70.2@2.7	84.4
HYPRO	Sup	RFS 10%@5yr	820	Int-high	78	64.6@3.4	90.4
US, Duke	Non-Inf	5yr-DFS HR<1.52	1115	Low	73.8	70@2.5	80
PROFIT	Non-Inf	5yr-DFS HR<1.32	1206	Int	78	60@3	77
CHHiP Trial	Non-Inf	BFR or CF HR<1.20	3216	All	74	60@3/ 57@3	77
Modena	**Retrosp**		**123**	**Int-High**		**70@2,5**	**80**

Courtesy of Dr. D'Angelillo (modified)

DISCUSSION -2
Results

Study	Type of Study	End-point	RTs	RT Hypo BED1.5	Results	
					RTs	RT Hypo
US, Miami	Sup	BCDF 15%@5yr	76	84.4	21.4%	23.3%
HYPRO	Sup	RFS 10%@5yr	78	90.4	77.1%	80.5%
US, Duke	Non-Inf	5yr-DFS HR<1.52	73.8	80	85.3%	86.3% HR 0.85 (0.67-1.14)
PROFIT	Non-Inf	5yr-DFS HR<1.32	78	77	79%	79% HR 0.99 (0.83-1.19)
CHHiP Trial	Non-Inf	BC or CF HR<1.208	74	77	88.3%	90.6% HR 0.84 (0.68-1.03)
Modena	**Retrosp**	**5yr-DFS**		80		**81,8%**

Courtesy of Dr. D'Angelillo (modified)

DISCUSSION -3
Toxicity

Study	RTs	RT Hypo BED3	%GU toxicity (≥G2)		%GI toxicity ≥G2	
			Acute	Late	Acute	Late
			H	H	H	H
US, Miami	76	80	nr	21.5	nr	18.1
HYPRO	78	82.7	23	41.3	13	21.9
US, Duke	73.8	77	27	29.7	10.7	22.4
PROFIT	78	72	4	2.1	0.7	1.3
CHHiP	74	72	49	2	38	3
Modena		**80**	**15,4**	**10**	**10**	**17,1**

Courtesy of Dr. D'Angelillo (modified)

CONCLUSIONS

Moderately Hypofractionated IG-IMRT using Tomotherapy was well tolerated, efficient and safe in terms of toxicities and clinical outcomes (**5-Yr OS=83,0%, 5Yr DFS =81,8%**)

Just 3 pts had to stop RT treatment (3-6 days) demonstrating an excellent tolerability profile even of RT treatment is associated to ADT

Any prognostic factor was found for DMFS e OS, but **Gleason Pattern Score and Nodal Involvement were found to be statistically significant indipendent prognostic factors in terms of DFS**

A longer follow-up is needed to confirm these findings waiting for the results of the «on-going» Phase III RCTs