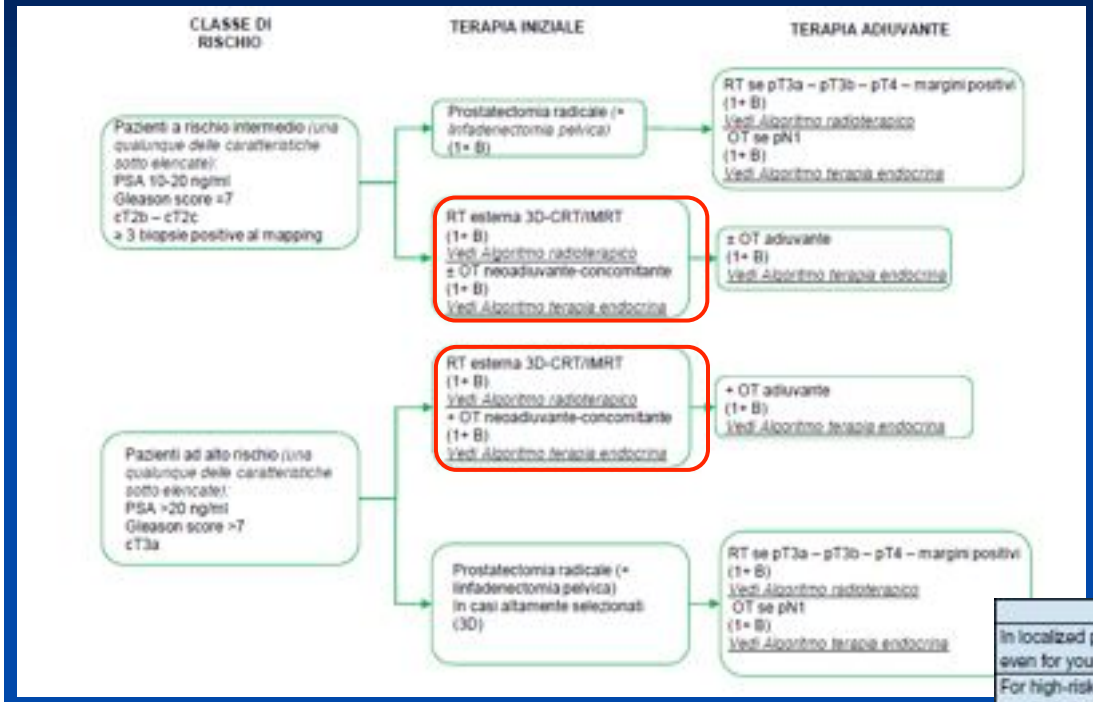
TOMO-RT moderatamente Ipofrazionata in pz con ADK Prostata a rischio intermedio/alto: outcomes clinici e tossicità in 85 pz trattati consecutivamente presso l' UO di RT di Modena.

A. Bruni, E. Mazzeo, B. Lanfranchi, P. Barbieri, C. Tata, L. Rubino,
L. M. Lamine, I. Valli, F. Bertoni
UO di Radioterapia Oncologica – Policlinico di Modena

6-8 Novembre 2014

INTRODUZIONE -1



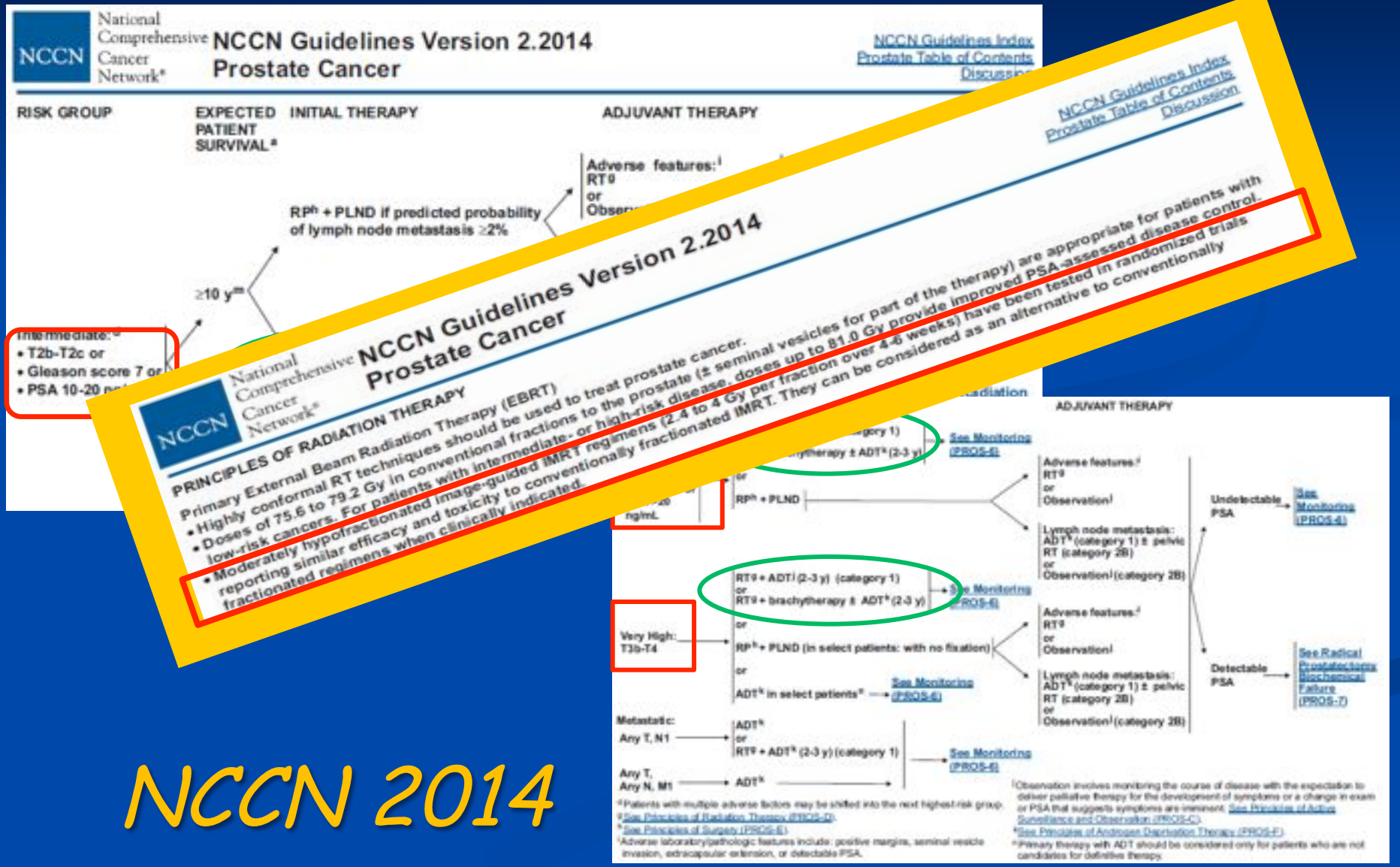
AIOM

eau
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

INTRODUZIONE -2



NCCN 2014

INTRODUZIONE -3

Eur Urol. 2014 Aug 26. pii: S0302-2838(14)00751-9. doi: 10.1016/j.eururo.2014.08.009. [Epub ahead of print] **In press**

A Systematic Review of Hypofractionation for Primary Management of Prostate Cancer.

Koontz BF[1], Bossi A[2], Cozzarini C[3], Wiegel T[4], D'Amico A[5].

Biomed Res Int. 2014;2014:781340. doi: 10.1155/2014/781340. Epub 2014 Apr 30. **2014**

Hypofractionation in prostate cancer: radiobiological basis and clinical appliance.

Mangoni M[1], Desideri I[1], Detti B[1], Bonomo P[1], Greto D[1], Paiar F[1], Simontacchi G[1], Meattini I[1], Scoccianti S[1], Masoni T[1], Ciabatti C[1], Turkai A[1], Semi S[2], Minervini A[2], Gacci M[2], Carini M[2], Livi L[1].

BioMed Research International

J Clin Oncol. 2013 Nov 1;31(31):3860-8. doi: 10.1200/JCO.2013.51.1972. Epub 2013 Oct 7. **2013**

Randomized trial of hypofractionated external-beam radiotherapy for prostate cancer.

Pollack A[1], Walker G, Horwitz EM, Price R, Feigenberg S, Konski AA, Stoyanova R, Movsas B, Greenberg RE, Uzzo RG, Ma C, Buyyounouski MK.

…PROs and CONTRAs…

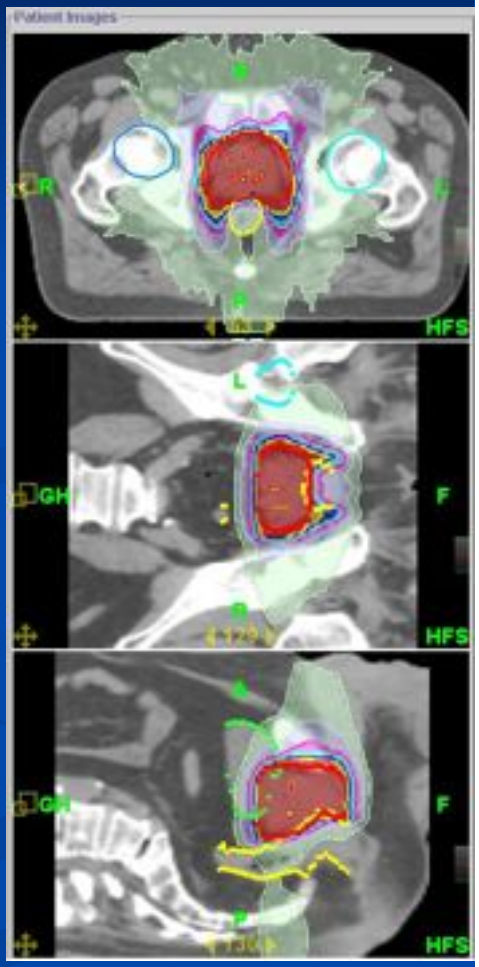
MATERIALI E METODI

85 pz trattati ***consecutivamente*** con RT radicale
Luglio 2008 - Settembre 2013

Età Media 71.2 aa
Età Mediana 72 aa
KPS 90-100 → 91,8%

GS <6 in 23 pz
=7 in 33 pz
>7 in 29 pz

	T1	T2	T3a	T3b	T4	TOT
N0	11	34	16	18	0	79
N1	0	2	0	4	0	6
TOT	11	36	16	22	0	85



32/85 (**37,6%**) pz a rischio **intermedio** 53/85 (**62,4%**) pz a rischio **alto**

RISULTATI-1

- Durata trattamento RT: media 42,8 ±5,9SD giorni
- Dosi medie complessive:

  PTV1: 70 ± 2,6SD Gy (range 54-76 Gy)

  PTV2: 62,2 ± 5,2SD Gy (range 54-70 Gy)

  PTV3: 51 Gy ±1,7SD Gy (range 50,4-58,8)

2,2 – 3,82 Gy/Die

SIB 90%

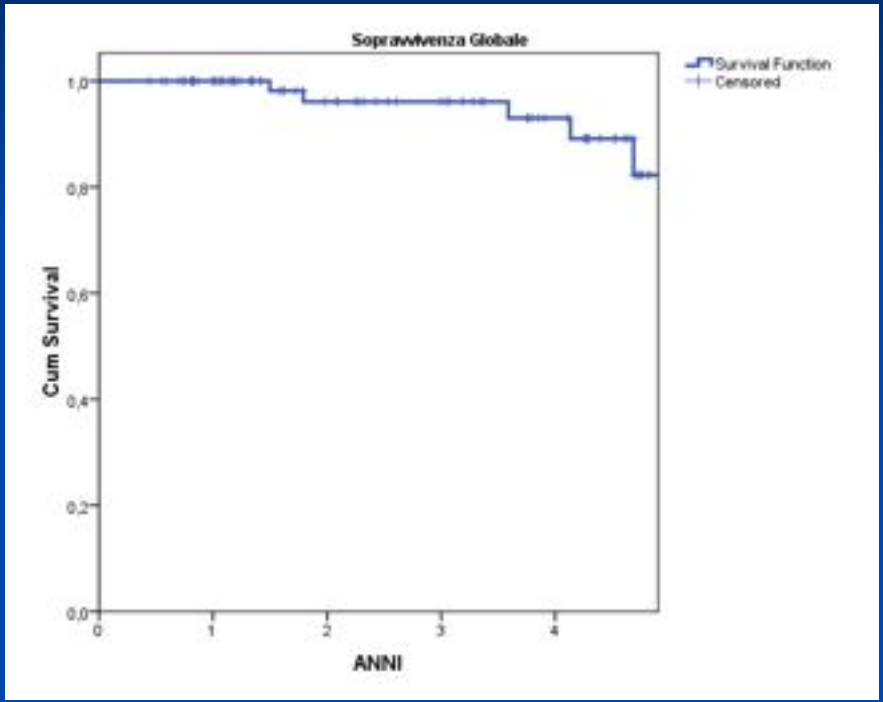
Tutti i pazienti hanno completato il trattamento di RT + OT

Sottoposti ad OT il 70,6% dei pazienti (60/85)

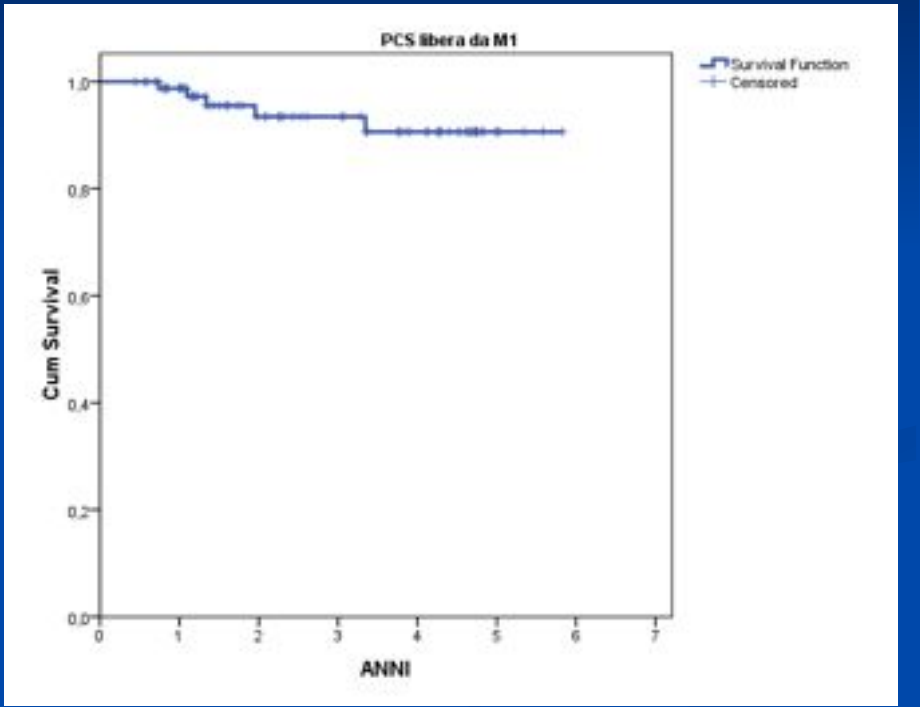
Follow-up mediano 27,7 mesi (range 5,4-70,9 mesi)

RISULTATI-2

Sopravvivenza Globale



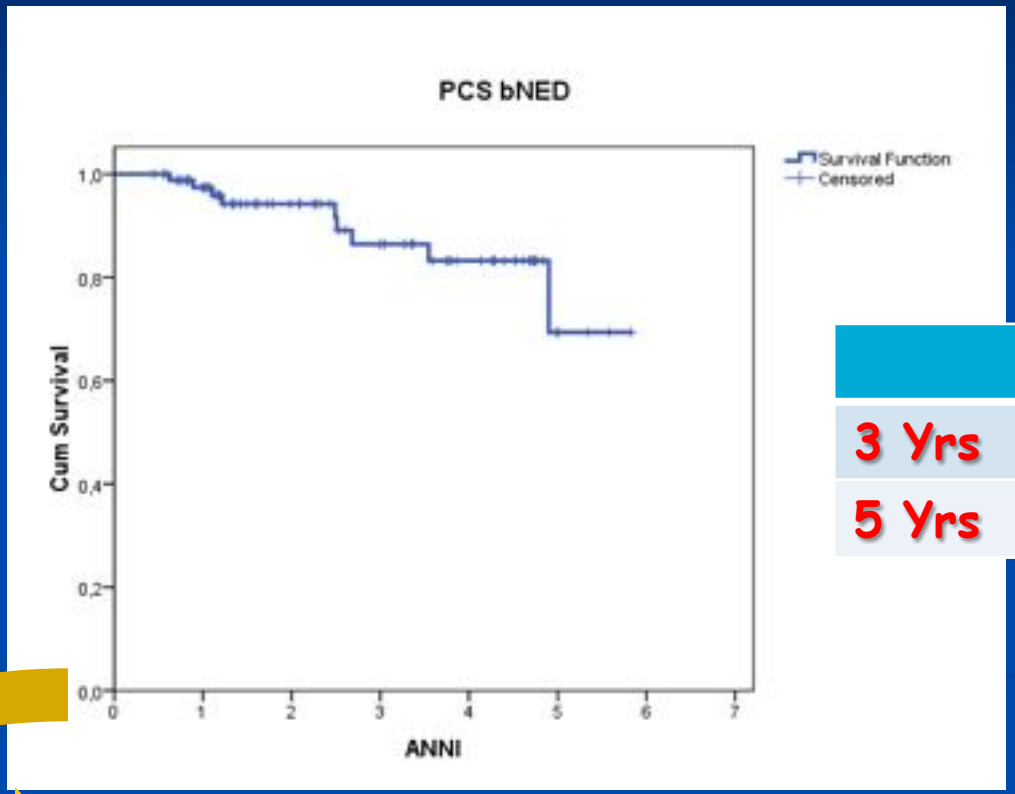
Sopravvivenza libera da MTS



	Overall Survival	Mts Free Survival
3 Yrs	96,0 +/- 2.7% ES	93,4 +/- 3,0%ES
5 Yrs	82,0 +/- 8,0% ES	90,6% +/- 4.0% ES

RISULTATI-3

Sopravvivenza libera da recidiva biochimica



	BF Survival
3 Yrs	86,4 +/- 5% ES
5 Yrs	70 +/- 13% ES

Analisi Univariata

Analisi Multivariata

RISULTATI-4

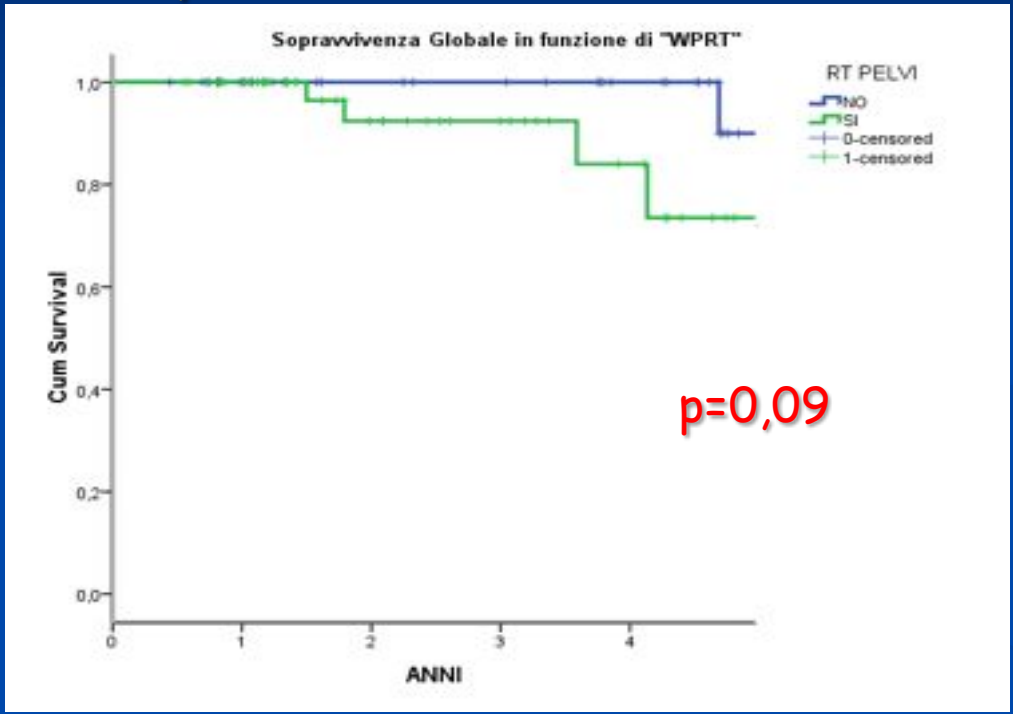
Analisi Univariata

	OS	DMFS	bNED
Età	NS	NS	NS
KPS	NS	NS	NS
Gleason PS	NS	P <0,05	p= 0,04
T	NS	NS	NS
N	NS	P <0,008	P <0,01
iPSA	NS	NS	NS
Risk Class	NS	NS	p=0,06
Dose RT	NS	NS	NS
WPRT	p= 0,09	P <0,02	NS
OT	NS	NS	p= 0,01
PSA Nadir	NS	p=0,09	p= 0,02
Durata OT	NS	NS	NS

RISULTATI-5

Analisi Univariata

Sopravvivenza Globale

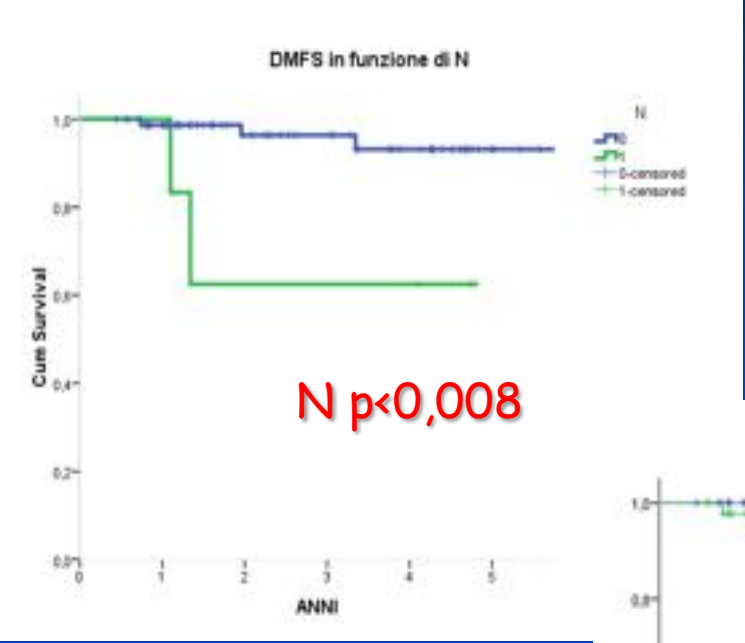


	3 YRS OS	5 YRS OS
NO WPRT	100% +/- 0,0 %ES	90 +/- 9,5%ES
YES WPRT	92,4 +/-5,2% ES	73,5% +/- 12,7% ES

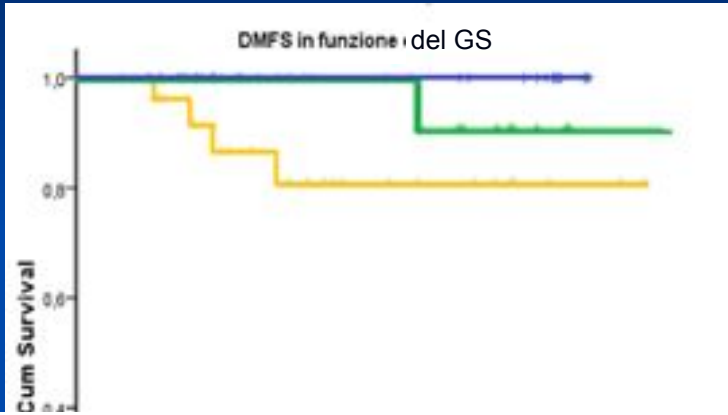
RISULTATI-6

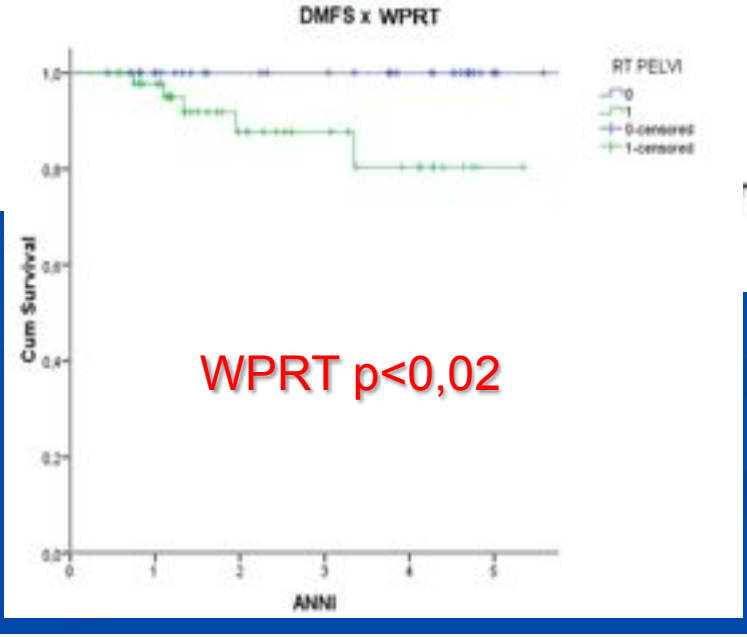
Analisi Univariata

Sopravvivenza libera da metastasi



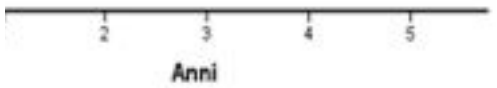
N p<0,008





WPRT p<0,02

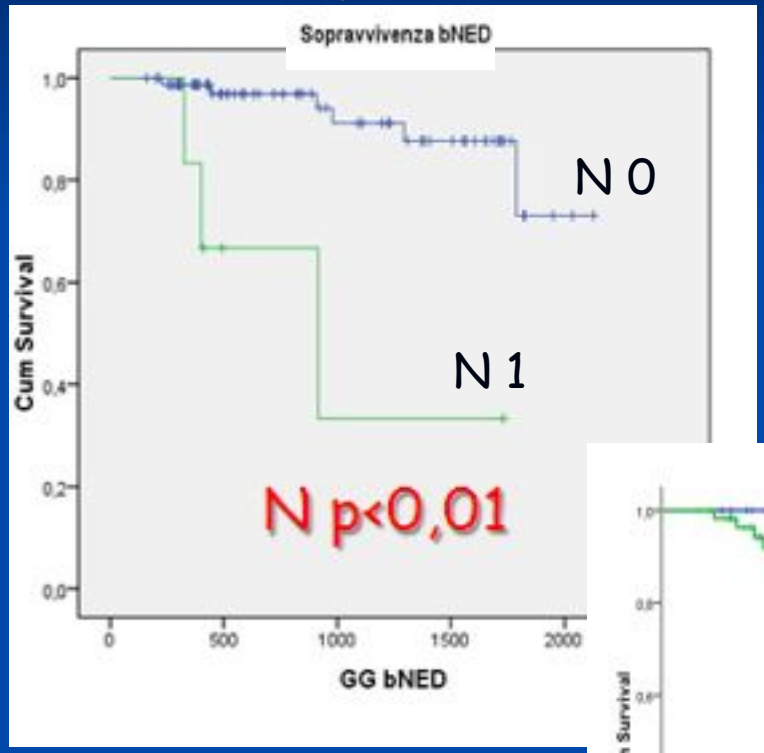
GS p<0,05

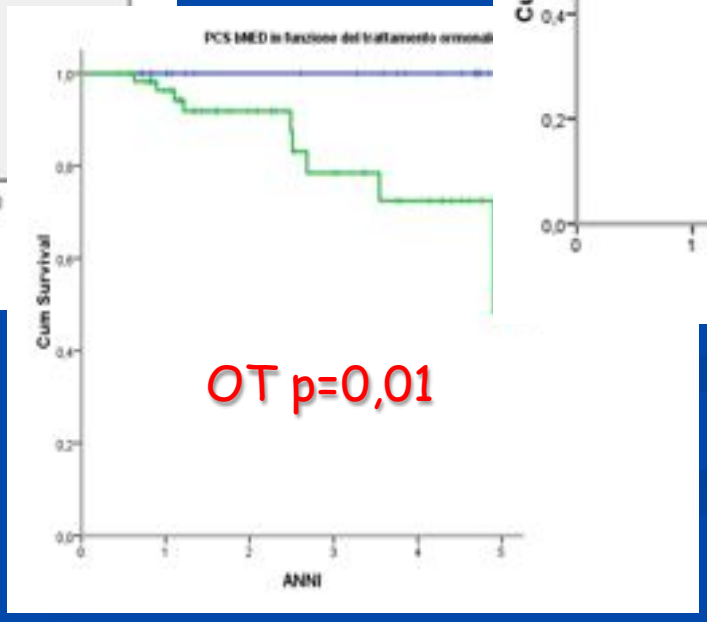


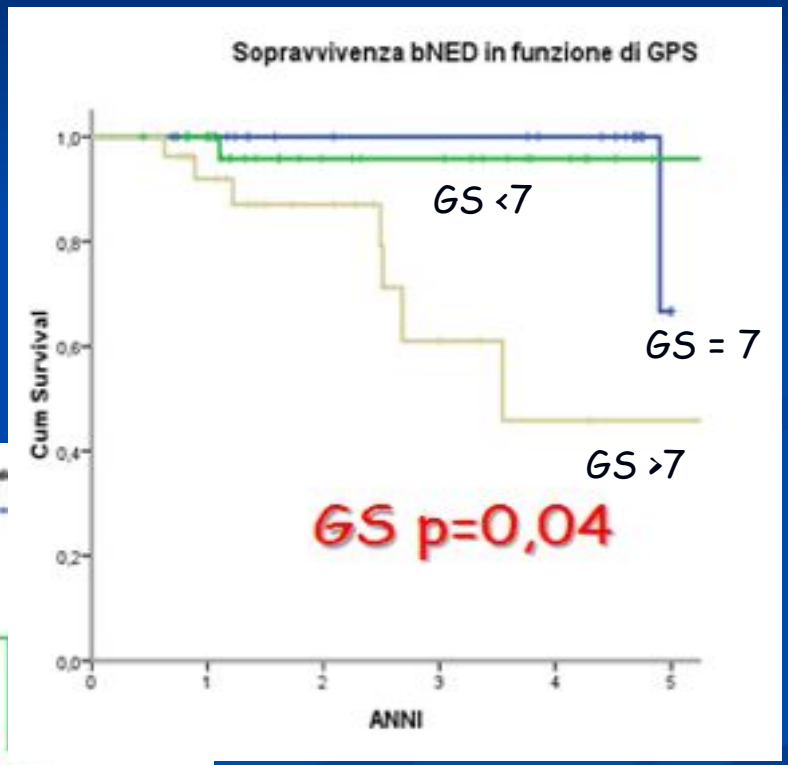
RISULTATI-7

Analisi Univariata

Sopravvivenza libera da recidiva biochimica







RISULTATI-8

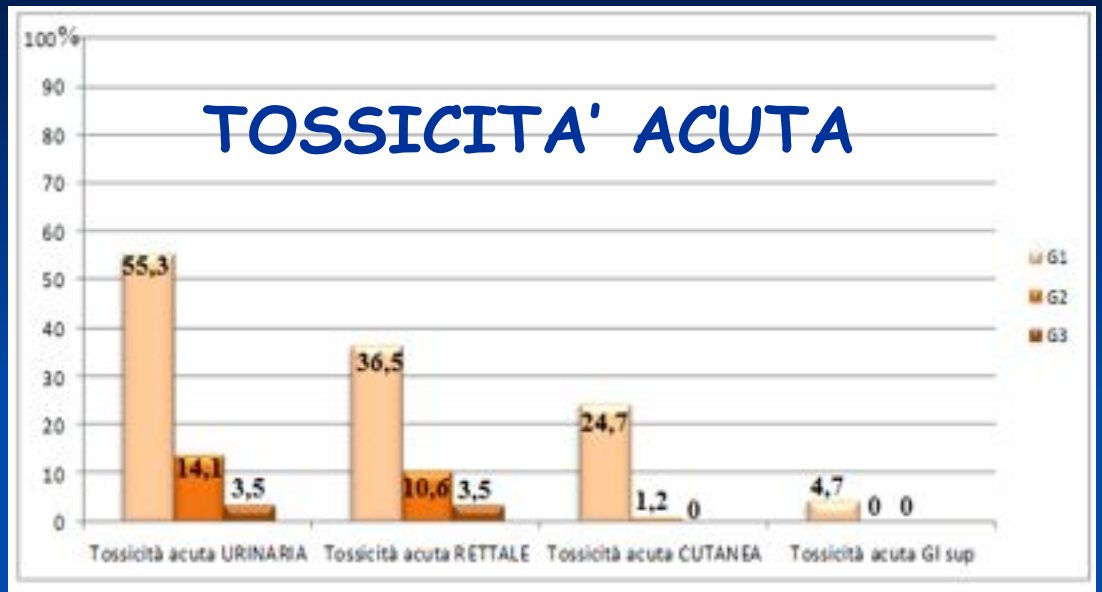
Analisi Multivariata

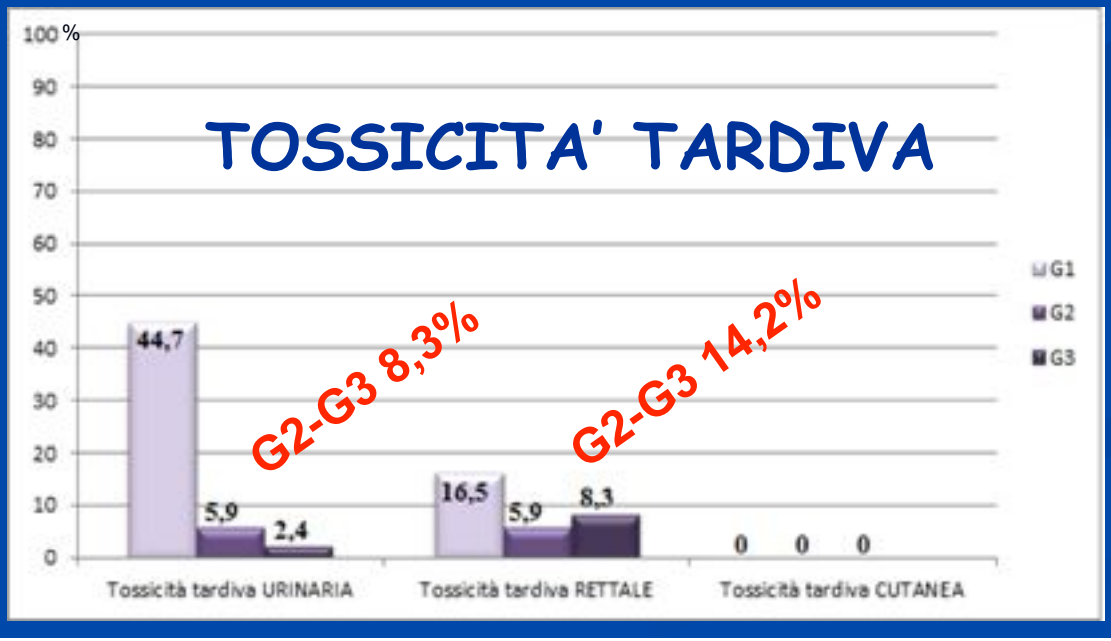
All'analisi multivariata *nessun fattore prognostico* è risultato statisticamente significativo per la *sopravvivenza globale e libera da metastasi a distanza*

MA…

	bNED
Gleason PS	p=0,005
Classe di rischio	p=0,09 (trend)
PSA Nadir	p=0,009

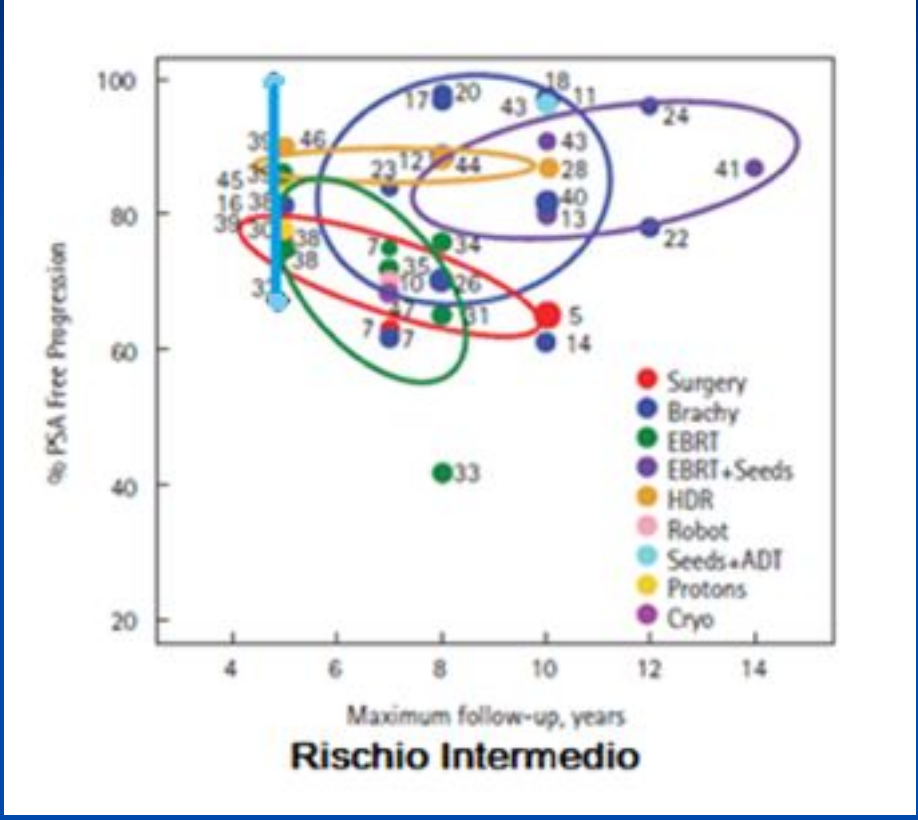
RISULTATI-9



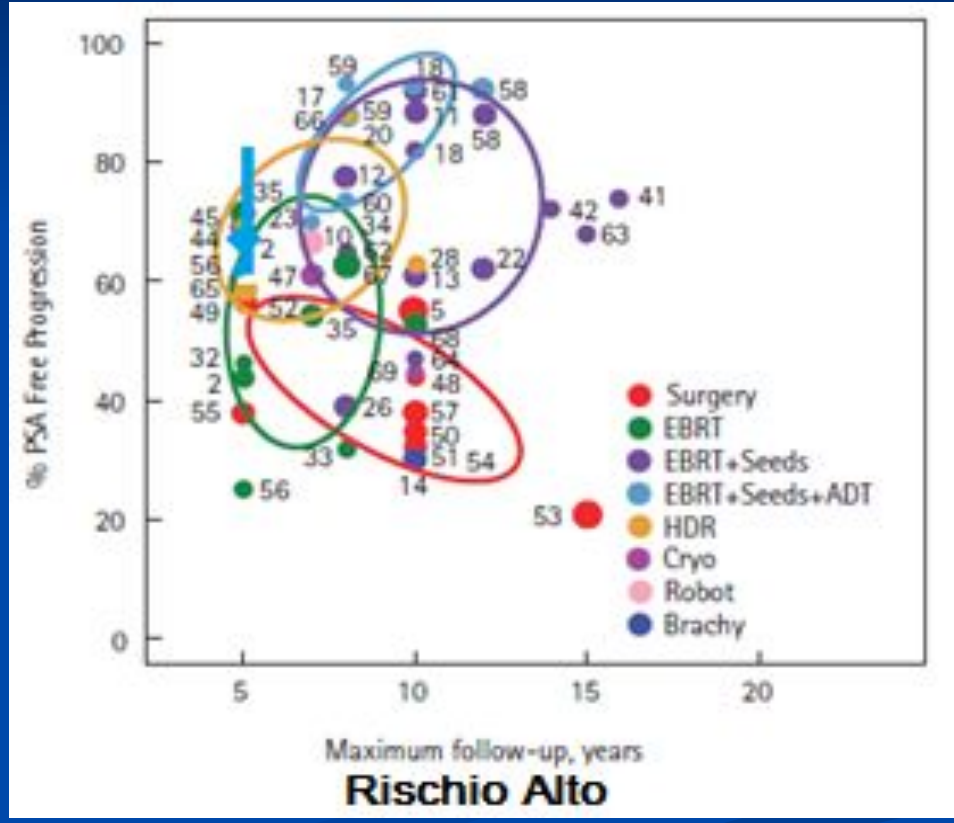


- 2 pz (2,4%) hanno dovuto sospendere temporaneamente il trattamento per tossicità acuta GI (1 pz per diarrea con febbre e leucocitosi, 1 pz per diarrea e rettorragia severa)
- 1 pz ha sospeso RT per 1 mese a causa di cistite batterica trattata con più linee antibiotiche non legata al trattamento radiante

DISCUSSIONE-1



Rischio Intermedio



Rischio Alto

P.Grimm et al, BJUI, 2012

DISCUSSIONE -2

HFRT

Dose: 66 – 80 Gy Tox GI tardiva ≥G2 (%): **1,9 – 14**

Reference	n	Risk groups	Median FU (months)	Total dose (Gy)	Total fractions	Gy/ fraction	BED (Gy), α/β = 1.5	BED (Gy), α/β = 10	RTOG late toxicity Grade ⩾2 (%) GU	RTOG late toxicity Grade ⩾2 (%) GI
Lukka[21]	470	Low, intermediate, high	64	66	33	2	154	79	1.3	1.9
	466			52.5	20	2.63	144	66	1.3	1.9
Yeoh[22,23]	109	NR	90	64	32	2	149	77	NR	NR
	108			55	20	2.75	156	70	NR	NR
Arcangeli[24-26]	85	High	35	80	40	2	187	96	16	17
	83			62	20	3.1	190	81	11	14
Pollack[27,28]	152	Intermediate, high	>60	76	38	2	177	91	8.3	5
	151			70.2	26	2.7	197	89	18.3	6.8
Kuban[29]	102	Mostly low, intermediate	56	75.6	42	1.80	166	89	19	6
	102			72	30	2.40	187	89	19	14

Zaorsky,N. et al. *Cancer Treat Rev*, 2013

CONCLUSIONI

Il trattamento moderatamente ipofrazionato con IG-IMRT mediante Tomoterapia si è dimostrato efficace con outcomes clinici soddisfacenti (**5-aa OS=82,0%+/-8,0% ES**)

Solo 2 pz hanno interrotto la RT (per 3-6 gg) dimostrando un' ottimo profilo di tollerabilità anche in trattamenti associati ad OT

Nessun fattore prognostico per DMFS e OS, tuttavia il **Gleason Pattern Score** ed il **PSA Nadir** sono risultati fattori prognostici indipendenti per **bNED**

Necessità di un follow-up più lungo per convalidare i risultati ottenuti oltre che di RCT di fase III.

PROSPETTIVE FUTURE