La re-irradiazione dopo primo trattamento dei pazienti affetti da ricorrenza rinofaringea di neoplasie del distretto cervico-cefalico

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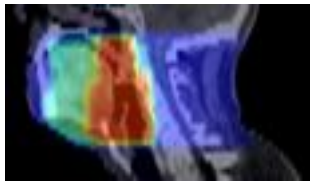
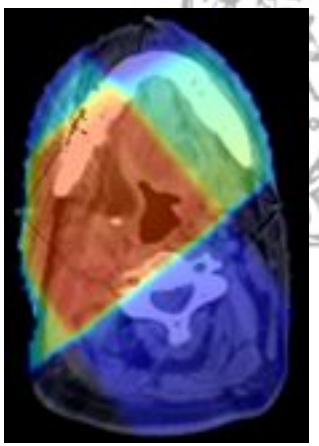
Il problema della recidiva in H&N

HNSCC

RT
chir + RT adiuv +/- CHT
RT radicale +/- chemioterapia
Chemioterapia neoadiuvante + RT +/- CHT

Risposta completa dopo il trattamento

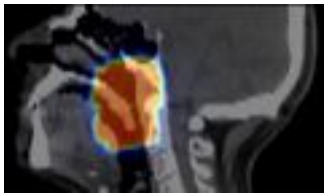


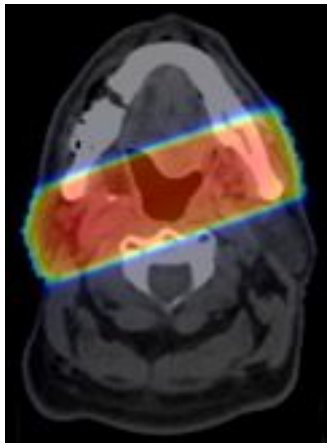


Secondo tumore primitivo SPT

Recidiva Locale LC

Re-irradiazione





Rinofaringe

	N. casi	%
Non fallimento	336	53,4
Solo su T	69	11
Solo su N	36	5.7
T + N	48	7.6
T/N + M1	54	8.6
Solo M1	82	13
Perso di vista	4	0.6

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1977-2000

- Le recidive su "T" sono presenti nel 40-50 % dei casi recidivati;
- sono espressione unica di recidiva di malattia ***solo in < 20 % dei pazienti (circa il 10% del totale dei trattati)***.

Controllo locale in "VECCHIE" casistiche retrospettive

Series	Patient No.	Year of primary radiotherapy	Dose of primary radiotherapy (Gy)*	Reirradiation dose* (Gy)	Local control rate (%)	5-year further survival rate (%)
Sooy *et al.* (12)	6	before 1956	Unknown	Unknown	50	—
Scanlon *et al.* (11)	38	1950–1960	Unknown	Unknown	—	16
Chen *et al.* (1)	9	1948–1967	30–70	40–60	22	—
Fu *et al.* (15)	42	1940–1974	34–70 (40% of patients ≥60)	11.9–63.3	26	41
Hoppe *et al.* (4)	13	1956–1973	range: 59.7–80.3 mostly: 65.0–70.0	42–60	29	29
Wang (13)	51	1950–1981	1950–1975 'suboptimal' 1975–1979 'qd program >1979 'bid program'	60–66 (38 patients) <60 (13 patients)	—	33 (38 patients) 0 (13 patients)
McNeese *et al.* (10)	30	1949–1976	≥60 (21 patients) 40–50 (9 patients)	60 (22 patients) ≥60 (8 patients)	34	20
Pryzant *et al.* (30)	53	1954–1989	30–70 (median 55)	27.5–99 (median 57)	35	21
Yan *et al.* (8)	219	1978	60	60	—	23
Vikram *et al.* (7)	10	1976–1981	50–75	≥100[¶]	60	1-year survival 90% 1-year disease-free survival 50%
Flores *et al.* (25)	22	1939–1980	40–70	40–60	36	—
Lee *et al.* (9)	15	1980–1984	60–65	50–66	47	2-year survival 27%
Sham *et al.* (6)	21	1985–1987	60–65	60–86	33	—
Zhang *et al.* (8)	133	1975	58–65	50–60	—	17
Choy *et al.* (2)	43	most 1986–1990 some before 1986	55.2–76 (median 60)	60[††]	80 (for persistence) 61 (for first recurrence)	82 (for persistence) 40 (for first recurrence)
Lee *et al.* (5)	706	1975–1985	60–66	<60 (532 patients) ≥60 (174 patients)	32	14
Teo *et al.* (present)	103	1984–1989	62.5 ± 20[§] ± 24[¶]	Mean 62.4: range 60–74	15.2	7.6

% di controllo locale tra 15 e 60

% di controllo locale aumenta con l'aumentare della dose

IJROBP 1998, 40 (4):897

Controllo locale in "VECCHIE" casistiche retrospettive

Senior author (reference)	Treatment method	Number of patients	Treatment period	Local salvage %	Late sequelae %
A. Reirradiation for the whole series					
Fu (6)	XRT ± brachy ± electrodesiccation	33	1940–74	15	27
McNeese (14)	XRT ± brachy ± chemotherapy	30	1949–76	33	>27
Wang (19)	XRT ± brachy	51	1950–81	NA	6
Yan (21)	XRT ± brachy	162[a]	1958–72	21	>29
Current	XRT ± brachy	654	1976–92	23 (32)[b]	26 (48)[b]
B. Reirradiation for recurrence confined to the nasopharynx					
Dickson (3)	Brachy	12	1971–80	25	minimal
Leung (13)	Brachy ± XRT	22	1990–92	45[c]	NA
McNeese (14)	XRT ± brachy ± chemotherapy	14	1949–76	43	NA
Sham (17)	Brachy ± XRT	18	1985–87	50	NA
Vikram (18)	Brachy	10	1980–81	60[d]	NA
Yan (21)	XRT ± brachy	20	1958–72	20	NA
Current	XRT	144	1976–92	41 (32)[b]	37 (53)[b]
	XRT + brachy	53		51 (45)[b]	26 (36)[b]
	brachy	31		29 (29)[b]	29 (35)[b]
C. Surgery					
Fee (4)	Surgery ± brachy	15	1984–89	34	27
Wei (20)	Surgery ± brachy	18	1989–93	42[c]	>27

30 % di tossicità tardiva

IJROBP 1998, 40 (4):897

DOSI EFFICACI PER UN RITRATTAMENTO

SALVAGE RADIATION THERAPY FOR LOCALLY RECURRENT NASOPHARYNGEAL CARCINOMA

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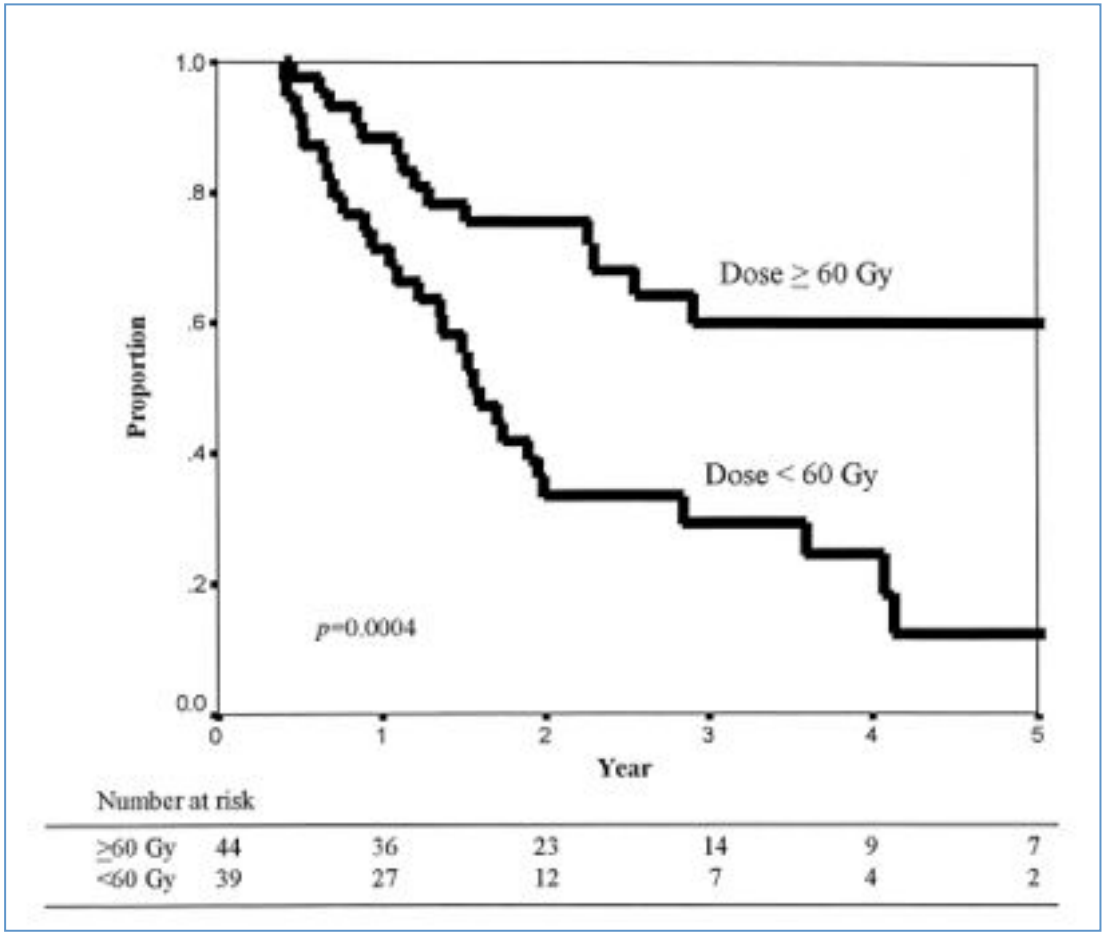
IJROBP 2000, 48 (5):1331



Number at risk

≥60 Gy	44	36	23	14	9	7
<60 Gy	39	27	12	7	4	2

IMRT

Eur J Cancer. 2012 Dec;48(18):3422-8. doi: 10.1016/j.ejca.2012.06.016. Epub 2012 Jul 25.

Long-term treatment outcome of recurrent nasopharyngeal carcinoma treated with salvage intensity modulated radiotherapy.

Hua YJ[1], Han F, Lu LX, Mai HQ, Guo X, Hong MH, Lu TX, Zhao C.

⊕ Author information

Abstract

PURPOSE: To evaluate the long-term treatment outcome in patients with recurrent nasopharyngeal carcinoma (NPC) treated with salvage intensity modulated radiotherapy (IMRT).

MATERIALS AND METHODS: One hundred and fifty one previously irradiation NPC patients with recurrent disease and re-irradiated by IMRT between 2001 and 2006 had been reviewed. The disease was re-stage I in 7, re-stage II in 21, re-stage III in 50 and re-stage IV in 73. Thirty-seven patients received concurrent chemotherapy, 39 had induction chemotherapy and 75 had radiotherapy alone.

RESULTS: All patients completed the planned IMRT. The median volume of the recurrent gross target volume of nasopharynx (rGTVnx) was 42.2 cm(3) (range 1.5-146.3 cm(3)). The median mean re-irradiation dose to the rGTVnx was 70.4Gy (range 62.1-77.6Gy). The median follow-up time after re-irradiation was 40.0 months (range 1.9-116.9 month). The 5-year local control rate (LCR) and overall survival rate (OS) for re-stage I, II, III, IV were 80.0%, 85.0%, 80.0%, 78.7% and 71.4%, 62.9%, 35.5%, 30.2%, respectively. Multivariate analysis indicated that rT classification (hazard ratio (HR), 2.02; 95%confidence interval (CI), 1.03-3.97; P=0.04) and the volume of rGTVnx (HR, 2.05; 95%CI, 1.31-3.22; P<0.01) were independent predictors for OS. Patients (39.0%) with re-stage III or IV disease experienced Grade 3 or 4 late toxicities.

CONCLUSION: Re-irradiation by IMRT for recurrent NPC resulted in encouraging local control. The clinical outcome for patients with early re-stage diseases was satisfactory. Further investigations, focus on optimising radiation dose and establishing effective treatment strategies, are warranted for advanced recurrent disease in order to improve overall survival and minimise late toxicity.

stereotassi

Author	Number of cases	Modalities	Dose of SRS/FSRT (Gy)	Results	Major complications
Cmelak *et al.* (1997) (14)	P: 11 (T2–4) R: 37 (SBM)*	SRS	P: 7–16 R: 7–35	P: 2-y LC 100% 2-y OS 100% R: 2-y LC 53%	8% (CNP 5%)
Kocher *et al.* (1998) (15)	R: 8	SRS	9–24	MST 9 months	63% (FICH 25%, IB 13%, TLN 25%)
Orecchia *et al.* (1999) (30)	R: 13 (rT1–4)	FSRT	24	3-y OS 31%	No
Chang *et al.* (1999) (16)	P: 23	SRS	7–15	2-y LC 100%	No
Tate *et al.* (1999) (17)	P: 23 (Stage III-IV)	SRS	7–15	2-y LC 100%	No
Ahn *et al.* (2000) (31)	P: 19 R: 12	FSRT	P: 8–40 R: 45–65	P: 4-y LC 89% 4-y OS 75% R: 2-y LC 92% 2-y OS 60%	LMN 5%
Chen *et al.* (2001) (27)	R:11 (SBI)	CRT +SRS	10–19	3 alive	FNH 9%
Xiao *et al.* (2001) (41)	R: 50	FSRT/RT+FSRT	14–35	3-y DFS 54% 3-y OS 60%	FNH 16%
Pai *et al.* (2002) (28)	R: 36	RT+SRS	8–20	3-y LC 56% 5-y OS 49%	22% (LMN 11%)
Le *et al.* (2003) (18)	P: 45 (Stage II-IV)	SRS	7–15	3-y LC 100% 3-y DFS 71% 3-y OS 75%	18% (CNP 9%, TLN 7%)
Chua *et al.* (2003) (19)	P: 7 R: 11 (rT1-2)	SRS	11–14	2-y LC 72% 2-y OS 86%	TLN 6%
Low *et al.* (2006) (29)	P: 5 R: 31 (rT1-2)	SRS+ICI	18	5-y LC 65% 5-y DFS 57% 5-y OS 62%	44% (CNP 20%, TLN 8%)

LC dal 53 al 100%

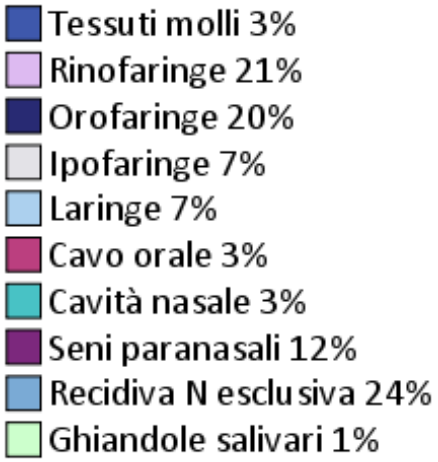
IJROBP 2007, 69(3): 761

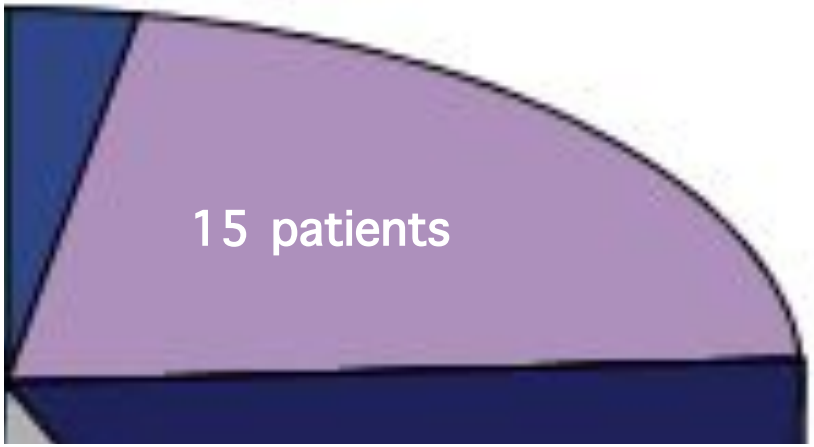
I problemi della re-irradiazione

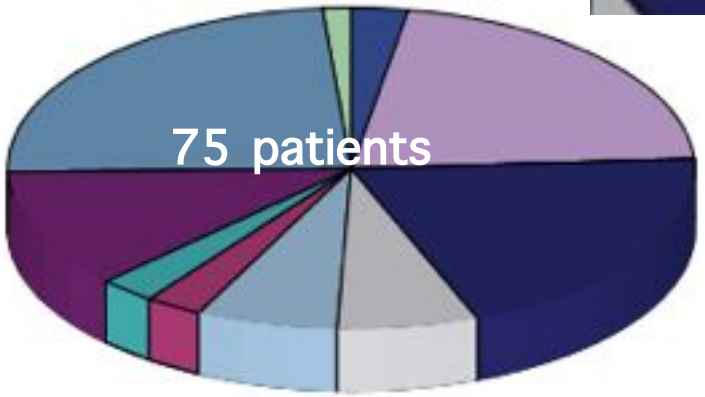
- a chi (selezione dei pazienti)
- come (CHT si vs no)
- come e quanto (tecniche e dosi)

Domande ancora aperte.....

Agosto 2005- Dicembre 2013

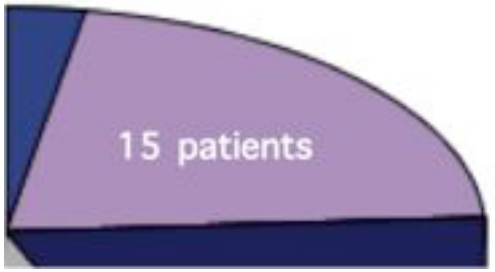






OBIETTIVI:

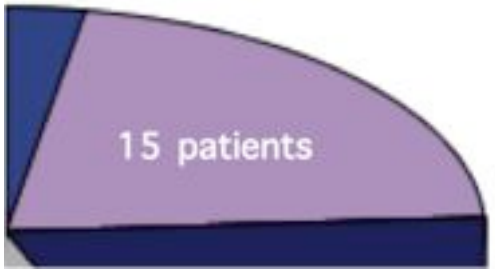
- Pazienti e tipo di trattamento
- Tossicita'
- Sopravvivenza



Caratteristiche dei pazienti

- Eta' media 59 yy
- IK 90-100 in 11 paz; 70-80 in 4 paz
- Indice di comorbidita' <2 in 13 pazienti

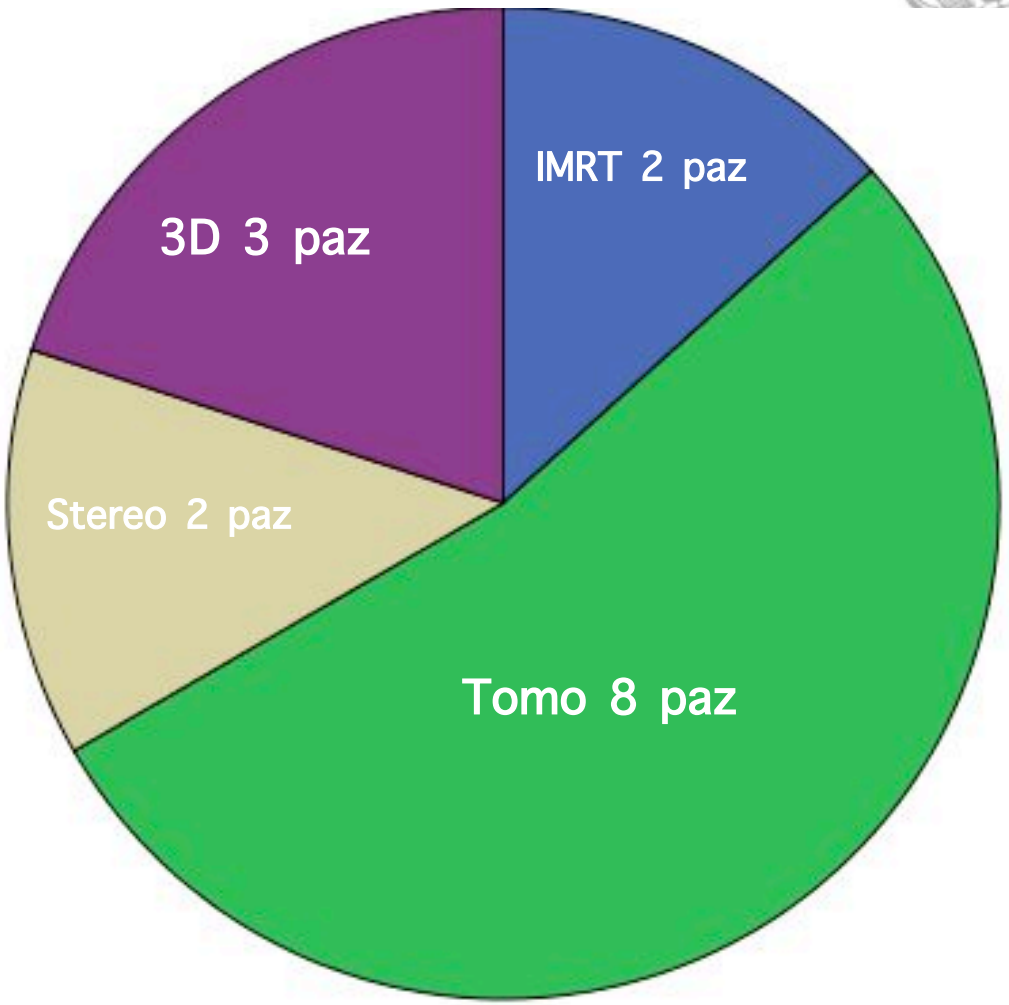
- Tempo medio I-II trattamento 34 mesi

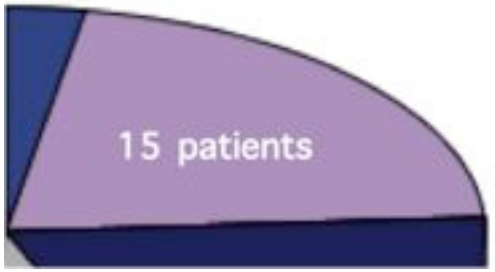


Caratteristiche del trattamento

- RT esclusiva in 13 paz
- RCT in 2

- Target: sede di rec





Caratteristiche del trattamento

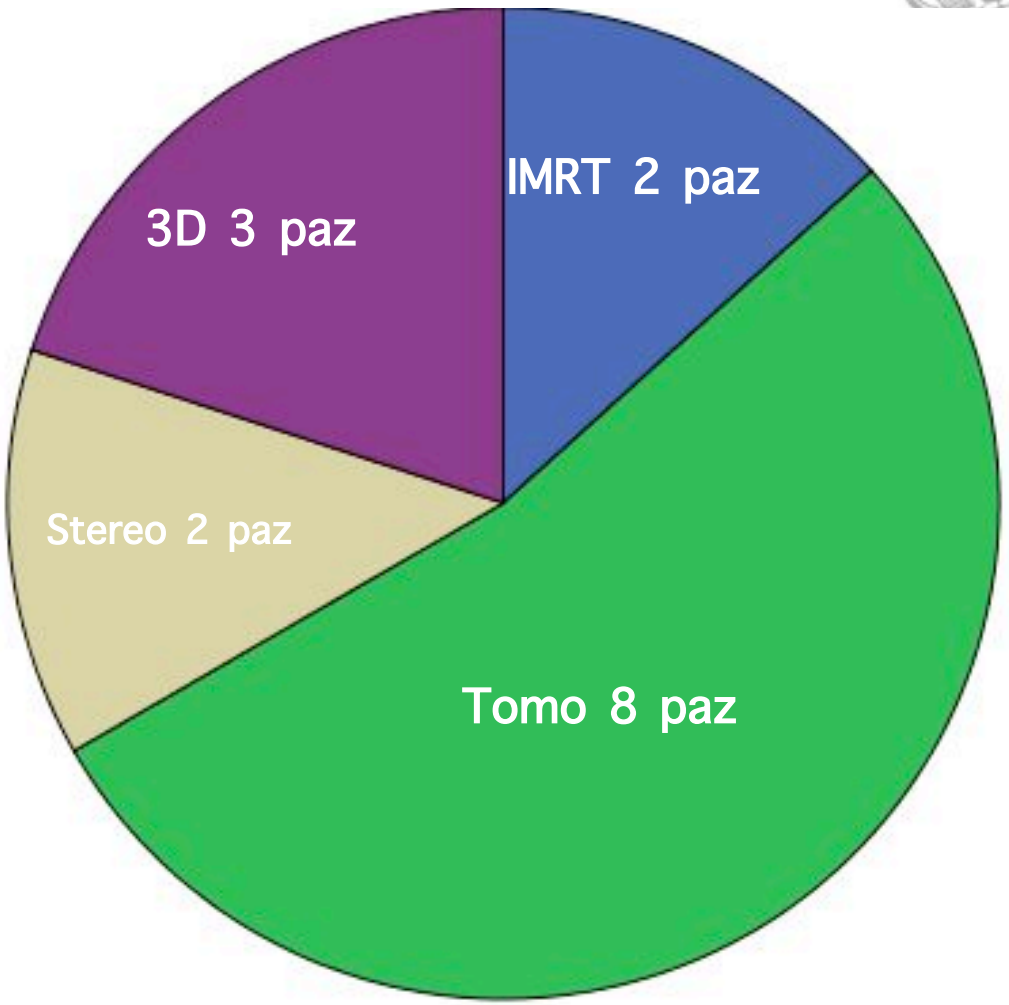
- RT esclusiva in 13 paz
- RCT in 2

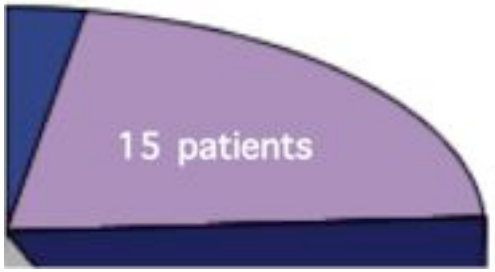
- Target: sede di rec

- Range dose

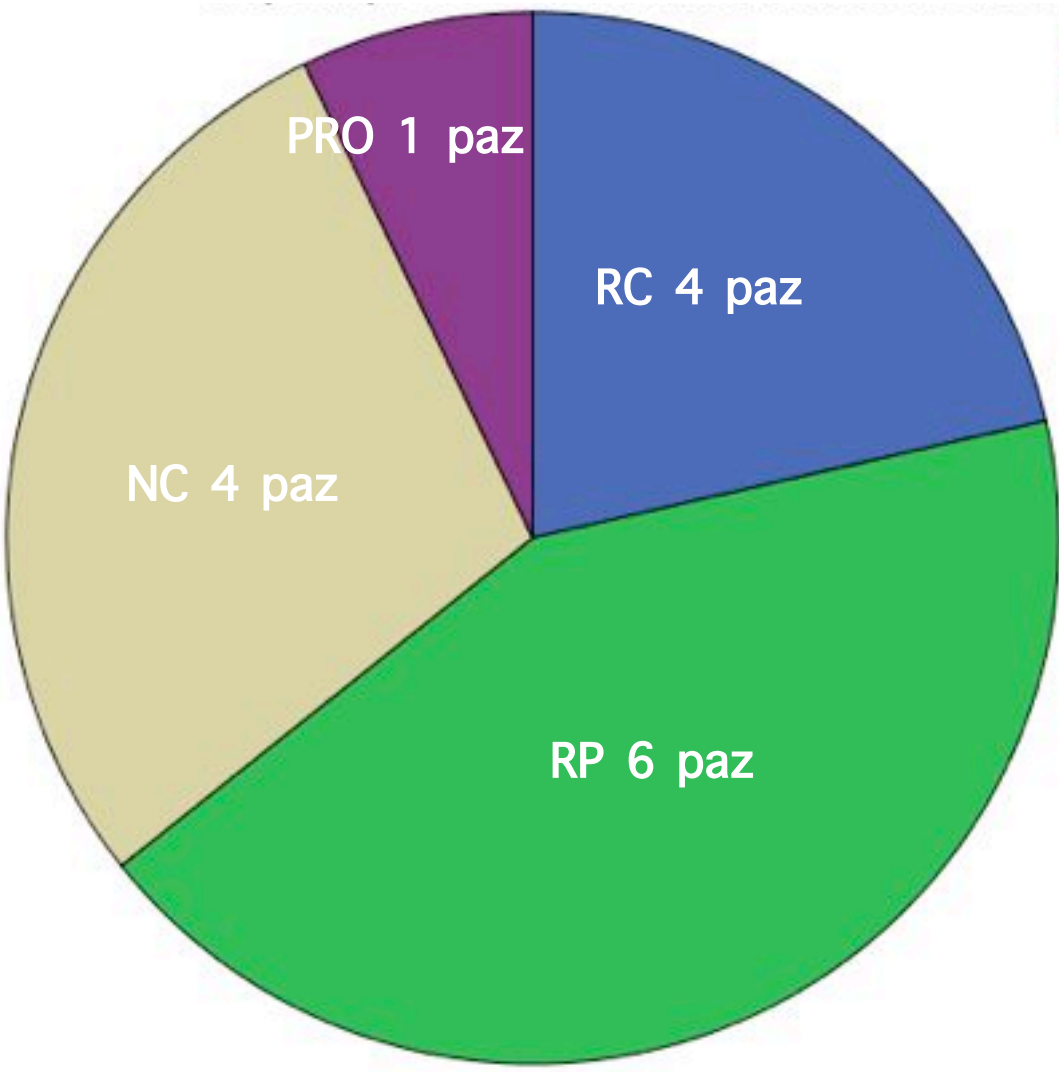
(non stereo) 33-66 Gy

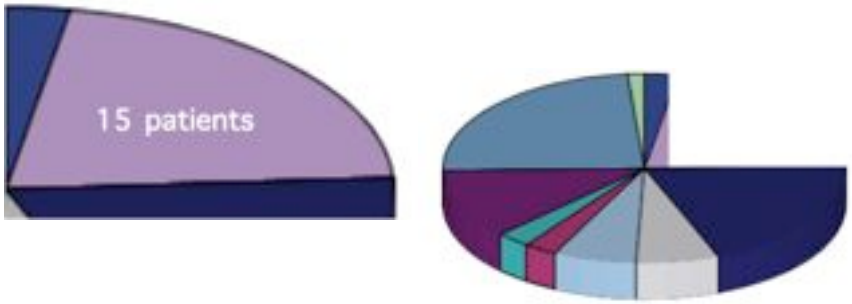
- Stereo: 6 Gy per 5 fr





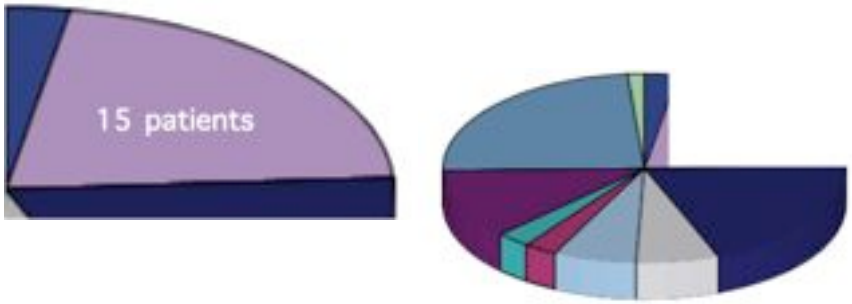
Risposta al trattamento 1° RMN





Tossicita' G4-G5

		G4		G5	
	TIPO	RR	nonRR	RR	nonRR
TOSSICITA' ACUTA	Salivary duct inflammation	0%	0%	0%	0%
	Mucositis oral	0%	0%	0%	0%
	Dermatitis radiation	0%	0%	0%	0%
	Dysphagia	0%	0%	0%	0%
TOSSICITA' TARDIVA	Dry mouth	0%	0%	0%	0%
	Superficial soft tissue fibrosis	0%	0%	0%	0%
	Trismus	0%	0%	0%	0%
	Dysphagia	0%	0%	0%	0%
	Myelitis	0%	0%	0%	0%
	Injury to carotid artery	0%	1%	7%	6%
	Thromboembolic event	0%	2%	0%	0%
	Head and neck soft tissue necrosis	0%	0%	0%	0%
	Osteonecrosis	0%	0%	0%	0%



Tossicita' G0-G2

		G0		G1		G2	
	TIPO	RR	nonRR	RR	nonRR	RR	nonRR
TOSSICITA' ACUTA	Salivary duct inflammation	80%	52%	20%	28%	0%	20%
	Mucositis oral	47%	37%	40%	33%	0%	27%
	Dermatitis radiation	87%	47%	7%	33%	0%	18%
	Dysphagia	47%	40%	47%	32%	7%	23%
TOSSICITA' TARDIVA	Dry mouth	60%	64%	27%	28%	13%	8%
	Superficial soft tissue fibrosis	93%	52%	7%	34%	0%	10%
	Trismus	100%	86%	0%	10%	0%	4%
	Dysphagia	67%	76%	13%	12%	13%	10%
	Myelitis	100%	100%	0%	0%	0%	0%
	Injury to carotid artery	93%	93%	0%	0%	0%	0%
	Thromboembolic event	100%	98%	0%	0%	0%	0%
	Head and neck soft tissue necrosis	100%	100%	0%	0%	0%	0%
	Osteonecrosis	100%	98%	0%	0%	0%	2%

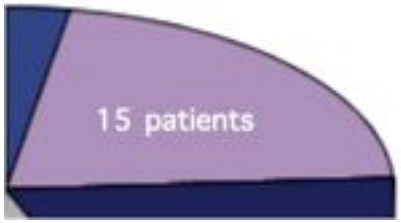
Istituto del Radio - BS 1977-2000

22 casi ritrattati con RTT (recidive locali e LR)

sequela	grado	n.	%
mucose	1	5	22.7
	2	14	63.6
	3	3	13.6
Osso/ATM	1	11	50
	2	9	40.9
	3	1	4.5
	4	1	4.5
udito	1	17	77.3
	2	4	18.2
	3	1	4.5

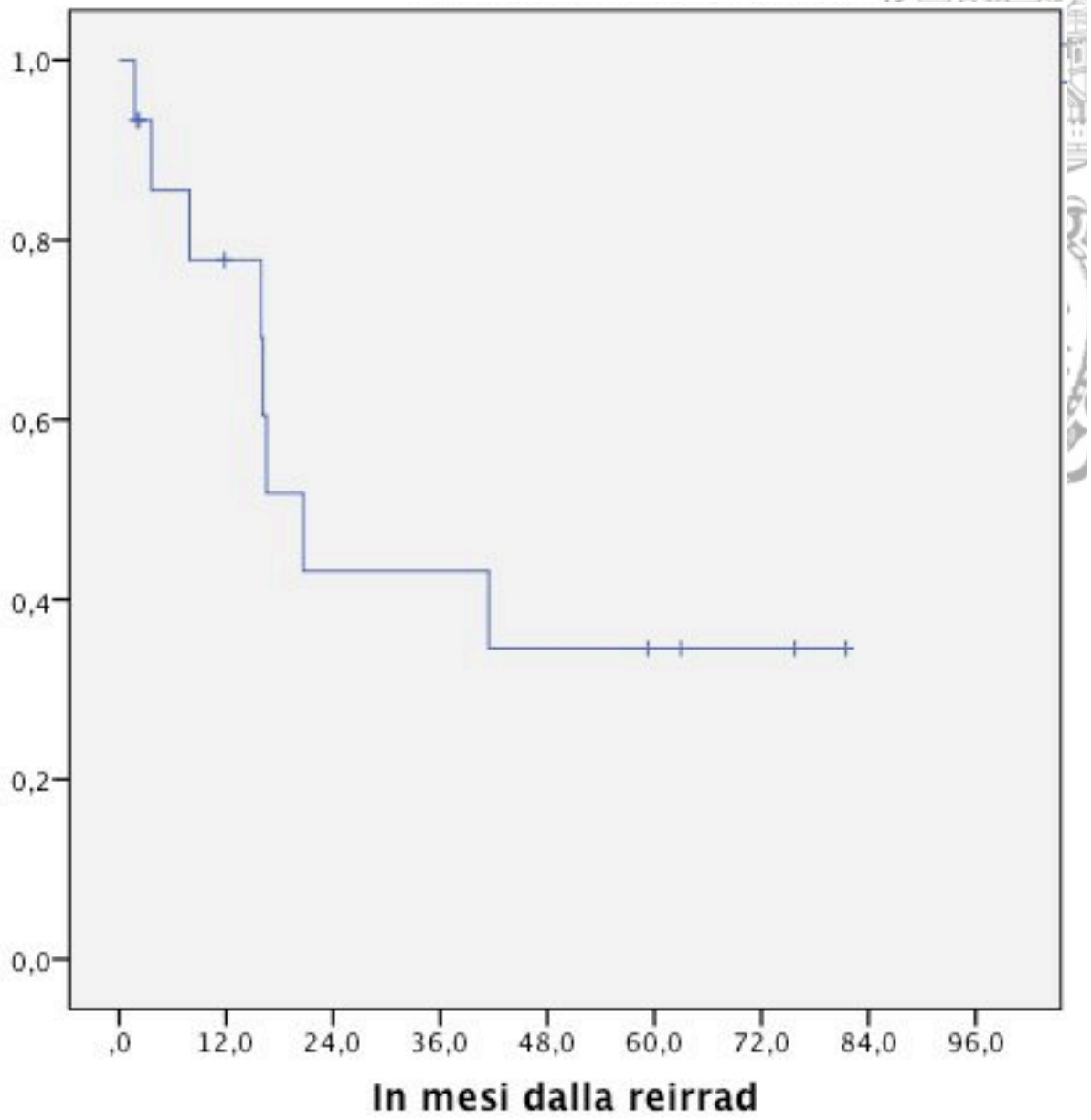
sequela	grado	n.	%
encefalo	1	16	72.7
	2	4	18.2
	3	2	9.1

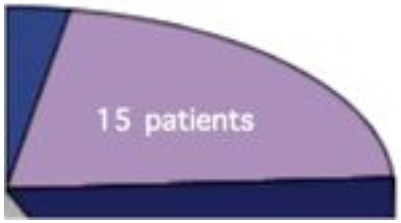
totali	1	5	22.7
	2	11	50
	3-4	6	27.3



Sopravvivenza - LC

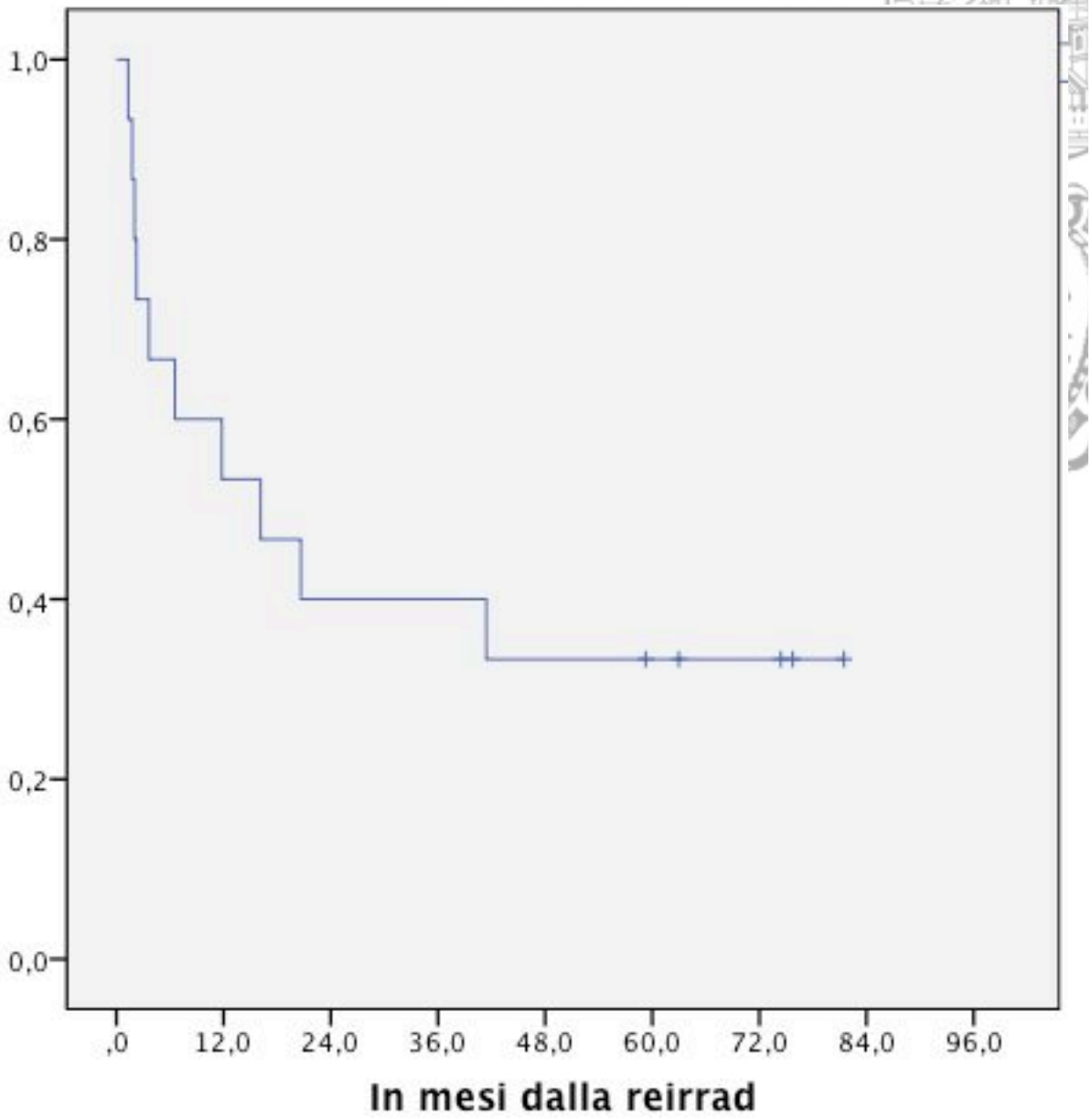
- Mediana 20 mesi
- 1 a: 79%
- 2 a: 43%

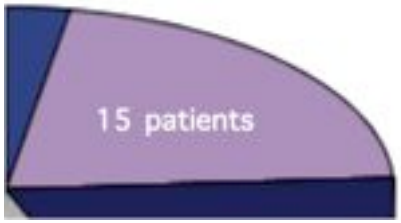




Sopravvivenza - PFS

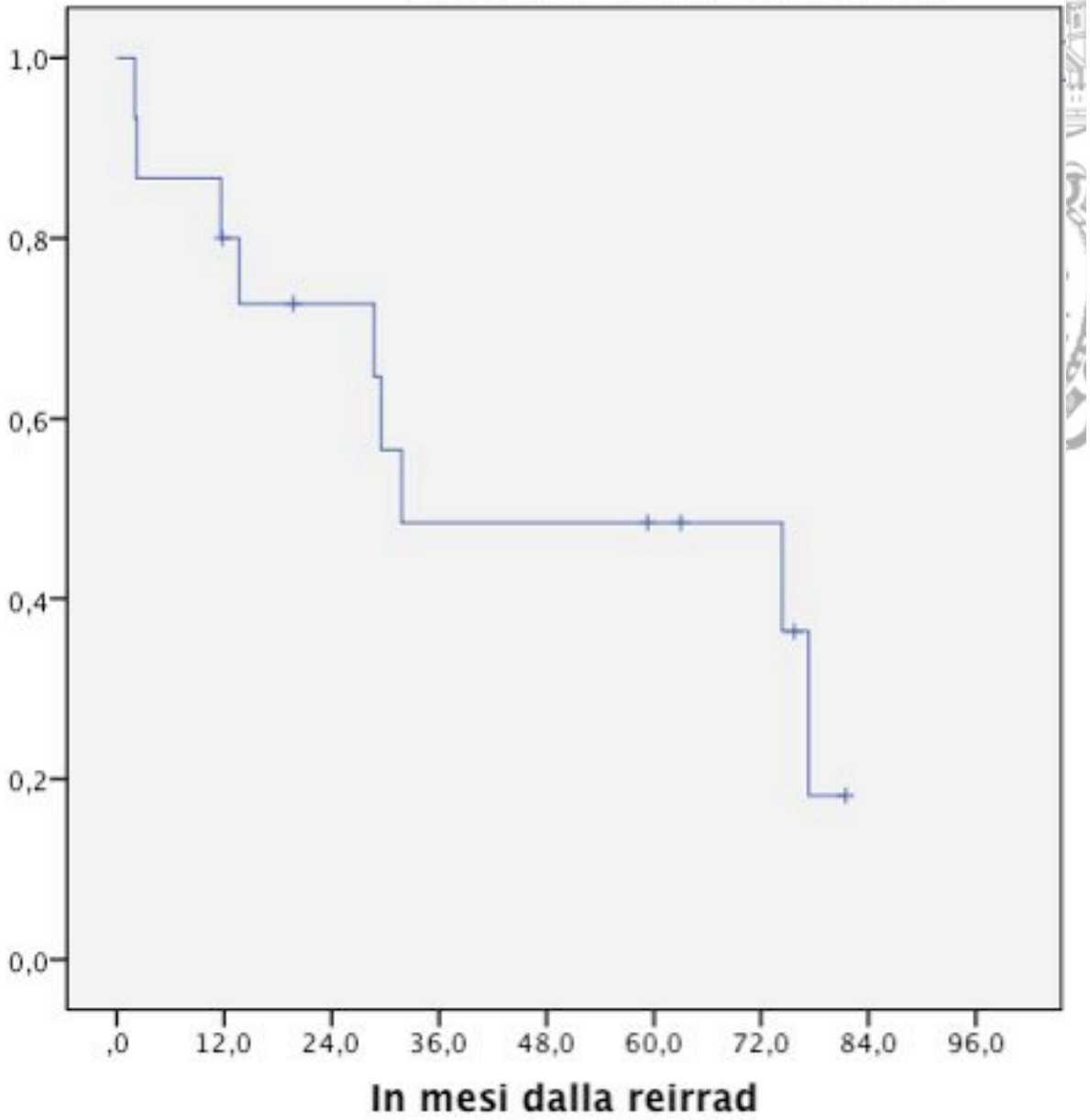
- Mediana 16 mesi
- 1 a: 53%
- 2 a: 40%

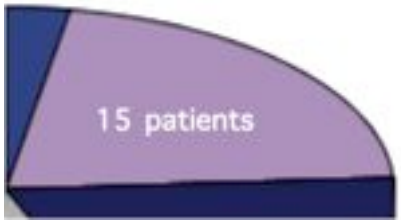




Sopravvivenza - OS

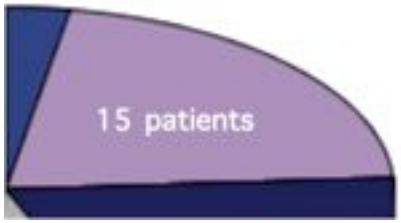
- Mediana 31 mesi
- 1 a: 80%
- 2 a: 73%





Univariata

- Nessuna delle variabili paziente ne' trattamento ha un impatto statisticamente significativo su nessuno degli *outcome* di sopravvivenza



Conclusioni

- La re-irradiazione e' possibile
- La selezione dei pazienti e' fondamentale
- La tossicita' acuta e tardiva e' accettabile quanto piu' il paziente e' ben selezionato;

- Le risposte alle domande ancora non le abbiamo con certezza e la valutazione clinica del "COMPLESSO PAZIENTE-MALATTIA" e' il momento fondamentale nel processo decisionale

- Non vi sono ancora dati SOLIDI che supportino la scelta di tecnica/dose


Thank
You!