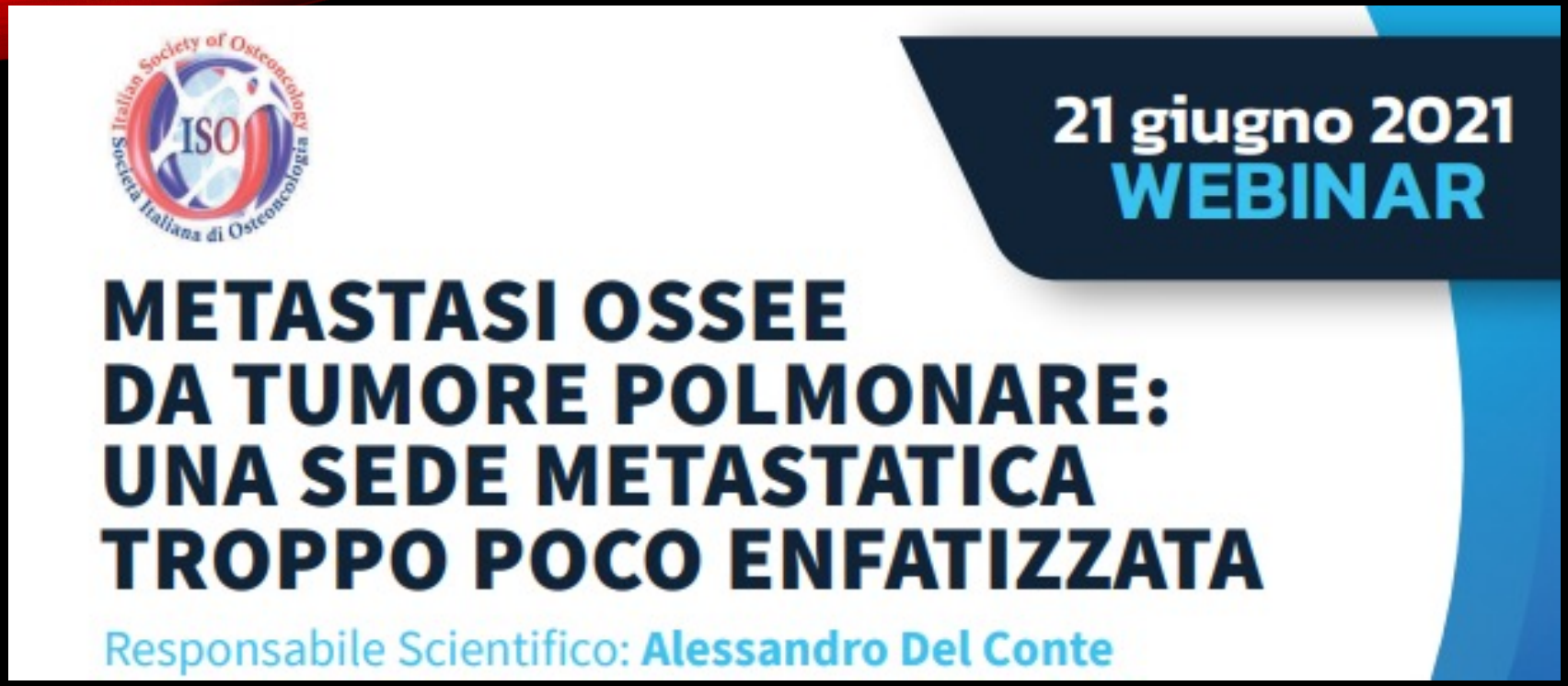


LA RADIOTERAPIA NELLE METASTASI OSSEE DA CARCINOMA POLMONARE

***Dott.* Revelant Alberto**

SOC Oncologia Radioterapica

CRO – Centro di Riferimento Oncologico

Aviano

LA RADIOTERAPIA

Trattamento di scelta (eccetto fratture → opzione chirurgica)

Pazienti fragili e spesso di difficile gestione

"Work-load": 30-40% attività struttura RT

GLI EFFETTI DELLA RADIOTERAPIA

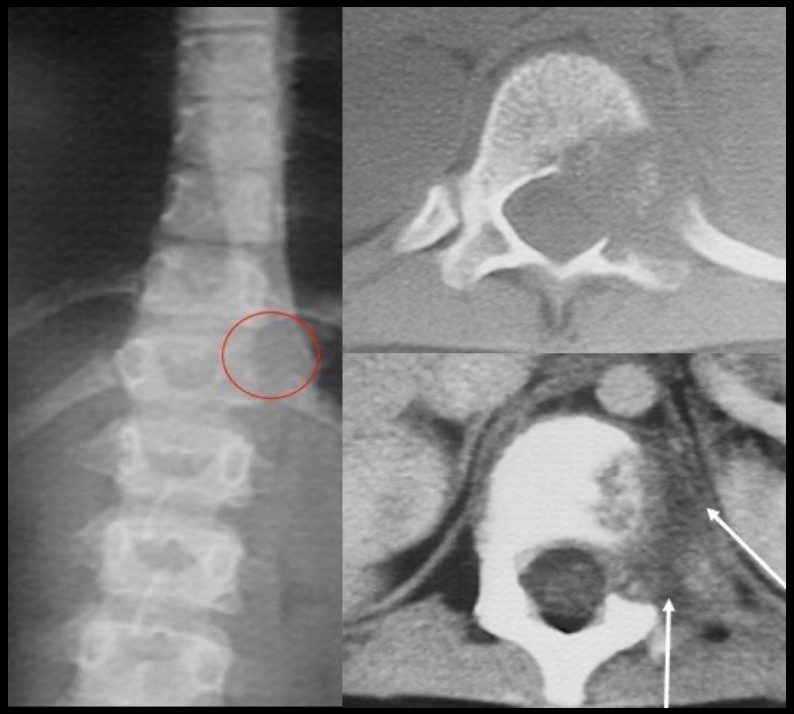
- Effetto antalgico nel 60-70% dei casi (studi randomizzati di fase III)
- Remissione completa del dolore in 1/3 dei casi
- Tempo d'azione: 2-6 settimane
- Durata mediana della risposta: 11-29 settimane
- Rischio recidiva del dolore (in caso di beneficio iniziale) nel 50% dei pazienti
- Ritrattamento efficace nel 60% dei casi
- Stessa efficacia in tutti i vari istotipi?

RADIOSENSIBILITÀ

Buona risposta	• Tumore mammario • Tumori ginecologici • Tumore prostatico
Risposta intermedia	• Tumori polmonari
Scarsa risposta	• Melanoma • Tumore a cellule renali

MECCANISMO D'AZIONE

- Eliminazione delle cellule neoplastiche -> riduzione del volume di malattia (Ferti et al. IJROBP 1985)
- Azione sul turnover dell'osso –> riduzione escrezione urinaria di prodotti della degradazione dell'osso -> inibizione dell'attività osteoclastica (RANK-RANKL) (Papatheofanis Br J Radiol 1997, Hoskin Lancet 2000)
- Effetto antalgico plurifattoriale (Allen et al. Cancer 1976)



LA CLASSIFICAZIONE

Complicate

- Frattura patologica\lesione ad alto rischio di frattura
- Invasione dei tessuti extraossei ed organi limitrofi
- Dolore neuropatico\sintomatologia neurologica

Non complicate

- Dolore
- Limitazione funzionale

I DOSAGGI IN RADIOTERAPIA

Singola frazione

- 8 Gy
- 10 Gy
- 12 Gy (SBRT)
- 14 Gy (SBRT)

Multiple frazioni

- 13 Gy / 2 fr
- 20 Gy / 5 fr
- 30 Gy / 10 fr
- 40 Gy / 20 fr (mieloma)
- 24 Gy / 3 fr (SBRT)
- 30 Gy / 5 fr (SBRT)

QUALE DOSAGGIO?

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Bone metastases

Overall response rates to radiation therapy for patients with painful uncomplicated bone metastases undergoing initial treatment and retreatment

- Singola frazione (SF) vs frazioni multiple (MF) -> stesso controllo del dolore
- Preferibile usare SF nelle lesioni non complicate
- Limitato utilizzo SF in caso di organi a rischio nelle vicinanze

LA SINGOLA FRAZIONE

Svantaggi

- Maggior necessità di ritrattamento (soprattutto nei pazienti 'long survivor')
- Aumento delle fratture patologiche (1,3% vs 3%)
- Riduzione della remineralizzazione ossea (1 solo studio)
- Rischio effetto 'Pain flare'

Vantaggi

- Raggiungimento più rapido controllo del dolore
- Maggior riduzione del dolore (soprattutto SBRT)
- Ripetibilità del trattamento (8Gy)
- Minor mobilizzazione di pazienti spesso 'fragili'

IL FENOMENO DEL PAIN FLARE

Table 3 Published studies evaluating prospectively the incidence of Pain Flare

Author	Number of evaluable patients	RT technique	RT dose schedules (Gy/fx)	Pain Flare Incidence (%)
Chow	88	3DCRT	8 Gy / 1fx	2 16 %
			20 Gy 5 fx	
			30 Gy /10 fx	
Loblaw	44	3DCRT	8Gy / fx	40.9 %
			20 Gy/ 5 fx	
Hird	111	3DCRT	8 Gy / 1 fx	40 %
			20 Gy 5 fx	
			30 Gy /10 fx	
Chiang	41	SBRT	20-24 Gy / 1 fx	68.3 %
			24 35 Gy / 2 5 fx	
Gomez-Iturriaga	135	3DCRT	8Gy / fx	37.7 %
			20 Gy/ 5 fx	

Abbreviations: 3DCRT: Tridimensional Conformal Radiotherapy; SBRT: Stereotactic Body Radiotherapy

SINGOLA O MULTIPLA?

Cosa guida la scelta del radioterapista

- Esperienza
- Linee guida
- Risorse tecnologiche
- Liste d'attesa
- Performance status ed età
- Sede da trattare (es. Vertebre cervicali)

IL RITRATTAMENTO

Single versus multiple fractions of repeat radiation for painful bone metastases: a randomised, controlled, non-inferiority trial

Edward Chow, Yvette M van der Linden, Daniel Roos, William F Hartsell, Peter Hoskin, Jackson S Y Wu, Michael D Brundage, Abdenour Nabid, Caroline J A Tissing-Tan, Bing Oei, Scott Babington, William F Demas, Carolyn F Wilson, Ralph M Meyer, Bingshu E Chen, Rebecca K S Wong

Tipo RT	8Gy/1 frazione	20Gy/5 frazioni	p
Risposta dolore	45%	51%	NS
Comparsa fratture	7%	5%	0.03
CMM	2%	<1%	NS
Diarrea	23%	31%	0.018
Inappetenza	56%	66%	0.011

SINGOLA O MULTIPLA?

Contents lists available at ScienceDirect

Journal of Bone Oncology

journal homepage: www.elsevier.com/locate/jbo

Review Article

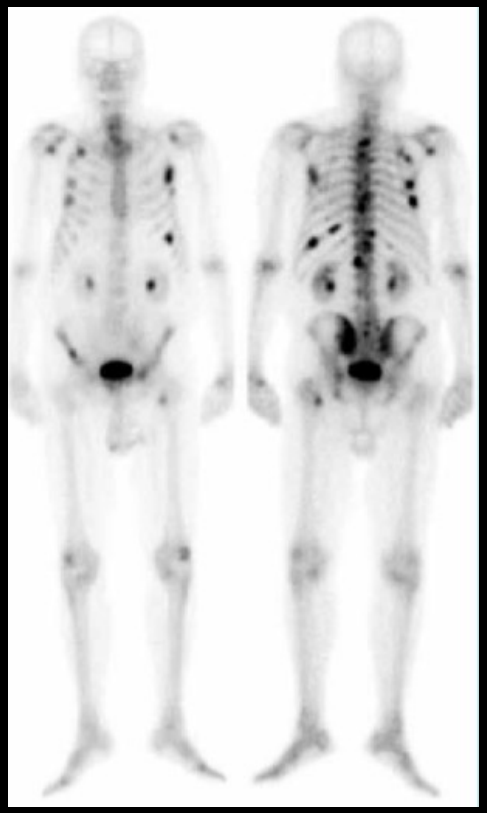
International patterns of practice in radiotherapy for bone metastases: A review of the literature

Rachel McDonald, Edward Chow, Henry Lam, Leigha Rowbottom, Hany Soliman *

"Despite the publication of robust randomized control trials, meta-analyses, and clinical practice guidelines recommending the use of a single treatment to palliate uncomplicated bone metastasis, SFRT is internationally underutilized"

SF STANDARD TERAPEUTICO?

- Dati di letteratura indicano che la Radioterapia in singola frazione viene utilizzata solo nel 10-30% dei casi



IL RISCHIO DI FRATTURA

La vecchia classificazione

- Lesione ossea di diametro > 2,5 cm (Keene JS Clin Orhop 1986)
- Lesione ossea che distrugge il 50% della corticale (Philips 1998)
- Avulsione piccolo trocantere (Metastatic Bone Disease: a guide to good practice)

Mirel's Scoring System

Mirel´s score

points	1	2	3
Localisation	Upper extr.	Lowe extr.	Pertrochant. region
Pain	low	medium	big
Type	Osteoplastic	mixed	Osteolytic
Size	<1/3 widht of bone	1/3 – 2/3 widht of bone	>2/3 widht of bone

IL RISCHIO DI FRATTURA DEL FEMORE

Simple radiographic parameter predicts fracturing in metastatic femoral bone lesions: results from a randomised trial

Yvette M. van der Linden[a,*], Herman M. Kroon[b], Sander P.D.S. Dijkstra[c], Judith J. Lok[d], Ed M. Noordijk[a], Jan Willem H. Leer[e], Corrie A.M. Marijnen[a], for the Dutch Bone Metastasis Study Group

Abstract

Background and purpose: In the randomised Dutch Bone Metastasis Study on the palliative effect of a single fraction (SF) of 8 Gy versus six fractions of 4 Gy on painful bone metastases, 14 fractures occurred in 102 patients with femoral metastases. Purpose of the present study was to identify lesional risk factors for fracturing and to evaluate the influence of the treatment schedule.

Material and methods: Pretreatment radiographs of femoral metastases were collected. Three observers separately measured the lesions and scored radiographic characteristics.

Results: Ten fractures occurred after median 7 weeks in 44 SF patients (23%) and four after median 20 weeks in 58 multiple fraction patients (7%) (UV, $P = 0.02$). In 110 femoral metastases, an axial cortical involvement >30 mm significantly predicted fracturing (MV, $P = 0.02$). Twelve out of 14 fractured lesions and 40 out of 96 non-fractured metastases had an axial cortical involvement >30 mm (negative predictive value, 97%). When correcting for the axial cortical involvement, the treatment schedule was not predictive anymore (MV, $P = 0.07$).

Conclusions: Fracturing of the femur mostly depended on the amount of axial cortical involvement of the metastasis. We recommend to treat femoral metastases with an axial cortical involvement ≤30 mm with an SF of 8 Gy for relief of pain. If the axial cortical involvement is >30 mm, prophylactic surgery should be performed to minimize the risk of pathological fracturing or, if the patient's condition is limited, irradiation to a higher total dose.

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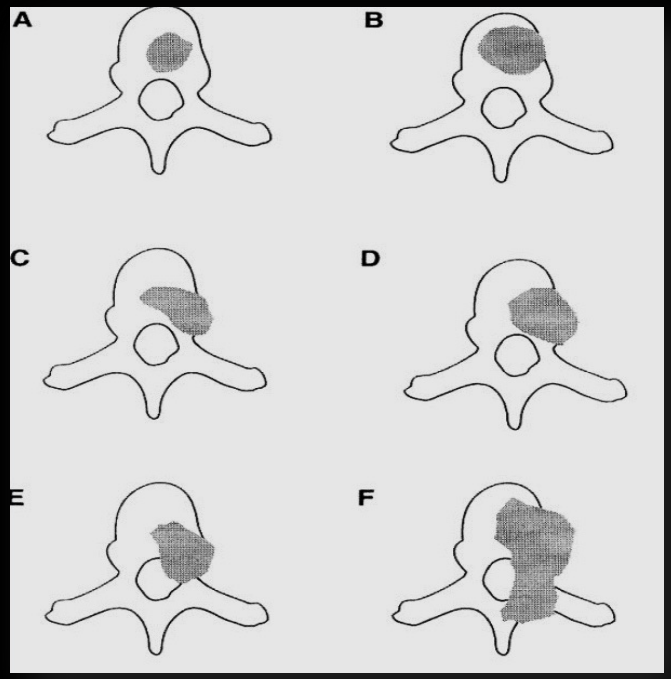
IL CROLLO VERTEBRALE

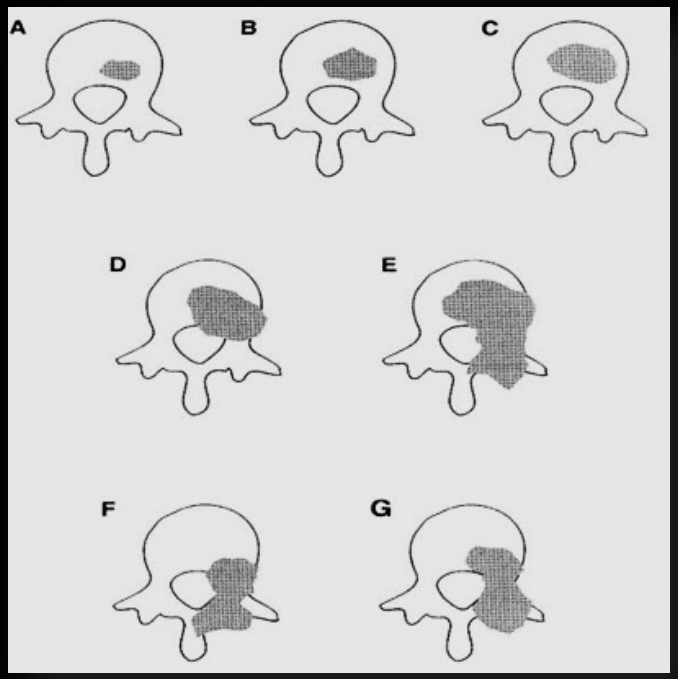
Risk Factors and Probability of Vertebral Body Collapse in Metastases of the Thoracic and Lumbar Spine

Taneichi, Hiroshi MD; Kaneda, Kiyoshi MD; Takeda, Naoki MD; Abumi, Kuniyoshi MD; Satoh, Shigenobu MD

Results. Significant risk factors were costovertebral joint destruction (odds ratio, 10.17; $P = 0.021$) and tumor size (odds ratio of every 10% increment in %TO, 2.44; $P = 0.032$) in the thoracic region (Th1-Th10), whereas, tumor size (odds ratio of every 10% increment in %TO, 4.35; $P = 0.002$) and pedicle destruction (odds ratio, 297.08; $P = 0.009$) were main factors in the thoracolumbar and lumbar spine (Th10-L5). The criteria of impending collapse were: 50-60% involvement of the vertebral body with no destruction of other structures, or 25-30% involvement with costovertebral joint destruction in the thoracic spine; and 35-40% involvement of vertebral body, or 20-25% involvement with posterior elements destruction in thoracolumbar and lumbar spine.

IL CROLLO VERTEBRALE





	A	B	C	D	E	F
%TO†	30%	60%	30%	60%	30%	60%
Costovertebral Joint Destruction	-	-	+	+	+	+
Pedicle Destruction	-	-	-	-	+	+
Posterior Elements Destruction	-	-	-	-	-	+
Predicted Probability of Collapse	0.13	0.68	0.57	0.96	0.71	0.98

	A	B	C	D	E	F	G
%TO†	20%	30%	40%	40%	60%	5%	20%
Pedicle Destruction	-	-	-	+	+	+	+
Posterior Elements Destruction	-	-	-	-	+	+	+
Predicted Probability of Collapse	0.07	0.25	0.60	0.99	0.99	0.06	0.38

IL CROLLO VERTEBRALE

A Novel Classification System for Spinal Instability in Neoplastic Disease

Spine 2010;35:E1221–E1229

An Evidence-Based Approach and Expert Consensus From the Spine Oncology Study Group

Element of SINS	Score
Location	
Junctional (occiput-C2, C7–T2, T11–L1, L5–S1)	3
Mobile spine (C3–C6, L2–L4)	2
Semi-rigid (T3–T10)	1
Rigid (S2–S5)	0
Pain relief with recumbency and/or pain with movement/loading of the spine	
Yes	3
No (occasional pain but not mechanical)	1
Pain free lesion	0
Bone lesion	
Lytic	2
Mixed (lytic/blastic)	1
Blastic	0
Radiographic spinal alignment	
Subluxation/translation present	4
De novo deformity (kyphosis/scoliosis)	2
Normal alignment	0
Vertebral body collapse	
>50% collapse	3
<50% collapse	2
No collapse with >50% body involved	1
None of the above	0
Posterolateral involvement of the spinal elements (facet, pedicle or CV joint fracture or replacement with tumor)	
Bilateral	3
Unilateral	1
None of the above	0

The SINS is generated by tallying each score from the 6 individual components. The minimum score is 0 and maximum is 18. Scores of 0 to 6 denote "stability," scores of 7 to 12 denote "indeterminate (possibly impending) instability," and scores of 13 to 18 denote "instability." Patients with SINS scores of 7 to 18 warrant surgical consultation.

SBRT NELLE METASTASI OSSEE

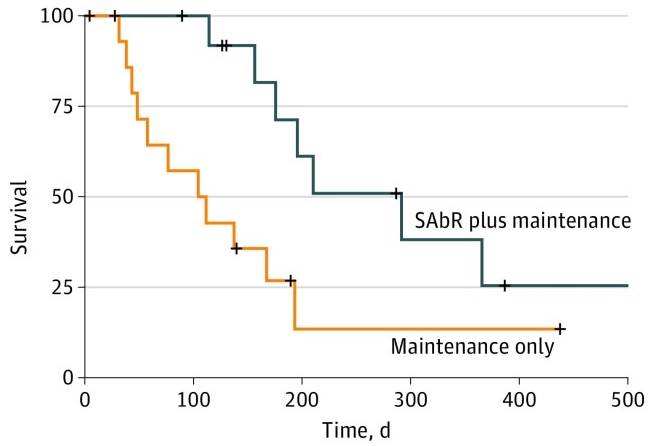
SBRT NELLE METASTASI OSSEE

Consolidative Radiotherapy for Limited Metastatic Non–Small-Cell Lung Cancer

JAMA Oncol. 2018 Jan; 4(1): e173501.

A Phase 2 Randomized Clinical Trial

Puneeth Iyengar, MD, PhD,[1] Zabi Wardak, MD,[1] David E. Gerber, MD,[2] Vasu Tumati, MD,[1] Chul Ahn, PhD,[3] Randall S. Hughes, MD,[2] Jonathan E. Dowell, MD,[2] Naga Cheedella, MD,[2] Lucien Nedzi, MD,[1] Kenneth D. Westover, MD, PhD,[1] Suprabha Pulipparacharuvil, PhD,[1] Hak Choy, MD,[1] and Robert D. Timmerman, MD[1]

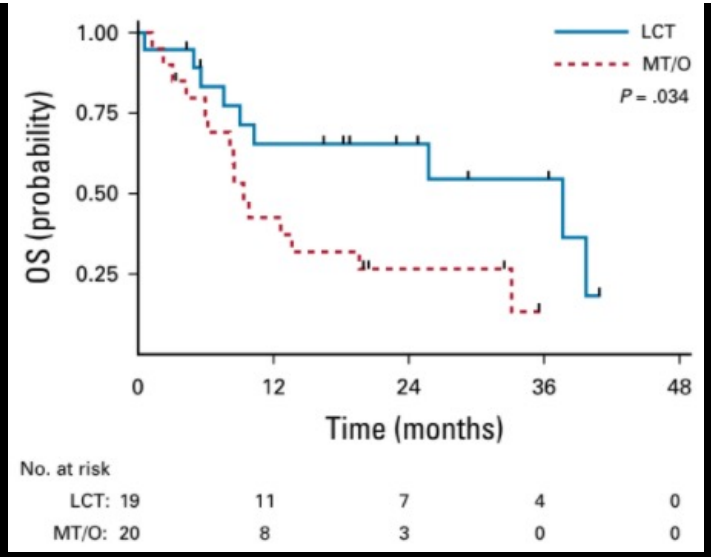


No. at risk					
SAbR plus maintenance	14	12	6	3	1
Maintenance only	15	8	1	1	1

RT ED SBRT NELLE METASTASI OSSEE

Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicentre, randomised, controlled, phase 2 study

Daniel R Gomez, George R Blumenschein Jr, J Jack Lee, Mike Hernandez, Rong Ye, D Ross Camidge, Robert C Doebele, Ferdinandos Skoulidis, Laurie E Gaspar, Don L Gibbons, Jose A Karam, Brian D Kavanagh, Chad Tang, Ritsuko Komaki, Alexander V Louie, David A Palma, Anne S Tsao, Boris Sepesi, William N William, Jianjun Zhang, Qiuling Shi, Xin Shelley Wang, Stephen G Swisher, John V Heymach**



GRAZIE PER L'ATTENZIONE!