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L'INNOVAZIONE TECNOLOGICA IN RADIOTERAPIA: NUOVI STANDARD CLINICI E PROBLEMATICHE GESTIONALI

Centro Congressi VILLA CAGNOLA

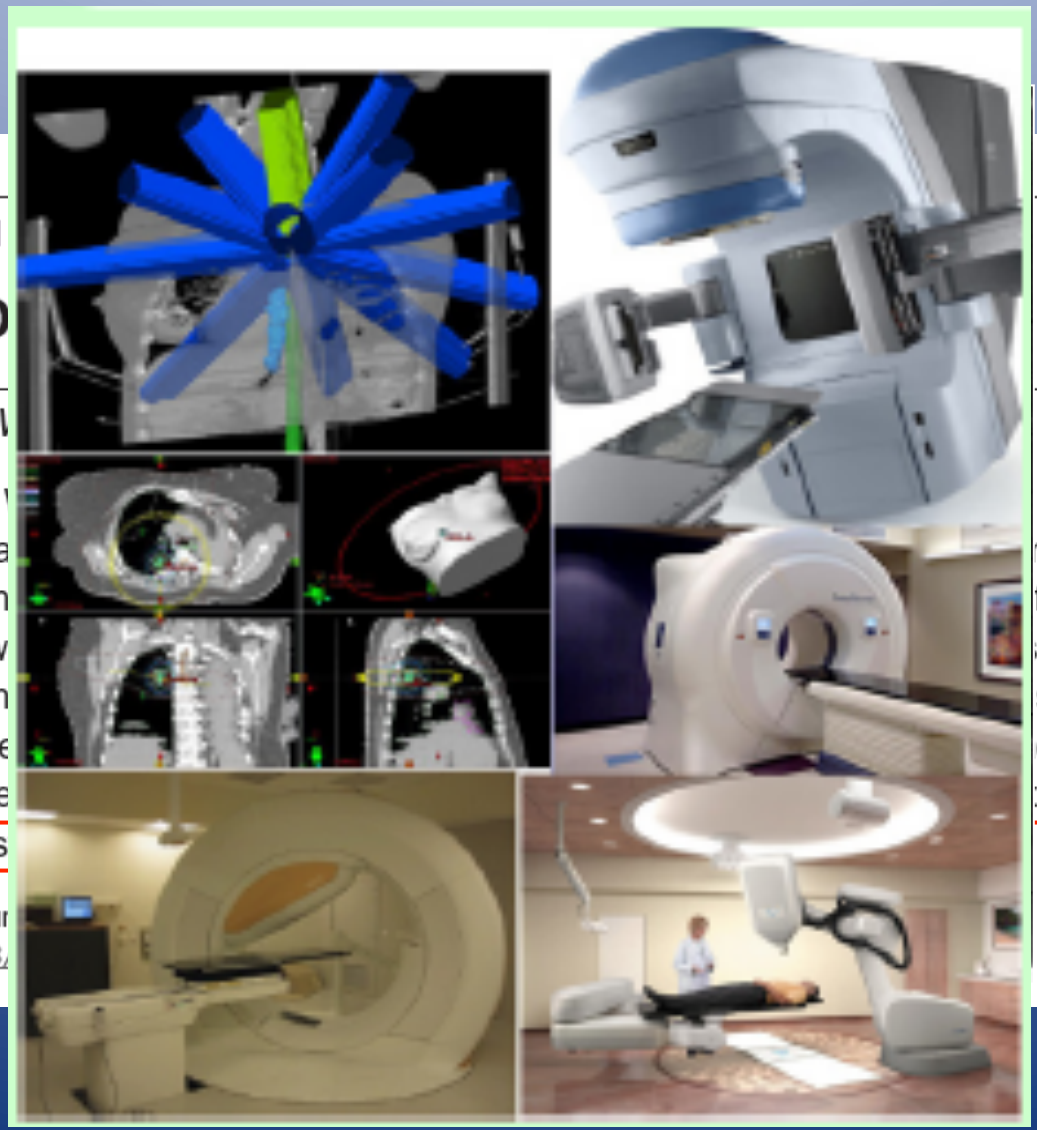
Via Cagnola, 19 - Gazzada Schianno (VA)

Sabato 29 novembre 2014

Localizzazioni secondarie scheletriche e linfonodali nel paziente oligometastatico

Dr. Dario Zerini – Divisione di Radioterapia – Istituto Europeo di Oncologia -Milano

Oligometastasi: una nuova era?



OPINION

Oligo

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Abstract |
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Weichselbaur
doi:10.1038/

March 2011;

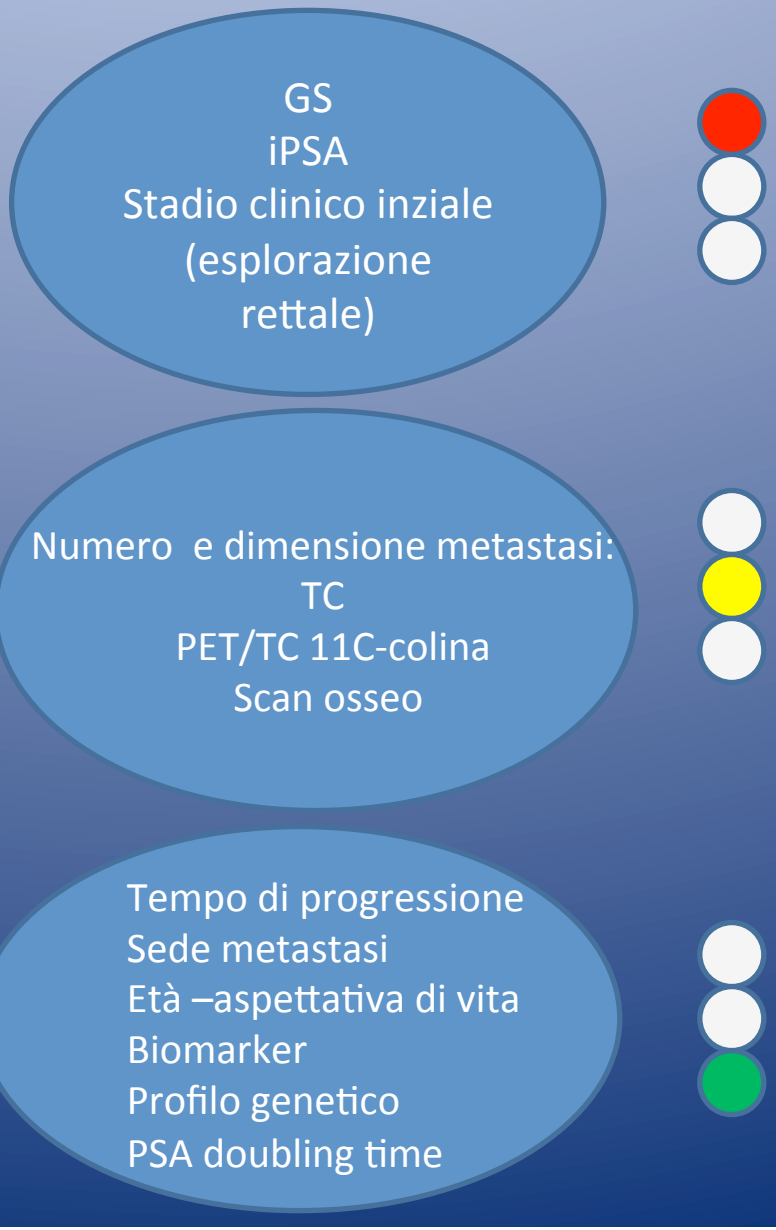
Il paziente oligometastatico

Pz con sino a 5 localizzazioni metastatiche e con non più di 3 localizzazioni in un singolo organo

Pz con ≤ 3 localizzazioni totali

Paziente oligometastatico: il “modello prostata”

Selezione dei pz in base a:



Decaestecker *et al. Radiation Oncology* 2014, **9**:135
http://www.ro-journal.com/content/9/1/135

RADIATION ONCOLOGY

RESEARCH Open Access

Repeated stereotactic body radiotherapy for oligometastatic prostate cancer recurrence

Karel Decaestecker[1], Gert De Meerleer[2], Bieke Lambert[3], Louke Delrue[4], Valérie Fonteyne[2], Tom Claeys[1], Filip De Vos[5], Wouter Huysse[4], Arne Hautekiet[2], Gaethan Maes[2] and Piet Ost[2*]

Abstract

Purpose: To assess the outcome of prostate cancer (PCa) patients diagnosed with oligometastatic disease at recurrence and treated with stereotactic body radiotherapy (SBRT).

Methods: Non-castrate patients with up to 3 synchronous metastases (bone and/or lymph nodes) diagnosed on positron emission tomography - computed tomography, following biochemical recurrence after local curative treatment, were treated with (repeated) SBRT to a dose of 50 Gy in 10 fractions or 30 Gy in 3 fractions. Androgen deprivation therapy-free survival (ADT-FS) defined as the time interval between the first day of SBRT and the initiation of ADT was the primary endpoint. ADT was initiated if more than 3 metastases were detected during follow-up even when patients were still asymptomatic. Secondary endpoints were local control, progression free survival (PFS) and toxicity. Toxicity was scored using the Common Terminology Criteria for Adverse Events.

Results: With a median follow-up from time of SBRT of 2 years, we treated 50 patients with 70 metastatic lesions with a local control rate of 100%. The primary involved metastatic sites were lymph nodes (54%), bone (44%), and viscera (2%). The median PFS was 19 mo (95% CI: 13–25 mo) with 75% of recurring patients having ≤3 metastases. A 2nd and 3rd course of SBRT was delivered in 19 and 6 patients respectively. This results in a median ADT-FS of 25 months (20–30 mo). On univariate analysis, only a short PSA doubling time was a significant predictor for both PFS (HR: 0.90, 95% CI: 0.82 – 0.99) and ADT-FS (HR: 0.83; 95% CI: 0.71 – 0.97). Ten patients (20%) developed toxicity following treatment, which was classified as grade I in 7 and grade II in 3 patients.

Conclusion: Repeated SBRT for oligometastatic prostate cancer postpones palliative androgen deprivation therapy with 2 years without grade III toxicity.

Keywords: Oligometastases, Prostate cancer, Recurrence, Salvage therapy, Stereotactic body radiotherapy

Int. J. Radiation Oncology Biol. Phys., Vol. 72, No. 5, pp. 1516–1522, 2008

0360-3016/08/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2008.03.044

CLINICAL INVES **Metastasis**

DESCRI TED WITH PY

MICHAEL T CHELL, PH.D.,

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Purpose: T ting oligometa-stases with ial lesions.
Methods an 1 patients with five or fewe rgery. For each lesion, the p ibed dose were ascertained (BED2), calculated using
Results: Lu ns were significantly larg ates were 77% and 73% re orse lesion LC. Lesions orig LC, as did lesions from d not correlate with impro
Conclusions od local tumor control. Bu

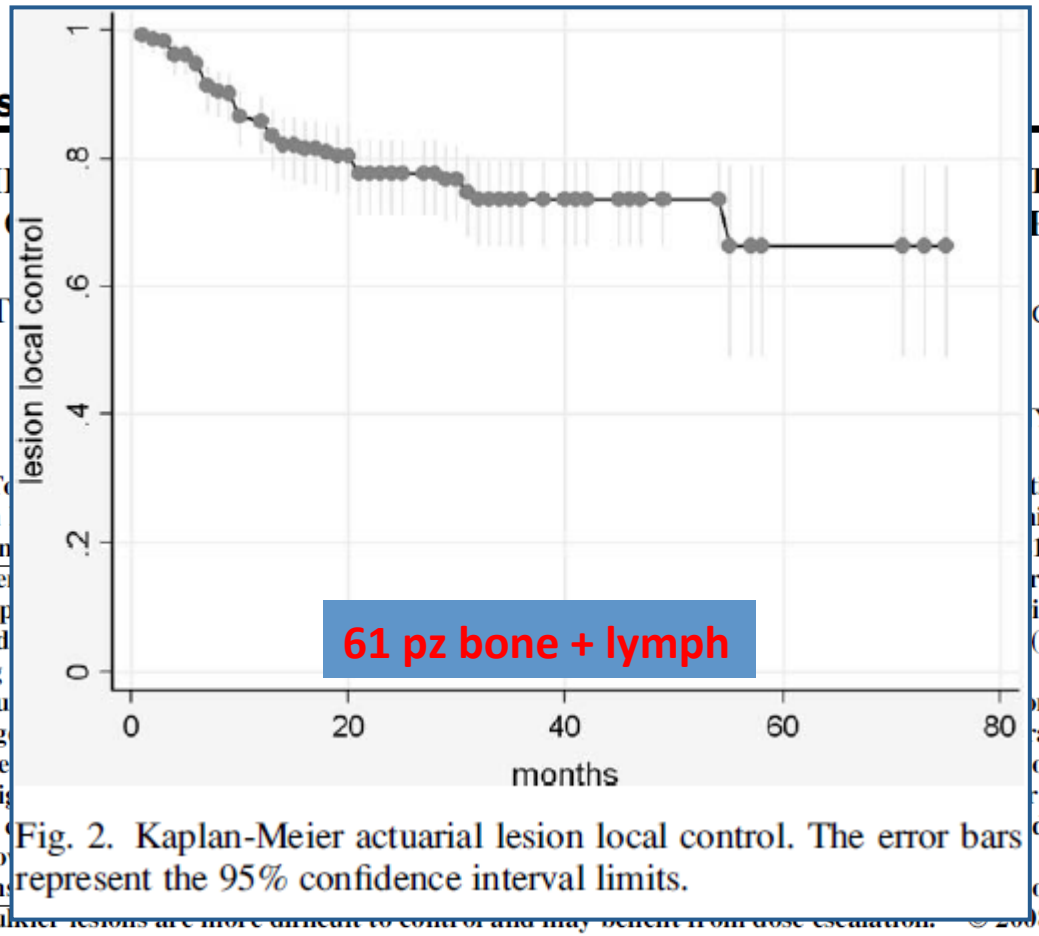

Fig. 2. Kaplan-Meier actuarial lesion local control. The error bars represent the 95% confidence interval limits.

Trattare la malattia oligometastatica con SBRT? Royal Marsden review

Panel: Evidence-based practice for extracranial oligometastases

- Stereotactic body radiotherapy results in a high control rate of treated metastases (~80%)
- About 20% of patients are progression free at 2–3 years after stereotactic body radiotherapy
- Toxicity is low
- Stereotactic body radiotherapy should be considered in patients with isolated metastases, especially if the disease-free interval is longer than 6 months
- Randomised trials are needed to establish whether stereotactic body radiotherapy improves progression free and/or overall survival
- Patients most likely to benefit from stereotactic body radiotherapy have:
  - Long disease-free interval
  - Breast histology
  - One to three metastases
  - Small metastases
  - Higher radiation dose delivered (biologic effective dose >100 Gy)

Tomotherapy per K colon oligometastatico

RESEARCH Open Access

Phase II study of helical tomotherapy in the multidisciplinary treatment of oligometastatic colorectal cancer

Benedikt Engels[1*], Thierry Gevaert[1], Hendrik Everaert[2], Peter De Coninck[1], Alexandra Sermeus[3], Nicolas Christian[1], Guy Storme[1], Dirk Verellen[1] and Mark De Ridder[1]

Abstract

Background: Complete metastasectomy provides a real chance for long-term survival in patients with oligometastatic colorectal cancer (CRC). For inoperable patients, we evaluated in this study intensity-modulated and image-guided radiotherapy (IMRT-IGRT) by helical tomotherapy.

Methods: Twenty-four CRC patients with ≤ 5 metastases were enrolled, receiving a dose of 50 Gy in fractions of 5 Gy. No limitations concerning dimension or localization of the metastases were imposed. Whole body PET-CT was performed at baseline and 3 months after the initiation of RT to evaluate the metabolic response rate according to PET Response Criteria in Solid Tumors (PERCIST) version 1.0.

Results: A total of 53 metastases were treated. Seventeen patients (71%) received previously ≥ 1 line of chemotherapy for metastatic disease, displaying residual (n = 7) or progressive (n = 10) metabolic active oligometastatic disease at time of inclusion. Most common sites were the lung, liver and lymphnodes. One patient (4%) experienced grade 3 dysphagia. Twenty-two patients were evaluated by post-treatment PET-CT. Twelve patients achieved a complete (n = 6) or partial (n = 6) metabolic response, resulting in an overall metabolic response rate of 55%. At a median follow-up of 10 months, 7 patients (29%) are in remission, of which 5 received previous chemotherapy with residual oligometastatic disease at time of inclusion. The actuarial 1-year local control, progression-free survival, and overall survival were 54%, 14% and 78%.

Conclusions: Helical tomotherapy delivering 10 fractions of 5 Gy resulted in a metabolic response rate of 55%, and appeared to be attractive as consolidation of inoperable oligometastatic disease after effective chemotherapy.

Trial registration: Eudract 2008-008300-40; NCT00807313

Keywords: Metastatic colorectal cancer, Oligometastases, Helical tomotherapy, IMRT-IGRT

Decision-making process for oligometastasis

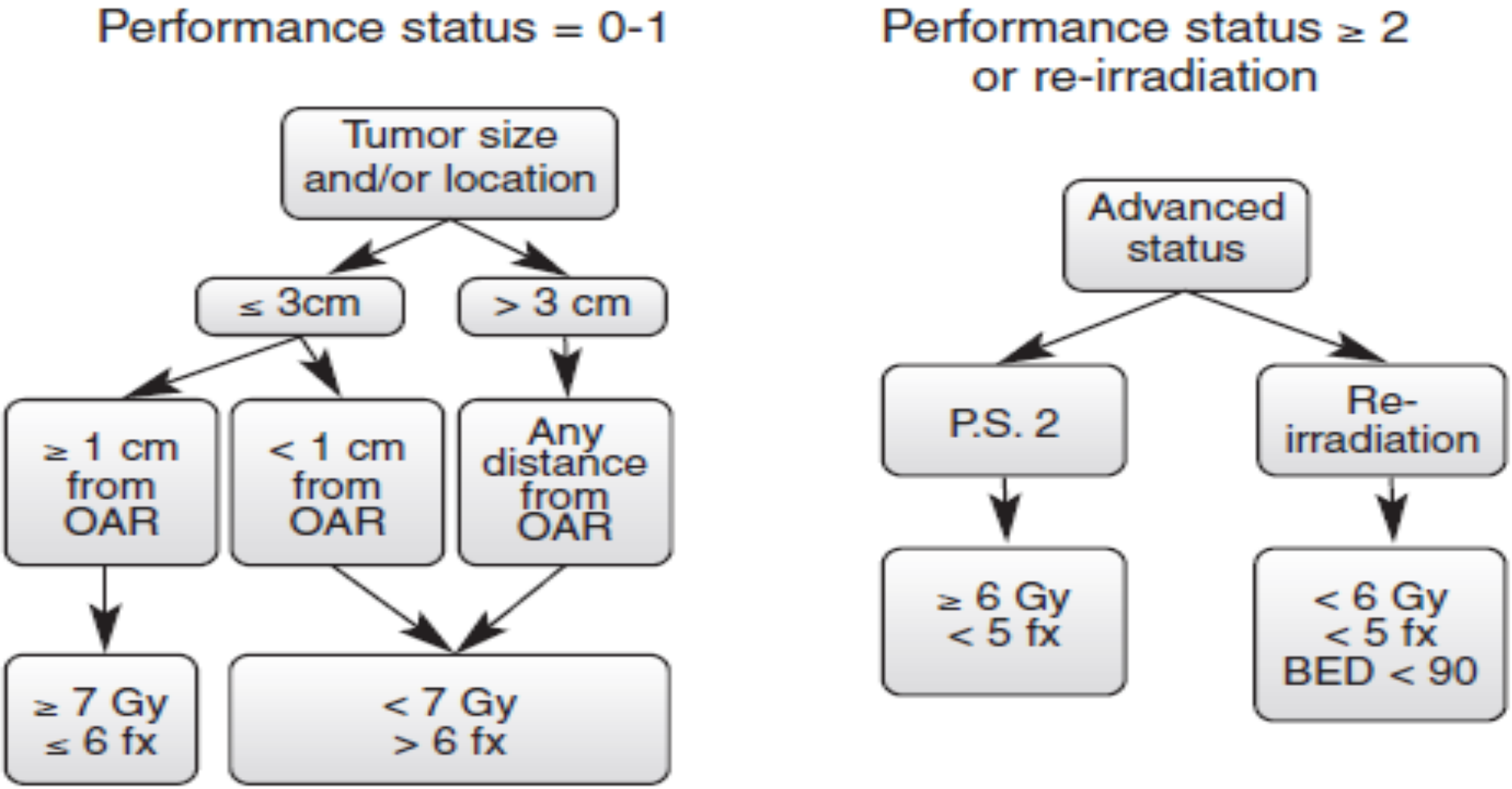

Figure 2 - Flow-chart of decisional steps followed to plan radiotherapy fractionation according to clinical and strumental parameters. OAR, organ-at-risk; BED, biological effective dose; fx, fraction.

Int. J. Radiation Oncology Biol. Phys., Vol. 81, No. 3, pp. 831–838, 2011

0360-3016/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2010.05.032

CLINICAL INVESTIGATION **Metastasis**

CLINICAL OUTCOME OF HYPOFRACTIONATED STEREOTACTIC RADIOTHERAPY FOR ABDOMINAL LYMPH NODE METASTASES

Mario Bignardi, M.D.,* Piera Navarria, M.D.,* Pietro Mancosu, M.Sc.,* Luca Cozzi, Ph.D.,† Antonella Fogliata, M.Sc.,† Angelo Tozzi, M.D.,* Simona Castiglioni, M.D.,* Carlo Carnaghi, M.D.,‡ Maria Chiara Tronconi, M.D.,‡ Armando Santoro, M.D.,‡ and Marta Scorsetti, M.D.*

*Radiation Oncology Department and ‡Medical Oncology Department, IRCCS Istituto Clinico Humanitas, Rozzano, Italy; and †Medical Physics Unit, Oncology Institute of Southern Switzerland, Bellinzona, Switzerland

Purpose: We report the medium-term clinical outcome of hypofractionated stereotactic body radiotherapy (SBRT) in a series of patients with either a solitary metastasis or oligometastases from different tumors to abdominal lymph nodes.

Methods and Materials: Between January 2006 and June 2009, 19 patients with unresectable nodal metastases in the abdominal retroperitoneal region were treated with SBRT. Of the patients, 11 had a solitary nodal metastasis and 8 had a dominant nodal lesion as part of oligometastatic disease, defined as up to five metastases. The dose prescription was 45 Gy to the clinical target volume in six fractions. The prescription had to be downscaled by 10% to 20% in 6 of 19 cases to keep within dose/volume constraints. The first 11 patients were treated with three-dimensional conformal techniques and the last 8 by volumetric intensity-modulated arc therapy. Median follow-up was 1 year.

Results: Of 19 patients, 2 had a local progression at the site of SBRT; both also showed concomitant tumor growth at distant sites. The actuarial rate of freedom from local progression was 77.8% ± 13.9% at both 12 and 24 months. Eleven patients showed progressive local and/or distant disease at follow-up. The 12- and 24-month progression-free survival rates were 29.5% ± 13.4% and 19.7% ± 12.0%, respectively. The number of metastases (solitary vs. nonsolitary oligometastases) emerged as the only significant variable affecting progression-free survival ($p < 0.0004$). Both acute and chronic toxicities were minimal.

Conclusions: Stereotactic body radiotherapy for metastases to abdominal lymph nodes was shown to be feasible with good clinical results in terms of medium-term local control and toxicity rates. Even if most patients eventually show progressive disease at other sites, local control achieved by SBRT may be potentially significant for preserving quality of life and delaying further chemotherapy. © 2011 Elsevier Inc.

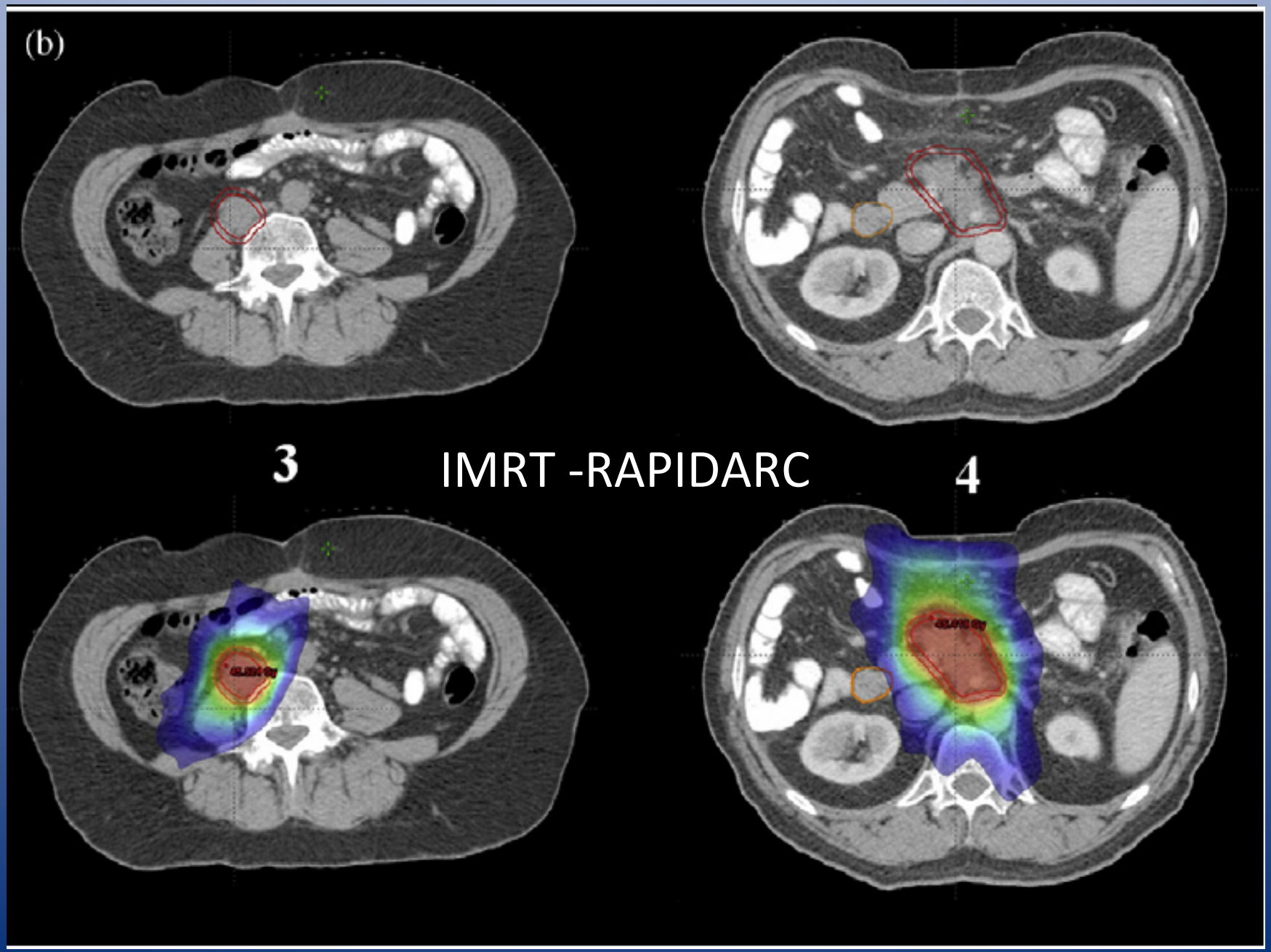
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Table 1. Patient characteristics

Variable group	Characteristics	Whole group	CRT patients	RA patients
Patient	Gender (No. of patients)			
	M	10	6	4
	F	9	5	4
	Age			
	M	62	61	64
	R	54–78	58–78	54–77
	ECO			
	0	15	9	6
	1	4	2	2
Tumor	Prin			
	C	5	3	2
	E	1	0	1
	S	1	1	0
	B	2	1	1
	P	1	0	1
	B	1	1	0
	K	2	1	1
	R	2	1	1
	L	1	1	0
	C	3	2	1
	No.			
	S	11	6	5
	C	8	5	3
	Max			
	M	30	30	30
	R	20–47	20–47	20–55
	CTV			
	M	17.4	20.5	14.3
	R	5.9–37.3	5.9–37.3	5.9–98.3
	M			
	M			
	PTV			
	M	39.6	39.6	31.5
	R	16.4–69.0	16.4–69.0	16.4–146.4
	Prev			
	Yes	11	7	4
	No	8	4	4
	Previous surgery at target site (No. of patients)			
	Yes	3	1	2
	No	16	10	6
	Total (No. of patients)	19	11	8

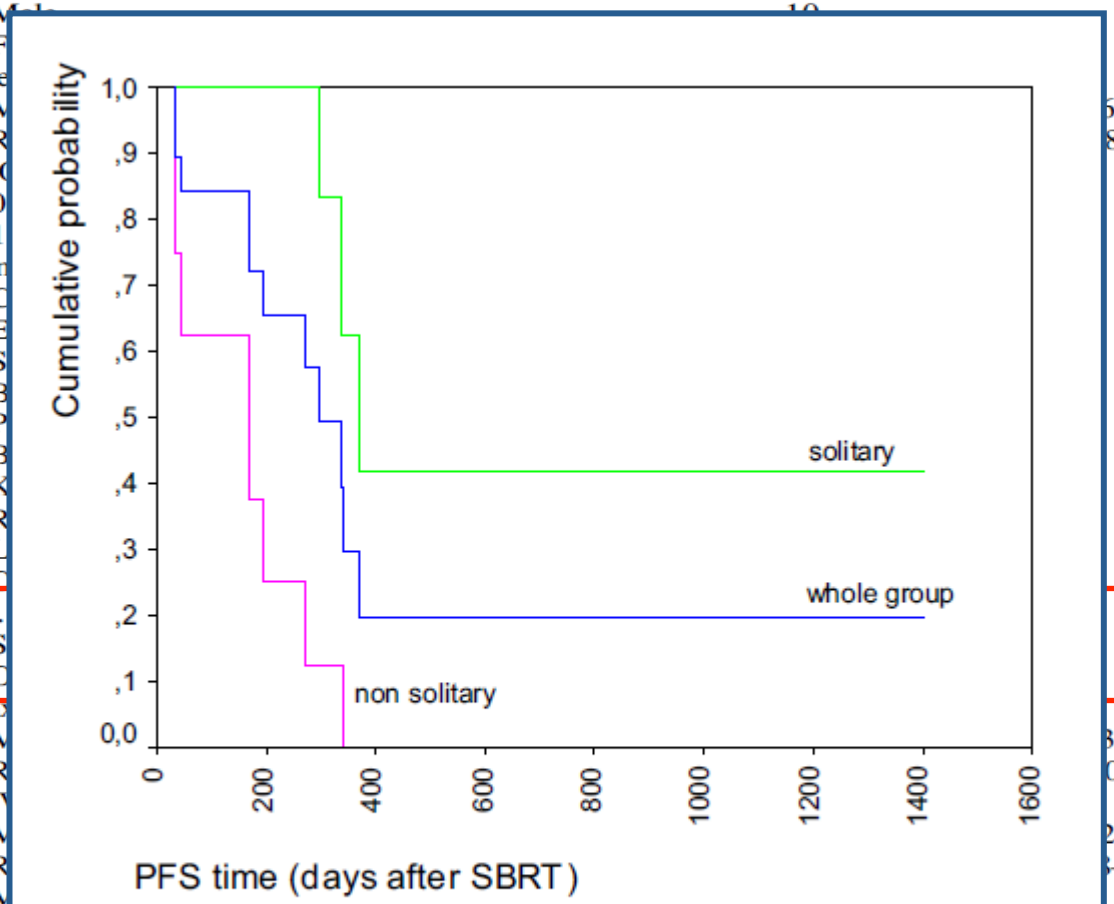


Fig. 3. Kaplan-Meier curve of progression-free survival (PFS): whole group vs. solitary metastases vs. nonsolitary oligometastases. SBRT = stereotactic body radiotherapy.

SBRT for oligometastatic patients with single abdominal lymph node recurrent cancer

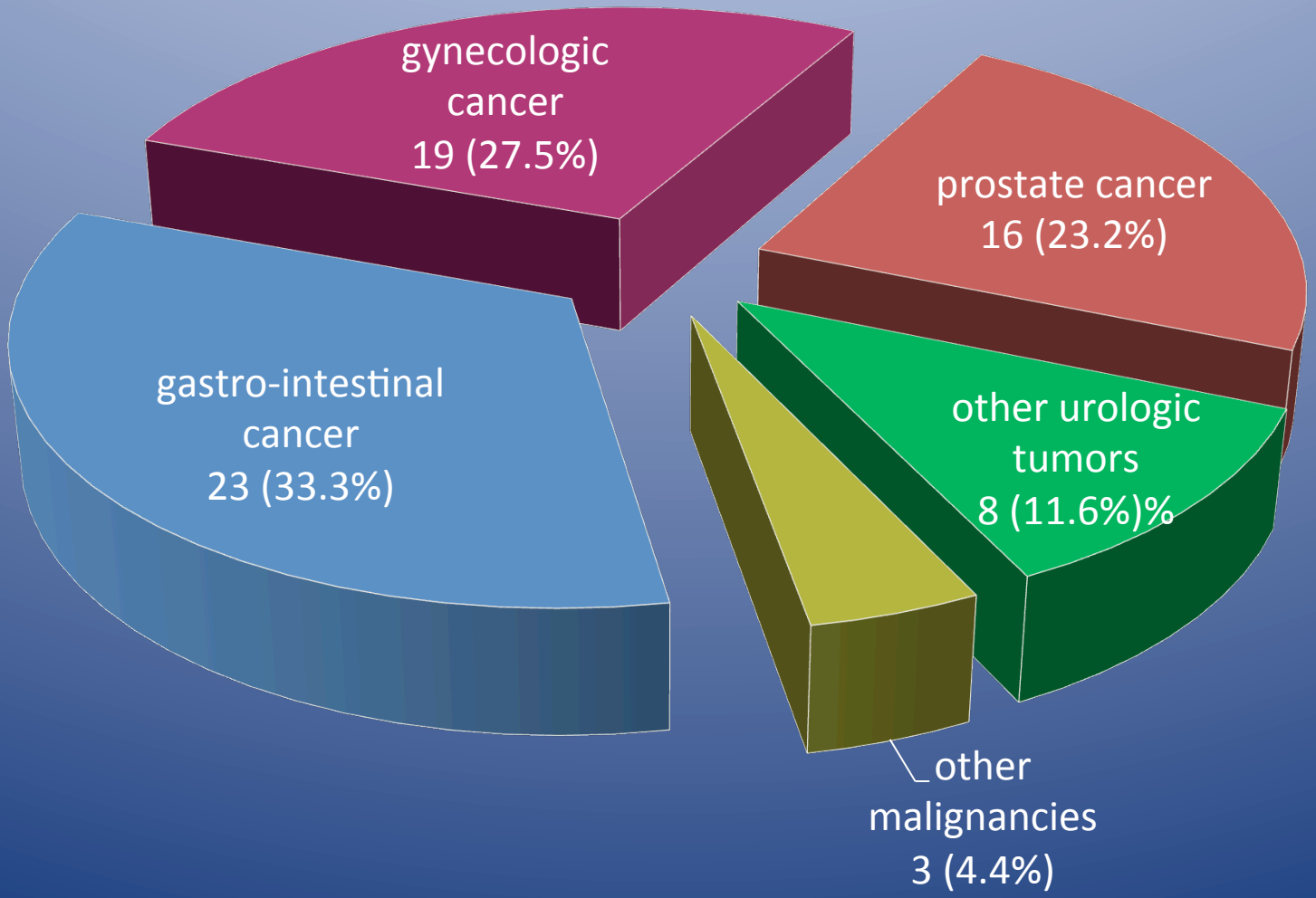
B. Jereczek-Fossa, G. Piperno, S. Ronchi, G. Catalano, C. Fodor, R. Cambria, P. Fossati, D. Zerini, C. Garibaldi, R. Orecchia,

UNIVERSITÀ DEGLI STUDI DI MILANO

European Institute of Oncology

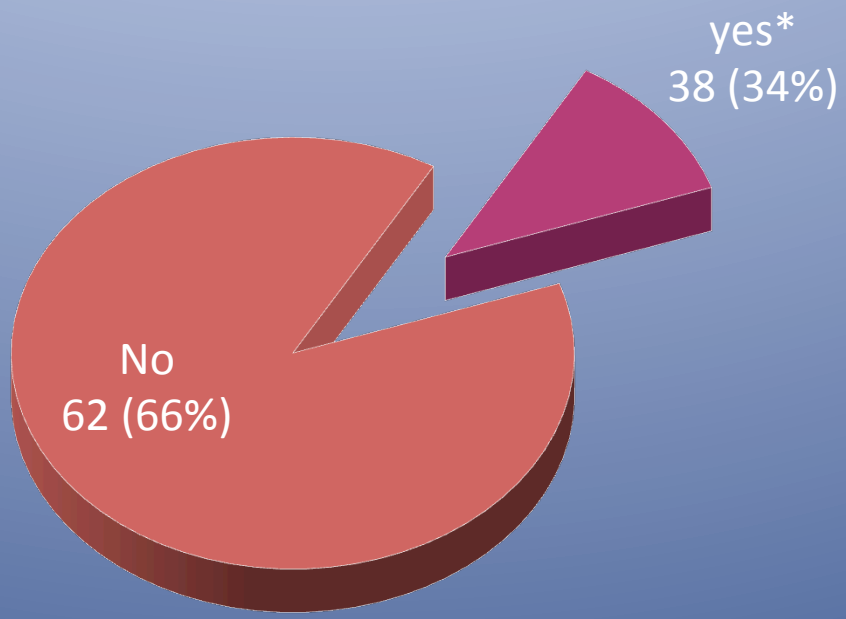
Characteristics	All patients N=69 or lesions n=94
Age (years), at the SBRT Mean±standard deviation	 63±11.4
Gender Male Female	 32 (46.4%) 37 (53.6%)
Interval between diagnosis of primary tumor and SBRT/per lesion (n=94) Mean (range) in months Median	 58 (3-251) **43**

Primary diagnosis (n=69 patients)



GTV volume **Median** Range GTV > 60 cc	**6.7 cc** 1.5-86.9 cc 3 lesions
PTV volume **Median** Range	**29.1 cc** 5-148.9 cc
SBRT regimens per lesion (n=94) **Median dose** Median BED_{2Gy} Median BED_{10Gy}	 **24 Gy/3 fr** 120 Gy (12-440 Gy) 43.2 Gy (7.2-120 Gy)

Acute toxicity (for all lesions, n=94)

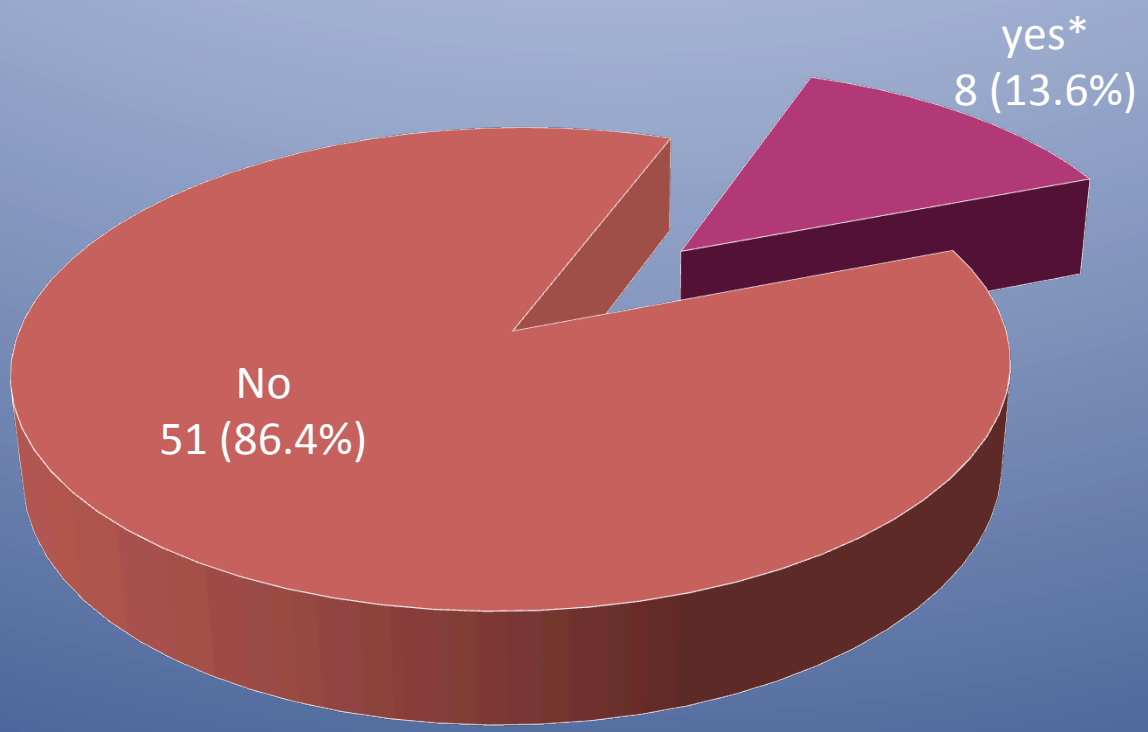


But only 2 RTOG/EORTC grade ≥3 acute events:

2 single events of urinary toxicity

-macroscopic hematuria
-urinary urgency and urethral stenosis; both: re-irradiation

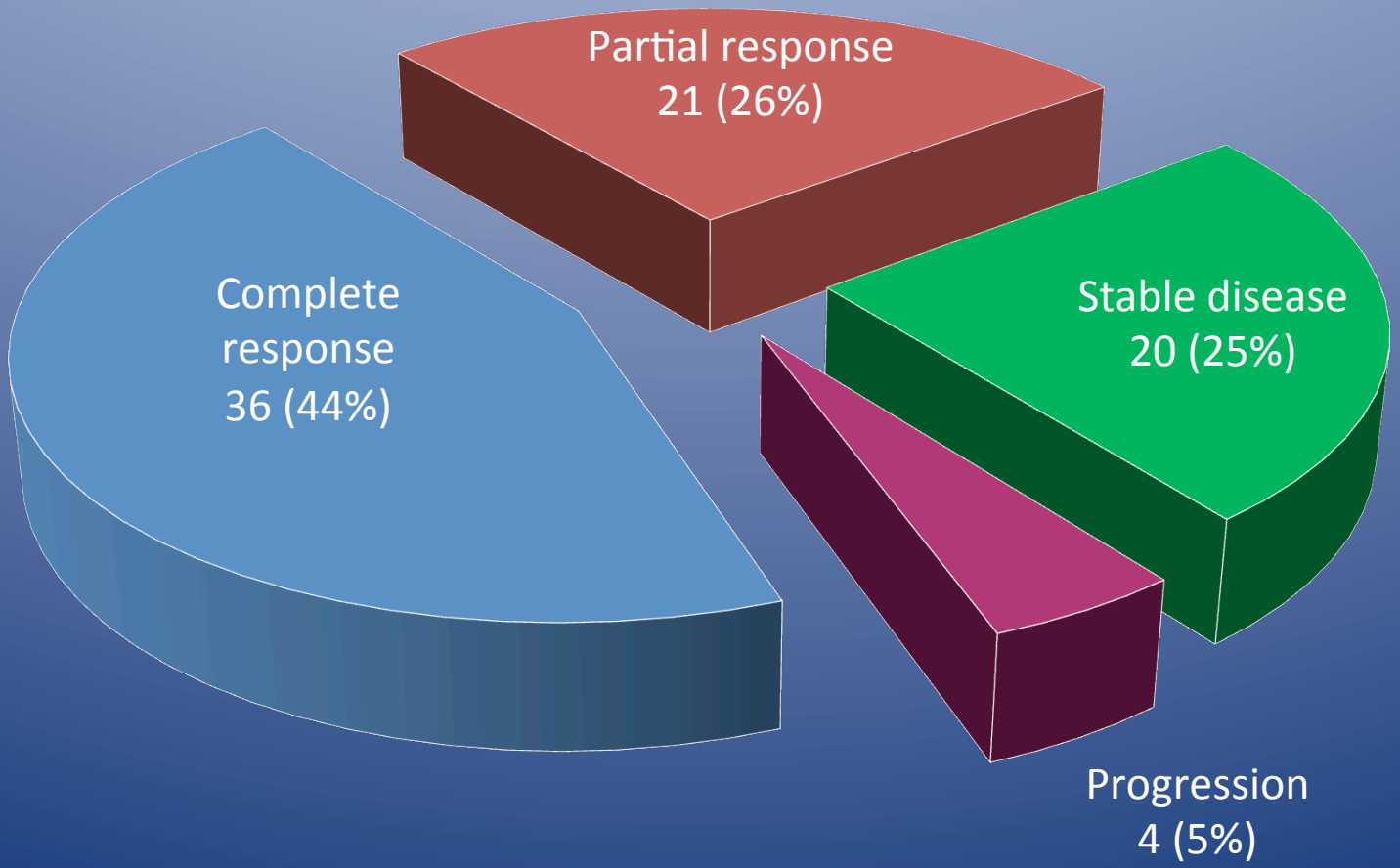
Late toxicity



1 severe late ≥ G3 event:

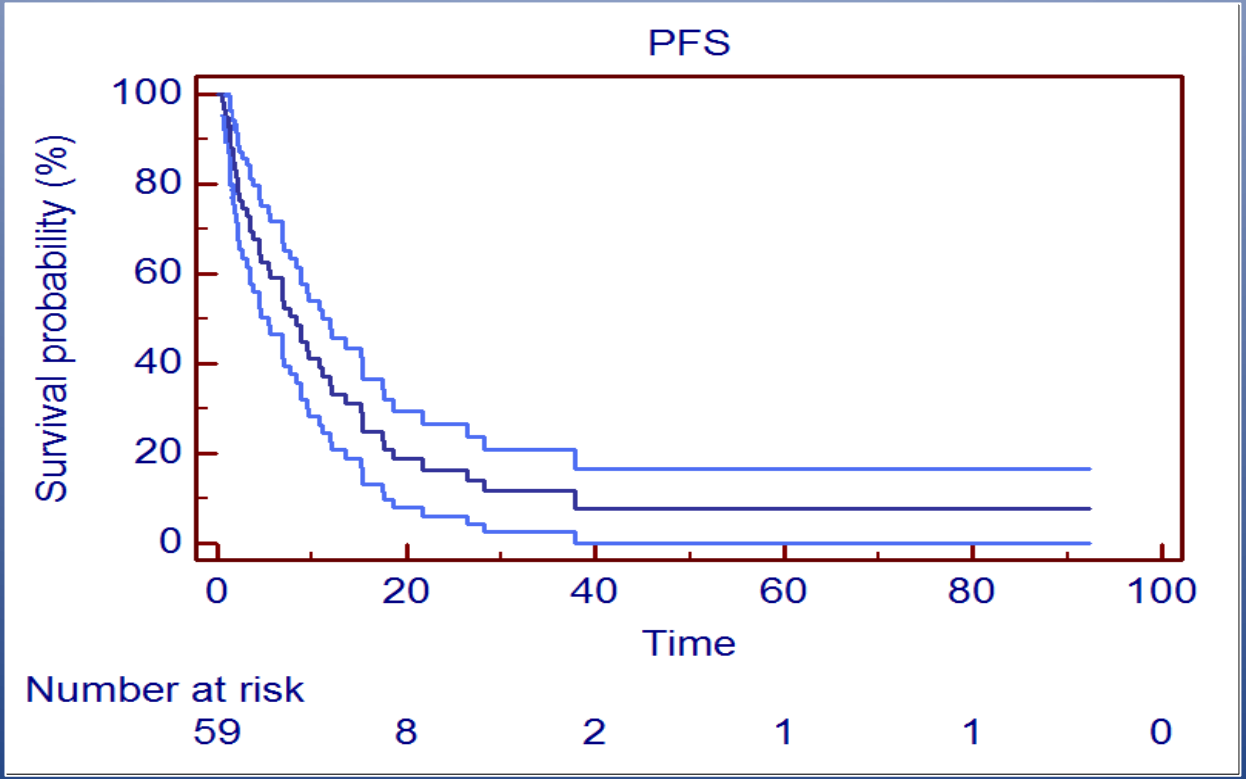
duodenal substenosis requiring endoscopic therapy

Radiological and/or FDG-or-choline-PET/CT response
(94 lesions, 81 evaluable)



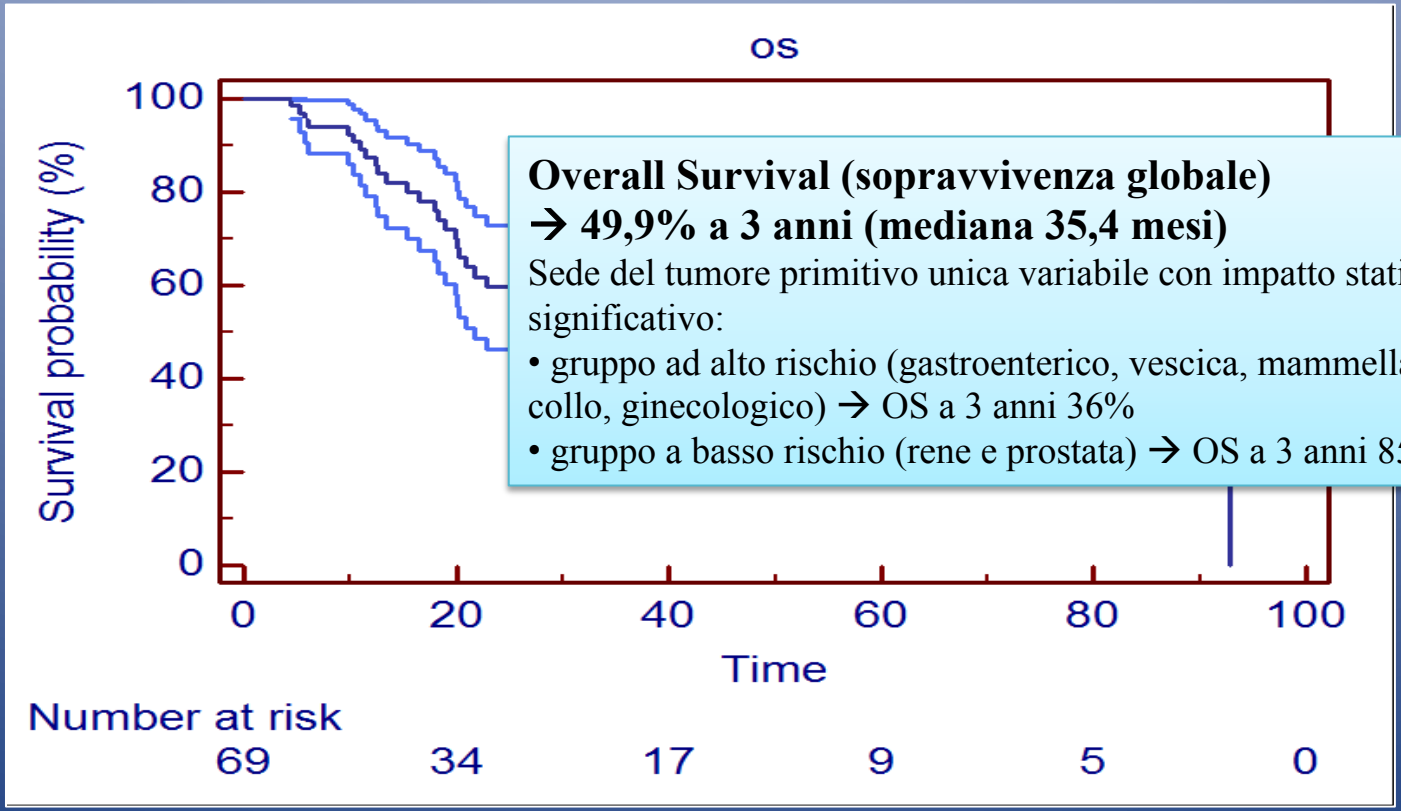
Progression free survival

actuarial 3-year progression free survival: 12%
patterns of failure: predominantly out-field



Overall survival

Actuarial 3-year overall survival:



Overall Survival (sopravvivenza globale)
→ 49,9% a 3 anni (mediana 35,4 mesi)
Sede del tumore primitivo unica variabile con impatto statisticamente significativo:
• gruppo ad alto rischio (gastroenterico, vescica, mammella, testa-collo, ginecologico) → OS a 3 anni 36%
• gruppo a basso rischio (rene e prostata) → OS a 3 anni 85%

Cancer/Radiothérapie 18 (2014) 342–349

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Revue générale

Radiothérapie stéréotaxique hypofractionnée des métastases osseuses

Hypofractionated stereotactic radiotherapy of bone metastases

B. Pichon[a], F. Thillays[a], C. Bourgier[b], M.-A. Mahé[a], S. Supiot[a,*]

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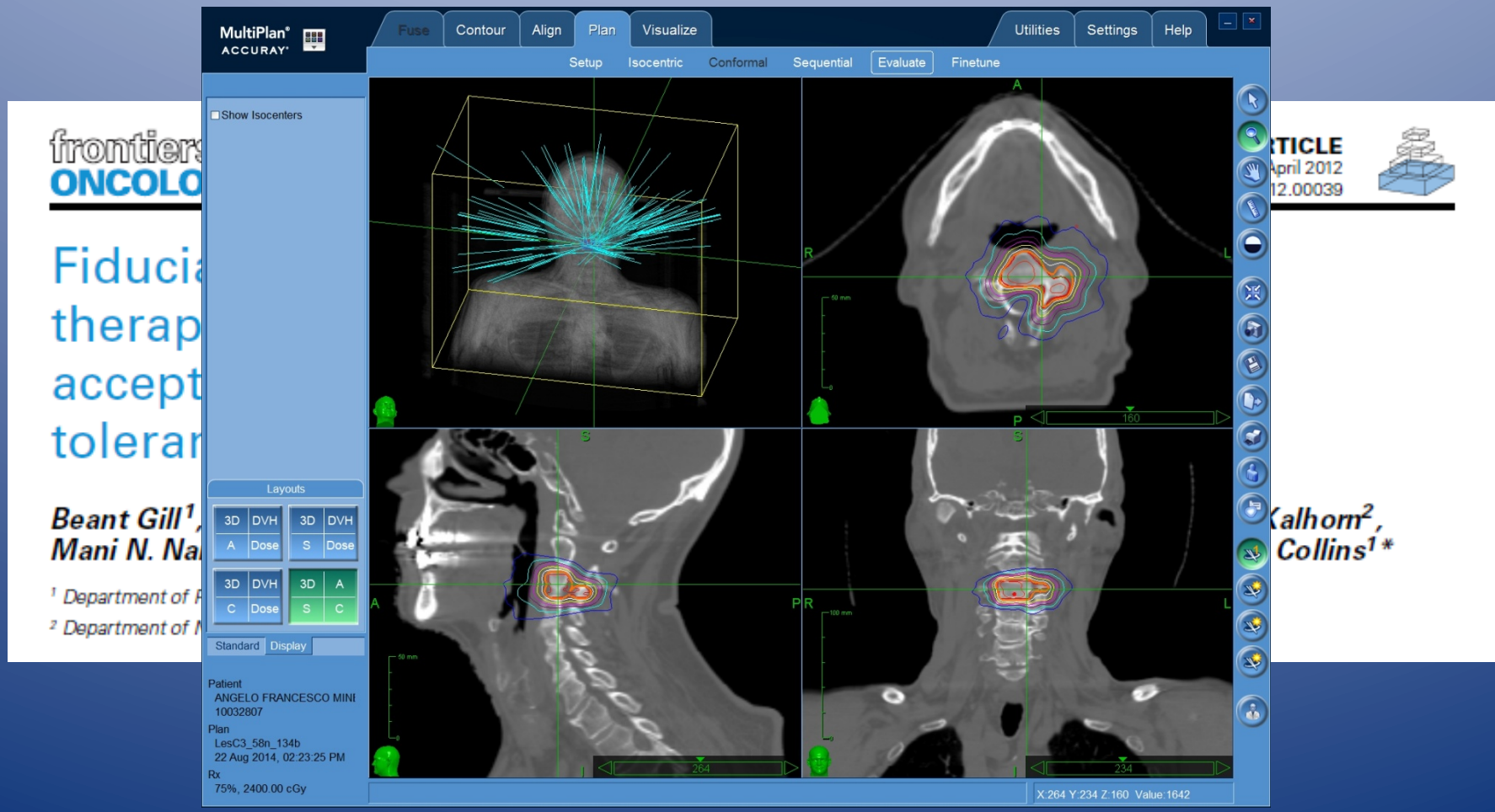
[b] *Service de radiothérapie, U896, institut régional du cancer de Montpellier, 34298 Montpellier, France*

Tableau 3
Contraintes aux organes à risque lors d'une irradiation stéréotaxique à fortes doses selon le fractionnement par Timmerman et al. [26].

	Cinq fractions	Trois fractions	Une seule séance
Moelle	Max 30 Gy $V22{,}5 < 0{,}25\ cm^3$ $V13{,}5 < 1{,}2\ cm^3$	Max 22 Gy $V18 < 0{,}25\ cm^3$ $V11 < 1{,}2\ cm^3$	Max 14 Gy $V10 < 0{,}25\ cm^3$ $V7 < 1{,}2\ cm^3$
Queue de cheval	Max 34 Gy $V30 < 5\ cm^3$	Max 24 Gy $V22 < 5\ cm^3$	Max 16 Gy $V14 < 5\ cm^3$
Œsophage	Max 32 Gy $V27{,}5 < 5\ cm^3$	Max 25 Gy $V21 < 5\ cm^3$	Max 19 Gy $V14 < 5\ cm^3$
Cœur	Max 38 Gy $V32 < 15\ cm^3$	Max 30 Gy $V24 < 15\ cm^3$	Max 22 Gy $V16 < 15\ cm^3$
Estomac	Max 32 Gy $V28 < 10\ cm^3$	Max 24 Gy $V21 < 5\ cm^3$	Max 16 Gy $V13 < 10\ cm^3$
Poumons (droit et gauche – volume-cible prévisionnel)	$V12{,}5 < 1500\ cm^3$ $V13{,}5 < 1000\ cm^3$	$V20\ Gy < 20\ \%$ $V10 < 30\ \%$ $V5 < 50\ \%$	$V5 < 50\ \%$ $V7 < 1500\ cm^3$
Peau	Max 32 Gy	Max 24 Gy	$V14 < 10\ cm^3$
Trachée	Max 38 Gy $V32 < 15\ cm^3$	Max 30 Gy $V24 < 15\ cm^3$	Max 22 Gy $V16 < 15\ cm^3$
Jéjunum/iléon	Max 35 Gy $V19{,}5 < 5\ cm^3$	Max 27 Gy $V16 < 5\ cm^3$	Max 19 Gy $V10 < 5\ cm^3$
Rectum	Max 38 Gy $V25 < 20\ cm^3$	Max 30 Gy $V20 < 20\ cm^3$	Max 22 Gy $V11 < 20\ cm^3$
Vessie	Max 38 Gy $V18{,}3 < 15\ cm^3$	Max 30 Gy $V15 < 15\ cm^3$	Max 22 Gy $V9 < 15\ cm^3$
Reins droit et gauche	$V17{,}5 < 200\ cm^3$	$V15 < 33\ \%$	$V8 < 200\ cm^3$

Vx : volume recevant *x* Gy ; Max : maximum.

Cyberknife per metastasi vertebrali: single shot



Clinical Study

Radiotherapy for Oligometastases and Oligo-Recurrence of Bone in Prostate Cancer

Ken-ichi Tabata,[1] Yuzuru Niibe,[2] Takefumi Satoh,[1] Hideyasu Tsumura,[1] Masaomi Ikeda,[1] Satoru Minamida,[1] Tetsuo Fujita,[1] Daisuke Ishii,[1] Masatsugu Iwamura,[1] Kazushige Hayakawa,[2] and Shiro Baba[1]

[1] *Department of Urology, Kitasato University School of Medicine, 1-15-1 Kitasato, Minami-ku, Sagamihara, Kanagawa 252-0375, Japan*

[2] *Department of Radiology and Radiation Oncology, Kitasato University School of Medicine, 1-15-1 Kitasato, Minami-ku, Sagamihara, Kanagawa 252-0375, Japan*

Table 2: Treatment characteristics.

Variables	Total $n = 35$
Total radiation dose (Gy)	40 (30–50)[†]
Biological effective dose (Gy_3)	67 (50–92)[†]
Reasons for radiotherapy	
Pain	16 (45.7%)
Spinal cord compression	2 (5.7%)
Prevention for SREs	17 (48.6%)
Treatment site	
Spine	15 (42.9%)
Femur	17 (48.6%)
Pelvis/hip	3 (8.6%)
Sternum	1 (2.8%)
Ribs	2 (5.7%)
Overall treatment time (days)	28 (12–43)[†]

Abbreviations. SREs: skeletal-related events.
[†]Median (range).

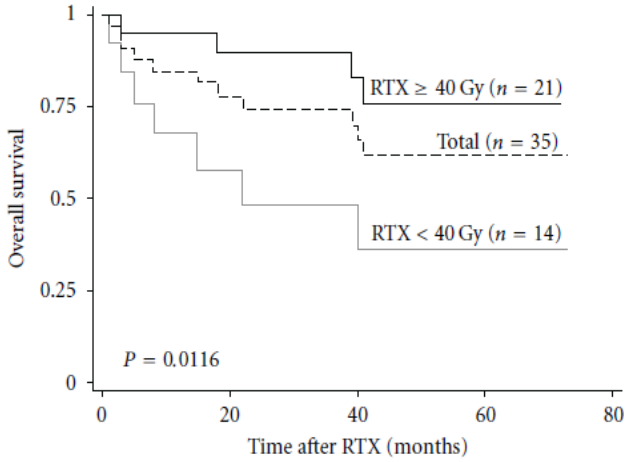
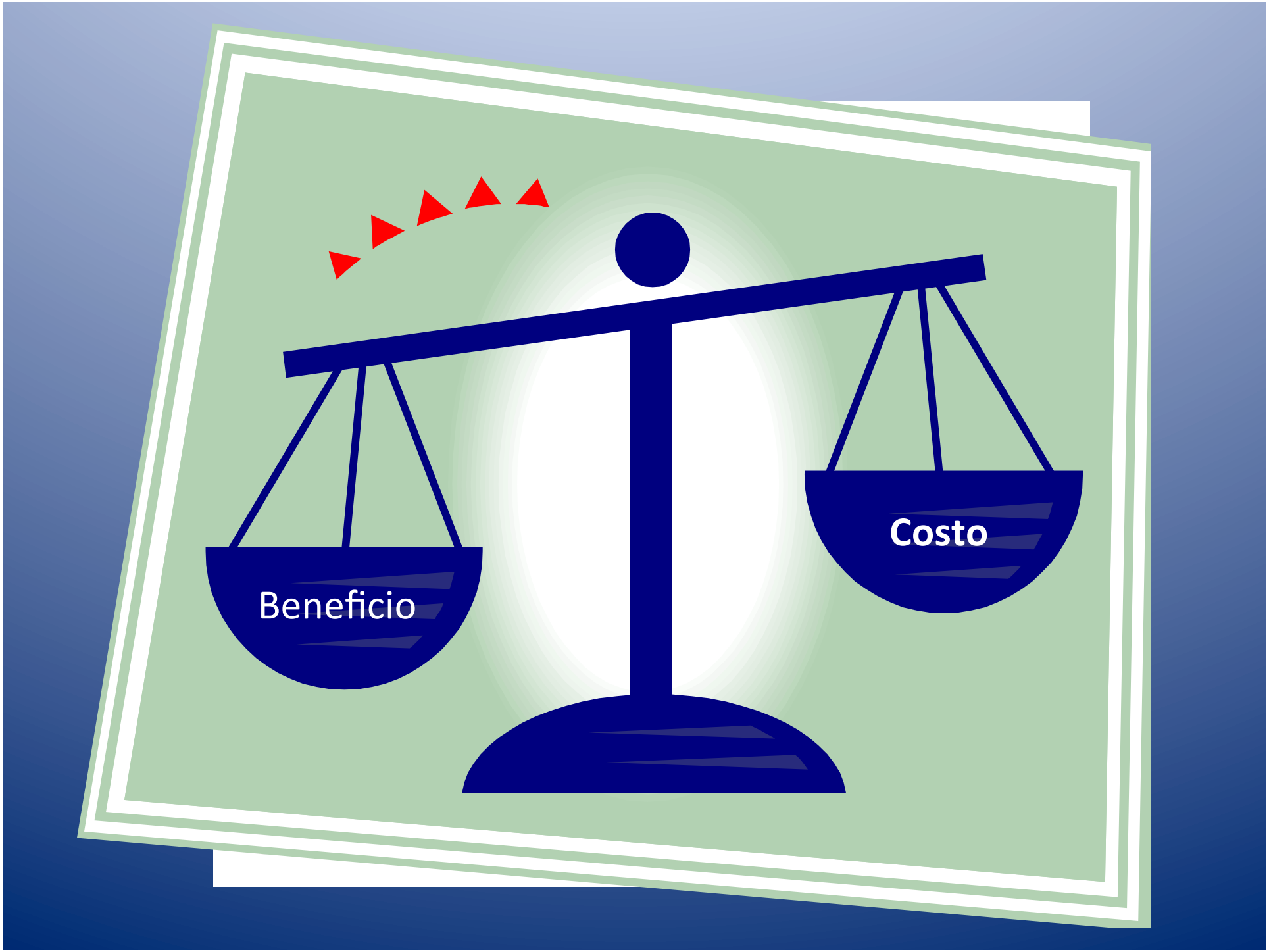


Figure 1: The overall survival curves for all patients ($n = 35$) and those that received a total radiotherapy dose of ≥40 Gy ($n = 21$) or <40 Gy ($n = 14$). RTX, radiotherapy.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European Association of Urology

Platinum Priority – Review – Prostate Cancer

Editorial by XXX on pp. x–y of this issue

Metastasis-directed Therapy of Regional and Distant Recurrences After Curative Treatment of Prostate Cancer: A Systematic Review of the Literature

Piet Ost[a,*], *Alberto Bossi*[b], *Karel Decaestecker*[c], *Gert De Meerleer*[a], *Gianluca Giannarini*[d], *R. Jeffrey Karnes*[e], *Mack Roach III*[f], *Alberto Briganti*[g]

Table 1 – Full-text publications of

Study	No. of patients	Adjuvant ADT (%)	Median duration ADT	Prophylactic nodal radiotherapy (%)
Casamassima et al. [23]	25	None	NA	7 (28)
Muacevic et al. [24]	40	27 (68)	NR	NA
Würschmidt et al. [25]	15	NR	NR	15 (100)
Ahmed et al. [26]	17	15 (88)	NR	NA
Jereczek-Fossa et al. [27]	19	19 (100)	12–17 mo	None
Schick et al. [28]	50	49 (98)	12 mo	25 (50)
Decaestecker et al. [29]	50	35 (70)	1 mo	None
Picchio et al. [30]	83	58 (70)	NR	77 (93)
Rinnab et al. [31]	15	11 (73)	NR	1 (7)
Schilling et al. [32]	10	6 (60)	NR	None
Winter et al. [33]	6	None	NA	None
Busch et al. [37]	6	6 (100)	Lifelong ADT	None
Jilg et al. [34]	47	34 (65)	NR	27 (52)
Martini et al. [35]	8	None	NA	None
Suardi et al. [36]	59	24 (41)	24 mo	21 (36)

ADT = androgen-deprivation therapy; C
resonance imaging; NA = not applicable
PSA = prostate-specific antigen; SBRT = s
* Mean numbers reported instead of me
** Median estimated from curves.

etastasis-directed therapy; MRI = magnetic
mography; PFS = progression-free survival;

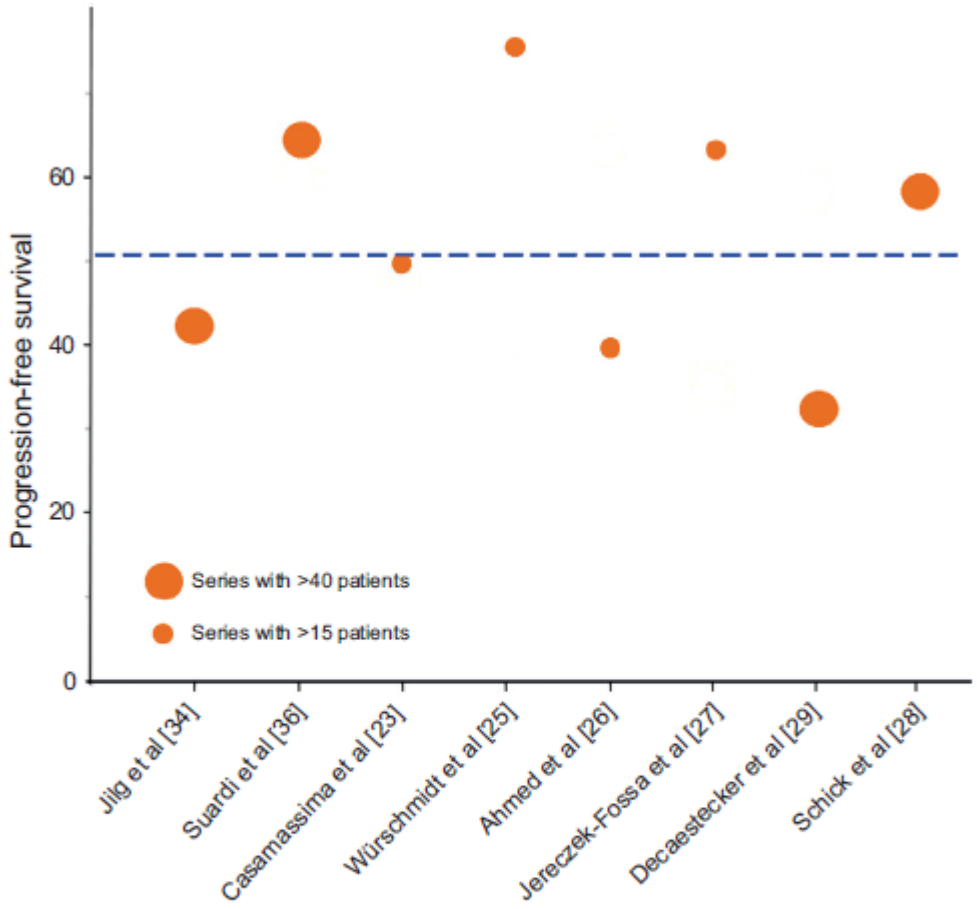

Fig. 2 – Progression-free survival in patients with oligometastatic prostate cancer recurrence at 1–3 yr of follow-up for studies with >15 patients. Dotted line represents mean proportion of patients who were progression free at the reported time point, weighted for the total number of patients.

Table 4 – Complications associated with metastasis-directed therapy for oligometastatic prostate cancer recurrence: (a) complications associated with radiotherapy according to Common Terminology Criteria for Adverse Events; (b) complications associated with salvage lymph node dissection according to the Clavien-Dindo classification

a.

Complication type	Muacevic et al. [24] (*n* = 40), no. (%)	Würschmidt et al.* [25] (*n* = 15), no. (%)	Ahmed et al. [26] (*n* = 17), no. (%)	Jereczek-Fossa et al. [27] (*n* = 19), no. (%)	Decaestecker et al. [29] (*n* = 50), no. (%)	Total (*n* = 141), no. (%)
Grade 1						
Bone pain	0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	3 (2)
Asymptomatic fracture	1 (2.5)	0 (0)	0 (0)	0 (0)	1 (2)	2 (1.4)
Fatigue	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (0.7)
Rectal toxicity	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	2 (1.4)
Urinary toxicity	0 (0)	0 (0)	0 (0)	2 (11)	0 (0)	2 (1.4)
Grade 2						
Nausea requiring antiemetics	5 (12.5)	0 (0)	0 (0)	0 (0)	0 (0)	5 (3.5)
Rectal toxicity	0 (0)	2 (13.3)	0 (0)	1 (5)	2 (4)	5 (3.5)
Urinary toxicity	0 (0)	0 (0)	0 (0)	1 (5)	1 (2)	2 (1.4)
Grade 3						
Urinary toxicity	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	1 (0.7)

b.

Complication type	Rinnab et al. [31] (*n* = 15), no. (%)	Busch et al. [37] (*n* = 6), no. (%)	Jilg et al. [34] (*n* = 47), no. (%)	Suardi et al. [36] (*n* = 59), no. (%)	Total (*n* = 127), no. (%)
Grade 1					
Lymphorrhea	0 (0)	0 (0)	4 (7.7)	12 (20.3)	16 (12.5)
Fever	0 (0)	0 (0)	3 (5.8)	18 (30.5)	21 (16.5)
Temporary weakness of the hip flexor	0 (0)	0 (0)	1 (1.9)	0 (0)	1 (0.8)
Wound dehiscence	0 (0)	0 (0)	3 (5.8)	0 (0)	3 (2.3)
Grade 2					
Deep vein thrombosis	0 (0)	0 (0)	0 (0)	1 (1.7)	1 (0.8)
Ileus	1 (7)	0 (0)	0 (0)	12 (20.3)	13 (10.2)
Grade 3a					
Lymphocele requiring drainage	1 (7)	0 (0)	2 (3.9)	7 (11.2)	10 (7.8)
Wound dehiscence	0 (0)	0 (0)	0 (0)	3 (5.1)	3 (2.3)
Hydronephrosis requiring stenting	1 (7)	0 (0)	0 (0)	0 (0)	1 (0.8)
Grade 3b					
Lymphocele requiring surgical drainage	0 (0)	0 (0)	0 (0)	1 (1.7)	1 (0.8)

* One patient experienced a grade 4 toxicity: bladder shrinkage requiring cystectomy with urinary derivation. This patient received radiotherapy to the prostate gland and metastatic nodes for a recurrence in the seminal vesicle and iliac nodes after previous brachytherapy to the prostate.


E domani……

SBRT per la malattia oligometastatica: disegno di studio randomizzato

Palma *et al. BMC Cancer* 2012, **12**:305
http://www.biomedcentral.com/1471-2407/12/305

BMC Cancer

STUDY PROTOCOL **Open Access**

Stereotactic ablative radiotherapy for comprehensive treatment of oligometastatic tumors (SABR-COMET): Study protocol for a randomized phase II trial

David A Palma[1*], Cornelis J A Haasbeek[2], George B Rodrigues[1], Max Dahele[2], Michael Lock[1], Brian Yaremko[1], Robert Olson[3], Mitchell Liu[3], Jason Panarotto[4], Gwendolyn H M J Griffioen[2], Stewart Gaede[1], Ben Slotman[2] and Suresh Senan[2]

Abstract

Background: Stereotactic ablative radiotherapy (SABR) has emerged as a new treatment option for patients with oligometastatic disease. SABR delivers precise, high-dose, hypofractionated radiotherapy, and achieves excellent rates of local control. Survival outcomes for patients with oligometastatic disease treated with SABR appear promising, but conclusions are limited by patient selection, and the lack of adequate controls in most studies. The goal of this multicenter randomized phase II trial is to assess the impact of a comprehensive oligometastatic SABR treatment program on overall survival and quality of life in patients with up to 5 metastatic cancer lesions, compared to patients who receive standard of care treatment alone.

Methods: After stratification by the number of metastases (1-3 vs. 4-5), patients will be randomized between Arm 1: current standard of care treatment, and Arm 2: standard of care treatment + SABR to all sites of known disease. Patients will be randomized in a 1:2 ratio to Arm 1:Arm 2, respectively. For patients receiving SABR, radiotherapy dose and fractionation depends on the site of metastasis and the proximity to critical normal structures. This study aims to accrue a total of 99 patients within four years. The primary endpoint is overall survival, and secondary endpoints include quality of life, toxicity, progression-free survival, lesion control rate, and number of cycles of further chemotherapy/systemic therapy.

Discussion: This study will provide an assessment of the impact of SABR on clinical outcomes and quality of life, to determine if long-term survival can be achieved for selected patients with oligometastatic disease, and will inform the design of a possible phase III study.

Trial registration: Clinicaltrials.gov identifier: NCT01446744

Keywords: Oligometastases, Stereotactic radiotherapy, Quality of life, Cancer, Survival

SABR-COMET

- Pz con sino a 5 M+ (osso, polmone,fegato, cervello) non più di 3 M+ per singolo organo e se possibile confermate da biopsia
- P.S.: ECOG 0-1, aspettativa di vita > 6 mesi
- Stratificazione pz: 1-3 vs 4-5 metastasi
- Randomizzazione: RT palliativa (schemi convenzionali) vs RT stereotassica
- No CHT concomitante; OT permessa

Palma *et al. BMC Cancer* 2012, **12**:305
http://www.biomedcentral.com/1471-2407/12/305

Arruolamento 2012→2016

Analisi dati 2017!

determine if long-term survival can be achieved for selected patients with oligometastatic disease, and will inform the design of a possible phase III study.

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Editorial

Prostate Radiotherapy for Men with Metastatic Disease: A New Comparison in the STAMPEDE Trial[1]

C.C. Parker [*], M.R. Sydes [†], M.D. Mason [‡], N.W. Clarke [§], D. Aebersold [¶], J.S. de Bono [**], D.P. Dearnaley [**], A.W.S. Ritchie [†], J.M. Russell [††], G. Thalmann [¶], M.K.B. Parmar [†], N.D. James [||]

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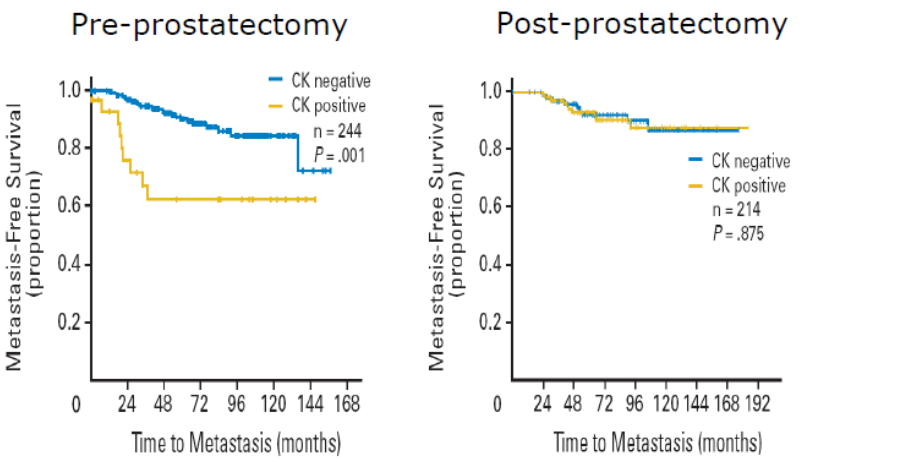
Received 9 January 2013; accepted 22 January 2013

Abscopal effect: prostate

Hypothesis

- The use of radiotherapy to the prostate will retard progression of the metastases in men presenting with metastatic prostate cancer

Supporting evidence: prostate cancer



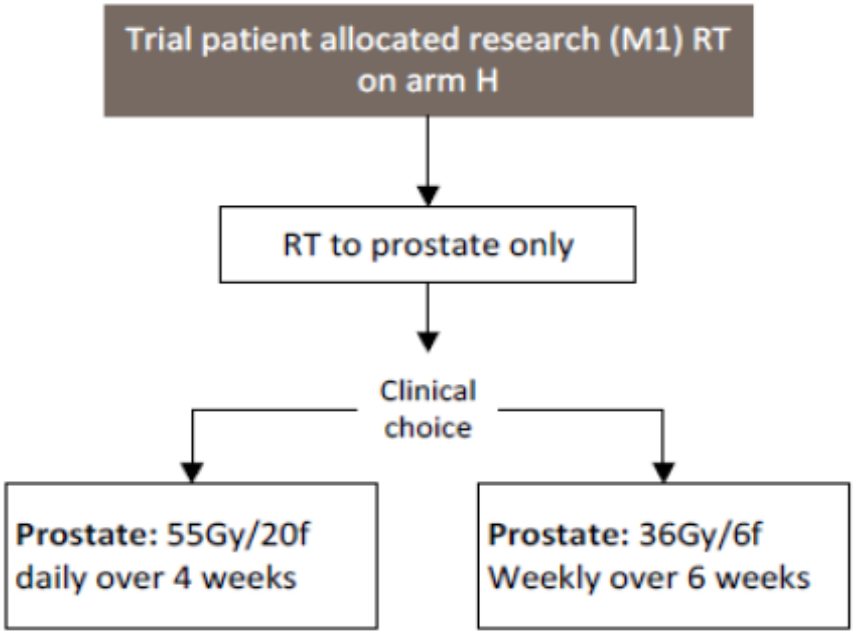
Weckermann JCO 2009; 27(10): 1549-56

Inference: The primary tumour may be required to stimulate disseminated tumour cells to grow into metastases

Current arms recruiting protocol 9.0

Patients eligible for STAMPEDE

Research (M1) Prostate Radiotherapy



[1] Except pts with a contra-indication to RT
[2] All suitable pts with newly diagnosed locally advanced disease should also have RT to the prostate

Decaestecker *et al. BMC Cancer* 2014, **14**:671
http://www.biomedcentral.com/1471-2407/14/671

BMC Cancer

STUDY PROTOCOL **Open Access**

Surveillance or metastasis-directed Therapy for OligoMetastatic Prostate cancer recurrence (STOMP): study protocol for a randomized phase II trial

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Background: Metastases-directed therapy (MDT) with surgery or stereotactic body radiotherapy (SBRT) is emerging as a new treatment option for prostate cancer (PCa) patients with a limited number of metastases (≤3) at recurrence – so called "oligometastases". One of the goals of this approach is to delay the start of palliative androgen deprivation therapy (ADT), with its negative impact on quality of life. However, the lack of a control group, selection bias and the use of adjuvant androgen deprivation therapy prevent strong conclusions from published studies.
The aim of this multicenter randomized phase II trial is to assess the impact of MTD on the start of palliative ADT compared to patients undergoing active surveillance.

Methods/Design: Patients with an oligometastatic recurrence, diagnosed on choline PET/CT after local treatment with curative intent, will be randomised in a 1:1 ratio between arm A: active surveillance only and arm B: MTD followed by active surveillance. Patients will be stratified according to the location of metastasis (node vs. bone metastases) and PSA doubling time (≤3 vs. > 3 months). Both surgery and SBRT are allowed as MDT. Active surveillance means 3-monthly PSA testing and re-imaging at PSA progression. The primary endpoint is ADT-free survival. ADT will be started in both arms at time of polymetastatic disease (>3 metastatic lesions), local progression or symptoms. The secondary endpoints include progression-free survival, quality of life, toxicity and prostate-cancer specific survival.

TAKE HOME MESSAGES

- Accurata selezione dei pz oligometastatici (N° lesioni, sede→ favorevole quella linfonodale ed ossea)
- Valutazione dei pz nell'ambito di gruppi multidisciplinari
- Ottimizzazione delle tecniche di imaging
- Utilizzo di tecniche radioterapiche speciali: controllo locoregionale con radioterapia stereotassica superiore ad altre potenziali cure oncologiche
- Partecipazione a protocolli di studio cooperativi