Associazione Italiana Radioterapia e Oncologia clinica

Società Italiana di Radiobiologia

EFFICACY AND SAFETY OF STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN OLIGOMETASTATIC UTERINE CANCER (MITO-RT2/RAD STUDY): A LARGE, MULTICENTER, RETROSPECTIVE STUDY IN COLLABORATION with MITO, AIRO GYN, and MaNGO GROUPS

Gabriella MACCHIA
on behalf of MITO, AIRO Gyn, and MANGO groups

UOS Radioterapia a Fasci Esterni Molise ART

Gemelli Molise - Campobasso

Associazione Italiana Radioterapia e Oncologia clinica
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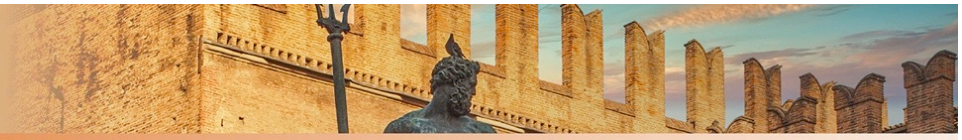


DICHIARAZIONE

Relatore: GABRIELLA MACCHIA

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(Consultant/MSD (Italia) s.r.l, a subsidiary of Merck & Co)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazione ad Advisory Board **(Relatore/AstraZeneca S.p.A.)**
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Altro

Recurrent/Metastatic Endometrial Cancer: Overview

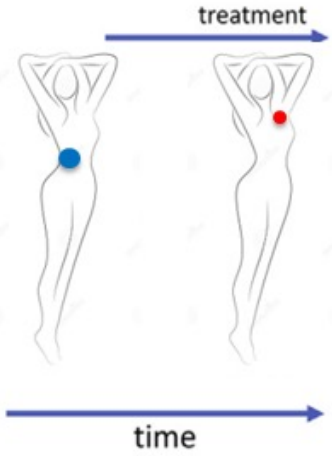
- EC is the most common gynecologic malignancy in women in the developed world with 65, 950 new EC diagnoses per year as well 12,550 deaths in 2022
- The incidence of EC is increasing annually by an estimated 1% to 2%; it is predicted to double by 2030 in the US
- Prognosis: 5-yr survival rates
  - Stage I: 95%
  - Stage IV: metastatic: 17.3%
- Systemic approaches: Chemotherapy, IO, Target, Hormonal therapies
- Locoregional approaches: Radiotherapy, Interventional radiology, chemoembolization, etc.

Zhang. Front Oncol. 2019;9:1440. Bray. CA Cancer J Clin. 2018;68:394. Siegel 2020. CA Cancer J Clin. 2020;70:7.

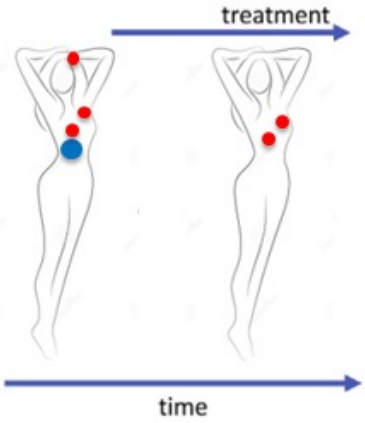
Oligometastatic scenario

De novo synchronous oligometastastic disease

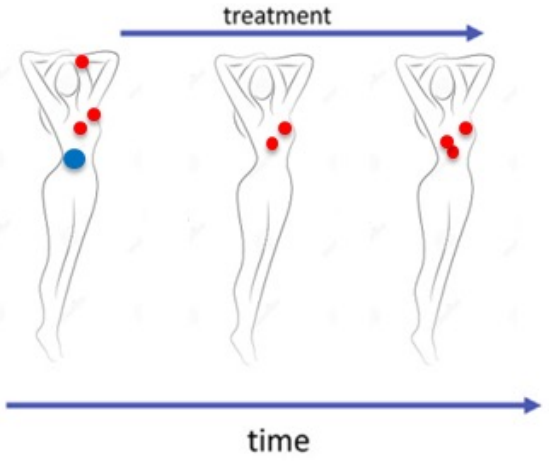
De novo metachronous oligometastastic disease



Oligopersistent disease

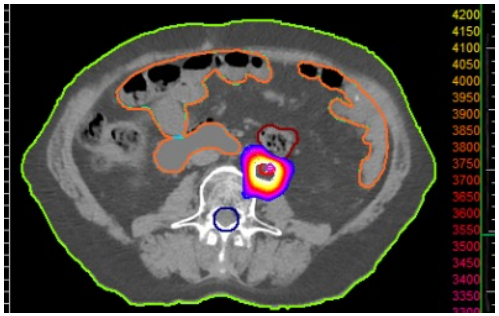


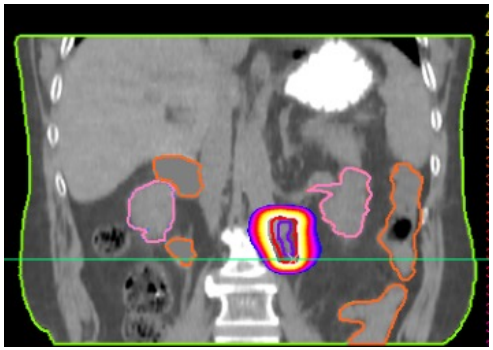
Oligoprogression

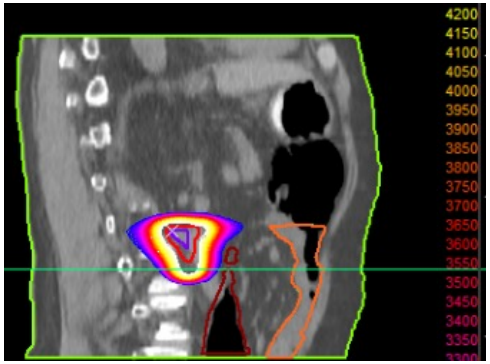


SBRT

- High dose/short time
- Minimally invasive
- Highly precise image-guided radiation delivery.
- High local control
- Minimal toxicities
- Retreatment
- Safely administered during CT
- Active in chemoresistant disease
- Immune response activator
- Synergic with immunotherapy and PARPi







Editorial

Stereotactic ablative radiotherapy: what's in a name?

Billy W. Loo Jr MD, PhD[a,*], Joe Y. Chang MD, PhD[b], Laura A. Dawson MD, FRCPC[c], Brian D. Kavanagh MD, MPH[d], Albert C. Koong MD, PhD[a], Suresh Senan MRCP, FRCR, PhD[e], Robert D. Timmerman MD[f]

Retrospective, multicenter study in a large, real-life dataset of MPR uterine patients

- Molise ART
- Gemelli ART Roma
- Pisa
- S. Raffaele-Milano
- Terni
- Campus Bio Medico-RM
- S. Andrea-RM
- Bologna
- Udine
- Biella
- Firenze
- Lecce
- Ancona
- S. Giovanni Rotondo

MITO RT-2

14 Centers, 157 patients, 272 lesions

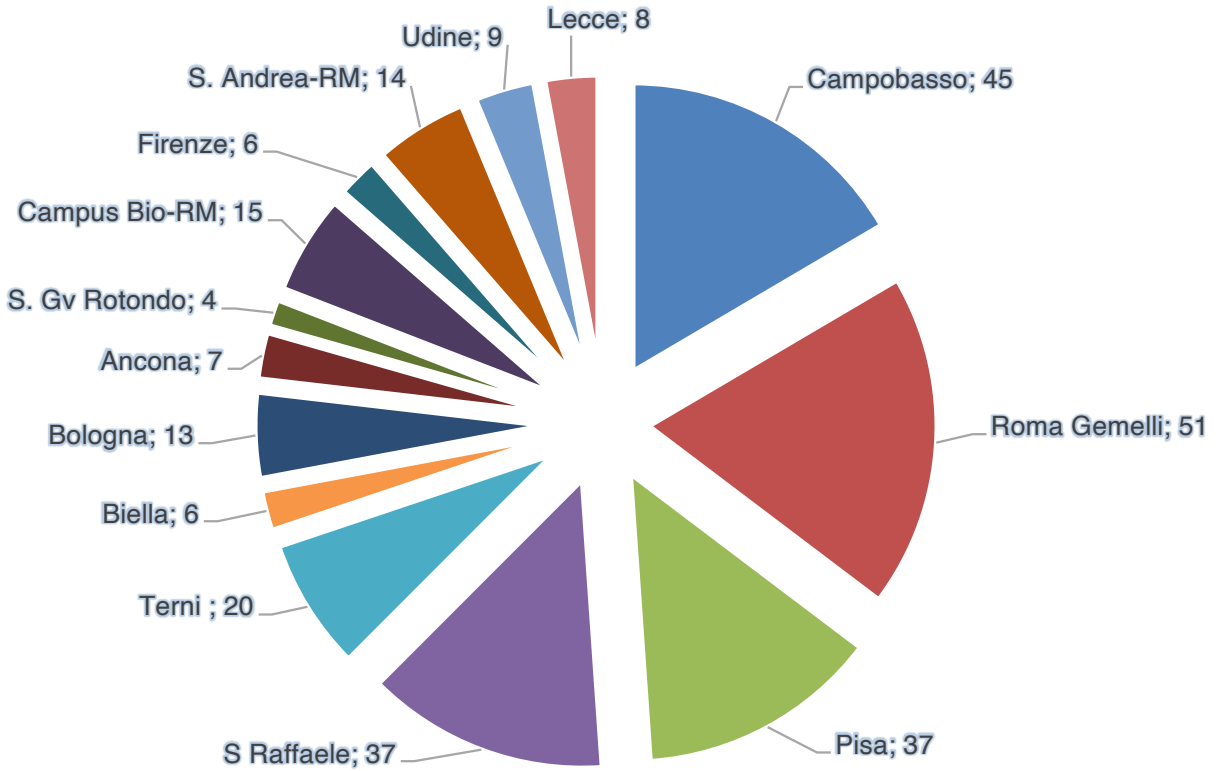
•Primary end-point:

Clinical complete response per lesion

•Secondary end-points:

•**Acute and Late Toxicities**

Lesions per Center



Patient characteristics

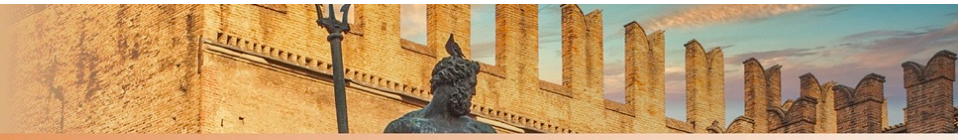
	N. (%)
All	157
Age, years	
Median (range)	69.7 (36.0-90.5)
Eastern Cooperative Oncology Group Performance Status	
0	111 (70.7)
1	40 (25.5)
2	6 (3.8)
Comorbidities per patient	
0	42 (26.9)
1	45 (28.8)
2	34 (21.8)
3	16 (10.3)
4	7 (4.6)
≥5	6 (3.8)
n.a.	6 (3.8)
Histotype	
Endometroid	116 (73.9)
Carcinosarcoma	14 (8.9)
Serous	13 (8.3)
Other	14 (8.9)

N. patients undergoing surgery before SBRT	
No	7 (4.5)
Yes	150 (95.5)
N. patients undergoing chemotherapy before SBRT	
No	42 (26.8)
Yes	110 (70.1)
n.a.	5 (3.1)
N. of lines of previous chemotherapies	
Median (range)	1 (1-6)
N. patients undergoing previous radiotherapy	
No	41 (26.1)
Yes	116 (73.9)
N. patients undergoing previous *in site*[a] radiotherapy	
No	91 (78.4)
Yes	25 (21.6)
N. of patients bearing	
1 lesion	97 (61.8)
2 lesions	34 (21.7)
3 lesions	14 (8.9)
4 lesions	1 (0.6)
5 lesions	8 (5.1)
>5 lesions	3 (1.9)

[a] calculated on the number of patients undergoing previous radiotherapy (N=116)

Features of lesions

	N.(%)
	272
Type of lesion(s)	
Lymph node	137 (50.4)
Parenchyma	135 (49.6)
Anatomical district	
Brain	16 (5.9)
Neck	2 (0.8)
Thorax	104 (38.3)
Abdomen	76 (27.9)
Pelvis	66 (24.2)
Bone	8 (2.9)
GTV	
Median, range (cm^3)	4.0 (0.05-181.10)
PTV	
Median, range (cm^3)	13.7 (2.0-196.5)



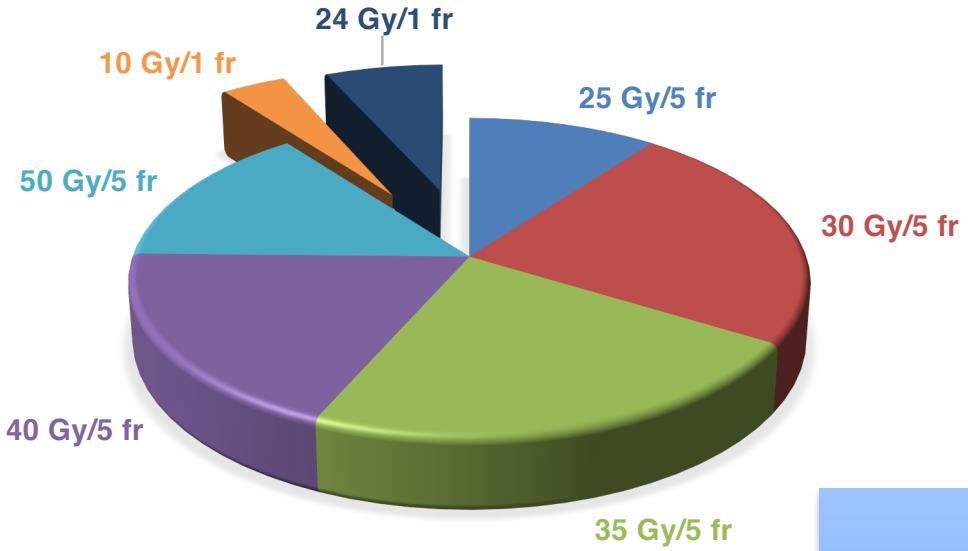
Details of treatment (272 lesions)

Total dose, Gy	
Median (range)	35 (10-75.2)
N. of fractions	
Median (range)	5 (1-10)
$BED_{\alpha/\beta 10}$	
Median (range)	59.5 (20.0-156.1)
Referral dose	
Specific isodose	120 (44.1)
Isocenter	88 (32.4)
Target mean	64 (23.5)

Type of treatment	N (%)
SBRT	242 (89.0)
SRS	30 (11.0)

Equipment	N (%)
Linear Accelerator (LINAC)	223 (82.0)
CyberKnife	44 (16.2)
Tomotherapy	5 (1.8)
Techniques	
VMAT	165 (60.7)
IMRT	93 (34.2)
3D-CRT	14 (5.1)

TOTAL DOSE/N° FRACTIONS



64% clinical CR
94.5% Clinical Benefit

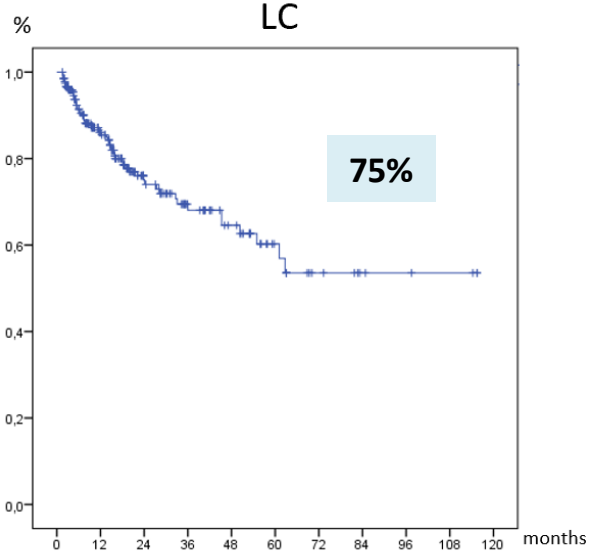
Results

Univariate and multivariate Cox regression analysis of variables predicting LC on "lesion" basis

		Univariate			Multivariate		
Variable	**N.**	**Hazard Ratio**	**95%CI**	**p-value**	**Hazard Ratio**	**95%CI**	**p-value**
Age Years		1.065					
≤69.9	148		0.637-1.783	0.809			
>69.9*	124						
Previous RT		0.425			0.570	0.268-1.215	
No	70		0.209-0.867	**0.019**			0.145
Yes*	201						
Previous RT in field		0.645			0.463	0.225-0.955	
No	230		0.3485-1.194	**0.162**			**0.037**
Yes*	42						
Histology		0.787					
Endometroid	182		0.458-1.351	0.384			
Other*	89						
Target		1.092					
Nodal	137		0.655-1.819	0.736			
Parenchimal*	135						
PTV		0.248			0.506	0.259-0.987	
≤13.7cc	**134**		0.132-0.469	**<0.001**			**0.046**
>13.7cc*	**134**						
BED		1.452			1.140	0.654-1.988	
≤59.5Gy	146		0.865-2.437	**0.158**			0.643
>59.5Gy*	126						
BED70		1.295					
≤70Gy	154		0.772-2.175	0.327			
>70Gy*	118						
Best Response		0.064			0.059	0.028-0.122	
CR	173		0.033-0.123	**<0.001**			**<0.001**
Not CR*	99						

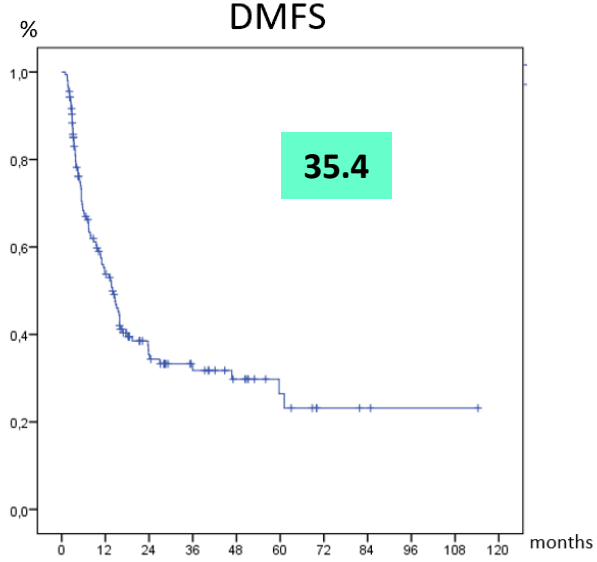
Results

LC



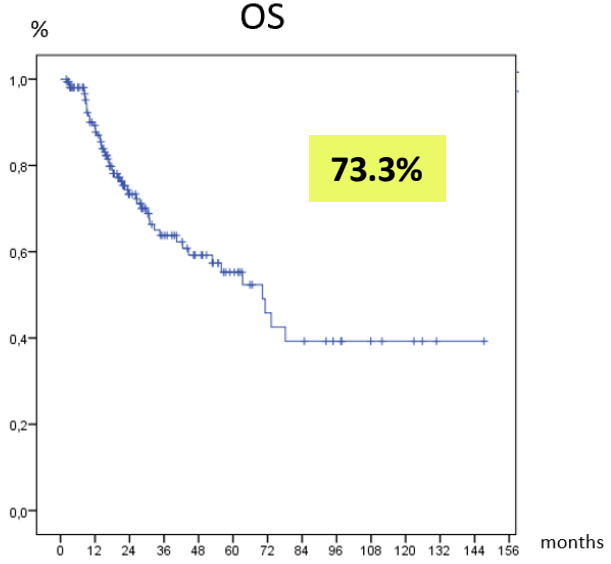
N events	0	32	48	54	56	58	60	60	60	60	60
N of cases	271	152	74	48	35	18	9	4	4	3	0

DMFS



N events	0	67	89	92	93	94	95	95	95	95	95
N of cases	157	72	34	21	14	8	3	1	1	1	0

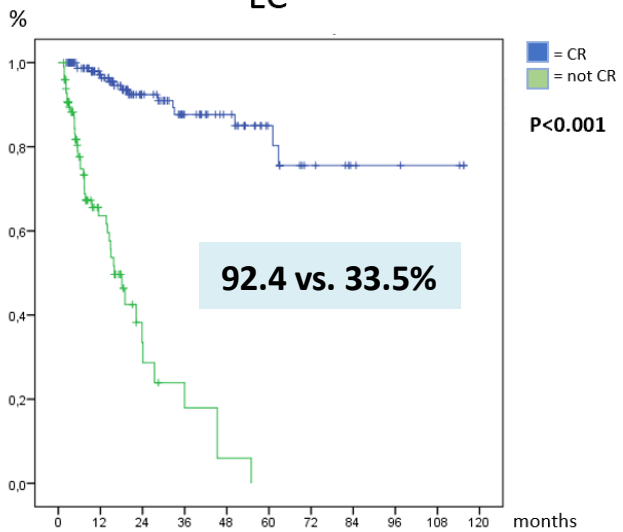
OS



N events	0	15	34	42	45	47	50	52	52	52	52	52	52	52
N of cases	157	118	70	50	35	23	14	12	9	5	4	1	1	0

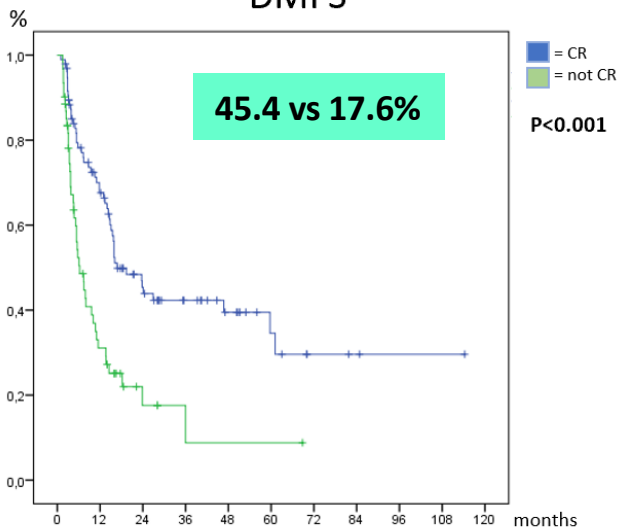
2y-impact of Complete Response achievement on outcomes

LC



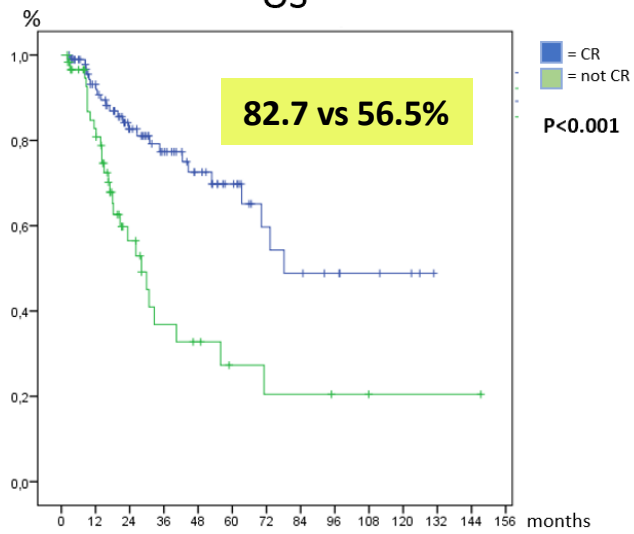
CR N events	0	4	9	12	12	13	15	15	15	15	15
CR N of cases	172	120	67	45	34	18	9	5	4	3	0
Not CR N events	0	28	39	42	44	45	45	45	45	45	45
Not CR N of cases	98	32	7	3	1	0	0	0	0	0	0

DMFS

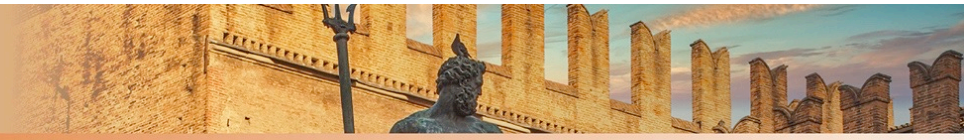


CR N events	0	29	46	48	49	50	51	51	51	51	51
CR N of cases	96	56	30	20	13	7	3	1	1	1	0
Not CR N events	0	38	43	44	44	44	44	44	44	44	44
Not CR N of cases	61	16	4	1	1	1	0	0	0	0	0

OS



CR N events	0	6	14	17	19	20	22	24	24	24	24	24	24	24
CR N of cases	96	76	53	39	28	19	11	9	7	4	3	0	0	0
Not CR N events	0	9	20	25	26	27	28	28	28	28	28	28	28	28
Not CR N of cases	61	42	17	9	7	4	3	3	2	1	1	1	1	0



Toxicities

Acute toxicity	
Patients	28 (17.8%)
Adverse Effects	58 (21 Grade 1; 7 Grade 2; 2 Grade 3, 1 Grade 4 & 1 grade 5 toxic death due to gastric perforation)

Most frequent toxicities ⇨ pain and lower gastrointestinal

Late toxicity	
Patients	18 (11.4%)

Adverse event (N°)	N°/ Grade
Pulmonary toxicity (5)	4 G1
	1 G2
Lower gastro-intestinal (4)	1 G2
	3 G3
Upper gastro-intestinal (2)	2 G3
Skin (3)	3 G1
Neurotoxicity (2)	1 G1
	1 G3
Pain (1)	1 G1
Hematological toxicity	1 G4

Conclusions

- The efficacy of SBRT in MPR-EC patients
- Low toxicity profile suggests a wider use of this treatment in this setting
- Combinations with new drugs are needed to improve outcomes

Pezzulla D, Bonome P, Cilla S, Deodato F

Campitelli M,
Laliscia C,
Fodor A, Zerbetto F,
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