

XXXIII CONGRESSO NAZIONALE AIRO

AIRO2023

BOLOGNA,
27-29 OTTOBRE 2023

PALAZZO DEI CONGRESSI

Radioterapia Oncologica: l'evoluzione al servizio dei pazienti



Associazione Italiana
Radioterapia e Oncologia clinica

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**STEREOTACTIC BODY RADIOTHERAPY AND ARTIFICIAL INTELLIGENCE IN
OLIGOMETASTATIC GYNAECOLOGIC CANCER: A LARGE, REAL-WORLD STUDY ON
RESPONSE PREDICTION, EFFICACY AND OUTCOMES**

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No conflict of interest



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Review



Role of stereotactic body radiotherapy in gynecologic radiation oncology

Conclusion and Future Directions

- SBRT active area of investigation
- a body of literature supports local control data in the setting of limited metastatic disease
- phase I and II trials have established the relative safety
- a dearth of phase III randomized evidence, including the use of immunotherapy

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A Large, Multicenter, Retrospective Study on Efficacy and Safety Of Stereotactic Body Radiotherapy (SBRT) in Oligometastatic Ovarian Cancer (MITO RT1 Study): A Collaboration of MITO, AIRO GYN, and MaNGO Groups

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Multicenter Study > Int J Gynecol Cancer. 2022 Jun 6;32(6):732-739.

doi: 10.1136/ijgc-2021-003237.

125 lesioni, 15 centri

Stereotactic body radiotherapy in oligometastatic cervical cancer (MITO-RT₂/RAD study): a collaboration of MITO, AIRO GYN, and MaNGO groups

Gabriella Macchia¹, Alessia Nardangeli², Concetta Laliscia³, Andrei Fodor⁴, Lorena Draghini⁵, Pier Carlo Gentile⁶, Giuseppe Roberto D'Agostino⁷, Vittoria Balcet⁸, Paolo Bonome⁹, Martina Ferioli¹⁰, Rosa Autorino², Lisa Vicenzi¹¹, Arcangela Raguso¹², Simona Borghesi¹³, Edy Ippolito¹⁴, Vanessa Di Cataldo¹⁵, Savino Cilla¹⁶, Elisabetta Perrucci¹⁷, Maura Campitelli², Maria Antonietta Gambacorta^{18,19}, Francesco Deodato^{9,19}, Giovanni Scambia²⁰, Gabriella Ferrandina²⁰

> Int J Radiat Oncol Biol Phys. 2023 May 5;S0360-3016(23)00417-0. doi: 10.1016/j.ijrobp.2023.04.025. Online ahead of print.

272 lesioni, 14 centri

EFFICACY AND SAFETY OF STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN OLIGOMETASTATIC UTERINE CANCER (MITO-RT₂/RAD STUDY): A LARGE, REAL-WORLD STUDY IN COLLABORATION WITH AIRO GYN, MITO and MaNGO Groups

Gabriella Macchia¹, Donato Pezzulla², Maura Campitelli³, Concetta Laliscia⁴, Andrei Fodor⁵, Paolo Bonome², Lorena Draghini⁶, Edy Ippolito⁷, Vitaliana DE Sanctis⁸, Martina Ferioli⁹, Francesca Titone¹⁰, Vittoria Balcet¹¹, Vanessa Di Cataldo¹², Donatella Russo¹³, Lisa Vicenzi¹⁴, Sabrina Cossa¹⁵, Simona Lucci³, Savino Cilla¹⁶, Francesco Deodato¹⁷, Maria Antonietta Gambacorta¹⁸, Giovanni Scambia¹⁹, Alessio Giuseppe Morganti⁹, Gabriella Ferrandina¹⁹

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Gynecological cancer prognosis using machine learning techniques: A systematic review of the last three decades (1990–2022)

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Results

validated. Twenty-three individual studies compared ML and non-ML methods. Study quality was highly variable and methodologies, statistical reporting and outcome measures were inconsistent, preventing generalized commentary or meta-analysis of performance outcomes.

Background

No accurate prediction models for clinical outcomes of gynaecologic oligometastatic cancer treated with SBRT exist

Nor is it clear if attaining a complete response (CR) following SBRT influences oncologic outcomes



AIM

- a **pooled analysis** of a large real-world multicentric dataset of ovarian, uterine and cervical oligometastatic lesions treated with SBRT in terms of **efficacy and clinical outcomes**
- in addition, an **exploratory machine learning analysis** able to identify the covariates able to predict the complete response after SBRT





Hystology		OC	UC	CC	All
Number of patients		261	157	83	501
Median age,yrs (range)		60 (28-85)	69.7 (36-90.5)	58 (30-92)	63 (28-92)
ECOG	0	111	111	56	357
	1	40	40	22	91
	2	6	6	4	48
	3	0	0	1	5
Comorbidities per patient	None	42	42	42	238
	1	45	45	21	144
	2	34	34	9	73
	3	16	16	5	27
	4	7	7	3	12
	>5	6	6	3	10
	n.a.	6	6	0	6
Patients undergoing surgery before SBRT	no	7	7	27	37
	yes	150	150	56	459
	n.a.	0	0	0	5
Patients undergoing chemotherapy before SBRT	no	42	42	21	63
	yes	110	110	61	427
	n.a.	5	5	1	6
Patients undergoing previous in site radiotherapy	no	91	91	55	393
	yes	25	25	28	62
	n.a.	0	0	0	5

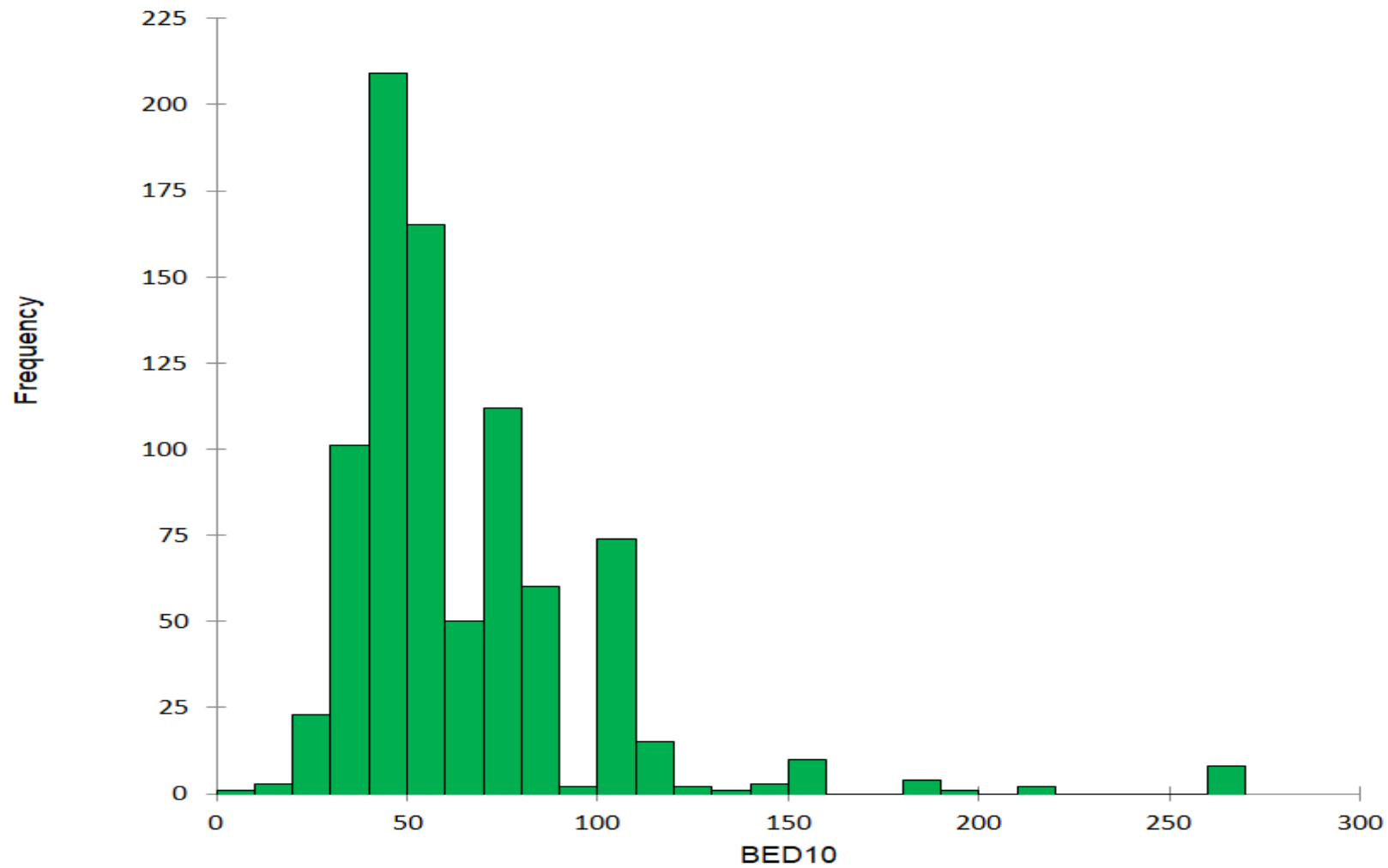
Abbreviations: yrs: years; OC: ovarian cancer; UC: uterine cancer; CC: cervical cancer; ECOG: Eastern Cooperative Oncology Group performance status; n.a.: not available; SBRT: stereotactic body radiotherapy



ALL

		4.5 (0.04-68.4)	4 (0.05-181.1)	4.3 (0.2-105.1)	4 (0.04-181)
GTV (range)		4.5 (0.04-68.4)	4 (0.05-181.1)	4.3 (0.2-105.1)	4 (0.04-181)
PTV (range)		17.9 (0.4-136.4)	13.7 (2-196.5)	15.7 (1.8-278.5)	16 (0.4-278.5)
Equipment	LINAC	401	115	223	739
	Ciberknife	34	10	44	88
	Tomotherapy	11	1	5	17
	Gammaknife	3	0	0	3
Techniques	VMAT	434	104	165	703
	IMRT	5	20	93	118
	3DCRT	8	1	14	23
	n.a.	0	0	0	0
Referral dose	Specificisodose	235	48	120	403
	Isocenter	159	31	88	278
	Target mean	55	46	64	165
Median Total dose (range)		25 (5-75)	35 (10-75.2)	35 (10-60)	30 (5-75.2)
Median number of fractions (range)		4 (1-13)	5 (1-10)	5 (1-10)	5 (1-13)
Median BED10 (range)		50.7(7.5-262.5)	59.5 (20-156.1)	59.5 (15-151.2)	51 (7.5-262.5)

Abbreviations: OC: ovarian cancer; UC: uterine cancer; CC: cervical cancer; GTV, gross tumor volume; PTV,



Efficacy

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Overall series

CR	538 (63.7%)
PR	189 (22.3%)
SD	80 (9.5%)
PD	38 lesions (4.5%)

Objective response rate (CR+PR): 85.9%

Clinical benefit (CR+PR+SD): 91.8%

OC

CR rate of 65.2%,



UC

CR rate of 64.0%



CC

CR rate of 58.4%



Variables selection and modelling

Least Absolute Shrinkage and Selection Operator (LASSO) method's application to all series → poor ability to forecast CR

Analysis of the 3 malignancies separately

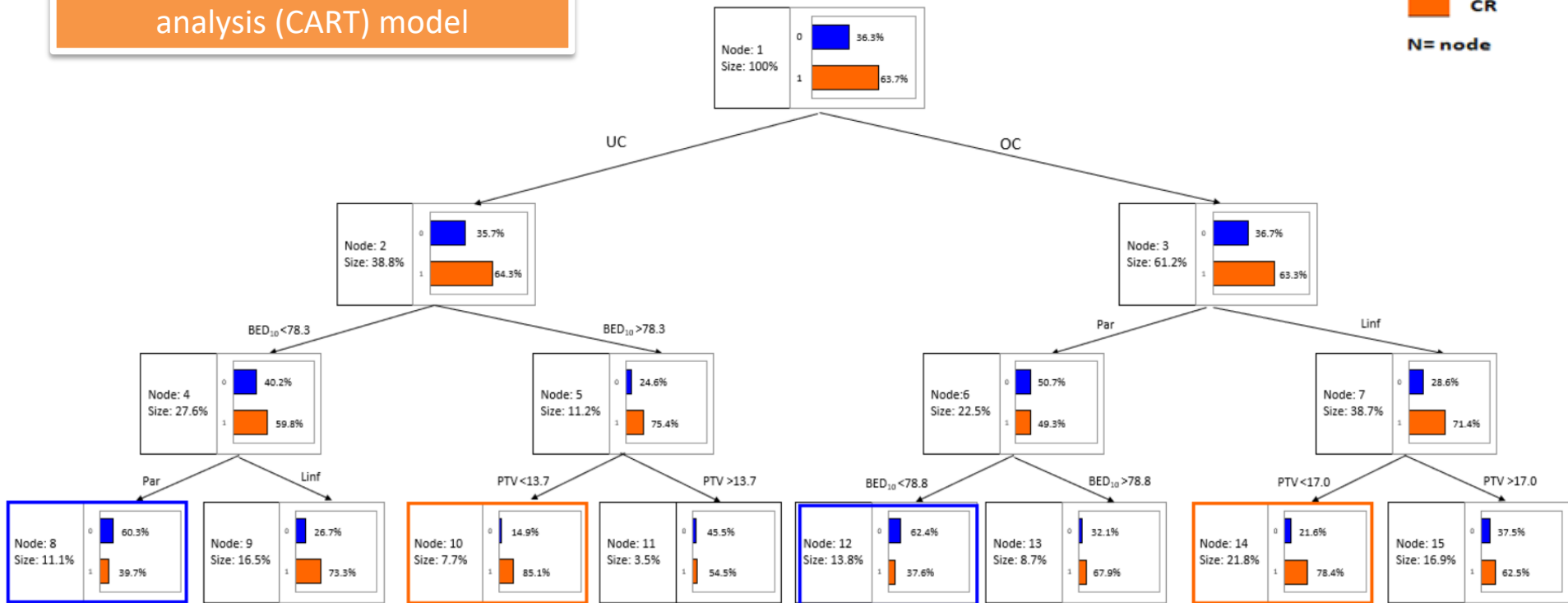
3 covariates predicted CR for ovarian or uterin lesion (LASSO coefficient not zero)

No covariates predictive for CR in cervical cancer lesions

Oligometastatic/persistent/recurrent gynecologic lesion

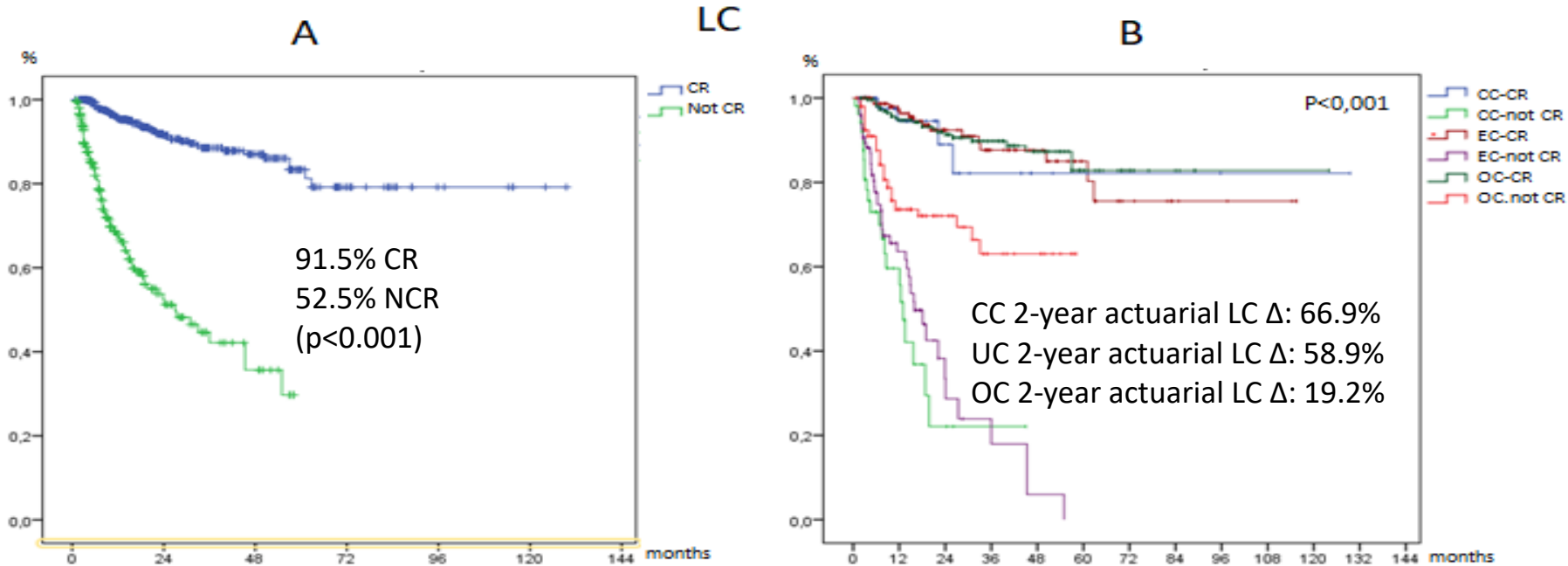
Classification And Regression Tree analysis (CART) model

 NCR
 CR
N= node



Clinical Outcomes 1

The overall 2-year actuarial local control rate: 79.2%



Median follow-up was 125 months (range: 1-316 months)

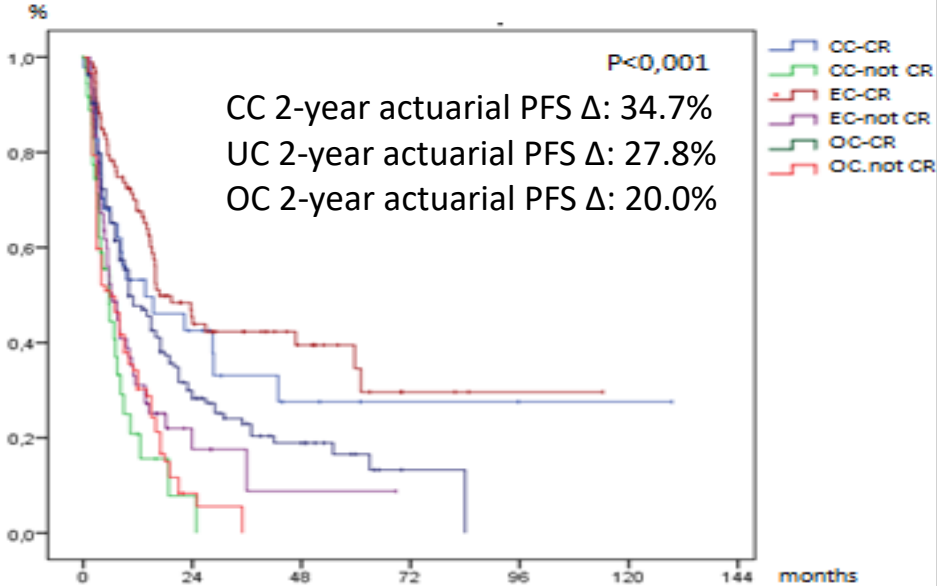
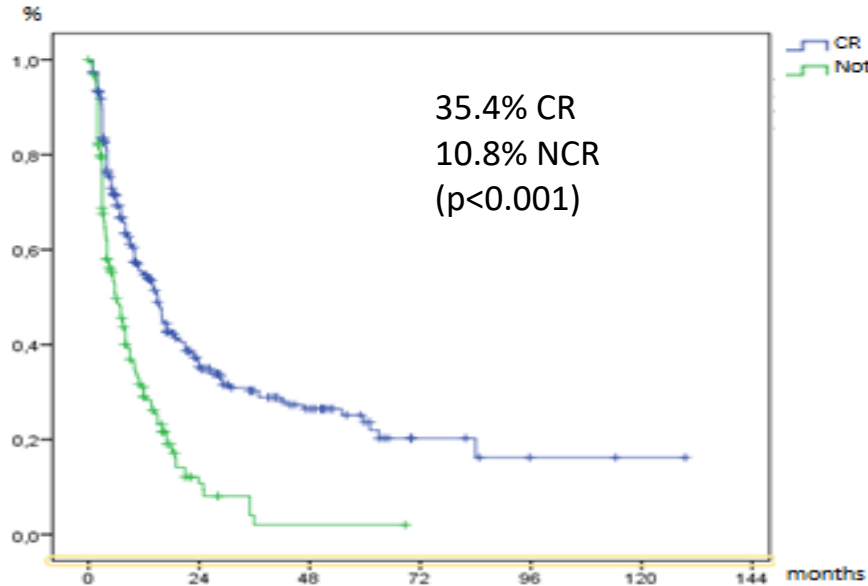
Clinical Outcomes 2

The overall 2-year actuarial PFS rate: 27.3%

C

PFS

D



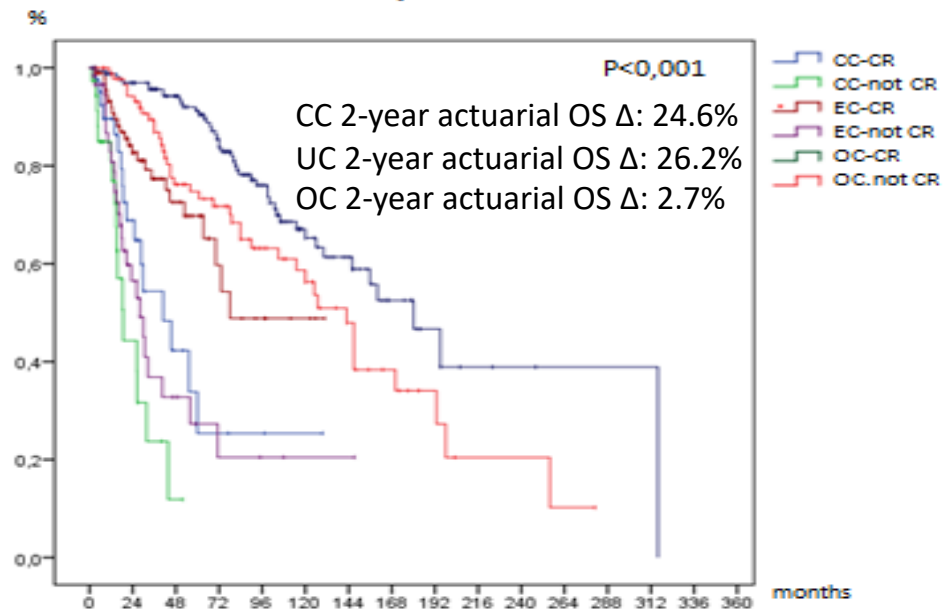
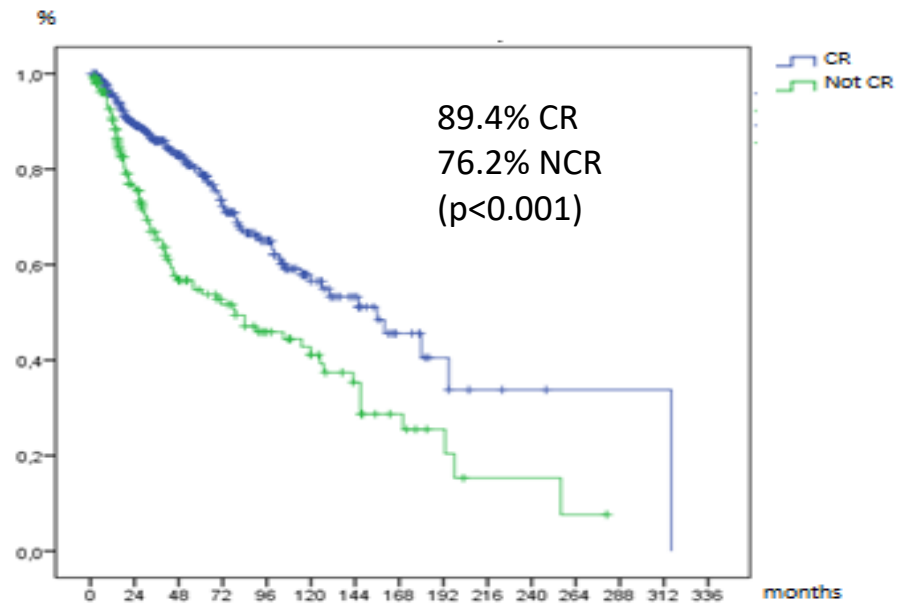
Clinical Outcomes 3

The overall 2-year actuarial OS rate: 84.7%

E

OS

F



Key points

- **21 radiation therapy centres have combined their data on 846 lesions from 501 patients** in an effort to identify complete response predictors and to strengthen the role of SBRT in the GYN setting
- The achievement of **complete response** acts as a **major driver**
- **SBRT gave a high and long-lasting Local Control rate (2-year rate: 79.2%)**
- **A robust and consistent CART model** employing 4 clinical variables, which **may lead oncologists via the rising chance of CR**
- For **OC** lesions, **the type of lesion (lymph node or parenchyma)** was the most important variable, whereas for **UC** lesions, the **BED₁₀** was the most important one.
- **the likelihood of receiving a complete response increases with decreasing volume** for both the ovarian and the uterine lesions. The size of the lesion offers for the radio-oncologist another degree of freedom on which he can partially infer
- For the setting of **cervical cancer**, however, it was **not** possible to identify any variables that were sufficiently predictive to create a **model**. The **lack** of some input factors, such as the **HPV status or other genetic/ epigenetic variables** able to better determine the core biology of the disease, **or the minimal** number of **inputs** might be the cause of this failure

Limits and strength

- the retrospective nature of the data.
- This ML model is based on a modest number of clinical and dosimetric parameters → other variables with potential influence on outcome prediction may be overlooked.
- The model was developed utilizing readily available data, which did not necessitate costly and time-consuming data processing (as in radiomics or genomics), resulting in more basic and understandable model that was also accurate. The low number of input variables should be viewed as a gain because such models will be less likely to overfit and easier to understand

Conclusions

- every effort must be made to obtain a **complete response** because seems to affects the outcomes
- the capacity to forecast it using artificial intelligence is critical in **boosting the chance of SBRT effectiveness** and driving treatment choices
- Further prospective studies to define doses, fractionations and volumes are needed, as well studies on the combination of SBRT with radiotherapy sensitizer, targeted drugs and immunotherapy.



Molise ART



*Ovunque vado in Molise ho un tetto,
ho un letto, ho una mesa, ho la fofole*
Giovanni Verga

Grazie

