OUTCOMES DEGLUTITORI SOGGETTIVI E OGGETTIVI DOPO RADIOTERAPIA AD INTENSITA' MODULATA CON RISPARMIO DEGLI ORGANI DELLA DEGLUTIZIONE NEI TUMORI DEL DISTRETTO TESTA E COLLO: RISULTATI DEFINITIVI DI UNO STUDIO PROSPETTICO DEL GRUPPO DI STUDIO TESTA COLLO DELLA SOCIETA' ITALIANA DI RADIOTERAPIA ONCOLOGICA

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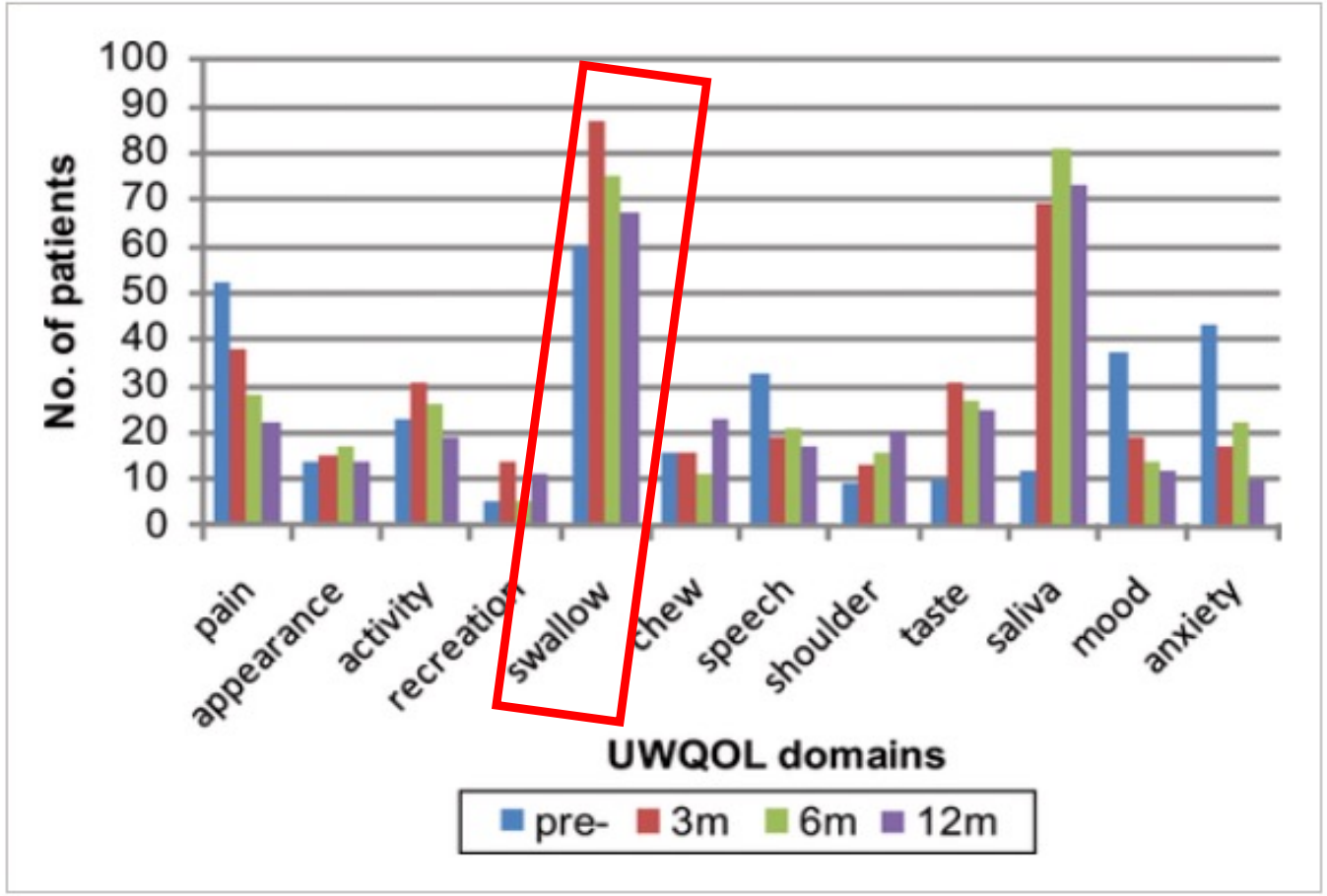
E’ un problema rilevante per i pazienti?



Patients’ selected priorities from University of Washington Quality of Life Questionnaire (UWQOL) domains at 4 time points.

Wilson, J.A., Carding, P.N. and Patterson, J.M. (2011), Otolaryngology–Head and Neck Surgery, 145: 767-771.

E’ un problema rilevante per i clinici?

- Il tasso di mortalità nei pazienti con disfagia che sviluppano polmonite da aspirazione dopo CCRT varia dal 9% al 34,6%.
- Il rischio di polmonite da aspirazione nei pazienti disfagici può verificarsi fino a 10 anni dopo il trattamento.
- La prevenzione della disfagia e soprattutto dell'aspirazione è fondamentale in questa popolazione.

Nguyen NP, Frank C, Moltz CC, et al. Aspiration rate following chemoradiation for head and neck cancer: an underreported occurrence. *Head Neck Radiother*. 2006; **80**: 302-306.

Perché MDADI? Perché PRO?

- è la metrica PRO più riconosciuta per la valutazione della qualità di vita (QoL) legata alla deglutizione
- E’ uno strumento di studio non di screening
- PRO: passare da «statistically significant» a «clinically meaningful»
- Una differenza di 10 punti = differenza minima clinicamente importante (MCID)

Per la disfagia non basta PRO

- Endpoint surrogati e poco chiari = dipendenza PEG o SNG, perdita di peso
- L'83% delle aspirazioni e il 100% delle penetrazioni nei pazienti trattati con CCRT sono silenti.
- Servono misure oggettive acquisite al basale e ripetute a vari time-points
- Fiberoptic Endoscopic Evaluation of Swallowing (FEES) e Videofluoroscopy (VFS)

No correlation between MDADI-C group (>80 and <80) and

FEES and VFS P-score at the 3 different time intervals (p>0,05)

Dysphagia. 2023; 38(1): 159–170.
Published online 2022 May 19. doi: 10.1007/s00455-022-10434-4
PMCID: PMC9118191
PMID: 35587295

Patient-Reported Outcomes After Swallowing (SWOARs)-Sparing IMRT in Head and Neck Cancers: Primary Results from a Prospective Study Endorsed by the Head and Neck Study Group (HNSG) of the Italian Association of Radiotherapy and Clinical Oncology (AIRO)

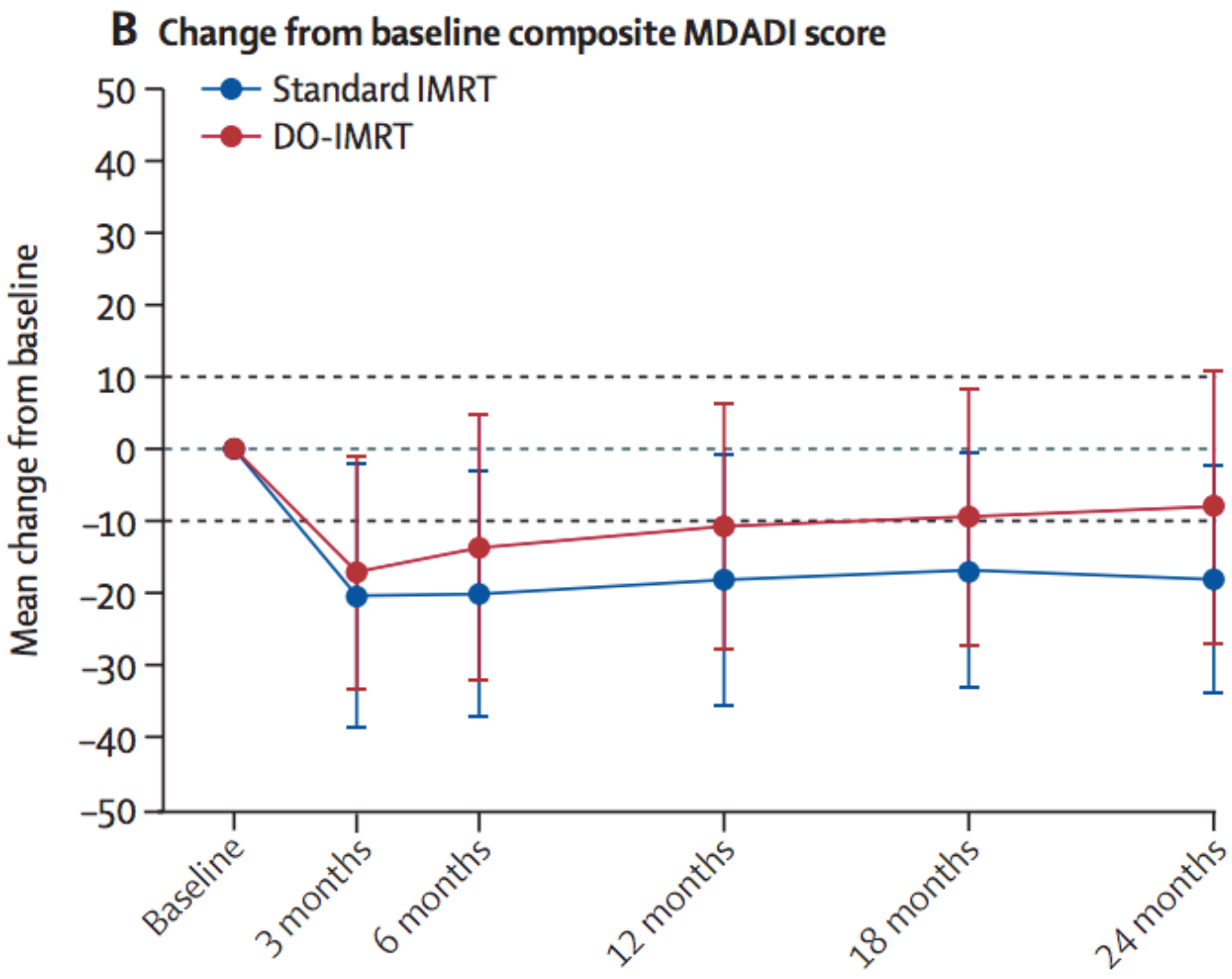
Stefano Ursino,[1] Elisa Calistri,[1] Francesca De Felice,[2] Pierluigi Bonomo,[3] Isacco Desideri,[3] Pierfrancesco Franco,[4] Francesca Arcadipane,[5] Caterina Colosimo,[1,6] Rosario Mazzola,[7] Marta Maddalo,[8] Alessandra Gonnelli,[1] Giulia Malfatti,[1] Riccardo Morganti,[9] Daniela Musio,[2] and Fabiola Paiar[1]

Lancet Oncol 2023; 24: 868–80

Dysphagia-optimised intensity-modulated radiotherapy versus standard intensity-modulated radiotherapy in patients with head and neck cancer (DARS): a phase 3, multicentre, randomised, controlled trial

Christopher Nutting, Laura Finneran, Justin Roe, Mark A Sydenham, Matthew Beasley, Shree Bhide, Cheng Boon, Audrey Cook, Emma De Winton, Marie Emson, Bernadette Foran, Robert Frogley, Imran Petkar, Laura Pettit, Keith Rooney, Tom Roques, Devraj Srinivasan, Justine Tyler, Emma Hall, on behalf of the DARS Trialist Group

- to detect a clinically relevant 10-point improvement in MDADI composite score
- 112 randomly assigned to DO(dysphagia-optimized)-IMRT or standard IMRT
- Median follow-up was 39·5 months

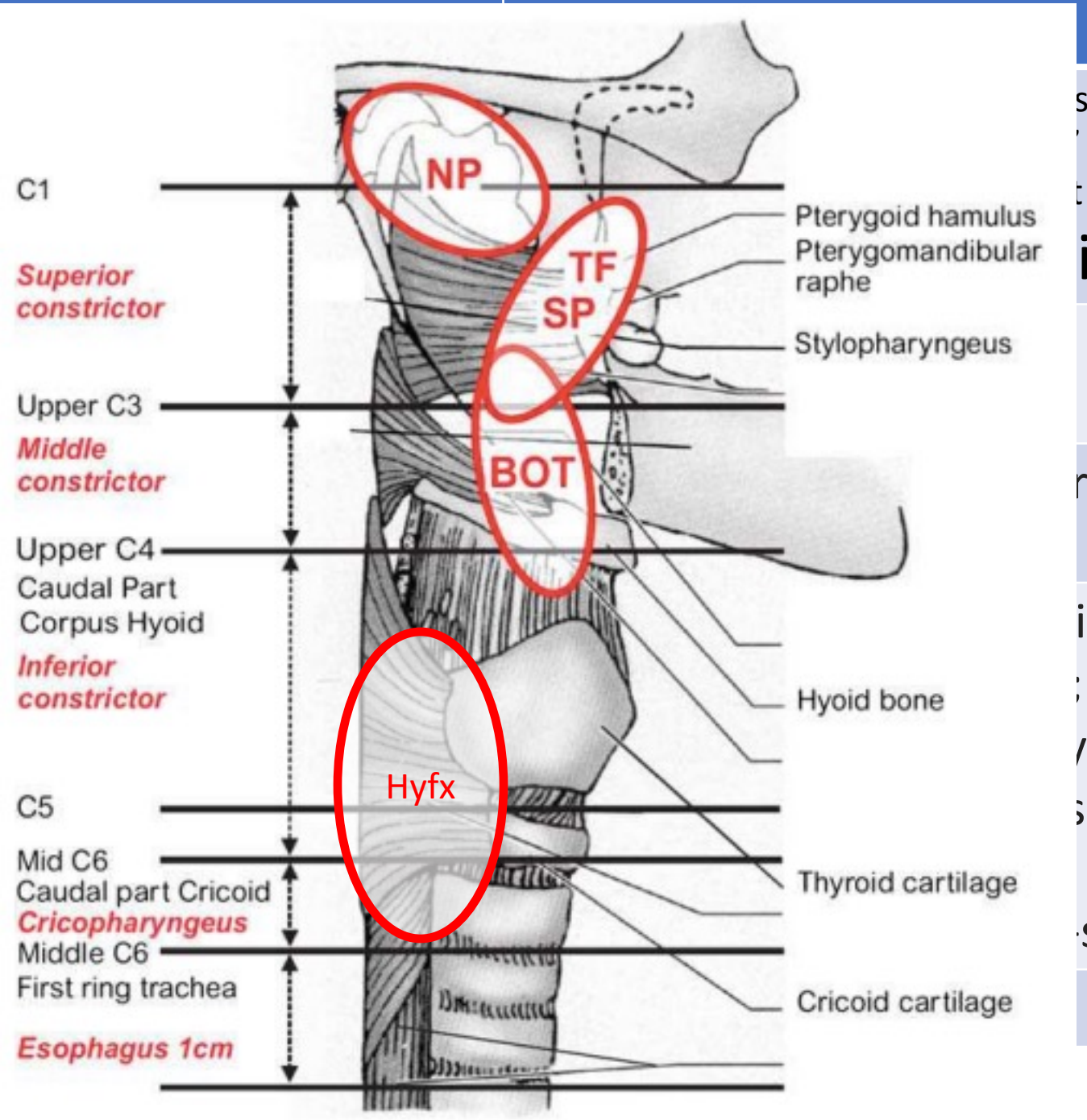


DO-IMRT mean difference 7·2 [95% CI 0·4–13·9]; p=0·037) than standard IMRT group

After adjusting for baseline score and clinical balancing factors, the mean difference was 9·8 (95% CI 3·5–16·0; p=0·0030).

differenza minima clinicamente importante (MCID) = 10 punti

Nutting	
7.2 (at best 9.8	sing to 76 at 12 months group. A statistically worsening for the i
88% of 24 centres de prophylactic swallow	
oropharyngeal or hy	ryngeal
Only the superior an constrictor muscles	ior, medium, and base of tongue; ynx; cricopharyngeal s) were defined to a dose reduction to sparing IMRT)
Only MDADI	



HIGHLY TAILORED ANAL CANCER MRI GUIDED INTERVENTIONAL RADIOTHERAPY: AGGIORNAMENTO DELLO STUDIO HIT-ART

B. Fionda[1], R. Bertolini[2], S. Manfrida[1], V. Deluca[1], A. Salvati[2], C. Mazzarella[1], V. Lancellotta[1], V. Frascino[1], F. G. Ciardo[2], L. Tagliaferri[1], M. A. Gambacorta[1|2].

1) UOC di Radioterapia Oncologica, Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Fondazione Policlinico Universitario A. Gemelli IRCCS

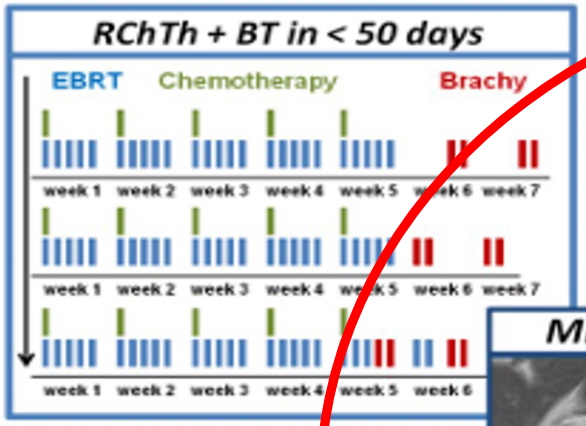
2) Istituto di Radiologia, Università Cattolica del Sacro Cuore

IGBT con MR ano: pochi dati

- Esistono pochi dati sull'approccio MR-guided nella brachiterapia per il cancro del canale anale.
- In una review di studi retrospettivi (R Frakulli J Contemp Brachytherapy 2018; 10, 3: 246–253) i risultati migliori in termini di LC e tossicità acuta sono stati registrati nello studio che usava BRT 3D-US-guidata

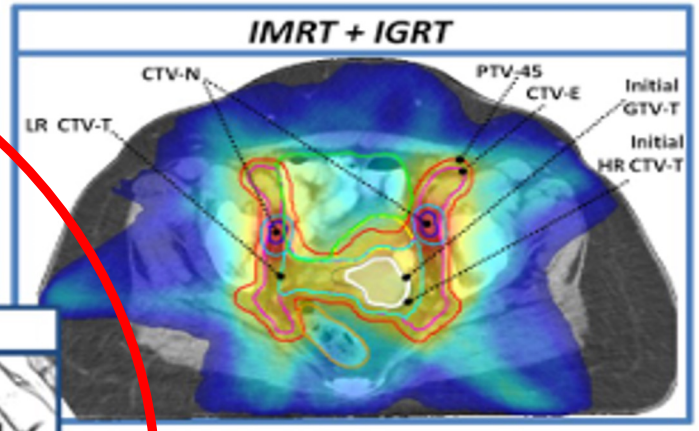
- Ecografia endoanale:
  - economica, sicura e ben tollerata,
  - dipendente dall'operatore
  - non è in grado di valutare i tumori stenotici.

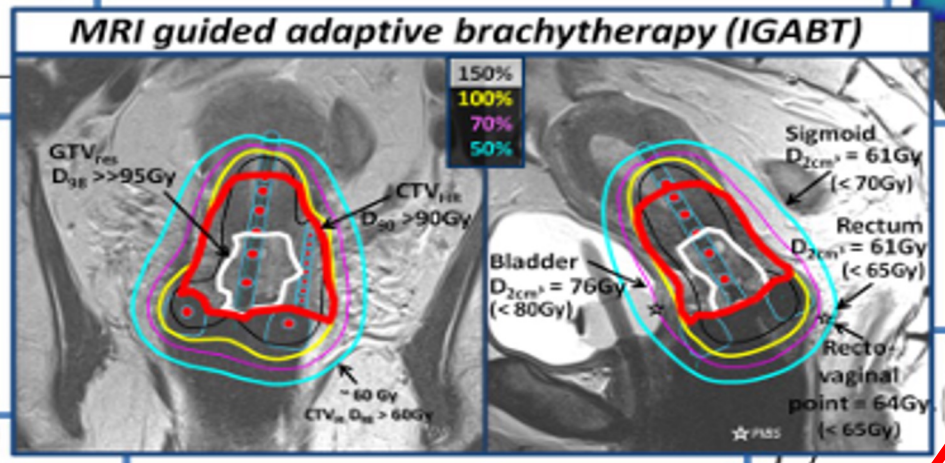
Lessons from retroEMBRACE and EMBRACE I



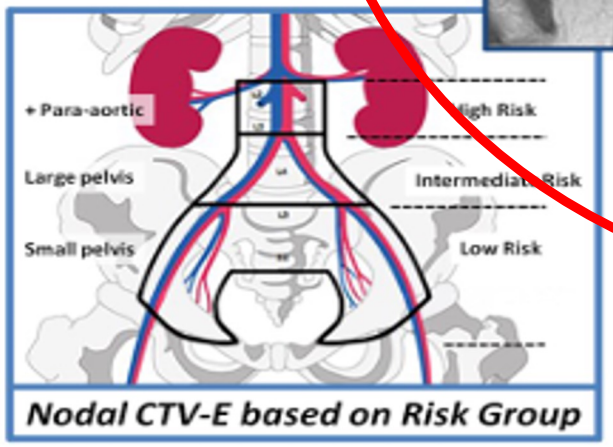
OTT

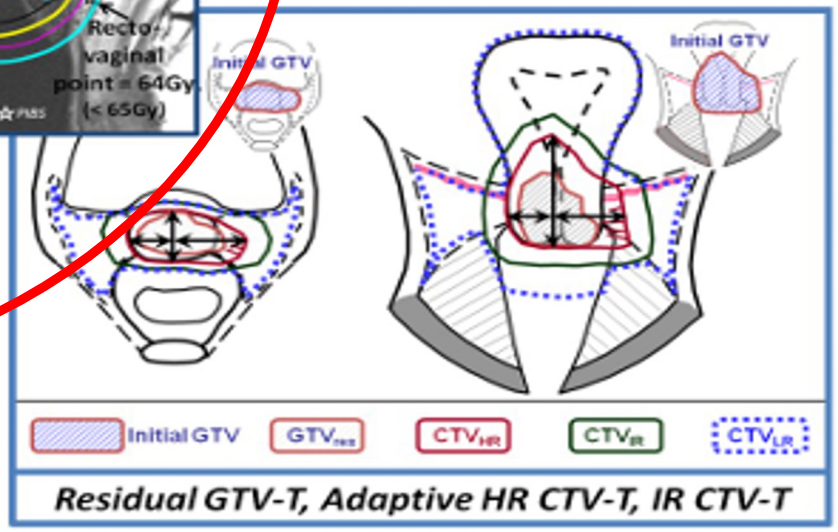
SIB-IMRT





MR-guided IRT





OTT

- Fionda et al.: revaluation after 2-3 weeks.
- The overall treatment time (OTT) and the time gap between the end of the primary EBRT and the sequential boost are prognostic factors for the local control rate and should be as short as possible.

	Dichotomous measure in days	endpoint
Cordoba et al.	58 days OTT	LC
Oblak et al.	73 days OTT	5y-LC 73% vs 56%
Deniaud-Alexandre et al.	38 days gap between EBRT and BRT	DFS
Weber et al.	37 days gap between EBRT and BRT	5y-LC 84% vs 61%
Fionda et al.	79 days OTT	OS

Dose

- After pelvic EBRT 45 Gy the exact dose of the brachytherapy boost, is still debated
  - dose ≥ 20 Gy EQD2 should be prescribed.
  - If CR ≤ 16 Gy EQD2
- an overall dose of at least 54 Gy EQD2 is needed
- Dose escalation for poor responders

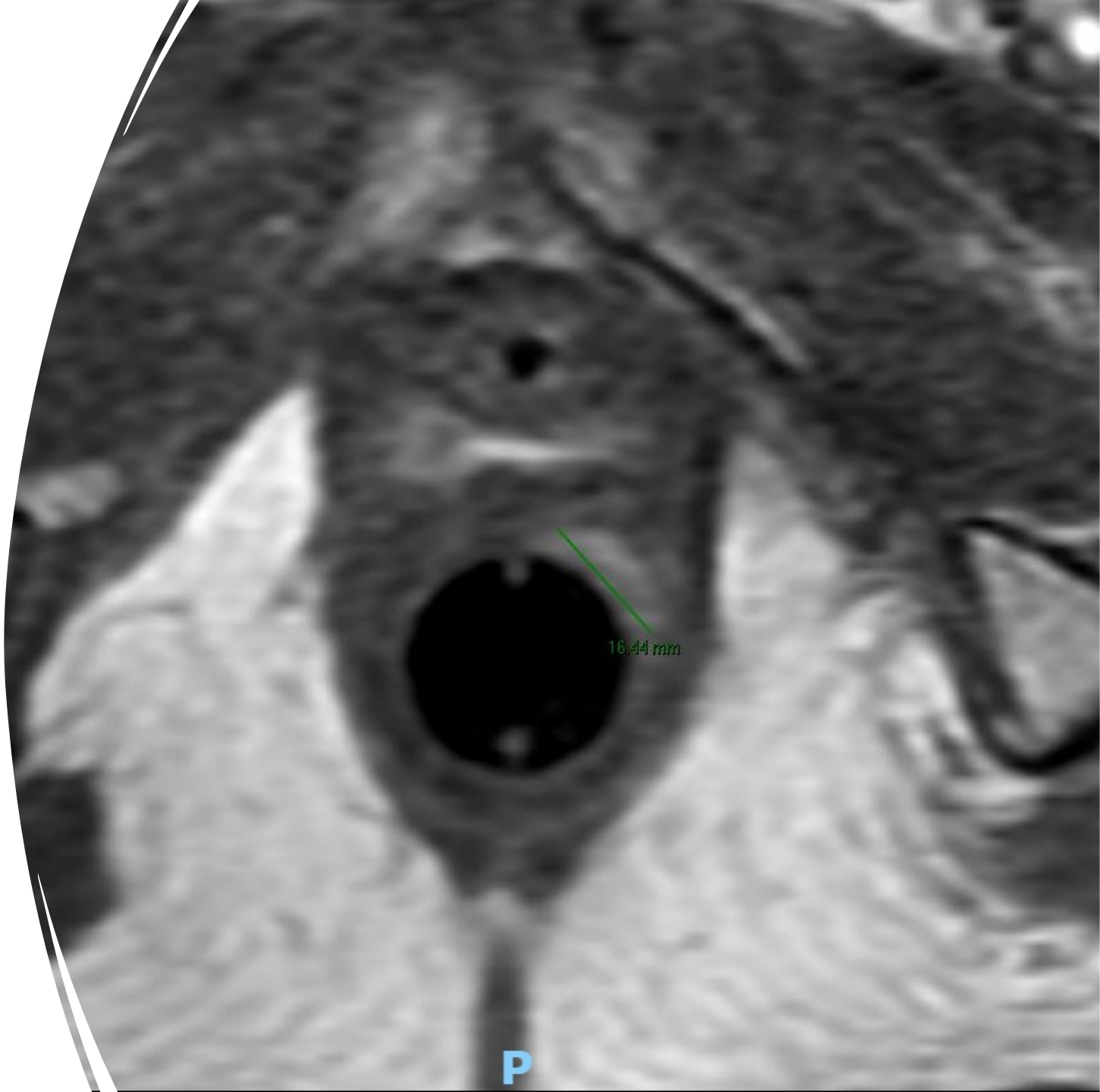
Qui strategia di personalizzazione della dose con EBRT e IRT

- EBRT: SIB-IMRT 45 to 55 Gy in 25 fx according to clinical stage.
- 2-3 weeks after CRT revaluation
- according to initial stage and tumor response, boost with IG-IRT with MRI with applicator on site
- When the BT dose exceeded 4 Gy delivered in 2 fractions with a 1 week interval

Volume

- CTV = initial GTV+ 5mm in all directions. THE GEC ESTRO HANDBOOK OF BRACHYTHERAPY | Part II Clinical Practice Version 1 - 01/03/2023

- Fionda: the CTV corresponded to residual tumor or scar



Risultati: mitigazione del fattore TNM: alta efficacia!

	5y LC	5y-CFS	5y-OS
Frakulli et al. (review)	78%	76.1%	64.1%
Fionda et al.	84%	74.1%	79.1%

T2-T4 (T2 43.5%, T3 19.4%, T4 25.8%) and 42 (67.7 %) had positive nodes.
Acute toxicity ≥G3 was recorded in 11 patients (17.7%).
No acute severe toxicity was recorded after boost IRT.
Late urinary tract toxicity levels were negligible (G1 in 4 pts).
No severe G4 late toxicity was recorded.

There was no correlation between outcomes and initial T and N stage

Domanda

- Vantaggio di MR nella cervice:
  - Adaptive (generalmente schedule con 4 frazioni)
  - BRT interstiziale ottimizzata
  - Diffusione di applicatori magneto-compatibili

- Nel canale anale:
  - margine di miglioramento rispetto a US (ottimizzazione interstiziale più che adaptive)? Schedule con 2 frazioni
  - Possibile diffusione della metodica

RADIOTERAPIA STEREOTASSICA E INTELLIGENZA ARTIFICIALE IN PAZIENTI OLIGOMETASTAICI DA NEOPLASIA GINECOLOGICA: UN GRANDE STUDIO REAL-WORLD SU PREDIZIONE DI RISPOSTA, EFFICACIA E OUTCOMES.

G. Macchia[1], S. Cilla[2], D. Pezzulla[1], M. Campitelli[3], C. Laliscia[4], R. Lazzari[5], L. Draghini[6], A. Fodor[7], G. R. D'agostino[8], D. Russo[9], V. Balcet[10], M. Ferioli[11], L. Vicenzi[12], S. Cossa[13], V. Di Cataldo[14], E. Perrucci[15], S. Borghesi[16], E. Ippolito[17], P. Gentile[18], V. De Sanctis[19], F. Titone[20], C. T. Delle Curti[21], A. Huscher[22], M. A. Gambacorta[3|23], G. Ferrandina[24], A. G. Morganti[25], F. Deodato[1|23].

1 Radiation Oncology Unit, Gemelli Molise Hospital

La maggior parte degli studi sono italiani!

- Macchia G., Lazzari R., Colombo N., Laliscia C., Capelli G., D'Agostino G.R., Deodato F., Maranzano E., Ippolito E., Ronchi S., et al. 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. *Oncologist.* 2020;25:e311–e320

- Iftode C., D'Agostino G.R., Tozzi A., Comito T., Franzese C., De Rose F., Franceschini D., Di Brina L., Tomatis S., Scorsetti M. Stereotactic Body Radiation Therapy in Oligometastatic Ovarian Cancer: A Promising Therapeutic Approach. *Int. J. Gynecol. Cancer.* 2018;28:1507–1513.

- Lazzari R., Ronchi S., Gandini S., Surgo A., Volpe S., Piperno G., Comi S., Pansini F., Fodor C., Orecchia R., et al. Stereotactic Body Radiation Therapy for Oligometastatic Ovarian Cancer: A Step Toward a Drug Holiday. *Int. J. Radiat. Oncol. Biol. Phys.* 2018;101:650–660.

- Macchia G., Nardangeli A., Laliscia C., Fodor A., Draghini L., Gentile P.C., D'Agostino G.R., Balcet V., Bonome P., Ferioli M., et al. Stereotactic Body Radiotherapy in Oligometastatic Cervical Cancer (MITO-RT2/RAD Study): A Collaboration of MITO, AIRO GYN, and MaNGO Groups. *Int. J. Gynecol. Cancer.* 2022;32:732–739.

- Cuccia F., Pastorello E., Vitale C., Nicosia L., Mazzola R., Figlia V., Giaj-Levra N., Ricchetti F., Rigo M., Attinà G., et al. The Use of SBRT in the Management of Oligometastatic Gynecological Cancer: Report of Promising Results in Terms of Tolerability and Clinical Outcomes. *J. Cancer Res. Clin. Oncol.* 2021;147:3613–3618

- Laliscia C., Fabrini M.G., Delishaj D., Morganti R., Greco C., Cantarella M., Tana R., Paiar F., Gadducci A. Clinical Outcomes of Stereotactic Body Radiotherapy in Oligometastatic Gynecological Cancer. *Int. J. Gynecol. Cancer.* 2017;27:396–402.

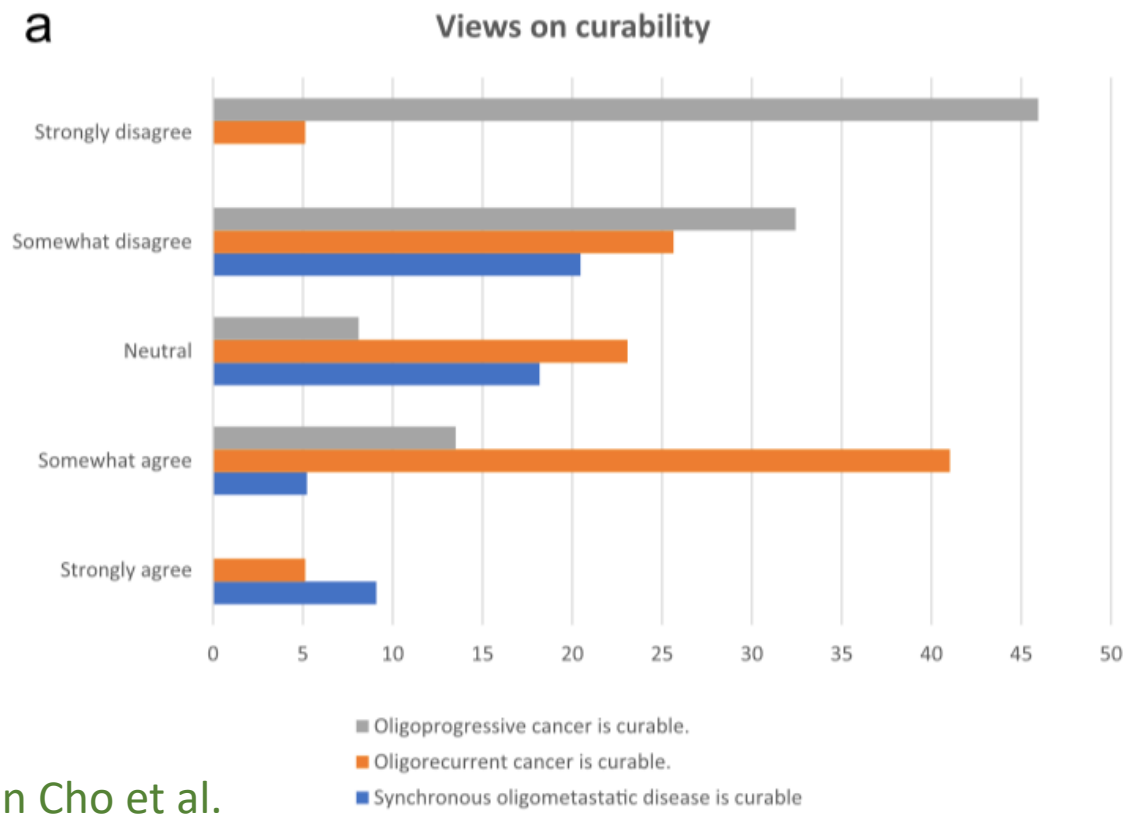
Domande di grande utilità clinica!

- Non esistono modelli di previsione accurati per gli esiti clinici del tumore ginecologico oligometastatico trattato con SBRT

- Non è chiaro se il raggiungimento di una risposta completa (CR) dopo SBRT influenzi gli esiti oncologici.

Veri oligometastatici = cura con MDT

- 52% di OM tra tutti i pazienti metastatici 7000 PET analizzate (Christ S.M et al. IJROBP 2022, 114, 596–602)
- long-term DFS 20% negli OM
- corrisponde a una prevalenza di veri OM di circa il 10% tra tutti i casi di cancro metastatico
- Dobbiamo rivedere le nostre aspettative



Hae Lin Cho et al.
Is Oligometastatic Cancer Curable? A Survey of Oncologist Perspectives, Decision Making, and Communication
Advances in Radiation Oncology (2023) 8, 101221

Beneficio clinico

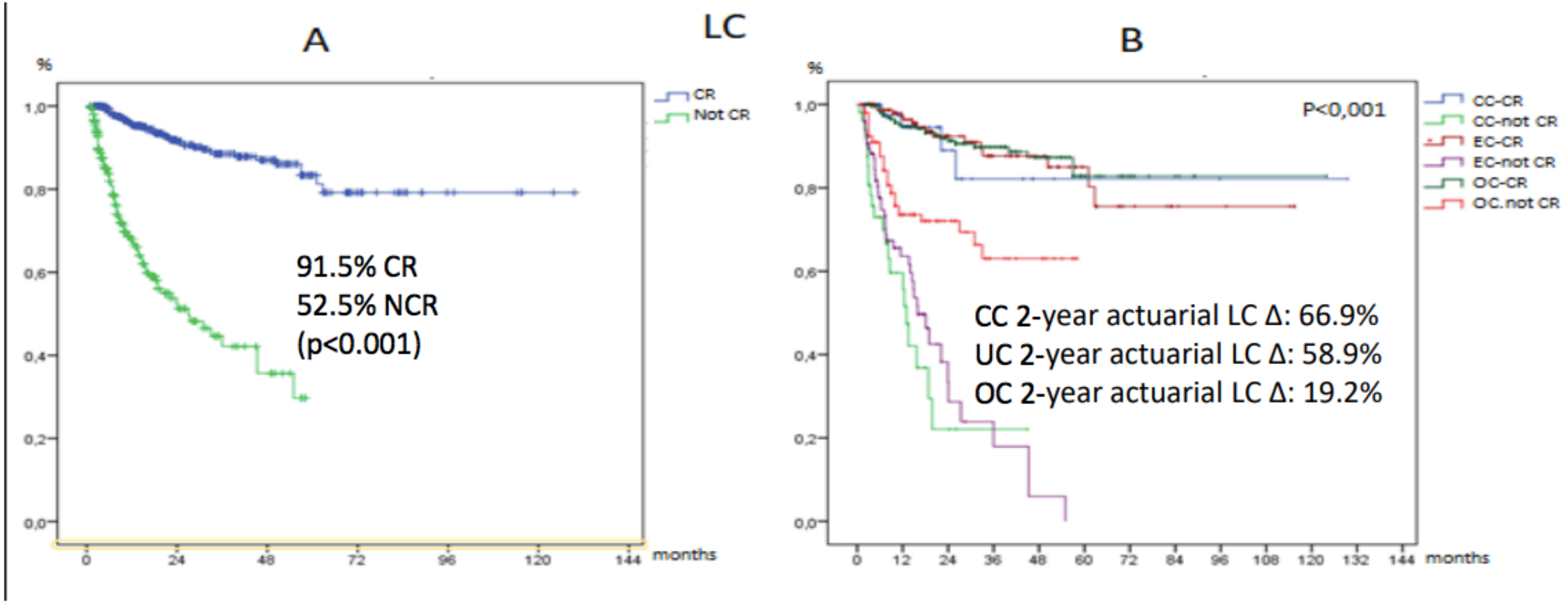
- Non è solo la curabilità, ma può essere il tempo alla progressione e all'inizio di una nuova terapia sistemica

- CR = 63.7%
- 2y PFS = 27,3%
- 2y OS = 71,0%
- differenze significative tra CR e non CR

- Domanda: data la discrepanza tra PFS e OS la SBRT cambia poco la traiettoria di malattia. CR è citoriduzione o fattore prognostico?

Clinical Outcomes 1

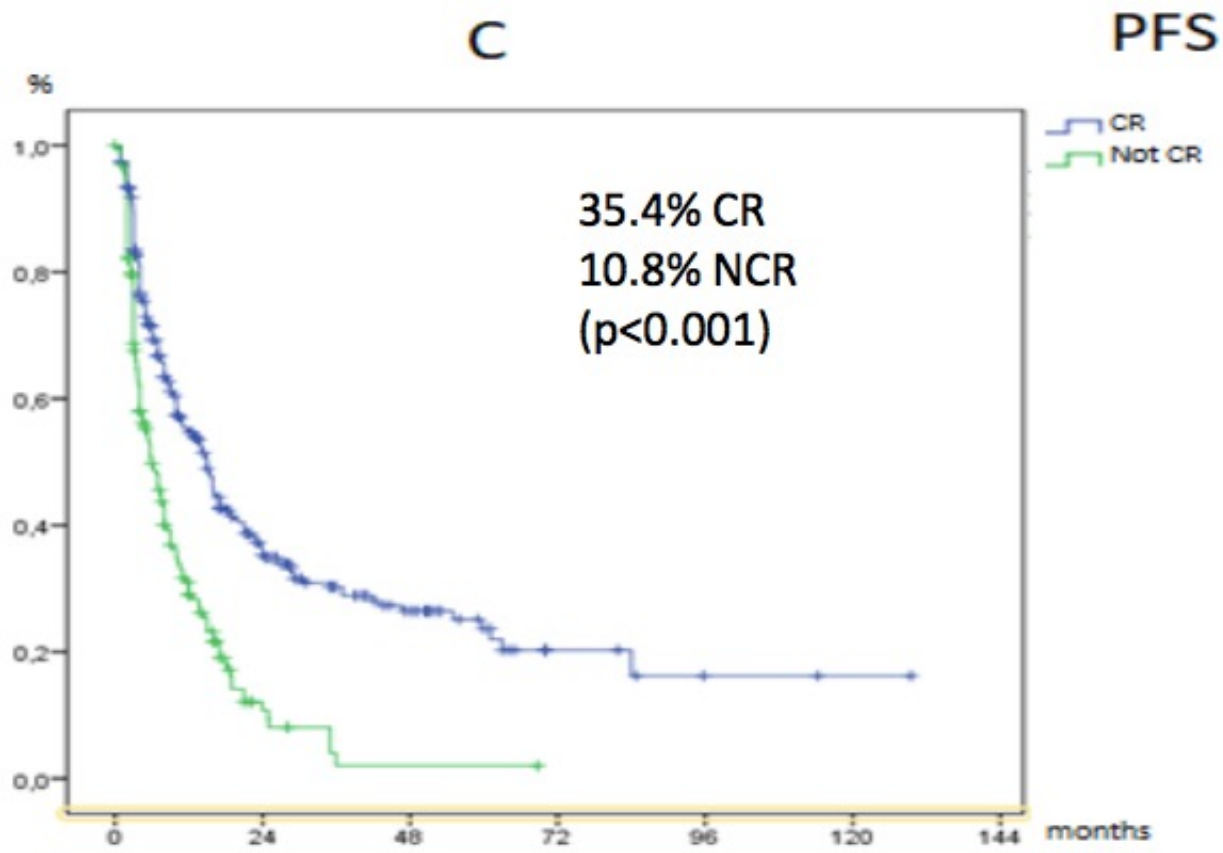
The overall 2-year actuarial local control rate:79.2%

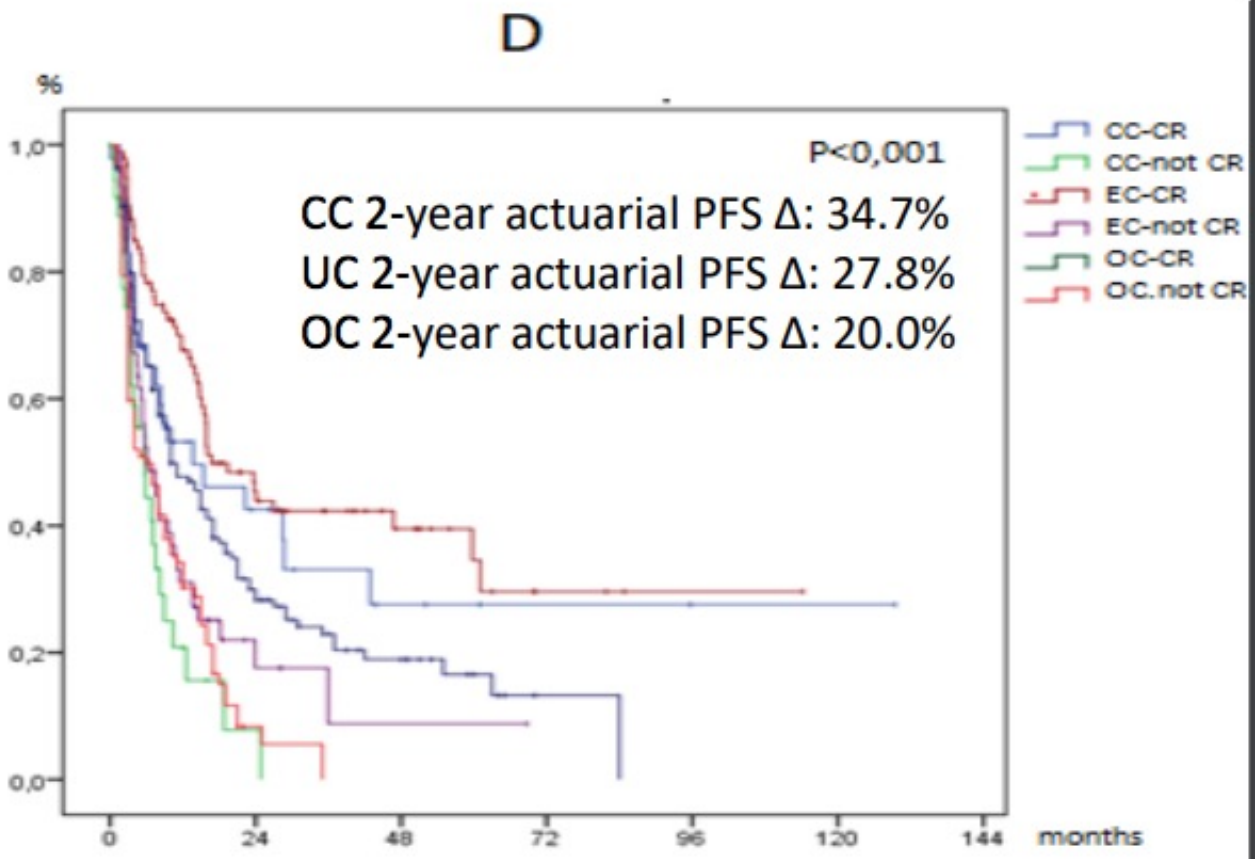


Median follow-up was 125 months (range: 1-316 months)

Clinical Outcomes 2

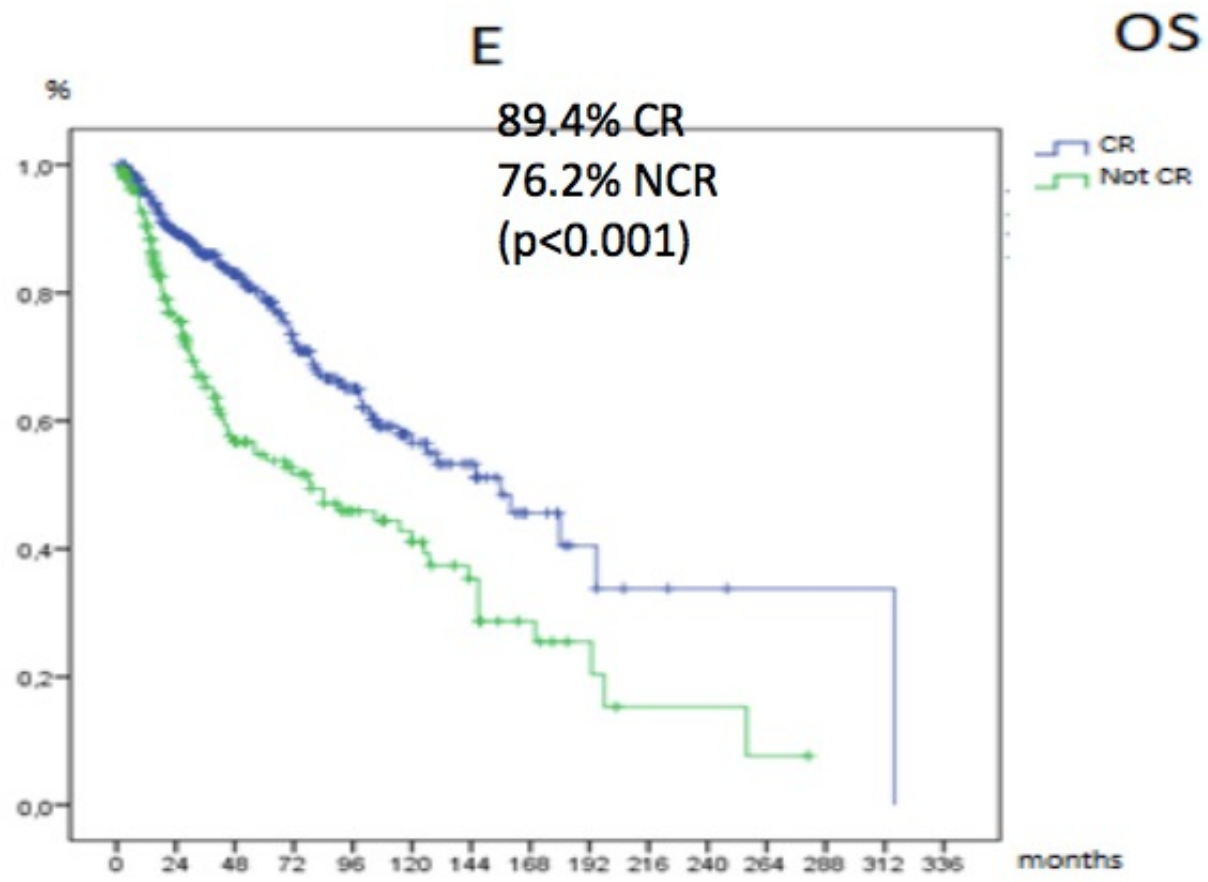
The overall 2-year actuarial PFS rate: 27.3%

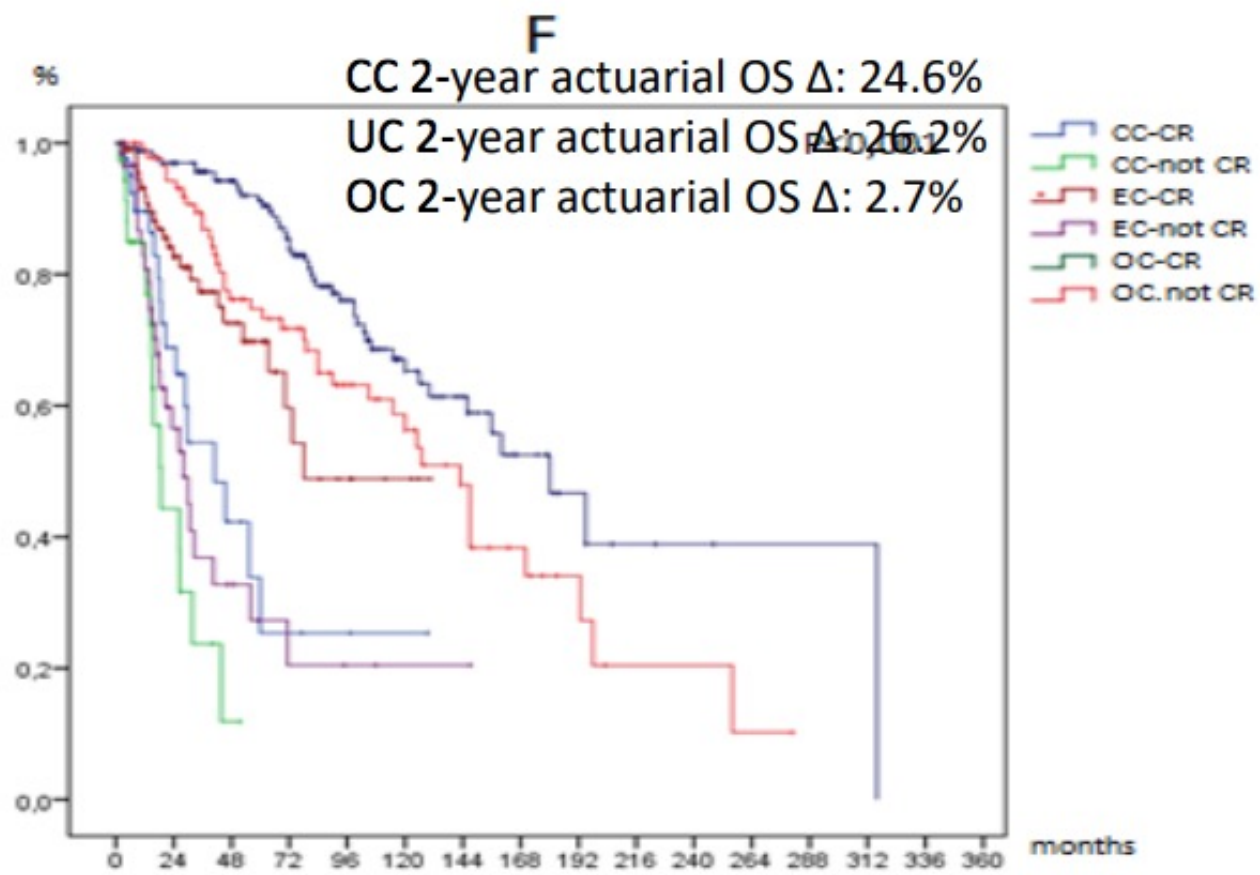




Clinical Outcomes 3

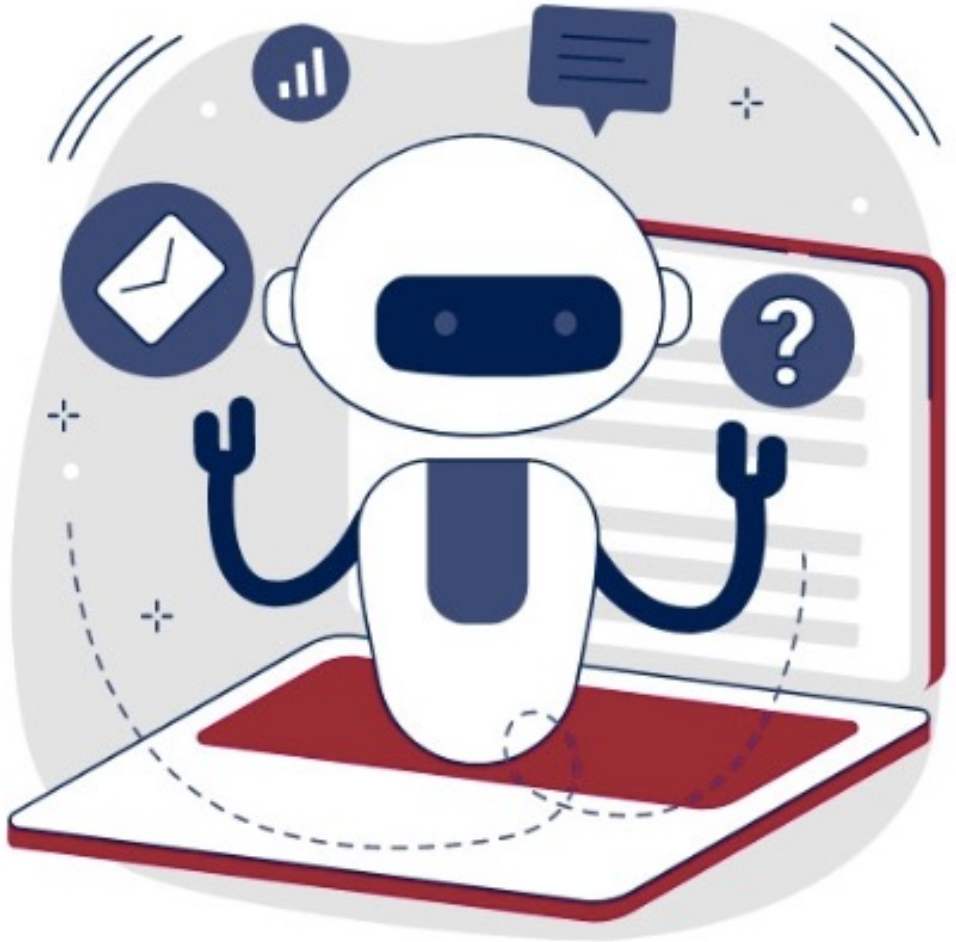
The overall 2-year actuarial OS rate: 84.7%





IA/machine learning = valore aggiunto

- machine learning model
- Utero:
  - BED10>78.3Gy CR 75.4%;
  - volume < 13.7cc CR 85.1%
- Ovaio:
  - lymph node = CR 71.4%
  - volume <17.0cc CR 78.4%.
- Cervice= nd



Clinical trial

Efficacy and safety of stereotactic body radiotherapy (SBRT) in oligometastatic/persistent/recurrent ovarian cancer: a prospective, multicenter phase II study (MITO-RT3/RAD)

Gabriella Macchia ,[1] Barbara Alicja Jereczek-Fossa,[2,3] Roberta Lazzari,[2] Annamaria Cerrotta,[4] Francesco Deodato,[1,5] Edy Ippolito,[6] Cynthia Aristei,[7] Maria Antonietta Gambacorta,[5,8] Giovanni Scambia,[9,10] Vincenzo Valentini,[5,8] Gabriella Ferrandina[9,10]

- PFS (progression of disease out of SBRT field)
- OS
- treatment-free interval (the interval from the SBRT and the start of a new systemic treatment or surgery)
- rate of toxicity and the 2-year actuarial late toxicity-free survival

ESTRO-ASTRO OMD consensus document Radiat Oncol 148:157-166, 2020

- The feasibility of safely delivering curative intent MDRT determines the maximum number of lesions and sites that can be treated with radiotherapy* in OMD

- ESTRO-ASTRO
- Macchia et al.
- Mito RT3-RAD