TRATTAMENTO ADIUVANTE DEL CARCINOMA DELL'ENDOMETRIO: STUDIO PROSPETTICO DI IRRADIAZIONE DELLA PELVI CON SOVRADOSAGGIO SIMULTANEO SULLA CUPOLA VAGINALE CON TECNICA VOLUMETRICA AD INTENSITA' MODULATA IN ALTERNATIVA AL TRATTAMENTO PELVICO E BRACHITERAPIA ENDOVAGINALE

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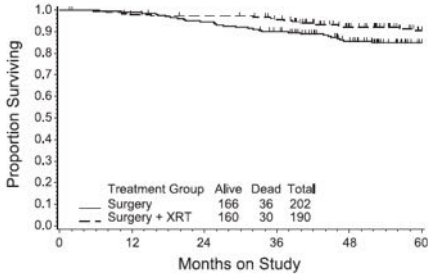
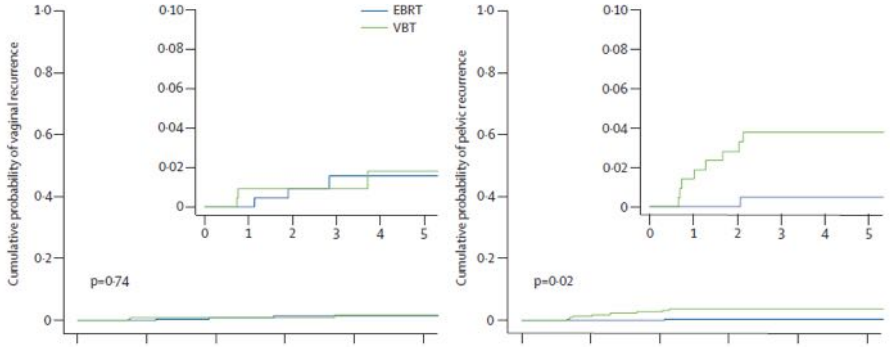
Background

Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomised trial

Lancet 2010; 375: 816–23



In intermediate-high risk endometrial cancer loco-regional control is improved by radiation therapy



✓ **Vaginal cuff recurrences account for approximately 75% without adjuvant RT**

✓ **Vaginal Brachytherapy represents the standard of care to ensure vaginal control**

✓**3D-conformal pelvic irradiation for endometrial cancer is associated to moderate-severe GI toxicity**

Portec-2 trial, Lancet, 2010
GOG-99 trial, Gynecologic Oncology, 2004

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Background

Impact of post operative intensity modulated radiotherapy on acute gastro-intestinal toxicity for patients with endometrial cancer: Results of the phase II RTCMIENDOMETRE French multicentre trial ☆

Radiotherapy and Oncology 111 (2014) 138–143

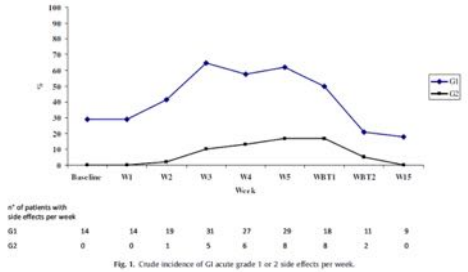
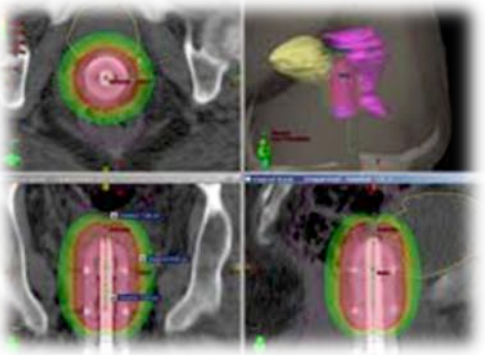


Fig. 1. Crude incidence of GI acute grade 1 or 2 side effects per week.

Post-operative IMRT resulted in low rate of acute GI grade 2 toxicity (CTCAE v3.0)

- ✓ **Volumetric-modulated arc therapy (VMAT) has been shown to be able to maintain a low-moderate GI toxicity profile in pelvic irradiation in other diseases**
- ✓ **VMAT showed a great potential for highly conformal dose to target volume**

In patients eligible to RT but unable to receive VBT or in case of patients refusing VBT, alternative RT option should be offered



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Alongi F. et al. Anticancer Res, 2013
Cozzi L. et al. Radiother Oncol, 2008

Study Design

To evaluate feasibility and tolerability of post-operative pelvic-VMAT for a total dose of 54Gy and simultaneous integrated boost to vaginal cuff for a total dose of 60Gy in 30 fractions

Primary Endpoints: LC and OS

Secondary Endpoint: Treatment-related Toxicity (GI and GU)

- *LC from the date of surgery to loco-regional recurrence (in the pelvis or the vaginal cuff)*
- *TTP from the date of surgery to the time of local recurrence or distant metastasis*
- *OS was calculated from the date of diagnosis to the death or last follow-up date*

Patients

Factors	%	n
Surgery		
Laparotomy	80	40
Laparoscopy	20	10
Histology		
Endometrioid	86	43
Clear Cells	6	3
Serous	8	4
Myometrial Infiltration		
≥ 50%	72	36
< 50%	28	14
Grading		
G1	12	6
G2	28	14
G3	60	30
FIGO stage		
IB1	20	10
IB2	28	14
IIA2	16	8
IIB	6	3
IIIA	2	1
IIIC	28	14
Pathologic nodes status		
N+	30	15
N-	70	35
Adjuvant chemotherapy		
Yes	56	28
No	44	22

50 patients

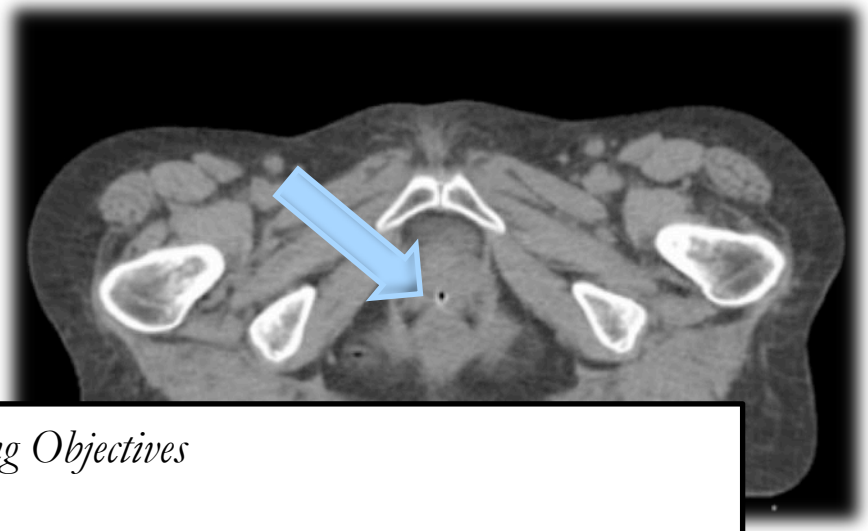
Median age: 68 y (62-78 y)

Median Follow Up: 30 months (16-43 months)

In case of stage ≥ II, RT was delivered sequentially not later than 4-6 weeks after Platinum-based chemotherapy

Treatment Procedure

- ✓ *MRI merged with CT-planning*
- ✓ *SIB: the upper 2/3 of vagina*
- ✓ *A 2 mm soft radiopaque transvaginal probe was used to define the vaginal cuff for all patients*
- ✓ *Daily correct*

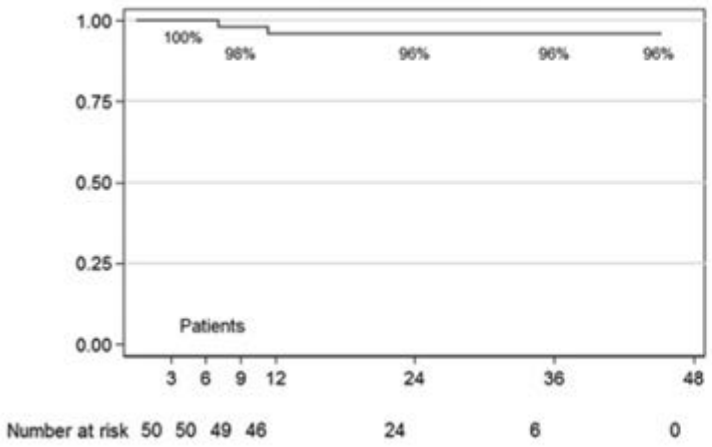


Planning Objectives

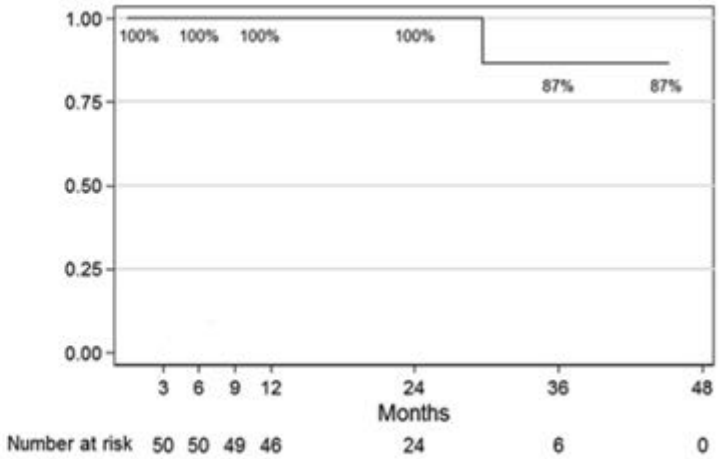
- ✓ *PTVs: 95% receiving at least 95% of each prescribed dose*
- ✓ *Rectum* $V50_{Gy} < 45\%$, $D_{max} < 70_{Gy}$
- ✓ *Bladder* $V60_{Gy} < 35\%$
- ✓ *Intestinal Cavity* $V20_{Gy} < 40\%$, $D_{mean} < 20_{Gy}$, $D_{max} < 48_{Gy}$
- ✓ *Femoral heads* $D1cc < 50_{Gy}$

Results

Local Control



Overall Survival

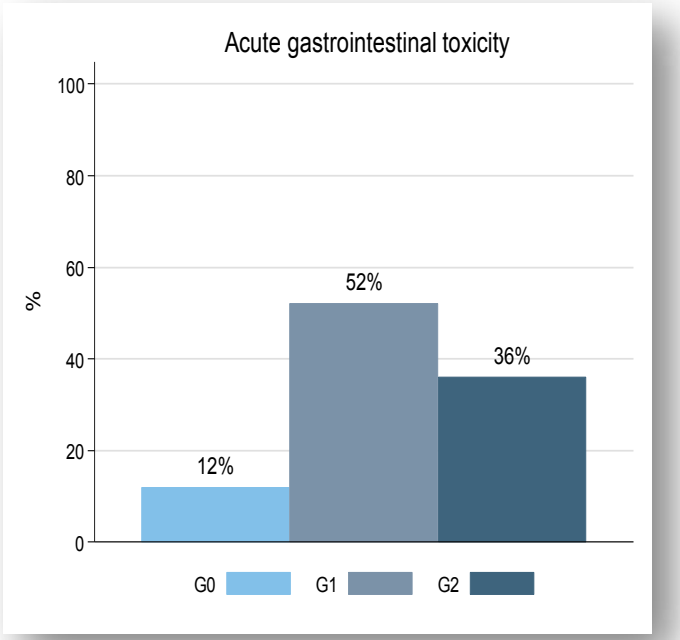


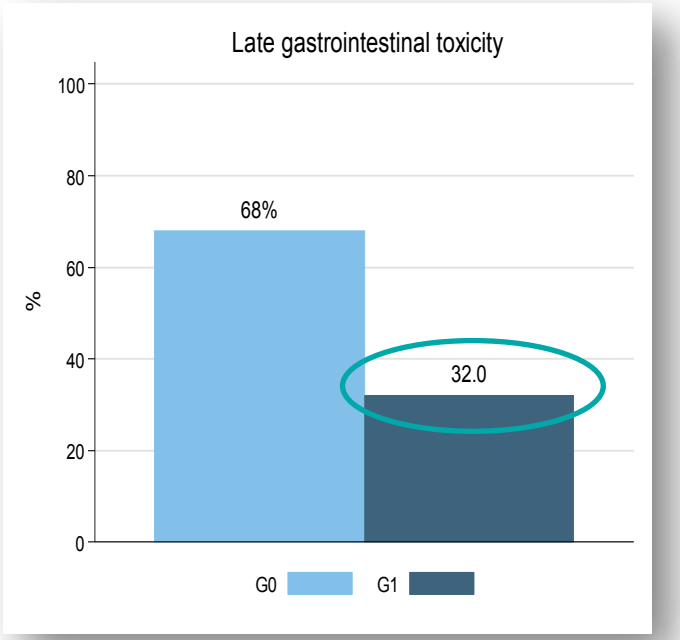
- ✓ **Median TTP: 25 months (range, 12-30 months)**
- ✓ **Five cases of systemic progression (2 peritoneal carcinosis, 1 liver metastases, 1 bone metastases, 1 sub-cutaneous metastases)**
- ✓ **Two loco-regional failures (pelvic nodes – Stage IIIC)**

No vaginal recurrence

Results

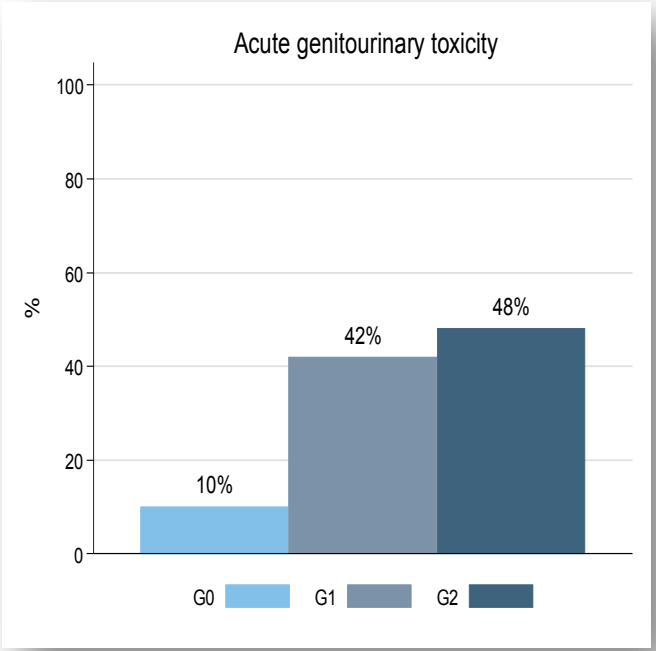
Gastrointestinal Toxicity **(CTCAE v4.0)**





Results

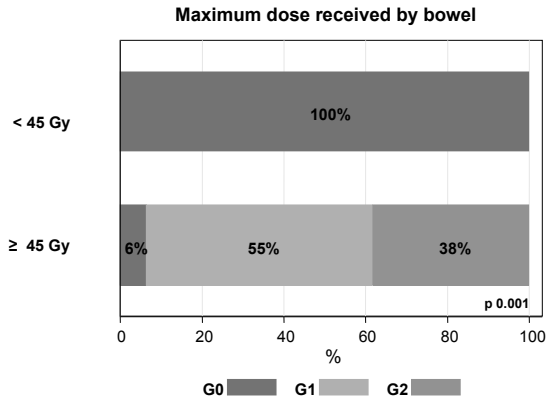
Genitourinary Toxicity **(CTCAE v4.0)**

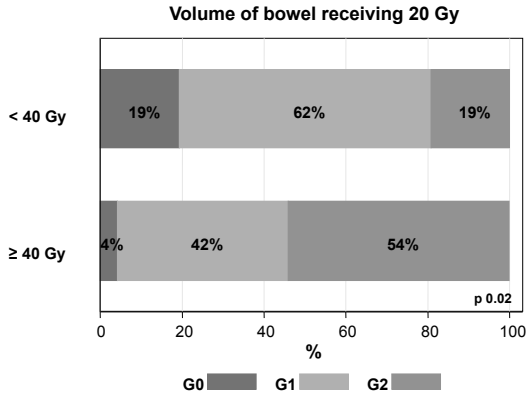


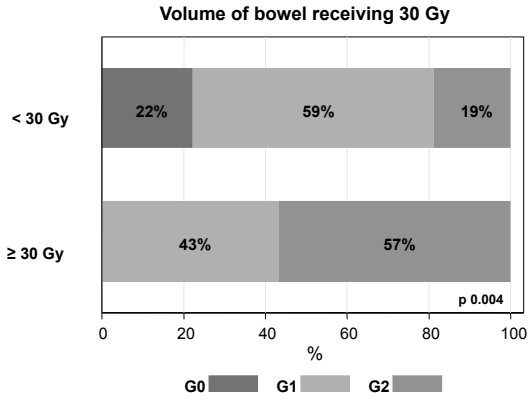
No late GU toxicity was registered

Results

Acute Toxicity: Dose-Volume Analysis







Acute G2 GI toxicity with intestinal cavity

- **Dmax ≥ 45 Gy**
- **$V20_{Gy}$ ≥ 40%**
- **$V30_{Gy}$ ≥ 30%**

No statistical correlation regarding GU toxicity

Conclusions

✓**Although our analysis presents several limitations due to the heterogeneity of the population, preliminary results in terms of tolerability and LC appear promising**

✓ **Pelvic-VMAT and SIB to vaginal cuff could be a viable alternative to pelvic-3D-CRT and VBT, when VBT is not logistically available or in case of patients refusing VBT**

<u>Prospective randomized trials are needed</u>

THANKS FOR ATTENTION!