CYCLE

Carbon ion radiation therapy in the treatment of mucosal melanomas of the female lower genital tract

Study Design	Monocentric, prospective phase II study
Statistical Considerations	Fleming one stage design
Treatment	The low-dose CTV (clinical target volume) will receive a total dose of 43 GyRBE in 10 fractions, 4 fractions per week. The high-dose CTV will receive a total dose of 68.8 GyRBE in 16 fractions, 4 fractions per week.
Endpoints	**The primary endpoint** of the study is to estimate **2-year PFS** in patients diagnosed with mucosal melanoma of the lower genital tract, treated with carbon ion radiation therapy. **Secondary endpoints:** •Overall survival (OS) •Toxicity according to Common Terminology Criteria for Adverse Events (CTCAE version 5.0) •Objective response rate (ORR) according to RECIST •Evaluation of the association between the clinical-radiological response at 6 weeks and the late response (> 6 months) •Quality of life.

CYCLE

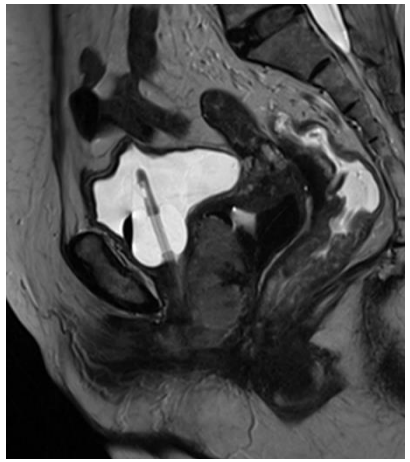
Carbon ion radiation therapy in the treatment of mucosal melanomas of the female lower genital tract

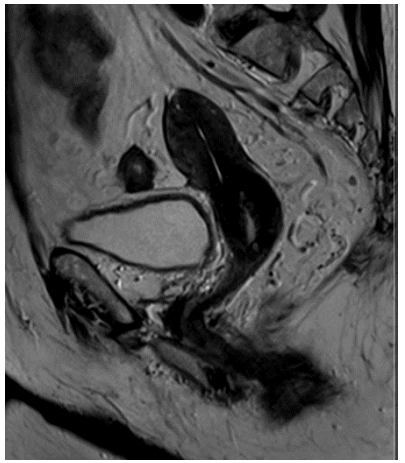
Inclusion Criteria	• **Histological diagnosis** • **N +** (only if confined to the groin and pelvis) • Age between **20-80 years** • ECOG 0-2 • **No evidence of metastasis** • At least **5 mm away with rectum and bladder wall** • **No previous RT** • Written informed consent • Patient's ability to understand the characteristics and consequences of the clinical trial • **Molecular characterization/ mutational state** • Disease staging (baseline exams)
Exclusion criteria	• Hip prosthesis, or metal prostheses or any other condition that prevents adequate imaging to identify the target volume and calculate the dose in the treatment plan • Psychic or other disorders that may prevent informed consent • Previous invasive tumor unless patient has been disease free for at least 3 years • **Contraindication to MRI** • Pregnancy or breastfeeding in progress

CYCLE

Carbon ion radiation therapy in the treatment of mucosal melanomas of the female lower genital tract

Enrollment	• **4/9**
Outcomes	• P1: CR (follow-up 24 months) • P2: CR (follow-up 13 months) • P3: PR (follow-up 8 months) • P4: PR (follow-up 4 months)





CYCLE – and now?

Carbon ion radiation therapy in the treatment of mucosal melanomas of the female lower genital tract

Inclusion Criteria	• **Histological diagnosis** • **N +** (only if confined to the groin and pelvis) • Age between **20-80 years** • ECOG 0-2 • **No evidence of metastasis** • At least **5 mm away with rectum and bladder wall** • **No previous RT** • Written informed consent • Patient's ability to understand the characteristics and consequences of the clinical trial • **Molecular characterization/ mutational state** • Disease staging (baseline exams)
Exclusion criteria	• Hip prosthesis, or metal prostheses or any other condition that prevents adequate imaging to identify the target volume and calculate the dose in the treatment plan • Psychic or other disorders that may prevent informed consent • Previous invasive tumor unless patient has been disease free for at least 3 years • **Contraindication to MRI** • Pregnancy or breastfeeding in progress

>20 years

(+3 pts between 2020-2022)

CYCLOPS

Study Design	Monocentric, prospective phase II study
Study Population	Patients affected by pelvic recurrence of gynecological neoplasia, already undergone to radiotherapy on pelvis, will be enrolled in the study.
Treatment	PTV will receive a total dose of 48-52.8 GyRBE in 12 fractions, 4 fractions per week. Treatment expected duration is 3 weeks, 4 fractions per week.
Statistical Considerations	Fleming one stage design
Aims	Primary endpoint: 1-year local control (LC) Secondary endpoints: • Overall survival (OS) • Toxicity according to Common Terminology Criteria for Adverse Events (CTCAE version 5.0) • Symptoms control, evaluating pain reduction (screened by NRS scale) and variation in the use of analgesic drugs (decrease or increase) • Subgroup success rate analysis with stratification according to: Histology (adenocarcinoma vs squamo-cellular)
Sample size	55 subjects

CYCLOPS

Inclusion Criteria

- Patients ≥ 18 years of age
- Karnofsky Index ≥ 70
- **Histological or radiological diagnosis** of pelvic recurrence
- **Contraindications for radical surgery**
- No other distant progression or stable disease (SD) of known secondarisms (≥6 months)
- Previous radiation therapy on pelvis
- Distance ≥ 10 mm between tumour and close intestinal tract (small intestine), radiologically evaluated
- **Possibility to perform a surgery to space the intestinal loops, in case of distance < 10mm**
- If needed, **spacer** in biocompatible material (silicon, goretex) or anatomical material (omentum, muscle patch), **non-absorbable.**
- DICOM images of the previous treatment plan availability

Exclusion criteria

- prosthesis, metal prostheses or any other condition that prevents adequate imaging to identify the target volume and calculate the dose in the treatment plan
- **Intestinal infiltration**
- **Bladder infiltration**
- **Vessel infiltration**
- Previous therapy with **anti-angiogenesis drugs**
- Psychic or other disorders that may prevent informed consent
- Previous invasive tumor, with the exception of skin cancer (excluding melanoma) unless disease-free for at least 3 years
- **Spacer in absorbable material (i.e. vycril)**
- Distance < 10 mm between tumour and close intestinal tract (small intestine), radiologically evaluated
- Impossibility to assess MRI

CYCLOPS

Enrollment	• **2/55**
Outcomes	• P1: local complete response (follow-up at 20 months) • P2: on treatment

CYCLOPS – how to improve the accrual?

Inclusion Criteria

- Patients ≥ 18 years of age
- Karnofsky Index ≥ 70
- Histological or radiological diagnosis of pelvic recurrence
- Contraindications for radical surgery
- No other distant progression or stable disease (SD) of known secondarisms (≥6 months)
- Previous radiation therapy on pelvis
- Distance ≥ 10 mm between tumour and close intestinal tract (small intestine), radiologically evaluated
- Possibility to perform a surgery to space the intestinal loops, in case of distance < 10mm
- If needed, spacer in biocompatible material (silicon, goretex) or anatomical material (omentum, muscle patch), non-absorbable.
- DICOM images of the previous treatment plan availability

Exclusion criteria

- prosthesis, metal prostheses or any other condition that prevents adequate imaging to identify the target volume and calculate the dose in the treatment plan
- **Intestinal infiltration**
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- Psychic or other disorders that may prevent informed consent
- Previous invasive tumor, with the exception of skin cancer (excluding melanoma) unless disease-free for at least 3 years
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- Impossibility to assess MRI

Contact

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