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PLENARY ABSTRACT | OVARIAN CANCER SESSION

Safety of Cytoreductive Surgery with Heated Intraperitoneal Gemcitabine and Systemic Dacarbazine for Recurrent Uterine Leiomyosarcoma – Preliminary Results of a Phase 2 Trial

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Disclosures

- I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

The off-label or investigational use of Gemcitabine will be addressed.

Background

- Uterine leiomyosarcoma (ULMS) is a rare but aggressive uterine malignancy
 - Incidence ~1 in 200,000 women
 - High rate of local recurrence within peritoneal cavity, eventual widespread metastases
 - Tumor rupture, morcellation, other
- Standard treatment: surgical resection + systemic gemcitabine/docetaxel
 - Combination therapy up to 40% response but ↑ toxicity
 - Despite therapy, recurrence rate even in Stage 1 disease >50%
- New therapies needed to improve progression-free survival and prognosis for ULMS patients

NCCN v 1.2022

Ganjoo, et al. Curr Probl Canc 2019



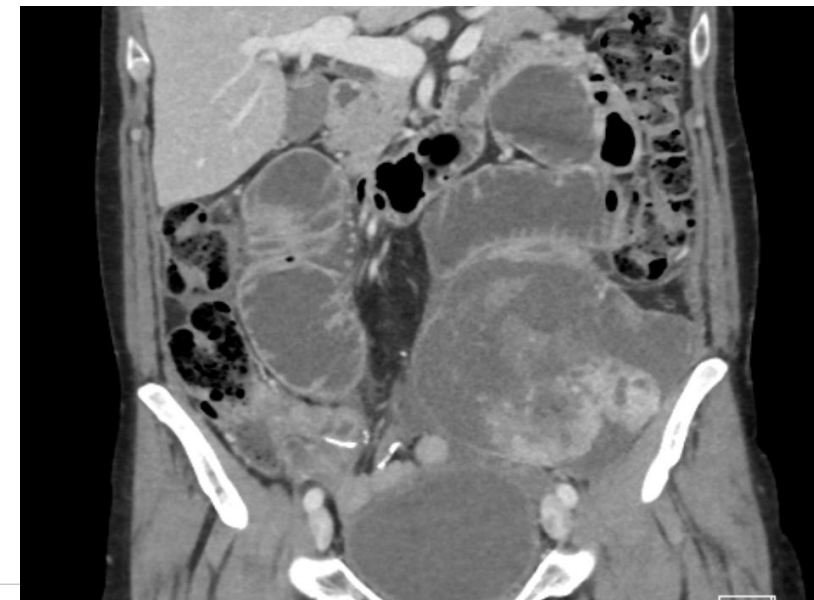
Recurrent ULMS



1 month post-op: NED



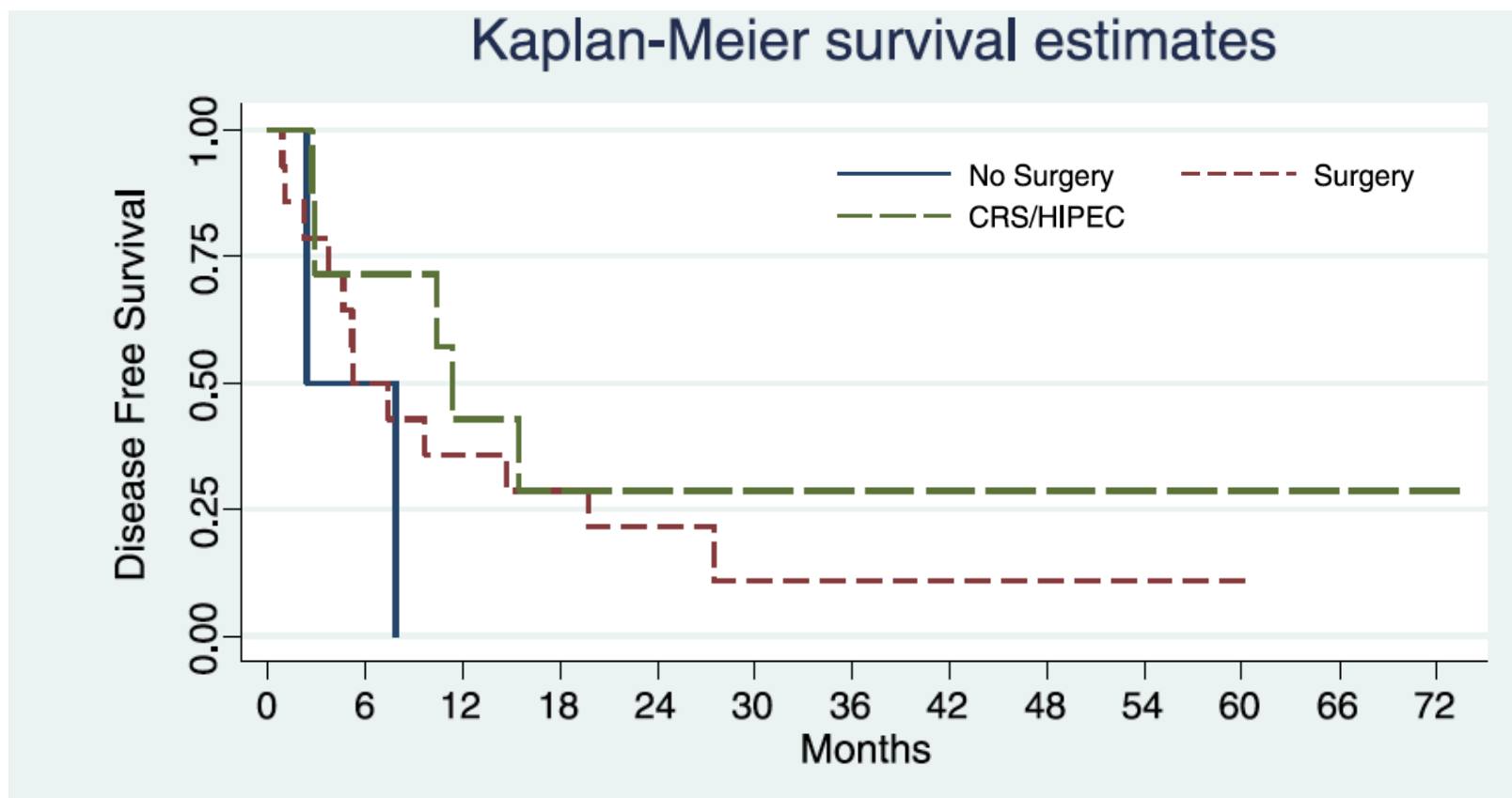
7 months post-op: Recurrence



Study Rationale

- Intraperitoneal chemotherapy in gynecological malignancies:
 - Improved progression-free and overall survival
 - Cytoreduction with HIPEC currently performed in ovarian & fallopian tube cancers
- ULMS recurs in the peritoneal cavity
 - HIPEC: increased regional concentration with decreased systemic toxicity
 - Gemcitabine with systemic activity against ULMS → consideration as perfusate
 - Dacarbazine exhibits activity against ULMS even as a single agent

CRS-HIPEC for Uterine Sarcoma



Diaz-Montes, et al., Int J Gynecol Cancer, 2019

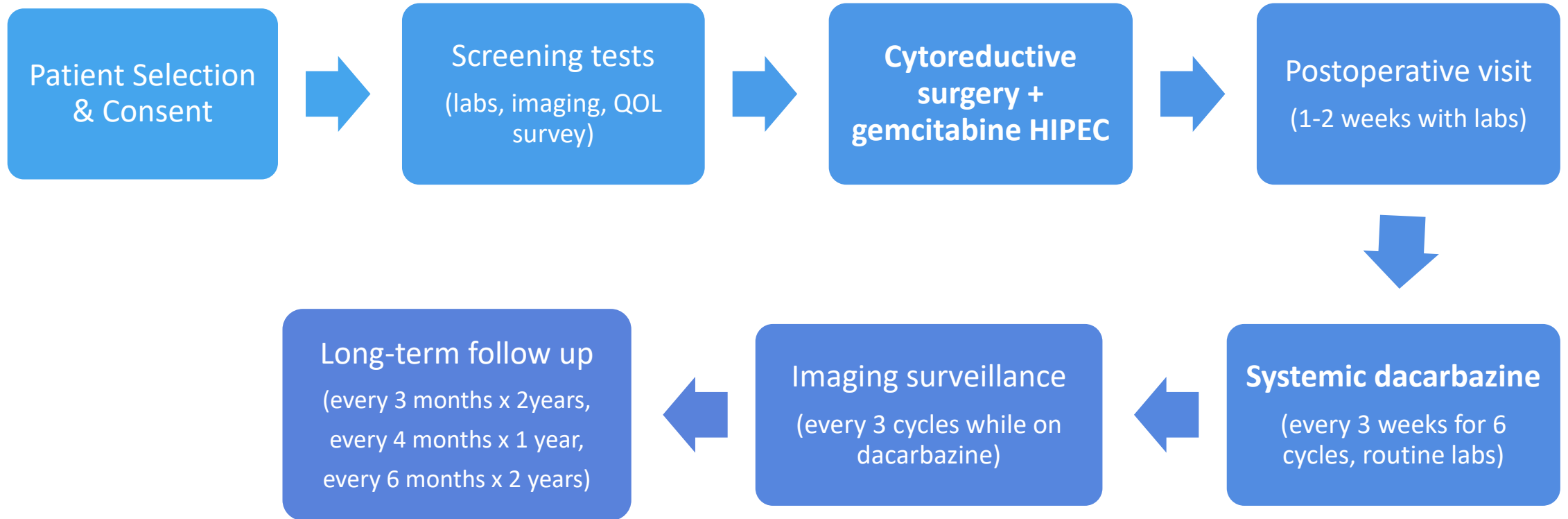
Study Intervention

1. Phase 2 Single Institution (NCT04727242)
2. Cytoreductive surgery
3. HIPEC with gemcitabine
(1000 mg/m² for 60 minutes at 42°C)
4. Systemic chemotherapy with dacarbazine
(1000 mg/m² every 3 weeks, for 6 cycles)

Study Design

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none">• Female ≥ 18 years with proven ULMS and recurrence• Imaging evidence of locally recurrent ULMS• Candidate for cytoreductive surgery per treating surgeon• Life expectancy > 3 months• ECOG functional status ≤ 2• Ability to consent for self to participate	<ul style="list-style-type: none">• Recurrence of ULMS < 6 months after systemic gemcitabine• Active extra-abdominal disease e.g. malignant pleural effusion. (May be included if treated and responded)• Prior neoadjuvant gemcitabine• Prior treatment with dacarbazine• Persistent toxicity from prior therapy• Metastatic disease to the liver• Pregnant or breastfeeding

Study Design



Study Objectives

- Primary endpoint:
 - **Progression-free survival**
- Secondary endpoints:
 - Safety profile of intervention
 - 6-month and 12-month recurrence-free survival
 - Quality of life metrics

Preliminary Results

Demographics

- 10 women with uterine leiomyosarcoma enrolled (March 2021 – July 2022)
 - Mean age: 58 years (31 - 84 years)
 - # prior abdominal surgeries: 1.5
 - History of morcellation: 50%
 - All ECOG: 0
 - BRCA: 10%

Preliminary Results

Operative factors

- 10 women with uterine leiomyosarcoma enrolled (March 2021 – July 2022)
 - Mean PCI 7.9 (6 - 14)
 - 90% CCR 0 achieved
 - Remaining had CCR 1
 - Mean Operative time: 346 minutes
 - Mean hospital LOS 6.9 days

Preliminary Results

Safety & complications

- 10 women with uterine leiomyosarcoma enrolled (March 2021 – July 2022)
 - No patient mortalities
 - 3 patients with complications related to CRS/HIPEC:
 - Bladder injury, ureteral transection, severe neutropenia
 - 2 patients with grade 3 or higher adverse effects
 - Lab abnormalities only

Preliminary Results

Outcomes

- 10 women with uterine leiomyosarcoma enrolled (March 2021 – July 2022)
 - Site of recurrence: Peritoneum >>> lung, bone
 - All patients currently alive: 40% no evidence of disease, 60% alive with disease

Conclusions

- ULMS is a rare STS with a high rate of recurrence despite optimal surgery and aggressive treatment
- CRS and HIPEC with Gemcitabine appears safe
- Study has not met accrual to date
 - Further follow up needed to assess efficacy

Thank you



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■ Primary Investigators

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