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and Peritoneum*



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

Beatrice Sun, MD

Resident, Department of Surgery
Stanford University School of Medicine

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
- Standard treatment: surgical resection + systemic gemcitabine/docetaxel
 - Combination therapy up to 40% response but ↑ toxicity
 - Despite therapy, recurrence rate even in Stage 1 disease is >50%
- New therapies are needed to improve progression-free survival and prognosis for ULMS patients

NCCN v 1.2022

Ganjoo, et al, *Curr Probl Canc*, 2019



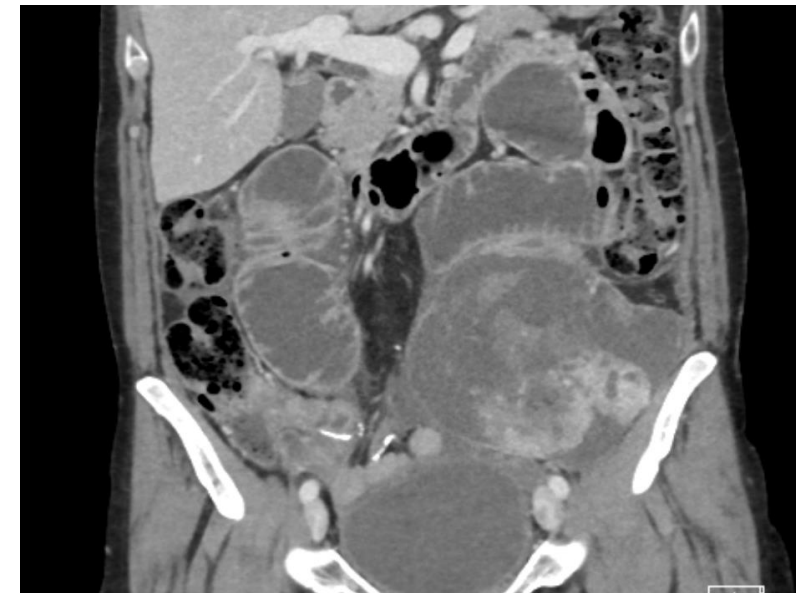
Recurrent ULMS



1 month post-op: NED

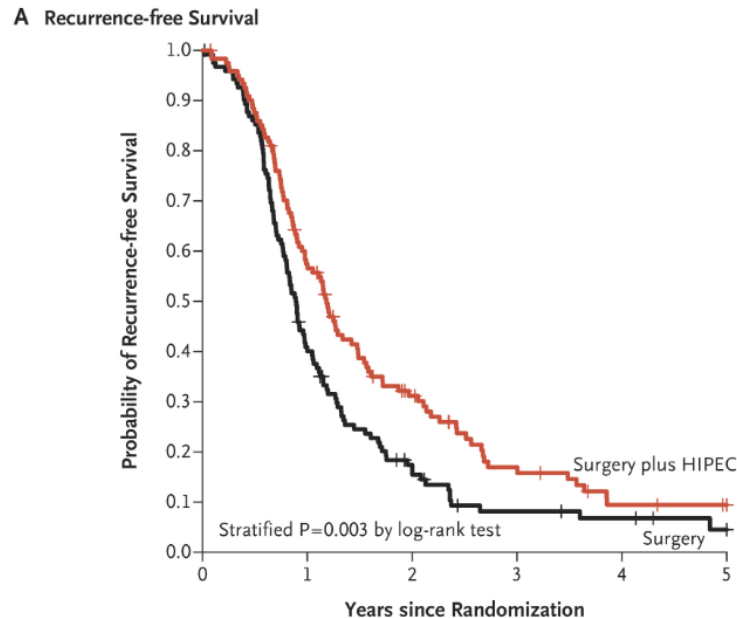


7 months post-op: Recurrence

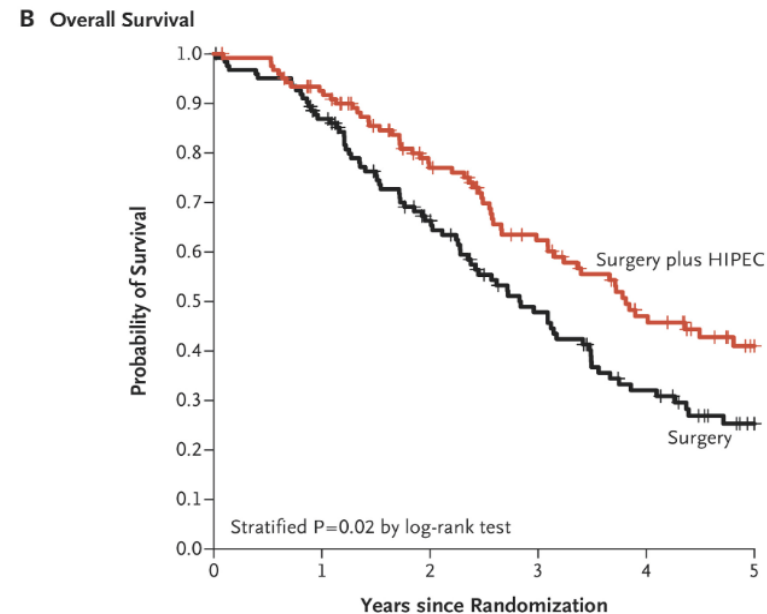


HIPEC in Gynecologic Malignancies

- Cytoreductive surgery (CRS) with HIPEC for ovarian & fallopian tube cancers
 - Improved recurrence-free and overall survival, no increased adverse effects



No. at Risk						
Surgery	123	48	18	7	5	2
Surgery plus HIPEC	122	67	31	15	7	5

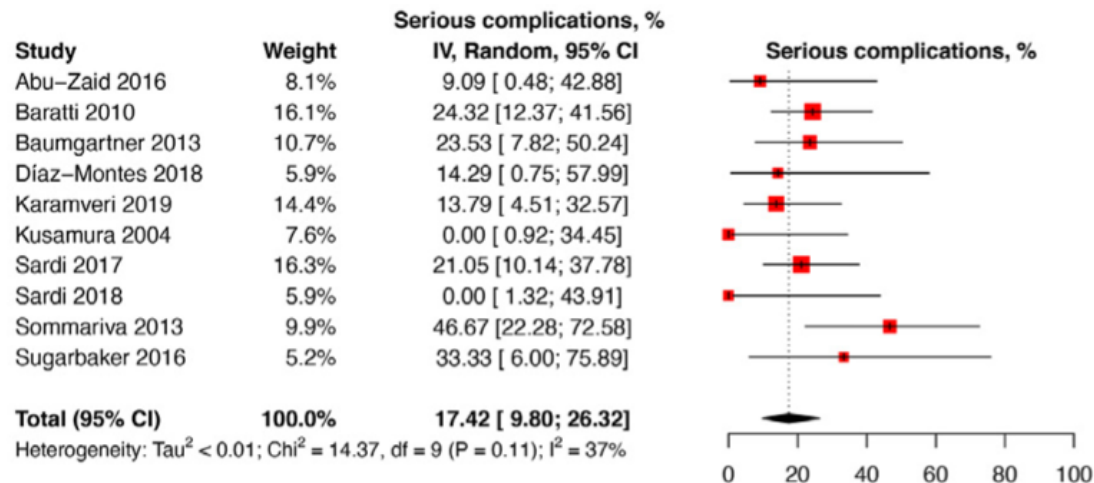


No. at Risk						
Surgery	123	103	70	44	27	12
Surgery plus HIPEC	122	108	79	56	37	20

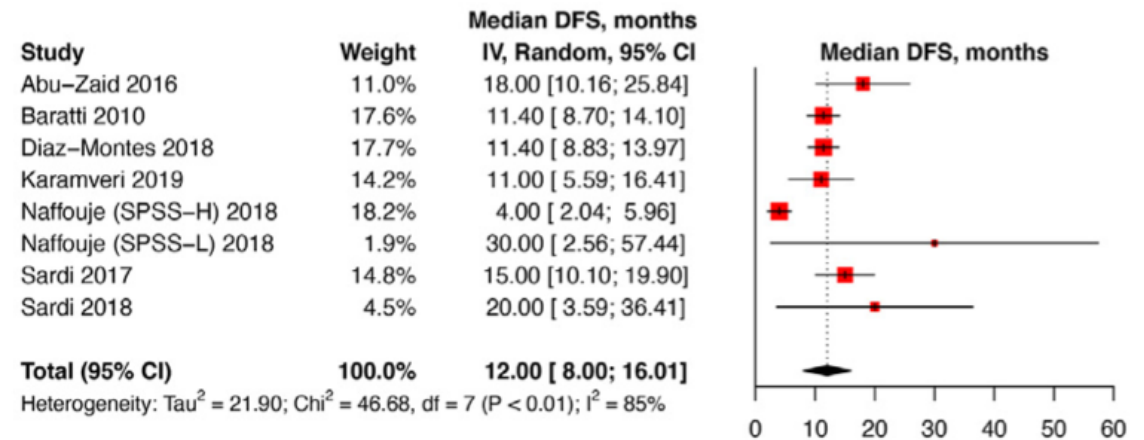
Van Driel et al. NEJM, 2018

HIPEC in Peritoneal Sarcomatosis

- Cisplatin + doxorubicin = most common perfusate



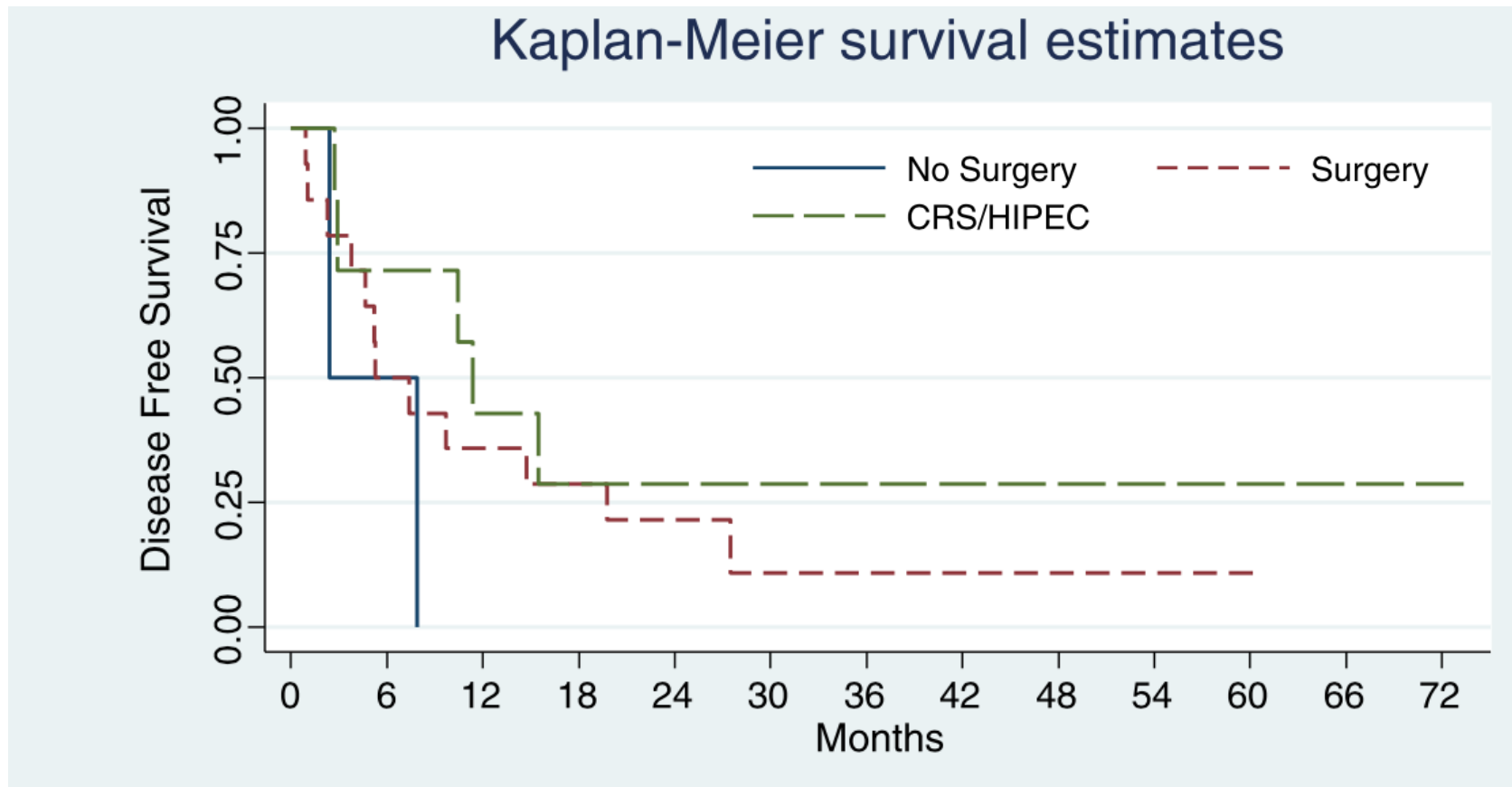
17% complications grade 3 or above



12 month disease-free survival

Wong et al. *EJSO*, 2022

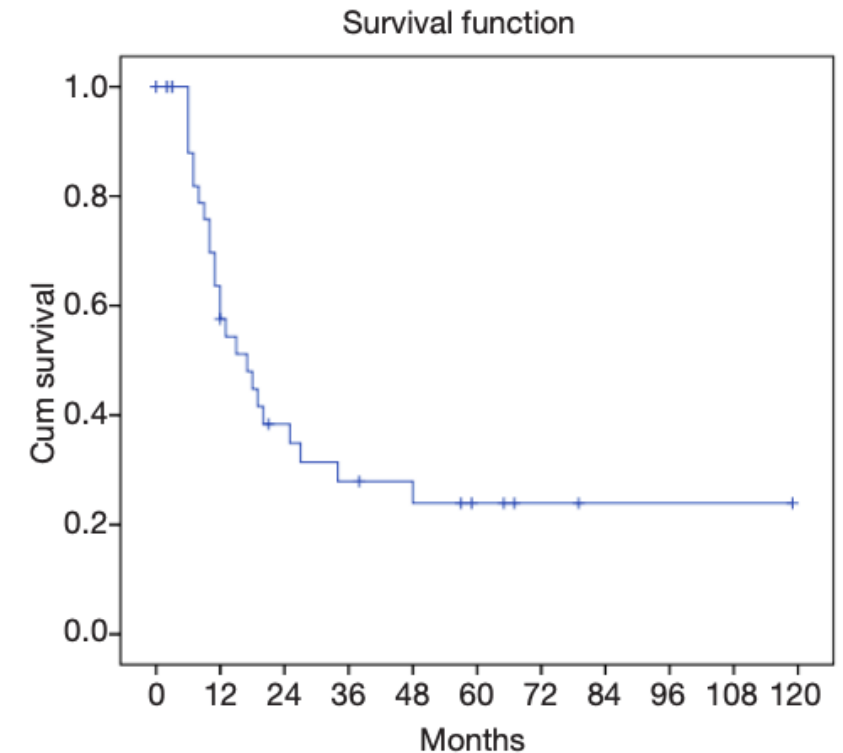
CRS-HIPEC for Uterine Sarcoma



Diaz-Montes, et al, Int J Gynecol Cancer, 2018

Gemcitabine in HIPEC

- 39 patients with resectable pancreatic adenocarcinoma
 - **R0 surgical resection + HIPEC with gemcitabine**
- Disease-free progression: 11 months
- Overall survival: 13 months
- **Good safety profile: 15% complications grade 3 or above**



Tentes. J Gastrointest Oncol, 2018

Study Rationale

- ULMS recurs in the peritoneal cavity
 - HIPEC: increased regional concentration with decreased systemic toxicity
 - Cisplatin has poor systemic efficacy in ULMS
 - **Gemcitabine** with systemic activity against ULMS → consideration as perfusate
 - **Dacarbazine** exhibits activity against ULMS even as a single agent

Study Intervention

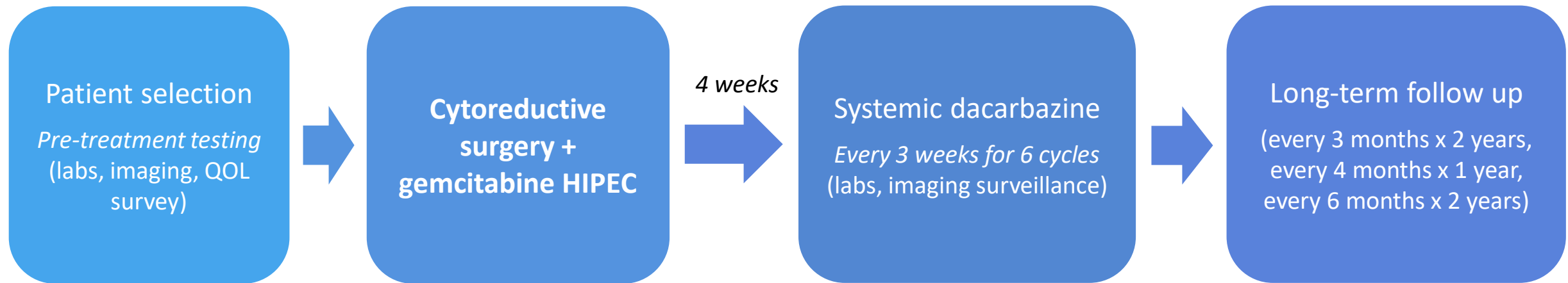
Phase 2 Trial, Single Institution (NCT04727242)

1. Cytoreductive surgery
2. HIPEC with gemcitabine
(1000 mg/m² for 60 minutes at 42°C)
3. 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 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

- 11 women with uterine leiomyosarcoma enrolled (March 2021 – Sept 2022)
 - Median age: 58 years (31 - 84 years)
 - # prior abdominal surgeries: 1.5
 - History of morcellation: 45%
 - BRCA: 9%
 - All ECOG 0

Preliminary Results

Operative factors

- 11 women with uterine leiomyosarcoma enrolled (March 2021 – Sept 2022)
 - Median PCI 7 (range 5 - 14)
 - >90% CCR 0 achieved
 - 1 patient with CCR 1
 - Median operative time: 341 minutes
 - Median hospital LOS: 6 days

Preliminary Results

Safety & complications

Patient	AE Grade Nausea	AE Grade Labs	AE Grade Hematologic	AE Grade Pain	AE Grade Functional	Surgical Complication
1	1	1	3	1	1	No
2	0	1	0	1	1	No
3	1	0	0	1	1	Yes → Bladder injury
4	0	0	0	0	0	No
5	0	0	0	0	0	No
6	0	0	0	1	1	No
7	2	1	3	0	1	No
8	0	0	0	0	0	No
9	0	0	0	0	0	No
10	1	1	1	0	0	Yes → Ureteral transection
11	0	0	0	0	0	No

Preliminary Results

Outcomes

Patient	Status	Recurrence Site(s)	Follow-Up (months)
1	AWD	Peritoneum	16
2	NED	Peritoneum, Bone	19
3	NED	N/A	12
4	AWD	Peritoneum, Lung	15
5	AWD	Peritoneum	14
6	NED	N/A	5
7	NED	N/A	12
8	AWD	Peritoneum	6
9	AWD	Peritoneum	19
10	AWD	Peritoneum	7
11	NED	N/A	1

Conclusions

- ULMS is a rare soft tissue sarcoma with high rate of recurrence despite optimal surgery and aggressive treatment
- CRS and HIPEC with gemcitabine appears safe
- Study has not met accrual to date (25 patients)
 - Further follow up needed to assess efficacy

Thank you



Stanford
MEDICINE

Department of Surgery
Surgical Oncology

■ Primary Investigators

- Kristen N. Ganjoo, MD
- Byrne Lee, MD FACS FSSO
- Nam Bui, MD
- Amer Karam, MD
- Oliver Dorigo, MD PhD

