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*International Society
for the Study of Pleura
and Peritoneum*



HEPATIC PANCREATIC BILIARY (HPB)

Cytoreductive Surgery and HIPEC for PDAC

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Advancing Innovative Therapies for Cancers That Invade the Peritoneum and the Pleura

Disclosures

- No 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/investigational use of Cisplatin, Mitomycin C, Nab-paclitaxel will be addressed.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

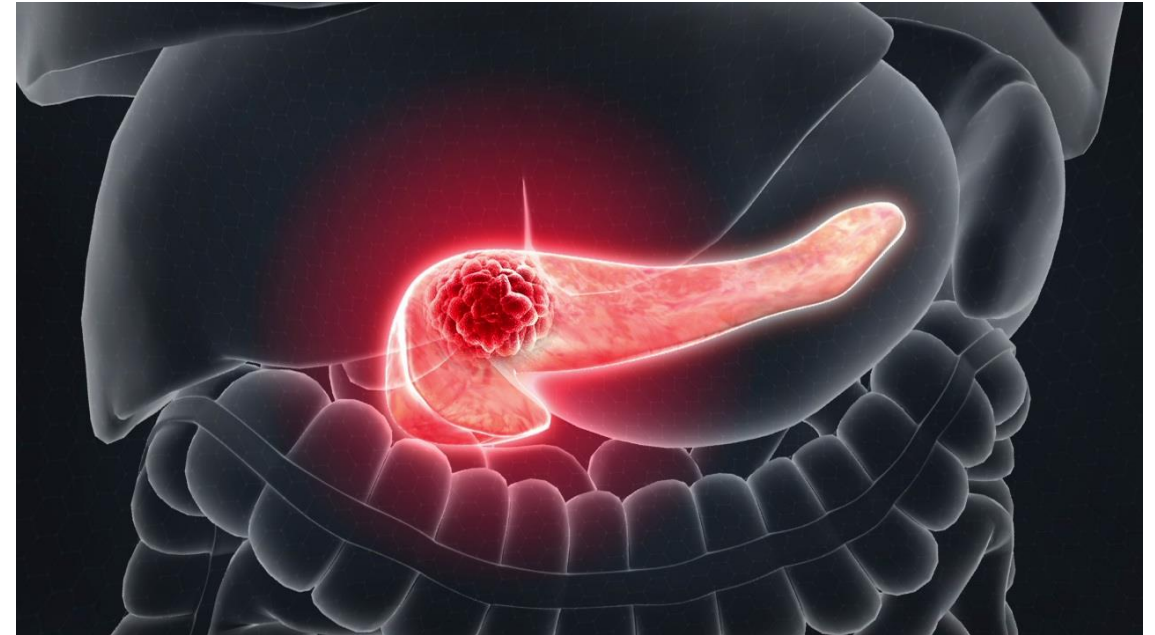
The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

The following CLC & IB components will be addressed in this presentation:

- Socioeconomic barriers to access to and acceptance of cytoreductive surgery and HIPEC.
- Implicit bias that many providers have that nothing can be done for metastatic pancreatic cancer to the peritoneum.

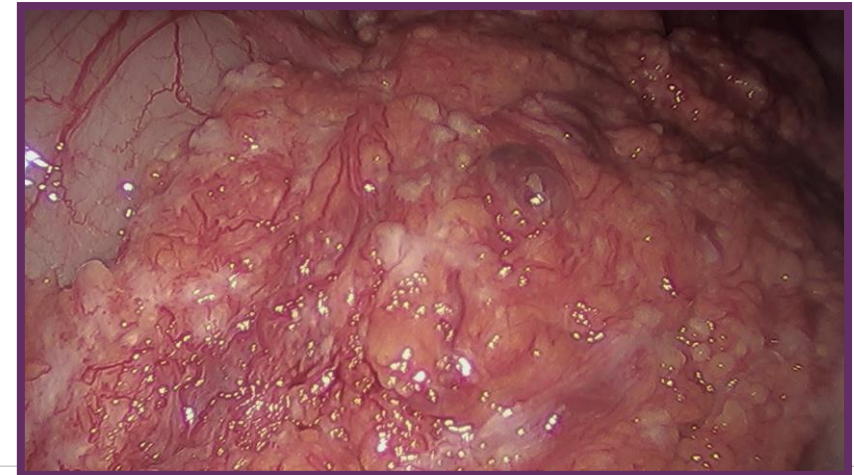
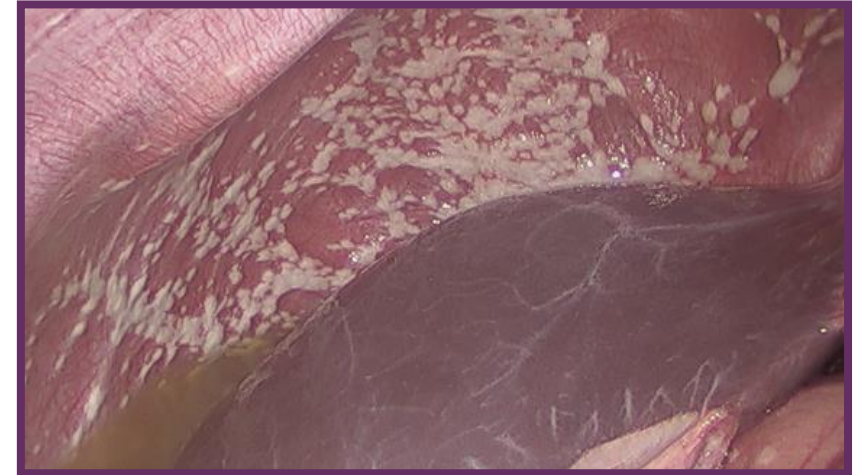
Pancreatic Ductal Adenocarcinoma (PDAC)

- Pancreatic cancer is highly fatal malignancy with ↑ incidence
- Most patients present with metastatic disease at diagnosis and even those who present with anatomically resectable local disease most will develop distant metastasis postoperatively
- Modern chemotherapy regimens have demonstrated improved responses and outcomes
- Thus, re-evaluation of resection of oligometastatic PDAC is warranted



Peritoneal Metastasis (PM)

- 1,004 staging laparoscopies for PDAC from 2017-2021
- 180 (18%) patients had radiographically occult PM and/or + cytology
- Median survival of patients was 13 months with no difference ($p=0.40$) between gross disease vs. + cytology alone



Hypothesis

- In patients with low volume peritoneal metastasis who demonstrate sustained objective response to prolonged induction chemotherapy that peritoneal limited metastasis could be treated with the goal of prolonging progression-free survival (PFS)

AIM OF CURRENT STUDY

- Determine safety and feasibility of (phase Ib/pilot) HIPEC + cytoreduction for patients with limited peritoneal metastasis

METHODS

18 Patients

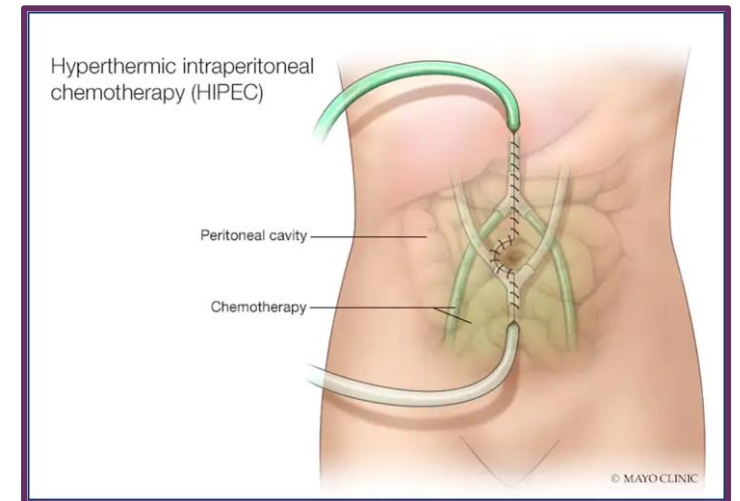
≥6 months FOLFIRINOX
and/or Gem/Abraxane

Radiographic, Metabolic,
and/or Biochemical
Response



Lap + HIPEC
Mitomycin C + Cisplatin

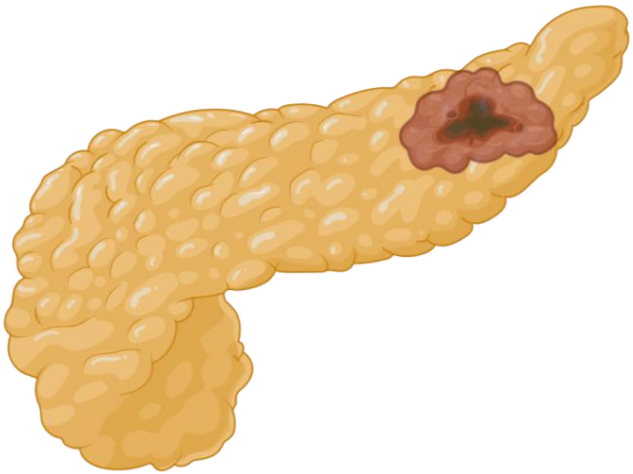
If amenable to CC-0



Cytoreduction + HIPEC
+
Treatment of Primary

TREATMENT OF PRIMARY

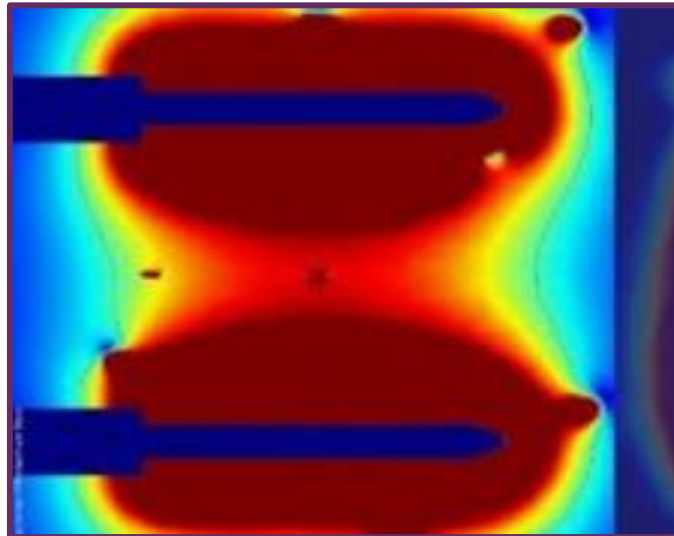
Formal Resection
(Distal Panc Or Total Panc)



Chemoradiation

+

IRE



IORT



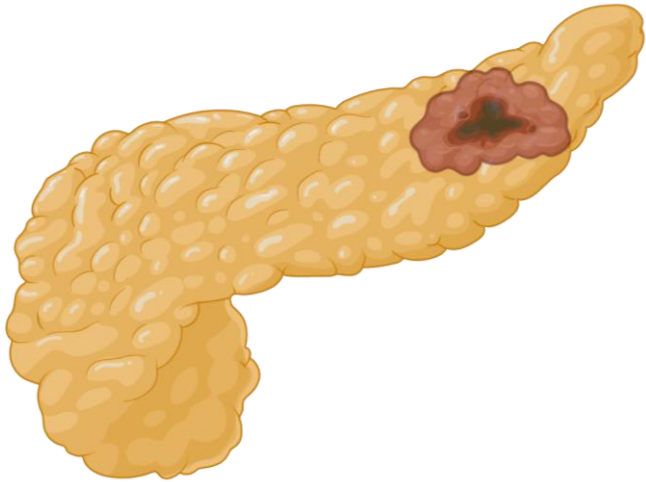
DEMOGRAPHICS

Pilot Cohort (n=18)

Median Age	57 (55-60)
Male / Female	44% / 56%
Median Chemo Cycles	14 (12-17)
Median CA19-9 at time of CRS/HIPEC	130 (35-273) U/mL
Gross Disease	50%
Median PCI at Staging Lap	0 (0-6)
Positive Cytology Only	50%

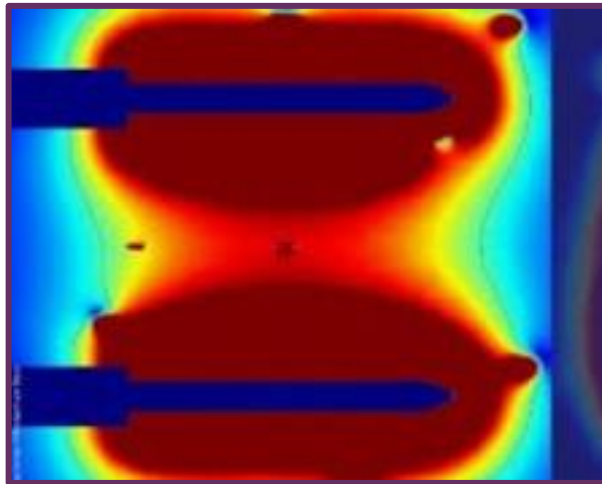
TREATMENT OF PRIMARY

Formal Resection



38%
(n=7)

IRE



56%
(n=10)

IORT



6%
(n=1)

RESULTS

Median (IQR) PCI at CRS + HIPEC
2 (0-4)

Complete Cyto reduction Achieved In All Cases

Path Response

Near-Complete Response

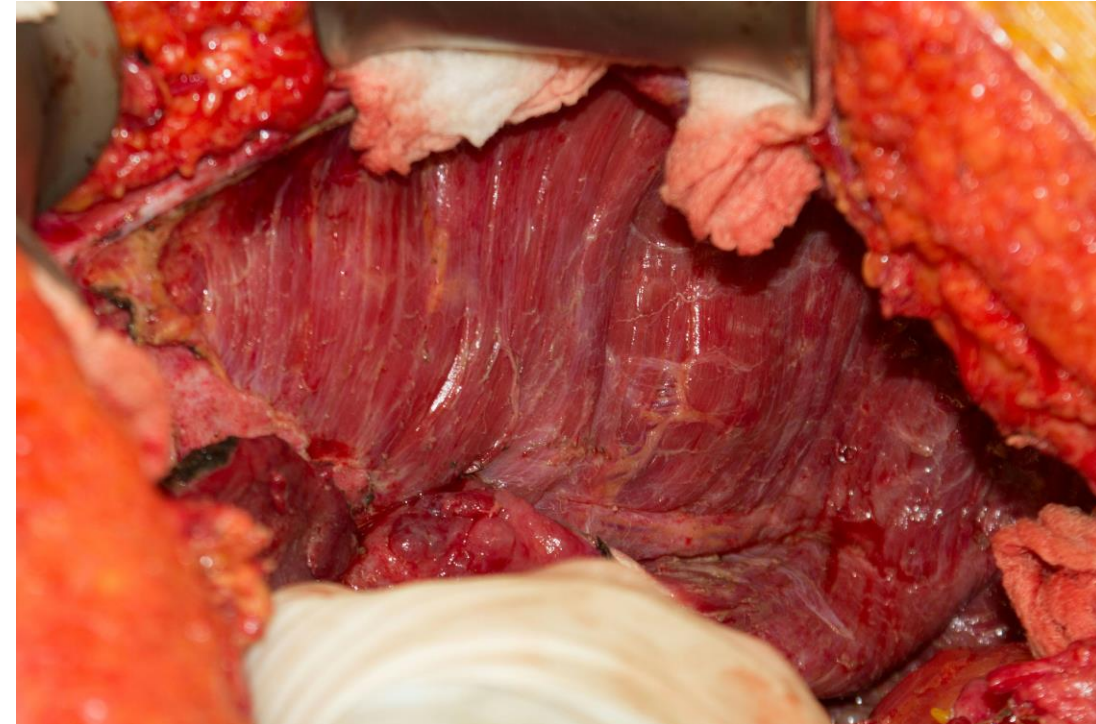
71% (5)

Moderate Response

29% (2)

CYTOREDUCTION

Omentectomy	94% (17)
Hemidiaphragm Peritonectomy	44% (8)
Pelvic Peritonectomy	22% (4)
Oophorectomy	22% (4)
Small Bowel Resection	22% (4)
Partial Colectomy	11% (2)
Splenectomy	11% (2)
Gastrectomy	6% (1)
Nephrectomy	6% (1)

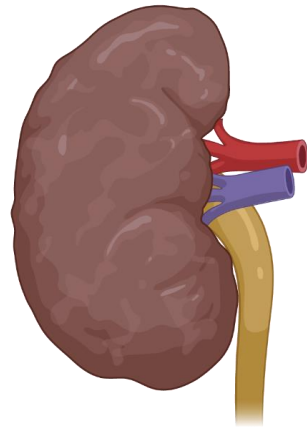


LAPAROSCOPIC HIPEC OUTCOMES

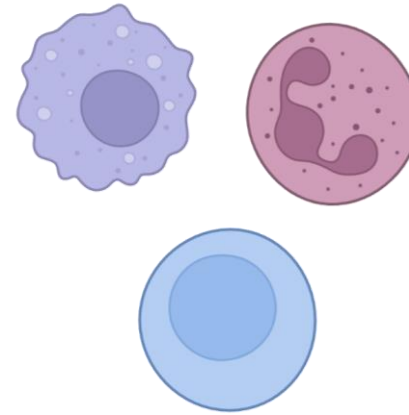
17/18 Patients Underwent Laparoscopic HIPEC



LOS
1 Day



AKI (rifle
criteria)
0%



- Grade ≥ 4
Cytopenia
 - 0%



Grade ≥ 3 Comp
0%

CRS PERI-OPERATIVE OUTCOMES



- Median Op Time
- 518 (473-616) mins



Median Blood Loss
375 (200-550) mL



Grade ≥ 3 Comp
44% (n=8)



30-day Mortality n=1
90-day Mortality n=2

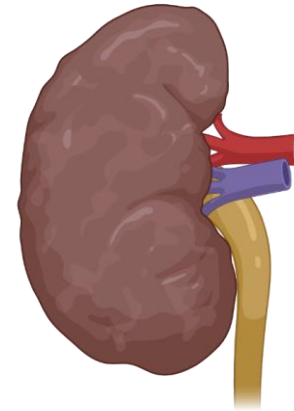
CRS + HIPEC PERI-OPERATIVE OUTCOMES



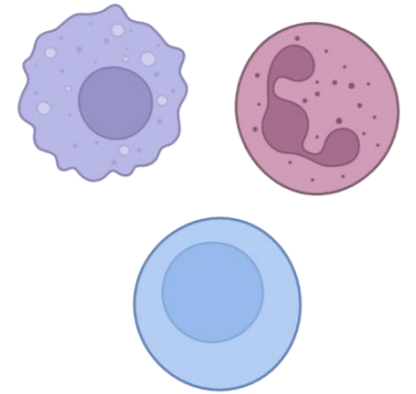
Median LOS
7 (6-8) Days



- 30-Day Readmit
39% (n=7)



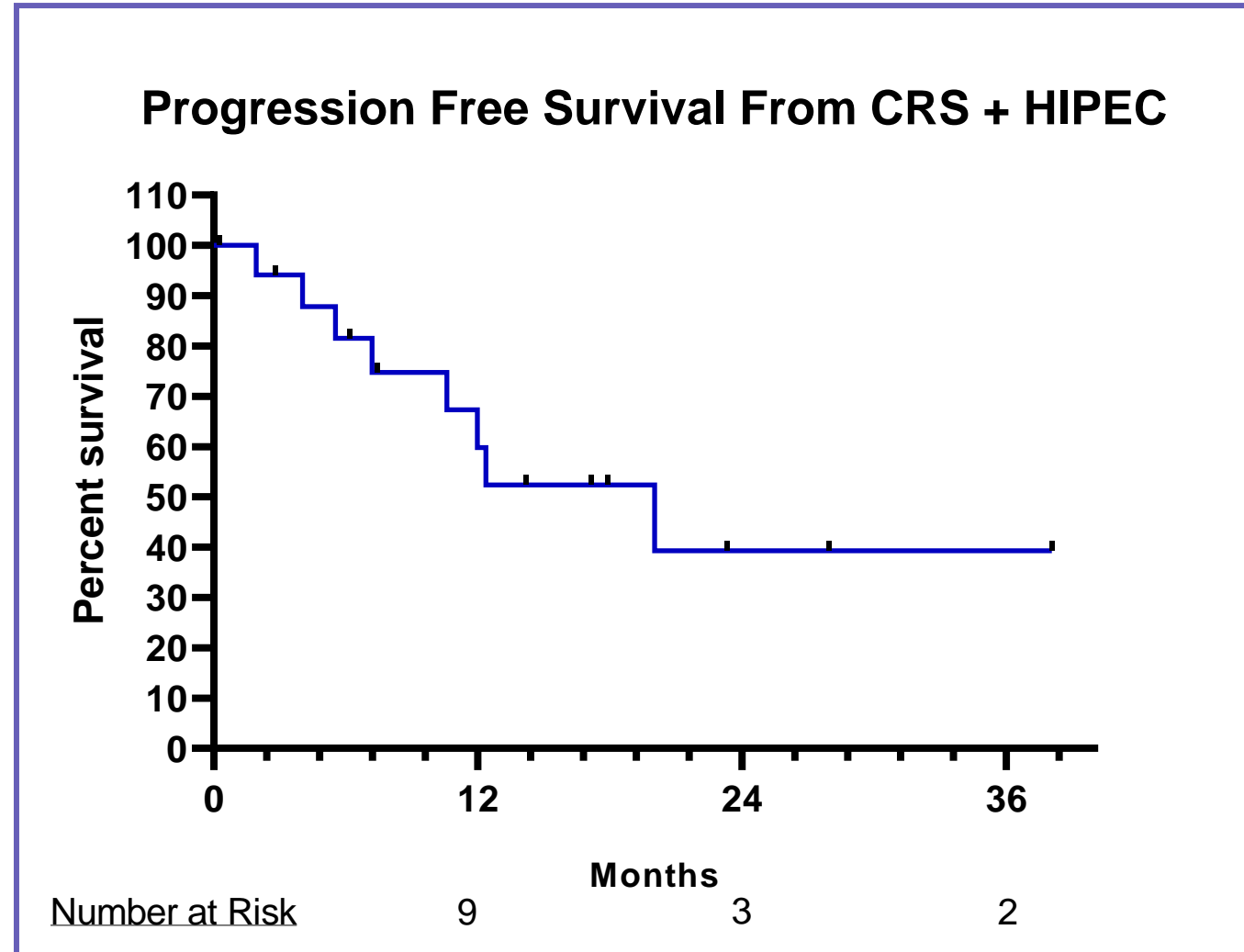
AKI
28% (n=5)



Grade ≥ 4
Cytopenia
11% (n=2)

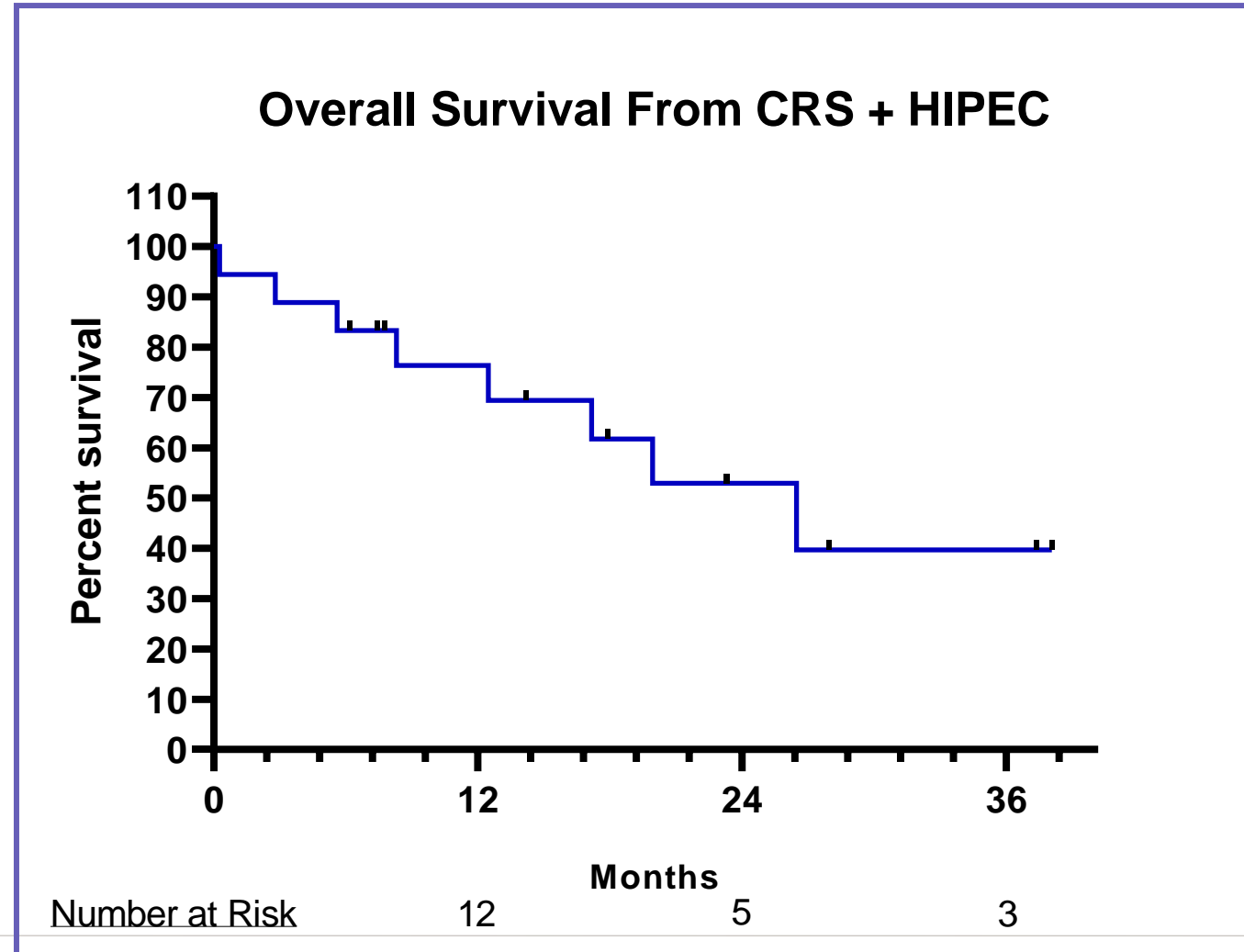
PROGRESSION-FREE SURVIVAL (PFS)

- Median PFS
20 months
- Disease Progression
44% (n=8)
- Most often in the peritoneum (63%, n=5) and less often in the liver (n=2), and other distant site (n=1).



OVERALL SURVIVAL

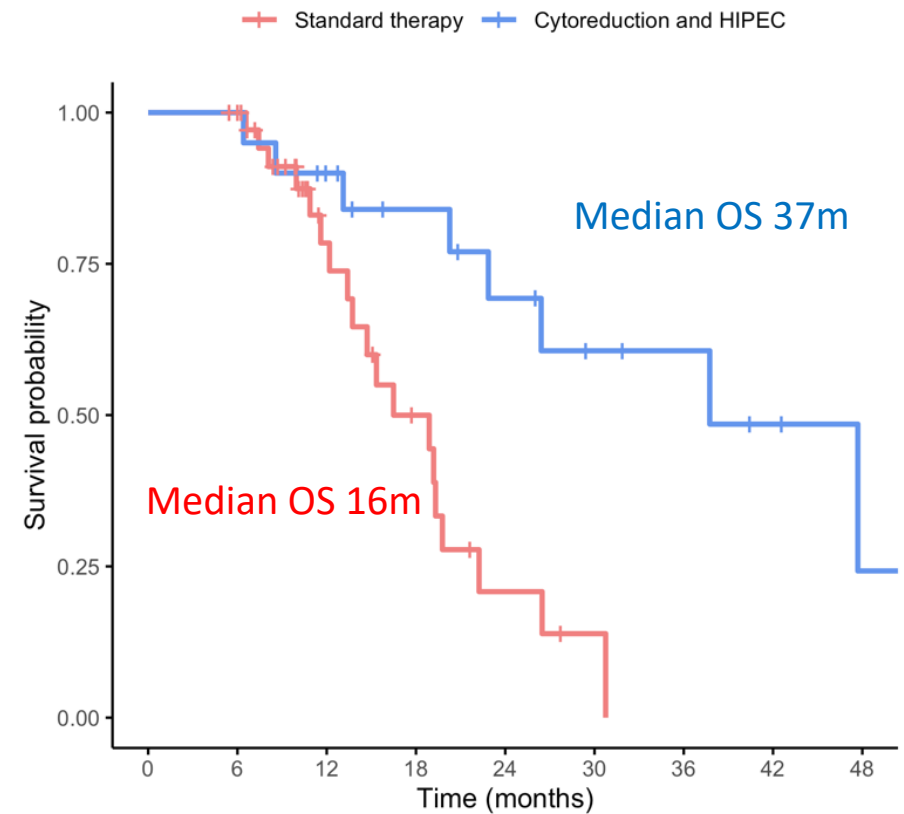
- Median Follow-Up
 - 16 (8-23) months
- Median Survival
 - 26 months



COMPARATIVE SURVIVAL

	Standard therapy (n=38)	HIPEC and resection/IRE (n=20)	p-value
Median age (years)	63 (IQR 53-69)	59 (IQR 55-66)	0.41
Female sex	19 (50%)	10 (50%)	>0.99
Distal tumor location	23 (61%)	15 (75%)	0.42
Median tumor size (mm)	35 (IQR 29-46)	38 (IQR 28-45)	0.63
BR/LA anatomy	31 (82%)	12 (60%)	0.14
Indeterminate peritoneal lesions on imaging	12 (32%)	6 (30%)	>0.99
Gross peritoneal metastases	27 (71%)	10 (50%)	0.19
Positive cytology	26 (84%) (avail in 31)	14 (88%) (avail in 16)	>0.99
Elevated peritoneal CA 19-9	11 (50%) (avail in 22)	9 (64%) (avail in 14)	0.62
Elevated peritoneal CEA	10 (45%) (avail in 22)	6 (43%) (avail in 14)	>0.99
Elevated serum CA 19-9	28 (82%) (avail in 34)	14 (74%) (avail in 19)	0.50
Median serum CA 19-9 level	172 (IQR 52-1071)	120 (IQR 36-280)	0.33
Elevated serum CEA	15 (52%) (avail in 29)	5 (38%) (avail in 13)	0.51
Median serum CEA level	3.1 (IQR 1.7-12.4)	2.2 (IQR 1.9-4.2)	0.35

OS from diagnosis of peritoneal metastases



CONCLUSIONS

- Cytoreduction + HIPEC is feasible with acceptable toxicity
- May prolong progression/survival in carefully selected patients
- Larger phase II Trial w/ cisplatin and nab-paclitaxel IP chemo is now enrolling (NCT04858009) with goal to enroll more diverse population