City of Hope

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OVARIAN CANCER

How Do IP Chemotherapies Fit in with Systemic Therapies in Ovarian Cancer?

Daphne Stewart, MD, MS

Associate Professor
Department of Medical Oncology
City of Hope

Disclosures

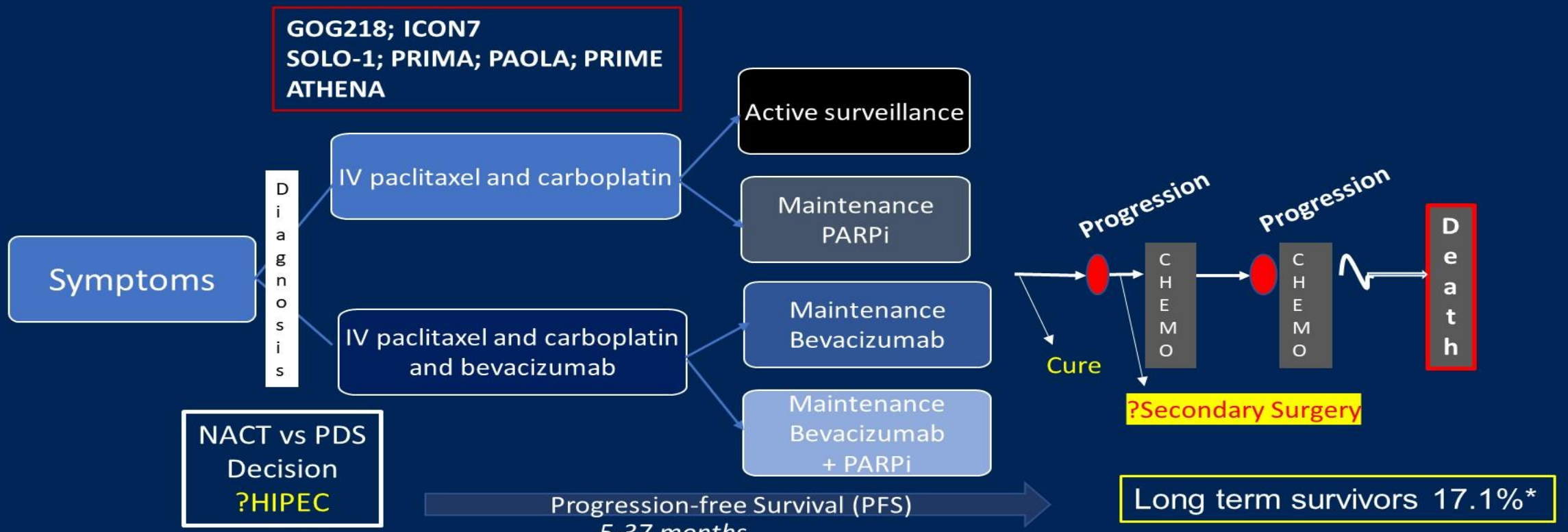
- I do not have any relevant financial relationships.

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

Ovarian cancer

- Majority present with spread to the peritoneal cavity at diagnosis and recurrence
- Peritoneal disease very symptomatic
- Peritoneal recurrence very hard to treat, devastating loss to function and life

Ovarian Cancer: 2022 Treatment Paradigm



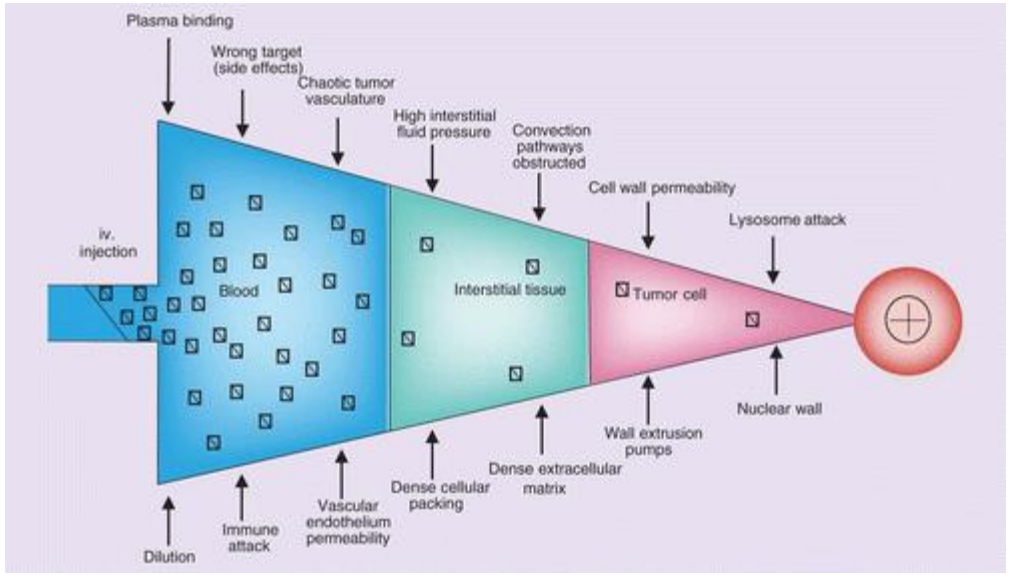
*SEER.cancer.gov accessed 2022

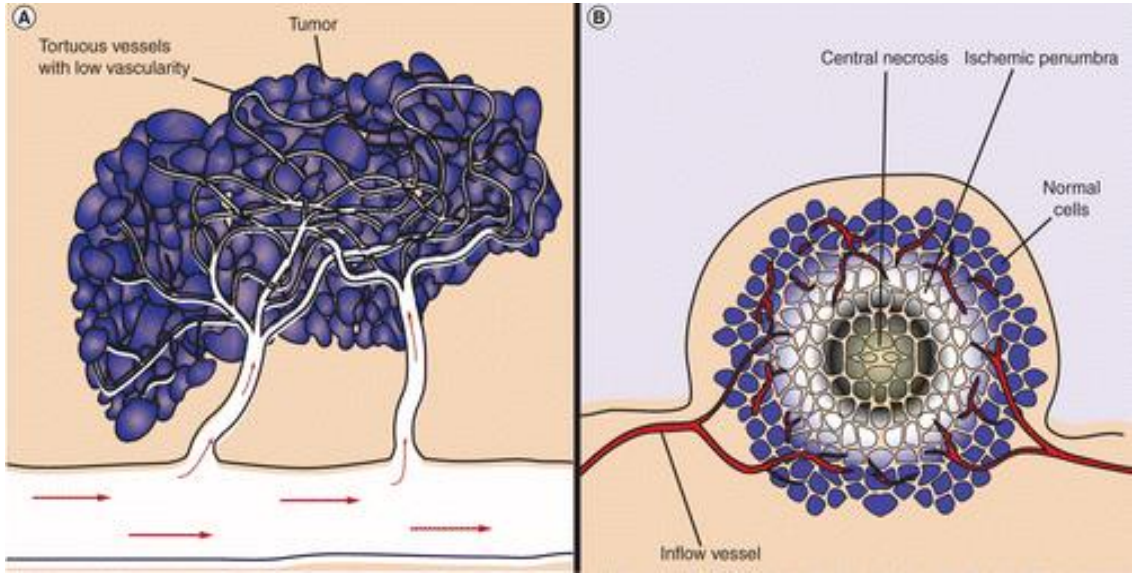
How can we further optimize treatment –

--thoughtful sequencing of available therapies, better maintenance, something curative??

--minimize barriers to care

Delivery of Systemic Chemotherapy

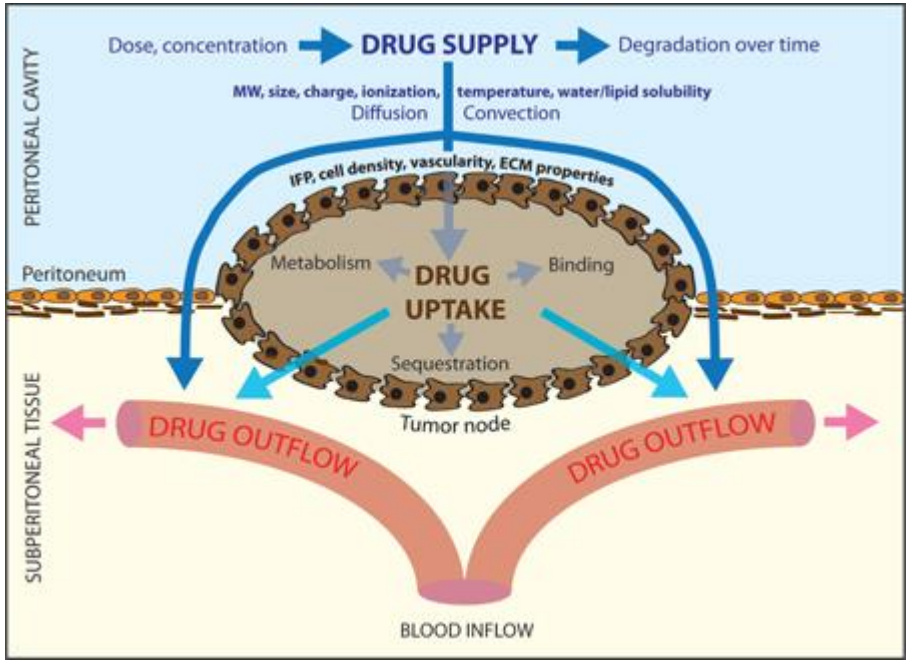




Delivery of chemotherapy requires diffusion across multiple spaces.

Intravascular delivery is hampered by high pressure and complicated tumor vasculature.

Benefits to IP chemotherapy



- High peritoneal to plasma ratio at peak concentration
  - Peritoneal plasma barrier blocks leakage to vessels and maintains high peritoneal concentration at tumors
  - Decreased systemic toxicity
- Lesions 2-3 mm (or smaller) avascular tumors will have higher drug exposure
- Poorly vascularized peritoneal tumors access high concentration drug delivery
- Risks: neurotoxicity, renal toxicity, catheter complications, abdominal pain

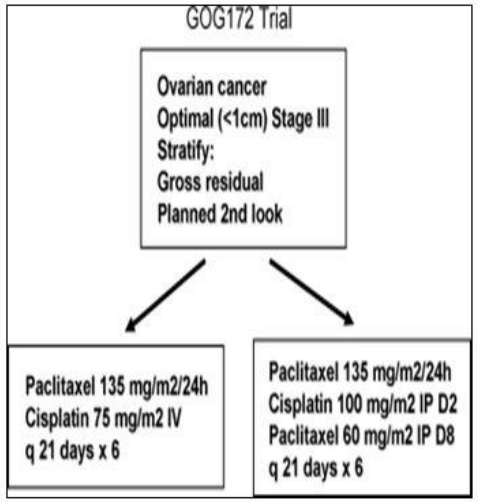
IP Therapies

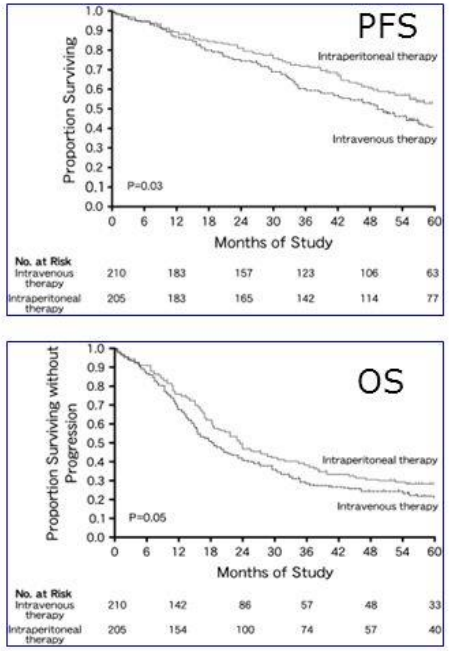
- IP
- IP/IV
- IV, interval CRS with HIPEC

IP v. IV chemotherapy

GOG 172

(Armstrong et al, 2006) CISPLATIN/PACLITAXEL IV vs. IP





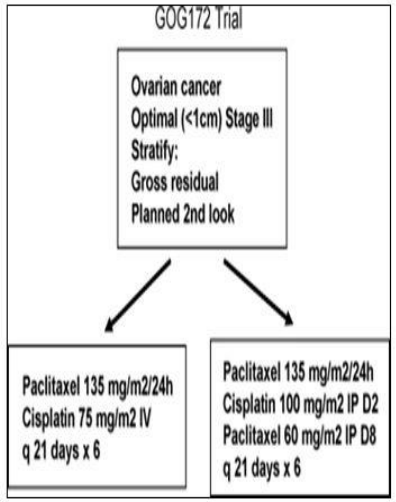
Results GOG 172
N =415

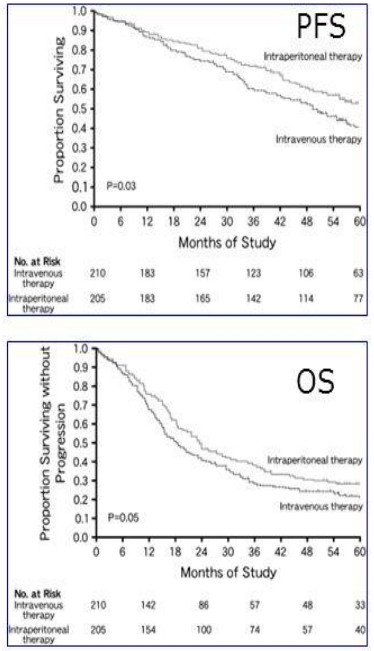
	IV	IP
Neg second look N=202	41%	57%
PFS	18.3 mos	23.8 mos
Overall Survival	49.7 mos	65.6 mos
Rel. Risk PFS		.77

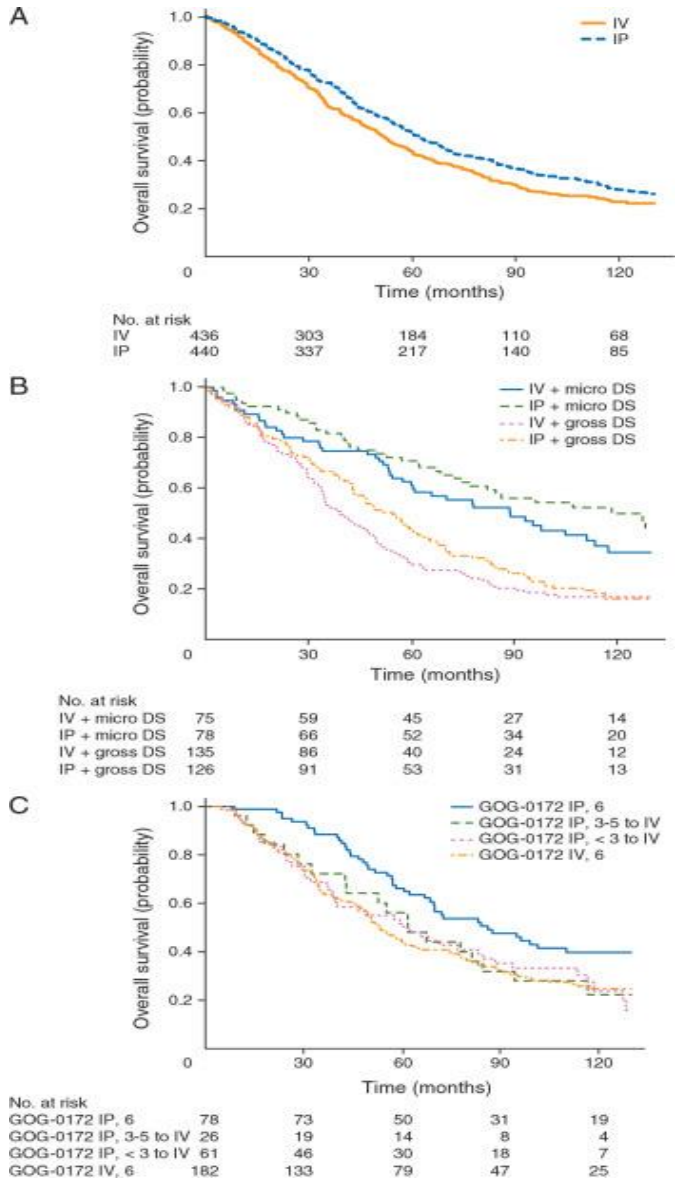
IP v. IV chemotherapy

GOG 172

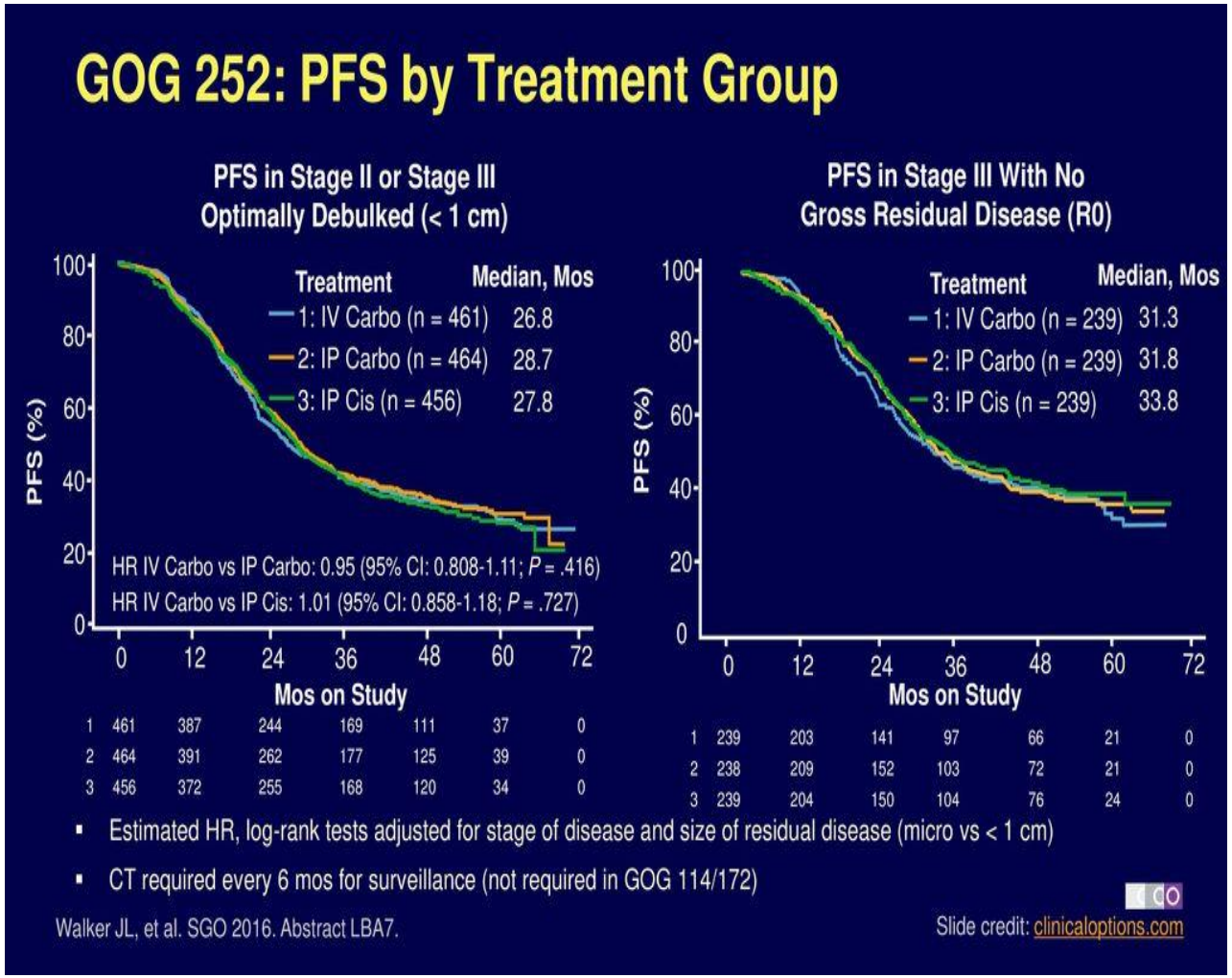
(Armstrong et al, 2006) CISPLATIN/PACLITAXEL IV vs. IP







IP v. IV chemotherapy



No benefit to IP chemotherapy in optimally debulked stage III ovarian cancer

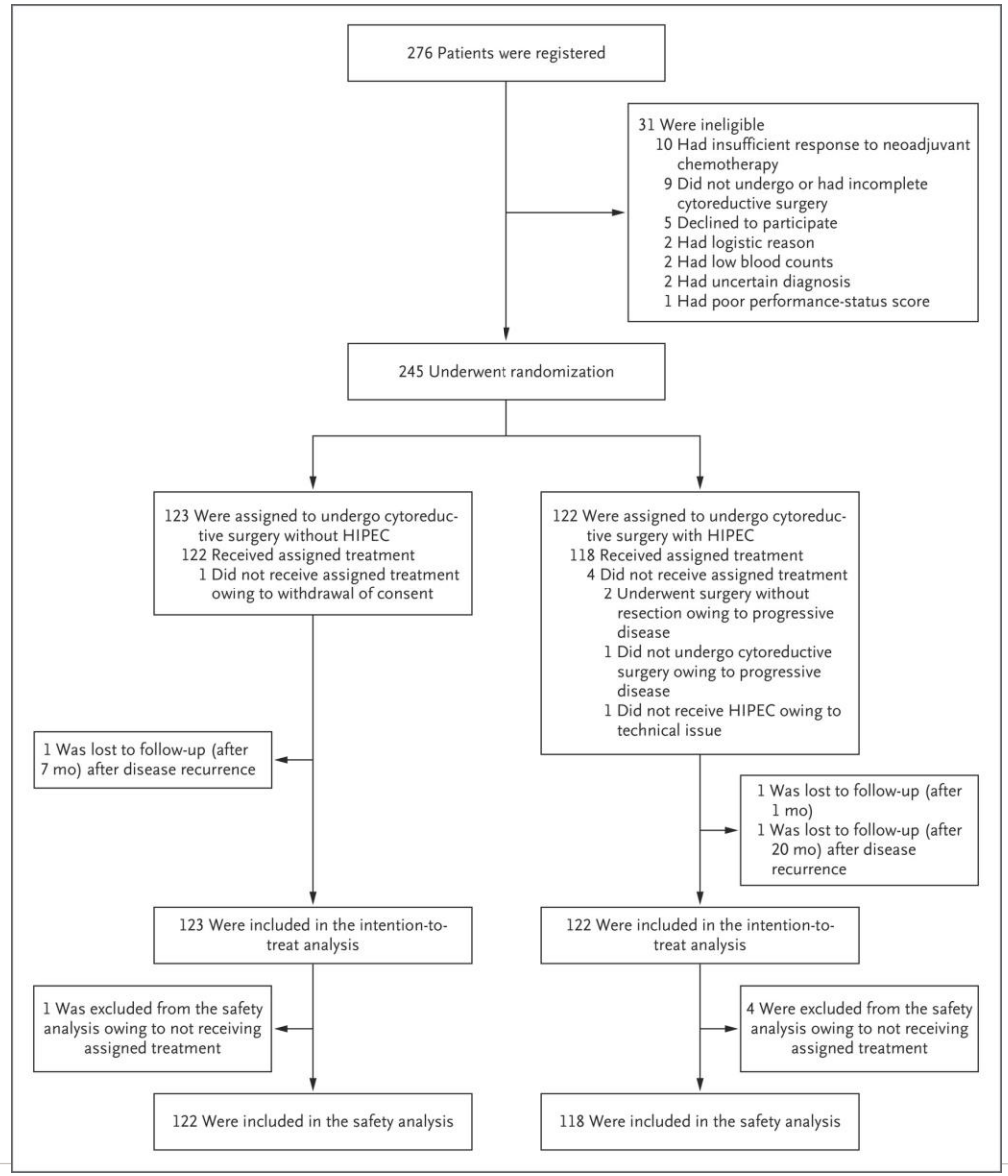
? Addition of Bev
?Dose dense Taxol

HIPEC in Addition to Systemic Therapy

Potential Timepoints for HIPEC

- Upfront CRS
- Interval CRS
- Secondary CRS for persistent disease
- Salvage CRS for recurrence
- Palliation for chemotherapy resistant ascites

OVHIPEC1; van Driel WJ et al, NEJM 2018



Ineligible for pCRS
NACT: 3 cycles carbo AUC 5-6, Taxol 175 mg/m2 with at least Stable disease

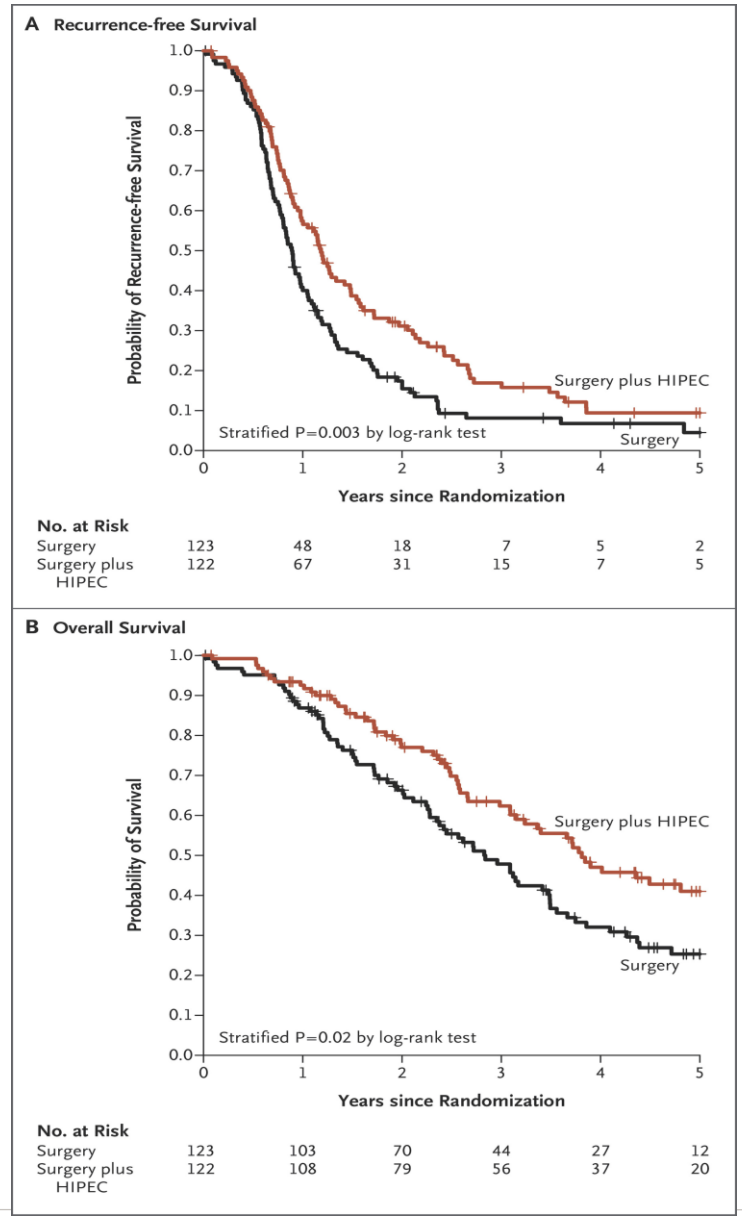
Randomization of patients in whom optimal CRS was anticipated

HIPEC: cisplatin 100 mg/m2 for 90 min at 42 deg C

3 cycles of adjuvant C/T

Primary EP: RFS

OVHIPEC1; van Driel WJ et al, NEJM 2018

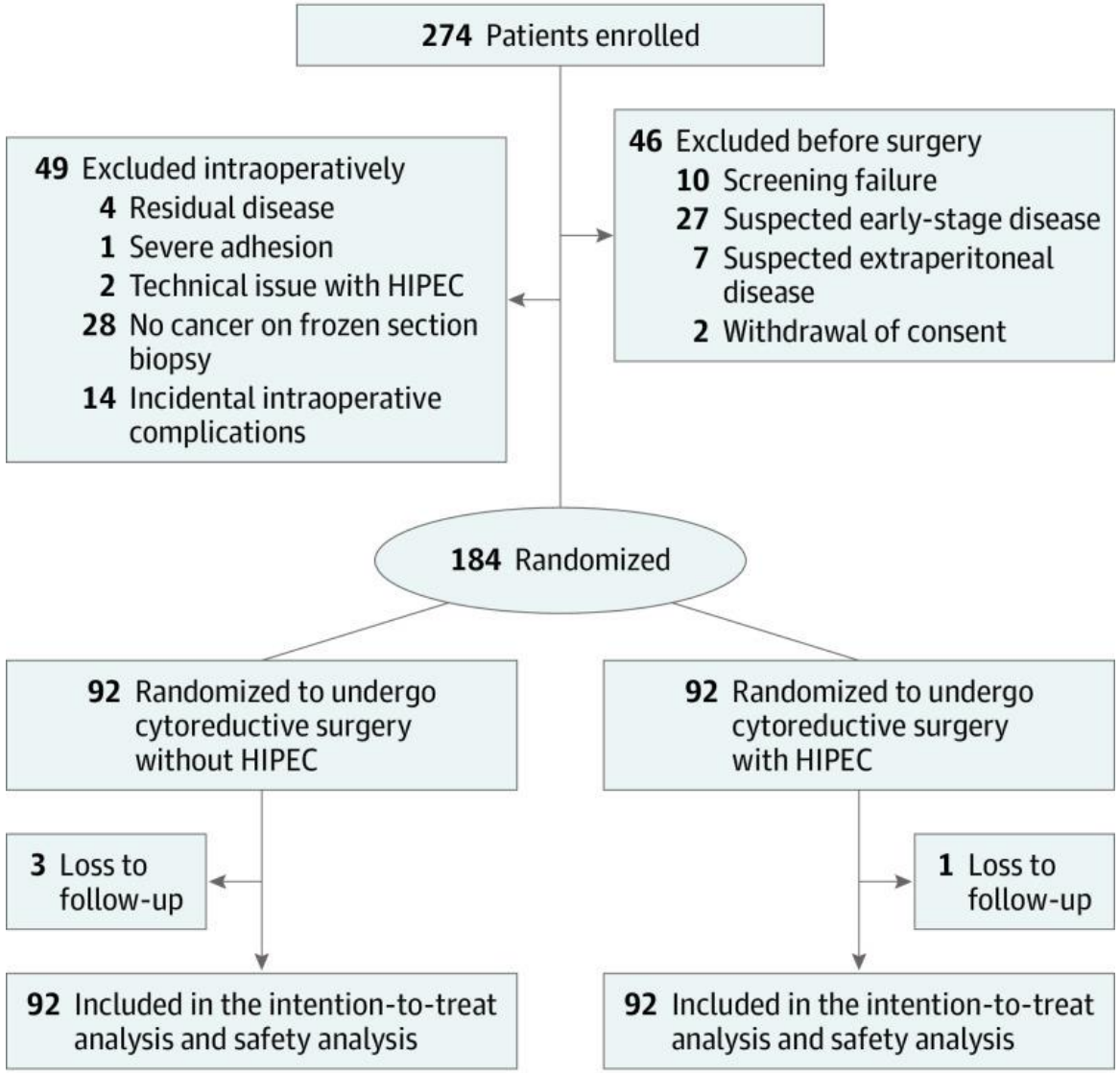


RFS at 3 yr 8% v 17% HR 0.66

OS at 3 yr: 48 v 62% HR 0.67

Completion of 3 cycles ACT: 90 v 94%

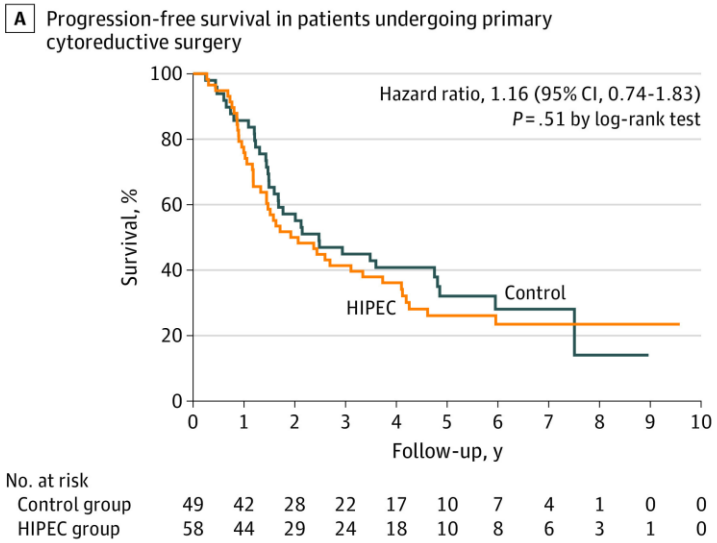
KOV-HIPEC-01

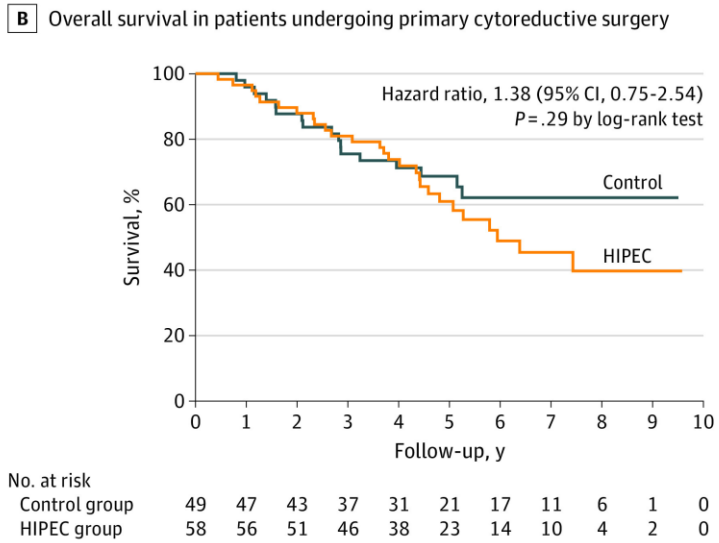


Ovarian cancer III/IV
NACT =77: chosen by Surgeon discretion
pCRS = 107
Adjuvant CT x 3 cycles

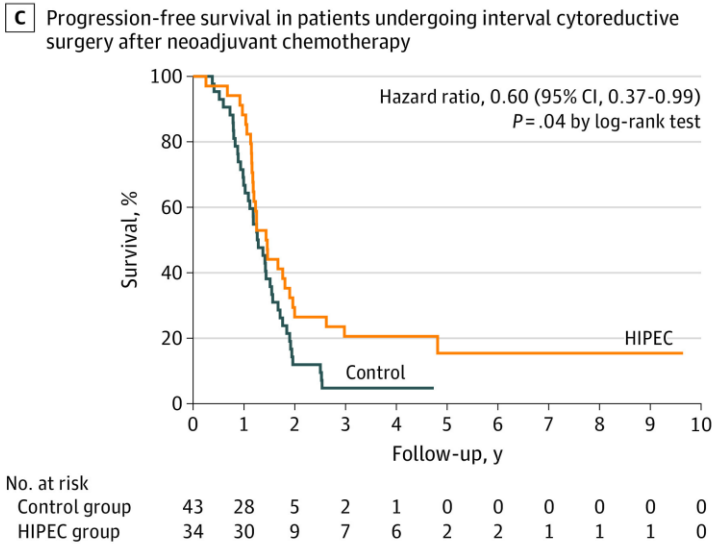
KOV-HIPEC-01, Lim et al 2022

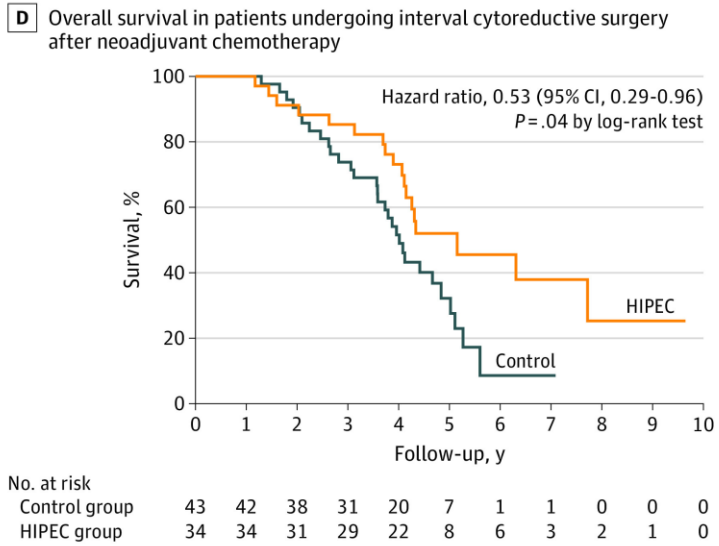
PCRS



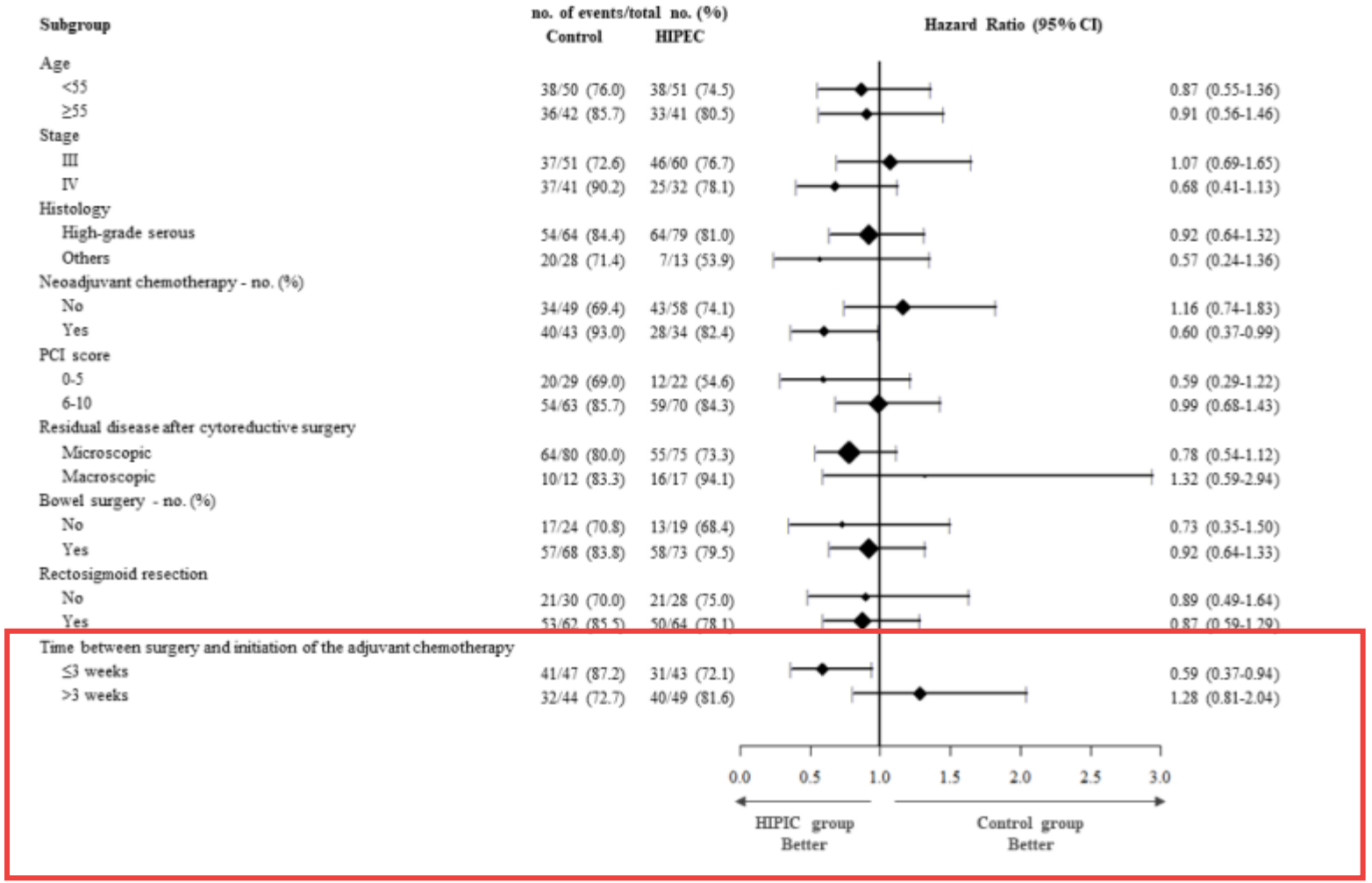


NACT, CRS





	IDS N=43	IDS+ HIPEC N=34	HR
PFS	15.4	17.4	0.60
OS	48.2	61.8	0.53


Subgroup
no. of events/total no. (%)
Control
HIPEC
Hazard Ratio (95% CI)
Age
<55 38/50 (76.0) 38/51 (74.5) 0.87 (0.55-1.36)
≥55 36/42 (85.7) 33/41 (80.5) 0.91 (0.56-1.46)
Stage
III 37/51 (72.6) 46/60 (76.7) 1.07 (0.69-1.65)
IV 37/41 (90.2) 25/32 (78.1) 0.68 (0.41-1.13)
Histology
High-grade serous 54/64 (84.4) 64/79 (81.0) 0.92 (0.64-1.32)
Others 20/28 (71.4) 7/13 (53.9) 0.57 (0.24-1.36)
Neoadjuvant chemotherapy - no. (%)
No 34/49 (69.4) 43/58 (74.1) 1.16 (0.74-1.83)
Yes 40/43 (93.0) 28/34 (82.4) 0.60 (0.37-0.99)
PCI score
0-5 20/29 (69.0) 12/22 (54.6) 0.59 (0.29-1.22)
6-10 54/63 (85.7) 59/70 (84.3) 0.99 (0.68-1.43)
Residual disease after cytoreductive surgery
Microscopic 64/80 (80.0) 55/75 (73.3) 0.78 (0.54-1.12)
Macroscopic 10/12 (83.3) 16/17 (94.1) 1.32 (0.59-2.94)
Bowel surgery - no. (%)
No 17/24 (70.8) 13/19 (68.4) 0.73 (0.35-1.50)
Yes 57/68 (83.8) 58/73 (79.5) 0.92 (0.64-1.33)
Rectosigmoid resection
No 21/30 (70.0) 21/28 (75.0) 0.89 (0.49-1.64)
Yes 53/62 (85.5) 50/64 (78.1) 0.87 (0.59-1.29)
Time between surgery and initiation of the adjuvant chemotherapy
≤3 weeks 41/47 (87.2) 31/43 (72.1) 0.59 (0.37-0.94)
>3 weeks 32/44 (72.7) 40/49 (81.6) 1.28 (0.81-2.04)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
HIPIC group Better
Control group Better

Preoperative Bevacizumab prior to HIPEC

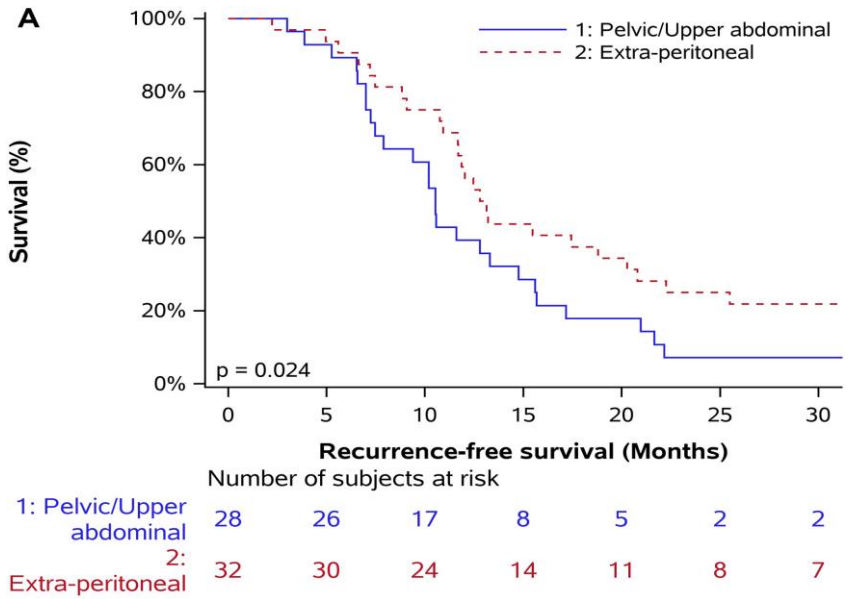
- King BH et al, 2020
  - Retrospective review of 499 HIPEC patients (UCSD)
    - 88 patients NACT: 54 in combination with bevacizumab versus 34 chemo alone
    - Per institutional guidelines Bevacizumab held for 6-8 weeks prior to CRS
- No increase in:
  - Gr III/IV morbidity: 9 v 6 OR 0.86
  - 60 day mortality: 0, 0

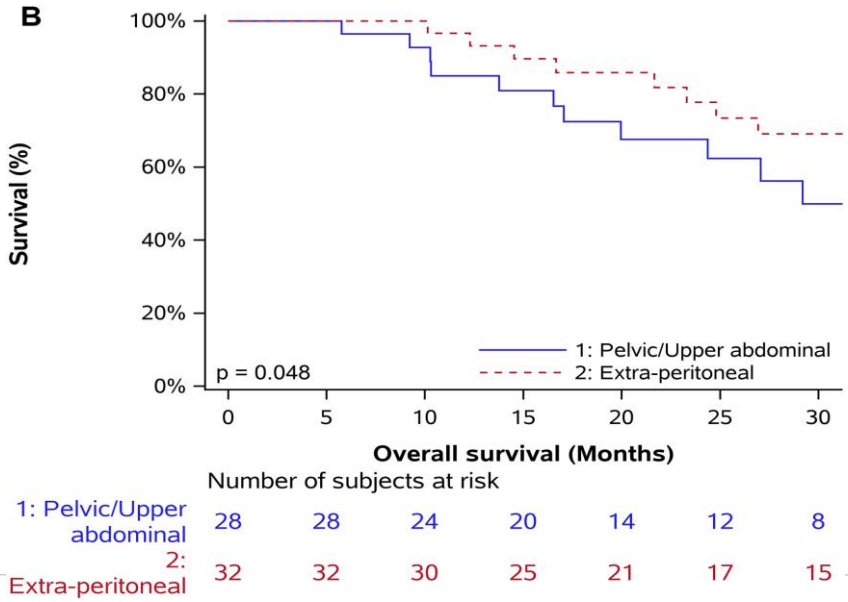
HIPEC Benefit in Combination with Systemic CT

- Benefit to IP chemotherapy under hyperthermia
- Additive benefit to intravascular therapy
    - Avoids delay in systemic therapy during surgical debulking
- May overcome platinum resistance: increased drug concentrations in tumor cells, direct cytotoxic effect of hyperthermia
- Concerns: increased time for post-op recovery, delay to systemic therapy, need to decrease dose intensity, patients may withdraw from subsequent therapy and worsen outcomes

Benefit to HIPEC at Interval Debulking

Reduced risk for peritoneal recurrence?
Can we identify optimal subgroup?



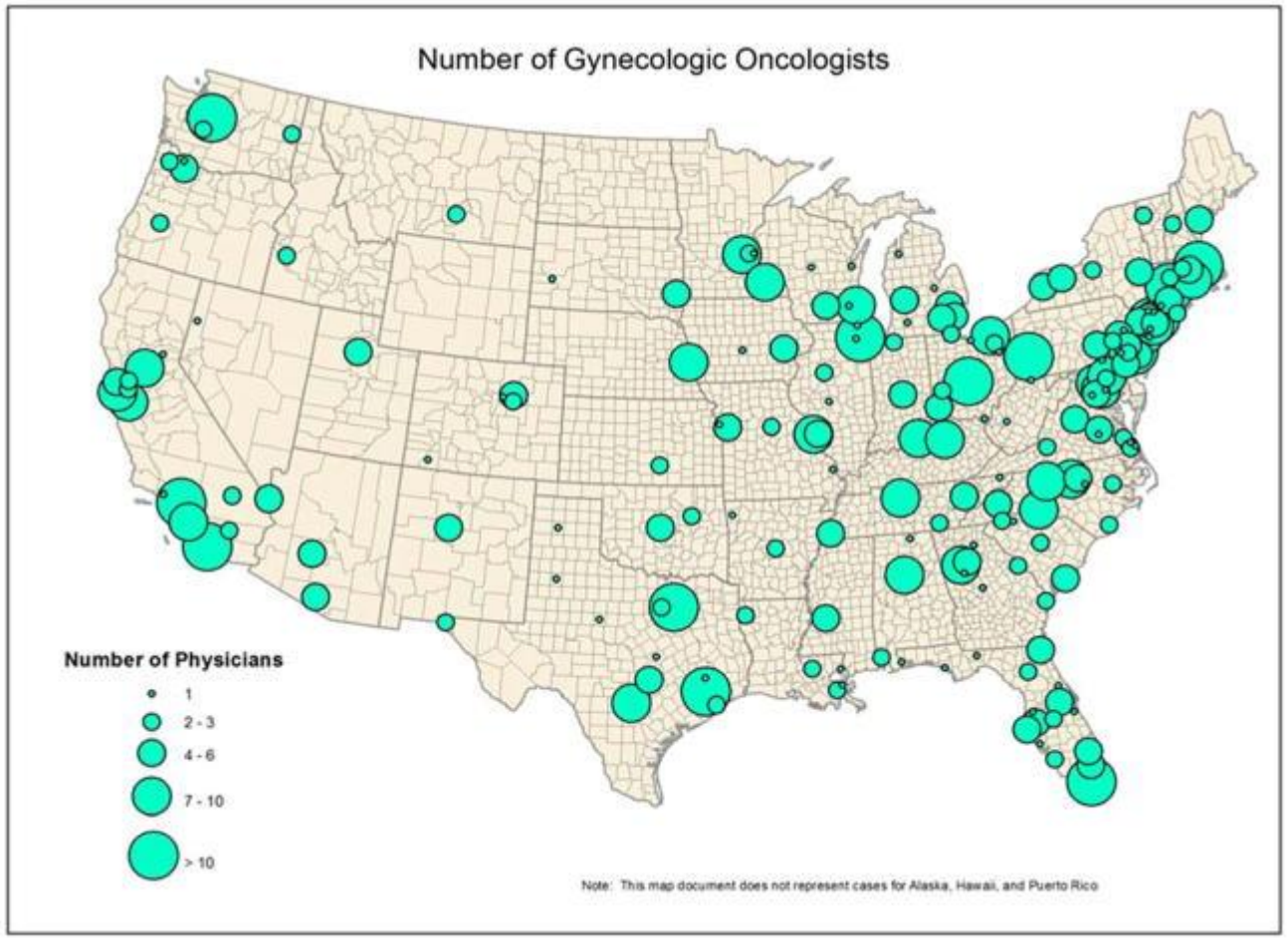


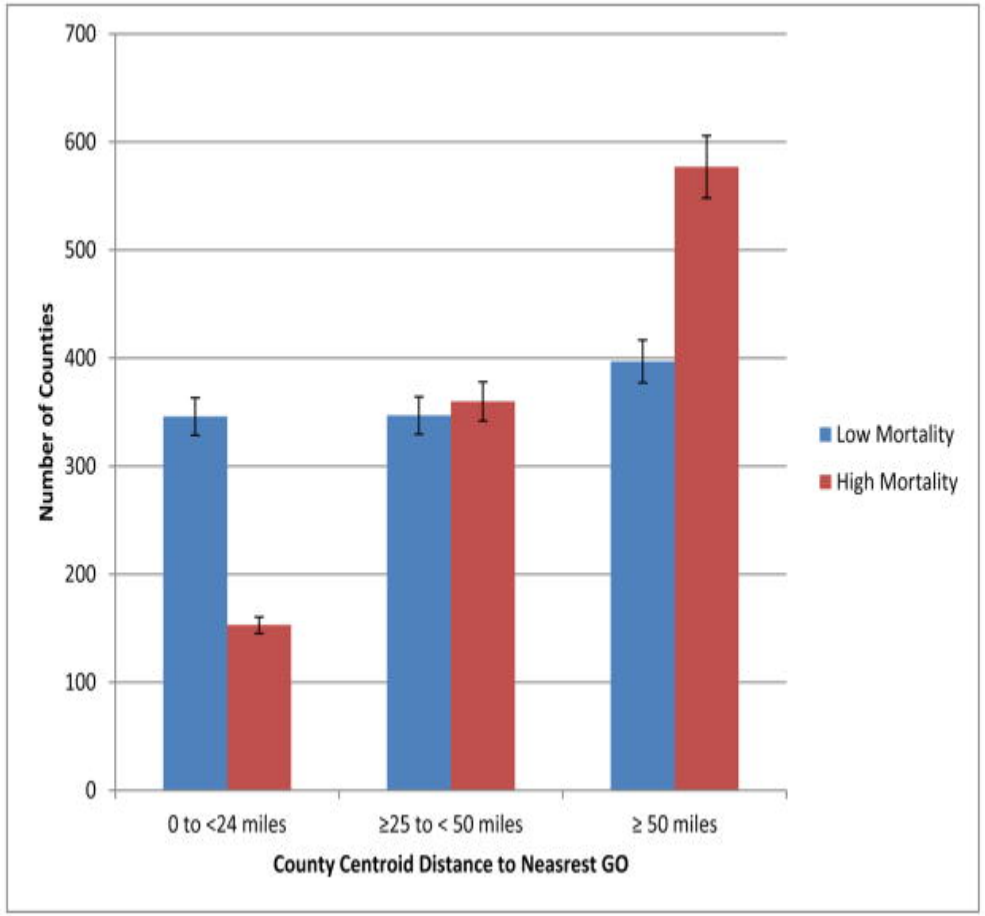
Chambers LM, Gyn Oncol 2021

Summary

- IP chemotherapy achieves different benefit compared with IV chemotherapy in peritoneal disease
- IP synergistic with hyperthermia
- 3 trials show benefit to interval debulking with HIPEC, do not increase systemic therapy complications
- Benefit: additional cycle of chemotherapy without delay? Decrease in rate of peritoneal recurrence?

Benefit to Comprehensive Care: Stewart SL et al 2014





Thank you