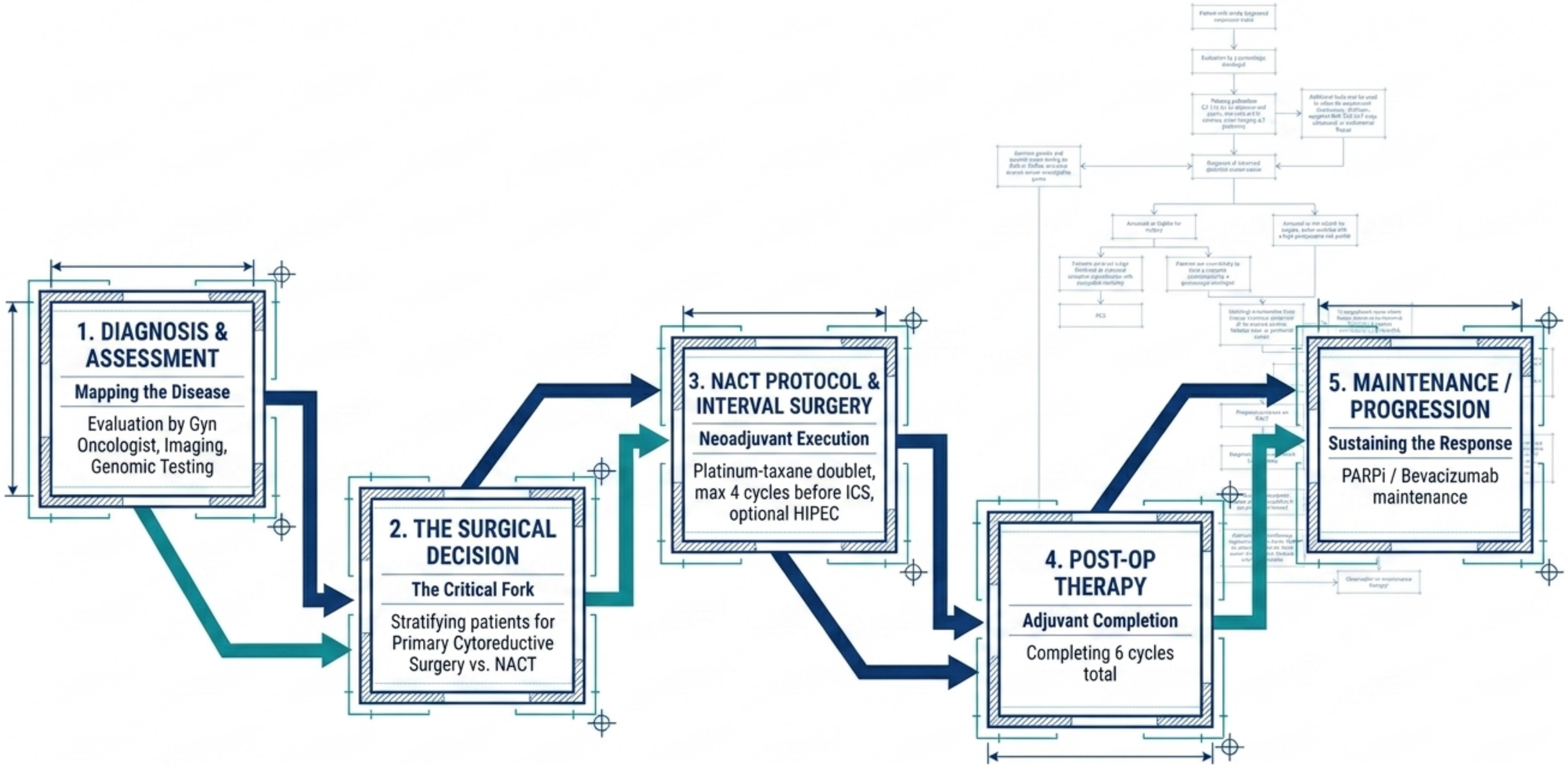
THE 2025 CLINICAL BLUEPRINT: NEOADJUVANT CHEMOTHERAPY IN ADVANCED OVARIAN CANCER

Distilling the ASCO Guideline Update for Frontline Practice

Endorsed by the Society of Gynecologic Oncology (SGO) | Designed for Clinical Pathway Navigation


1. DIAGNOSIS & ASSESSMENT
Mapping the Disease
Evaluation by Gyn Oncologist, Imaging, Genomic Testing
2. THE SURGICAL DECISION
The Critical Fork
Stratifying patients for Primary Cytoreductive Surgery vs. NACT
3. NACT PROTOCOL & INTERVAL SURGERY
Neoadjuvant Execution
Platinum-taxane doublet, max 4 cycles before ICS, optional HIPEC
4. POST-OP THERAPY
Adjuvant Completion
Completing 6 cycles total
5. MAINTENANCE / PROGRESSION
Sustaining the Response
PARPi / Bevacizumab maintenance

NODE 1: LAYING THE GROUNDWORK — INITIAL CLINICAL EVALUATION

[Strong Recommendation | Moderate Evidence] **Primary Evaluation**

[Strong Recommendation | High Evidence] **Genetic Testing**

The Expert Assessment

All patients with suspected stage III/IV EOC must be evaluated by a gynecologic oncologist to determine PCS candidacy.

The Imaging & Biomarker Baseline

Mandatory: CA-125 serum test, CT of abdomen/pelvis (oral/IV contrast), and chest imaging (CT preferred).

The Molecular Blueprint

Offer germline and somatic testing for *BRCA1/BRCA2* at diagnosis. Somatic testing must include measures of homologous recombination (HRD).

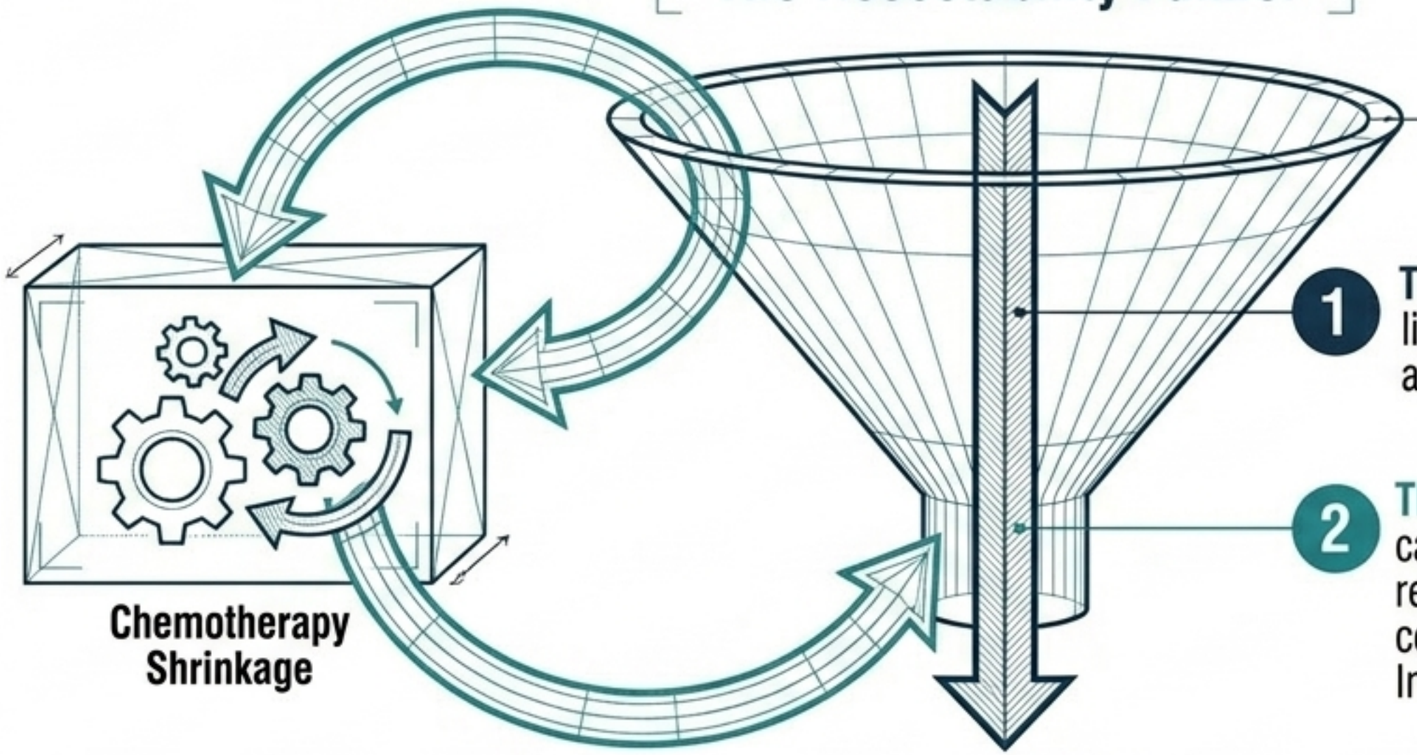
EVALUATING RESECTABILITY: THE DIAGNOSTIC TOOLKIT

	**Staging Laparoscopy**	**Clinical Utility** [Conditional Rec] Highly reliable predicting optimal cytoreduction. Reduces unnecessary laparotomies. Lower suboptimal cytoreduction rates (2.0%) vs. CT (11.1%).
	**Whole-Body DWI/MRI**	**Clinical Utility** [Conditional Rec] Superior performance compared to CT in specific sites (mesentery, lumbo-aortic lymph nodes). Accuracy ~88%, High specificity (98%).
	**FDG-PET Scan**	**Clinical Utility** [Conditional Rec] Reflects overall tumor burden; highly sensitive/specific for predicting complete cytoreduction likelihood.
	**Ultrasound (Expert)**	**Clinical Utility** [Conditional Rec] Reliable alternative to CT/MRI for predicting non-resectability (98% specificity) when performed by expert sonographers.

DIFFERENTIAL DIAGNOSIS ALERT: Consider endometrial to rut advanced endometrial cancer, cancer, which can mimic EOC presentation.

NODE 2: THE ULTIMATE GOAL — NAVIGATING THE CYTOREDUCTION FUNNEL

The Resectability Funnel



High Tumor Burden / Extensive Carcinomatosis

1 **THE PCS PATH:** For patients highly likely to achieve R0 upfront with acceptable morbidity.

2 **THE NACT PATH:** For patients who cannot pass the funnel upfront. NACT reduces tumor volume and surgical complexity, enabling a successful Interval Cytoreductive Surgery (ICS).

Target Output: R0
(No Macroscopic Residual Disease)

CLINICAL INSIGHT: Residual tumor volume is the most critical predictor of Overall Survival. The goal is no gross residual disease. Choose the pathway that guarantees safe passage through the funnel.

THE CRUCIAL FORK: PCS VS. NACT PATIENT PROFILER

PCS - PRIMARY CYTOREDUCTIVE SURGERY

[Conditional Rec | Moderate Evidence]

Ideal Candidate Profile

- Medically fit for complex surgery.
- High likelihood of achieving complete cytoreduction (R0).
- Acceptable predicted perioperative morbidity.

Clinical Directive

PCS remains the standard of care for medically fit patients with resectable disease at diagnosis. Routine use of NACT-ICS is cautioned against for this specific group.

NACT - NEOADJUVANT CHEMOTHERAPY

[Strong Rec | High Evidence]

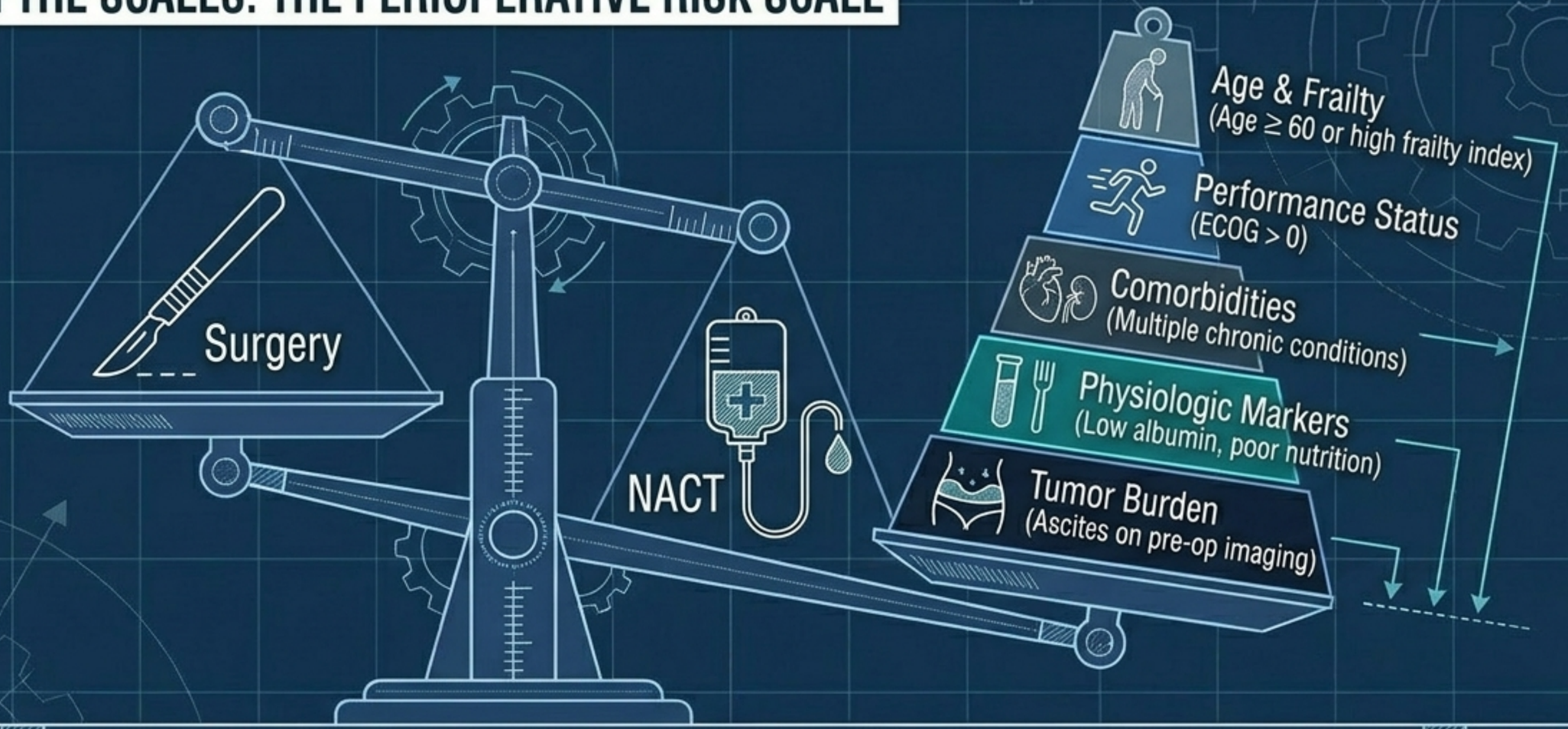
Ideal Candidate Profile

- Deemed unlikely to have complete cytoreduction by a Gyn Oncologist, OR possesses a high perioperative risk profile.

Clinical Directive

NACT is strongly recommended. It decreases surgical complexity, reduces severe post-op complications, and allows time for medical optimization.

TIPPING THE SCALES: THE PERIOPERATIVE RISK SCALE



TAKEAWAY: Patients requiring highly complex procedures (e.g., splenectomy, colon surgery, peritoectomy) to achieve cytoreduction inherently face higher morbidity, strengthening the case for NACT.

NODE 3: SECURING THE PRE-NACT DIAGNOSIS

[Conditional Rec | Moderate Evidence]

Step 1: **Histologic Confirmation** (Gold Standard)

Core tissue biopsy is strongly preferred. Fine-needle aspirates (FNA) are inadequate.

WHY?

Crucial for genetic/somatic tumor testing and distinguishing borderline from invasive cancer cells.

Step 2: **The Exceptional Case** Alternate Pathway

If biopsy is impossible, cytologic evaluation combined with a serum CA-125 to CEA ratio > 25 is acceptable.

Step 3: **Rule Out Mimics**

Approximately 3% of patients in key trials had non-ovarian cancers.
Rule out GI, breast, and endometrial primaries before initiating NACT.

THE EVIDENCE BASELINE: MAJOR RCTS SHAPING NACT

CHORUS

Type: Non-inferiority
Primary Outcome: NACT non-inferior to PCS for OS.
Takeaway: Proved NACT is at least as effective as primary surgery. Lower severe nausea/vomiting and post-op deaths.

OS Data:	NACT	PCS	HR (95% CI)
Median OS (mos)	24.1	22.6	HR, 0.87 (95% CI, 0.72 to 1.05)

EORTC 55971

Type: Non-inferiority
Primary Outcome: NACT non-inferior to PCS for OS.
Takeaway: Comparable survival outcomes. Lower severe post-op complications and deaths.

OS Data:	NACT	PCS	HR (95% CI)
Median OS (mos)	12.0	10.7	HR, 0.91 (95% CI, 0.76 to 1.09)

SCORPION

Type: Superiority (high tumor load)
Primary Outcome: Did NOT show superiority of NACT over PCS for Progression-Free Survival (14.0 vs 15.0 mos).
Takeaway: Significantly reduced severe complications in NACT arm.

PFS Data:	NACT	PCS	HR (95% CI)
Median PFS (mos)	14.0	15.0	HR, 1.05 (95% CI, 0.84 to 1.33)

JCOG0602

Type: Non-inferiority
Primary Outcome: Did not statistically confirm non-inferiority.
Takeaway: Overall Survival and Progression-Free Survival were similar between groups.

PFS & OS Data:	NACT	PCS	HR (95% CI)
Median PFS (mos)	16.4	15.1	HR, 0.96 (95% CI, 0.75 to 1.23)
Median OS (mos)	44.3	49.0	HR, 1.05 (95% CI, 0.84 to 1.33)

SYNTHESIS: Meta-analyses confirm NACT reduces surgical morbidity and perioperative mortality, with comparable survival outcomes for high-risk and high-tumor-burden patients.

CONSTRUCTING THE NACT REGIMEN

[Strong Rec | High Evidence] Standard

[Conditional Rec | Moderate Evidence] Alternatives

VULNERABLE OLDER ADULTS

Monitor closely for neuropathy; utilize geriatric assessment tools for personalized dose adjustments.

PRIMARY STANDARD OF CARE

Target: High-grade serous or endometrioid ovarian cancer.

Regimen: PLATINUM-TAXANE DOUBLET (Carboplatin + Paclitaxel, once every 3 weeks).

⚠ Single-agent carboplatin yields worse survival outcomes even in vulnerable populations; the doublet is strictly preferred.

RARE HISTOLOGIES

Consider PCS over NACT for low-grade serous or clear cell (low chemo response rates).

Consider fluorouracil-based regimens for mucinous histology.

Note: Adding bevacizumab to NACT improves surgical operability, but complete macroscopic response rates remain <10%.

THE NACT TO ICS CHRONOMETER

[Conditional Rec | Low Evidence]

THE SURGICAL WINDOW

THE ASSESSMENT WINDOW

THE RADIOGRAPHIC CHECKPOINT

DIMINISHING RETURNS

Administer NACT.
Measure CA-125 with each cycle.
Calculate KELIM score (marker of chemosensitivity).

Perform imaging to compare with baseline.

Interval Cytoreductive Surgery (ICS) should be performed after ≤ 4 cycles for patients responding or stable.

Meta-analyses show receiving 5 or more NACT cycles before surgery indicates a potential decline in survival outcomes.

CLINICAL IMPERATIVE: Perform standard ICS earlier rather than delaying.
Early surgery enables earlier initiation of highly effective maintenance therapies.

THE INTRAOPERATIVE PIVOT: CRITERIA FOR HIPEC

[Conditional Rec | Moderate Evidence]

The Eligibility Gate

(All criteria must be met)

- [ ] FIGO Stage III Disease
- [ ] Treated initially with NACT
- [ ] Good Performance Status (PS)
- [ ] Adequate Renal Function (CrCl > 30, Serum Cr < 1.5)

Operational Reality

RESOURCE & SAFETY WARNING

- Requires trained multidisciplinary staff (pharmacy, nursing, anesthesia, surgery).
- Cisplatin (100 mg/m^2) is highly nephrotoxic and emetogenic.
- Requires IV sodium thiosulfate (prevent nephrotoxicity), strict goal-directed fluid therapy, and aggressive antiemetic protocols.

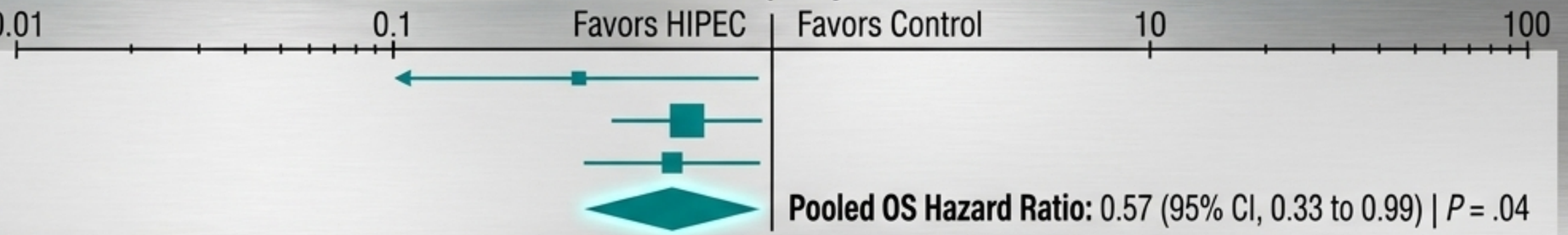
THE EVIDENCE FOR HEAT: HIPEC TRIALS OVERVIEW

Trial Name	HIPEC Regimen (Dose/Time/Temp)	Median Follow-Up	Overall Survival (OS) HR	Disease-Free Survival (DFS) HR
OVHIPEC-1 (Aronson 2023) | n = 122 (HIPEC), n = 123 (Control)	Cisplatin 100 mg/m² | 90 min | 40-42°C	10.4 years	0.70 (0.53 to 0.92)	0.63 (0.48 to 0.83)
Lim 2022	Cisplatin 75 mg/m² | 90 min | 41.5°C	69.4 months	0.53 (0.35 to 0.80)	0.60 (0.40 to 0.90)
Antonio 2022 | n = 35 (HIPEC), n = 36 (Control)	Cisplatin 75 mg/m² | 60 min | 42-43°C	32 months	0.05 (0.00 to 0.80)	0.12 (0.02 to 0.72)

Across diverse dosing and timing regimens, the addition of heated intraperitoneal cisplatin during ICS **consistently demonstrates profound improvements** in both **DFS** and **OS**.

VISUALIZING THE HIPEC SURVIVAL ADVANTAGE

OVERALL SURVIVAL (OS)

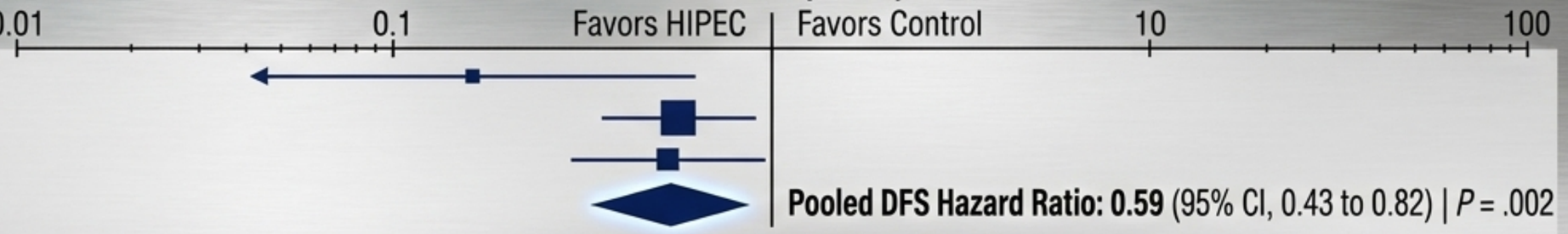


Pooled OS Hazard Ratio: 0.57 (95% CI, 0.33 to 0.99) | *P* = .04

Test for overall effect: Z = 2.01 (*P* = .04)
Heterogeneity: $Tau^2 = 0.11$; $chi^2 = 4.00$, df = 2 (*P* = .14); $I^2 = 50\%$

A 43% reduction in the risk of death.

DISEASE-FREE SURVIVAL (DFS)



Pooled DFS Hazard Ratio: 0.59 (95% CI, 0.43 to 0.82) | *P* = .002

Test for overall effect: Z = 3.16 (*P* = .002)
Heterogeneity: $Tau^2 = 0.02$; $chi^2 = 2.59$, df = 2 (*P* = .27); $I^2 = 23\%$

A 41% reduction in the risk of disease progression.

Note: These survival advantages predated the modern era of PARP inhibitors, emphasizing the need for shared decision-making regarding future maintenance options.

NODE 4: COMPLETING THE CIRCUIT — POST-ICS CHEMOTHERAPY

[Strong Rec | High Evidence]

TARGET: 6 TOTAL CYCLES OF PLATINUM-TAXANE DOUBLET

Timing:

Initiate post-operative chemotherapy within 4-6 weeks after surgery to avoid detrimental delays.

Modifications:

Adjust doses or discontinue components if cumulative toxicity (e.g., neuropathy) demands it.

Targeted Additions:

IV Bevacizumab may be added for high-risk patients (Stage IV, suboptimal ICS), but should only start at post-op cycle 2 to allow surgical healing.

NODE 5: SECURING THE GAINS — FRONTLINE MAINTENANCE THERAPIES

[Strong Rec | Moderate Evidence]

Complete or Partial Response to Platinum

***BRCA* Pathogenic Variant**	Therapy Output: PARP Inhibitors (Olaparib or Niraparib)
	SOLO1 trial showed profound PFS improvement (HR 0.30).
HRD Positive (BRCA wild-type)	Therapy Output: Niraparib monotherapy **OR** Olaparib + Bevacizumab (PAOLA-1 trial)
HRD Proficient / Negative	Therapy Output: Niraparib (PRIMA trial) or Observation
	PAOLA-1 showed no benefit for Olaparib+Bev in this specific group.
Bevacizumab Continuation	Therapy Output: If Bevacizumab started with chemo, continue up to 12 months or progression.

THE PIVOT POINT: MANAGING PROGRESSION ON NACT

[Conditional Rec | Mod Evidence]
Re-biopsy

[Strong Rec | Mod Evidence]
Avoiding surgery / initiating end-of-life care

CLINICAL REALITY CHECK:
Progression on 1st-line platinum implies platinum-refractory disease (median OS < 1 year).

RE-ROUTING

RECONFIRM DIAGNOSIS

Repeat core tissue biopsy (rule out other othery primary primary cancers).

Ensure germline/somatic profiling is complete.

HALT SURGICAL PLANS

Surgery is **NOT** advised and unlikely to achieve cytoreduction.

Reserve surgery strictly for palliation (e.g., bowel obstruction ostomy).

SWITCH SYSTEMIC STRATEGIES

Transition to alternative, non-cross-resistant chemotherapy (gemcitabine, liposomal doxorubicin, bevacizumab) or clinical trials.

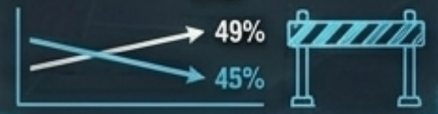
PRIORITIZE PALLIATION

Early engagement of palliative care to optimize symptom management and quality of life.

BRIDGING THE GAPS: THE HEALTH EQUITY IMPERATIVE

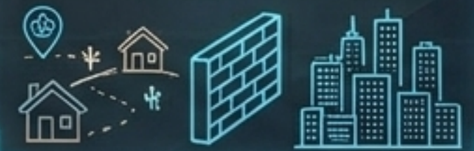
The Surgical Access Gap

Black women have a significantly lower 5-year OS (49%) vs White women (60%), driven by lower rates of optimal debulking and NACT access due to income and insurance disparities. Black patients are 38% less likely to undergo CRS.



The Geographic Wall

Only 21% of non-metropolitan US counties have a practicing oncologist, leading to higher mortality rates for rural patients.



The Genomic Testing Void

Lower rates of germline *BRCA1/2* testing are observed among Asian, Black, and Hispanic patients compared to White patients.

CLINICAL CALL-TO-ACTION: True guideline implementation requires active mitigation of social determinants. Care teams must address transportation, insurance status, and systemic bias to ensure equitable access to gynecologic oncologists and quality surgical care.

THE 2025 ASCO MASTER TREATMENT ALGORITHM