0.53 [95% CI, 0.29 to 0.97]) and a median DFS of 17.4 months versus 15.4 months (HR, 0.60 [95% CI, 0.37 to 0.97]).[22] Another HIPEC trial[23] found an OS of 52 months in the HIPEC group compared to 45 months in the control group (HR, 0.05 [95% CI, 0.00 to 0.80]) and a DFS of 18 months versus 12 months (HR, 0.12 [95% CI, 0.02 to 0.72]).

Pooled data from these studies (Table 4) show that HIPEC, when added to NACT and CRS, significantly improves OS (HR, 0.57 [95% CI, 0.33 to 0.99], $P = .04$; Fig 2) and DFS (HR, 0.59 [95% CI, 0.43 to 0.82], $P = .002$; Fig 3) with moderate heterogeneity. These results indicate that incorporating HIPEC into the treatment regimen for qualifying patients with advanced ovarian cancer may lead to better survival outcomes and support the recommendation for its use in clinical practice.

### *Clinical Interpretation*

The use of HIPEC during ICS has shown significant improvement in OS across several studies, although this evidence predates the introduction of PARPi in the maintenance setting. If HIPEC is given, patients should be carefully informed and consent to the reported risks and benefits of HIPEC in context of future maintenance options. Given high-dose cisplatin (100 mg/m$^2$) is used, significant renal dysfunction would exclude HIPEC administration (Creatinine Clearance <30 or serum Creatinine <1.5). In addition, careful consideration should be given to patients with diabetes, neuropathy, hearing loss, or advanced age.

Due to the resource intensity required to administer HIPEC, availability is limited to centers that have adequately trained staff and dedicated resources. In preparation for HIPEC administration, multidisciplinary coordination with pharmacy, nursing, anesthesia, and surgery is vital to guarantee safe delivery of intraoperative chemotherapy. Proper training in HIPEC administration and supportive medication is essential. Surgeons should minimize nephrotoxins (ie, contrast scans, anti-inflammatories) perioperatively and postoperatively. Baseline laboratory studies, specifically renal function and blood counts, should be within the week prior to ICS or HIPEC. Since cisplatin has high emetic potential, standard preventive antiemetic treatment should be provided such as intravenous palonosetron, aprepitant, and dexamethasone.[113] Perioperative, goal-directed fluid therapy approaches should be implemented to maintain optimal hemodynamic indices, maximize tissue oxygenation, and avoid volume overload, which can delay postoperative recovery and increase postoperative complications.[114] Sodium thiosulfate (bolus at start of HIPEC followed by continuous infusion) should be administered to prevent nephrotoxicity. In the postoperative period, careful assessment for cisplatin side effects is warranted as well as an antiemetic regimen (dexamethasone, ondansetron, and/or olanzapine) and close monitoring of kidney function, electrolytes, glucose,



**TABLE 3.** Results of HIPEC Trials

| Author Year of Publication | HIPEC Arm | Control Arm | HIPEC | | | NACT Scheme | Median Follow-Up, Months | Median OS, Months, HR (95% CI) | Median DFS, Months, HR (95% CI) |
|---|---|---|---|---|---|---|---|---|---|
| | | | HIPEC Scheme | Duration, Minutes | Temperature, °C | | | | |
| Aronson 2023[20] Van Driel 2018[21] OVHIPEC-1 Final Long-Term Analysis | NACT + CRS + HIPEC + ASC n = 122 | NACT + CRS + ASC n = 123 | Cisplatin (100 mg/m$^2$) | 90 | 40-42 | Carboplatin (AUC 5-6 mg/mL/min) + paclitaxel (175 mg/m$^2$ BSA) | 10.4 years in HIPEC 10.1 years in surgery-alone | HIPEC: 44.9 Control: 33.3 HR, 0.70 (0.53 to 0.92) | PFS HIPEC: 14.3 Control: 10.7 HR, 0.63 (0.48 to 0.83) |
| Lim 2022[22] | NACT + CRS + HIPEC + ASC n = 34 | NACT + CRS + ASC n = 43 | Cisplatin (75 mg/m$^2$) | 90 | 41.5 | Carboplatin (AUC 5 mg/mL/min) + paclitaxel (175 mg/m$^2$ BSA) | 69.4 | HIPEC: 61.8 Control: 48.2 HR, 0.53 (0.29 to 0.96) | PFS HIPEC: 17.4 Control: 15.4 HR, 0.60 (0.37 to 0.99) |
| Antonio 2022[23] | NACT + CRS + HIPEC + ASC n = 35 | NACT + CRS + ASC n = 36 | Cisplatin (75 mg/m$^2$) | 60 | 42-43 | Carboplatin (AUC 5) + paclitaxel (175 mg/m$^2$) | 32 | HIPEC: 52 Control: 45 HR, 0.05 (0.00 to 0.80) | HIPEC: 18 Control: 12 HR, 0.12 (0.02 to 0.72) |

Abbreviations: ASC, adjuvant systemic chemotherapy; BSA, body-surface area; HIPEC, hyperthermic intraperitoneal chemotherapy; CRS, cytoreductive surgery; DFS, disease-free survival; HR, hazard ratio; NACT, neoadjuvant chemotherapy; OS, overall survival; PFS, progression-free survival.