# Colorectal Cancer & HIPEC Randomized Trials

| Study | Type | Patients | Arms | Primary Endpoint | Main Result | Strengths | Limitations | Interpretation |
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| PRODIGE7[23] (France) | RCT, multicenter | PCI<25 (n=265) | CRS alone vs CRS/HIPEC | OS | Median OS: 41.2 vs 41.7 months, p=0.99 | -Proves role of complete CRS, with impressive OS in both arms<br>-Subanalysis showed significant effect of HIPEC in patients with PCI 11-15<br>-Complete CRS only | -Study design overestimated presumed survival benefit so sample size may be inadequate<br>-PFS may be more appropriate endpoint since HIPEC is a locoregional treatment<br>-Patients in CRS alone arm who had recurrence were offered CRS/HIPEC<br>-No assessment of PCI prior to start of NACT<br>-HIPEC perfusion only 30 min with oxaliplatin | -No additional OS benefit with CRS + oxaliplatin-based HIPEC compared to CRS alone<br>-Complete CRS is an essential component for achieving long-term survival |
| PROPHYLOCHIP -PRODIGE 15[24] (France) | RCT, multicenter | High-risk for PM after initial resection of primary tumor + systemic chemo (n=150) | Follow-up vs second-look CRS/HIPEC | 3-year peritoneal DFS | 53% vs 44%, p=0.82 | -Highlighted the occurrence of peritoneal metastases found during second-look surgeries, prompting more careful resection during initial surgery and confirming the low sensitivity of standard imaging in detecting PM | -HIPEC perfusion with oxaliplatin<br>-Large portion of follow-up only patients may have been treated at an early stage<br>-Synchronous PM and T4 lesions are different cohorts with unique prognoses, but were combined here | -Second-look surgery + oxaliplatin-based HIPEC did not improve DFS compared to standard surveillance and resulted in a significant rate of serious complications |
| COLOPEC[25] (Netherlands) | RCT, multicenter | High-risk (T4/perforated without PM) after resection of primary tumor (n=204) | Systemic chemo alone vs systemic chemo + CRS/HIPEC | 18-month peritoneal DFS | 76.2% vs 80.9%, p=0.28 | -Confirms that patients with locally advanced CRC are at a high risk for quick peritoneal relapse | -HIPEC perfusion with oxaliplatin<br>-Significant amount of patients were found to have PM at diagnosis<br>-Delayed postoperative chemo start in HIPEC group<br>-Diagnostic lap was too invasive an approach to determine the primary endpoint and almost 40% of the cohort did not undergo one | -Adjuvant CRS + oxaliplatin-based HIPEC did not improve DFS compared to standard adjuvant systemic chemotherapy |

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| HIPECT4[26] (Spain) | RCT, multicenter | Locally advanced (T4M0) (n-184) | CRS alone vs CRS/HIPEC | 3-year locoregional (peritoneal) control rate | 87.6% vs 97.6%, p=0.03 | -Important step for treating challenging T4 lesions that have limited evidence to support the use of systemic chemo and are at high risk for developing peritoneal metastases<br>-Demonstrates that CRS alone and CRS/HIPEC with mitomycin-C can be performed with similar morbidity rates<br>-HIPEC perfusion with mitomycin-C<br>-Majority of patients were able to start adjuvant chemo on time | -Failed to show a difference in DFS or OS<br>-May require additional metrics to help evaluate benefits of HIPEC for local control, such as rates of bowel obstructions or other symptom causing sites<br>-Fails to address quality of life | -The addition of HIPEC with mitomycin-C to complete CRS improved the locaoregional control rate compared to CRS alone at the time of resection of the primary tumor |
| Verwaal et al.[19] (Netherlands) | RCT, single center | Known PM or positive ascites (n=105) | Systemic chemo +/- palliative surgery vs CRS/HIPEC + systemic chemo | OS | Median OS: 12.6 vs 22.4 months, p=0.032 | -HIPEC perfusion for 90 minutes with Mitomycin-C<br>-Emphasizes the importance of complete CRS and extent of disease as major prognostic factors | -Single center<br>-Open technique HIPEC perfusion | -CRS/HIPEC with Mitomycin-C improves survival compared to a palliative approach, especially in patients with limited disease |