Review

Catheter Based Intraperitoneal Administration of Paclitaxel for Peritoneal Metastases From Gastrointestinal Cancer

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Catheter Based Intraperitoneal Administration of Paclitaxel for Peritoneal Metastases from Gastrointestinal Cancer

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Simple Summary

Peritoneal metastasis (PM) is a common and highly lethal form of spread in gastrointestinal cancers. Conventional systemic chemotherapy is ineffective because poor tumor vascularization and the peritoneal–plasma barrier limit drug delivery to peritoneal tumors. Catheter-based normothermic intraperitoneal chemotherapy (CBIP) offers a practical alternative by enabling repeated drug administration through an implanted port and easy combination with systemic therapy. Paclitaxel (PTX) is particularly well suited for this approach because of its favorable pharmacokinetic properties, and accumulating clinical evidence supports the efficacy and safety of PTX-based CBIP. Future innovations may further improve outcome of the patients with PM.

Abstract

Peritoneal metastasis (PM) is the most frequent and lethal pattern of dissemination in gastrointestinal malignancies. Despite advances in systemic chemotherapy, outcomes remain poor because the unique biology of PM, characterized by poor vascularization and the peritoneal–plasma barrier (PPB), limits drug penetration and contributes to treatment resistance. To address these challenges, several locoregional treatment strategies have been developed, including cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy (CRS+HIPEC) and pressurized intraperitoneal aerosol chemotherapy (PIPAC). However, their widespread adoption is constrained by invasiveness, strict patient selection, and inconsistent survival benefits. Catheter-based normothermic intraperitoneal chemotherapy (CBIP) has emerged as a practical and less invasive alternative, particularly in East Asia. Through an implanted intraperitoneal port, CBIP enables repeated drug administration, providing sustained regional exposure while imposing minimal procedural burden. Importantly, it can be readily integrated with systemic chemotherapy, making it suitable for long-term multimodal treatment. Among available agents, paclitaxel (PTX) is particularly well suited for intraperitoneal administration because of its prolonged retention within the peritoneal cavity and limited systemic absorption. These pharmacokinetic properties allow high local drug concentrations with relatively low systemic toxicity. Consequently, PTX-based CBIP represents a biologically rational and clinically feasible treatment strategy for PM. This review summarizes the pharmacological rationale, clinical evidence, and emerging innovations in drug formulation and delivery that may further enhance the efficacy of PTX-based intraperitoneal chemotherapy for this challenging disease.

Keywords: peritoneal metastasis; peritoneal–plasma barrier catheter-based intraperitoneal chemotherapy; Paclitaxel; conversion surgery; nanoparticle

1. Introduction

The incidence of peritoneal metastasis (PM) in gastrointestinal malignancies varies substantially according to the primary tumor origin; however, it consistently represents one of the major patterns of metastatic spread in advanced disease. In gastric cancer, synchronous PM is reported in

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approximately 10–21% of patients at initial diagnosis. However, when occult disease detected by peritoneal cytology, staging laparoscopy, recurrent cases, and autopsy findings are taken into account, the lifetime incidence of PM is estimated to reach 30–50%. [1-3] In pancreatic cancer, radiologically detectable synchronous PM is observed in approximately 9–14% of patients, whereas PM is identified in 20–50% of advanced cases when staging laparoscopy and autopsy data are included[4, 5], indicating a high prevalence of occult peritoneal disease. In colorectal cancer, the incidence of synchronous PM is relatively lower, ranging from 4–8% at diagnosis; however, the cumulative incidence increases to approximately 8–25%. [6, 7] Among hepatobiliary malignancies, gallbladder cancer and cholangiocarcinoma exhibits synchronous PM in approximately 10–20% of patients, whereas hepatocellular carcinoma shows a lower incidence of only 2–6%. [8]

Despite advances in systemic chemotherapy and molecular-targeted therapy, the prognosis of patients with PM remains substantially worse than that of patients with other metastatic patterns, even within the same stage IV category. [9-11] This unfavorable outcome is largely attributable to the unique biological and anatomical characteristics of PM[12], including sparse vascularization[13], dense stromal fibrosis[14], the peritoneal–plasma barrier (PPB) [15], and a profoundly immunosuppressive microenvironment. [16] Especially, the PPB critically influences drug delivery in peritoneal metastasis.[15, 17] This dynamic barrier, composed of the mesothelium, interstitium, and microvasculature, enables prolonged retention of intraperitoneally administered drugs while simultaneously limiting penetration of systemically delivered agents into peritoneal tumors. Drug transport is strongly affected by molecular size, solubility, fibrosis, and extracellular matrix density.[18, 19] Consequently, achieving deep drug penetration into metastatic nodules remains a major therapeutic challenge.

These anatomical and pharmacologic characteristics provide a strong rationale for intraperitoneal (IP) chemotherapy. By directly delivering anticancer agents into the peritoneal cavity, IP administration can achieve markedly higher local drug exposure while limiting systemic toxicity. Among various locoregional approaches, cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) has been widely adopted, particularly in Western countries. HIPEC combines macroscopic tumor debulking with heat-enhanced cytotoxicity and improved tissue penetration [20], and has demonstrated survival benefit in selected patients with ovarian [21] and colorectal [22] cancers. CRS+HIPEC has been reported to be beneficial also for selected patients with gastric [23, 24] and pancreatic [25]cancers, although the benefit remains highly dependent on tumor biology, completeness of cytoreduction, and patient selection. Another emerging strategy is pressurized intraperitoneal aerosol chemotherapy (PIPAC), which was developed mainly in Europe. PIPAC delivers aerosolized chemotherapy under pressure to improve intraperitoneal distribution and tissue penetration, and early studies have demonstrated favorable pathological responses and promising survival outcomes [26-29]. However, the absence of randomized evidence and standardized treatment protocols remains a major limitation.

In contrast, repeated normothermic IP chemotherapy delivered through a subcutaneous access port and intraperitoneal catheter, referred to as catheter-based intraperitoneal chemotherapy (CBIP), represents a more practical and minimally invasive therapeutic strategy (Fig. 1A). CBIP provides a platform for sustained and repeated IP drug administration via an implanted port system, enabling non-invasive weekly delivery of high local concentrations of anticancer agents over prolonged periods. In addition, the system allows serial sampling of peritoneal fluid for cytological and biomarker-based disease monitoring. Unlike HIPEC or PIPAC, CBIP does not require repeated general anesthesia and is therefore better suited for long-term treatment. In this review, we summarize the mechanistic rationale, pharmacologic basis, clinical evidence, and future perspectives of PTX-based catheter-based intraperitoneal chemotherapy for gastrointestinal cancers with PM.

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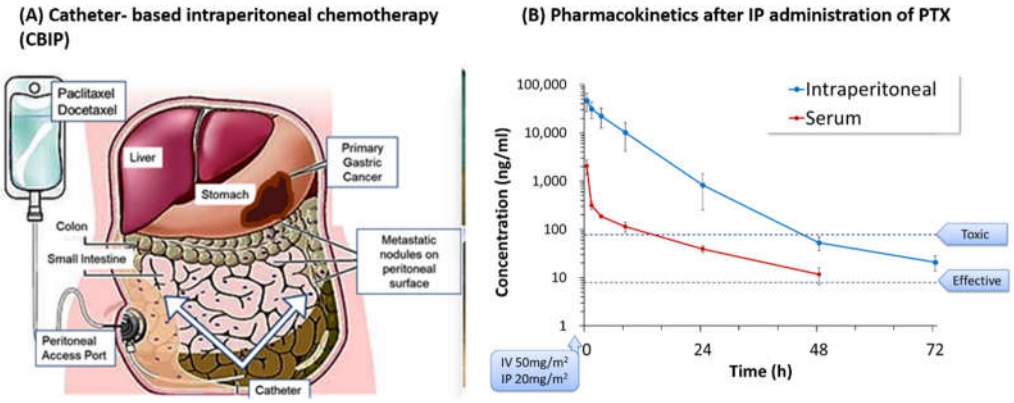

Figure 1. Catheter-based intraperitoneal chemotherapy (CBIP) using paclitaxel. (A) CBIP using an implantable port system. (B) Time-course changes in paclitaxel (PTX) concentrations in serum and peritoneal fluid in a representative patient following intravenous (50 mg) and intraperitoneal (20 mg) administration of PTX.

2. Characteristics of PM from a Pharmacokinetic Perspective

The peritoneal cavity is the largest enclosed compartment in the human body, lined by a mesothelial monolayer and characterized by abundant visceral adipose tissue and a unique local immune microenvironment. Despite its large surface area, effective peritoneal blood flow is remarkably low, estimated at only 60–100 mL/min (approximately 1–2% of cardiac output). This distinctive physiological feature fundamentally differentiates the peritoneum from other visceral organs and contributes to the limited efficacy of systemic chemotherapy against peritoneal malignancies.[13, 30]

A key determinant of drug disposition within the peritoneal cavity is the peritoneal–plasma barrier (PPB).[15, 17] Rather than a single anatomical structure, the PPB is a dynamic, multilayered interface composed of the mesothelium, submesothelial interstitium, and subperitoneal microvasculature. Drug transport across this barrier occurs through interstitial diffusion and microvascular absorption, providing the pharmacokinetic basis for intraperitoneal (IP) chemotherapy by enabling high local drug concentrations and prolonged peritoneal residence compared with intravenous administration. Classical studies identified the microvascular endothelium as the principal rate-limiting component, with transport kinetics largely determined by molecular size, charge, and solubility.[17, 18] Consequently, larger molecules exhibit slower clearance and higher peritoneal-to-plasma area-under-the-curve (AUC) ratios.[31, 32] In addition, the submesothelial interstitium, particularly extracellular matrix composition and collagen density, plays a critical role in regulating solute diffusion.[19, 33] Recent studies have further implicated the endothelial glycocalyx, including hyaluronan, in controlling macromolecular permeability.[34] These observations highlight the PPB as a highly dynamic interface that is continuously remodeled by physiological and pathological processes. Inflammation and tumor infiltration induce angiogenesis, fibrosis, and mesothelial injury, thereby altering transport characteristics and drug distribution.

Importantly, the PPB acts bidirectionally. While it limits systemic absorption of IP-administered drugs and thereby maintains high intraperitoneal exposure, it also restricts the penetration of systemically administered agents into peritoneal tumors. This challenge is further exacerbated by tumor-associated fibrosis and desmoplasia, which increase interstitial density and pressure, creating a formidable barrier to drug diffusion from both the bloodstream and the peritoneal cavity. Therefore, the major therapeutic challenge in PM is not merely achieving high drug concentrations within the peritoneal cavity, but ensuring sufficient penetration into metastatic nodules.

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3. Pharmacological Characteristics of PTX

Among the available agents, PTX possesses particularly favorable pharmacokinetic properties for CBIP. PTX, originally isolated from the bark of Taxus brevifolia (Pacific yew), is highly hydrophobic and is therefore formulated as large micelles with Cremophor and ethanol. As a result, PTX forms micellar particles with a relatively large molecular diameter (approximately 10–12 nm) in solution. These micelles are absorbed predominantly through the lymphatic system, leading to prolonged retention within the peritoneal cavity and limited systemic exposure.[35] Accordingly, after IP administration, the peritoneal-to-plasma area under the concentration–time curve (AUC) ratio for PTX has been reported to be approximately 1000,[36] with more recent studies showing a range of 550–2300, substantially higher than that observed with many hydrophilic agents.[37, 38] Indeed, pharmacokinetic study demonstrated that intraperitoneal concentration of PTX maintain above effective dose for 3 days after IP administration of PTX. [39] (Fig.1 B)

In addition, PTX exerts antifibrotic effects, including inhibition of fibroblast proliferation and extracellular matrix deposition [40, 41], resulting no peritoneal adhesion even after repeated IP administration. These characteristics enable sustained exposure of peritoneal tumor surfaces to cytotoxic concentrations while minimizing systemic toxicity, making PTX one of the most suitable agents for repeated CBIP chemotherapy.

4. Pharmacological Characteristics of PTX

The PPB limits drug diffusion from both the bloodstream and the peritoneal cavity; thus, the key challenge is not simply achieving high intraperitoneal drug concentrations, but ensuring deep penetration into metastatic nodules. Preclinical studies have demonstrated that IP PTX achieves direct penetration into peritoneal metastatic nodules.[42-44] However, despite achieving high intraperitoneal concentrations, tumor penetration remains limited. Experimental studies using radiolabeled PTX have demonstrated that drug infiltration is limited to less than 100 μm from the tumor surface in xenograft models.[45] Other studies employing fluorescein-labeled PTX have shown penetration extending several hundred micrometers beneath the surface of peritoneal nodules. (Fig.2) [46] While this superficial distribution can effectively destroy peripheral tumor cells, it is unlikely to eradicate deeply located lesions, making repeated administration essential.

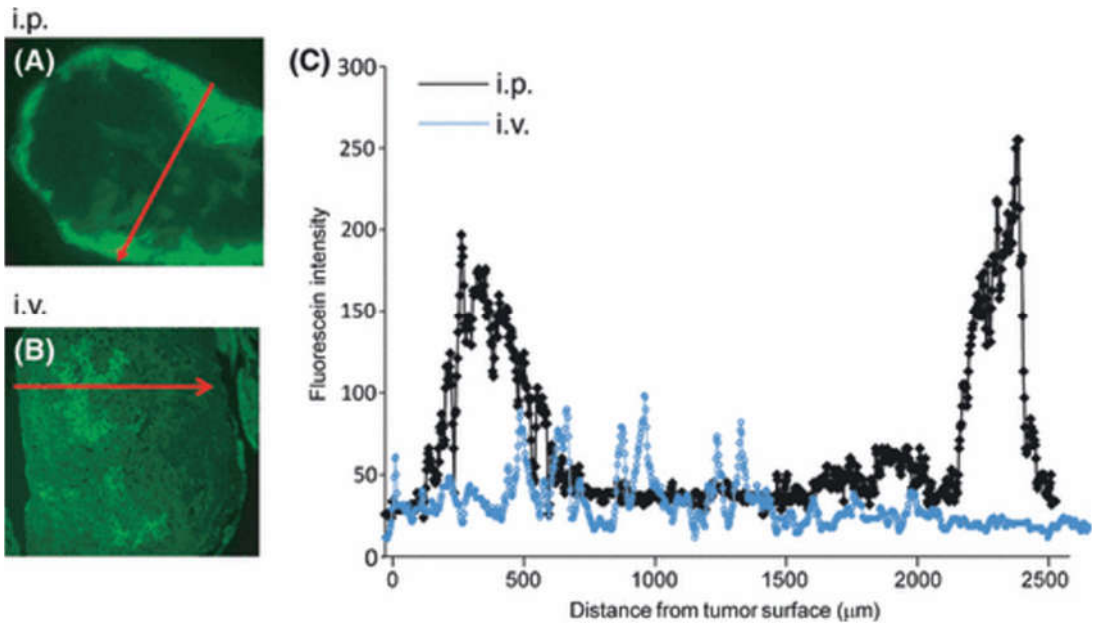

Figure 2. Infiltration of paclitaxel (PTX) into peritoneal tumor after intraperitoneal administration. Intratumoral distribution in peritoneal tumors after intravenous (IV) or intraperitoneal (IP) injection of PTX nanoparticles. Peritoneal tumors were established by IP inoculation of the human gastric cancer cell line

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MKN45P. Oregon Green–conjugated PTX nanoparticles (100 μg) were administered either IV via the tail vein or directly into peritoneal cavity (IP). After 24 h, peritoneal tumors were resected, and fluorescein intensity was evaluated in tissue sections. A representative line corresponding to the deepest apparent penetration of green fluorescent PTX was defined (red arrow), and fluorescence intensity along the line was measured and plotted. The maximal depth of PTX penetration after IP administration in each tumor is objectively measured.

However, even repeated IP therapy has limited penetration depth and minimal activity against extra-peritoneal disease. In addition, postoperative adhesions may impair drug distribution within the peritoneal cavity. These limitations support the rationale for combining IP and systemic chemotherapy. Preclinical studies have demonstrated complementary distribution patterns, with IV-administered PTX localizing mainly to perivascular regions, whereas IP-delivered PTX accumulates in relatively avascular tumor areas.[46, 47] (Fig.2) In addition, PTX has been shown to induce marked destruction microvessels in the tumor periphery.[48], which may disrupt tumor architecture and reduce interstitial fluid pressure, thereby facilitating deeper penetration of IV administered agents. Recent experimental data show that IP PTX enhances the intratumoral concentration of IV administered Carboplatin [49], providing direct evidence for the synergistic potential of sequential IP and systemic chemotherapy. Collectively, these findings support combination of CBIP-PTX with systemic chemotherapy as a rational strategy to overcome spatial drug-delivery barriers in PM.

5. Clinical Results of CBIP-PTX with Systemic Chemotherapy for Patients with PM

5.1. Gastric Cancer

CBIP-PTX was developed for gastric cancer with PM (GCPM) in Japan. First regimen consisted of oral S-1 (80 mg/m², days 1–14), weekly intravenous (IV) paclitaxel (PTX, 50 mg/m²), and IP-PTX administered via an implanted peritoneal port. A phase I study established the recommended IP dose at 20 mg/m². [39] Early phase II studies demonstrated encouraging outcomes in patients with macroscopic PM or positive peritoneal cytology with a 1-year overall survival (OS) rate of 78% with a median survival time (MST) of 22.5 months, which was reproduced comparable results in another prospective cohort. [50, 51] Importantly, repeated second-look laparoscopies frequently demonstrated substantial regression of peritoneal nodules and disappearance of ascites, allowing conversion gastrectomy in selected responders. Postoperative continuation of IP chemotherapy was also feasible. Then, randomized phase III PHOENIX-GC trial was conducted, which compared IP+IV PTX plus S-1 against standard cisplatin plus S-1 (SP). [52] Although the primary analysis narrowly failed to achieve statistical significance (MST 17.7 vs. 15.2 months; HR 0.72; p=0.08), several important findings strongly supported the efficacy of IP therapy. First, protocol violations substantially affected interpretation, including crossover to IP treatment in approximately 12% of patients assigned to the control arm. Second, the IP group included a greater proportion of patients with massive ascites, representing a biologically unfavorable subgroup. When analyses were restricted to the per-protocol population, the survival benefit became significant (HR 0.64; p=0.022), and adjustment for ascites imbalance further strengthened the effect (HR 0.59; p=0.008). Moreover, the IP arm achieved markedly superior ascites control and cytological conversion rates (76% vs. 33%), indicating stronger suppression of peritoneal disease biology.

Subsequent studies consistently reproduced favorable outcomes across multiple systemic chemotherapy backbones. (Table 1) Combination regimens incorporating SOX [53-57], FOLFOX [58, 59], capecitabine/oxaliplatin or cisplatin [60, 61], or S1/cisplatin [62] generally achieved 1-year OS rates of approximately 70–80% and MSTs around 15–22 months. Notably, escalation of IP-PTX doses to 40–80 mg/m² did not clearly improve survival outcomes, suggesting that pharmacologic saturation within the peritoneal cavity may already be achieved at moderate doses. Most recently, the Chinese multicenter phase III DRAGON-01 trial provided further high-level evidence. In this study, IP-PTX combined with IV PTX and S-1 significantly improved survival compared with systemic

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chemotherapy alone, achieving an MST of 19.4 months versus 13.9 months (p=0.0054). Importantly, survival benefits persisted in long-term follow-up, including improvements in 1-, 2-, 3-, and 5-year OS rates, suggesting durable disease control in selected patients.[63]

Table 1. Efficacy of Catheter-based intraperitoneal chemotherapy (CBIP) using PTX for Patients with PM.

Author, Year	PTX dose (mg/m2)	Systemic regimen	Study	n	MST	1y-OS	Response rate	Cytology negative conversion rate	conversion Surgery rate	Grade3/4 Neutro-penia	Major Grade3/4 non-hematological Toxicity	Ref.
Gastric cancer												
Ishigami H, 2010	20	S-1+PTX	P2	40	22.5 M	78.0 %	10/18 (55.6%)	86.0%	37.5%	38.0%	Nausea vomit: 8%, Anorexia: 5%	45
Yamaguchi H, 2013	20	S-1+PTX	P2	35	17.6 M	77.1 %	5/7 (71.4%)	97.0%	31.4%	34.0%	Nausea vomit:3%	46
Ishigami H, 2016	20	S-1+PTX	P3	114	17.7 M	71.9 %	9/17 (52.9%)	95.0%	45.7%	50.0%	Nausea vomit: 10%, Anorexia 10%, Febrile neutropenia 8%	47
Fujiwara, 2016	40	S-1+L-OHP	P2	60	ND	71.5 %	4/6 (67.7%)	71.0%	35..9%	50.0%	Anorexia 12%, Febrile neutropenia 6%	48
Saito S, 2021	40	S-1+L-OHP	P2	44	25.8 M	79.5 %	2/3(67.7 %)	86.0%	45.0%	39.0%	Febrile neutropenia 5%	49
Chia, DKA, 2023	40	Cap+L-OHP	P2	44	14.6 M	67.8 %	ND	70.5%	29.5%	18.0%	Febrile neutropenia 14%	55
Tu, L, 2023	80	S-1+L-OHP	P2	49	16.9 M	81.6 %	21/47 (51.2%)	ND	26.5%	40.8%	Nausea vomit: 22.5%, Diarrhea 12.2%,	52
Yang ZY, 2022	20	S-1+PTX	P2	67	19.3 M	67.2 %	22/64 (34.4%)	67.2%	62.9%	26.9%	Liver dysfunction 9%	59
Zhao S, 2022	80	mFOLFOX	P2	29	11.0 M	ND	11/29 (37.9%)	ND	ND	34.5%	Diarrhea2 0.7%	54
Seo WL, 2025	80	Cap+CDDP	P2	28	ND	76.9 %	10/24 (41.7%)	ND	ND	41.7%		51

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Kobayashi D, 2024	20	S1+CDDP	P2	53	19.4 M	73.6 %	ND	64.0%	30.0%	24.0%	Diarrhea 13%, Anorexia 17%	57
Yan C, 2026	20	S-1+PTX	P3	148	17.7 M	69.6 %	ND	ND	50.7%	19.9%	Fatigue 7.7%,Anorexia 5.1%	58
Pancreatic cancer												
Satoi S, 2017	20	S-1+PTX	P2	33	16.3 M	62.0 %	12/33(36.4%)	55.0%	24.2%	42.0%	Febrile neutropenia 14% Anorexia 12%	67
Yamada S, 2020	20	GEM+nab-PTX	P1/2	46	14.5 M	61.0 %	21/46 (45.6%)	76.0%	39.1%	69.6%	Anorexia 20%	68
Colorectal cancer												
Murono K, 2019	20	mFOLFOX6+Bmab or CapeOX+Bmab	P1/2	6	29.3 M	ND	3/6(25%)	ND	ND	16.7%	Nausea vomit: 16.7%, Abdominal pain:16.7%	81

One of the most clinically important aspects of IP-taxane therapy is its ability to induce cytological conversion and facilitate conversion surgery. Across studies, conversion from positive to negative peritoneal cytology (CY1→CY0) occurred in 64–97% of patients[50-54, 58, 60, 62, 64], substantially exceeding rates typically achieved with systemic chemotherapy alone. Conversion gastrectomy became feasible in 26–63% of cases, and patients undergoing surgery often achieved prolonged survival, with reported MSTs ranging from 24 to 42 months. [50-55, 57] [58, 62, 63] [60, 64] These findings suggest that IP-PTX may convert selected stage IV patients into candidates for potentially curative-intent treatment.

The toxicity profile of CBIP-taxane appears manageable and generally comparable to conventional systemic chemotherapy. The most common adverse events are hematologic toxicities, including grade 3/4 leukopenia and neutropenia, which are usually manageable with dose modifications or temporary interruption. [50-52] [53-57] [58, 59] [60, 61] [62, 63] Non-hematologic toxicities, such as neuropathy, gastrointestinal symptoms, fatigue, or hepatic dysfunction, are relatively infrequent. Importantly, severe abdominal pain is uncommon despite repeated IP administration. An additional issue unique to CBIP is port-related complications. In a University of Tokyo cohort, approximately 20% of patients experienced complications including inflow obstruction, infection, reflux, or fistula formation. [65]However, severe complications requiring major surgical intervention were uncommon, and most studies reported low rates of grade 3/4 port-related adverse events.

IP-PTX therapy may also have important roles beyond macroscopic peritoneal metastasis. In patients with microscopic peritoneal disease (P0CY1), several studies reported cytological conversion rates exceeding 75–95% with encouraging survival outcomes. [66] Furthermore, preliminary evidence suggests that postoperative IP-PTX may help prevent peritoneal recurrence in high-risk patients with serosal invasion. [67] Even in highly advanced cases with massive malignant ascites and poor performance status, IP therapy has shown potential benefit. Because systemic drug delivery into peritoneal lesions is particularly impaired in these patients, IP-PTX may partially overcome this limitation. Combination approaches integrating cell-free and concentrated ascites reinfusion therapy

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(CART) with IP-PTX have demonstrated encouraging survival outcomes despite historically dismal prognoses. [68]

In Western populations, clinical evidence remains limited but is steadily emerging. In the United States, the prospective phase II STOPGAP study, [69] evaluating IP-PTX in combination with 5-fluorouracil and leucovorin, has been completed and has subsequently progressed to a phase III trial (STOPGAP II). (https://clinicaltrials.gov/study/NCT07001748) In Europe, a phase III study, IPa-Gastric trial, is currently evaluating the added benefit of IP-PTX to standard fluoropyrimidine- and oxaliplatin-based systemic regimens.(https://clinicaltrials.gov/study/NCT07304271) These studies are expected to clarify the generalizability of IP taxane–based strategies beyond East Asian populations and to better define their role within global treatment paradigms.

5.2. Pancreatic Cancer

Pancreatic ductal adenocarcinoma (PDAC) remains one of the deadliest malignancies, with a 5-year survival rate below 10%.[70] Peritoneal metastasis (PM) is a frequent and highly lethal metastatic pattern, with reported median survival of only 2–3 months and 1-year overall survival (OS) rates of 10–14%.[71] Although modern systemic regimens such as FOLFIRINOX and gemcitabine plus nab-paclitaxel (GEM+nab-PTX) have improved outcomes in metastatic PDAC,[72] their efficacy specifically against PM remains unclear. In contrast, HIPEC has been poorly investigated in PDAC because of the aggressive biology and poor prognosis of the disease.

Two phase II studies have suggested promising activity of CBIP using PTX. Satoi et al. evaluated IV/IP PTX plus S-1 and reported a median OS of 16.3 months, with response and disease control rates of 36% and 82%, respectively.[73] Patients who underwent conversion surgery achieved significantly longer survival than those who did not (27.8 vs. 14.2 months). Yamada et al. subsequently investigated IV gemcitabine and nab-PTX combined with IP PTX, demonstrating a median OS of 14.5 months, a response rate of 50%, and a disease control rate of 95%, with cytology conversion observed in 39% of patients.[74] Conversion surgery was again associated with markedly prolonged survival.

Based on these encouraging findings, an ongoing phase III trial is comparing IP PTX–based therapy with standard systemic GEM+nab-PTX in patients with PDAC and PM.[75] This multicenter study will directly evaluate whether bidirectional chemotherapy using IP PTX can improve survival outcomes in this highly refractory disease.

5.3. Colorectal Cancer

Colorectal cancer (CRC) accounts for approximately 10.2% of all newly diagnosed cancers worldwide, and second leading cause of cancer-related death. [76]. PM is one of the most frequent metastatic patterns in CRC and is associated with particularly poor prognosis. Population-based studies have shown that synchronous PM is present in approximately 4–7% of patients at the time of initial CRC diagnosis, while an additional 4–6% develop metachronous PM during the disease course.[77, 78] Historically, PM from CRC has been regarded as a terminal condition with substantially worse prognosis than hematogenous metastases such as liver or lung metastases. Large registry analyses reported median OS of only 5–9 months in untreated patients [79] and approximately 12–16 months with modern systemic chemotherapy alone. [80]

In selected patients, however, CRS plus HIPEC has significantly improved outcomes. The randomized trial by Verwaal et al. demonstrated superior survival with CRS+HIPEC compared with systemic chemotherapy alone,[81] and subsequent cohort studies reported median OS exceeding 30–40 months with 5-year survival rates of 30–45% after complete cytoreduction.[82, 83] Prognosis is strongly influenced by the PCI, completeness of cytoreduction, tumor biology, and histological subtype. Patients with low PCI and complete cytoreduction achieve the best outcomes, whereas signet-ring cell carcinoma and extensive small bowel involvement are associated with poor survival.[84] Nevertheless, recurrence remains frequent, and many patients are not candidates for aggressive surgery because of diffuse disease or poor performance status.

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PIPAC has emerged as a promising alternative for CRC with PM. Recent studies have shown that oxaliplatin-based PIPAC is feasible, safe, and well tolerated. Lurvink et al. reported median OS of 15–27 months,[85] while Sleiman et al., in an analysis of 949 patients from 11 studies, reported median OS ranging from 8 to 37.8 months, with most patients completing the planned treatment cycles.[86] These findings are consistent with the pooled median OS of approximately 16 months reported by Alyami et al.[26] Histopathologic response rates were also encouraging, including complete response in nearly 50% of patients and major regression in 29%. [85] Toxicity was generally mild, with most adverse events limited to grade 1–2 abdominal pain or nausea, whereas grade ≥3 toxicities occurred in only 12–15% of patients and no treatment-related deaths were reported.[26, 86] Quality of life was largely preserved during treatment.

CBIP-PTX therapy has been employed in Japan for treatment of PM from CRC. A preceding phase I study demonstrated favorable safety and preliminary efficacy, with a response rate of 25%, improvement in PCI in 50% of patients, complete conversion to negative peritoneal cytology, median progression-free survival (PFS) of 8.8 months, and median OS of 29.3 months.[87] Based on these encouraging results, the subsequent iPac-02 study was conducted as a single-arm, multicenter phase II trial enrolling 38 patients with isolated unresectable colorectal PMs.[88] Patients received weekly intraperitoneal PTX (20 mg/m²) combined with FOLFOX- or CAPOX-bevacizumab. The primary endpoint was response rate, while secondary endpoints included PFS, OS, PCI improvement, conversion to negative peritoneal cytology, and safety.

6. Clinical Results of CBIP-PTX with Systemic Chemotherapy for Patients with PM

6.1. Seek the Optimal Systemic Chemotherapy to Combine with IP-PTX

IP-PTX should be recognized fundamentally as a locoregional treatment, with limited activity against extraperitoneal disease. Given that PM frequently coexists with systemic dissemination, the integration of effective and well-tolerated systemic chemotherapy is essential to optimize overall patient outcomes. In this context, combination strategies incorporating contemporary molecularly targeted agents and immunotherapies are particularly promising. In this context, recent phase II studies have incorporated IP-PTX into modern systemic regimens, thereby enabling the concurrent use of biomarker-driven therapies, including anti–PD-1 inhibitors and HER2-targeted agents. Kang et al. reported outcomes in 22 patients with GCPM treated with FOLFOX with or without nivolumab in combination with IP-PTX (60 mg/m²), demonstrating a median overall survival of 20.2 months. [89] Yang et al. are currently investigating a combination regimen comprising cadonilimab (a dual CTLA-4/PD-1 inhibitor), LM-302 (a claudin 18.2–targeted antibody–drug conjugate), and S-1 with IP-PTX (20 mg/m²) in patients with CLDN18.2-positive GC (NCT06519591). Claudin 18.2 has emerged as a promising molecular target in gastric cancer, and its monoclonal antibody, zolbetuximab, has recently been approved as a first-line treatment for metastatic disease. [90, 91] Claudin 18.2 is preferentially expressed in diffuse-type and poorly differentiated gastric cancers, histological subtypes that are strongly associated with peritoneal dissemination. [92, 93] Therefore, combining IP-PTX with zolbetuximab represents a biologically rational therapeutic strategy and may provide excellent efficacy in patients with GCPM. In addition, a phase II trial (NCT05185947) is evaluating the combination of IP/IV PTX with the tyrosine kinase inhibitor nilotinib across multiple malignancies, including, but not limited to, gastric cancer. [94] These ongoing efforts are expected to refine the optimal systemic partners for IP-PTX–based therapy and to further enhance clinical outcomes through a rational, multimodal treatment approach.

6.2. Modification of PTX for IP Specific Drug

Another promising strategy for improving IP chemotherapy is the development of IP-specific anticancer formulations. Increasing preclinical evidence suggests that advanced biomaterials, including hydrogels, nanoparticles, and implantable delivery systems, can achieve sustained

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locoregional drug release within the peritoneal cavity, thereby enhancing therapeutic exposure while reducing systemic toxicity.[95] For paclitaxel (PTX), both chemical modification and formulation-based approaches have demonstrated superior antitumor efficacy compared with conventional formulations in murine PM models. Li et al. showed that PTX solubilized with poly(L-glutamic acid) improved biodistribution and drug delivery efficiency in ovarian cancer PM.[96] Yamada et al. reported that hyaluronic acid (HA)-based formulations prolonged intraperitoneal retention of PTX and enhanced antitumor effects in nude mice.[97] Similarly, Bajaj et al. demonstrated that HA-based in situ crosslinkable hydrogels improved PTX retention and therapeutic efficacy after IP administration.[98] Soma et al. developed a nanomicellar PTX formulation using a PMB polymer, an amphiphilic copolymer composed of 2-MPC and n-BMA, which enhanced direct penetration into peritoneal tumors.[47] Emoto et al. further showed that NK105, a “core-shell”-type polymeric micellar PTX nanoparticle, enhanced antitumor activity against both peritoneal and extraperitoneal lesions.[99] In addition, De Clercq et al. demonstrated that PTX-loaded genipin-crosslinked gelatin microspheres prolonged intraperitoneal drug retention and improved therapeutic outcomes in advanced ovarian cancer models. More sophisticated nanocarrier systems, including pH-sensitive polymersomes and tumor-penetrating peptide (iRGD)-functionalized nanoparticles, have further improved tumor accumulation and intratumoral penetration after IP administration.[100, 101] Collectively, these studies suggest that physicochemical modification of nanomicellar structures, including particle size, surface charge, and solvent polymer characteristics, critically influences the therapeutic efficacy of IP-PTX. Although no anticancer agents have yet been specifically approved for IP chemotherapy, the development of optimized nanodrugs for locoregional delivery may represent a major breakthrough in the treatment of PM.

6.3. Modification of Intraperitoneal Immune Microenvironment

Another important consideration in CBIP is its impact on the peritoneal immune microenvironment. The high local concentrations achieved by IP-PTX may exert substantial cytotoxic effects not only on tumor cells but also on resident and infiltrating immune cells, potentially resulting in profound local immunosuppression. The peritoneal cavity harbors a unique immune milieu that is generally immunosuppressive and plays a critical role in regulating tumor progression and therapeutic response in PM.[16, 102, 103] Recent analyses of ascitic immune cells have shown that IP-PTX treatment reduces the proportion of CD8(+) T cells while increasing CD11b(+) myeloid cells. Notably, a marked expansion of CD16(−)CCR3(+) eosinophils was observed in a subset of patients and was associated with enhanced tumor regression and improved survival outcomes.[104] These findings suggest that the therapeutic effects of IP-PTX may be mediated, at least in part, through modulation of the local immune environment. Given the pivotal role of the immune microenvironment in determining chemosensitivity and treatment outcomes,[105] strategies aimed at restoring or enhancing antitumor immunity within the peritoneal cavity may represent an important avenue for maximizing the efficacy of CBIP.

6. Conclusion

CBIP-PTX represents a biologically rational treatment strategy for PM from gastrointestinal cancers, and accumulating clinical evidence increasingly supports its therapeutic utility, particularly in East Asian populations. A major advantage of this approach is its repeatability which enables prolonged locoregional treatment for peritoneal tumors. Moreover, it can be safely combined with various systemic regimens, including recently developed molecularly targeted agents and immune-based therapies. With further optimization of treatment protocols and continued clinical validation, CBIP-PTX may become an important component of future multimodal treatment strategies for this highly lethal disease.

 doi:10.20944/preprints202606.0429.v1

References

1. Thomassen I, van Gestel YR, van Ramshorst B, Luyer MD, Bosscha K, Nienhuijs SW, et al. Peritoneal carcinomatosis of gastric origin: a population-based study on incidence, survival and risk factors. Int J Cancer. 2014;134(3):622-8. Epub 20130805. doi: 10.1002/ijc.28373. PubMed PMID: 23832847.
2. Sirody J, Kaji AH, Hari DM, Chen KT. Patterns of gastric cancer metastasis in the United States. Am J Surg. 2022;224(1 Pt B):445-8. Epub 2022/02/12. doi: 10.1016/j.amjsurg.2022.01.024. PubMed PMID: 35144812.
3. Rijken A, Pape M, Simkens GA, de Hingh I, Luyer MDP, van Sandick JW, et al. Peritoneal metastases from gastric cancer in a nationwide cohort: Incidence, treatment and survival. Int J Cancer. 2024;154(6):992-1002. Epub 2023/11/02. doi: 10.1002/ijc.34780. PubMed PMID: 37916797.
4. Vincent A, Herman J, Schulick R, Hruban RH, Goggins M. Pancreatic cancer. Lancet. 2011;378(9791):607-20. Epub 20110526. doi: 10.1016/S0140-6736(10)62307-0. PubMed PMID: 21620466; PubMed Central PMCID: PMCPMC3062508.
5. Wu G, Standring OJ, King DA, Gholami S, Devoe CE, Thiels CA, et al. Management of Peritoneal Metastasis in Patients with Pancreatic Ductal Adenocarcinoma. Curr Oncol. 2025;32(2). Epub 20250212. doi: 10.3390/curroncol32020103. PubMed PMID: 39996904; PubMed Central PMCID: PMCPMC11854847.
6. Koppe MJ, Boerman OC, Oyen WJ, Bleichrodt RP. Peritoneal carcinomatosis of colorectal origin: incidence and current treatment strategies. Ann Surg. 2006;243(2):212-22. doi: 10.1097/01.sla.0000197702.46394.16. PubMed PMID: 16432354; PubMed Central PMCID: PMCPMC1448921.
7. Baaten I, West NP, Quyn AJ, Seymour MT, Seligmann JF. Colorectal cancer peritoneal metastases: Biology, treatment and next steps. Eur J Surg Oncol. 2020;46(4 Pt A):675-83. Epub 20191031. doi: 10.1016/j.ejso.2019.10.035. PubMed PMID: 31806517.
8. Rijken A, Bakkers C, Klumpen HJ, van der Geest LG, de Vos-Geelen J, van Erning FN, et al. Insights into synchronous peritoneal metastases from hepatobiliary origin: Incidence, risk factors, treatment, and survival from a nationwide database. Eur J Surg Oncol. 2023;49(8):1436-43. Epub 20230305. doi: 10.1016/j.ejso.2023.03.004. PubMed PMID: 36898900.
9. Koemans WJ, Lurvink RJ, Grootscholten C, Verhoeven RHA, de Hingh IH, van Sandick JW. Synchronous peritoneal metastases of gastric cancer origin: incidence, treatment and survival of a nationwide Dutch cohort. Gastric Cancer. 2021;24(4):800-9. Epub 2021/01/27. doi: 10.1007/s10120-021-01160-1. PubMed PMID: 33495964.
10. Franko J, Shi Q, Goldman CD, Pockaj BA, Nelson GD, Goldberg RM, et al. Treatment of colorectal peritoneal carcinomatosis with systemic chemotherapy: a pooled analysis of north central cancer treatment group phase III trials N9741 and N9841. J Clin Oncol. 2012;30(3):263-7. doi: 10.1200/JCO.2011.37.1039. PubMed PMID: 22162570; PubMed Central PMCID: PMC3269953.
11. Wu L, Zhu L, Xu K, Zhou S, Zhou Y, Zhang T, et al. Clinical significance of site-specific metastases in pancreatic cancer: a study based on both clinical trial and real-world data. J Cancer. 2021;12(6):1715-21. Epub 20210118. doi: 10.7150/jca.50317. PubMed PMID: 33613759; PubMed Central PMCID: PMCPMC7890328.
12. Cortes-Guiral D, Hubner M, Alyami M, Bhatt A, Ceelen W, Glehen O, et al. Primary and metastatic peritoneal surface malignancies. Nat Rev Dis Primers. 2021;7(1):91. Epub 2021/12/18. doi: 10.1038/s41572-021-00326-6. PubMed PMID: 34916522.
13. Solass W, Horvath P, Struller F, Konigsrainer I, Beckert S, Konigsrainer A, et al. Functional vascular anatomy of the peritoneum in health and disease. Pleura Peritoneum. 2016;1(3):145-58. Epub 2016/09/01. doi: 10.1515/pp-2016-0015. PubMed PMID: 30911618; PubMed Central PMCID: PMCPMC6328070.
14. Fujimori D, Kinoshita J, Yamaguchi T, Nakamura Y, Gunjigake K, Ohama T, et al. Established fibrous peritoneal metastasis in an immunocompetent mouse model similar to clinical immune microenvironment of gastric cancer. BMC cancer. 2020;20(1):1014. Epub 2020/10/22. doi: 10.1186/s12885-020-07477-x. PubMed PMID: 33081727; PubMed Central PMCID: PMCPMC7574408.
15. Jacquet P, Sugarbaker PH. Peritoneal-plasma barrier. Cancer Treat Res. 1996;82:53-63. PubMed PMID: 8849943.

 doi:10.20944/preprints202606.0429.v1

16. Kim H, Kwon M, Lee SK, Son SM, Lee OJ, Man Yoon S, et al. Distinct Immunosuppressive Tumor Microenvironment in Gastric Cancer With Peritoneal Metastasis. J Gastric Cancer. 2025;25(4):605-20. Epub 2025/10/16. doi: 10.5230/jgc.2025.25.e46. PubMed PMID: 41093779; PubMed Central PMCID: PMCPMC12536193.
17. Dedrick RL, Myers CE, Bungay PM, DeVita VT, Jr. Pharmacokinetic rationale for peritoneal drug administration in the treatment of ovarian cancer. Cancer Treat Rep. 1978;62(1):1-11. PubMed PMID: 626987.
18. Markman M. Intraperitoneal antineoplastic drug delivery: rationale and results. Lancet Oncol. 2003;4(5):277-83. Epub 2003/05/07. doi: 10.1016/s1470-2045(03)01074-x. PubMed PMID: 12732164.
19. Ceelen WP, Flessner MF. Intraperitoneal therapy for peritoneal tumors: biophysics and clinical evidence. Nat Rev Clin Oncol. 2010;7(2):108-15. doi: 10.1038/nrclinonc.2009.217. PubMed PMID: 20010898.
20. Oleson JR, Calderwood SK, Coughlin CT, Dewhirst MW, Gerweck LE, Gibbs FA, Jr., et al. Biological and clinical aspects of hyperthermia in cancer therapy. Am J Clin Oncol. 1988;11(3):368-80. Epub 1988/06/01. PubMed PMID: 3289367.
21. van Driel WJ, Koole SN, Sikorska K, Schagen van Leeuwen JH, Schreuder HWR, Hermans RHM, et al. Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer. N Engl J Med. 2018;378(3):230-40. Epub 2018/01/18. doi: 10.1056/NEJMoa1708618. PubMed PMID: 29342393.
22. Mirnezami R, Mehta AM, Chandrakumaran K, Cecil T, Moran BJ, Carr N, et al. Cytoreductive surgery in combination with hyperthermic intraperitoneal chemotherapy improves survival in patients with colorectal peritoneal metastases compared with systemic chemotherapy alone. Br J Cancer. 2014;111(8):1500-8. Epub 2014/09/17. doi: 10.1038/bjc.2014.419. PubMed PMID: 25225906; PubMed Central PMCID: PMCPMC4200082.
23. Pelc Z, Sedlak K, Endo Y, Van Sandick J, Gisbertz S, Pera M, et al. Hyperthermic intraperitoneal chemotherapy (HIPEC) for gastric cancer with peritoneal metastasis - Joint analysis of European GASTRODATA and American national cancer database. Am J Surg. 2025;242:116235. Epub 2025/02/16. doi: 10.1016/j.amjsurg.2025.116235. PubMed PMID: 39954554.
24. Tops-Welten MW, Galanos LJK, Creemers GJ, Luyer MDP, De Hingh I, van Hellemond IEG. Gastrointestinal CancerEmerging treatment modalities for gastric cancer with peritoneal metastases: a systematic review. Oncologist. 2025;30(9). Epub 2025/08/12. doi: 10.1093/oncolo/oyaf219. PubMed PMID: 40794565; PubMed Central PMCID: PMCPMC12445643.
25. Gudmundsdottir H, Yonkus JA, Thiels CA, Warner SG, Cleary SP, Kendrick ML, et al. Oncologic Outcomes of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Highly Selected Patients with Metastatic Pancreatic Ductal Adenocarcinoma. Ann Surg Oncol. 2023;30(12):7833-9. Epub 20230819. doi: 10.1245/s10434-023-14138-3. PubMed PMID: 37596449.
26. Alyami M, Hubner M, Grass F, Bakrin N, Villeneuve L, Laplace N, et al. Pressurised intraperitoneal aerosol chemotherapy: rationale, evidence, and potential indications. Lancet Oncol. 2019;20(7):e368-e77. Epub 2019/07/04. doi: 10.1016/S1470-2045(19)30318-3. PubMed PMID: 31267971.
27. Struller F, Horvath P, Solass W, Weinreich FJ, Strumberg D, Kokkalis MK, et al. Pressurized intraperitoneal aerosol chemotherapy with low-dose cisplatin and doxorubicin (PIPAC C/D) in patients with gastric cancer and peritoneal metastasis: a phase II study. Ther Adv Med Oncol. 2019;11:1758835919846402. Epub 2019/06/18. doi: 10.1177/1758835919846402. PubMed PMID: 31205501; PubMed Central PMCID: PMCPMC6535725.
28. Ellebaek SB, Graversen M, Detlefsen S, Lundell L, Fristrup CW, Pfeiffer P, et al. Pressurized intraperitoneal aerosol chemotherapy (PIPAC) of peritoneal metastasis from gastric cancer: a descriptive cohort study. Clin Exp Metastasis. 2020;37(2):325-32. Epub 2020/02/01. doi: 10.1007/s10585-020-10023-5. PubMed PMID: 32002724.
29. Chen R, Yang Z, Li R, Yang Y, Zheng J, Wang J, et al. Pressurized intraperitoneal aerosol chemotherapy in advanced gastric cancer with peritoneal metastases: a comprehensive meta-analysis of feasibility, efficacy, and safety. Gastroenterol Rep (Oxf). 2025;13:goaf040. Epub 2025/06/16. doi: 10.1093/gastro/goaf040. PubMed PMID: 40520131; PubMed Central PMCID: PMCPMC12167634.

 doi:10.20944/preprints202606.0429.v1

30. Perl J, Bargman JM. Peritoneal dialysis: from bench to bedside and bedside to bench. Am J Physiol Renal Physiol. 2016;311(5):F999-F1004. Epub 2016/03/25. doi: 10.1152/ajprenal.00012.2016. PubMed PMID: 27009336.
31. de Bree E, Michelakis D, Stamatiou D, Romanos J, Zoras O. Pharmacological principles of intraperitoneal and bidirectional chemotherapy. Pleura Peritoneum. 2017;2(2):47-62. Epub 2017/06/01. doi: 10.1515/pp-2017-0010. PubMed PMID: 30911633; PubMed Central PMCID: PMCPMC6405033.
32. Rietveld PCS, Guchelaar NAD, Sassen SDT, Koch BCP, Mathijssen RHJ, Koolen SLW. A Clinical Pharmacological Perspective on Intraperitoneal Chemotherapy. Drugs. 2025;85(7):931-43. Epub 2025/05/25. doi: 10.1007/s40265-025-02195-9. PubMed PMID: 40411722; PubMed Central PMCID: PMCPMC12185600 manuscript.
33. Flessner MF. The transport barrier in intraperitoneal therapy. Am J Physiol Renal Physiol. 2005;288(3):F433-42. Epub 2005/02/05. doi: 10.1152/ajprenal.00313.2004. PubMed PMID: 15692055.
34. Kamiya K, Hatayama N, Tawada M, Asai A, Yamauchi M, Kinashi H, et al. Role of endothelial hyaluronan in peritoneal membrane transport and disease conditions during peritoneal dialysis. Sci Rep. 2024;14(1):7412. Epub 2024/03/29. doi: 10.1038/s41598-024-58148-x. PubMed PMID: 38548914; PubMed Central PMCID: PMCPMC10978880.
35. Singla AK, Garg A, Aggarwal D. Paclitaxel and its formulations. International journal of pharmaceutics. 2002;235(1-2):179-92. PubMed PMID: 11879753.
36. Markman M. Intraperitoneal chemotherapy in the management of malignant disease. Expert review of anticancer therapy. 2001;1(1):142-8. Epub 2002/07/13. doi: 10.1586/14737140.1.1.142. PubMed PMID: 12113122.
37. Sugarbaker PH. Intraperitoneal paclitaxel: pharmacology, clinical results and future prospects. J Gastrointest Oncol. 2021;12(Suppl 1):S231-S9. Epub 2021/05/11. doi: 10.21037/jgo-2020-03. PubMed PMID: 33968440; PubMed Central PMCID: PMCPMC8100710.
38. Guchelaar NAD, Noordman BJ, Koolen SLW, Mostert B, Madsen EVE, Burger JWA, et al. Intraperitoneal Chemotherapy for Unresectable Peritoneal Surface Malignancies. Drugs. 2023;83(2):159-80. Epub 2023/01/13. doi: 10.1007/s40265-022-01828-7. PubMed PMID: 36633826; PubMed Central PMCID: PMCPMC9908703 Mostert received consulting fees from Lilly, Servier and BMS, and research funding from Sanofi, Pfizer and BMS. Niels A.D. Guchelaar, Bo J. Noordman, Stijn L.W. Koolen, Eva V.E. Madsen, Jacobus W.A. Burger, Alexandra R.M. Brandt-Kerkhof, Geert-Jan Creemers, Ignace H.J.T. de Hingh, Misha Luyer, Sander Bins, Esther van Meerten, Sjoerd M. Lagarde, Cornelis Verhoef and Ron. H.J. Mathijssen declare that they have no conflicts of interest that might be relevant to the contents of this manuscript.
39. Ishigami H, Kitayama J, Otani K, Kamei T, Soma D, Miyato H, et al. Phase I pharmacokinetic study of weekly intravenous and intraperitoneal paclitaxel combined with S-1 for advanced gastric cancer. Oncology. 2009;76(5):311-4. doi: 10.1159/000209277. PubMed PMID: 19299904.
40. Jackson JK, Skinner KC, Burgess L, Sun T, Hunter WL, Burt HM. Paclitaxel-loaded crosslinked hyaluronic acid films for the prevention of postsurgical adhesions. Pharm Res. 2002;19(4):411-7. Epub 2002/05/30. doi: 10.1023/a:1015175108183. PubMed PMID: 12033372.
41. Choung HK, Jin SE, Lee MJ, Kim CK, Hwang JM. Slow-releasing paclitaxel in polytetrafluoroethylene/polylactide-co-glycolide laminate delays adjustment after strabismus surgery in rabbit model. Invest Ophthalmol Vis Sci. 2008;49(12):5340-5. Epub 2008/08/19. doi: 10.1167/iovs.08-1694. PubMed PMID: 18708626.
42. Innocenti F, Danesi R, Di Paolo A, Agen C, Nardini D, Bocci G, et al. Plasma and tissue disposition of paclitaxel (taxol) after intraperitoneal administration in mice. Drug Metab Dispos. 1995;23(7):713-7. Epub 1995/07/01. PubMed PMID: 7587959.
43. Mohamed F, Sugarbaker PH. Intraperitoneal taxanes. Surg Oncol Clin N Am. 2003;12(3):825-33. Epub 2003/10/22. doi: 10.1016/s1055-3207(03)00038-3. PubMed PMID: 14567034.
44. Soma D, Kitayama J, Ishigami H, Kaisaki S, Nagawa H. Different tissue distribution of paclitaxel with intravenous and intraperitoneal administration. J Surg Res. 2009;155(1):142-6. Epub 2009/03/31. doi: 10.1016/j.jss.2008.06.049. PubMed PMID: 19328496.

 doi:10.20944/preprints202606.0429.v1

45. Kyle AH, Huxham LA, Yeoman DM, Minchinton AI. Limited tissue penetration of taxanes: a mechanism for resistance in solid tumors. Clin Cancer Res. 2007;13(9):2804-10. Epub 2007/05/03. doi: 10.1158/1078-0432.Ccr-06-1941. PubMed PMID: 17473214.
46. Kamei T, Kitayama J, Yamaguchi H, Soma D, Emoto S, Konno T, et al. Spatial distribution of intraperitoneally administrated paclitaxel nanoparticles solubilized with poly (2-methacryloxyethyl phosphorylcholine-co n-butyl methacrylate) in peritoneal metastatic nodules. Cancer Sci. 2011;102(1):200-5. Epub 2010/10/15. doi: 10.1111/j.1349-7006.2010.01747.x. PubMed PMID: 20942868.
47. Soma D, Kitayama J, Konno T, Ishihara K, Yamada J, Kamei T, et al. Intraperitoneal administration of paclitaxel solubilized with poly(2-methacryloxyethyl phosphorylcholine-co n-butyl methacrylate) for peritoneal dissemination of gastric cancer. Cancer Sci. 2009;100(10):1979-85. Epub 2009/07/17. doi: 10.1111/j.1349-7006.2009.01265.x. PubMed PMID: 19604244.
48. Kitayama J, Emoto S, Yamaguchi H, Ishigami H, Watanabe T. Intraperitoneal paclitaxel induces regression of peritoneal metastasis partly by destruction of peripheral microvessels. Cancer Chemother Pharmacol. 2014;73(3):605-12. Epub 2014/01/28. doi: 10.1007/s00280-014-2393-0. PubMed PMID: 24464356.
49. Tamura K, Kimura N, Ohzawa H, Miyato H, Sata N, Koyanagi T, et al. Optimizing Timing of Intraperitoneal Chemotherapy to Enhance Intravenous Carboplatin Concentration. Cancers (Basel). 2024;16(16). Epub 2024/08/31. doi: 10.3390/cancers16162841. PubMed PMID: 39199611; PubMed Central PMCID: PMCPMC11352839.
50. Ishigami H, Kitayama J, Kaisaki S, Hidemura A, Kato M, Otani K, et al. Phase II study of weekly intravenous and intraperitoneal paclitaxel combined with S-1 for advanced gastric cancer with peritoneal metastasis. Ann Oncol. 2010;21(1):67-70. Epub 2009/07/17. doi: 10.1093/annonc/mdp260. PubMed PMID: 19605503.
51. Yamaguchi H, Kitayama J, Ishigami H, Emoto S, Yamashita H, Watanabe T. A phase 2 trial of intravenous and intraperitoneal paclitaxel combined with S-1 for treatment of gastric cancer with macroscopic peritoneal metastasis. Cancer. 2013;119(18):3354-8. Epub 2013/06/26. doi: 10.1002/cncr.28204. PubMed PMID: 23798046.
52. Ishigami H, Fujiwara Y, Fukushima R, Nashimoto A, Yabusaki H, Imano M, et al. Phase III Trial Comparing Intraperitoneal and Intravenous Paclitaxel Plus S-1 Versus Cisplatin Plus S-1 in Patients With Gastric Cancer With Peritoneal Metastasis: PHOENIX-GC Trial. J Clin Oncol. 2018;36(19):1922-9. Epub 2018/05/11. doi: 10.1200/jco.2018.77.8613. PubMed PMID: 29746229.
53. Fujiwara Y, Ishigami H, Miwa H, Tanaka T, Kodera Y, Imamoto H, et al. Phase II study of intraperitoneal paclitaxel plus S-1/oxaliplatin for gastric cancer with peritoneal metastasis: SOX+IP PTX trial. Journal of Clinical Oncology. 2016;34(15(suppl)):Abst. 4040.
54. Saito S, Yamaguchi H, Ohzawa H, Miyato H, Kanamaru R, Kurashina K, et al. Intraperitoneal Administration of Paclitaxel Combined with S-1 Plus Oxaliplatin as Induction Therapy for Patients with Advanced Gastric Cancer with Peritoneal Metastases. Ann Surg Oncol. 2021;28(7):3863-70. Epub 2020/12/04. doi: 10.1245/s10434-020-09388-4. PubMed PMID: 33270170; PubMed Central PMCID: PMCPMC8184712.
55. Shi M, Yang Z, Lu S, Liu W, Ni Z, Yao X, et al. Oxaliplatin plus S-1 with intraperitoneal paclitaxel for the treatment of Chinese advanced gastric cancer with peritoneal metastases. BMC cancer. 2021;21(1):1344. Epub 2021/12/20. doi: 10.1186/s12885-021-09027-5. PubMed PMID: 34922478; PubMed Central PMCID: PMCPMC8684127.
56. Seo WJ, Kim DW, Lee CM, Park JY, Jang YJ, Park JM, et al. Intraperitoneal paclitaxel with systemic S-1 plus oxaliplatin for advanced or recurrent gastric cancer with peritoneal metastasis: A single-arm, multicenter phase II clinical trial. Eur J Surg Oncol. 2025;51(6):109603. Epub 2025/02/27. doi: 10.1016/j.ejso.2025.109603. PubMed PMID: 40009925.
57. Tu L, Zhang W, Ni L, Xu Z, Yang K, Gou H, et al. Study of SOX combined with intraperitoneal high-dose paclitaxel in gastric cancer with synchronous peritoneal metastasis: A phase II single-arm clinical trial. Cancer Med. 2023;12(4):4161-9. Epub 2022/09/27. doi: 10.1002/cam4.5277. PubMed PMID: 36161282; PubMed Central PMCID: PMCPMC9972103.

 doi:10.20944/preprints202606.0429.v1

58. Kang SH, Min SH, Kim JW, Lee E, Park SW, Lee S, et al. Safety and Efficacy of Intraperitoneal Paclitaxel Plus Intravenous Fluorouracil, Leucovorin, and Oxaliplatin (FOLFOX) for Gastric Cancer with Peritoneal Metastasis. Ann Surg Oncol. 2022;29(8):5084-91. Epub 2022/03/25. doi: 10.1245/s10434-022-11582-5. PubMed PMID: 35322307.
59. Zhao S, Su L, Chen Y, Li X, Lin P, Chen W, et al. Phase 2 randomized controlled trial of intravenous or intraperitoneal paclitaxel plus mFOLFOX6 vs. mFOLFOX6 as first-line treatment of advanced gastric cancer. Front Oncol. 2022;12:850242. Epub 2022/09/27. doi: 10.3389/fonc.2022.850242. PubMed PMID: 36158665; PubMed Central PMCID: PMCPMC9491235.
60. Chia DKA, Sundar R, Kim G, Ang JJ, Shabbir A, So JBY, et al. Outcomes of a Phase II Study of Intraperitoneal Paclitaxel Plus Systemic Capecitabine and Oxaliplatin (XELOX) for Gastric Cancer with Peritoneal Metastases. Ann Surg Oncol. 2023;30(3):1889-90. Epub 2022/12/24. doi: 10.1245/s10434-022-12877-3. PubMed PMID: 36564654.
61. Vatandoust S, Bright T, Roy AC, Abbas MN, Watson DI, Gan S, et al. Phase 1 trial of intraperitoneal paclitaxel in combination with intravenous cisplatin and oral capecitabine in patients with advanced gastric cancer and peritoneal metastases (IPGP study). Asia Pac J Clin Oncol. 2022;18(4):404-9. Epub 2021/11/24. doi: 10.1111/ajco.13659. PubMed PMID: 34811896.
62. Kobayashi D, Kodera Y, Fukushima R, Morita M, Fushida S, Yamashita N, et al. Phase II Study of Intraperitoneal Administration of Paclitaxel Combined with S-1 and Cisplatin for Gastric Cancer with Peritoneal Metastasis. Ann Surg Oncol. 2024;31(2):735-43. Epub 2023/11/12. doi: 10.1245/s10434-023-14240-6. PubMed PMID: 37952018.
63. Yan C, Yang Z, Shi Z, Lu S, Shi M, Nie M, et al. Intraperitoneal and Intravenous Paclitaxel Plus S-1 for Gastric Cancer With Peritoneal Metastasis: A Phase 3 Randomized Clinical Trial. JAMA Oncol. 2026. Epub 20260521. doi: 10.1001/jamaoncol.2026.1347. PubMed PMID: 42166134; PubMed Central PMCID: PMCPMC13195509.
64. Yang ZY, Yuan F, Lu S, Xu W, Wu JW, Xi WQ, et al. Efficacy and Safety of Conversion Therapy by Intraperitoneal and Intravenous Paclitaxel Plus Oral S-1 in Gastric Cancer Patients With Peritoneal Metastasis: A Prospective Phase II Study. Front Oncol. 2022;12:905922. Epub 2022/07/08. doi: 10.3389/fonc.2022.905922. PubMed PMID: 35795055; PubMed Central PMCID: PMCPMC9251062.
65. Emoto S, Ishigami H, Hidemura A, Yamaguchi H, Yamashita H, Kitayama J, et al. Complications and management of an implanted intraperitoneal access port system for intraperitoneal chemotherapy for gastric cancer with peritoneal metastasis. Jpn J Clin Oncol. 2012;42(11):1013-9. Epub 2012/08/09. doi: 10.1093/jjco/hys129. PubMed PMID: 22872745.
66. Aizawa M, Ishigami H, Yabusaki H, Nashimoto A, Imamoto H, Imano M, et al. Phase II study of intraperitoneal paclitaxel plus S-1/paclitaxel for gastric cancer with positive peritoneal cytology: CY-PHOENIX trial. Journal of Clinical Oncology. 2017;35(4(Suppl)):96(Abst).
67. Kitayama J, Ishigami H, Yamaguchi H, Emoto S, Watanabe T. Intraperitoneal Paclitaxel is useful as adjuvant chemotherapy for advanced gastric cancer with serosal exposure. Case Rep Oncol. 2014;7(1):58-64. Epub 2014/02/28. doi: 10.1159/000358379. PubMed PMID: 24575018; PubMed Central PMCID: PMCPMC3934609.
68. Yamaguchi H, Kitayama J, Emoto S, Ishigami H, Ito T, Hanafusa N, et al. Cell-free and concentrated ascites reinfusion therapy (CART) for management of massive malignant ascites in gastric cancer patients with peritoneal metastasis treated with intravenous and intraperitoneal paclitaxel with oral S-1. Eur J Surg Oncol. 2015;41(7):875-80. doi: 10.1016/j.ejso.2015.04.013. PubMed PMID: 25986856.
69. Senthil M, Dayyani F. Phase II clinical trial of sequential treatment with systemic chemotherapy and intraperitoneal paclitaxel for gastric and gastroesophageal junction peritoneal carcinomatosis - STOPGAP trial. BMC cancer. 2023;23(1):209. Epub 2023/03/05. doi: 10.1186/s12885-023-10680-1. PubMed PMID: 36870941; PubMed Central PMCID: PMCPMC9985848.
70. Mizrahi JD, Surana R, Valle JW, Shroff RT. Pancreatic cancer. Lancet. 2020;395(10242):2008-20. doi: 10.1016/S0140-6736(20)30974-0. PubMed PMID: 32593337.

 doi:10.20944/preprints202606.0429.v1

71. Mackay TM, van Erning FN, van der Geest LGM, de Groot JWB, Haj Mohammad N, Lemmens VE, et al. Association between primary origin (head, body and tail) of metastasised pancreatic ductal adenocarcinoma and oncologic outcome: A population-based analysis. Eur J Cancer. 2019;106:99-105. Epub 20181123. doi: 10.1016/j.ejca.2018.10.008. PubMed PMID: 30476732.
72. Boileve A, Mercier L, Bonnet B, Tarabay A, Blanchet-Deverly S, Hollebecque A, et al. Lung-only metastatic pancreatic cancer: Differences in patients 'characteristics, molecular profile and survival. Eur J Cancer. 2026;235:116227. Epub 20260109. doi: 10.1016/j.ejca.2026.116227. PubMed PMID: 41547177.
73. Satoi S, Fujii T, Yanagimoto H, Motoi F, Kurata M, Takahara N, et al. Multicenter Phase II Study of Intravenous and Intraperitoneal Paclitaxel With S-1 for Pancreatic Ductal Adenocarcinoma Patients With Peritoneal Metastasis. Ann Surg. 2017;265(2):397-401. Epub 2017/01/07. doi: 10.1097/SLA.0000000000001705. PubMed PMID: 28059968.
74. Yamada S, Fujii T, Yamamoto T, Takami H, Yoshioka I, Yamaki S, et al. Phase I/II study of adding intraperitoneal paclitaxel in patients with pancreatic cancer and peritoneal metastasis. Br J Surg. 2020;107(13):1811-7. Epub 2020/07/09. doi: 10.1002/bjs.11792. PubMed PMID: 32638367; PubMed Central PMCID: PMCPMC7689756.
75. Yamamoto T, Fujii T, Hirano S, Motoi F, Honda G, Uemura K, et al. Randomized phase III trial of intravenous and intraperitoneal paclitaxel with S-1 versus gemcitabine plus nab-paclitaxel for pancreatic ductal adenocarcinoma with peritoneal metastasis (SP study). Trials. 2022;23(1):119. Epub 2022/02/07. doi: 10.1186/s13063-022-06049-7. PubMed PMID: 35123553; PubMed Central PMCID: PMCPMC8817533.
76. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-63. Epub 2024/04/04. doi: 10.3322/caac.21834. PubMed PMID: 38572751.
77. Lemmens VE, Klaver YL, Verwaal VJ, Rutten HJ, Coebergh JW, de Hingh IH. Predictors and survival of synchronous peritoneal carcinomatosis of colorectal origin: a population-based study. Int J Cancer. 2011;128(11):2717-25. Epub 20101013. doi: 10.1002/ijc.25596. PubMed PMID: 20715167.
78. Segelman J, Granath F, Holm T, Machado M, Mahteme H, Martling A. Incidence, prevalence and risk factors for peritoneal carcinomatosis from colorectal cancer. Br J Surg. 2012;99(5):699-705. Epub 20120127. doi: 10.1002/bjs.8679. PubMed PMID: 22287157.
79. Jayne DG, Fook S, Loi C, Seow-Choen F. Peritoneal carcinomatosis from colorectal cancer. Br J Surg. 2002;89(12):1545-50. doi: 10.1046/j.1365-2168.2002.02274.x. PubMed PMID: 12445064.
80. Franko J, Shi Q, Meyers JP, Maughan TS, Adams RA, Seymour MT, et al. Prognosis of patients with peritoneal metastatic colorectal cancer given systemic therapy: an analysis of individual patient data from prospective randomised trials from the Analysis and Research in Cancers of the Digestive System (ARCAD) database. Lancet Oncol. 2016;17(12):1709-19. Epub 20161012. doi: 10.1016/S1470-2045(16)30500-9. PubMed PMID: 27743922.
81. Verwaal VJ, van Ruth S, de Bree E, van Sloothen GW, van Tinteren H, Boot H, et al. Randomized trial of cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy and palliative surgery in patients with peritoneal carcinomatosis of colorectal cancer. J Clin Oncol. 2003;21(20):3737-43. doi: 10.1200/JCO.2003.04.187. PubMed PMID: 14551293.
82. Elias D, Lefevre JH, Chevalier J, Brouquet A, Marchal F, Classe JM, et al. Complete cytoreductive surgery plus intraperitoneal chemohyperthermia with oxaliplatin for peritoneal carcinomatosis of colorectal origin. J Clin Oncol. 2009;27(5):681-5. doi: 10.1200/JCO.2008.19.7160. PubMed PMID: 19103728.
83. Cashin PH, Graf W, Nygren P, Mahteme H. Cytoreductive surgery and intraperitoneal chemotherapy for colorectal peritoneal carcinomatosis: prognosis and treatment of recurrences in a cohort study. Eur J Surg Oncol. 2012;38(6):509-15. doi: 10.1016/j.ejso.2012.03.001. PubMed PMID: 22475555.
84. Goere D, Malka D, Tzanis D, Gava V, Boige V, Eveno C, et al. Is there a possibility of a cure in patients with colorectal peritoneal carcinomatosis amenable to complete cytoreductive surgery and intraperitoneal chemotherapy? Ann Surg. 2013;257(6):1065-71. doi: 10.1097/SLA.0b013e31827e9289. PubMed PMID: 23299520.

 doi:10.20944/preprints202606.0429.v1

85. Lurvink RJ, Rauwerdink P, Rovers KP, Wassenaar ECE, Deenen MJ, Nederend J, et al. First-line palliative systemic therapy alternated with electrostatic pressurised intraperitoneal aerosol chemotherapy (oxaliplatin) for isolated unresectable colorectal peritoneal metastases: protocol of a multicentre, single-arm, phase II study (CRC-PIPAC-II). BMJ Open. 2021;11(3):e044811. Epub 20210330. doi: 10.1136/bmjopen-2020-044811. PubMed PMID: 33785492; PubMed Central PMCID: PMCPMC8011718.
86. Sleiman MJ, Jelip A, Buchs N, Toso C, Liot E, Koessler T, et al. Pressurized Intraperitoneal Aerosol Chemotherapy for Peritoneal Carcinomatosis in Colorectal Cancer Patients: A Systematic Review of the Evidence. Cancers (Basel). 2024;16(21). Epub 20241030. doi: 10.3390/cancers16213661. PubMed PMID: 39518099; PubMed Central PMCID: PMCPMC11544814.
87. Murono K, Nagata H, Ishimaru K, Emoto S, Kaneko M, Hiyoshi M, et al. Safety of intraperitoneal paclitaxel combined with conventional chemotherapy for colorectal cancer with peritoneal carcinomatosis: a phase I trial. Cancer Chemother Pharmacol. 2019;83(1):145-50. Epub 20181101. doi: 10.1007/s00280-018-3714-5. PubMed PMID: 30386886.
88. Murono K, Yokoyama Y, Nozawa H, Sasaki K, Emoto S, Matsuzaki H, et al. Intraperitoneal paclitaxel combined with FOLFOX/CAPOX plus bevacizumab for colorectal cancer with peritoneal carcinomatosis (the iPac-02 trial): study protocol of a single arm, multicenter, phase 2 study. Int J Colorectal Dis. 2023;38(1):173. Epub 20230620. doi: 10.1007/s00384-023-04434-5. PubMed PMID: 37340243; PubMed Central PMCID: PMCPMC10282041.
89. Kang SH, Kim JW, Lee E, Yoo M, Jeon D, Park W, et al. Intraperitoneal paclitaxel plus intravenous fluorouracil, leucovorin, oxaliplatin (FOLFOX) and nivolumab for gastric cancer with peritoneal metastasis: results from the IPLUS Phase II study. Gastric Cancer. 2026. Epub 2026/04/20. doi: 10.1007/s10120-026-01741-y. PubMed PMID: 42001371.
90. Shitara K, Lordick F, Bang YJ, Enzinger P, Ilson D, Shah MA, et al. Zolbetuximab plus mFOLFOX6 in patients with CLDN18.2-positive, HER2-negative, untreated, locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma (SPOTLIGHT): a multicentre, randomised, double-blind, phase 3 trial. Lancet. 2023;401(10389):1655-68. Epub 20230415. doi: 10.1016/S0140-6736(23)00620-7. PubMed PMID: 37068504.
91. Shah MA, Shitara K, Ajani JA, Bang YJ, Enzinger P, Ilson D, et al. Zolbetuximab plus CAPOX in CLDN18.2-positive gastric or gastroesophageal junction adenocarcinoma: the randomized, phase 3 GLOW trial. Nat Med. 2023;29(8):2133-41. Epub 20230731. doi: 10.1038/s41591-023-02465-7. PubMed PMID: 37524953; PubMed Central PMCID: PMCPMC10427418.
92. Zhong F, Ren Z, Li W, Jones T, Zeng X, Wang S, et al. The sensitivity and specificity of Claudin18.2 and MUC6 in the differential diagnosis of endocervical gastric-type glandular lesions. Hum Pathol. 2025;160:105837. Epub 20250607. doi: 10.1016/j.humpath.2025.105837. PubMed PMID: 40490055.
93. Luchini C, Matkowskyj KA, Kuwata T, Longacre TA, Schirmacher P, Takamatsu M, et al. Claudin-18.2 immunohistochemical evaluation in pancreatic cancer specimens: review and recommendations for routine testing and scoring. Virchows Arch. 2025;487(3):487-99. Epub 20250821. doi: 10.1007/s00428-025-04222-2. PubMed PMID: 40835751; PubMed Central PMCID: PMCPMC12488767.
94. Gallanis AF, Perati SR, Canady SN, Epstein M, Moore N, Satterwhite AA, et al. Efficacy of Bidirectional Paclitaxel plus Capecitabine or Nilotinib for Peritoneal Carcinomatosis: A Single Institution Analysis of Two Phase II Clinical Trials. Ann Surg Oncol. 2026;33(5):4679-89. Epub 2026/01/17. doi: 10.1245/s10434-025-18967-2. PubMed PMID: 41545610; PubMed Central PMCID: PMCPMC13083422.
95. Nowacki M, Peterson M, Kloskowski T, McCabe E, Guiral DC, Polom K, et al. Nanoparticle as a novel tool in hyperthermic intraperitoneal and pressurized intraperitoneal aerosol chemotheprapy to treat patients with peritoneal carcinomatosis. Oncotarget. 2017;8(44):78208-24. Epub 2017/11/05. doi: 10.18632/oncotarget.20596. PubMed PMID: 29100461; PubMed Central PMCID: PMCPMC5652850.
96. Li C, Newman RA, Wu QP, Ke S, Chen W, Hutto T, et al. Biodistribution of paclitaxel and poly(L-glutamic acid)-paclitaxel conjugate in mice with ovarian OCa-1 tumor. Cancer Chemother Pharmacol. 2000;46(5):416-22. Epub 2000/12/29. doi: 10.1007/s002800000168. PubMed PMID: 11127947.

 doi:10.20944/preprints202606.0429.v1

97. Yamada J, Kitayama J, Tsuno NH, Yamashita H, Miyato H, Soma D, et al. Intra-peritoneal administration of paclitaxel with non-animal stabilized hyaluronic acid as a vehicle--a new strategy against peritoneal dissemination of gastric cancer. Cancer Lett. 2008;272(2):307-15. Epub 2008/09/05. doi: 10.1016/j.canlet.2008.07.024. PubMed PMID: 18768251.
98. Bajaj G, Kim MR, Mohammed SI, Yeo Y. Hyaluronic acid-based hydrogel for regional delivery of paclitaxel to intraperitoneal tumors. J Control Release. 2012;158(3):386-92. doi: 10.1016/j.jconrel.2011.12.001. PubMed PMID: 22178261; PubMed Central PMCID: PMC3319161.
99. Emoto S, Yamaguchi H, Kishikawa J, Yamashita H, Ishigami H, Kitayama J. Antitumor effect and pharmacokinetics of intraperitoneal NK105, a nanomicellar paclitaxel formulation for peritoneal dissemination. Cancer Sci. 2012;103(7):1304-10. Epub 2012/03/21. doi: 10.1111/j.1349-7006.2012.02274.x. PubMed PMID: 22429777; PubMed Central PMCID: PMCPMC7659395.
100. Simon-Gracia L, Hunt H, Scodeller P, Gaitzsch J, Kotamraju VR, Sugahara KN, et al. iRGD peptide conjugation potentiates intraperitoneal tumor delivery of paclitaxel with polymersomes. Biomaterials. 2016;104:247-57. Epub 2016/07/30. doi: 10.1016/j.biomaterials.2016.07.023. PubMed PMID: 27472162; PubMed Central PMCID: PMCPMC5687559.
101. Simon-Gracia L, Hunt H, Scodeller PD, Gaitzsch J, Braun GB, Willmore AM, et al. Paclitaxel-Loaded Polymersomes for Enhanced Intraperitoneal Chemotherapy. Mol Cancer Ther. 2016;15(4):670-9. doi: 10.1158/1535-7163.MCT-15-0713-T. PubMed PMID: 26880267; PubMed Central PMCID: PMCPMC4873343.
102. Liu M, Silva-Sanchez A, Randall TD, Meza-Perez S. Specialized immune responses in the peritoneal cavity and omentum. J Leukoc Biol. 2021;109(4):717-29. Epub 20200902. doi: 10.1002/JLB.5MIR0720-271RR. PubMed PMID: 32881077; PubMed Central PMCID: PMCPMC7921210.
103. Takahashi K, Kurashina K, Yamaguchi H, Kanamaru R, Ohzawa H, Miyato H, et al. Altered intraperitoneal immune microenvironment in patients with peritoneal metastases from gastric cancer. Front Immunol. 2022;13:969468. Epub 2022/09/20. doi: 10.3389/fimmu.2022.969468. PubMed PMID: 36119051; PubMed Central PMCID: PMCPMC9478385.
104. Matsumiya M, Sonoda H, Yamashita H, Kurashina K, Takahashi K, Ohzawa H, et al. Intraperitoneal Paclitaxel-Induced Eosinophil Recruitment as a Potential Mediator of Tumor Response in Peritoneal Metastases from Gastric Cancer. Ann Surg Oncol. 2026. Epub 2026/01/29. doi: 10.1245/s10434-025-19075-x. PubMed PMID: 41609927.
105. Galluzzi L, Buque A, Kepp O, Zitvogel L, Kroemer G. Immunogenic cell death in cancer and infectious disease. Nat Rev Immunol. 2017;17(2):97-111. Epub 2016/11/01. doi: 10.1038/nri.2016.107. PubMed PMID: 27748397.