Protocol

Cytoreductive Surgery and Perioperative Intraperitoneal Chemotherapy for Select Intra-Abdominal and Pelvic Malignancies

(20307)

Medical Benefit		**Effective Date**: 07/01/15	**Next Review Date**: 03/18
Preauthorization	Yes	**Review Dates**: 01/11, 01/12, 01/13, 01/14, 01/15, 03/15, 03/16, 03/17	

Preauthorization is required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With pseudomyxoma peritonei	Interventions of interest are: • Cytoreductive surgery and perioperative intraperitoneal chemotherapy	Comparators of interest are: • Cytoreductive surgery	Relevant outcomes include: • Overall survival • Change in disease status • Quality of life • Treatment-related morbidity
Individuals: • With peritoneal carcinomatosis of colorectal origin	Interventions of interest are: • Cytoreductive surgery and perioperative intraperitoneal chemotherapy	Comparators of interest are: • Cytoreductive surgery • Systemic chemotherapy	Relevant outcomes include: • Overall survival • Change in disease status • Quality of life • Treatment-related morbidity
Individuals: • With peritoneal carcinomatosis of gastric origin	Interventions of interest are: • Cytoreductive surgery and perioperative intraperitoneal chemotherapy	Comparators of interest are: • Cytoreductive surgery • Systemic chemotherapy	Relevant outcomes include: • Overall survival • Change in disease status • Quality of life • Treatment-related morbidity
Individuals: • With peritoneal carcinomatosis of endometrial origin	Interventions of interest are: • Cytoreductive surgery and perioperative intraperitoneal chemotherapy	Comparators of interest are: • Cytoreductive surgery • Systemic chemotherapy	Relevant outcomes include: • Overall survival • Change in disease status • Quality of life • Treatment-related morbidity
Individuals: • With peritoneal mesothelioma	Interventions of interest are: • Cytoreductive surgery and perioperative intraperitoneal chemotherapy	Comparators of interest are: • Cytoreductive surgery • Systemic chemotherapy • Radiotherapy	Relevant outcomes include: • Overall survival • Change in disease status • Quality of life • Treatment-related morbidity
Individuals: • With ovarian cancer	Interventions of interest are: • Cytoreductive surgery and perioperative intraperitoneal chemotherapy	Comparators of interest are: • Cytoreductive surgery • Systemic chemotherapy	Relevant outcomes include: • Overall survival • Change in disease status • Quality of life • Treatment-related morbidity

Populations	Interventions	Comparators	Outcomes
Individuals: • With appendiceal goblet cell tumors	Interventions of interest are: • Cytoreductive surgery and perioperative intraperitoneal chemotherapy	Comparators of interest are: • Cytoreductive surgery • Systemic chemotherapy	Relevant outcomes include: • Overall survival • Change in disease status • Quality of life • Treatment-related morbidity

Description

Cytoreductive surgery (CRS) comprises peritonectomy (i.e., peritoneal stripping) procedures and multivisceral resections, depending on the extent of intra-abdominal tumor dissemination. The surgical procedure may be followed intraoperatively by infusion of hyperthermic chemotherapy, referred to as hyperthermic intraperitoneal chemotherapy (HIPEC). CRS and HIPEC have been proposed for a number of intra-abdominal and pelvic malignancies such as pseudomyxoma peritonei and peritoneal carcinomatosis from colorectal, gastric, or endometrial cancer.

Summary of Evidence

For individuals who have pseudomyxoma peritonei who receive cytoreductive surgery and perioperative intraperitoneal chemotherapy, the evidence includes cohort studies and a systematic review. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related morbidity. Uncontrolled studies of primary treatment of pseudomyxoma peritonei with CRS and HIPEC have reported median and five-year overall survival ranging from 47 to 156 months and 41% to 96%, respectively. One retrospective study of 26 patients who underwent CRS and HIPEC for recurrence indicated five year overall survival of 34%. Procedure-related morbidity and mortality have generally decreased over time. Controlled studies are needed to draw conclusions about the efficacy and safety of CRS and HIPEC compared with standard treatment (CRS alone). The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have peritoneal carcinomatosis of colorectal origin who receive cytoreductive surgery and perioperative intraperitoneal chemotherapy, the evidence includes one randomized controlled trial (RCT), a systematic review, and observational studies. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related morbidity. The RCT found significantly higher median overall survival in the CRS and HIPEC group than in the standard care group. However, the RCT had methodologic limitations including an inability to differentiate between benefits of CRS and HIPEC. Additional controlled trials reporting quality of life as well as survival outcomes are needed to evaluate the impact on the net health outcome. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have peritoneal carcinomatosis of gastric origin who receive cytoreductive surgery and perioperative intraperitoneal chemotherapy, the evidence includes two small RCTs and two small retrospective comparative studies. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related morbidity. The evidence is insufficient to determine the effects of the technology on health outcomes. Given that patients eligible for CRS and HIPEC must be surgical candidates, the most appropriate comparator would be gastric resection with or without systemic chemotherapy administered to both treatment groups in a comparative study. The only RCT that used this design reported reduced survival in the CRS and HIPEC group, although the trial was small (N=26) and statistical testing was not reported. Additional trials are needed using the appropriate comparator and with appropriate sample sizes and statistical analysis reporting. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have peritoneal carcinomatosis of endometrial origin who receive cytoreductive surgery and perioperative intraperitoneal chemotherapy, the evidence includes cohort studies. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related morbidity. Only uncontrolled studies were available and they had small sample sizes (< 25 patients). Randomized trials that compare CRS plus HIPEC to standard treatment (e.g., CRS alone or systemic chemotherapy alone). The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have peritoneal mesothelioma who receive cytoreductive surgery and perioperative intraperitoneal chemotherapy, the evidence includes retrospective cohort studies and systematic reviews. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related morbidity. Uncontrolled studies have shown median and five-year overall survival ranging from 30 to 92 months and 33% to 68%, respectively, for patients with peritoneal mesothelioma who are treated with CRS and HIPEC. Reported procedure-related morbidity and mortality were approximately 35% and 5%, respectively. Controlled studies are needed to draw conclusions about the efficacy and safety of CRS and HIPEC compared with standard treatment (CRS alone). The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have ovarian cancer who receive cytoreductive surgery and perioperative intraperitoneal chemotherapy, the evidence includes one RCT, systematic reviews, and uncontrolled studies. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related morbidity. Results from one RCT with methodologic flaws, case-control studies, and cohort studies are inconsistent; the RCT and case-control studies showed improved survival with CRS plus HIPEC in the second-line setting compared with CRS without HIPEC, but retrospective cohort studies have not shown a clear survival advantage compared with current treatment in the first- or the second-line setting. Results of at least some of these studies were confounded by prognostic factors (completeness of cytoreduction, extent of peritoneal carcinomatosis, chemosensitivity to platinum). Well-designed, RCTs are needed to control for potential covariates and to demonstrate improvements in net health outcomes compared with current treatment approaches (i.e., CRS with systemic chemotherapy). The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy

Cytoreductive surgery and perioperative intraperitoneal chemotherapy may be considered **medically necessary** for the treatment of**:**

- pseudomyxoma peritonei; and
- diffuse malignant peritoneal mesothelioma.

Cytoreductive surgery and perioperative intraperitoneal chemotherapy is considered **investigational** for:

- peritoneal carcinomatosis from colorectal cancer, gastric cancer, or endometrial cancer
- ovarian cancer; and
- all other indications, including goblet cell tumors of the appendix.

Background

Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy

CRS comprises peritonectomy (i.e., peritoneal stripping) procedures and multivisceral resections, depending on the extent of intra-abdominal tumor dissemination.[1] The surgical procedure may be followed intraoperatively by the infusion of hyperthermic chemotherapy, most commonly mitomycin C. Inflow and outflow catheters are

placed in the abdominal cavity, along with temperature probes to monitor temperature. The skin is then temporarily closed during the chemotherapy perfusion, which typically runs for one to two hours. This procedure is referred to as HIPEC.

Pseudomyxoma Peritonei

Pseudomyxoma peritonei is a clinicopathologic entity characterized by the production of mucinous ascites and mostly originates from epithelial neoplasms of the appendix. Appendix cancer is diagnosed in fewer than 1000 Americans each year; less than half are epithelial neoplasms.[2] As mucin-producing cells of the tumor proliferate, the narrow lumen of the appendix becomes obstructed and subsequently leads to appendiceal perforation. Neoplastic cells progressively colonize the peritoneal cavity and produce copious mucin, which collects in the peritoneal cavity. Pseudomyxoma peritonei ranges from benign (disseminated peritoneal adenomucinosis) to malignant (peritoneal mucinous carcinomatosis), with some intermediate pathologic grades. Clinically, this syndrome ranges from early pseudomyxoma peritonei, fortuitously discovered on imaging or during a laparotomy performed for another reason, to advanced cases with a distended abdomen, bowel obstruction, and starvation. The conventional treatment of pseudomyxoma peritonei is surgical debulking repeated as necessary to alleviate pressure effects. However, repeated debulking surgeries become ever more difficult due to progressively thickened intra-abdominal adhesions, and this treatment is palliative, leaving visible or occult disease in the peritoneal cavity.[3] Five-year overall survival (OS) depends on tumor histology and ranges from 6% for high-grade tumors to 75% for low-grade tumors.[4, 5]

Gastrointestinal Cancers (Colorectal, Gastric) and Peritoneal Carcinomatosis

Peritoneal dissemination develops in approximately 10% to 15% of patients with colon cancer and, despite the use of increasingly effective regimens of chemotherapy and biologic agents in the treatment of advanced disease, peritoneal metastases are associated with a median survival of six to seven months.

Peritoneal carcinomatosis is detected in more than 30% of patients with advanced gastric cancer and is a poor prognostic indicator. Median survival is three months, and five-year survival is less than 1%.[6] Sixty percent of deaths from gastric cancer are attributed to peritoneal carcinomatosis.[7] Current chemotherapy regimens are nonstandard, and peritoneal seeding is considered unresectable for cure.[8]

Peritoneal Mesothelioma

Malignant mesothelioma is a relatively uncommon malignancy that may arise from the mesothelial cells lining the pleura, peritoneum, pericardium, and tunica vaginalis testis. In the United States, 200 to 400 new cases of diffuse malignant peritoneal mesothelioma (DMPM) are registered every year, accounting for 10% to 30% of all-type mesothelioma.[9] DMPM has traditionally been considered as a rapidly lethal malignancy with limited and ineffective therapeutic options.[9] The disease is usually diagnosed at an advanced stage and is characterized by multiple variably sized nodules throughout the abdominal cavity. As the disease progresses, the nodules become confluent to form plaques, masses, or uniformly cover peritoneal surfaces. In most patients, death eventually results from locoregional progression within the abdominal cavity. In historical case series, treatment by palliative surgery, systemic or intraperitoneal chemotherapy, and abdominal irradiation resulted in a median survival of approximately 12 months.[9]

Surgical cytoreduction (resection of visible disease) in conjunction with HIPEC is designed to remove visible tumor deposits and residual microscopic disease. By delivering chemotherapy intraperitoneally, drug exposure to the peritoneal surface is increased some 20-fold compared with systemic exposure. In addition, previous animal and in vitro studies have suggested that the cytotoxicity of mitomycin C is enhanced at temperatures greater than 39° C (102.2° F).

Ovarian Cancer

Several different types of malignancies can arise in the ovary; epithelial carcinoma is the most common type, accounting for 90% of malignant ovarian tumors. Epithelial ovarian cancer is the fifth most common cause of cancer death in women in the United States. New cases and deaths from ovarian cancer in 2014 were estimated at 21,980 and 14,270, respectively.[10] Most ovarian cancer patients (> 70%) present with widespread disease, and annual mortality is approximately 65% of the incidence rate.

Current management of advanced epithelial ovarian cancer is CRS followed by combination chemotherapy. Treatment guidelines recommend intraperitoneal chemotherapy for patients with optimally debulked (< 1 cm) stage 2 disease (pelvic extension of tumor) or stage 3 disease (peritoneal extension of tumor).[11] Estimated median OS is 66 months with and 37 to 49 months without intraperitoneal chemotherapy, respectively.[12, 13] However, tumor recurrences are common, and prognosis for recurrent disease is poor.

CRS plus HIPEC in combination with systemic chemotherapy is being studied for primary and recurrent disease. Because HIPEC is administered at the time of surgery, treatment-related morbidity may be reduced compared with intraperitoneal chemotherapy administered postoperatively.

Regulatory Status

Mitomycin, carboplatin, and other drugs used for hyperthermic intraperitoneal chemotherapy (HIPEC) have not been approved by the U.S. Food and Drug Administration (FDA) for this indication. Cyclophosphamide and nitrogen mustard are FDA-approved for intraperitoneal administration, but neither drug is used regularly for this purpose.[14]

Several peritoneal lavage systems (Product Code LGZ) have been cleared for marketing by FDA through the 510(k) process to provide "warmed, physiologically compatible sterile solution" (e.g., Performer® HT perfusion system; RanD Srl, Medolla, Italy[15]). None has received marketing approval or clearance to administer chemotherapy. FDA has issued warning letters to manufacturers of devices that are FDA-cleared for peritoneal lavage using sterile saline solutions when these devices are marketed for off-label use in HIPEC (e.g., ThermaSolutions, Minneapolis, MN[16]; Belmont Instrument, Billerica, MA[17]).

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

1. Glockzin G, Ghali N, Lang SA, et al. Results of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal carcinomatosis from colorectal cancer. J Surg Oncol. Sep 15 2009; 100(4):306-310. PMID 19697436
2. Maggiori L, Elias D. Curative treatment of colorectal peritoneal carcinomatosis: current status and future trends. Eur J Surg Oncol. Jul 2010; 36(7):599-603. PMID 20605396
3. Elias D, Honore C, Ciuchendea R, et al. Peritoneal pseudomyxoma: results of a systematic policy of complete cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. Br J Surg. Sep 2008; 95(9):1164-1171. PMID 18690633
4. Chua TC, Moran BJ, Sugarbaker PH, et al. Early- and long-term outcome data of patients with pseudomyxoma peritonei from appendiceal origin treated by a strategy of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. J Clin Oncol. Jul 10 2012; 30(20):2449-2456. PMID 22614976
5. Nakakura EK. Pseudomyxoma peritonei: more questions than answers. J Clin Oncol. Jul 10 2012; 30(20):2429-2430. PMID 22614983
6. Yonemura Y, Kawamura T, Bandou E, et al. Advances in the management of gastric cancer with peritoneal dissemination. Recent Results Cancer Res. 2007; 169:157-164. PMID 17506258
7. Yonemura Y, Endou Y, Shinbo M, et al. Safety and efficacy of bidirectional chemotherapy for treatment of patients with peritoneal dissemination from gastric cancer: Selection for cytoreductive surgery. J Surg Oncol. Sep 15 2009; 100(4):311-316. PMID 19697437
8. Delotte J, Desantis M, Frigenza M, et al. Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy for the treatment of endometrial cancer with peritoneal carcinomatosis. Eur J Obstet Gynecol Reprod Biol. Jan 2014; 172:111-114. PMID 24300558
9. Baratti D, Kusamura S, Deraco M. Diffuse malignant peritoneal mesothelioma: systematic review of clinical management and biological research. J Surg Oncol. Jun 2011; 103(8):822-831. PMID 21283990
10. MD Anderson Cancer Center. Appendix cancer: basics. 2015. http://www.mdanderson.org/patient-and-cancer-information/cancer-information/cancer-types/appendix-cancer/index.html. Accessed June 24, 2016.
11. Abu-Zaid A, Azzam AZ, Alomar O, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for managing peritoneal carcinomatosis from endometrial carcinoma: a single-center experience of 6 cases. Ann Saudi Med. Mar-Apr 2014; 34(2):159-166. PMID 24894786
12. Armstrong DK, Bundy B, Wenzel L, et al. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. N Engl J Med. Jan 5 2006; 354(1):34-43. PMID 16394300
13. Cannistra SA. Intraperitoneal chemotherapy comes of age. N Engl J Med. Jan 5 2006; 354(1):77-79. PMID 16394306
14. Yan TD, Cao CQ, Munkholm-Larsen S. A pharmacological review on intraperitoneal chemotherapy for peritoneal malignancy. World J Gastrointest Oncol. Feb 15 2010; 2(2):109-116. PMID 21160929
15. U.S. Food and Drug Administration. Devices@FDA. RanD S.R.L. Performer HT/Hang & Go HT Basic. 510(k) number K120026. 05/08/2012. http://www.accessdata.fda.gov/scripts/cdrh/devicesatfda/index.cfm?db=pmn&id=K120026. Accessed June 24, 2016.
16. U.S. Food and Drug Administration (FDA). Warning letter: Therma Solutions, Inc., 05/07/2012. http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2012/ucm307258.htm. Accessed June 24, 2016.
17. U.S. Food and Drug Administration (FDA). Warning letter: Belmont Instrument Corporation, 05/07/2012. http://www.fda.gov/iceci/enforcementactions/warningletters/2012/ucm306771.htm. Accessed June 24, 2016.
18. Jimenez W, Sardi A, Nieroda C, et al. Predictive and prognostic survival factors in peritoneal carcinomatosis from appendiceal cancer after cytoreductive surgery with hyperthermic intraperitoneal chemotherapy. Ann Surg Oncol. Dec 2014; 21(13):4218-4225. PMID 24986239

19. Marcotte E, Dube P, Drolet P, et al. Hyperthermic intraperitoneal chemotherapy with oxaliplatin as treatment for peritoneal carcinomatosis arising from the appendix and pseudomyxoma peritonei: a survival analysis. World J Surg Oncol. 2014; 12:332. PMID 25380618
20. Glehen O, Gilly FN, Boutitie F, et al. Toward curative treatment of peritoneal carcinomatosis from nonovarian origin by cytoreductive surgery combined with perioperative intraperitoneal chemotherapy: a multi-institutional study of 1,290 patients. Cancer. Dec 15 2010; 116(24):5608-5618. PMID 20737573
21. Chua TC, Yan TD, Smigielski ME, et al. Long-term survival in patients with pseudomyxoma peritonei treated with cytoreductive surgery and perioperative intraperitoneal chemotherapy: 10 years of experience from a single institution. Ann Surg Oncol. Jul 2009; 16(7):1903-1911. PMID 19387742
22. Vaira M, Cioppa T, G DEM, et al. Management of pseudomyxoma peritonei by cytoreduction+HIPEC (hyperthermic intraperitoneal chemotherapy): results analysis of a twelve-year experience. In Vivo. Jul-Aug 2009; 23(4):639-644. PMID 19567401
23. Yan TD, Black D, Savady R, et al. A systematic review on the efficacy of cytoreductive surgery and perioperative intraperitoneal chemotherapy for pseudomyxoma peritonei. Ann Surg Oncol. Feb 2007; 14(2):484-492. PMID 17054002
24. Sardi A, Jimenez WA, Nieroda C, et al. Repeated cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in peritoneal carcinomatosis from appendiceal cancer: analysis of survival outcomes. Eur J Surg Oncol. Nov 2013; 39(11):1207-1213. PMID 24007834
25. Elias D, Gilly F, Quenet F, et al. Pseudomyxoma peritonei: a French multicentric study of 301 patients treated with cytoreductive surgery and intraperitoneal chemotherapy. Eur J Surg Oncol. 2010; 36(5):456-462. PMID
26. Lord AC, Shihab O, Chandrakumaran K, et al. Recurrence and outcome after complete tumour removal and hyperthermic intraperitoneal chemotherapy in 512 patients with pseudomyxoma peritonei from perforated appendiceal mucinous tumours. Eur J Surg Oncol. Mar 2015; 41(3):396-399. PMID 25216980
27. Elias D, Mariani A, Cloutier AS, et al. Modified selection criteria for complete cytoreductive surgery plus HIPEC based on peritoneal cancer index and small bowel involvement for peritoneal carcinomatosis of colorectal origin. Eur J Surg Oncol. Nov 2014; 40(11):1467-1473. PMID 25086990
28. Nikolic S, Dzodic R, Zegarac M, et al. Survival prognostic factors in patients with colorectal peritoneal carcinomatosis treated with cytoreductive surgery and intraoperative hyperthermic intraperitoneal chemotherapy: a single institution experience. J BUON. Jan-Mar 2014; 19(1):66-74. PMID 24659645
29. Tabrizian P, Shrager B, Jibara G, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal carcinomatosis: outcomes from a single tertiary institution. J Gastrointest Surg. May 2014; 18(5):1024-1031. PMID 24577736
30. Vallicelli C, Cavaliere D, Catena F, et al. Management of peritoneal carcinomatosis from colorectal cancer: review of the literature. Int J Colorectal Dis. Aug 2014; 29(8):895-898. PMID 24915844
31. Levine EA, Stewart JHt, Shen P, et al. Intraperitoneal chemotherapy for peritoneal surface malignancy: experience with 1,000 patients. J Am Coll Surg. Apr 2014; 218(4):573-585. PMID 24491244
32. Teo MC, Tan GH, Tham CK, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in Asian patients: 100 consecutive patients in a single institution. Ann Surg Oncol. Sep 2013; 20(9):2968-2974. PMID 23504144
33. Esquivel J, Lowy AM, Markman M, et al. The American Society of Peritoneal Surface Malignancies (ASPSM) multiinstitution evaluation of the Peritoneal Surface Disease Severity Score (PSDSS) in 1,013 patients with colorectal cancer with peritoneal carcinomatosis. Ann Surg Oncol. Dec 2014; 21(13):4195-4201. PMID 24854493
34. Baratti D, Kusamura S, Iusco D, et al. Postoperative complications after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy affect long-term outcome of patients with peritoneal metastases from colorectal cancer: a two-center study of 101 patients. Dis Colon Rectum. Jul 2014; 57(7):858-868. PMID 24901687

35. Huang CQ, Feng JP, Yang XJ, et al. Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy improves survival of patients with peritoneal carcinomatosis from colorectal cancer: a case-control study from a Chinese center. J Surg Oncol. Jun 2014; 109(7):730-739. PMID 24374987
36. de Cuba EM, Kwakman R, Knol DL, et al. Cytoreductive surgery and HIPEC for peritoneal metastases combined with curative treatment of colorectal liver metastases: Systematic review of all literature and meta-analysis of observational studies. Cancer Treat Rev. Jun 2013; 39(4):321-327. PMID 23244778
37. Klaver YL, Chua TC, Verwaal VJ, et al. Secondary cytoreductive surgery and peri-operative intraperitoneal chemotherapy for peritoneal recurrence of colorectal and appendiceal peritoneal carcinomatosis following prior primary cytoreduction. J Surg Oncol. May 2013; 107(6):585-590. PMID 23280508
38. Rampone B, Schiavone B, Martino A, et al. Current role of hyperthermic intraperitoneal chemotherapy in the treatment of peritoneal carcinomatosis from colorectal cancer. World J Gastroenterol. Mar 21 2010; 16(11):1299-1302. PMID 20238394
39. Elias D, Lefevre JH, Chevalier J, et al. Complete cytoreductive surgery plus intraperitoneal chemohyperthermia with oxaliplatin for peritoneal carcinomatosis of colorectal origin. J Clin Oncol. Feb 10 2009; 27(5):681-685. PMID 19103728
40. van Leeuwen BL, Graf W, Pahlman L, et al. Swedish experience with peritonectomy and HIPEC. HIPEC in peritoneal carcinomatosis. Ann Surg Oncol. Mar 2008; 15(3):745-753. PMID 18057988
41. Glehen O, Kwiatkowski F, Sugarbaker PH, et al. Cytoreductive surgery combined with perioperative intraperitoneal chemotherapy for the management of peritoneal carcinomatosis from colorectal cancer: a multi-institutional study. J Clin Oncol. Aug 15 2004; 22(16):3284-3292. PMID 15310771
42. Verwaal VJ, van Ruth S, de Bree E, 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. Oct 15 2003; 21(20):3737-3743. PMID 14551293
43. Williams BH, Alzahrani NA, Chan DL, et al. Repeat cytoreductive surgery (CRS) for recurrent colorectal peritoneal metastases: yes or no? Eur J Surg Oncol. Aug 2014; 40(8):943-949. PMID 24378009
44. Turaga K, Levine E, Barone R, et al. Consensus guidelines from The American Society of Peritoneal Surface Malignancies on standardizing the delivery of hyperthermic intraperitoneal chemotherapy (HIPEC) in colorectal cancer patients in the United States. Ann Surg Oncol. May 2014; 21(5):1501-1505. PMID 23793364
45. Verwaal VJ, Bruin S, Boot H, et al. 8-year follow-up of randomized trial: cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy in patients with peritoneal carcinomatosis of colorectal cancer. Ann Surg Oncol. Sep 2008; 15(9):2426-2432. PMID 18521686
46. Mahteme H, Hansson J, Berglund A, et al. Improved survival in patients with peritoneal metastases from colorectal cancer: a preliminary study. Br J Cancer. Jan 26 2004; 90(2):403-407. PMID 14735184
47. Shan LL, Saxena A, Shan BL, et al. Quality of life after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal carcinomatosis: A systematic review and meta-analysis. Surg Oncol. Oct 28 2014; 23(4):199-210. PMID 25466850
48. Seretis C, Youssef H. Quality of life after cytoreductive surgery and intraoperative hyperthermic intraperitoneal chemotherapy for peritoneal surface malignancies: A systematic review. Eur J Surg Oncol. Dec 2014; 40(12):1605-1613. PMID 25242382
49. Passot G, Bakrin N, Roux AS, et al. Quality of life after cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy: a prospective study of 216 patients. Eur J Surg Oncol. May 2014; 40(5):529-535. PMID 24370285
50. Rudloff U, Langan RC, Mullinax JE, et al. Impact of maximal cytoreductive surgery plus regional heated intraperitoneal chemotherapy (HIPEC) on outcome of patients with peritoneal carcinomatosis of gastric origin: results of the GYMSSA trial. J Surg Oncol. Sep 2014; 110(3):275-284. PMID 25042700

51. Yarema RR, Ohorchak MA, Zubarev GP, et al. Hyperthermic intraperitoneal chemoperfusion in combined treatment of locally advanced and disseminated gastric cancer: results of a single-centre retrospective study. Int J Hyperthermia. May 2014; 30(3):159-165. PMID 24641798
52. Kim KW, Chow O, Parikh K, et al. Peritoneal carcinomatosis in patients with gastric cancer, and the role for surgical resection, cytoreductive surgery, and hyperthermic intraperitoneal chemotherapy. Am J Surg. Jan 2014; 207(1):78-83. PMID 24157224
53. Yang XJ, Huang CQ, Suo T, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy improves survival of patients with peritoneal carcinomatosis from gastric cancer: final results of a phase III randomized clinical trial. Ann Surg Oncol. Jun 2011; 18(6):1575-1581. PMID 21431408
54. Coccolini F, Cotte E, Glehen O, et al. Intraperitoneal chemotherapy in advanced gastric cancer. Meta-analysis of randomized trials. Eur J Surg Oncol. Jan 2014; 40(1):12-26. PMID 24290371
55. Bakrin N, Cotte E, Sayag-Beaujard A, et al. Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy for the treatment of recurrent endometrial carcinoma confined to the peritoneal cavity. Int J Gynecol Cancer. Jul 2010; 20(5):809-814. PMID 20973274
56. Robella M, Vaira M, Mellano A, et al. Treatment of diffuse malignant peritoneal mesothelioma (DMPM) by cytoreductive surgery and HIPEC. Minerva Chir. Feb 2014; 69(1):9-15. PMID 24675242
57. Alexander HR, Jr., Bartlett DL, Pingpank JF, et al. Treatment factors associated with long-term survival after cytoreductive surgery and regional chemotherapy for patients with malignant peritoneal mesothelioma. Surgery. Jun 2013; 153(6):779-786. PMID 23489943
58. Yan TD, Deraco M, Baratti D, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for malignant peritoneal mesothelioma: multi-institutional experience. J Clin Oncol. Dec 20 2009; 27(36):6237-6242. PMID 19917862
59. Shetty SJ, Bathla L, Govindarajan V, et al. Comparison of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy with mitomycin or carboplatin for diffuse malignant peritoneal mesothelioma. Am Surg. Apr 2014; 80(4):348-352. PMID 24887664
60. Helm JH, Miura JT, Glenn JA, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for malignant peritoneal mesothelioma: a systematic review and meta-analysis. Ann Surg Oncol. May 2015; 22(5):1686-1693. PMID 25124472
61. Massari R, Barone M, Basilico R, et al. Peritonectomy and hyperthermic chemotherapy in patients with advanced or recurrent ephitelial ovarian cancer: a single center cohort study. Minerva Chir. Feb 2014; 69(1):17-26. PMID 24675243
62. Robella M, Vaira M, Marsanic P, et al. Treatment of peritoneal carcinomatosis from ovarian cancer by surgical cytoreduction and hyperthermic intraperitoneal chemotherapy (HIPEC). Minerva Chir. Feb 2014; 69(1):27-35. PMID 24675244
63. Konigsrainer I, Horvath P, Struller F, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in recurrent epithelial ovarian cancer with peritoneal metastases: a single centre experience. Langenbecks Arch Surg. Jun 2014; 399(5):589-594. PMID 24817542
64. Chiva LM, Gonzalez-Martin A. A critical appraisal of hyperthermic intraperitoneal chemotherapy (HIPEC) in the treatment of advanced and recurrent ovarian cancer. Gynecol Oncol. Jan 2015; 136(1):130-135. PMID 25434634
65. Bakrin N, Classe JM, Pomel C, et al. Hyperthermic intraperitoneal chemotherapy (HIPEC) in ovarian cancer. J Visc Surg. Oct 2014; 151(5):347-353. PMID 25168575
66. Spiliotis J, Halkia E, Lianos E, et al. Cytoreductive surgery and HIPEC in recurrent epithelial ovarian cancer: a prospective randomized phase III study. Ann Surg Oncol. May 2015; 22(5):1570-1575. PMID 25391263
67. Fagotti A, Costantini B, Petrillo M, et al. Cytoreductive surgery plus HIPEC in platinum-sensitive recurrent ovarian cancer patients: a case-control study on survival in patients with two year follow-up. Gynecol Oncol. Dec 2012; 127(3):502-505. PMID 23022234

68. Spiliotis J, Vaxevanidou A, Sergouniotis F, et al. The role of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in the management of recurrent advanced ovarian cancer: a prospective study. J BUON. Jan-Mar 2011; 16(1):74-79. PMID 21674853
69. Muñoz-Casares FC, Rufian S, Rubio MJ, et al. The role of hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC) in the treatment of peritoneal carcinomatosis in recurrent ovarian cancer. Clin Transl Oncol. Nov 2009; 11(11):753-759. PMID 19917539
70. Helm CW, Richard SD, Pan J, et al. Hyperthermic intraperitoneal chemotherapy in ovarian cancer: first report of the HYPER-O registry. Int J Gynecol Cancer. Jan 2010; 20(1):61-69. PMID 20130504
71. Huo YR, Richards A, Liauw W, et al. Hyperthermic intraperitoneal chemotherapy (HIPEC) and cytoreductive surgery (CRS) in ovarian cancer: A systematic review and meta-analysis. Eur J Surg Oncol. Dec 2015; 41(12):1578-1589. PMID 26453145
72. Le Brun JF, Campion L, Berton-Rigaud D, et al. Survival benefit of hyperthermic intraperitoneal chemotherapy for recurrent ovarian cancer: a multi-institutional case control study. Ann Surg Oncol. Oct 2014; 21(11):3621-3627. PMID 24819120
73. Cascales-Campos PA, Gil J, Feliciangeli E, et al. The role of hyperthermic intraperitoneal chemotherapy using paclitaxel in platinum-sensitive recurrent epithelial ovarian cancer patients with microscopic residual disease after cytoreduction. Ann Surg Oncol. Mar 2015; 22(3):987-993. PMID 25212832
74. Coccolini F, Campanati L, Catena F, et al. Hyperthermic intraperitoneal chemotherapy with cisplatin and paclitaxel in advanced ovarian cancer: a multicenter prospective observational study. J Gynecol Oncol. Jan 2015; 26(1):54-61. PMID 25376916
75. Roy P, Chetty R. Goblet cell carcinoid tumors of the appendix: An overview. World J Gastrointest Oncol. Jun 15 2010; 2(6):251-258. PMID 21160637
76. McConnell YJ, Mack LA, Gui X, et al. Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy: an emerging treatment option for advanced goblet cell tumors of the appendix. Ann Surg Oncol. Jun 2014; 21(6):1975-1982. PMID 24398544
77. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: colon cancer. Version 2.2016. http://www.nccn.org/professionals/physician_gls/PDF/colon.pdf. Accessed June 24, 2016.
78. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: rectal cancer. Version 2.2016. http://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed June 24, 2016.
79. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: gastric cancer. Version 2.2016. http://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed June 24, 2016.
80. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: uterine neoplasms. Version 2.2016. http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed June 24, 2016.
81. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: ovarian cancer including fallopian tube cancer and primary peritoneal cancer. Version 1.2016. http://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed June 24, 2016.
82. Chang GJ, Kaiser AM, Mills S, et al. Practice parameters for the management of colon cancer. Dis Colon Rectum. Aug 2012; 55(8):831-843. PMID 22810468
83. Esquivel J, Sticca R, Sugarbaker P, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in the management of peritoneal surface malignancies of colonic origin: a consensus statement. Society of Surgical Oncology. Ann Surg Oncol. Jan 2007; 14(1):128-133. PMID 17072675
84. Dube P, Sideris L, Law C, et al. Guidelines on the use of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in patients with peritoneal surface malignancy arising from colorectal or appendiceal neoplasms. Curr Oncol. Apr 2015; 22(2):e100-112. PMID 25908915