
Supplementary information

Primary and metastatic peritoneal surface malignancies

In the format provided by the
authors and unedited

Supplementary Table 1: Treatment modalities for primary and metastatic PSMs

Pathologies	Neoadjuvant treatments	Surgery	HIPEC	Targeted therapies	Intraperitoneal treatments	Systemic chemotherapy
Pseudomyxoma peritonei and PM from appendiceal cancers						
• curative	No	Upfront CC-0 or CC-1 CRS	recommended	No	Option of EPIC	Adjuvant if poor prognostic factors
• palliative	-	Upfront CC-2 or 3 CRS	recommended	Antiangiogenic* Bromelain and Acetylcysteine (BroMac) in early clinical development	PIPAC under evaluation	Palliative according to right-sided colorectal cancer*
Malignant peritoneal mesothelioma						
• curative	Intraperitoneal chemotherapy, NIPS and PIPAC under evaluation	Upfront CC-0 CC-1 CRS	recommended	No standard recommendation*	Option of EPIC	Adjuvant if poor prognostic factors to be considered*
• palliative		No	No	Immunotherapy, PARP-inhibition and other targeted agents under evaluation*	Option of long-term intraperitoneal chemotherapy or PIPAC	Palliative Platinum-/Pemetrexed-based regimens
PM from Ovarian Cancer						
• 1st line	Systemic chemotherapy if CC-0 CRS not possible	Upfront or interval CC-0 CRS	Option in interval surgery	Antiangiogenic or PARP-inhibition	No	Adjuvant Platinum-/Taxane-based
• Platin sensitive recurrence	Systemic chemotherapy if CC-0 CRS not possible	Upfront or delayed CC-0 CRS	Under evaluation into RCT	Antiangiogenic or PARP-inhibition	PIPAC under evaluation	Palliative Platinum-based
• Platin resistant recurrence	Systemic chemotherapy if CC-0 CRS not possible	Option if CC-0 CRS	Option if CC-0 CRS	Antiangiogenic	PIPAC under evaluation	Palliative Topotecan or Anthracyclines
PM from colorectal cancer						
• curative	Option of systemic chemotherapy Intraperitoneal chemotherapy, NIPS and PIPAC under evaluation	CC-0 CRS	Option into specialized centers	No standard recommendation*	PIPAC under evaluation	Adjuvant if poor prognostic factors*
• palliative	-	No	No	Antiangiogenic and anti-EGFR according to mutational status and sidedness of primary tumor Immunotherapy in MSI patients	PIPAC under evaluation	Palliative Oxaliplatin/Fluoropyrimidine based or Irinotecan/Fluoropyrimidine or Trifluridine-Tipiracil (3 rd -line)
PM from gastric cancer						
• curative	Option of systemic chemotherapy Intraperitoneal chemotherapy and NIPS, PIPAC under evaluation	CC-0 CRS in patients with low PCI	Option in combination with CC-0 CRS	No standard recommendation*	PIPAC under evaluation	Adjuvant
• palliative	PIPAC under evaluation	No	Under evaluation	Trastuzumab in Her 2 positive patients Immunotherapy in MSI and under further evaluation in MSS	PIPAC under evaluation	Palliative Platinum/Fluoropyrimidine based 1 st -line, Taxane (2 nd -line) or Irinotecan or Trifluridine-Tipiracil (3 rd -line)
PM from others malignancies						
• curative	To select adequate candidate	Only in case of CC-0 CRS	Option in combination with CC-0 CRS	-		Optional
• palliative	-	No	Option in malignant ascites	-	Optional	Registered and established disease specific regimens

CRS: cytoreductive surgery; CC-0 CRS: complete CRS; CC-1 CRS: sub-complete CRS; CC-2 and 3: Incomplete CRS; PARP: Poly (ADP-ribose) polymerase; PCI: Peritoneal Cancer Index; PM: peritoneal metastasis; HIPEC: hyperthermic intraperitoneal chemotherapy; EPIC: early postoperative intraperitoneal chemotherapy; MSI: microsatellite instability; MSS: Microsatellite stable; PIPAC: Pressurized intraperitoneal aerosolized chemotherapy; NIPS: neoadjuvant intraperitoneal and systemic chemotherapy.

*No definitive evidence from controlled trials available.

Supplementary Table 2: Principal results of largest trials evaluating curative treatment of peritoneal surface malignancies

Authors	Year	Type of trial	Treatment modalities	N	5 yr OS (%)	Median OS	Severe morbidity (%)	Mortality (%)
Pseudomyxoma peritonei								
Ansari et al.(1)	2016	Retrospective Monocentric	CRS + HIPEC	738	87.4	Not reached	15.2	0.8
Kusamura et al.(2)	2021	Retrospective Multicentric	CRS alone CRS + HIPEC	1924 376 1548	46.2 57.8	Not reached	28.9 32.6	8.5 3.1
Peritoneal Mesothelioma								
Alexander et al.(3)	2013	Retrospective Multicentric	CRS + perioperative intraperitoneal chemotherapy	211	26	38.7 months	30	2.3
Yan et al.(4)	2010	Retrospective Multicentric	CRS +/- HIPEC	401	47	53 months	31	2
Colorectal PM								
Verwaal et al.(5)	2003	Prospective Randomized	Systemic chemotherapy CRS + HIPEC	51 54	-	12.6 months 22.3 months	- -	- 8
Elias et al.(6)	2010	Retrospective Multicentric	CRS + HIPEC	523	27	30.1 months	31	3
Esquivel et al.(7)	2014	Retrospective Multicentric	Systemic chemotherapy CRS + HIPEC	308 705	19 58	10 months 41 months	- -	- -
Quenet et al.(8)	2021	Prospective Randomized	CRS alone CRS + HIPEC	132 133	13.1 14.8	41.2 months 41.7 months	30 40	2.3 3
Gastric PM								
Yang et al.(9)	2011	Prospective Randomized	CRS alone CRS + HIPEC	34 34	- -	6.5 months 11 months	11.7 14.7	- -
Cambay et al.(10)	2013	Retrospective Monocentric	NIPS + CRS + HIPEC	194	10.7	15.8 months	23.6	3.9
Bonnot et al.(11)	2019	Retrospective Multicentric	CRS alone CRS + HIPEC	97 180	6.4 19.9	12.1 months 18.8 months	55.3 53.7	10.1 7.4
Ovarian PM 1st line								
Eisenkop et al.(12)	2003	Prospective	CRS alone	408	49	58 months	-	-
Amstrong et al.(13)	2006	Prospective Randomized	CRS and LT IP chemotherapy CRS alone	214 215	- -	66 months 50 months	- -	- -
Van Driel et al.(14)	2018	Prospective Randomized	CRS alone CRS + HIPEC	123 122	- -	33.9 months 45.7 months	25 27	4 1
Ovarian PM recurrence								
Harter et al.(15)	2006	Retrospective	Complete CRS Incomplete CRS	170 47	-	45 months 20 months	- -	- -
Bakrin et al.(16)	2013	Retrospective Multicentric	CRS and HIPEC	566	-	35.4 months	31.3	0.8
Spiliotis et al.(17)	2015	Prospective Randomized	CRS alone CRS + HIPEC	60 60	- -	13.4 months 26.7 months	- -	- -

CRS: Cytoreductive surgery, HIPEC: Hyperthermic intraperitoneal chemotherapy, LT IP chemotherapy: Long term intraperitoneal chemotherapy

References

1. Ansari N, Chandrakumaran K, Dayal S, Mohamed F, Cecil TD, Moran BJ. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in 1000 patients with perforated appendiceal epithelial tumours. *Eur J Surg Oncol*. 2016;42(7):1035-41.
2. Kusamura S, Barretta F, Yonemura Y, Sugarbaker PH, Moran BJ, Levine EA, et al. The Role of Hyperthermic Intraperitoneal Chemotherapy in Pseudomyxoma Peritonei After Cytoreductive Surgery. *JAMA Surg*. 2021:e206363.
3. Alexander HR, Bartlett DL, Pingpank JF, Libutti SK, Royal R, Hughes MS, et al. Treatment factors associated with long-term survival after cytoreductive surgery and regional chemotherapy for patients with malignant peritoneal mesothelioma. *Surgery*. 2013;153(6):779-86.
4. Yan TD, Deraco M, Baratti D, Kusamura S, Elias D, Glehen O, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for malignant peritoneal mesothelioma: multi-institutional experience. *J Clin Oncol*. 2009;27(36):6237-42.
5. 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.
6. Elias D, Gilly F, Boutitie F, Quenet F, Bereder JM, Mansvelt B, et al. Peritoneal colorectal carcinomatosis treated with surgery and perioperative intraperitoneal chemotherapy: retrospective analysis of 523 patients from a multicentric French study. *J Clin Oncol*. 2010;28(1):63-8.
7. Esquivel J, Lowy AM, Markman M, Chua T, Pelz J, Baratti D, 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*. 2014;21(13):4195-201.
8. Quénet F, Elias D, Roca L, Goéré D, Ghouti L, Pocard M, et al. Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy versus cytoreductive surgery alone for colorectal peritoneal metastases (PRODIGE 7): a multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol*. 2021;22(2):256-66.
9. Yang XJ, Huang CQ, Suo T, Mei LJ, Yang GL, Cheng FL, 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*. 2011;18(6):1575-81.
10. Canbay E, Mizumoto A, Ichinose M, Ishibashi H, Sako S, Hirano M, et al. Outcome data of patients with peritoneal carcinomatosis from gastric origin treated by a strategy of bidirectional chemotherapy prior to cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in a single specialized center in Japan. *Ann Surg Oncol*. 2014;21(4):1147-52.
11. Bonnot PE, Piessen G, Kepenekian V, Decullier E, Pocard M, Meunier B, et al. Cytoreductive Surgery with and without Hyperthermic Intraperitoneal Chemotherapy for Gastric Cancer with Peritoneal Metastasis (CYTO-CHIP study): A Propensity-Score Analysis. *J Clin Oncol*. 2019;37(23):2028-2040.
12. Eisenkop SM, Spirtos NM, Friedman RL, Lin WC, Pisani AL, Peticucci S. Relative influences of tumor volume before surgery and the cytoreductive outcome on survival for patients with advanced ovarian cancer: a prospective study. *Gynecol Oncol*. 2003;90(2):390-6.
13. Armstrong DK, Bundy B, Wenzel L, Huang HQ, Baergen R, Lele S, et al. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. *N Engl J Med*. 2006;354(1):34-43.
14. 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.
15. Harter P, du Bois A, Hahmann M, Hasenburg A, Burges A, Loibl S, et al. Surgery in recurrent ovarian cancer: the Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) DESKTOP OVAR trial. *Ann Surg Oncol*. 2006;13(12):1702-10.
16. Bakrin N, Bereder JM, Decullier E, Classe JM, Msika S, Lorimier G, et al. Peritoneal carcinomatosis treated with cytoreductive surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for advanced ovarian carcinoma: a French multicentre retrospective cohort study of 566 patients. *Eur J Surg Oncol*. 2013;39(12):1435-43.
17. Spiliotis J, Halkia E, Lianos E, Kalantzi N, Grivas A, Efstathiou E, et al. Cytoreductive surgery and HIPEC in recurrent epithelial ovarian cancer: a prospective randomized phase III study. *Ann Surg Oncol*. 2015;22(5):1570-5.