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Short Report

Pressurized intraperitoneal aerosol chemotherapy (PIPAC): updated systematic review using the IDEAL framework

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Introduction

Pressurized intraperitoneal aerosol chemotherapy (PIPAC) is a surgical innovation deployed to treat peritoneal metastases. Traditionally, peritoneal metastases have been treated with systemic chemotherapy, but this approach is limited by poor peritoneal perfusion. Intra-abdominal chemotherapy in the form of heated lavage (hyperthermic intraperitoneal chemotherapy (HIPEC)) is currently used alongside cytoreductive surgery. The use of aerosolized agents in a laparoscopic setting was first described in 2000 in a swine model[1]; since then, a number of PIPAC studies have been reported. The IDEAL framework[2] provides recommendations for the design, development, and reporting of studies for novel surgical interventions (*Table 1*). It recommends that innovations move through stages (idea, development, exploration, assessment, and long-term studies).

This paper provides an update of the previously performed PIPAC IDEAL review[3], to include updated research. There are almost double the number of PIPAC papers now (165 *versus* 86), compared with the search completed 3 years ago. This review was performed on behalf of the PIPAC UK collaborative.

Methods

This systematic review was conducted with the MEDLINE and Embase databases, up to 28 February 2022. Included studies were assigned a stage (0, 1, 2a, 2b, 3, or 4), using the IDEAL guidelines[4]. Full methodological details, including the PRISMA checklist/flow chart, are available in the *supplementary material*.

Results

After screening, 18 trial registrations and 147 published papers were included[1,5–151]. IDEAL stage allocation can be viewed online (*supplementary material*).

Stage 0: idea (preclinical)

The first description of a 'therapeutic pneumoperitoneum' in a swine model was published in 2000[1]. Studies successfully demonstrated the superiority of PIPAC over conventional lavage with regard to peritoneal distribution and drug penetration using methylene blue dye, and Dbait with a fluorescent marker[5,6]. Further studies demonstrated drug penetration was highest closest to the delivery device, and that aerosol distribution was heterogenous[7–9]. Studies found that increasing the intra-abdominal pressure to 15 mmHg (from 12 mmHg) increased the cytotoxic action of oxaliplatin on a cell line[10], but a higher temperature did not have a significant effect.

Some units investigated how to improve chemotherapy delivery; demonstrating the stability of nano- or microparticles during PIPAC[11,12]. Further experiments addressed non-homogenous drug distribution with the use of a rotational/multidirectional nozzle[13,14]. Another modification involved the use of electrostatic precipitation, and was named ePIPAC[15].

Stage 1: idea

The first in-human studies performed on patients with peritoneal metastases were published in 2013 and 2014[16,17]. They demonstrated peritoneal tumour regression in the three patients treated, with limited renal and liver toxicity. The PIPAC technique was described as follows: pressurized aerosolization of cisplatin and doxorubicin; 12 mmHg CO_2 pneumoperitoneum over 30 minutes; and a temperature of 37°C. The dosage of cisplatin (7.5 mg/m^2 body surface) and doxorubicin (1.5 mg/m^2 body surface) were set as 10 per cent of the usual HIPEC dose. Occupational health studies demonstrated safety for theatre staff[18], with most new PIPAC groups each performing their own occupational safety tests[19–25].

Stage 2a: development

Early perioperative complications included rare but life-threatening instances of severe peritoneal sclerosis or severe

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Table 1 Summary of the stages of surgical innovation according to the IDEAL framework

Stage of innovation	Description	No. of patients	Proposed method of investigation	Studies included in this review
0: idea (preclinical)	Feasibility and definition of procedure	None	Simulated, cadaver, animal, modelling	Preclinical studies in animals (*in vivo* and post-mortem models) and *in vitro*
1: idea	Proof of concept; first in human	Very few	Case reports, small case series	Case reports, small case series, occupational health and safety studies; data relate to safety and technical feasibility
2a: development	Therapy evolving; refining and modifying the technique	Usually < 30	Prospective development studies	Larger case series, non-randomized studies; prospective and retrospective case series; single centre
2b: exploration	Learning curves progressing, indication expanding	Many	Prospective series, multisite, feasibility RCT	Large multicentre case series, studies looking at new indication
3: assessment	Procedure has clear definition and used by many surgeons but needs to be tested against standard of care	Many	RCT	RCT and RCT protocols
4: long-term	Long-term follow-up with registry data, to monitor late/rare complications	Many	Registry, late/rare case reports	NA

RCT, randomized clinical trial; NA, not applicable.

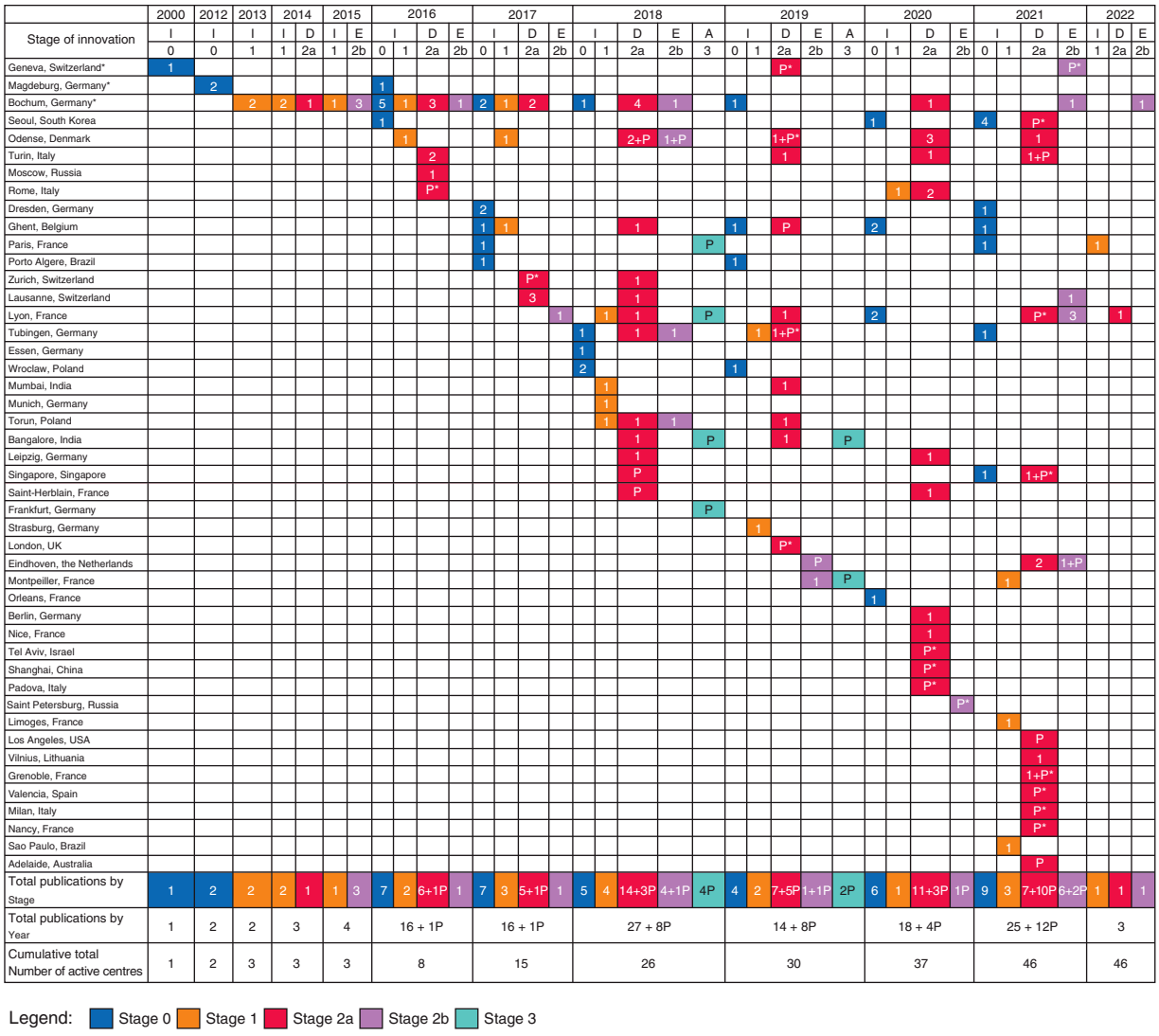

Fig. 1 Identified studies were assigned a stage and displayed by year and location

Study centres are described by city where the institution of the lead author was located, or where the pressurized intraperitoneal aerosol chemotherapy (PIPAC) was performed. An asterisk (*) next to location indicates the original PIPAC group moved (now Bochum). I, idea; D, development; E, exploration; A, assessment; P, published protocol paper; P*, protocol from ClinicalTrials.gov or clinicaltrialsregister.eu.

hypersensitivity reactions to platinum[26,27]. A systematic review included 28 clinical studies involving more than 1500 patients, and showed that 45 per cent of patients developed a grade 1 adverse event, but only 1.6 per cent of patients had a grade 5 adverse event (death)[42]. No significant renal, hepatic, or haematological toxicity was described. One study assessed quality of life (QoL) in 91 patients and demonstrated no therapy-related decrease in QoL score[28].

The most common PIPAC chemotherapy regimen is either oxaliplatin as a sole agent or cisplatin with doxorubicin. Formal dose-escalation studies include a phase 1 study that found patients undergoing PIPAC could tolerate an increase in the dose of cisplatin and doxorubicin up to 10.5 and 2.1 mg/m^2, respectively[29]. Another unit found that the maximum tolerated dose of oxaliplatin was 90 mg/m^2 [30]. However, another phase 1 dose-escalation study found that three patients could tolerate a maximum dose of 135 mg/m^2 [31], with no dose-limiting toxicity observed. They also looked at cisplatin and doxorubicin, and found a maximum tolerated dose of 30 mg/m^2 and 6 mg/m^2, respectively—significantly higher than doses used in any previous PIPAC application. Common adverse events across all these studies included nausea, vomiting, and abdominal pain. While earlier trials assessed PIPAC in ovarian and colorectal peritoneal metastases, indications have expanded, and include cholangiocarcinoma[32], pancreas[33], breast and endometrial origins[35].

Stage 2b: exploration

There has been rapid expansion of PIPAC from Germany[28,35] to nearby countries, including France, Switzerland, and the Netherlands[36–38]. Its wide acceptance into practice has led some papers to describe as many as 1200 PIPAC treatments[49]. Its safety has been demonstrated, with minimal risks and impact on QoL, and ePIPAC has been shown to be feasible, safe, and repeatable in patients[40]. There is also evidence that PIPAC may be used as a neoadjuvant treatment, with downstaging of peritoneal disease enabling transition from unresectable to resectable tumours in a small number of patients[41].

Stage 3: assessment

The penultimate IDEAL stage involves testing the proposed surgical innovation against the standard of care. To date there have been six stage 3 published protocols, but no results have yet been published. Half of the protocols compare cycles of PIPAC + systemic chemotherapy with systemic chemotherapy; the other half compare PIPAC alone with systemic chemotherapy. Both the disease targeted and the primary outcomes evaluated are variable. The lack of a consistent outcome measurement in these trials may make it more difficult to compare results. Two-thirds of the proposed studies will be multicentred, with collaboration across the European PIPAC units.

Discussion

Since 2019, there has been an increase in the number of studies on PIPAC published (165 *versus* 86), as well as the number of units using PIPAC (46 *versus* 28). As *Fig. 1* demonstrates, there is a general progression through the IDEAL stages, although published randomized clinical trials (RCTs) are still lacking. A PIPAC online registry (https://isspp.org) has been set up by the International Society of the Study of Pleura and Peritoneum and, if utilized by the PIPAC community, should provide the foundation for future stage 4 reports.

According to the IDEAL framework, surgical innovation should progress through the stages in a step-wise fashion, but this does not mean that each new unit need regress to stage 0 if little is being changed. This paper also highlights the need for all clinical trials to be prospectively registered, as only a fraction appear prospectively on clinical trials registries, if at all.

Given that the use of PIPAC to treat peritoneal disease has been practised, mostly in Europe, for the past decade, it is imperative that robust RCTs are set up to compare this intervention with the standard of care. There is a risk that in some units the use of PIPAC is so widespread that it may be a barrier to patient recruitment into the non-PIPAC arm within a RCT. The lack of robust evidence for efficacy means that in the UK PIPAC remains categorized within the National Institute of Health and Care Excellence guidelines for use in clinical trials only[152]. The PIPAC UK collaborative has been formed in response to this recommendation. Through the collaboration, the UK is ideally placed to carry out a multicentre RCT. This would allow the effectiveness of PIPAC to be demonstrated definitively and place this innovation within routine care pathways.

Collaborators

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Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS* online.

Data availability

Data obtained from the IDEAL review process is available on request.

References

1. Reymond MA, Hu B, Garcia A, Reck T, Köckerling F, Hess J *et al.* Feasibility of therapeutic pneumoperitoneum in a large animal model using a microvaporisator. *Surg Endosc* 2000; **14**:51–55
2. McCulloch P, Altman DG, Campbell WB, Flum DR, Glasziou P, Marshall JC *et al.* Surgical innovation and evaluation 3: no surgical innovation without evaluation: the IDEAL recommendations. *Lancet* 2009;**374**:1105–1112
3. Tate SJ, Torkington J. Pressurized intraperitoneal aerosol chemotherapy: a review of the introduction of a new surgical technology using the IDEAL framework. *BJS Open* 2020;**4**: 206–215
4. IDEAL collaboration. *IDEAL Flowchart and Guidebook*. https://www.ideal-collaboration.net/wp-content/uploads/2021/04/IDEAL-Stages-Guidebook-Final.pdf (accessed 30 March 2022)
5. Solaß W, Hetzel A, Nadiradze G, Sagynaliev E, Reymond MA. Description of a novel approach for intraperitoneal drug delivery and the related device. *Surg Endosc* 2012;**26**:1849–1855
6. Solass W, Herbette A, Schwarz T, Hetzel A, Sun JS, Dutreix M *et al.* Therapeutic approach of human peritoneal carcinomatosis with Dbait in combination with capnoperitoneum: proof of concept. *Surg Endosc* 2012;**26**: 847–852
7. Khosrawipour V, Khosrawipour T, Diaz-Carballo D, Förster E, Zieren J, Giger-Pabst U. Exploring the spatial drug distribution pattern of pressurized intraperitoneal aerosol chemotherapy (PIPAC). *Ann Surg Oncol* 2016;**23**:1220–1224
8. Khosrawipour V, Khosrawipour T, Kern AJP, Osma A, Kabakci B, Diaz-Carballo D *et al.* Distribution pattern and penetration depth of doxorubicin after pressurized intraperitoneal aerosol chemotherapy (PIPAC) in a postmortem swine model. *J Cancer Res Clin Oncol* 2016;**142**:2275–2280
9. Bellendorf A, Khosrawipour V, Khosrawipour T, Siebigteroth S, Cohnen J, Diaz-Carballo D *et al.* Scintigraphic peritoneography reveals a non-uniform 99mTc-Pertechnetat aerosol distribution pattern for pressurized intra-peritoneal aerosol chemotherapy (PIPAC) in a swine model. *Surg Endosc* 2018;**32**: 166–174
10. Khosrawipour V, Diaz-Carballo D, Acikelli AH, Khosrawipour T, Falkenstein TA, Wu D *et al.* Cytotoxic effect of different treatment parameters in pressurized intraperitoneal aerosol chemotherapy (PIPAC) on the in vitro proliferation of human colonic cancer cells. *World J Surg Oncol* 2017;**15**:43
11. Shariati M, Lollo G, Matha K, Descamps B, Vanhove C, Van de Sande L *et al.* Synergy between intraperitoneal aerosolization (PIPAC) and cancer nanomedicine: cisplatin-loaded polyarginine-hyaluronic acid nanocarriers efficiently eradicate peritoneal metastasis of advanced human ovarian cancer. *ACS Appl Mater Interfaces* 2020;**12**: 29024–29036
12. Mikolajczyk A, Khosrawipour V, Schubert J, Chaudhry H, Pigazzi A, Khosrawipour T. Particle stability during pressurized intra-peritoneal aerosol chemotherapy (PIPAC). *Anticancer Res* 2018;**38**:4645–4649
13. Seitenfus R, Ferreira PRW, Santos GOD, Alves RJV, Kalil AN, Barros ED *et al.* A prototype single-port device for pressurized intraperitoneal aerosol chemotherapy. Technical feasibility and local drug distribution. *Acta Cir Bras* 2017;**32**:1056–1063
14. Park SJ, Lee EJ, Lee HS, Kim J, Park S, Ham J *et al.* Development of rotational intraperitoneal pressurized aerosol chemotherapy to enhance drug delivery into the peritoneum. *Drug Deliv* 2021;**28**:1179–1187
15. Kakchekeeva T, Demtröder C, Herath NI, Griffiths D, Torkington J, Solaß W *et al.* *In vivo* feasibility of electrostatic precipitation as an adjunct to pressurized intraperitoneal aerosol chemotherapy (ePIPAC). *Ann Surg Oncol* 2016;**23**:592–598
16. Solass W, Kerb R, Mürdter T, Giger-Pabst U, Strumberg D, Tempfer C *et al.* Intraperitoneal chemotherapy of peritoneal carcinomatosis using pressurized aerosol as an alternative to liquid solution: first evidence for efficacy. *Ann Surg Oncol* 2014;**21**:553–559
17. Blanco A, Giger-Pabst U, Solass W, Zieren J, Reymond MA. Renal and hepatic toxicities after pressurized intraperitoneal aerosol chemotherapy (PIPAC). *Ann Surg Oncol* 2013;**20**: 2311–2316
18. Solass W, Giger-Pabst U, Zieren J, Reymond MA. Pressurized intraperitoneal aerosol chemotherapy (PIPAC): occupational health and safety aspects. *Ann Surg Oncol* 2013;**20**:3504–3511
19. Willaert W, Sessink P, Ceelen W. Occupational safety of pressurized intraperitoneal aerosol chemotherapy (PIPAC). *Pleura Peritoneum* 2017;**2**:121–128
20. Roussin F, Taibi A, Canal-Raffin M, Cantournet L, Durand-Fontanier S, Druet-Cabanac M *et al.* Assessment of workplace environmental contamination and occupational exposure to cisplatin and doxorubicin aerosols during electrostatic pressurized intraperitoneal aerosol chemotherapy. *Eur J Surg Oncol* 2021;**47**:2939–2947
21. Ndaw S, Hanser O, Kenepekian V, Vidal M, Melczer M, Remy A *et al.* Occupational exposure to platinum drugs during intraperitoneal chemotherapy. Biomonitoring and surface contamination. *Toxicol Lett* 2018;**298**:171–176
22. Larroque M, Arnaudguilhem C, Bouyssiere B, Quenet F, Bouazza N, Jarlier M *et al.* Evaluation of the environmental contamination and exposure risk in medical/non-medical staff after oxaliplatin-based pressurized intraperitoneal aerosol chemotherapy. *Toxicol Appl Pharmacol* 2021;**429**:115694
23. Ametsbichler P, Böhlandt A, Nowak D, Schierl R. Occupational exposure to cisplatin/oxaliplatin during pressurized intraperitoneal aerosol chemotherapy (PIPAC)? *Eur J Surg Oncol* 2018;**44**:1793–1799
24. Graversen M, Pedersen PB, Mortensen MB. Environmental safety during the administration of pressurized intraperitoneal aerosol chemotherapy (PIPAC). *Pleura Peritoneum* 2016;**1**:203–208
25. Delhorme JB, Klipfel A, D'Antonio F, Greget MC, Diemunsch P, Rohr S *et al.* Occupational safety of pressurized intraperitoneal aerosol chemotherapy (PIPAC) in an operating room without laminar airflow. *J Visc Surg* 2019;**156**:485–488
26. Graversen M, Detlefsen S, Pfeiffer P, Lundell L, Mortensen MB. Severe peritoneal sclerosis after repeated pressurized intraperitoneal aerosol chemotherapy with oxaliplatin (PIPAC OX): report of two cases and literature survey. *Clin Exp Metastasis* 2018;**35**:103–108
27. Siebert M, Alyami M, Mercier F, Gallice C, Villeneuve L, Bérard F *et al.* Severe hypersensitivity reactions to platinum compounds

post-pressurized intraperitoneal aerosol chemotherapy (PIPAC): first literature report. *Cancer Chemother Pharmacol* 2019;**83**:425–430
28. Odendahl K, Solass W, Demtröder C, Giger-Pabst U, Zieren J, Tempfer C *et al.* Quality of life of patients with end-stage peritoneal metastasis treated with pressurized intraperitoneal aerosol chemotherapy (PIPAC). *Eur J Surg Oncol* 2015;**41**:1379–1385
29. Tempfer CB, Giger-Pabst U, Seebacher V, Petersen M, Dogan A, Rezniczek GA. A phase I, single-arm, open-label, dose escalation study of intraperitoneal cisplatin and doxorubicin in patients with recurrent ovarian cancer and peritoneal carcinomatosis. *Gynecol Oncol* 2018;**150**:23–30
30. Dumont F, Passot C, Raoul JL, Kepenekian V, Lelièvre B, Boisdron-Celle M *et al.* A phase I dose-escalation study of oxaliplatin delivered via a laparoscopic approach using pressurised intraperitoneal aerosol chemotherapy for advanced peritoneal metastases of gastrointestinal tract cancers. *Eur J Cancer* 2020;**140**:37–44
31. Robella M, De Simone M, Berchialla P, Argenziano M, Borsano A, Ansari S *et al.* A phase I dose escalation study of oxaliplatin, cisplatin and doxorubicin applied as PIPAC in patients with peritoneal carcinomatosis. *Cancers (Basel)* 2021; **13**:1060
32. Falkenstein TA, Götze TO, Ouaissi M, Tempfer CB, Giger-Pabst U, Demtröder C. First clinical data of pressurized intraperitoneal aerosol chemotherapy (PIPAC) as salvage therapy for peritoneal metastatic biliary tract cancer. *Anticancer Res* 2018;**38**:373–378
33. Khosrawipour T, Khosrawipour V, Giger-Pabst U. Pressurized intra peritoneal aerosol chemotherapy in patients suffering from peritoneal carcinomatosis of pancreatic adenocarcinoma. *PLoS One* 2017;**12**:e0186709
34. Rezniczek GA, Giger-Pabst U, Thaher O, Tempfer CB. Pressurized intraperitoneal aerosol chemotherapy (PIPAC) for rare gynecologic indications: peritoneal metastases from breast and endometrial cancer. *BMC Cancer* 2020;**20**:1122
35. Demtröder C, Solass W, Zieren J, Strumberg D, Giger-Pabst U, Reymond MA. Pressurized intraperitoneal aerosol chemotherapy with oxaliplatin in colorectal peritoneal metastasis. *Colorectal Dis* 2016;**18**:364–371
36. Hübner M, Grass F, Teixeira-Farinha H, Pache B, Mathevet P, Demartines N. Pressurized intraperitoneal aerosol chemotherapy—practical aspects. *Eur J Surg Oncol* 2017;**43**: 1102–1109
37. 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**:e044811
38. Alyami M, Gagniere J, Sgarbura O, Cabelguenne D, Villeneuve L, Pezet D *et al.* Multicentric initial experience with the use of the pressurized intraperitoneal aerosol chemotherapy (PIPAC) in the management of unresectable peritoneal carcinomatosis. *Eur J Surg Oncol* 2017;**43**:2178–2183
39. Giger-Pabst U, Tempfer CB. How to perform safe and technically optimized pressurized intraperitoneal aerosol chemotherapy (PIPAC): experience after a consecutive series of 1200 procedures. *J Gastrointest Surg* 2018;**22**:2187–2193
40. Taibi A, Teixeira Farinha H, Durand Fontanier S, Sayedalamin Z, Hübner M, Sgarbura O. Pressurized intraperitoneal aerosol chemotherapy enhanced by electrostatic precipitation (ePIPAC) for patients with peritoneal metastases. *Ann Surg Oncol* 2021;**28**:3852–3860
41. Alyami M, Mercier F, Siebert M, Bonnot PE, Laplace N, Villeneuve L *et al.* Unresectable peritoneal metastasis treated by pressurized intraperitoneal aerosol chemotherapy (PIPAC) leading to cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. *Eur J Surg Oncol* 2021;**47**:128–133
42. Tempfer C, Giger-Pabst U, Hilal Z, Dogan A, Rezniczek GA. Pressurized intraperitoneal aerosol chemotherapy (PIPAC) for peritoneal carcinomatosis: systematic review of clinical and experimental evidence with special emphasis on ovarian cancer. *Arch Gynecol Oster* 2018;**298**:243–257
43. Khosrawipour V, Bellendorf A, Khosrawipour C, Hedayat-Pour Y, Diaz-Carballo D, Förster E *et al.* Irradiation does not increase the penetration depth of doxorubicin in normal tissue after pressurized intra-peritoneal aerosol chemotherapy (PIPAC) in an *ex vivo* model. *In Vivo* 2016;**30**:593–597
44. Khosrawipour V, Giger-Pabst U, Khosrawipour T, Pour YH, Diaz-Carballo D, Förster E *et al.* Effect of irradiation on tissue penetration depth of doxorubicin after pressurized intra-peritoneal aerosol chemotherapy (PIPAC) in a novel *ex-vivo* model. *J Cancer* 2016;**7**:910–914
45. Khosrawipour V, Khosrawipour T, Falkenstein TA, Diaz-Carballo D, Förster E, Osma A *et al.* Evaluating the effect of Micropump© position, internal pressure and doxorubicin dosage on efficacy of pressurized intra-peritoneal aerosol chemotherapy (PIPAC) in an *ex vivo* model. *Anticancer Res* 2016;**36**:4595–4600
46. Khosrawipour V, Khosrawipour T, Hedayat-Pour Y, Diaz-Carballo D, Bellendorf A, Böse-Ribeiro H *et al.* Effect of whole-abdominal irradiation on penetration depth of doxorubicin in normal tissue after pressurized intraperitoneal aerosol chemotherapy (PIPAC) in a post-mortem swine model. *Anticancer Res* 2017;**37**:1677–1680
47. Khosrawipour V, Mikolajczyk A, Schubert J, Khosrawipour T. Pressurized intra-peritoneal aerosol chemotherapy (PIPAC) via endoscopical microcatheter system. *Anticancer Res* 2018; **38**:3447–3452
48. Khosrawipour V, Reinhard S, Martino A, Khosrawipour T, Arafkas M, Mikolajczyk A. Increased tissue penetration of doxorubicin in pressurized intraperitoneal aerosol chemotherapy (PIPAC) after high-intensity ultrasound (HIUS). *Int J Surg Oncol* 2019;**2019**:6185313
49. Göhler D, Große S, Bellendorf A, Falkenstein TA, Ouaissi M, Zieren J *et al.* Hyperthermic intracavitary nanoaerosol therapy (HINAT) as an improved approach for pressurised intraperitoneal aerosol chemotherapy (PIPAC): Technical description, experimental validation and first proof of concept. *Beilstein J Nanotechnol* 2017;**8**:2729–2740
50. Göhler D, Khosrawipour V, Khosrawipour T, Diaz-Carballo D, Falkenstein TA, Zieren J *et al.* Technical description of the microinjection pump (MIP®) and granulometric characterization of the aerosol applied for pressurized intraperitoneal aerosol chemotherapy (PIPAC). *Surg Endosc* 2017;**31**:1778–1784
51. Minnaert A-K, Dakwar GR, Benito JM, García Fernández JM, Ceelen W, De Smedt SC *et al.* High-pressure nebulization as application route for the peritoneal administration of siRNA complexes. *Macromol Biosci* 2017;**17**
52. Van de Sande L, Rahimi-Gorji M, Giordano S, Davoli E, Matteo C, Detlefsen S *et al.* Electrostatic intraperitoneal aerosol delivery of nanoparticles: proof of concept and preclinical validation. *Adv Healthc Mater* 2020;**9**:e2000655

53. Van de Sande L, Willaert W, Cosyns S, De Clercq K, Shariati M, Remaut K *et al.* Establishment of a rat ovarian peritoneal metastasis model to study pressurized intraperitoneal aerosol chemotherapy (PIPAC). *BMC Cancer* 2019;**19**:424
54. Davigo A, Passot G, Vassal O, Bost M, Tavernier C, Decullier E *et al.* PIPAC versus HIPEC: cisplatin spatial distribution and diffusion in a swine model. *Int J Hyperthermia* 2020;**37**:144–150
55. Tavernier C, Passot G, Vassal O, Allaouchiche B, Decullier E, Bakrin N *et al.* Pressurized intraperitoneal aerosol chemotherapy (PIPAC) might increase the risk of anastomotic leakage compared to HIPEC: an experimental study. *Surg Endosc* 2020;**34**:2939–2946
56. Rezniczek GA, Buggisch J, Sobilo J, Launay A, Lerondel S, Le Pape A *et al.* Establishment of a mouse ovarian cancer and peritoneal metastasis model to study intraperitoneal chemotherapy. *Cancers (Basel)* 2020;**12**:3818
57. Eveno C, Haidara A, Ali I, Pimpie C, Mirshahi M, Pocard M. Experimental pharmacokinetics evaluation of chemotherapy delivery by PIPAC for colon cancer: first evidence for efficacy. *Pleura Peritoneum* 2017;**2**:103–109
58. Mimouni M, Richard C, Adenot P, Letheule M, Tarrade A, Sandra O *et al.* Pressurized intra-peritoneal aerosol chemotherapy (PIPAC): increased intraperitoneal pressure does not affect distribution patterns but leads to deeper penetration depth of doxorubicin in a sheep model. *BMC Cancer* 2021;**21**:461
59. Seitenfus R, Kalil AN, de Barros ED, Galeano Zettler C, Dos Santos GO, Glehen O *et al.* Assessment of the aerosol distribution pattern of a single-port device for intraperitoneal administration of therapeutic substances. *Surg Endosc* 2019; **33**:3503–3510
60. Lee HS, Kim J, Lee EJ, Park SJ, Mun J, Paik H *et al.* Evaluation of a novel prototype for pressurized intraperitoneal aerosol chemotherapy. *Cancers (Basel)* 2020;**12**:633
61. Mun J, Park SJ, Kim HS. Rotational intraperitoneal pressurized aerosol chemotherapy in a porcine model. *Gland Surg* 2021;**10**: 1271–1275
62. Jung DH, Son SY, Oo AM, Park YS, Shin DJ, Ahn SH *et al.* Feasibility of hyperthermic pressurized intraperitoneal aerosol chemotherapy in a porcine model. *Surg Endosc* 2016; **30**:4258–4264
63. Tan HL, Kim G, Charles CJ, Li RR, Jang CJM, Shabbir A *et al.* Safety, pharmacokinetics and tissue penetration of PIPAC paclitaxel in a swine model. *Eur J Surg Oncol* 2021;**47**: 1124–1131
64. Keck HS, Weinreich F-J, Shegokar R, Königsrainer A, Reymond MA, Nadiradze G. Experimental evaluation of icodextrin delivery as pressurized aerosol (PIPAC): antiadhesive and cytotoxic effects. *Eur J Surg Oncol* 2021;**47**:1434–1440
65. Weinreich J, Struller F, Sautkin I, Giuashvili S, Reymond M, Königsrainer A *et al.* Chemosensitivity of various peritoneal cancer cell lines to HIPEC and PIPAC: comparison of an experimental duplex drug to standard drug regimens *in vitro*. *Invest New Drugs* 2019;**37**:415–423
66. Mikolajczyk A, Khosrawipour V, Schubert J, Grzesiak J, Chaudhry H, Pigazzi A *et al.* Effect of liposomal doxorubicin in pressurized intra-peritoneal aerosol chemotherapy (PIPAC). *J Cancer* 2018;**9**:4301–4305
67. Schubert J, Khosrawipour V, Chaudhry H, Arafkas M, Knoefel WT, Pigazzi A *et al.* Comparing the cytotoxicity of taurolidine, mitomycin C, and oxaliplatin on the proliferation of in vitro colon carcinoma cells following pressurized intra-peritoneal aerosol chemotherapy (PIPAC). *World J Surg Oncol* 2019;**17**:93
68. Park S, Park SJ, Lee HS, Ham J, Lee EJ, Kim J *et al.* Establishment of an experimental system for intraperitoneal chemotherapy in a rat model. *In Vivo* 2021;**35**:2703–2710
69. Piao J, Park SJ, Lee H, Kim J, Park S, Lee N *et al.* Ideal nozzle position during pressurized intraperitoneal aerosol chemotherapy in an *ex vivo* model. *Anticancer Res* 2021;**41**: 5489–5498
70. Braet H, Rahimi-Gorji M, Debbaut C, Ghorbaniasl G, Van Walleghem T, Cornelis S *et al.* Exploring high pressure nebulization of Pluronic F127 hydrogels for intraperitoneal drug delivery. *Eur J Pharm Biopharm* 2021;**169**:134–143
71. Göhler D, Geldner A, Gritzki R, Lohse F, Große S, Sobilo J *et al.* Development of a rat capnoperitoneum phantom to study drug aerosol deposition in the context of anticancer research on peritoneal carcinomatosis. *Sci Rep* 2021;**11**:21843
72. Tempfer CB, Hartmann F, Hilal Z, Rezniczek GA. Intraperitoneal cisplatin and doxorubicin as maintenance chemotherapy for unresectable ovarian cancer: a case report. *BMC Cancer* 2017;**17**:26
73. Tempfer CB, Solass W, Buerkle B, Reymond MA. Pressurized intraperitoneal aerosol chemotherapy (PIPAC) with cisplatin and doxorubicin in a woman with pseudomyxoma peritonei: a case report. *Gynecol Oncol Rep* 2014;**10**:32–35
74. Reymond M, Demtroeder C, Solass W, Winnekendonk G, Tempfer C. Electrostatic precipitation pressurized intraperitoneal aerosol chemotherapy (ePIPAC): first in-human application. *Pleura Peritoneum* 2016;**1**:109–116
75. Giger-Pabst U, Solass W, Buerkle B, Reymond MA, Tempfer CB. Low-dose pressurized intraperitoneal aerosol chemotherapy (PIPAC) as an alternative therapy for ovarian cancer in an octogenarian patient. *Anticancer Res* 2015;**35**:2309–2314
76. Solanki SL, Kumar PP, DeSouza A, Saklani AP. Perioperative concerns and management of pressurised intraperitoneal aerosolised chemotherapy: report of two cases. *Indian J Anaesth* 2018;**62**:225–228
77. Graversen M, Detlefsen S, Bjerregaard JK, Pfeiffer P, Mortensen MB. Peritoneal metastasis from pancreatic cancer treated with pressurized intraperitoneal aerosol chemotherapy (PIPAC). *Clin Exp Metastasis* 2017;**34**:309–314
78. Rotolo S, Ferracci F, Santullo F, Lodoli C, Inzani F, Abatini C *et al.* Systemic chemotherapy and pressurized intraperitoneal aerosol chemotherapy (PIPAC): a case report of a multimodal treatment for peritoneal metastases of pancreatic origin. *Int J Surg Case Rep* 2020;**77S**:S75–S78
79. Nowacki M, Grzanka D, Zegarski W. Pressurized intraperitoneal aerosol chemotherapy after misdiagnosed gastric cancer: case report and review of the literature. *World J Gastroenterol* 2018;**24**:2130–2136
80. Horvath P, Yurttas C, Struller F, Bösmüller H, Lauer UM, Nadalin S *et al.* Pressurized intraperitoneal aerosol chemotherapy (PIPAC) for peritoneal metastases in solid organ graft recipients: first experience. *Ann Transplant* 2019;**24**:30–35
81. Ezanno AC, Malgras B, Aoun O, Delarge A, Doreille A, Pocard M. A severe oxaliplatin immune-induced syndrome after oxaliplatin-based pressurized intraperitoneal aerosol chemotherapy (PIPAC). *Pleura Peritoneum* 2022;**7**:35–38
82. Akaishi EH, da Silva DG V, Lima HVG, Grapperon-Mathis RLM, Arakaki MS, Galindo IVA *et al.* Pressurized intraperitoneal aerosol chemotherapy (PIPAC): the first reported case in Brazil using standardized technique with the Capnopen® nebulizer device. *Am J Case Rep* 2021;**22**:e933906
83. Somashekhar SP, Ashwin KR, Kumar CR, Rauthan A, Rakshit SH. Pressurized intraperitoneal aerosol chemotherapy

procedure for nonresectable peritoneal carcinomatosis: first Indian study. *South Asian J Cancer* 2019;**8**:27–30
84. Somashekhar SP, Rajagopal AK, Zaveri SS, Chandrashekhar RK, Rauthan A, Rakshit SH. First Indian study on pressurized intraperitoneal aerosol chemotherapy (PIPAC) procedure for advanced peritoneal carcinomatosis secondary to epithelial ovarian cancer. *Indian J Gynecol Oncol* 2018;**16**:25
85. Feldbrügge L, Gronau F, Brandl A, Auer TA, Oeff A, Thuss-Patience P *et al.* Systemic chemotherapy including ramucirumab in combination with pressurized intra-peritoneal aerosol chemotherapy is a safe treatment option for peritoneal metastasis of gastric cancer. *Front Oncol* 2020;**10**:610572
86. Tempfer CB, Celik I, Solass W, Buerkle B, Pabst UG, Zieren J *et al.* Activity of pressurized intraperitoneal aerosol chemotherapy (PIPAC) with cisplatin and doxorubicin in women with recurrent, platinum-resistant ovarian cancer: preliminary clinical experience. *Gynecol Oncol* 2014;**132**:307–311
87. Tempfer CB, Hilal Z, Dogan A, Petersen M, Rezniczek GA. Concentrations of cisplatin and doxorubicin in ascites and peritoneal tumor nodules before and after pressurized intraperitoneal aerosol chemotherapy (PIPAC) in patients with peritoneal metastasis. *Eur J Surg Oncol* 2018;**44**:1112–1117
88. Rezniczek GA, Jüngst F, Jütte H, Tannapfel A, Hilal Z, Hefler LA *et al.* Dynamic changes of tumor gene expression during repeated pressurized intraperitoneal aerosol chemotherapy (PIPAC) in women with peritoneal cancer. *BMC Cancer* 2016;**16**:654
89. Gockel I, Jansen-Winkeln B, Haase L, Niebisch S, Moulla Y, Lyros O *et al.* Pressurized intraperitoneal aerosol chemotherapy (PIPAC) in patients with peritoneal metastasized colorectal, appendiceal and small bowel cancer. *Tumori* 2020;**106**:70–78
90. Gockel I, Jansen-Winkeln B, Haase L, Rhode P, Mehdorn M, Niebisch S *et al.* Pressurized intraperitoneal aerosol chemotherapy (PIPAC) in gastric cancer patients with peritoneal metastasis (PM): results of a single-center experience and register study. *J Gastric Cancer* 2018;**18**:379
91. Graversen M, Detlefsen S, Asmussen J, Mahdi B, Fristrup C, Pfeiffer P *et al.* Treatment of peritoneal carcinomatosis with pressurized intraperitoneal aerosol chemotherapy—PIPAC-OPC2. *Pleura Peritoneum* 2018;**3**:20180108
92. Graversen M, Detlefsen S, Bjerregaard JK, Fristrup CW, Pfeiffer P, Mortensen MB. Prospective, single-center implementation and response evaluation of pressurized intraperitoneal aerosol chemotherapy (PIPAC) for peritoneal metastasis. *Ther Adv Med Oncol* 2018;**10**:1758835918777036
93. Graversen M, Detlefsen S, Ellebaek SB, Fristrup C, Pfeiffer P, Mortensen MB. Pressurized intraperitoneal aerosol chemotherapy with one minute of electrostatic precipitation (ePIPAC) is feasible, but the histological tumor response in peritoneal metastasis is insufficient. *Eur J Surg Oncol* 2020;**46**:155–159
94. Graversen M, Fristrup C, Kristensen TK, Larsen TR, Pfeiffer P, Mortensen MB *et al.* Detection of free intraperitoneal tumour cells in peritoneal lavage fluid from patients with peritoneal metastasis before and after treatment with pressurised intraperitoneal aerosol chemotherapy (PIPAC). *J Clin Pathol* 2019;**72**:368–372
95. Robella M, Berchialla P, Borsano A, Cinquegrana A, Ilari Civit A, De Simone M *et al.* Study protocol: phase I dose escalation study of oxaliplatin, cisplatin and doxorubicin applied as PIPAC in patients with peritoneal metastases. *Int J Environ Res Public Health* 2021;**18**:5656
96. Robella M, Vaira M, Argenziano M, Spagnolo R, Cavalli R, Borsano A *et al.* Exploring the use of pegylated liposomal doxorubicin (Caelyx®) as pressurized intraperitoneal aerosol chemotherapy. *Front Pharmacol* 2019;**10**:669
97. Robella M, Vaira M, De Simone M. Safety and feasibility of pressurized intraperitoneal aerosol chemotherapy (PIPAC) associated with systemic chemotherapy: an innovative approach to treat peritoneal carcinomatosis. *World J Surg Oncol* 2016;**14**:128
98. Vaira M, Robella M, Borsano A, De Simone M. Single-port access for pressurized intraperitoneal aerosol chemotherapy (PIPAC): technique, feasibility and safety. *Pleura Peritoneum* 2016;**1**:217–222
99. Kuchen N, Cereser T, Hailemariam S, Schoeb O. Safety and efficacy of pressurized intraperitoneal/intrathoracic aerosol chemotherapy (PIPAC/PITAC) in patients with peritoneal and/or pleural carcinomatosis: a preliminary experience. *J Med Ther* 2018;**2**:2–6
100. Račkauskas R, Baušys A, Lukšta M, Jurgaitis J, Paškonis M, Strupas K. Pressurized intraperitoneal aerosol chemotherapy (PIPAC) for peritoneal malignancy: initial experience of the first program in the Baltic countries. *World J Surg Oncol* 2021;**19**:236
101. Di Giorgio A, Schena CA, El Halabieh MA, Abatini C, Vita E, Strippoli A *et al.* Systemic chemotherapy and pressurized intraperitoneal aerosol chemotherapy (PIPAC): a bidirectional approach for gastric cancer peritoneal metastasis. *Surg Oncol* 2020;**34**:270–275
102. Di Giorgio A, Sgarbura O, Rotolo S, Schena CA, Bagalà C, Inzani F *et al.* Pressurized intraperitoneal aerosol chemotherapy with cisplatin and doxorubicin or oxaliplatin for peritoneal metastasis from pancreatic adenocarcinoma and cholangiocarcinoma. *Ther Adv Med Oncol* 2020;**12**:1758835920940887
103. Giger-Pabst U, Demtröder C, Falkenstein TA, Ouaissi M, Götze TO, Rezniczek GA *et al.* Pressurized intraperitoneal aerosol chemotherapy (PIPAC) for the treatment of malignant mesothelioma. *BMC Cancer* 2018;**18**:442
104. Hilal Z, Rezniczek GA, Klenke R, Dogan A, Tempfer CB. Nutritional status, cachexia, and anorexia in women with peritoneal metastasis and intraperitoneal chemotherapy: a longitudinal analysis. *J Gynecol Oncol* 2017;**28**:e80
105. Nadiradze G, Giger-Pabst U, Zieren J, Strumberg D, Solass W, Reymond MA. Pressurized intraperitoneal aerosol chemotherapy (PIPAC) with low-dose cisplatin and doxorubicin in gastric peritoneal metastasis. *J Gastrointest Surg* 2016;**20**:367–373
106. Lurvink RJ, Tajzai R, Rovers KP, Wassenaar ECE, Moes DJAR, Pluimakers G *et al.* Systemic pharmacokinetics of oxaliplatin after intraperitoneal administration by electrostatic pressurized intraperitoneal aerosol chemotherapy (ePIPAC) in patients with unresectable colorectal peritoneal metastases in the CRC-PIPAC trial. *Ann Surg Oncol* 2021;**28**:265–272
107. Willaert W, Van de Sande L, Van Daele E, Van De Putte D, Van Nieuwenhove Y, Pattyn P *et al.* Safety and preliminary efficacy of electrostatic precipitation during pressurized intraperitoneal aerosol chemotherapy (PIPAC) for unresectable carcinomatosis. *Eur J Surg Oncol* 2019;**45**:2302–2309
108. Hübner M, Teixeira Farinha H, Grass F, Wolfer A, Mathevet P, Hahnloser D *et al.* Feasibility and safety of pressurized intraperitoneal aerosol chemotherapy for peritoneal carcinomatosis: a retrospective cohort study. *Gastroenterol Res Pract* 2017;**2017**:6852749

109. Farinha HT, Grass F, Kefleyesus A, Achtari C, Romain B, Montemurro M *et al.* Impact of pressurized intraperitoneal aerosol chemotherapy on quality of life and symptoms in patients with peritoneal carcinomatosis: a retrospective cohort study. *Gastroenterol Res Pract* 2017;**2017**:4596176
110. Farinha HT, Grass F, Labgaa I, Pache B, Demartines N, Hübner M. Inflammatory response and toxicity after pressurized intraperitoneal aerosol chemotherapy. *J Cancer* 2018;**9**:13–20
111. Larbre V, Alyami M, Mercier F, Vantard N, Bonnefoy I, Opsomer MA *et al.* No renal toxicity after repeated treatment with pressurized intraperitoneal aerosol chemotherapy (PIPAC) in patients with unresectable peritoneal metastasis. *Anticancer Res* 2018;**38**:6869–6875
112. Khomyakov V, Ryabov A, Ivanov A, Bolotina L, Utkina A, Volchenko N *et al.* Bidirectional chemotherapy in gastric cancer with peritoneal metastasis combining intravenous XELOX with intraperitoneal chemotherapy with low-dose cisplatin and doxorubicin administered as a pressurized aerosol: an open-label, phase-2 study (PIPAC-GA2). *Pleura Peritoneum* 2016;**1**:159–166
113. Katdare N, Prabhu R, Mishra S, Mehta S, Bhatt A. Pressurized intraperitoneal aerosol chemotherapy (PIPAC): initial experience from Indian centers and a review of literature. *Indian J Surg Oncol* 2019;**10**:24–30
114. Ceribelli C, Debs T, Chevallier A, Piche MA, Bereder JM. Initial experience of pressurized intraperitoneal aerosol chemotherapy (PIPAC) in a French hyperthermic intraperitoneal chemotherapy (HIPEC) expert center. *Surg Endosc* 2020;**34**:2803–2806
115. Ellebæk 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**:325–332
116. Ellebæk SB, Graversen M, Detlefsen S, Lundell L, Fristrup CW, Pfeiffer P *et al.* Pressurized intraperitoneal aerosol chemotherapy (PIPAC)-directed treatment of peritoneal metastasis in end-stage colo-rectal cancer patients. *Pleura Peritoneum* 2020;**5**:20200109
117. Nielsen M, Graversen M, Ellebæk SB, Kristensen TK, Fristrup C, Pfeiffer P *et al.* Next-generation sequencing and histological response assessment in peritoneal metastasis from pancreatic cancer treated with PIPAC. *J Clin Pathol* 2021;**74**:19–24
118. Kim G, Tan HL, Sundar R, Lieske B, Chee CE, Ho J *et al.* PIPAC-OX: a phase I study of oxaliplatin-based pressurized intraperitoneal aerosol chemotherapy in patients with peritoneal metastases. *Clin Cancer Res* 2021;**27**:1875–1881
119. Nowacki M, Nowacka K, Głowacka I, Zegarska B, Zegarski W. Overall clinical and trichoscopic analysis performed in patients who underwent pressurized intraperitoneal aerosol chemotherapy (PIPAC) treatment for peritoneal carcinomatosis—initial trial preliminary report. *Postepy Dermatol Alergol* 2019;**36**:461–467
120. Nowacki M, Zegarski W. The scientific report from the first pressurized intraperitoneal aerosol chemotherapy (PIPAC) procedures performed in the eastern part of Central Europe. *J Int Med Res* 2018;**46**:3748–3758
121. Horvath P, Beckert S, Struller F, Königsrainer A, Reymond MA. Pressurized intraperitoneal aerosol chemotherapy (PIPAC) for peritoneal metastases of pancreas and biliary tract cancer. *Clin Exp Metastasis* 2018;**35**:635–640
122. Struller F, Horvath P, Solass W, Weinreich F-J, 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**:175883591984640
123. De Simone M, Vaira M, Argenziano M, Berchialla P, Pisacane A, Cinquegrana A *et al.* Pressurized intraperitoneal aerosol chemotherapy (PIPAC) with oxaliplatin, cisplatin, and doxorubicin in patients with peritoneal carcinomatosis: an open-label, single-arm. phase II clinical trial. *Biomedicines* 2020;**8**:102
124. Kepenekian V, Péron J, You B, Bonnefoy I, Villeneuve L, Alyami M *et al.* Non-resectable malignant peritoneal mesothelioma treated with pressurized intraperitoneal aerosol chemotherapy (PIPAC) plus systemic chemotherapy could lead to secondary complete cytoreductive surgery: a cohort study. *Ann Surg Oncol* 2022;**29**:2104–2113
125. Tidadini F, Abba J, Quesada JL, Baudrant M, Bonne A, Foote A *et al.* Effect of pressurized intraperitoneal aerosol chemotherapy on the survival rate of patients with peritoneal carcinomatosis of gastric origin. *J Gastrointest Cancer* 2021. doi:10.1007/s12029-021-00698-8. Epub ahead of print. PMID: 34677795
126. Lurvink RJ, Rovers KP, Wassenaar ECE, Bakkers C, Burger JWA, Creemers GJM *et al.* Patient-reported outcomes during repetitive oxaliplatin-based pressurized intraperitoneal aerosol chemotherapy for isolated unresectable colorectal peritoneal metastases in a multicenter, single-arm, phase 2 trial (CRC-PIPAC). *Surg Endosc* 2022;**36**:4486–4498
127. Van De Sande L, Graversen M, Hubner M, Pocard M, Reymond M, Vaira M *et al.* Intraperitoneal aerosolization of albumin-stabilized paclitaxel nanoparticles (Abraxane™) for peritoneal carcinomatosis—a phase I first-in-human study. *Pleura Peritoneum* 2018;**3**:20180112
128. Raoof M, Malhotra G, Kohut A, O'Leary M, Frankel P, Tran T *et al.* PIPAC for the treatment of gynecologic and gastrointestinal peritoneal metastases: technical and logistic considerations of a phase 1 trial. *Ann Surg Oncol* 2022;**29**:175–185
129. Dumont F, Senellart H, Pein F, Campion L, Glehen O, Goere D *et al.* Phase I/II study of oxaliplatin dose escalation via a laparoscopic approach using pressurized aerosol intraperitoneal chemotherapy (PIPOX trial) for nonresectable peritoneal metastases of digestive cancers (stomach, small bowel and colorectal): Rationale and design. *Pleura Peritoneum* 2018;**3**:20180120
130. Kim G, Tan HL, Chen E, Teo SC, Jang CJM, Ho J *et al.* Study protocol: phase 1 dose escalating study of Pressurized Intra-Peritoneal Aerosol Chemotherapy (PIPAC) with oxaliplatin in peritoneal metastasis. *Pleura Peritoneum* 2018;**3**:20180118
131. Reid JL, Kanhere HA, Hewett PJ, Price TJ, Maddern GJ, Trochsler MI. Can pressurised intraperitoneal aerosol chemotherapy with oxaliplatin (PIPAC-O+) be added to standard treatment for resectable high-risk gastric cancer patients? a study protocol. *Pleura Peritoneum* 2021;**6**:151–154
132. Girshally R, Demtröder C, Albayrak N, Zieren J, Tempfer C, Reymond MA. Pressurized intraperitoneal aerosol chemotherapy (PIPAC) as a neoadjuvant therapy before cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. *World J Surg Oncol* 2016;**14**:253
133. Tempfer CB, Rezniczek GA, Ende P, Solass W, Reymond MA. Pressurized intraperitoneal aerosol chemotherapy with cisplatin and doxorubicin in women with peritoneal carcinomatosis: a cohort study. *Anticancer Res* 2015;**35**:6723–6729

134. Tempfer CB, Winnekendonk G, Solass W, Horvat R, Giger-Pabst U, Zieren J *et al.* Pressurized intraperitoneal aerosol chemotherapy in women with recurrent ovarian cancer: a phase 2 study. *Gynecol Oncol* 2015;**137**:223–228
135. Rovers KP, Lurvink RJ, Wassenaar EC, Kootstra TJ, Scholten HJ, Tajzai R *et al.* Repetitive electrostatic pressurised intraperitoneal aerosol chemotherapy (ePIPAC) with oxaliplatin as a palliative monotherapy for isolated unresectable colorectal peritoneal metastases: protocol of a Dutch, multicentre, open-label, single-arm, phase II study (CRC-PIPAC). *BMJ Open* 2019;**9**:e030408
136. Rovers KP, Wassenaar ECE, Lurvink RJ, Creemers G-JM, Burger JWA, Los M *et al.* Pressurized intraperitoneal aerosol chemotherapy (oxaliplatin) for unresectable colorectal peritoneal metastases: a multicenter, single-arm, phase II trial (CRC-PIPAC). *Ann Surg Oncol* 2021;**28**:5311–5326
137. Alyami M, Bonnot P-E, Mercier F, Laplace N, Villeneuve L, Passot G *et al.* Pressurized intraperitoneal aerosol chemotherapy (PIPAC) for unresectable peritoneal metastasis from gastric cancer. *Eur J Surg Oncol* 2021;**47**:123–127
138. Siebert M, Alyami M, Mercier F, Gallice C, Villeneuve L, Laplace N *et al.* Pressurized intraperitoneal aerosol chemotherapy (PIPAC) in association with systemic chemotherapy and bevacizumab, evaluation of safety and feasibility. A single center comparative study. *Eur J Surg Oncol* 2021;**47**:139–142
139. Sgarbura O, Hübner M, Alyami M, Eveno C, Gagnière J, Pache B *et al.* Oxaliplatin use in pressurized intraperitoneal aerosol chemotherapy (PIPAC) is safe and effective: a multicenter study. *Eur J Surg Oncol* 2019;**45**:2386–2391
140. Graversen M, Detlefsen S, Fristrup C, Pfeiffer P, Mortensen MB. Adjuvant pressurized intraperitoneal aerosol chemotherapy (PIPAC) in resected high-risk colon cancer patients—study protocol for the PIPAC-OPC3 Trial. A prospective, controlled phase 2 Study. *Pleura Peritoneum* 2018;**3**:20180107
141. Graversen M, Lundell L, Fristrup C, Pfeiffer P, Mortensen MB. Pressurized intraperitoneal aerosol chemotherapy (PIPAC) as an outpatient procedure. *Pleura Peritoneum* 2018;**3**:20180128
142. Nowacki M, Alyami M, Villeneuve L, Mercier F, Hubner M, Willaert W *et al.* Multicenter comprehensive methodological and technical analysis of 832 pressurized intraperitoneal aerosol chemotherapy (PIPAC) interventions performed in 349 patients for peritoneal carcinomatosis treatment: an international survey study. *Eur J Surg Oncol* 2018;**44**:991–996
143. Kurtz F, Struller F, Horvath P, Solass W, Bösmüller H, Königsrainer A *et al.* Feasibility, safety, and efficacy of pressurized intraperitoneal aerosol chemotherapy (PIPAC) for peritoneal metastasis: a registry study. *Gastroenterol Res Pract* 2018;**2018**:2743985
144. Sindayigaya R, Dogan C, Demtröder CR, Fischer B, Karam E, Buggisch JR *et al.* Clinical outcome for patients managed with low-dose cisplatin and doxorubicin delivered as pressurized intraperitoneal aerosol chemotherapy for unresectable peritoneal metastases of gastric cancer. *Ann Surg Oncol* 2022; **29**:112–123
145. Tabchouri N, Buggisch J, Demtröder CR, Thiery J, Rezniczek G, Tempfer CB *et al.* Pressurized intraperitoneal aerosol chemotherapy for colorectal peritoneal metastases. *Ann Surg Oncol* 2021;**28**:5275–5286
146. Somashekhar SP, Ashwin KR, Rauthan A, Rohit KC. Pressurized intraperitoneal aerosol chemotherapy vs. intravenous chemotherapy for unresectable peritoneal metastases secondary to platinum resistant ovarian cancer—study protocol for a randomized control trial. *Pleura Peritoneum* 2019;**4**:20180111
147. Somashekhar SP, Ashwin KR, Rauthan CA, Rohit KC. Randomized control trial comparing quality of life of patients with end-stage peritoneal metastasis treated with pressurized intraperitoneal aerosol chemotherapy (PIPAC) and intravenous chemotherapy. *Pleura Peritoneum* 2018;**3**:20180110
148. Goetze T O, Al-Batran S-E, Pabst U, Reymond M, Tempfer C, Bechstein WO *et al.* Pressurized intraperitoneal aerosol chemotherapy (PIPAC) in combination with standard of care chemotherapy in primarily untreated chemo naïve upper GI-adenocarcinomas with peritoneal seeding—a phase II/III trial of the AIO/CAOGI/ACO. *Pleura Peritoneum* 2018;**3**:20180113
149. Bakrin N, Tempfer C, Scambia G, De Simone M, Gabriel B, Grischke E-M *et al.* PIPAC-OV3: a multicenter, open-label, randomized, two-arm phase III trial of the effect on progression-free survival of cisplatin and doxorubicin as Pressurized Intra-Peritoneal Aerosol Chemotherapy (PIPAC) vs. chemotherapy alone in patients with platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer. *Pleura Peritoneum* 2018;**3**:20180114
150. Sgarbura O, Gourgou S, Tosi D, Bakrin N, Bouazza N, Delaine S *et al.* MESOTIP: phase II multicenter randomized trial evaluating the association of PIPAC and systemic chemotherapy vs. systemic chemotherapy alone as 1st-line treatment of malignant peritoneal mesothelioma. *Pleura Peritoneum* 2019;**4**:20190010
151. Eveno C, Jouvin I, Pocard M. PIPAC EstoK 01: pressurized intraperitoneal aerosol chemotherapy with cisplatin and doxorubicin (PIPAC C/D) in gastric peritoneal metastasis: a randomized and multicenter phase II study. *Pleura Peritoneum* 2018;**3**:20180116
152. National Institute for Health and Care Excellence. Pressurised intraperitoneal aerosol chemotherapy for peritoneal carcinomatosis. https://www.nice.org.uk/guidance/ipg681/chapter/1-Recommendations (accessed 30 March 2022)

European Colorectal Congress

28 November – 1 December 2022, St.Gallen, Switzerland

Monday, 28 November 2022

09.50
Opening and welcome
Jochen Lange, St.Gallen, CH

10.00
It is leaking! Approaches to salvaging an anastomosis
Willem Bemelman, Amsterdam, NL

10.30
Predictive and diagnostic markers of anastomotic leak
Andre D'Hoore, Leuven, BE

11.00
SATELLITE SYMPOSIUM
ETHICON

11.45
Of microbes and men – the unspoken story of anastomotic leakage
James Kinross, London, UK

12.15
LUNCH

13.45
Operative techniques to reduce anastomotic recurrence in Crohn's disease
Laura Hancock, Manchester, UK

14.15
Innovative approaches in the treatment of complex Crohn Diseases perianal fistula
Christianne Buskens, Amsterdam, NL

14.45
To divert or not to divert in Crohn surgery – technical aspects and patient factors
Pär Myrelid, Linköping, SE

15.15
COFFEE BREAK

15.45
Appendiceal neoplasia – when to opt for a minimal approach, when and how to go for a maximal treatment
Tom Cecil, Basingstoke, Hampshire, UK

16.15
SATELLITE SYMPOSIUM
Medtronic
Further,Together

17.00
Outcomes of modern induction therapies and Wait and Watch strategies, Hope or Hype
Antonino Spinelli, Milano, IT

17.30
EAES Presidential Lecture - Use of ICG in colorectal surgery: beyond bowel perfusion
Salvador Morales-Conde, Sevilla, ES

18.00
Get-Together with your colleagues
Industrial Exhibition

Tuesday, 29 November 2022

9.00
CONSULTANT'S CORNER
Michel Adamina, Winterthur, CH

10.30
COFFEE BREAK

11.00
SATELLITE SYMPOSIUM
INTUITIVE

11.45
Trends in colorectal oncology and clinical insights for the near future
Rob Glynne-Jones, London, UK

12.15
LUNCH

13.45
VIDEO SESSION

14.15
SATELLITE SYMPOSIUM
BD

15.00
COFFEE BREAK

15.30
The unsolved issue of TME: open, robotic, transanal, or laparoscopic – shining light on evidence and practice
Des Winter, Dublin, IE
Jim Khan, London, UK
Brendan Moran, Basingstoke, UK

16.30
SATELLITE SYMPOSIUM
Takeda

17.15
Lars Pahlman lecture
Søren Laurberg, Aarhus, DK

Thursday, 1 December 2022
Masterclass in Colorectal Surgery
Proctology Day

Wednesday, 30 November 2022

9.00
Advanced risk stratification in colorectal cancer – choosing wisely surgery and adjuvant therapy
Philip Quirke, Leeds, UK

09.30
Predictors for Postoperative Complications and Mortality
Ronan O'Connell, Dublin, IE

10.00
Segmental colectomy versus extended colectomy for complex cancer
Quentin Denost, Bordeaux, FR

10.30
COFFEE BREAK

11.00
Incidental cancer in polyp - completion surgery or endoscopy treatment alone?
Laura Beyer-Berjot, Marseille, FR

11.30
SATELLITE SYMPOSIUM
EVOLUZIONE DISPOSITIVI MEDICI

12.00
Less is more – pushing the boundaries of full-thickness rectal resection
Xavier Serra-Aracil, Barcelona, ES

12.30
LUNCH

14.00
Management of intestinal neuroendocrine neoplasia
Frédéric Ris, Geneva, CH

14.30
Poster Presentation & Best Poster Award
Michel Adamina, Winterthur, CH

15.00
SATELLITE SYMPOSIUM
OLYMPUS

15.45
COFFEE BREAK

16.15
Reoperative pelvic floor surgery – dealing with perineal hernia, reoperations, and complex reconstructions
Guillaume Meurette, Nantes, FR

16.45
Salvage strategies for rectal neoplasia
Roel Hompes, Amsterdam, NL

17.15
Beyond TME – technique and results of pelvic exenteration and sacrectomy
Paris Tekkis, London, UK

19.30
FESTIVE EVENING

Information & Registration **www.colorectalsurgery.eu**