ulusal CERRAHİ ONKOLOJİ KONGRESİ 6
24 - 27 Şubat 2022 | Gloria Golf Resort – ANTALYA

Dr. Ali Duran
BALIKESİR ÜNV. TIP FAKÜLTESİ GENEL CERRAHİ ANABİLİM DALI

EPİC, PİPAC, BANC, İNTRAPERİTONEAL İMMÜNOTERAPİ ve ÖTESİ

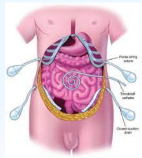
EPİC

(Early Postoperative Intraperitoneal Chemotherapy)

-Sitoredüktif Cerrahi

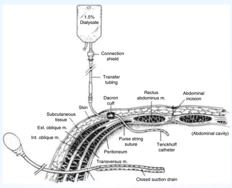
-Drenler ve Kateter

-Sızıntı testi



EPİC

(Early Postoperative Intraperitoneal Chemotherapy)



EPİC

(Early Postoperative Intraperitoneal Chemotherapy)

- **Postoperatif** %1.5 Dex. Periton Diyaliz solüsyonu ile irrigasyon
- **1. Gün:** % 1.5 Dex. Diyaliz solüsyonu 1L (10 mg/m² Mitomisin C)
- **1-5. Gün:** % 1.5 Dex. Diyaliz solüsyonu 1L (700 mg/m² 5-FU+ 50 mEq NaHCO3)

Major series on IPHC and/or EPIC after cytoreductive surgery for PMP, DMPM, and CRPC

Chief investigator	Year	Treatment center	Type	n	Intraperitoneal chemotherapy	Survival (%) 3-yr	Survival (%) 5-yr
Piso et al[1]	2001	Hanover, Germany	PMP	17	IPHC: cisplatin	75	-
Butterworth et al[2]	2002	Vancouver, Canada	PMP	11	EPIC: 5-FU + mitomycin	60	-
Witkamp et al[3]	2001	Amsterdam, Netherlands	PMP	46	IPHC: mitomycin	81	-
Sugarbaker et al[4]	2001	Washington, USA	PMP	501	EPIC: 5-FU + mitomycin	-	80
					IPHC: mitomycin		
Loggie et al[5]	2001	Winston-Salem, USA	DMPM	12	IPHC: mitomycin	50	-
Sebbag et al[6]	2000	Washington, USA	DMPM	33	IPHC: cisplatin + doxorubicin	56	47
Sugarbaker et al[7]	2003	Washington, USA	DMPM	68	IPHC: cisplatin + doxorubicin	60	50
					EPIC: paclitaxel		
Feldman et al[8]	2003	Bethesda, USA	DMPM	49	IPHC: cisplatin ± paclitaxel	-	59
Fujimura et al[9]	1999	Kanazawa, Japan	CRPC	14	IPHC: cisplatin + mitomycin + etoposide	21	-
Witkamp et al[10]	2001	Amsterdam, Netherlands	CRPC	29	IPHC: mitomycin	23	-
Elias et al[11]	2001	Villejuif, France	CRPC	64	IPHC: mitomycin ± cisplatin	47	27
					EPIC: mitomycin + 5-FU		
Pestieau et al[12]	2000	Washington, USA	CRPC	104	IPHC: mitomycin	45	30
					EPIC: 5-FU		
Zoetmulder et al[13]	2002	Amsterdam, Netherlands	CRPC	94	IPHC: mitomycin	-	30
Shen et al[14]	2004	Winston-Salem, USA	CRPC	77	IPHC: mitomycin	25	17
Glehen et al[15]	2004	Multi-institutions	CRPC	506	IPHC or EPIC	-	-

IPHC: Intraperitoneal hyperthermic chemotherapy; EPIC: Early postoperative intraperitoneal chemotherapy; PMP: Pseudo-myxoma peritonei; DMPM: Diffuse malignant peritoneal mesothelioma; CRPC: Colo-rectal peritoneal carcinomatosis.

Drug	Type	Molecular weight	AUC ratio	Dose	Carrier solution	Incompatibility in solution	Heat synergy	Heat stability	Stability in solution at room temperature	Depth of penetration	Unusual local toxicity	Metabolism
Doxorubicin	Antitumor Antibiotic	579.99	230	15 mg/m²	1.5% dextrose dialysis solution	Heparin Fluorouracil	Yes	42.0	7 days	4–6 cell layers	Peritoneal sclerosis, abdominal pain with instillation	Hepatic metabolism with biliary excretion: 40%–50% Renal: 4%–5%
Melphalan	Alkylator	305.2	93	70 mg/m²	0.9% sodium chloride	N/A	Marked	42.0	2 hours	N/A	N/A	Primarily non-renal
Mitomycin C	Antitumor Antibiotic	334.3	23.5	35 mg/m²	1.5% dextrose dialysis solution	Bleomycin	Yes	42.5	58 ± 10 minutes in perfusate	2,000 μ	Bowel perforation, anastomotic dehiscence	25% first pass. Urine excretion: 10%–30%
Cisplatin	Alkylator	300.1	7.8	90 mg/m²	0.9% sodium chloride	N/A	Yes	41.5	20 hours	1–3 mm	N/A	Nonenzymatic conversion, renal excretion
Gemcitabine	Pyrimidine antagonist	299.5	500	1,000 mg/m²	0.9% sodium chloride	N/A	At 48 hours	42.5	Stable	N/A	N/A	Intracellular metabolism, renal excretion
Mitoxantrone	Antitumor Antibiotic	517.41	115–255	28 mg/m²	0.9% sodium chloride, lactated Ringer's solution	Heparin	Yes	43.0	7 days undiluted	5–6 cellular layers	Abdominal pain, adhesion formation	Excretion: urine and feces
Oxaliplatin	Alkylator	397.3	16	460 mg/m²	5% dextrose	Aluminum alkaline or NaCl solutions	Yes	46.0	6 hours	1–2 mm	N/A	Nonenzymatic biotransformation. Eliminated renal 54% and fecal 2%
Etoposide	Antitumor Antibiotic	588.58	65	25–350 mg/m²	5% dextrose	Plastic devices, acrylic, antibiotics	Yes	42.0	24–96 hours	N/A	N/A	Hepatic metabolism, elimination renal 44%–60%, fecal 16%, bile 6%

Drug	Type	Molecular weight	AUC ratio	Dose	Carrier solution	Incompat-ibility in solution	Heat synergy	Heat stability	Stability in solution at room temperature	Depth of penetration	Unusual local toxicity	Metabolism
Irinotecan	Antitumor Antibiotic	677.19	N/A				No	44.0	12 hours	N/A	N/A	Hepatic bio-transformation SN-38, renal excretion 11%–20%
Paclitaxel	Antimitotic	853.9	1,000	120-180 mg total dose	1.5% dextrose dialysis solution, 6% hetastarch	Plastic containers and tubes	No	42.5	27 hours	>80 cell layers	May leach carcinogen from soft plastic	Hepatic biotrans-formation. Excretion: renal 16% and bile 14%
Docetaxel	Antimitotic	861.9	552	45 mg/m²	0.9% sodium chloride	Plastic containers and tubes	No	N/A	Use within 4 hours	N/A	May leach carcinogen from soft plastic	Excretion: fecal 75% and renal 6%
5-Fluorouracil	Anti-metabolite	130.08	250	650 mg/m² × 5 days	0.9% sodium chloride, Icodextrin, 1.5% dextrose dialysis solution	Daunorubicin, doxorubicin, idaurubicin, cisplatin, icytarabine, diazepan	Minimal	43.0		0.2 mm	Increased with prior radiation therapy	Hepatic degradation 90%, renal 7%-20%
Floxuridine (FUDR)	Anti-metabolite	246.2	75	500 mg/m² twice daily × 3 days	0.9% sodium chloride	N/A	Minimal	43.0	7 days	N/A	Chemical peritonitis	Hepatic degradation 100%
Carboplatin	Alkylator	371.25	10		0.9% sodium chloride	N/A	Yes	41.5	N/A	0.5 mm	N/A	Renal clearance 67%

'Doses are given for use as a single agent.
N/A = information not available

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MİTOMİSİN C

- Nefrotoksik
- Yara iyileşmesi
- Anastomoz kaçağı
- Fistül

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5-FU

- Kc'de metabolize (KC yetmezliğinde dikkat!!!)
- Tek başına 700-800 mg/m²/gün (Mitomisin C ile birlikte 600-650 mg/m²/gün)

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PAKLİTAKSEL

- DMPM(Diffüz Malign Peritoneal Mezotelyoma)
- Diethylhexylphthalate (DEHP) içermeyen setlerle işlem yapılmalı

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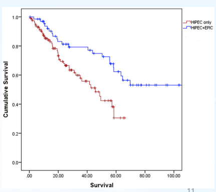
Early postoperative intraperitoneal chemotherapy is associated with survival benefit for appendiceal adenocarcinoma with peritoneal dissemination

Yeqian Huang [a], Nayef A. Alzahrani [a, b], Winston Liauw [c], Hussein Soudy [a, d], Abdulaziz M. Alzahrani [a], David L. Morris [a]

	HIPEC	HIPEC + EPIC	p
Total n = 185	118 (63.8)	67 (36.2)	
Overall OS median (months) (95%CI)	45.6 (33.2–58.1)	NR	0.003
Overall 1yr OS (%)	85.1	93.6	
Overall 3yr OS (%)	57.9	79.2	
Overall 5yr OS (%)	30.5	62.3	
Recurrence rate n (%)	64 (54.2)	42 (62.7)	0.264
DFS median (months) (95%CI)	12.3 (8.5–16.0)	18.9 (12.5–25.2)	0.044
1yr DFS (%)	50.8	61.9	
3yr DFS (%)	3.3	14.3	
5yr DFS (%)	0	7.1	



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Early Postoperative Intraperitoneal Chemotherapy for Low-Grade Appendiceal Mucinous Neoplasms with Pseudomyxoma Peritonei: Is it Beneficial?

Yeqian Huang BMed, MD, Nayef A. Alzahrani MBBS, Winston Liauw MBBS, MMedSci, Thamer B. Traiki MBBS & David L. Morris MD, PhD

	HIPEC + EPIC	HIPEC	*p*-value
Total *n* = 250	176 (70.4)	74 (29.6)	
Sex [*n* (%)]			0.068
Male	60 (44.1)	33 (56.9)	
Female	76 (55.9)	25 (43.1)	
Age, years [mean (SD)]	52.0 (12.9)	55.9 (13.2)	0.033
PCI [mean (SD)]	22.3 (10.5)	21.4 (12.2)	0.485
PCI score [*n* (%)]			0.203
<20	69 (39.2)	35 (47.9)	
≥20	107 (60.8)	38 (52.1)	
Pathology [*n* (%)]			0.393
LAMN–NEA	74 (42.0)	35 (47.9)	
LAMN–NEP	102 (58.0)	39 (52.1)	
Operation hours [mean (SD)]	9.7 (2.5)	9.6 (3.6)	0.916
Transfusion [mean (SD)]	5.5 (7.8)	7.1 (8.9)	0.166
CEA, mg/L [mean (SD)]	25.1 (49.4)	37.8 (68.4)	0.112
CA19-9, U/mL [mean (SD)]	116.9 (322.0)	124.2 (212.9)	0.867
CA125, U/mL [mean (SD)]	45.6 (47.7)	43.3 (67.5)	0.779
Hospital mortality (%)	1 (0.6)	2 (2.7)	0.153
Major morbidity, grade III/IV [*n* (%)]	85 (48.3)	33 (44.6)	0.593
ICU stay, days [mean (SD)]	4.6 (8.8)	5.0 (10.6)	0.764
HDU stay, days [mean (SD)]	6.0 (3.9)	3.6 (4.0)	<0.001
Total stay, days [mean (SD)]	29.7 (23.3)	30.0 (25.0)	0.927

HIPEC hyperthermic intraperitoneal chemotherapy, *EPIC* early postoperative intraperitoneal chemotherapy, *SD* standard deviation, *PCI* Peritoneal Cancer Index, *LAMN–NEA* low-grade appendiceal mucinous neoplasms with neoplastic epithelium absent, *LAMN–NEP* low-grade appendical mucinous neoplasms with neoplastic epithelium present, *CEA* carcinoembryonic antigen, *ICU* intensive care unit, *HDU* high dependency unit

	HIPEC + EPIC	HIPEC	*p*-value
All patients			
Median overall OS, months (95 % CI)	NR	89.1 (–)	0.001
Overall 1-year OS (%)	97.7	94.7	
Overall 3-year OS (%)	95.7	78.6	
Overall 5-year OS (%)	93.0	64.5	
Recurrence rate [*n* (%)]	49 (33.8)	18 (42.9)	0.281
Disease-free survival, months (95 % CI)	17.3 (11.9–22.8)	9.2 (4.2–14.3)	0.618
PCI > 20 subgroup			
Median overall OS, months (95 % CI)	103.59 (79.97–127.21)	89.07 (17.02–161.12)	0.025
Overall 1-year OS (%)	95.4	96.6	
Overall 3-year OS (%)	93.6	77.4	
Overall 5-year OS (%)	89.5	60.3	
Recurrence rate [*n* (%)]	38 (39.6)	17(51.5)	0.232
Disease-free survival, months (95 % CI)	15.0 (10.9–19.1)	9.2 (5.2–13.3)	0.854
LAMN–NEA subgroup			
Median overall OS, months (95 % CI)	NR	NR	0.053
Overall 1-year OS (%)	100	100	
Overall 3-year OS (%)	100	75.0	
Overall 5-year OS (%)	100	75.0	
LAMN–NEP subgroup			
Median overall OS, months (95 % CI)	NR	NR	0.005
Overall 1-year OS (%)	97.0	93.8	
Overall 3-year OS (%)	94.6	79.7	
Overall 5-year OS (%)	91.4	62.1	

HIPEC hyperthermic intraperitoneal chemotherapy, *EPIC* early postoperative intraperitoneal chemotherapy, *OS* overall survival, *CI* confidence interval, *NR* not reported, *PCI* Peritoneal Cancer Index, *LAMN–NEA* low-grade appendiceal mucinous neoplasms with neoplastic epithelium absent, *LAMN–NEP* low-grade appendical mucinous neoplasms with neoplastic epithelium present

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Does early post-operative intraperitoneal chemotherapy (EPIC) for patients treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) make a difference?

Grace Hwei Ching Tan, Whee Sze Ong, Claramae Shulyn Chia, Chee Kian Tham, Khee Chee Soo & Melissa Ching Ching Teo

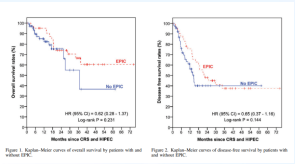

Figure 1. Kaplan–Meier curves of overall survival by patients with and without EPIC.

Figure 2. Kaplan–Meier curves of disease-free survival by patients with and without EPIC.

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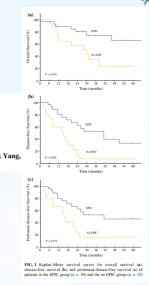
Efficacy of Early Postoperative Intraperitoneal Chemotherapy After Complete Surgical Resection of Peritoneal Metastasis from Colorectal Cancer: A Case–Control Study from a Single Center

Soo Yeun Park, MD[1], Gyu-Seog Choi, MD, PhD[1], Jun Seok Park, MD, PhD[1], Hye Jin Kim, MD[1], Chun-Seok Yang, MD[1], Jong Gwang Kim, MD, PhD[2], and Byung Woog Kang, MD, PhD[2]



- Mitomycin C (10 mg/ m2 /gün)

ve 5-fluorouracil (5-FU; 700 mg/m2 /gün)

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PIPAC

(Pressurized Intraperitoneal Aerosol Chemotherapy)

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KİMLERE YAPALIM?

- Tedavi altında ilerleyen hastalık
- KT istememe ya da KT'ye karşı ciddi yan etki
- SRC+HİPEC tedavisine rağmen ilerleyen hastalık
- SRC+HİPEC ya da başka tedavilere uygun olmayan hastalar

(PSI indeksi yüksek, genel durumu agresif cerrahiyi kaldıramayacak, SRC sonrası CCS 0-1 olamayacak hastalar, taşlı yüzük hücreli kanser, diffüz ince barsak tutulumu olan, SRC+HİPEC tedavisini istemeyen hastalar)

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KİMLERE YAPMAYALIM?

- Karın dışı metastaz (izole malign plevral efüzyon hariç)
- Genel durumu kötü hastalar (Karnofsky <%50, ECOG Skoru >2)
- Barsaklarda tam obstrüksiyon

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AVANTAJLARI

- Düşük morbidite
- Asit ve ağrı palyasyonu
- Yüksek intraperitoneal konsantrasyon
- Düşük sistemik toksisite
- Daha iyi dağılım ve penetrasyon

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TEKNİK

- Aerosol tedavi 1999 'dan beri mevcut (Aerosol itici olarak kullanılır)
- PİPEC son 10 yıl
- **PİPAC esnasında** sıvı ilaç solüsyonu özel bir cihaz (Kapnopen-Mikropompa –MIP) vasıtasıyla karın içine aerosolize edilir.
- **PİPAC esnasında** üretilen mikrodamlacıkların boyutu yaklaşık 11 mikron düzeyindedir.

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NASIL UYGULANIR?

- Karın 37 ° C sıcaklıkta karbondioksitle şişirildikten sonar iki adet balonlu trokar karın duvarına yerleştirilir.
- Karın içi laparoskopik olarak eksplore edilir ve PCI belirlenir.
- Asit boşaltılır ve karın duvarından biyopsiler alınır. Klips ile işaretleme.
- Mikropompa, yüksek-basınç enjektörüne bağlanır ve trokardan geçirilerek karın içine yerleştirilir.
- Karın içi basınç 12 mm-Hg
- İlaç 30 dakika insüfle edilir (150-200 PSİ, akış hızı 0.5 ml/sn)
- Kapalı drenaj sistemi ile batın içi aspire edilir.

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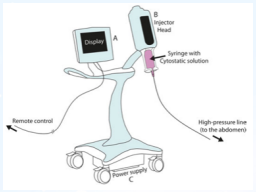

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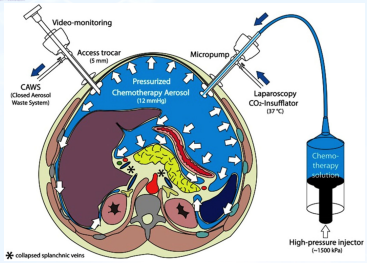

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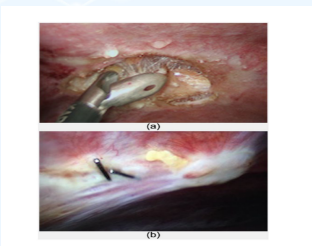

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BASINÇ

- Tümör içine nüfuz eden ilaç konsantrasyonunu arttırır.
- Deneysel hayvan çalışmalarında karın içi basıncın arttırılmasıyla karın içine uygulanan doxorubicin ve cisplatin'in antitümoral etkilerinin ve antitümoral birikimlerinin arttığı gösterilmiştir.
- İlacın periton boşluğundan subperitoneal alana geçişi sağlanmış olur.
- Hidrolik kapiller basınç üzerinde karşı çekim oluşturup ilacın vücut bölümlerinden dışarı atılmasını yavaşlatır.

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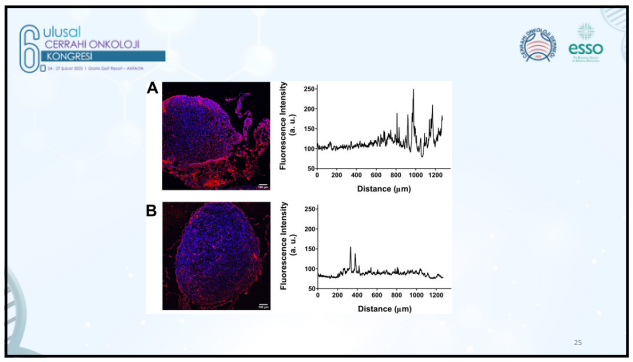
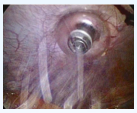
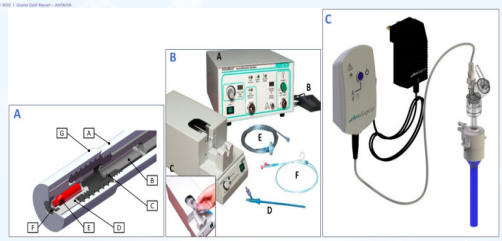


MİKROPOMPA

- 12mm balonlu trokar içinden yerleştirilir 9 mm çapındadır.
- Bağlantı girişi, gövde kısmı ve püskürtücü uç olmak üzere üç bölümden oluşur.
- MIP sadece laminer akımlı ameliyathanede yapılmalı, maksimum her dört dakikada tüm havanın değişimi sağlanmalıdır.

Mikropompa





Yüksek-Basınçlı Enjektör

- Yüksek-basınç enjektörü yüksek basınç bağlantı hattıyla mikropompaya bağlanır, hazırlanan ilaç 20 bar basınç ile mikropompaya ulaştırılır.

- Kolorektal ve appediküler kanserlerde oxaloplatin (92 mg/m² 150 ml %5 dex içinde)
- Diğerlerinde doxorubusin (1.5 mg/m² 50 ml %0.9 izotonik)+ cisplatin (7.5 mg/m² 150 ml %0.9 izotonik) kullanılıyor.
- Mitomisin C (1.5 mg/m² 50 mL NaCl %0.9) (Platin bazlı ajanlara allerjisi olan Kolorektal kanserlerde)

GÜVENLİK

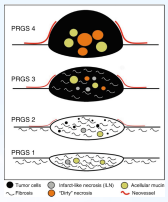
- Özel filtre (Buffalo filtre)
- Laminer akım
- Çift eldiven, gözlük, 3M maske
- Hasta üzeri örtü
- Medikal atıklar

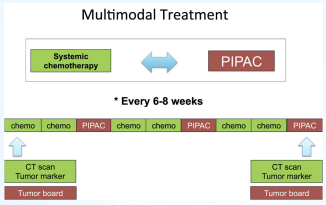
YANIT DEĞERLENDİRME

- Biyopsi ve sitoloji (ikinci PIPAC sırasında)
- PKI
- Yaşam kalitesi
- Radyoloji

YANIT DEĞERLENDİRME

Peritoneal Regression Grading System (PRGS)		
Grade	**Tumor cells**	**Regression features**
PRGS 1 – complete response	No tumor cells	Abundant fibrosis and/or acellular mucin pools and/or infarct-like necrosis
PRGS 2 – major response	Few tumor cells (isolated or small clusters)	Fibrosis and/or acellular mucin pools and/or infarct-like necrosis predominant over tumor cells
PRGS 3 – minor response	Predominant tumor cells	Tumor cells predominant over fibrosis and/or acellular mucin pools and/or infarct-like necrosis
PRGS 4 – no response	Visible tumor cells (at lowest magnification)	No regressive changes





Research Article

Feasibility, Safety, and Efficacy of Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) for Peritoneal Metastasis: A Registry Study

Florian Kurtz,[1] Florian Struller,[1] Philipp Horvath,[1] Wiebke Solass,[2] Hans Bösmüller,[3] Alfred Königsrainer,[1] and Marc A. Reymond[1,4]

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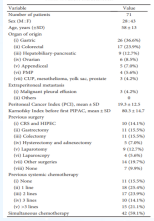

Table 1: Patient characteristics.

Variable	Value
Number of patients	71
Sex (M : F)	28 : 43
Age, years (±SD)	58 ± 13
Origin of origin	
(i) Gastric	26 (36.6%)
(ii) Colorectal	17 (23.9%)
(iii) Hepatobiliary-pancreatic	9 (12.7%)
(iv) Ovarian	7 (9.9%)
(v) Appendiceal	5 (7.0%)
(vi) PMP	4 (5.6%)
(vii) CUP, mesothelioma, yolk sac, prostate	3 (4.2%)
Extraperitoneal metastasis	
(i) Malignant pleural effusion	3 (4.2%)
(ii) Others	0
Peritoneal Cancer Index (PCI), mean ± SD	19.3 ± 12.3
Karnofsky Index before first PIPAC, mean ± SD	80.3 ± 14.7
Previous surgery	
(i) CRS and HIPEC	10 (14.1%)
(ii) Gastrectomy	11 (15.5%)
(iii) Colectomy	11 (15.5%)
(iv) Hysterectomy and adnexectomy	5 (7.0%)
(v) Laparotomy	9 (12.7%)
(vi) Laparoscopy	4 (5.6%)
(vii) Other surgeries	14 (19.7%)
(viii) None	7 (9.9%)
Previous systemic chemotherapy	
(i) None	11 (15.5%)
(ii) 1 line	16 (22.5%)
(iii) 2 lines	17 (23.9%)
(iv) 3 lines	10 (14.1%)
(v) >3 lines	15 (21.1%)
Simultaneous chemotherapy	42 (59.1%)

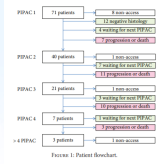

Figure 1: Patient flowchart.

Table 2: Adverse events.

Intraoperative			
Type of complication			
(i) Bowel injury	3*		
(ii) Lung aspiration	1		
(iii) Bleeding	1		
Total	4 (5.6%)		
Postoperative	Dindo-Clavien	CTCAE	
Type of complication			
(i) Abdominal wall infiltration	2	1	N/A
(ii) Leucopenia	1	N/A	3
(iii) Ascites leakage	1	1	N/A
(iv) Nausea/vomiting	1	2	2
(v) Hematoma, transfusion	1	2	N/A
(vi) Hospital mortality	1*	5	5
Total		7 (9.9%)	

*Resected and repaired intraoperatively; *ASA IV patient, 4500 ml ascites, unrelated to procedure.

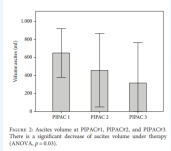

Figure 2: Ascites volume at PIPAC#1, PIPAC#2, and PIPAC#3. There is a significant decrease of ascites volume under therapy (ANOVA, $p < 0.03$).

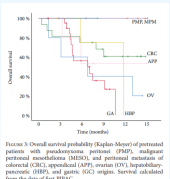

Figure 3: Overall survival probability (Kaplan-Meyer) of pretreated patients with pseudomyxoma peritonei (PMP), malignant peritoneal mesothelioma (MESO), and peritoneal metastasis of colorectal (CRC), appendiceal (APP), ovarian (OV), hepatobiliary-pancreatic (HBP), and gastric (GC) origins. Survival calculated from the date of first PIPAC.

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Prospective, single-center implementation and response evaluation of pressurized intraperitoneal aerosol chemotherapy (PIPAC) for peritoneal metastasis

Martin Graversen, Sönke Detlefsen, Jon Kroll Bjerregaard, Claus Wilki Fristrup, Per Pfeiffer and Michael Bau Mortensen

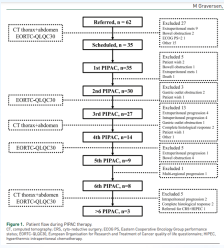

Figure 1. Patient flow during PIPAC therapy.

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Table 3. Feasibility and response evaluation data.

Procedures			
Total no. PIPAC procedures		129	
PIPAC/pt, mean (SD)		3.44 (1.95)	
PIPAC/pt, median (range)		3 (1–9)	
Technical aspects	PIPAC 1 (n = 35)	PIPAC 2 (n = 27)	
Iatrogen femoral access, no. patients (%)	35 (100%)	27 (100%)	
Procedure time, minutes (range)	180 (71–156)	93 (77–129)	
Days of admission, median (range)	1 (1–6)	1 (0–2)	
Discharge day D/T, no. patients (%)	28 (80%)	24 (89%)	
Pain/NSAID			
Postoperative pain*, median (range)	3 (0–10)	3 (0–7)	
Postoperative nausea, no. patients			
None	24	16	
Mild	2	4	
Moderate	1	5	
Severe	8	5	
Postoperative vomiting, no. patients			
None	26	18	
1 vomit	2	1	
2–3 vomits	3	2	
>3 vomits	4	5	
Response evaluation	PIPAC 1	PIPAC 2	
PRSS, mean (SD)	2.85 (0.66)	1.56 (0.52)	$p = 0.0004$
PRSS, maximum value	4	3	
PRSS improvement, patients (%)		16/27 (67%)	
Malignant cells in peritoneal lavage	13/22 (59%)	9/22 (41%)	
Conversion nonmalignant → malignant		1/22 (4.5%)	
Conversion malignant → nonmalignant		5/22 (23%)	
No conversion		8/22 (36%)	

* Visual Analog Scale 1–10.
PIPAC, pressurized intraperitoneal aerosol chemotherapy; PONV, postoperative nausea and vomiting; PRSS, peritoneal regression grading score; PI, patient; SD, standard deviation.

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Table 2
Ongoing prospective clinical trials using PIPAC in patients with peritoneal metastases, listed on clinicaltrials.gov.

No.	Study type	Cancer type	Chemotherapy	NCT number
1	Phase 1	Ovarian, oeso-gastric, pancreatic and primary peritoneal tumors	Nab-paclitaxel (7.5–70 mg/m²) and Cisplatin (10.5 mg/m²)	NCT04000906
2	Phase 1	Colorectal Ovarian, uterine and gastric	Oxaliplatin 92 mg/m² Cisplatin 10.5 mg/m² + Doxorubicin 2.1 mg/m²	NCT04329494
3	Phase 1	Gastric	Oxaliplatin 90 mg/m² + IV nivolumab 240 mg q2w	NCT03172416
4	Phase 1	Gastric	Cisplatin 10.5 mg/m² + Doxorubicin 2.1 mg/m² after laparoscopic gastrectomy	NCT04047004
5	Phase 1/2	Gastric	Docetaxel	NCT04410887
6	Phase 1/2	Colorectal and gastric	Oxaliplatin (90–300 mg/m²)	NCT03294252
7	Phase 2	Colorectal and appendical Other gastrointestinal and gynecological	Oxaliplatin 92 mg/m² Cisplatin 7.5 mg/m² + Doxorubicin 1.2 mg/m²	NCT03287375
8	Phase 2	Colon	Oxaliplatin 92 mg/m²	NCT03280511
9	Phase 2	Colorectal	Oxaliplatin 92 mg/m²	NCT03808228
10	Phase 2 randomized trial	Mesothelioma	Cisplatin 10.5 mg/m² + Doxorubicin 2.1 mg/m² + IV Cisplatin and Permetrexed vs. IV Cisplatin and Permetrexed	NCT03875144
11	Phase 2 randomized trial	Gastric	Cisplatin 10.5 mg/m² + Doxorubicin 2.1 mg/m² + IV chemotherapy vs. IV chemotherapy	NCT04065139
12	Observational	Colorectal Ovarian, gastric, pancreatic and primary peritoneal tumors	Oxaliplatin 92 mg/m² Cisplatin 7.5 mg/m² + Doxorubicin 1.2 mg/m²	NCT03100708
13	Observational	Ovarian, gastric, and colorectal	Oxaliplatin 92 mg/m²	NCT04122885
14	International registry	Any	Not specified	NCT03210298

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BANC

(Bidirectional Adjuvant Normothermic Chemotherapy)

- İntraabdominal kateter (Primer cerrahi ya da second look)
- Port kateter
- Diyaliz kateteri

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Alternative intraperitoneal chemotherapy regimens for optimally debulked ovarian cancer

Heidi J Gray, Chirag A Shah, Ron E Swensen, Hisham K Tamimi, Barbara A Goff

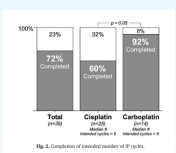
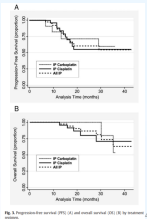


Fig. 2. Completion of intended number of IP cycles.



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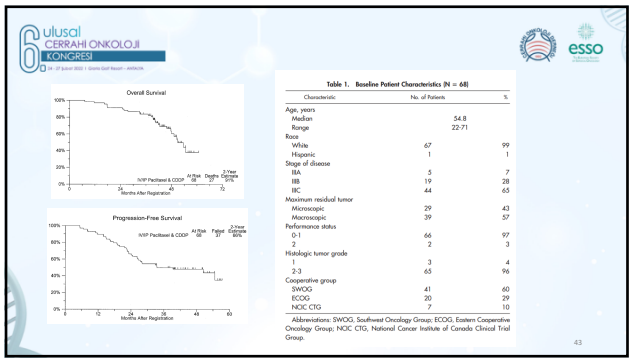
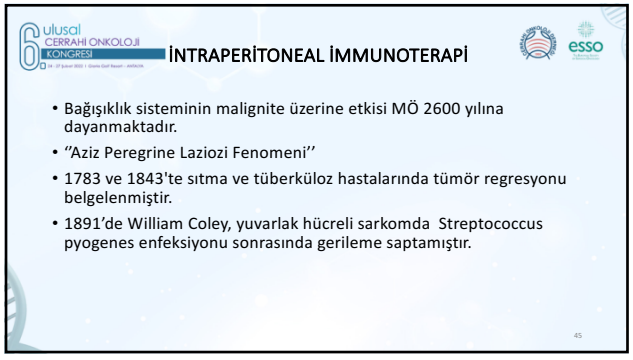
Combined Intraperitoneal and Intravenous Chemotherapy for Women With Optimally Debulked Ovarian Cancer: Results From an Intergroup Phase II Trial

By Mace L. Rothenberg, P.Y. Liu, Patricia S. Braly, Sharon P. Wilczynski, Edward V. Hannigan, Scott Wadler, Gavin Stuart, Caroline Jung, Maurie Markman, and David S. Alberts

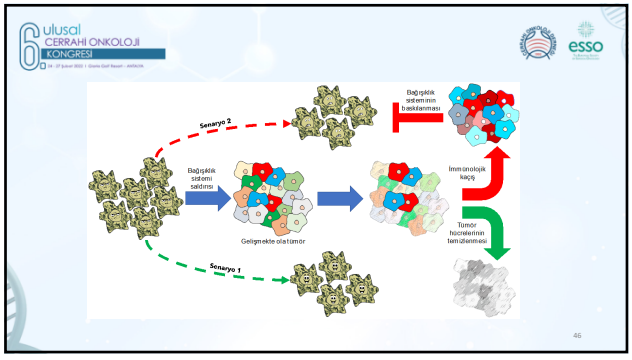
- Tenckoff kateter ya da port kateter sonrasında
- 1 ve 2. Günlerde 24 saat boyunca 135 mg/m² İV paklitaksel
- 2.günde 100 mg/m² 2 L izotonik içerirsnde İP sisplatin ve 8. Günde 60 mg/m² paklitaksel İP uygulandı.
- 21 günlük 6 kür tedavi planlandı.
- 2 yıllık sağkalım oranı %91 idi ve medyan sağkalım süresi 51 aydı

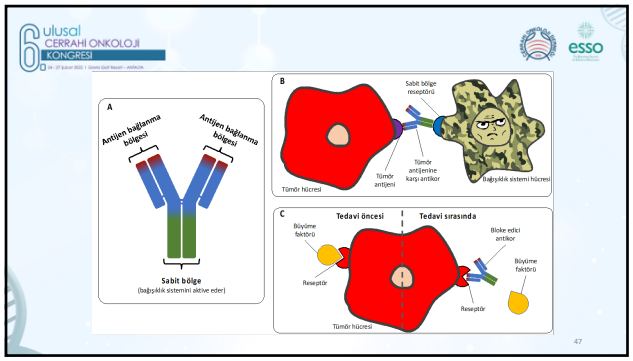


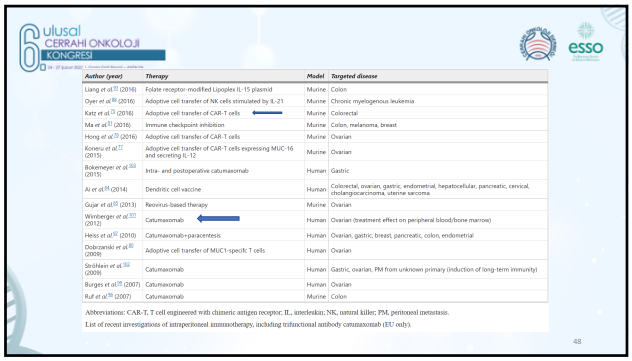

- Nötropeni (%79)
- Bulantı (%50)
- Kusma (%34)
- Yorgunluk/halsizlik/uyuşukluk (%24)

İNTRAPERİTONEAL İMMUNOTERAPİ

- Bağışıklık sisteminin malignite üzerine etkisi MÖ 2600 yılına dayanmaktadır.
- ‘’Aziz Peregrine Laziozi Fenomeni’’
- 1783 ve 1843'te sıtma ve tüberküloz hastalarında tümör regresyonu belgelenmiştir.
- 1891’de William Coley, yuvarlak hücreli sarkomda Streptococcus pyogenes enfeksiyonu sonrasında gerileme saptamıştır.







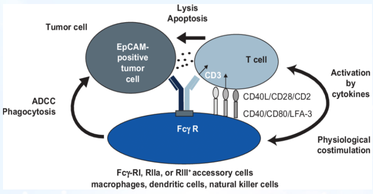
Author (year)	Therapy	Model	Targeted disease
Liang et al.[71] (2016)	Folate receptor-modified Lipoplex IL-15 plasmid	Murine	Colon
Oyer et al.[46] (2016)	Adoptive cell transfer of NK cells stimulated by IL-21	Murine	Chronic myelogenous leukemia
Katz et al.[23] (2016)	Adoptive cell transfer of CAR-T cells	Murine	Colorectal
Ma et al.[51] (2016)	Immune checkpoint inhibition	Murine	Colon, melanoma, breast
Hong et al.[70] (2016)	Adoptive cell transfer of CAR-T cells	Murine	Ovarian
Koneru et al.[72] (2015)	Adoptive cell transfer of CAR-T cells expressing MUC-16 and secreting IL-12	Murine	Ovarian
Bokemeyer et al.[202] (2015)	Intra- and postoperative catumaxomab	Human	Gastric
Ai et al.[58] (2014)	Dendritic cell vaccine	Human	Colorectal, ovarian, gastric, endometrial, hepatocellular, pancreatic, cervical, cholangiocarcinoma, uterine sarcoma
Gujar et al.[69] (2013)	Reovirus-based therapy	Murine	Ovarian
Wimberger et al.[203] (2012)	Catumaxomab	Human	Ovarian (treatment effect on peripheral blood/bone marrow)
Heiss et al.[67] (2010)	Catumaxomab+paracentesis	Human	Ovarian, gastric, breast, pancreatic, colon, endometrial
Dobrzanski et al.[66] (2009)	Adoptive cell transfer of MUC1-specific T cells	Human	Ovarian
Ströhlein et al.[202] (2009)	Catumaxomab	Human	Gastric, ovarian, PM from unknown primary (induction of long-term immunity)
Burges et al.[59] (2007)	Catumaxomab	Human	Ovarian
Ruf et al.[56] (2007)	Catumaxomab	Murine	Colon

Abbreviations: CAR-T, T cell engineered with chimeric antigen receptor; IL, interleukin; NK, natural killer; PM, peritoneal metastasis.
List of recent investigations of intraperitoneal immunotherapy, including trifunctional antibody catumaxomab (EU only).

6. ulusal CERRAHİ ONKOLOJİ KONGRESİ

Extraperitoneal response to intraperitoneal immunotherapy with catumaxomab in a patient with cutaneous lymphangiosis carcinomatosa from ovarian cancer: a case report and review of the literature

H. Woopen, K. Pietzner, S. Darb-Esfahani, G. Oskay-Oezcelik & J. Sehouli



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- Asit miktarı azalmış
- IL-2 seviyeleri artmış
- Ca-125 seviyeleri azalmış (57.8'den 29.7 U/ml)
- Cilt metastazı gerilemiş.

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6. ulusal CERRAHİ ONKOLOJİ KONGRESİ

Regional CAR-T cell infusions for peritoneal carcinomatosis are superior to systemic delivery

SC Katz[1,2], GR Point[1], M Cunetta[1], M Thorn[1], P Guha[1], NJ Espat[1,2], C Boutros[3], N Hanna[3] and RP Junghans[4]

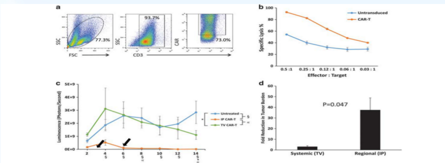

Figure 1. Optimization of chimeric antigen receptor T cell (CAR-T) delivery for treatment of peritoneal tumors. CAR-Ts were generated from murine splenocytes and were characterized for expression of CD3 and the anti-CEA CAR (**a**). *In vitro* CAR-T tumor killing was tested with bioluminescence assays, in which CAR-Ts or untransduced T cells were co-cultured with MC38CEA-luc at various effector:target ratios (**b**). CAR-Ts were tested *in vivo* via intraperitoneal (IP) or tail vein (TV) infusion, and peritoneal tumor killing was monitored by changes in bioluminescence. Arrows indicate the CAR-T injection time points. Each line on the plot is representative of the average of four mice. Symbols denoting significance ($P < 0.05$) are found below the x axis (**c**). Fold reduction in tumor luminescence was calculated between days 4 and 14 of the *in vivo* study, comparing TV with IP CAR-T delivery (**d**). Error bars are representative of s.e.m. values. *P*-values were calculated using the Student's *t*-test. CEA, carcinoembryonic antigen.

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Randomised phase II trial to investigate catumaxomab (anti-EpCAM × anti-CD3) for treatment of peritoneal carcinomatosis in patients with gastric cancer

Maren Knödler[1], Justus Körfer[1], Volker Kunzmann[2], Jörg Trojan[3], Severin Daum[4], Michael Schenk[5], Frank Kullmann[6], Sebastian Schroll[7], Dirk Behringer[8], Michael Stahl[9], Salah-Eddin Al-Batran[10], Ulrich Hacker[1], Stefan Ibach[11], Horst Lindhofer[12] and Florian Lordick[1]

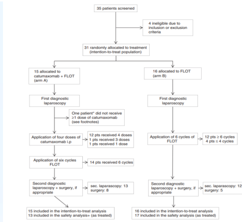

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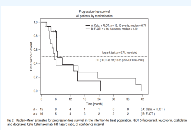
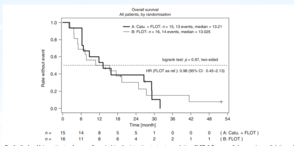
Table 2. Response rate

Macroscopic complete remission of peritoneal carcinomatosis	Catumaxomab + FLOT ($N = 15$)	FLOT ($N = 16$)
Complete remission (CR)	4 (27%)	3 (19%)
Non CR	9 (60%)	9 (56%)
No data	2 (13%)	4 (25%)
Clinical response (RECIST)	Catumaxomab + FLOT ($N = 13$)	FLOT ($N = 13$)
Partial response	6 (46%)	6 (46%)
Stable disease	3 (23%)	2 (15%)
Progressive disease	3 (23%)	5 (38%)
Not evaluated	1 (8%)	–

CR complete remission, *RECIST* response evaluation criteria in solid tumours





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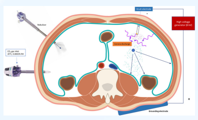
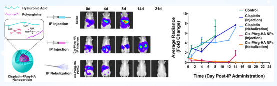
GELECEK

- Elektrostatik PIPAC



- Nano Partikül PIPAC



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- IP Nanopartikül uygulamaları
- Manyetik Nanopartiküller
- Aşılar
- İntraperitoneal Fitoterapiler
- İntraperitoneal RT

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TEŞEKKÜRLER…

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