



THIRD ANNUAL
ISSPP
Congress 2022

*International Society
for the Study of Pleura
and Peritoneum*



GASTRIC CANCERS

Rationale and Outcomes for PIPAC in Gastric Cancer

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Advancing Innovative Therapies for Cancers That Invade the Peritoneum and the Pleura

Disclosures

- I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

The off-label/investigational use of Cisplatin, and Doxorubicin will be discussed.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

This presentation is dedicated solely to research or other issues that do not contain a direct patient care component.

Gastric peritoneal carcinomatosis

Major problem of the disease evolution

More than 50% of potentially curable gastric cancer died of peritoneal recurrence

60% of all causes of gastric cancer deaths is from peritoneal carcinomatosis

No improvement in median survival for patients with metastatic gastric cancer despite increased use of chemotherapy

N. Bernards^{1,2*}, G. J. Creemers², G. A. P. Nieuwenhuijzen³, K. Bosscha⁴, J. F. M. Pruijt⁵ & V. E. P. P. Lemmens^{1,6}

¹Eindhoven Cancer Registry, Comprehensive Cancer Centre South, Eindhoven; Departments of ²Internal Medicine; ³Surgery, Catharina Hospital, Eindhoven; Departments of ⁴Surgery; ⁵Internal Medicine, Jeroen Bosch Hospital, 's-Hertogenbosch; ⁶Department of Public Health, Erasmus MC University Medical Centre, Rotterdam, The Netherlands

ANNALS OF
ONCOLOGY



Figure 1. Prescription of chemotherapy for patients with metastatic gastric cancer over time, 1990–2011.

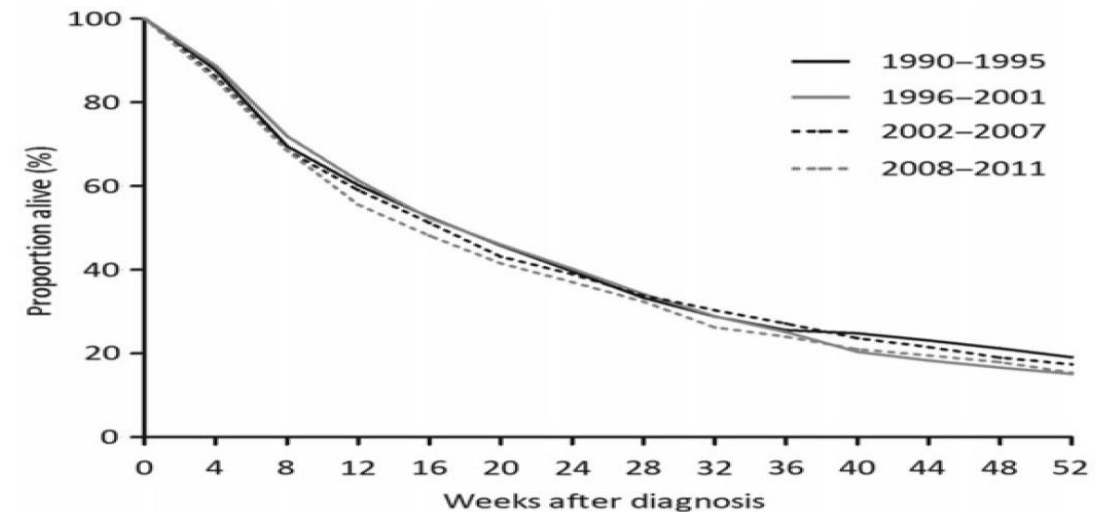
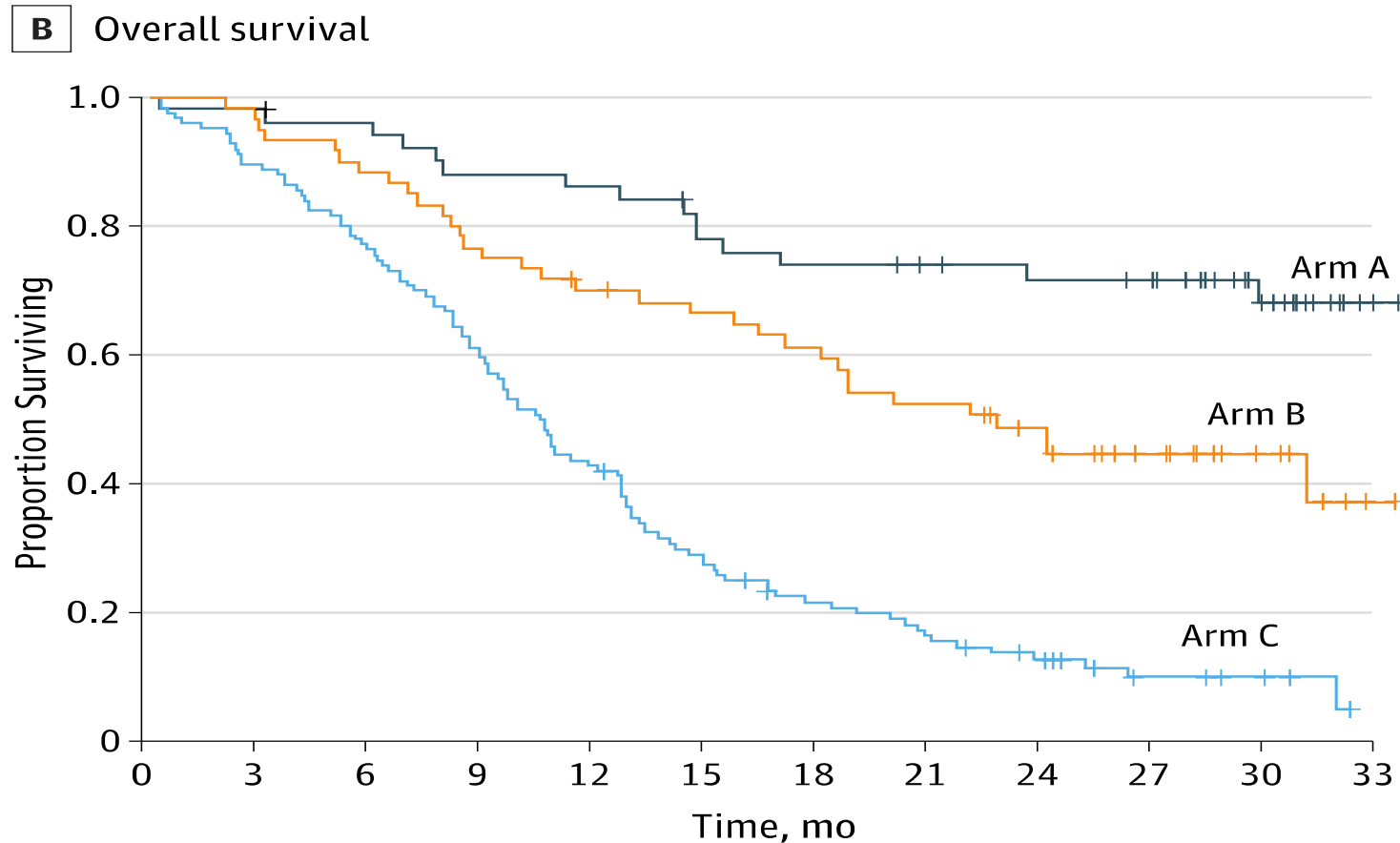


Figure 2. The overall survival of patients with metastatic gastric cancer in weeks.

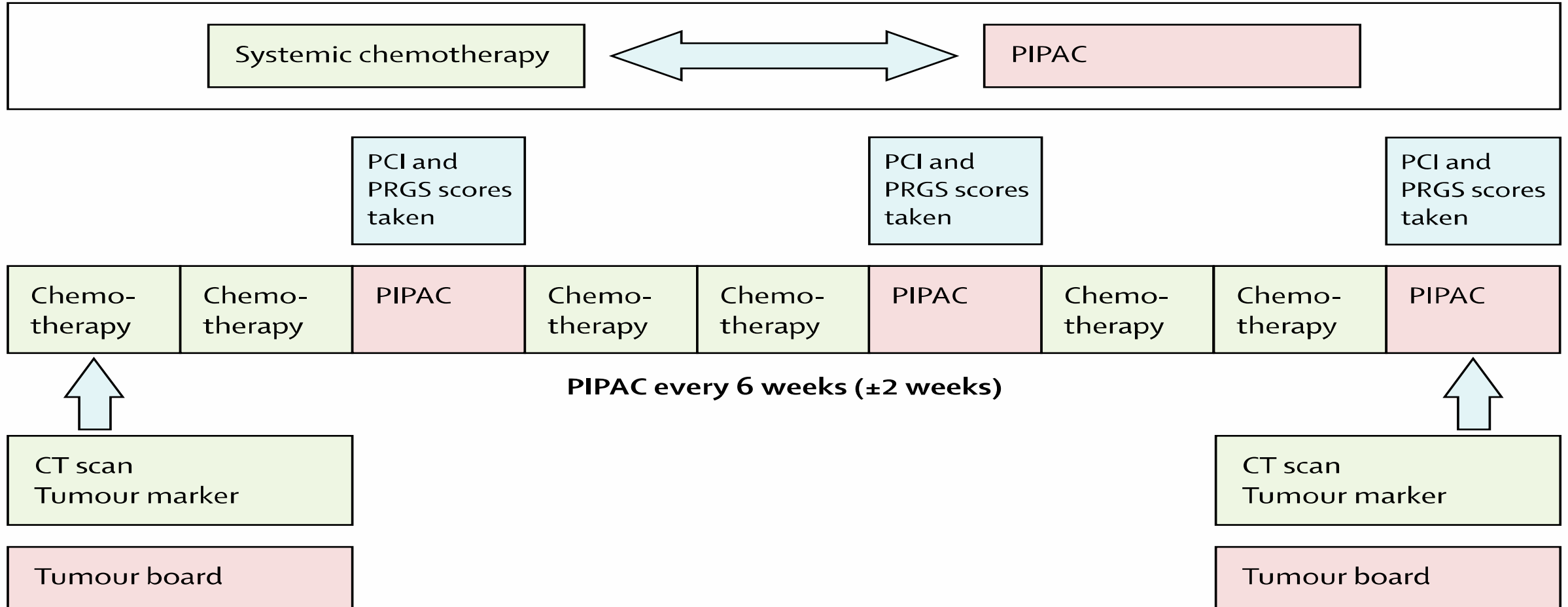
FLOT in advanced gastric cancer



Median survival of 11 months

2017 JAMA Oncology

PIPAC in combination with IV chemotherapy



Alyami , hubner et al Lancet Oncol 2019

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

25 patients	Cisplatin-doxorubicin
AGE	55.1
PCI	15
Complications NCI CTCAE V4: (III, IV)	3 (12%)
Mortality	0
Median survival	6.7 month

Struller et al Ther Adv Med oncol 2019

Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) with Low-Dose Cisplatin and Doxorubicin in Gastric Peritoneal Metastasis

24 patients	Cisplatin-doxorubicin
AGE	56
PCI	16
Complications NCI CTCAE V4: (III, IV) Mortality	7 (29.1%) 2 (8.3%) , 1 (4.15%) related
Median survival	15.4 month

Nadiradze et al, J Gastrointest Surg (2016)

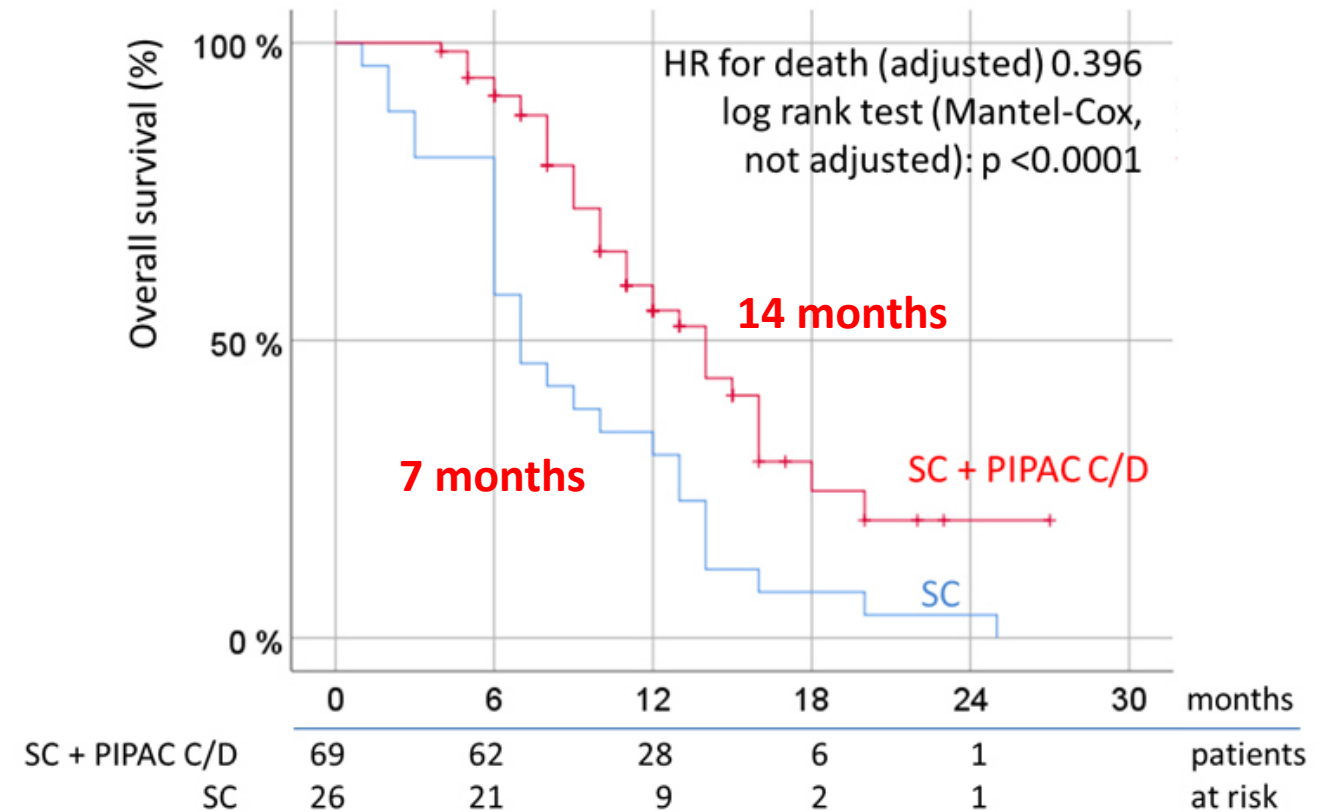
Bidirectional chemotherapy in gastric cancer with peritoneal metastasis combining intravenous XELOX with intraperitoneal chemotherapy with low dose cisplatin and Doxorubicin administered as a pressurized aerosol: an open label, Phase-2 study (PIPAC-GA2)

31 patients	Cisplatin-doxorubicin
AGE	52
PCI	16
Complications NCI CTCAE V4: (III, IV) Mortality	1 (3.2%) 0
Median survival	13 month
Complete pathological response	27%
Partial pathological response	33%

Khomyakov et al, Pleura and Peritoneum 2016

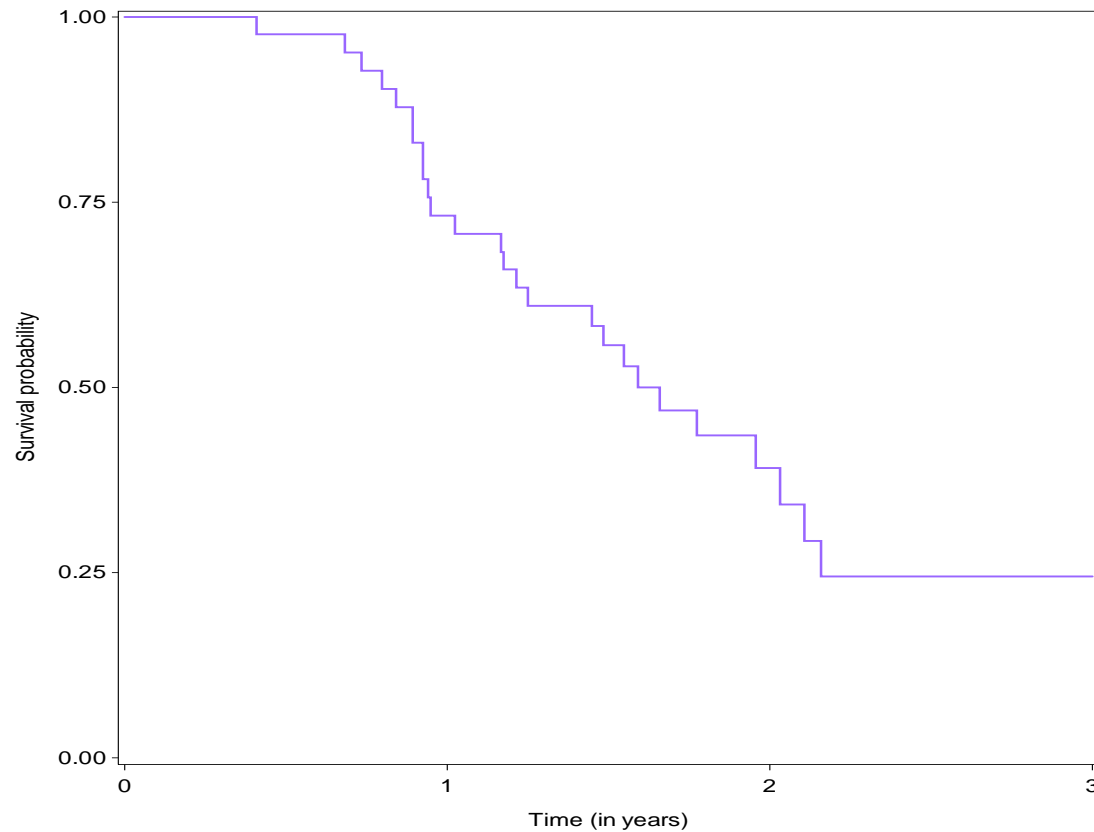
Palliative Systemic Chemotherapy with or without Pressurized IntraPeritoneal Aerosol Chemotherapy with Cisplatin and Doxorubicin (PIPAC C/D) for Gastric Cancer with Peritoneal Metastasis: A Propensity Score Analysis.

95 Patients	69 SC + PIPAC	26 SC alone
AGE	52.8	60.6
Median survival	14 month	7 month



Khomiakov et al ASCO GI 2020

Pressurized intraperitoneal aerosol chemotherapy (PIPAC) for nonresectable peritoneal metastasis from gastric cancer.



Overall Survival

19.1 months
(IC 95% : 14.1 -25.3)

16 patients (38.1%) Alive

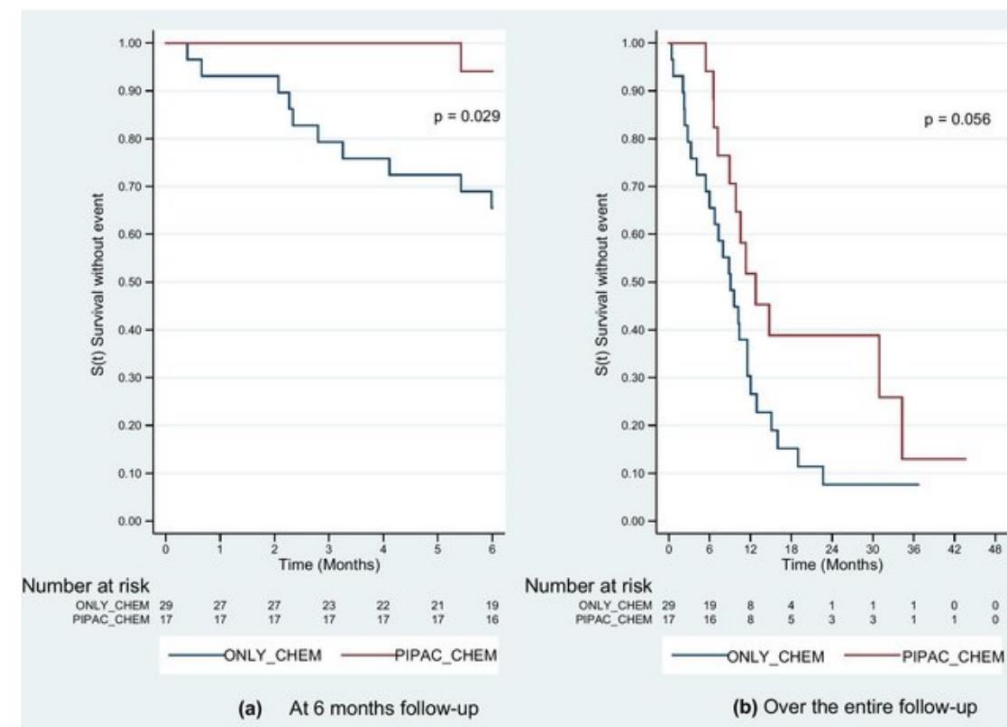
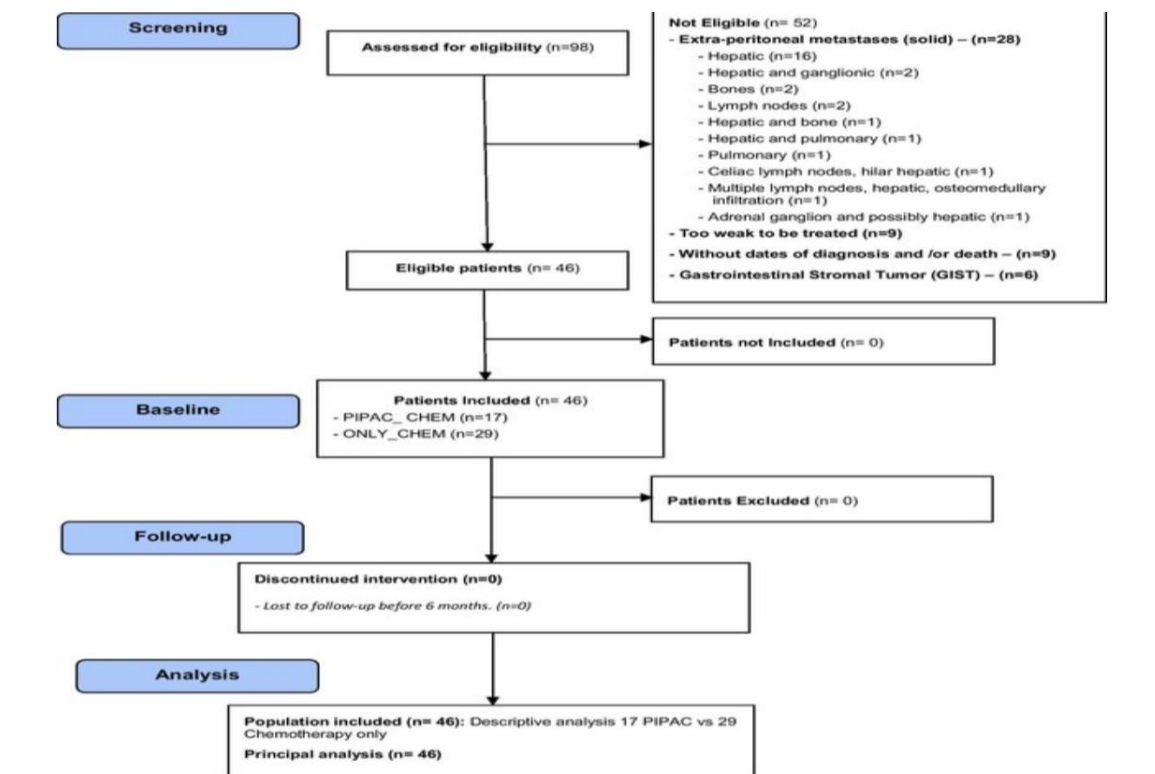
Alyami et al , EJSO, 2019

Clinical outcome for patients managed with Low-Dose Cisplatin and Doxorubicin delivered as Pressurized Intraperitoneal Aerosol Chemotherapy for unresectable Gastric Peritoneal Metastasis

131 patients	296 Cisplatin-doxorubicin
AGE	57
Complications NCI CTCAE V4: (III, IV) Mortality	7 (4.9) 2 (1.4)
Overall survival >3 pipac	11 months 16 months

Sindayigaya R et al, Ann Surg oncol (2021)

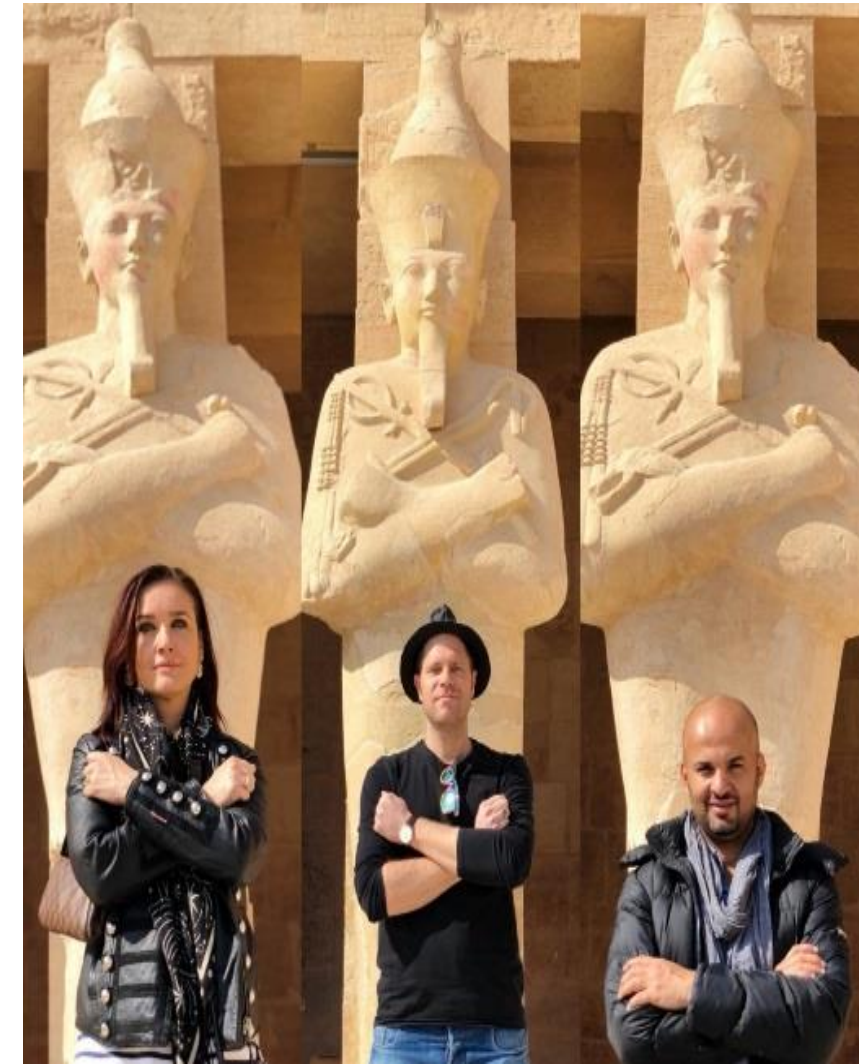
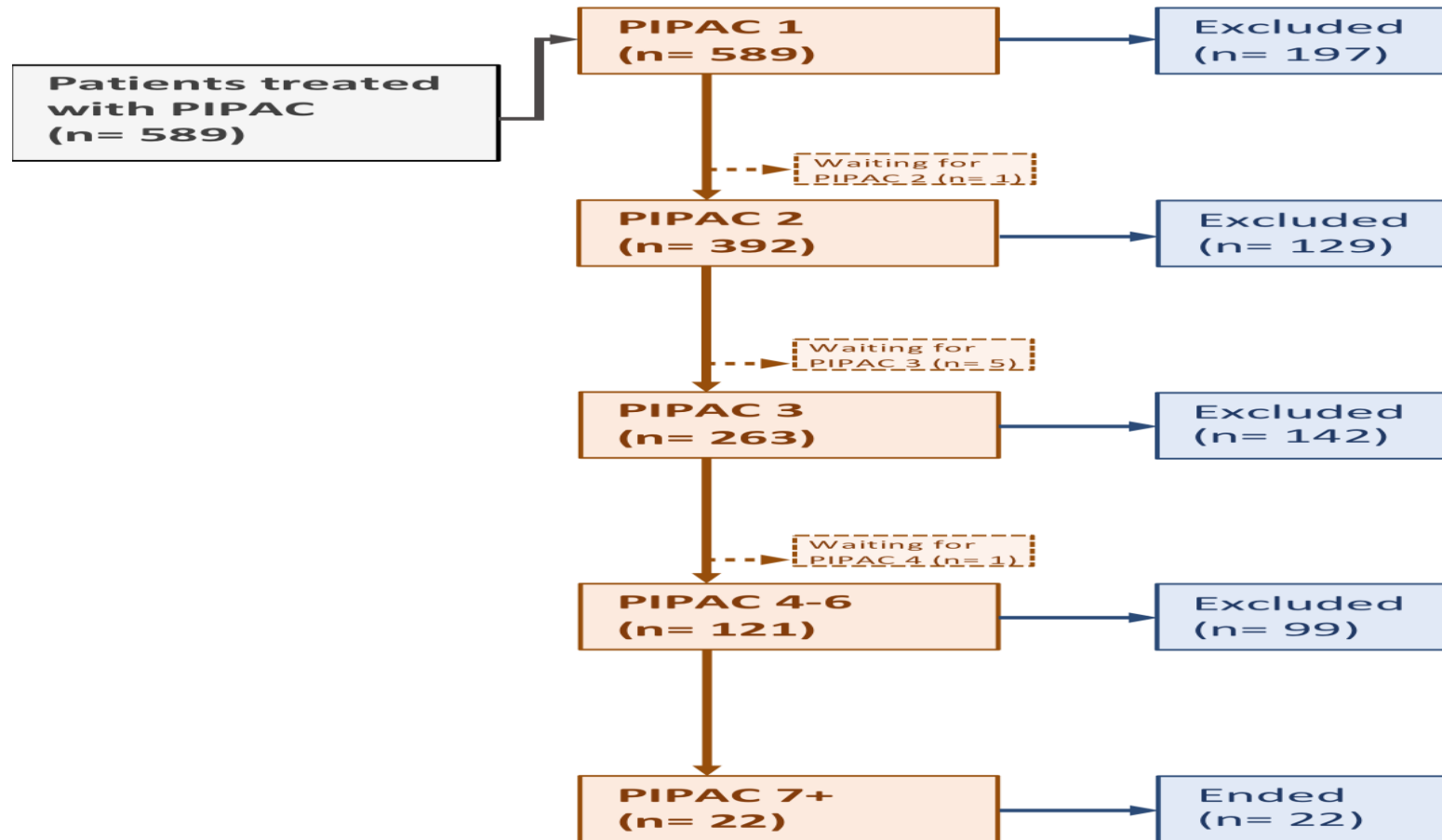
Effect of Pressurized intraperitoneal aerosol chemotherapy on the survival rate of patients with peritoneal carcinomatosis of gastric origin.



Tidadini et al J Gastroint cancer , 2021

PIPAC Cohort study

Flow chart



Alyami et al ASCO GI 2022

		Ovarian	Colorectal	Gastric	Mesothelioma	HPB	Total (PIPAC)	
	Ahmedabad	9	7	5	2	-	23 (62)	
	Barcelona	8	4	11	-	4	27 (60)	
	Dijon	15	10	5	2	5	37 (95)	
	Ghent	8	36	26	-	-	70 (215)	
	Grenoble	3	14	11	2	2	32 (96)	
	Lausanne	42	47	13	6	6	114 (280)	
	Leipzig	4	23	36	6	16	85 (175)	
	Lyon	41	52	105	26	12	236 (810)	
	Manipal	22	10	2	2	-	36 (62)	
	Montpellier	21	18	22	6	13	80 (240)	
	Moscow	10	1	191	-	-	202 (380)	
	Paris	2	12	29	5	-	134 (48)	
	Regenburg	6	9	19	-	2	36 (120)	
	Rome	-	17	31	2	17	67 (110)	
	Salzburg	8	-		6	3	17 (102)	
	Strasbourg	11	7	17	5	1	41 (100)	
	Torino	24	45	39	7	4	119 (250)	
	Tübingen	8	23	33	2	20	86 (150)	
	TOTAL	242	335	595	79	105	1356 (3441)	

Characteristic	Overall, N = 589 ¹	1-3 PIPAC, N = 468 ¹	>3 PIPAC, N = 121 ¹	p-value ²
Age (median)	56 (47, 64)	56 (46, 64)	57 (49, 63)	0.4
Age (stratified)				0.13
<50	200 (34%)	165 (35%)	35 (29%)	
50-70	339 (58%)	260 (56%)	79 (65%)	
>70	50 (8.5%)	43 (9.2%)	7 (5.8%)	
Gender				0.2
Male	272 (46%)	223 (48%)	49 (40%)	
Female	317 (54%)	245 (52%)	72 (60%)	
BMI (median)	22.0 (19.4, 24.5)	22.0 (19.2, 24.7)	22.0 (20.1, 24.2)	0.7
BMI (stratified)				0.6
(0,17]	23 (6.5%)	19 (6.7%)	4 (5.4%)	
(17,22]	161 (45%)	125 (44%)	36 (49%)	
(22,30]	159 (45%)	129 (46%)	30 (41%)	
(30,100]	13 (3.7%)	9 (3.2%)	4 (5.4%)	
ASA score				<0.001
1	42 (13%)	32 (12%)	10 (14%)	
2	192 (58%)	137 (54%)	55 (75%)	
3	95 (29%)	87 (34%)	8 (11%)	
ECOG				0.019
0	248 (51%)	204 (52%)	44 (47%)	
1	190 (39%)	143 (36%)	47 (50%)	
2	44 (9.0%)	41 (10%)	3 (3.2%)	
3	6 (1.2%)	6 (1.5%)	0 (0%)	

Alyami et al ASCO GI 2022

Characteristic	Overall, N = 589 ¹	1-3 PIPAC, N = 468 ¹	>3 PIPAC, N = 121 ¹	p-value ²
differentiation				
well-mod. diff.	66 (13%)			
poorly diff.	133 (25%)			
SRC	327 (62%)			
PC chronology				>0.9
synchrone	406 (72%)	326 (72%)	80 (72%)	
metachrone	155 (28%)	124 (28%)	31 (28%)	
History of CRS-HIPEC	16 (2.7%)	15 (3.2%)	1 (0.8%)	0.2
History of gastrectomy	165 (28%)	128 (27%)	37 (31%)	0.5
PIPAC modality				0.4
concomittant CT	253 (86%)	187 (85%)	66 (89%)	
exclusive PIPAC	40 (14%)	32 (15%)	8 (11%)	
Nb of PIPAC	2.00 (1.00, 3.00)	2.00 (1.00, 3.00)	5.00 (4.00, 6.00)	<0.001
CTCAE 3+ complications	29 (5.1%)	20 (4.4%)	9 (7.6%)	0.2
30d POM	11 (1.9%)	11 (2.4%)	0 (0%)	0.13

¹ Median (IQR); n (%)

² Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

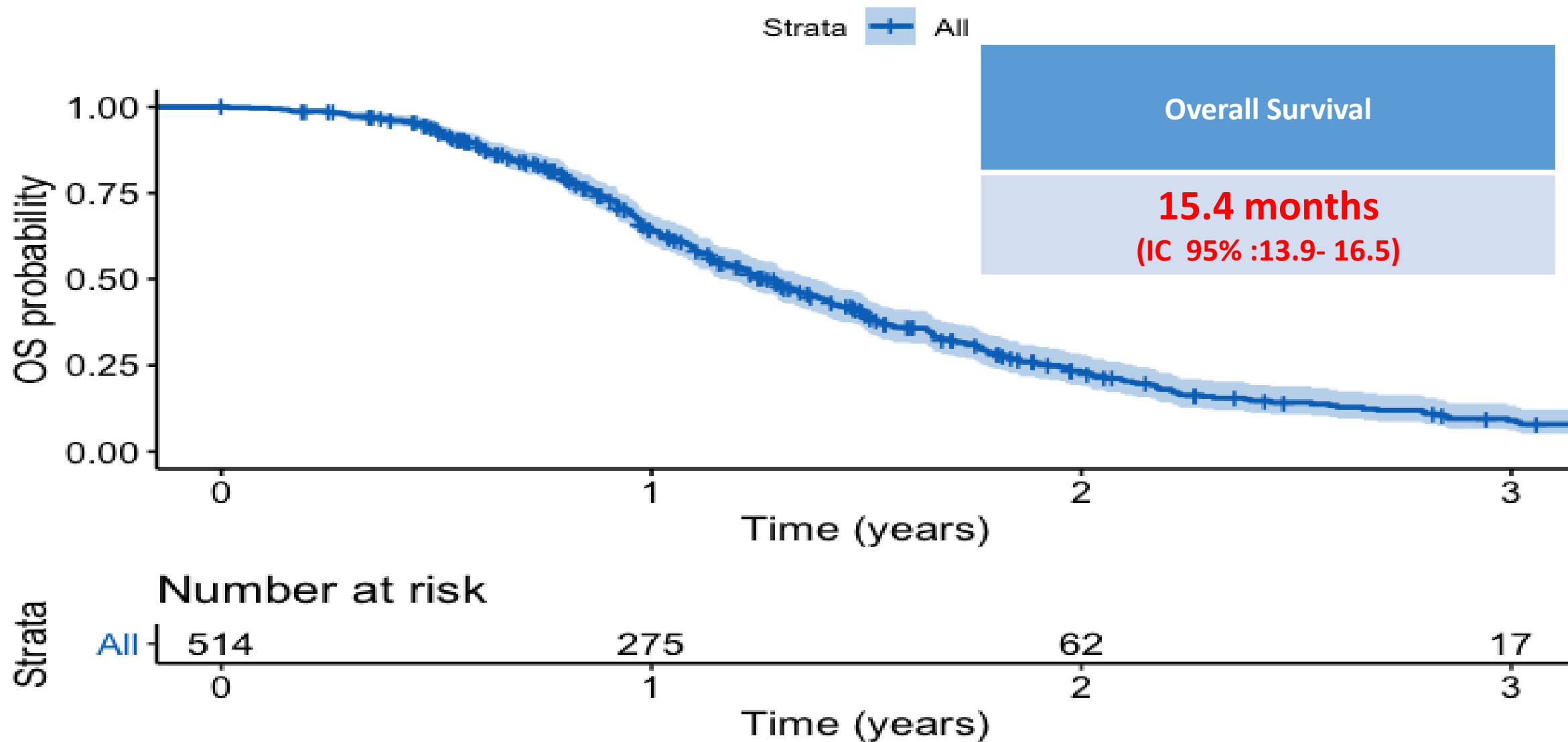
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Characteristic	before PIPAC, N = 392 ¹	after ≥ 3 PIPAC, N = 392 ¹	p-value ²
PCI	13 (7, 21)	13 (7, 22)	0.8
cytology	85 (22%)	60 (16%)	0.027
ascites	71 (18%)	80 (21%)	0.4
pain	132 (34%)	157 (40%)	0.057
dysphagia	52 (13%)	36 (9.2%)	0.074
occlusion	35 (8.9%)	83 (21%)	<0.001
nausea	40 (10%)	80 (21%)	<0.001
EORTC	54 (35, 73)	53 (6, 67)	0.4
RECIST			
complete	0 (NA%)	9 (3.7%)	
partial/stable	0 (NA%)	138 (57%)	
progression	0 (NA%)	97 (40%)	
PRGS			
PRGS1-2	0 (NA%)	206 (71%)	
PRGS3-4	0 (NA%)	85 (29%)	

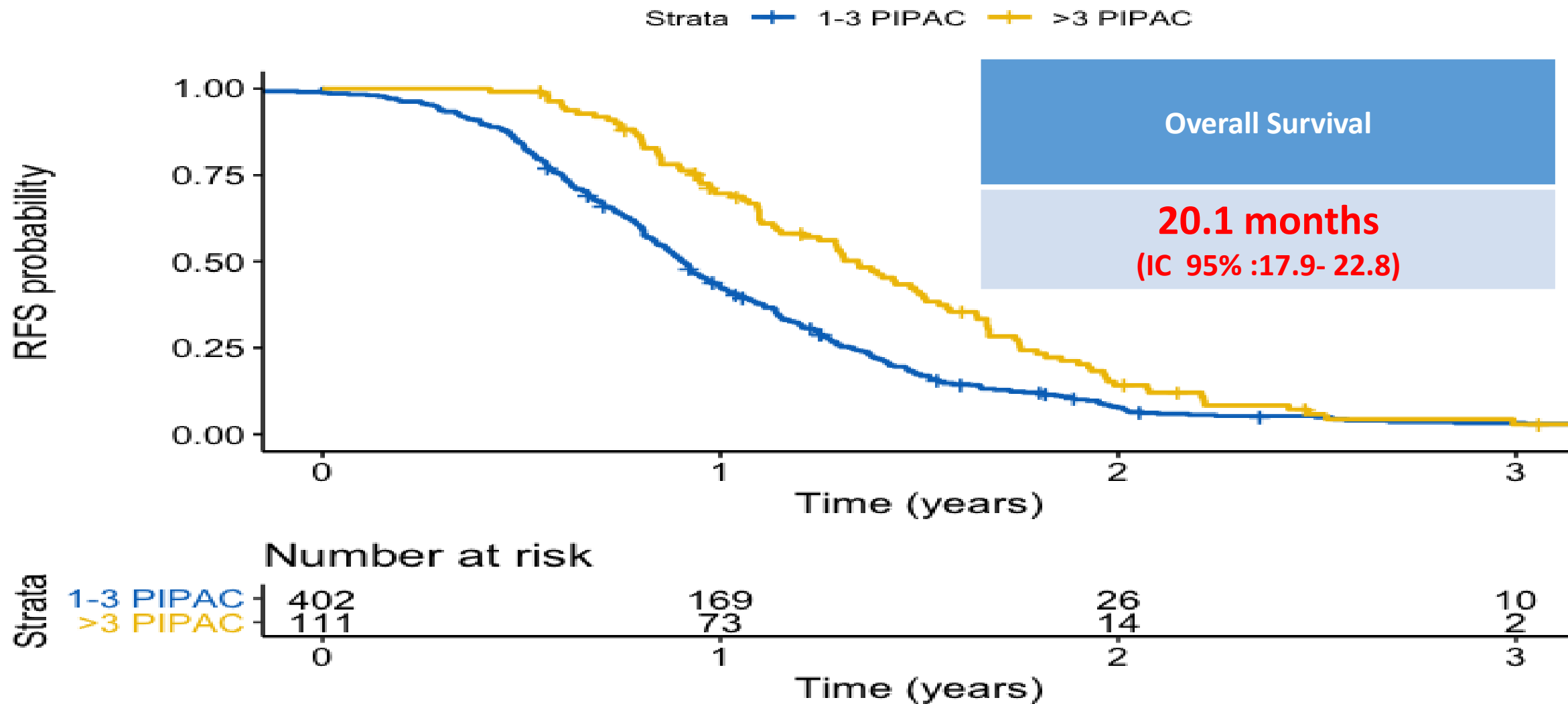
¹ Median (IQR); n (%)

² Wilcoxon rank sum test; Pearson's Chi-squared test

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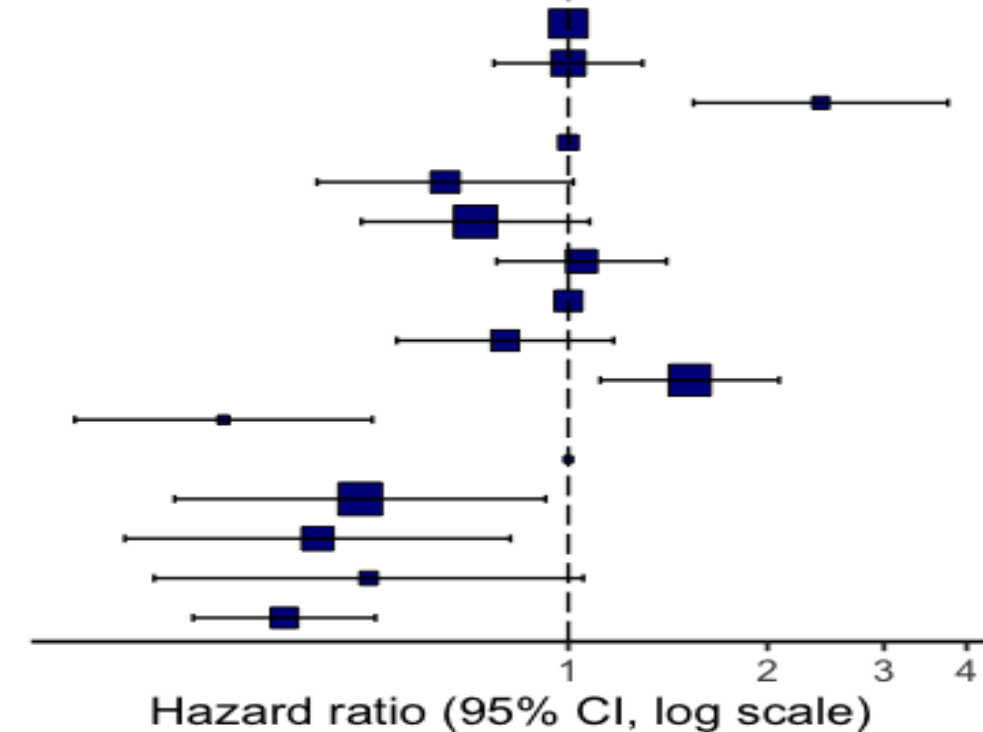
Alyami et al ASCO GI 2022



Alyami et al ASCO GI 2022

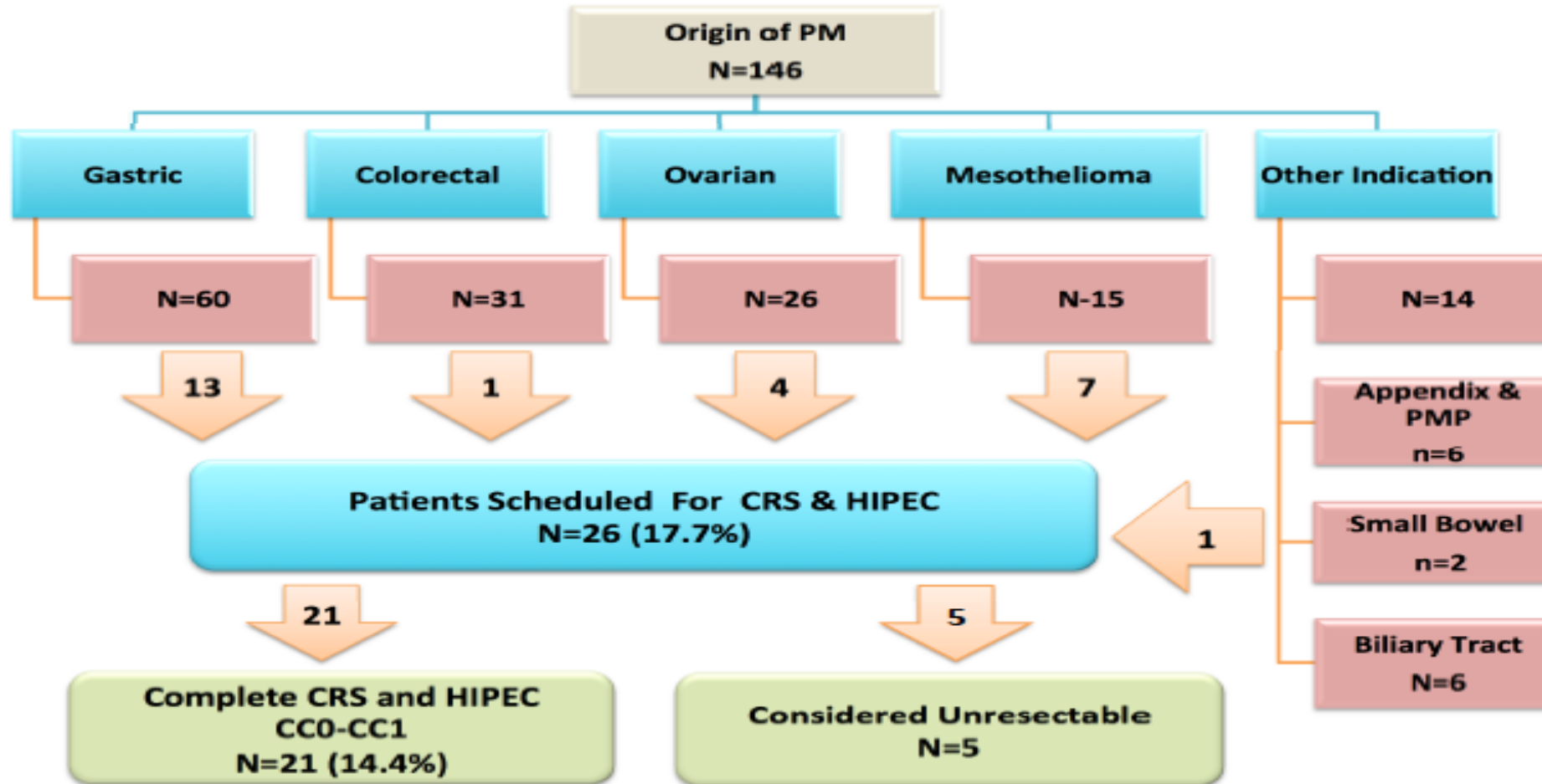
Survival: HR (95% CI, p-value)

ECOG.factor	0	-
	1	1.00 (0.77-1.29, p=0.999)
	2-3	2.41 (1.55-3.75, p<0.001)
differentiation	well-mod. diff.	-
	poorly diff.	0.65 (0.42-1.02, p=0.060)
	SRC	0.72 (0.49-1.08, p=0.111)
synchronic	metachrone	1.05 (0.78-1.41, p=0.757)
PCI.initial.cat	<7	-
	7-12	0.80 (0.55-1.17, p=0.254)
	>12	1.53 (1.12-2.08, p=0.008)
HIPEC_postPIPAC	yes	0.30 (0.18-0.51, p<0.001)
PIPAC_line	1st line	-
	2nd line	0.48 (0.25-0.92, p=0.028)
	3rd line	0.42 (0.21-0.82, p=0.011)
	4th line	0.50 (0.24-1.05, p=0.068)
PIPAC3	>3 PIPAC	0.37 (0.27-0.51, p<0.001)



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Unresectable Peritoneal Metastasis treated by Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) leading to Cytoreductive Surgery And Hyperthermic Intraperitoneal Chemotherapy.

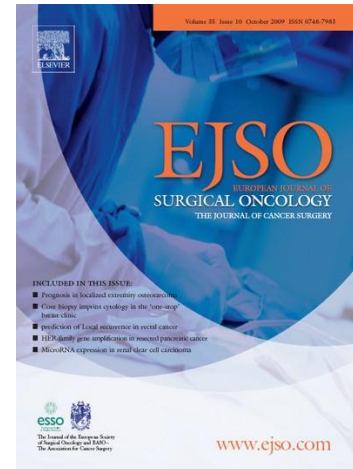


Alyami et al , EJSO, 2019



Unresectable Peritoneal Metastasis treated by Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) leading to Cytoreductive Surgery And Hyperthermic Intraperitoneal Chemotherapy.

Patient	Primary Malignancy	CC score	HIPEC drug used	Follow up (Month)	Status (Dead, Alive with recurrence, Alive free of disease)	Site of recurrence (comment)
1	Gastric	1	Mitomycin C	5	Dead	Peritoneal
2	Gastric	0	Mitomycin C	18	Alive with recurrence	Peritoneal / Bone
3	Gastric	0	Cisplatin	6	Dead	Peritoneal
4	Gastric	0	Oxaliplatin	21	Alive free of disease	N/A
5	Gastric	0	Mitomycin C	14	Alive with recurrence	Breast
6	Gastric	0	Cisplatin	9	Alive free of disease	N/A
7	Gastric	0	Cisplatin	7	Alive free of disease	N/A
8	Gastric	0	Cisplatin	9	Alive free of disease	N/A
9	Gastric	0	Mitomycin C	1	Dead	(Bowel ischemia)
10	Gastric	0	Cisplatin+Doxo	7	Alive free of disease	N/A
11	Malignant mesothelioma	1	Cisplatin+Doxo	26	Alive free of disease	N/A
12	Malignant mesothelioma	1	Cisplatin+Doxo	25	Alive free of disease	N/A
13	Malignant mesothelioma	1	Cisplatin+Doxo	5	Dead	Pleura
14	Malignant mesothelioma	1	Cisplatin+Doxo	9	Dead	Peritoneal
15	Malignant mesothelioma	1	Cisplatin+Doxo	4	Alive free of disease	N/A
16	Malignant mesothelioma	0	Cisplatin+Doxo	6	Alive free of disease	N/A
17	Ovarian	0	Cisplatin	22	Alive free of disease	N/A
18	Ovarian	0	Cisplatin+Doxo	7	Alive free of disease	N/A
19	Ovarian	1	Cisplatin+Doxo	6	Alive free of disease	N/A
20	Ovarian	1	Cisplatin	3	Alive free of disease	N/A
21	Small bowel	0	Mitomycin C	18	Alive free of disease	N/A



Alyami et al , EJSO, 2019

Comprehensive Treatment Algorithms of the Swiss Peritoneal Cancer Group for Peritoneal Cancer of Gastrointestinal Origin

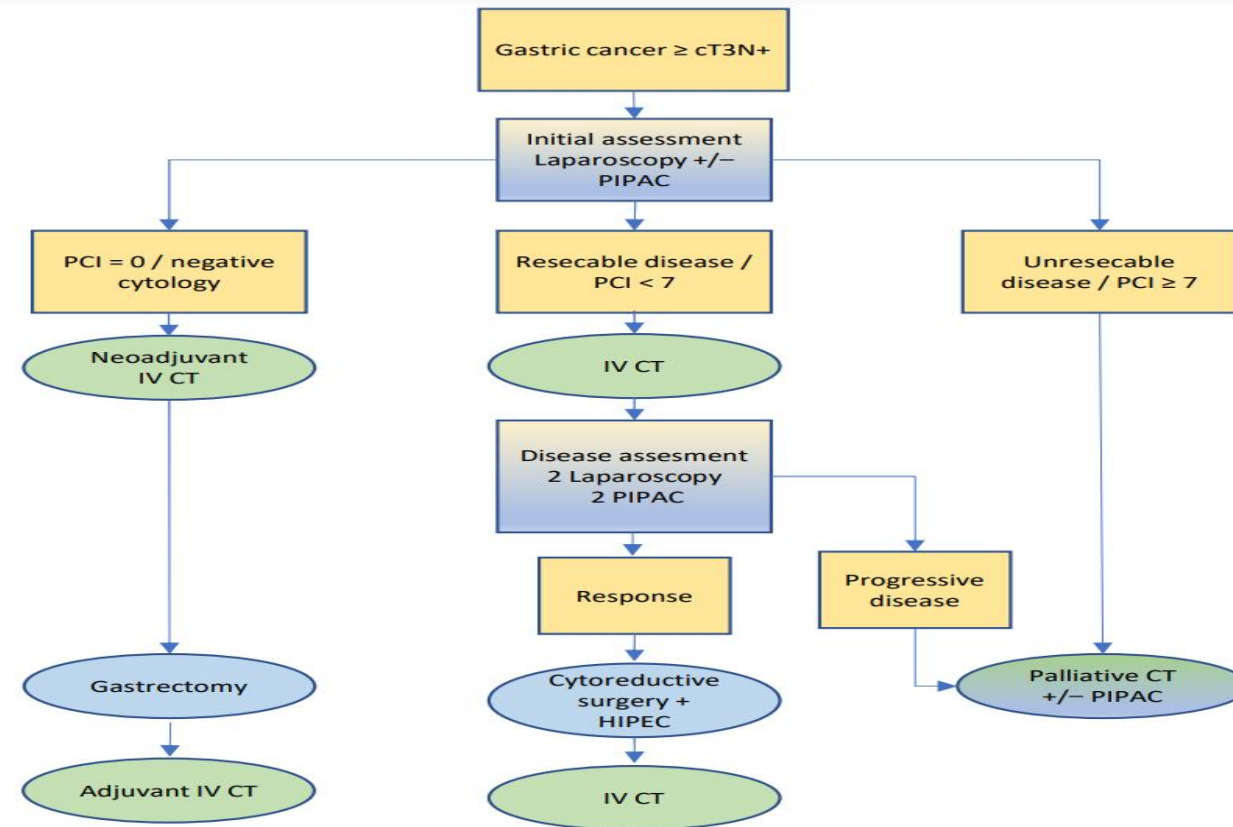
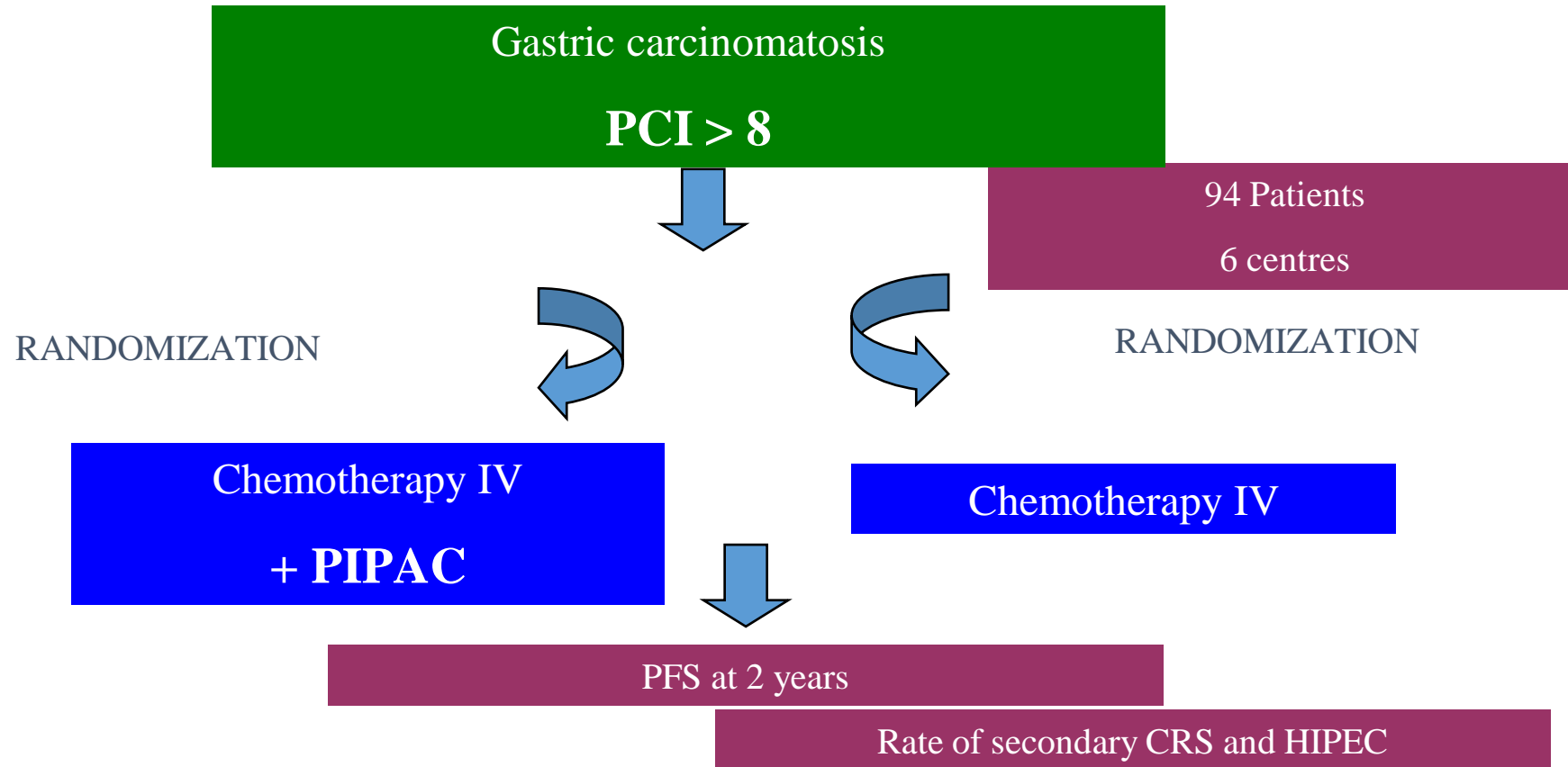


Figure 3. Treatment algorithm for gastric cancer.

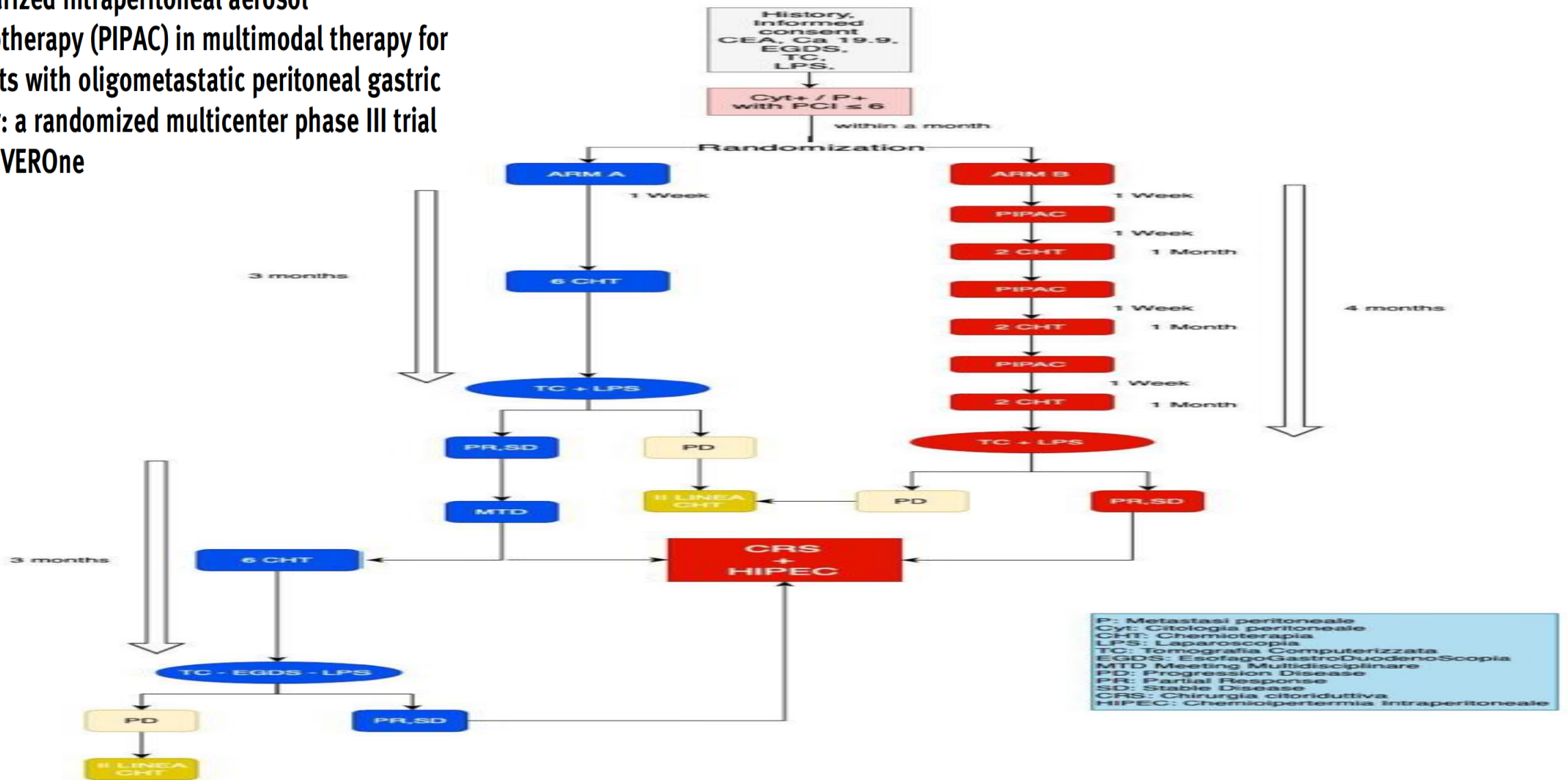
Adamina m et Cancer 2022



PIPAC EstoK 01 (Eveno) ***Multicentric randomized phase III study***



Pressurized intraperitoneal aerosol chemotherapy (PIPAC) in multimodal therapy for patients with oligometastatic peritoneal gastric cancer: a randomized multicenter phase III trial PIPAC VEROne



Casella et Pleura & peritoneum 2022

Conclusions

- **PIPAC appears promising technic for peritoneal metastasis from gastric cancer and should be combined to IV chemotherapy**
- **Interesting tolerance, response rates and survival**
- **PIPAC do better when the full protocol proposed**
- **Neoadjuvant PIPAC may appropriately select patients for curative approach or surgery and should be evaluated into phase III studies**

1st middle east PSOGI meeting 4-6/2/2023

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