Papel de la quimioterapia sistémica en la PREVENCIÓN de la carcinomatosis peritoneal (de origen gástrico y colorrectal) y su integración en el abordaje proactivo

Ana Ruiz Casado
Servicio de Oncología Médica

SaludMadrid
Hospital Universitario Puerta de Hierro Majadahonda
Comunidad de Madrid

QUIMIOTERAPIA ADYUVANTE EN CÁNCER DE COLON Y CÁNCER GÁSTRICO

- ¿Es eficaz la QT en la prevención de la carcinomatosis peritoneal metacrónica tras la cirugía con intención curativa del cáncer de colon y gástrico?

- ¿Hay algún esquema más eficaz?

ESQUEMA

- Un poco de historia: toma de conciencia sobre la existencia del problema
- Cuanto más se busca más se encuentra
- Pero sigue siendo un problema al que se le presta poca atención

PATTERNS OF RECURRENCE FOLLOWING SURGERY ALONE FOR ADENOCARCINOMA OF THE COLON AND RECTUM

ALLAN W. CASS, MD,* RODNEY R. MILLION, MD,† AND WILLIAM W. PFAFF, MD‡

TABLE 4. Specific Areas of Local Recurrences as Related to Large Bowel Site of Origin

Large bowel site	Contiguous to operative area	Abdominal incision	Peritoneal implants	TOTAL
Cecum	10	—	1	11/28 (39%)
Ascending colon	—	—	—	0/15 (0%)
Transverse colon	3	1	—	4/15 (26%)
Descending-sigmoid colon*	10	6	2	18/71 (25%)
Rectum–rectosigmoid†	42	—	3	45/151 (30%)
TOTAL	65/78 (83%)	7/78 (9%)	6/78 (8%)	78/280 (28%)‡

* Includes two anastomotic recurrences.
† Includes six perineal, four vaginal, two bladder, and eight anastomotic recurrences.
‡ Actual recurrence rate is 30%, or 78 of 256 patients surviving the operation.

in the remaining 17% (13/78). It is a moot point whether peritoneal implants are an aftermath of the operative procedure or occur as part of the natural pattern of spread.

Cancer 37:2861–2865, 1976.

Cancer, 1984

TABLE 5. Presence of Cancer at Autopsy by Assigned Therapy

Autopsy findings	Treated No.	Treated %	Control No.	Control %
Total autopsies	26	100.0	21	100.0
Recurrent cancer found	14	53.8	15	71.4
Cancer at operative site				
No cancer	13	50.0	13	61.9
Cancer found	12	46.2	6	28.6
At anastomosis	1	3.8	1	4.8
Intraperitoneal	9	34.6	4	19.0
Under pelvic floor	2	7.7	1	4.8
Abdominal scar	1	3.8	1	4.8
Unknown	1	3.8	2	9.5
Metastases				
None	12	46.2	5	23.8
One or more	14	53.8	12	57.1
Lung	5	19.2	5	23.8
Brain	0	0.0	0	0.0
Bone	1	3.8	0	0.0
Adrenals	2	7.7	1	4.8
Liver	9	34.6	11	52.4
Other sites	14	53.8	7	33.3
Unknown	0	0.0	4	19.0

Cancer, 1985

Thirty-four of 53 patients (64%) had retroperitoneal lymph node involvement at autopsy. Of 22 patients who did not have lymph node involvement on the original operative specimen (Stages A, B1, B2, B3), 11 patients (50%) had retroperitoneal lymph node involvement at autopsy. This apparent paradox may in part be explained by the observation that 7 of these 11 patients had peritoneal seeding, which provided an alternative pathway for spread to the retroperitoneal nodes; an additional 3 patients had operative-bed or anastomotic recurrences.

NEJM, Dukes C 1990

Table 1. Clinical and Pathological Characteristics in the Stage C Colon-Cancer Study.

	OBSERVATION (N = 315)	LEVAMISOLE (N = 310)	LEV + 5-FU (N = 304)
Age — median (range)	60 (18–84)	61 (26–83)	61 (25–80)
		percent of patients	
Sex — male	53	57	46
Days since surgery			
7–20	29	26	25
21–35	71	74	75
Location of primary tumor			
Cecum and right colon	31	35	34
Flexures and transverse colon	14	19	17
Left colon	6	5	4
Sigmoid and rectosigmoid	47	38	43
Multiple primaries	3	3	2
Depth of invasion			
Submucosa	3	1	3
Muscular layer	12	12	10
Serosa	85	87	86
Adjacent organ involvement			
Adhesion	15	16	13
Invasion	8	7	3
Obstruction	20	20	18
Perforation	3	4	3
Regional peritoneal implants	5	6	7
No. of nodes involved			
1–4	72	71	74
>4	28	29	26
Histologic differentiation			
Well	9	12	10
Moderately well	73	71	71
Poor	17	14	18
Unknown	2	3	2

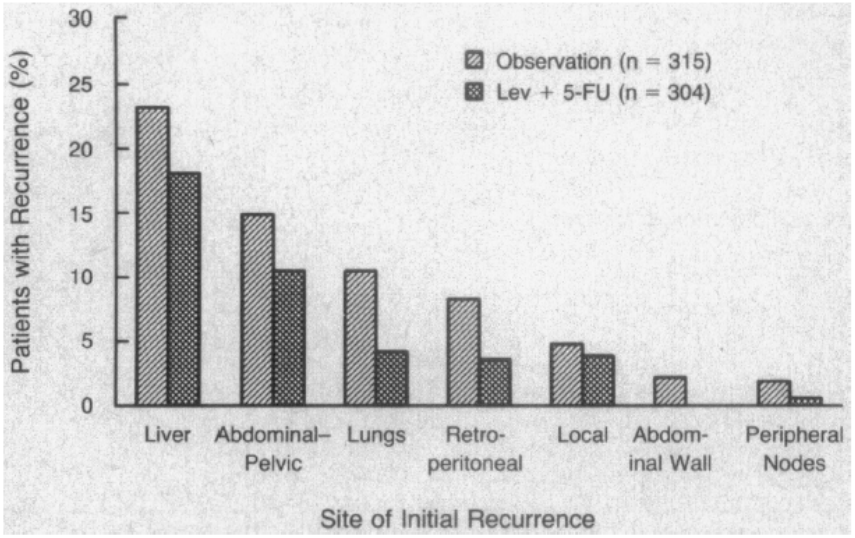

Figure 2. Site of Initial Recurrence, According to Study Arm.

Moertel et al, NEJM 1990

EPIDEMIOLOGÍA DE CARCINOMATOSIS PERITONEAL DE ORIGEN COLORRECTAL

- 4,2% de los pacientes con CCR I-III desarrollarán CP
- CP METACRÓNICA
  - 19% (1/5) de los pacientes que desarrollan metástasis tienen CP
    - 41% única localización
    - 59% metástasis también en otros órganos
- Mediana del tiempo al diagnóstico: 18 meses
  - 16 para cáncer de colon
  - 21 para cáncer de recto
- 73% de pacientes con carcinomatosis fue diagnosticada como primera metástasis (única o con otras)

Segelman J et al. Br J Surg 2012; 99: 699-705
vanGestel et al. EJSO 2014; 963-969

FACTORES DE RIESGO

- T4
- N+
- Ciego
- Mucinoso
- Margen afectado
- Margen desconocido
- Grado de diferenciación desconocido

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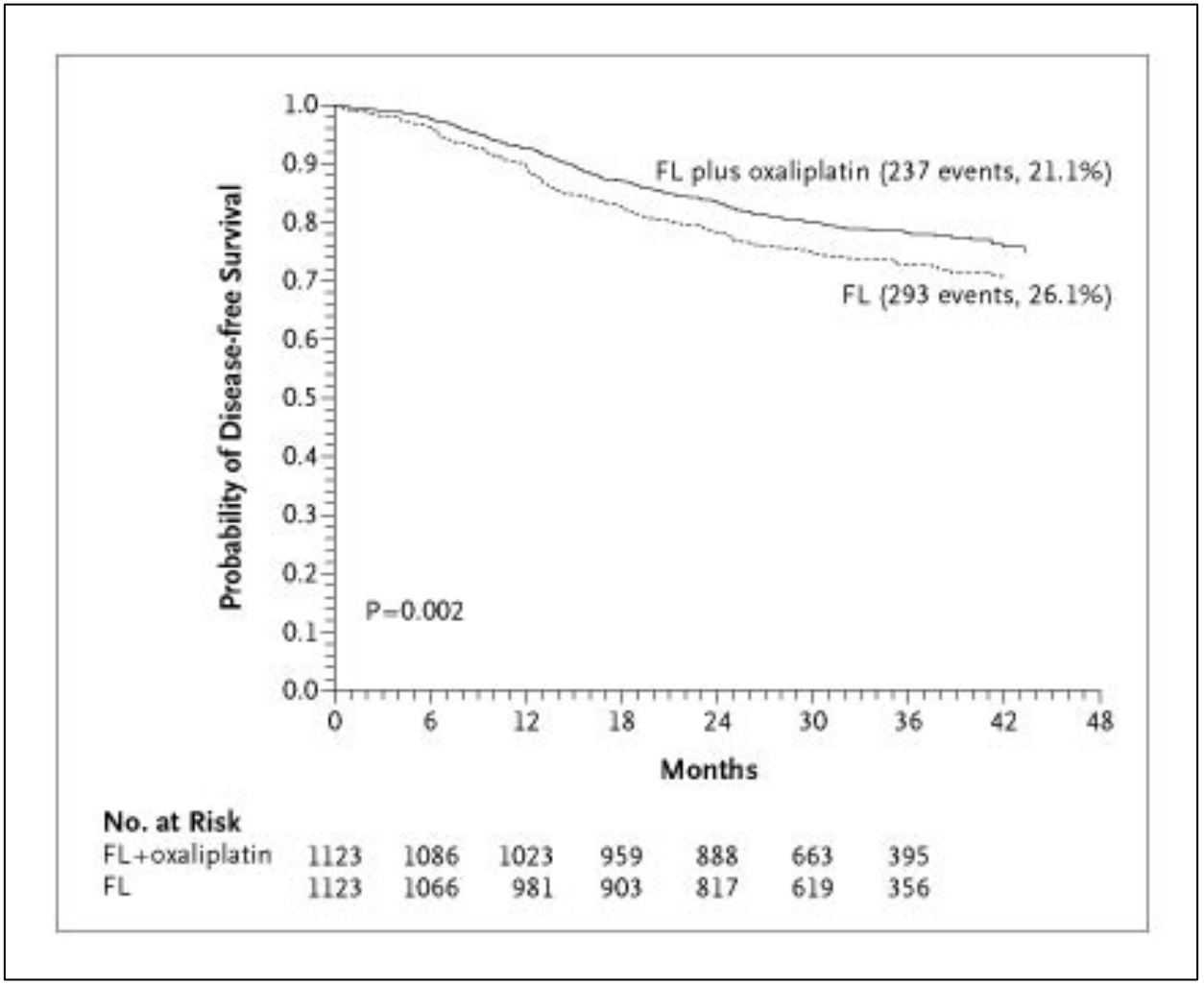
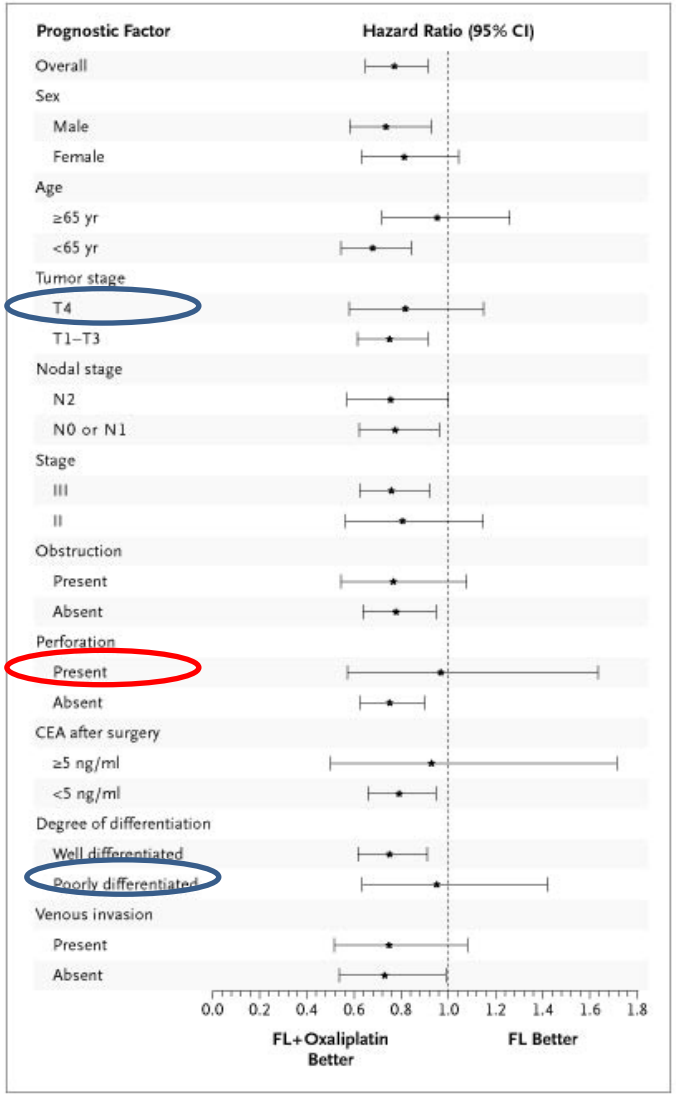


André T et al. N Engl J Med 2004;350:2343-2351.

Hazard Ratios and 95 Percent Confidence Intervals for Recurrence in the Group Given Fluorouracil and Leucovorin (FL) plus Oxaliplatin, as Compared with the FL Group, According to Baseline Prognostic Factors and the Intention to Treat.



André T et al. N Engl J Med 2004;350:2343-2351.

EPIDEMIOLOGÍA DE CARCINOMATOSIS PERITONEAL DE ORIGEN GÁSTRICO

- 1108 pts (1986-2013) con un seguimiento de 37 meses
- Mediana del tiempo al diagnóstico: 17,7 meses
  - 16 para cáncer de colon y 21 para cáncer de recto
- CP METACRÓNICA
  - 15,5% de los pacientes
- Factores de riesgo:
  - Afectación de la serosa
  - N+
  - Clas en anillo de sello
  - Poco diferenciado

Seyfried et al. BMC Cancer 2015

Table 2 Overview of the therapy all patients received during the three treatment time periods

Therapy (all patients n = 1108)	Time period I (1986–1994)	Time period II (1995–2003)	Time period III (2004 – 2013)	p-value*	All time periods
Any therapy	341 (93.9%)	331 (94.8%)	382 (96.5%)	0.260	1054 (95.1%)
Any operation	332 (91.5%)	318 (91.1%)	347 (87.6%)	0.148	996 (90.0%)
D2 gastrectomy	178 (53.3%)	196 (61.6%)	231 (66.8%)	0.001	605 (60.7%)
30d mortality	3 (1.7%)	2 (1,0%)	7 (3.0%)	0.314	12 (2.0%)
90d mortality	8 (4.5%)	9 (4.6%)	16 (6.9%)	0.456	33 (5.5%)
tumor-free	157 (88.2%)	184 (93.9%)	219 (94.8%)	0.085	560 (92.6%)
Thereof w/o 30d-mortality	155 (98.7%)	182 (98.9%)	213 (97.3%)	0.390	550 (98.2%)
Chemotherapy	45 (12.4%)	60 (17.2%)	211 (53.3%)	<0.001	316 (28.5%)
5-FU	40 (11.0%)	45 (12.9%)	3 (0.8%)	<0.001	88 (7.9%)
Combination*	5 (1.4%)	4 (1.1%)	101 (25.5%)	<0.001	110 (9.9%)
Combination + antibody**	0 (0%)	0 (0%)	16 (4%)	<0.001	16 (1.4%)
Chemoregimen undocumented	0 (0%)	11 (3.2%)	91 (8.2%)	<0.001	102 (9.2%)
Perioperative chemotherapy in curative treated and R0 patients (N = 550)					
Patients	155	182	213		550
Perioperative therapy	0 (0%)	0 (0%)	64 (30.0%)	<0.001	65 (11.6%)
No perioperative therapy	155 (100%)	182 (100%)	148 (70.0%)	<0.001	485 (88.4%)

Chemotherapy includes perioperative as well as second-line and palliative therapy. Information on neoadjuvant chemotherapy is provided on 550 patients after R0 gastrectomy and D2 lymphadenectomy.
*Combination of 5-FU and/or oxaliplatin, irinotecane, cisplatin, epirubicin, doxorubicin, cyclophosphamide **combination as described above + antibody therapies (Trastuzumab, Panitumumab, Catumaxumab).

Seyfried et al. BMC Cancer 2015

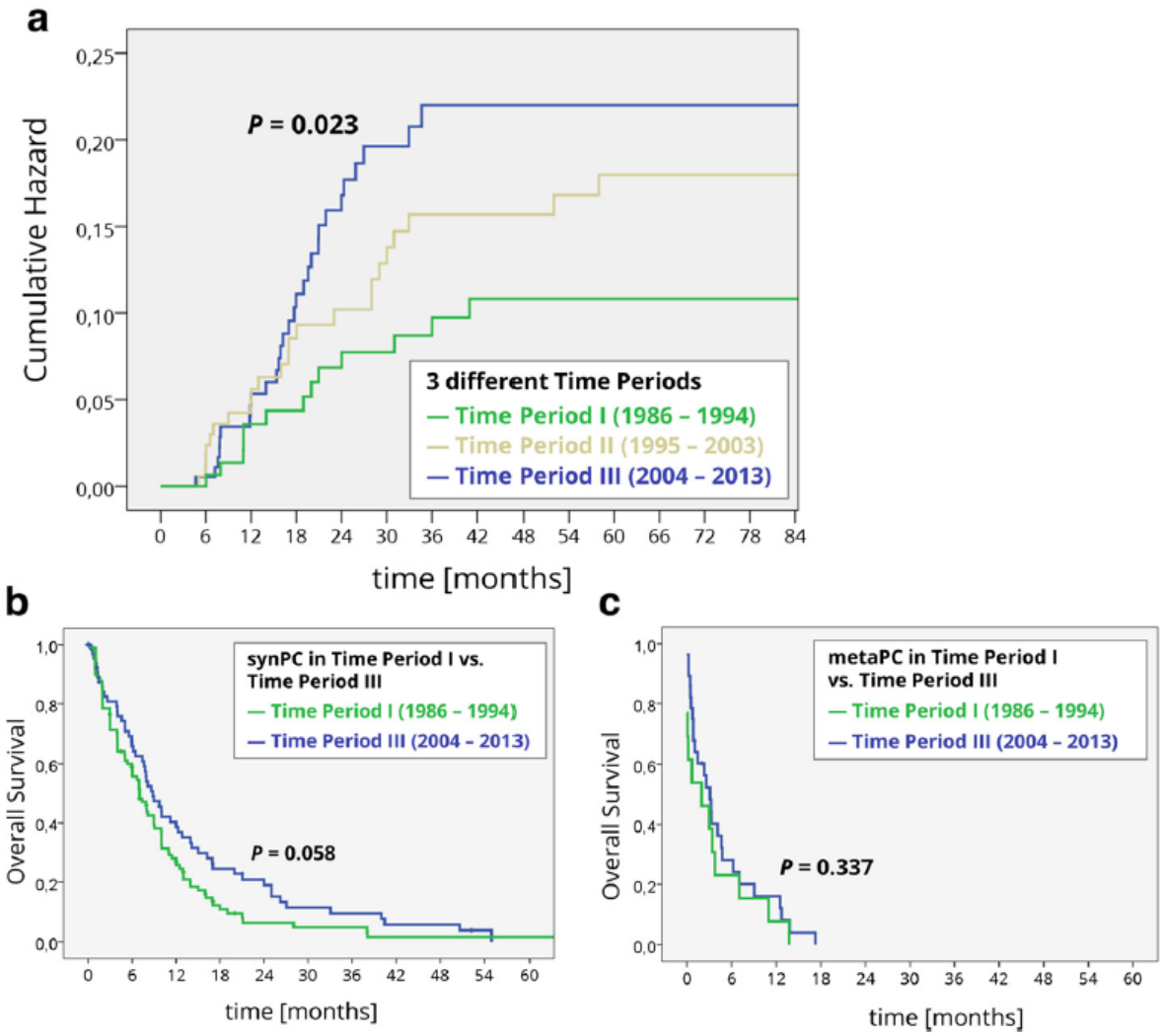


Figure 2 Peritoneal carcinomatosis. a) Cumulative hazard ratio for the development of metaPC (550 after R0 resection, stratified for the three time periods.) **b)** Tumour related overall survival of 167 patients with synchronous peritoneal carcinomatosis (synPC) stratified for time periods I and III. **c)** Tumour related overall survival from the time of diagnosis metachronous peritoneal carcinomatosis (metaPC) in the group of 550 patients that were R0 after initial therapy.

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CONCLUSIONES

- La CP constituye un problema de magnitud mal conocida
- La precocidad del diagnóstico podría estar relacionada con la intensidad de los seguimientos
- No hay datos fiables de la eficacia de la quimioterapia en su prevención