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*International Society
for the Study of Pleura
and Peritoneum*



OVARIAN CANCER

Patient Selection and Timing of HIPEC in Ovarian Cancer

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

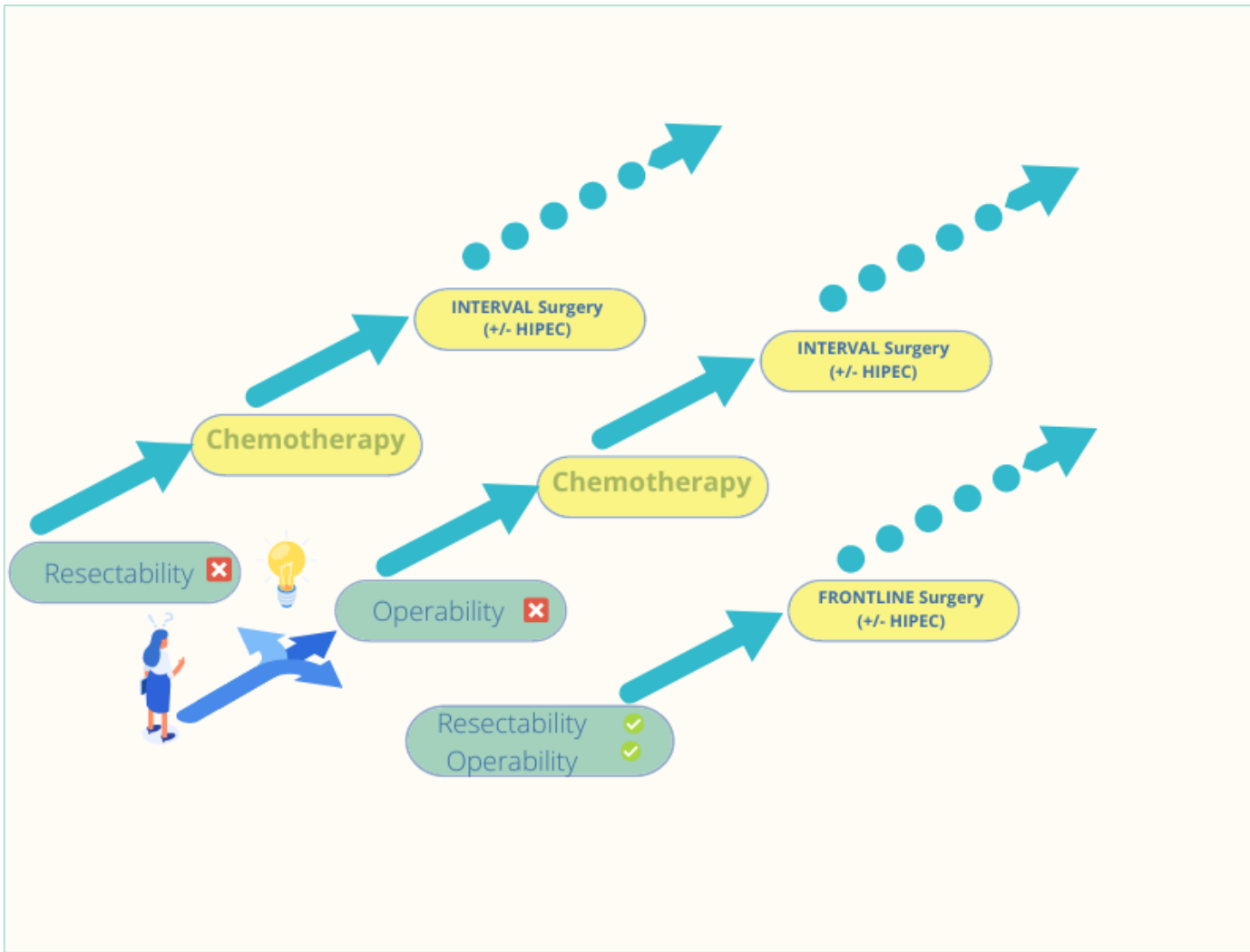
Disclosures

- Consultant for GlaxoSmithKline.

This presentation and/or comments will be free of any bias toward or promotion of the above referenced company or their product(s) and/or other business interests.

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

Timepoint : a surrogate for patient selection process

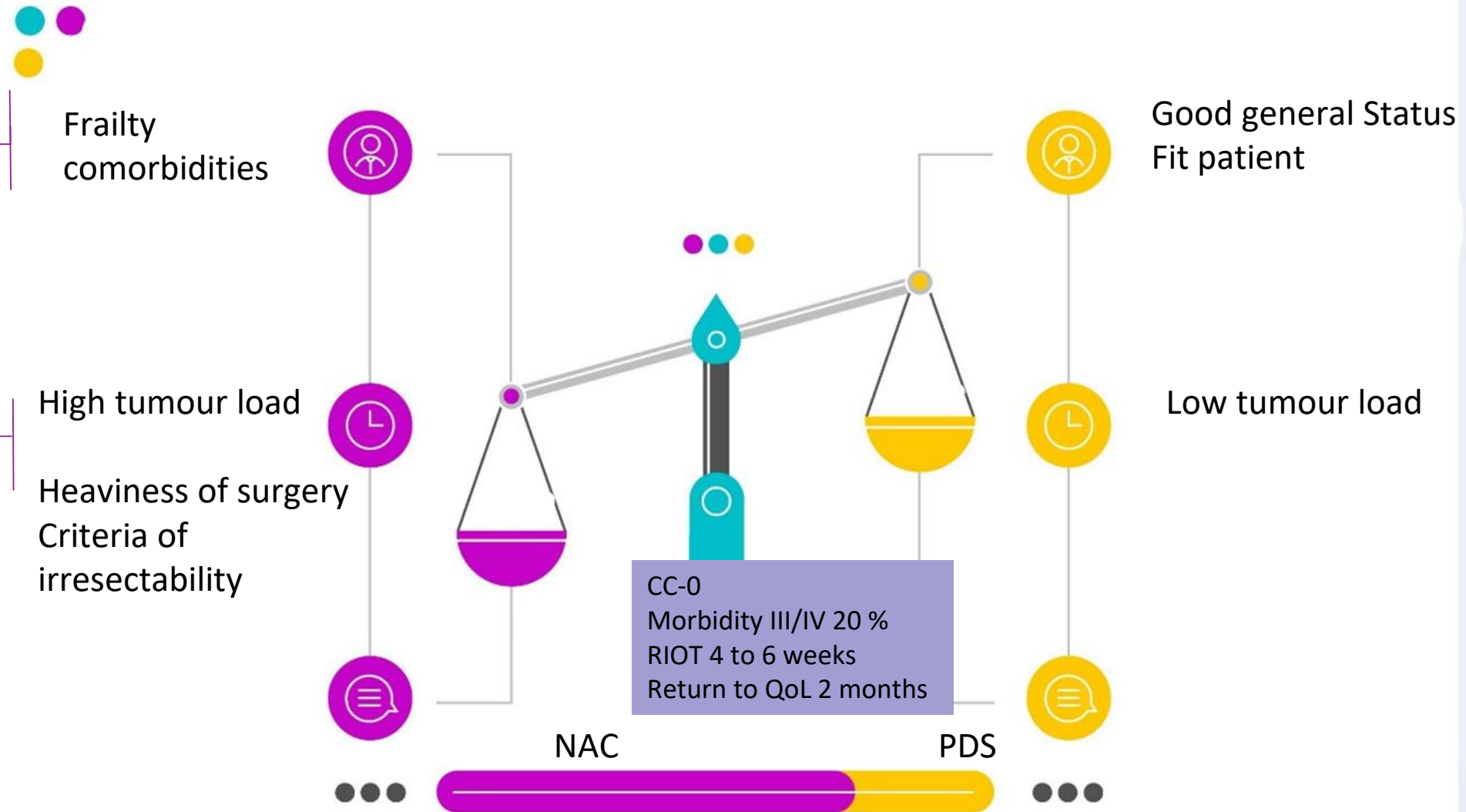


Prerequisite :

1/ Surgery : **Complete** AND the **sooner** the better

2/ **Multidisciplinary** team

CRS and HIPEC : timepoint

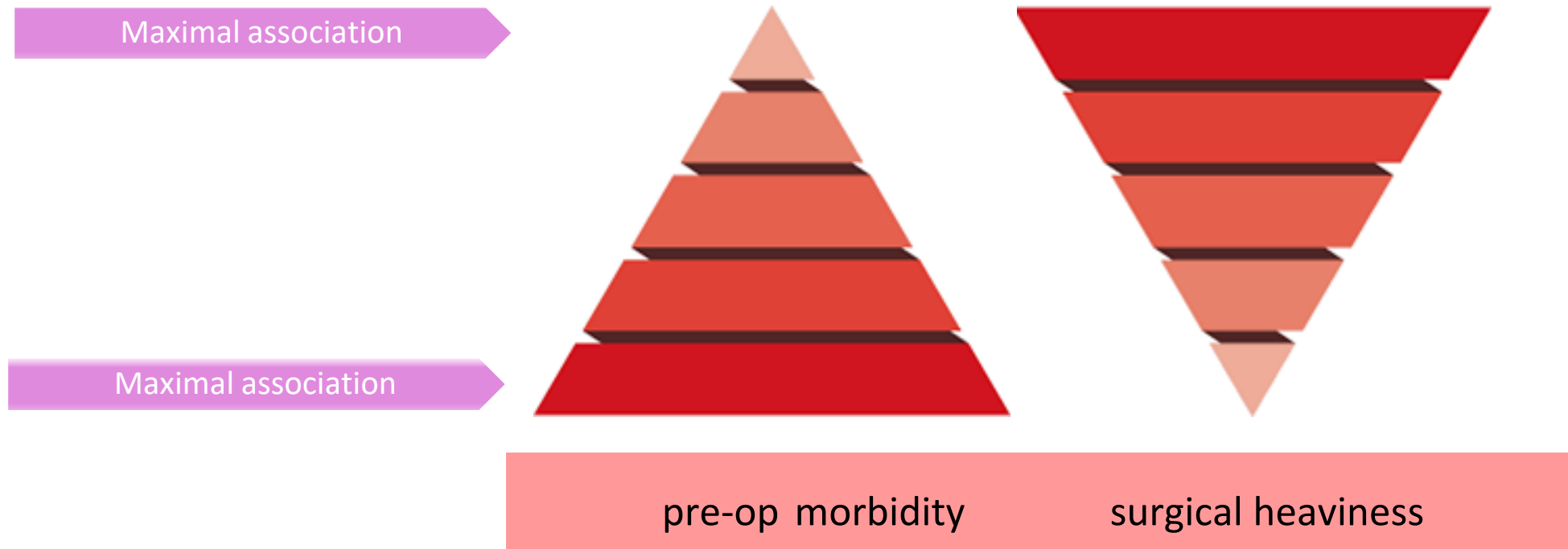


Frailed patients and Elderly

The german quality assurance programm QS-OVAR 2001, 2004 and 2008: OS for patients with intended standard strategy CRS->CT	FIGO IIIB-IV	FIGO IIIB-IV		
		75+ years	Comorbidity	75+ yrs plus comorbidity
	(n = 1436)	(N = 289)	(N = 436)	(N = 166)
	(E = 896)	(E = 243)	(E = 333)	(E = 146)
OS in months				
median	30,3	14,1	17,3	10,6
95% CI	28,1 - 32,8	11,9 - 16,4	15,2 - 20,6	7,6 - 14,0
OS-rates in %				
3 months	90,2	80,0	3 months mortality rate: 27,7% 6 months mortality rate: 40,0%	
6 months	85,5	69,1		
9 months	81,7	61,6		
12 months	76,9	55,2		




≈12 % of all pts

adapt surgery to general status ?

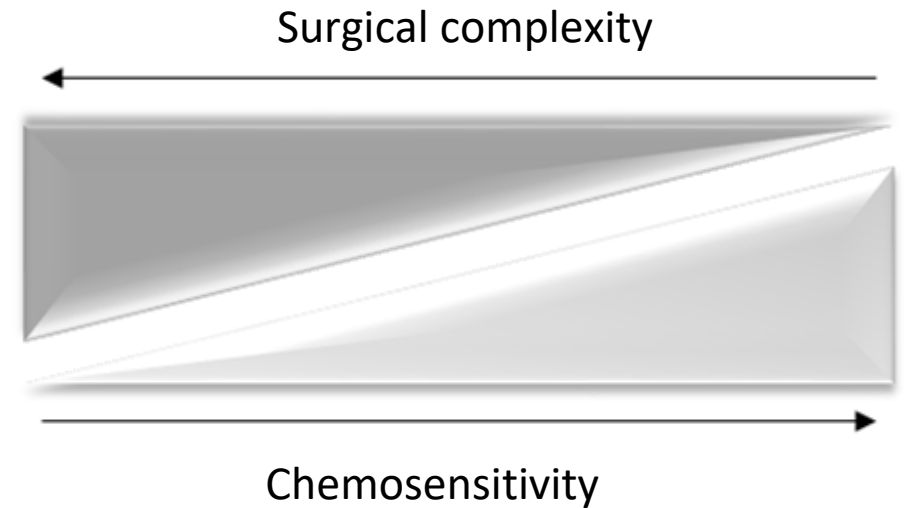
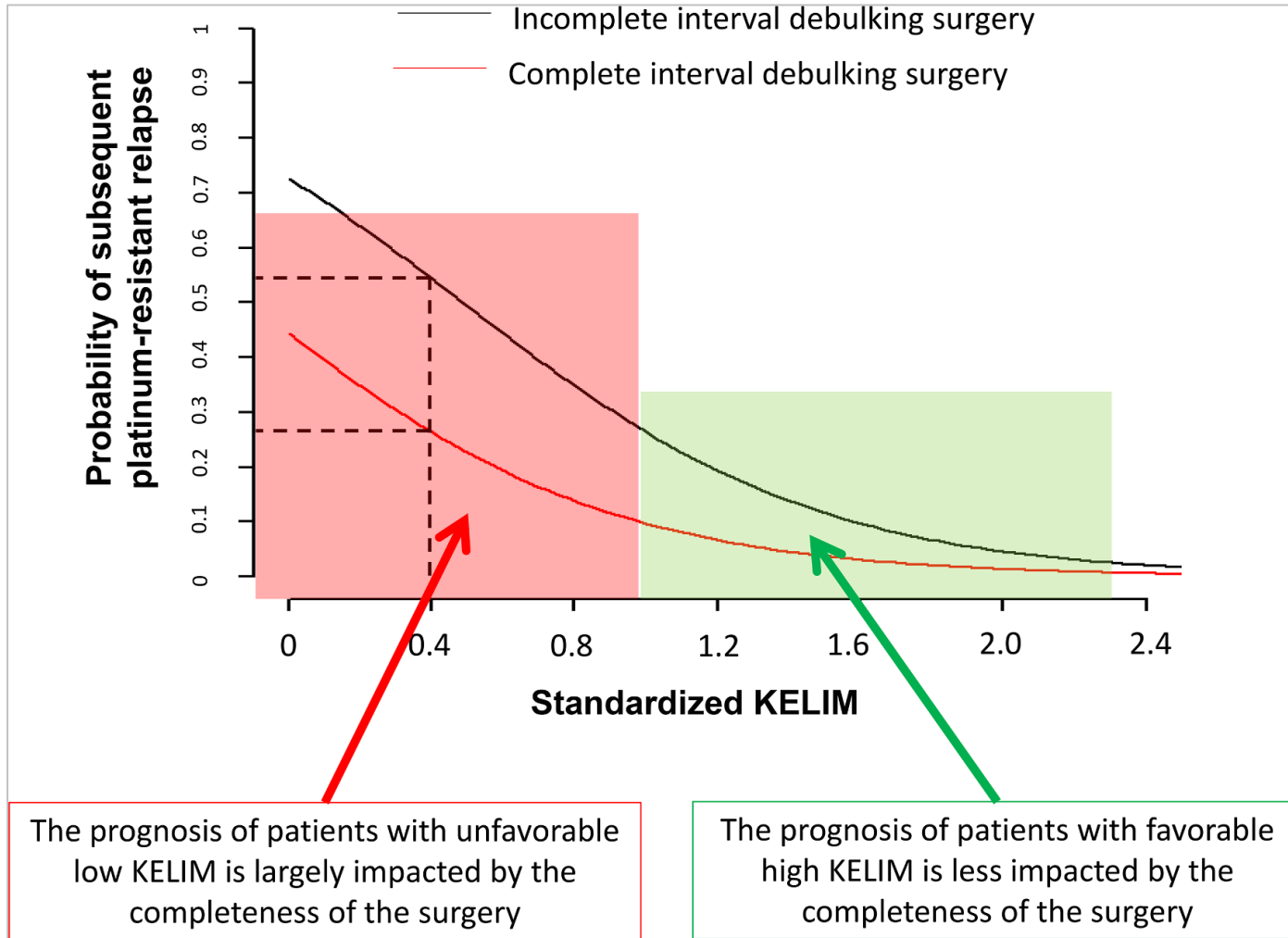


Adapt surgery to disease extent

- Laparoscopy
- CT Scan
- MRI

	Laparoscopic assessment
	<ul style="list-style-type: none"> - Peritonectomies (including diaphragmatic domes) - Splenectomy - 1 or 2 digestive anastomoses
	<ul style="list-style-type: none"> - Protection ileostomy - More than 2 digestive anastomoses - Extensive lymphadenectomy (risk of <u>lymphorrhea</u>)
	<ul style="list-style-type: none"> - Univocal irresectability criteria: <ul style="list-style-type: none"> - Mesentery root retraction - Small intestine serosa military - Invasion of the hepatic pedicle (≠ carcinosis of the peritoneum of the pedicle) - Invasion of the <u>cavo-sus-hepatic confluence</u> (theoretical, satellite of massive carcinomas which combine other criteria of <u>irresectability</u>) - unreasonable surgical procedures <ul style="list-style-type: none"> - Total colectomy - Total / subtotal gastrectomy

Should we adapt surgery to biology ?



Assessment of the respective contributions of surgery and of the tumor primary chemosensitivity relative to the success of the first-line treatment in **CHIVA trial**. Probability of subsequent platinum-resistant relapse according to the completeness of interval debulking surgery and the tumor primary chemosensitivity measured during neoadjuvant chemotherapy

Should we adapt HIPEC to biology ?

TUMOR MARKERS AND SIGNATURES

Effect of HIPEC according to HRD/*BRCA*wt genomic profile in stage III ovarian cancer: Results from the phase III OVHIPEC trial

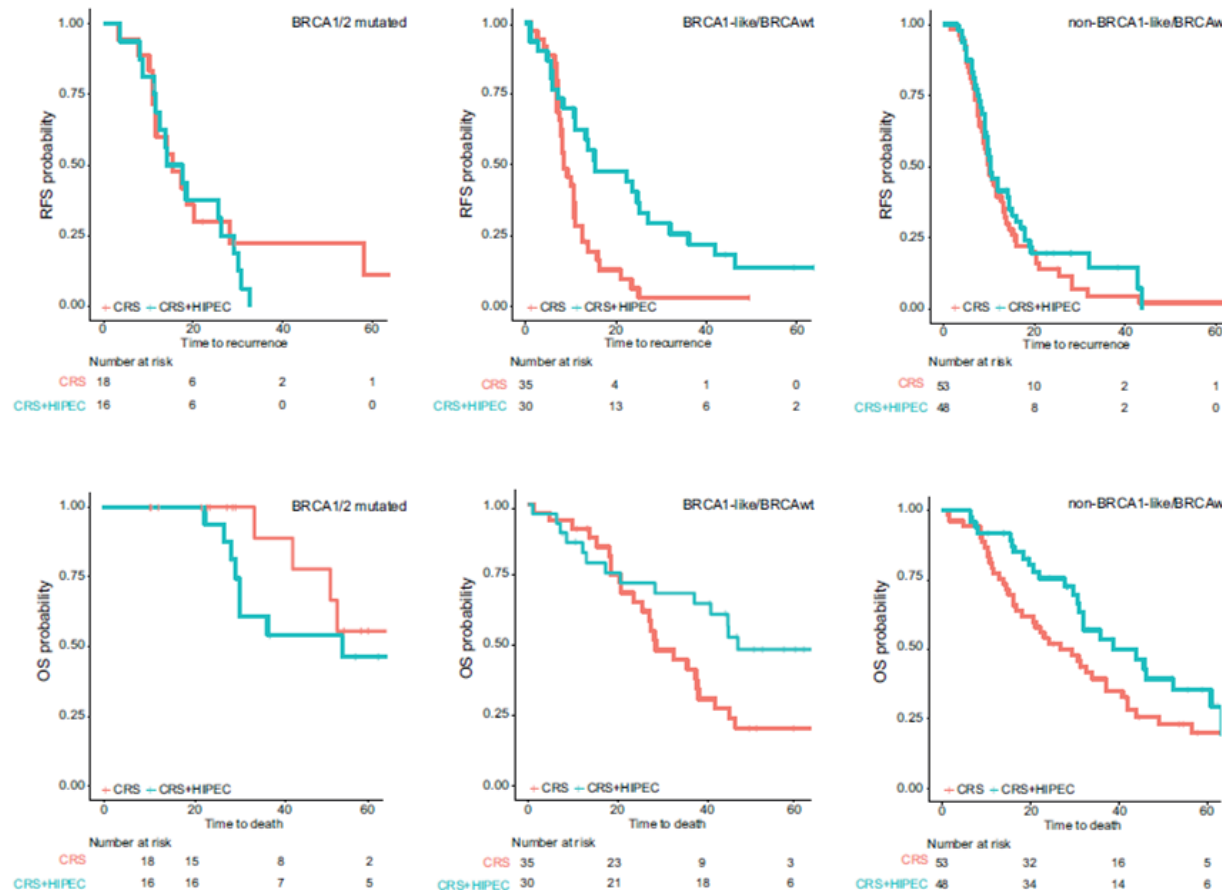


FIGURE 3 Kaplan-Meier curves for *BRCA*mut, *BRCA*1-like/*BRCA*wt and non-*BRCA*1-like patients for RFS and OS by treatment arm [Color figure can be viewed at wileyonlinelibrary.com]

HIPEC (cddp 100 mg 90 min)

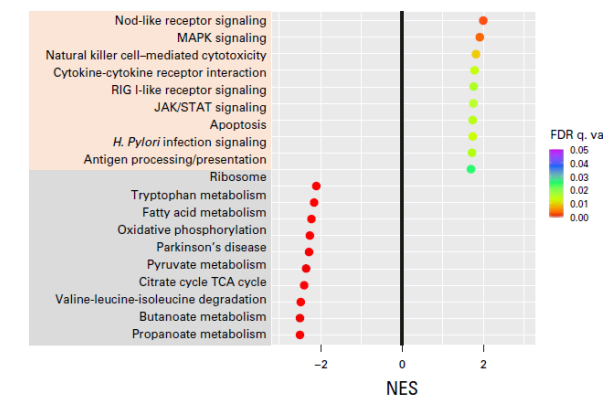
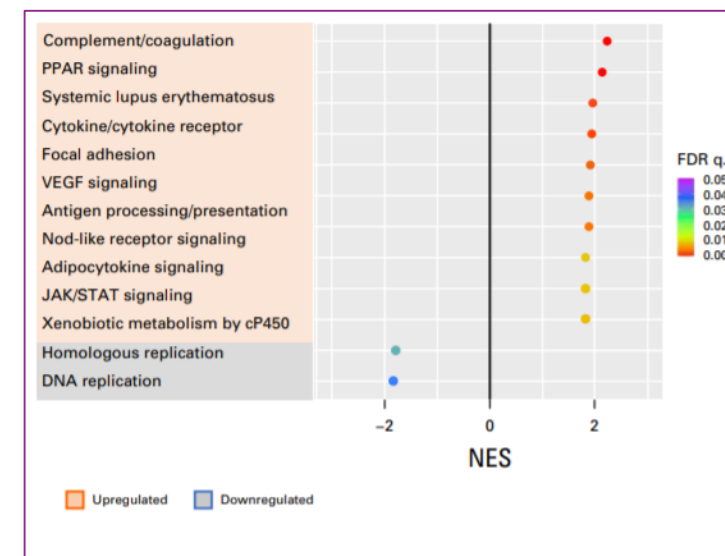
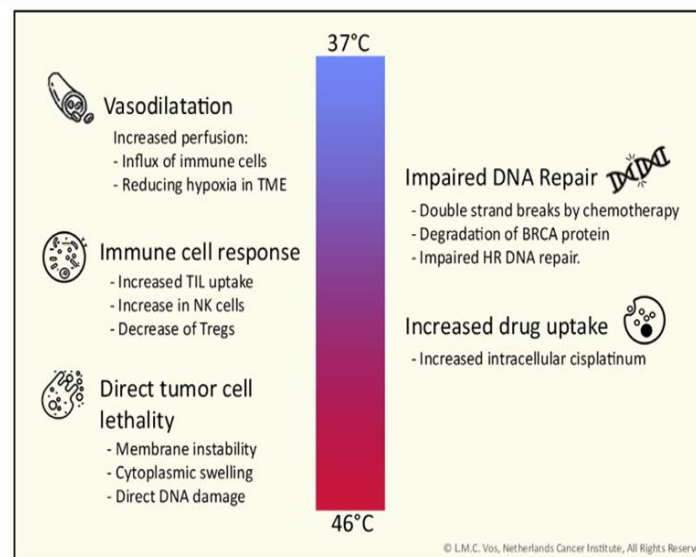
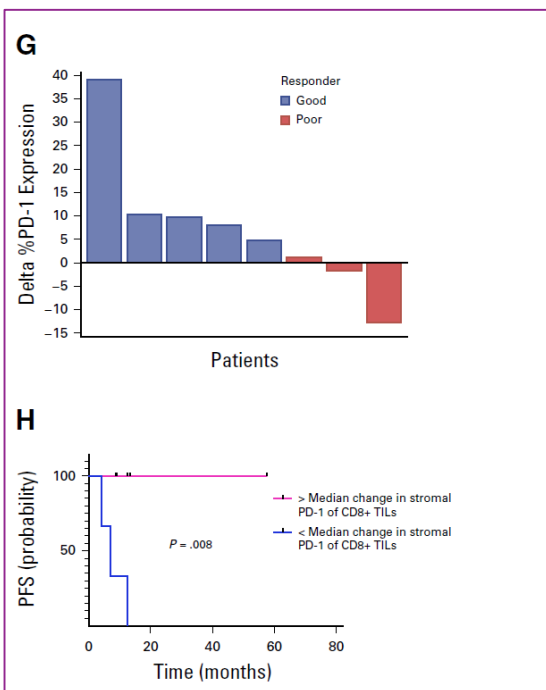
→ *BRCA* mutated : no benefit

→ HRD

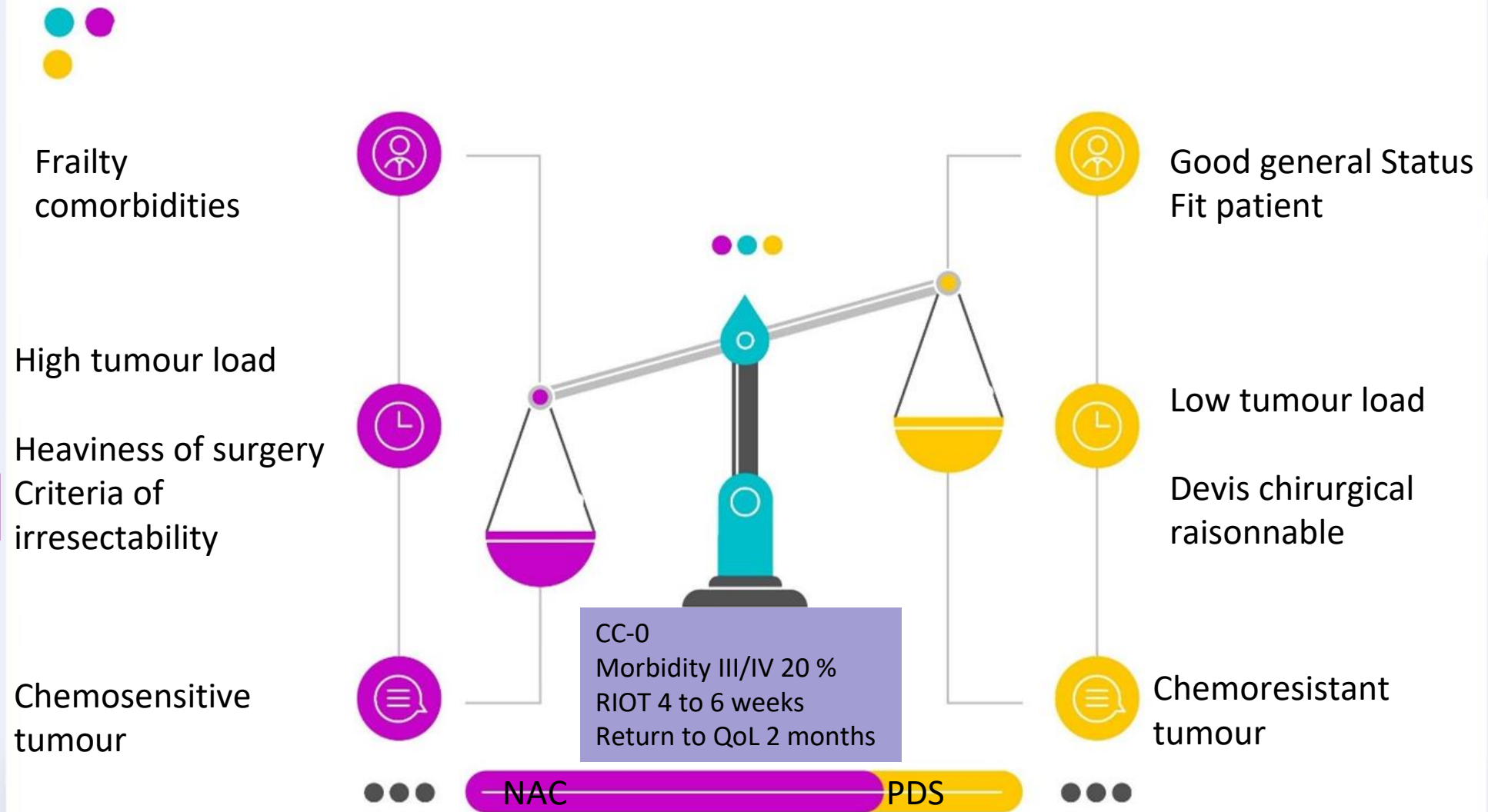
→ HRP

} Benefit OS/PFS

Should we adapt HIPEC to biology ?



CRS and HIPEC : the timepoint



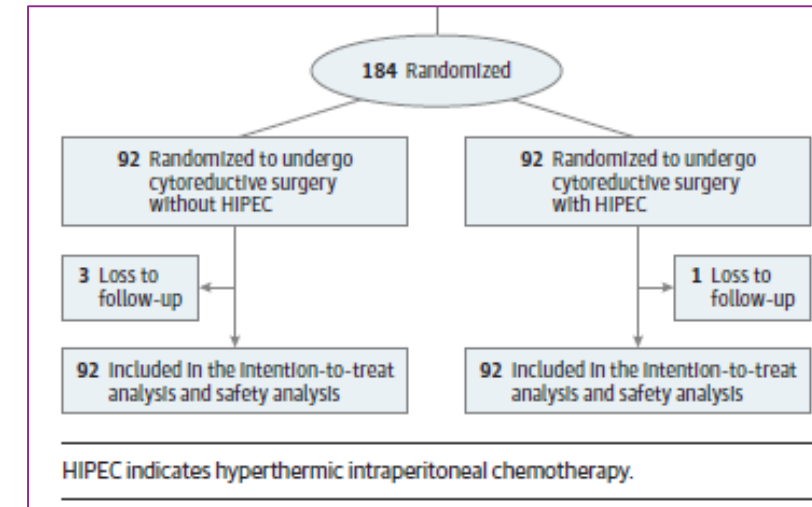
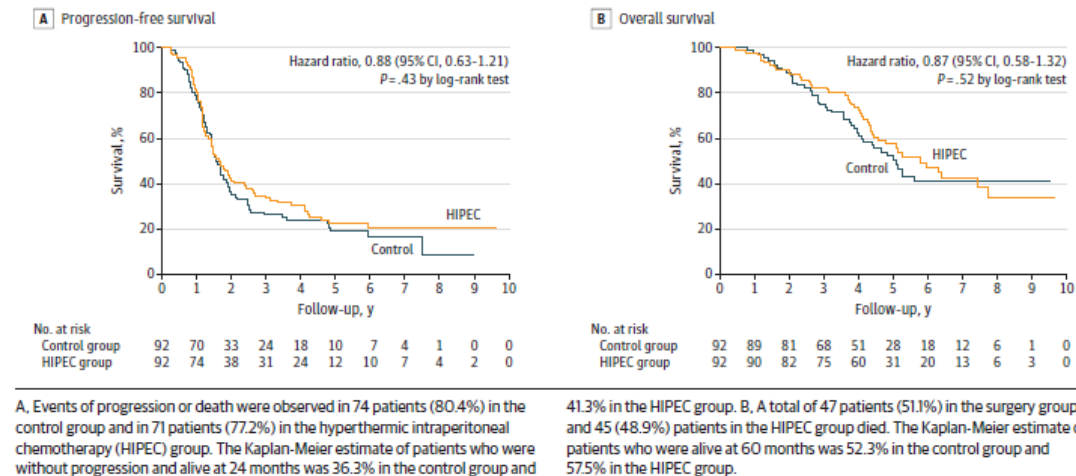
CRS and HIPEC : the timepoint Frontline

JAMA Surgery | Original Investigation

Survival After Hyperthermic Intraperitoneal Chemotherapy and Primary or Interval Cytoreductive Surgery in Ovarian Cancer A Randomized Clinical Trial

Myong Cheol Lim, MD, PhD; Suk-Joon Chang, MD, PhD; Boram Park, PhD; Heon Jong Yoo, MD, PhD; Chong Woo Yoo, MD, PhD; Byung Ho Nam, PhD; Sang-Yoon Park, MD, PhD; for the HIPEC for Ovarian Cancer Collaborators

Figure 2. Kaplan-Meier Estimates of Progression-Free Survival and Overall Survival as Preplanned Intention to Treat



→ HIPEC (cddp 75 mg 90 min)

→ Mixed frontline AND interval surgery

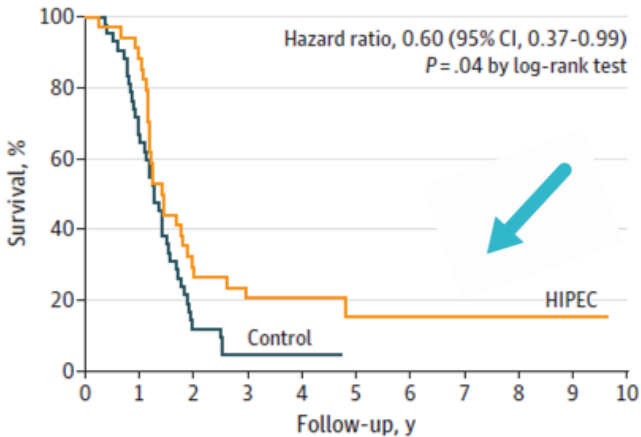
CRS and HIPEC : the timepoint Interval

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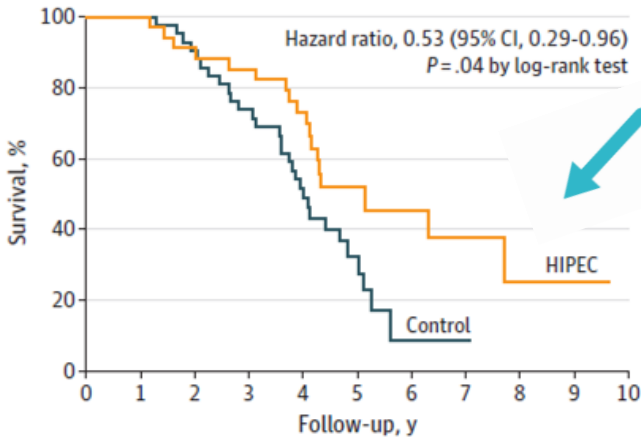
Myong Cheol Lim, MD, PhD; Suk-Joon Chang, MD, PhD; Boram Park, PhD; Heon Jong Yoo, MD, PhD; Chong Woo Yoo, MD, PhD;
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C Progression-free survival in patients undergoing interval cytoreductive surgery after neoadjuvant chemotherapy



No. at risk										
Control group	43	28	5	2	1	0	0	0	0	0
HIPEC group	34	30	9	7	6	2	2	1	1	0

D Overall survival in patients undergoing interval cytoreductive surgery after neoadjuvant chemotherapy



No. at risk										
Control group	43	42	38	31	20	7	1	1	0	0
HIPEC group	34	34	31	29	22	8	6	3	2	0

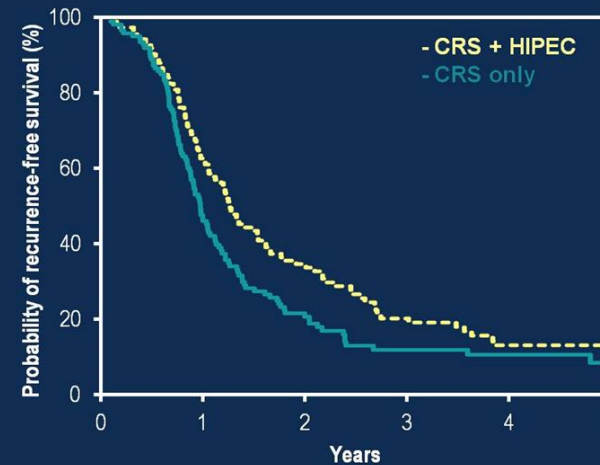
CRS and HIPEC : the timepoint Interval

Results

	CRS + HIPEC N=122	
Surgical result, n (%)		
0 mm (complete)	83 (68)	
0 - 2.5 mm	22 (18)	
2.5 mm – 10 mm	13 (11)	
> 10 mm/no resection	4 (3)	
Post-surgical complications, n (%)		
Infections	17 (14)	9 (7)
Surgery related	14 (11)	17 (14)
Six cycles chemotherapy completed, n (%)	115 (94)	109 (89)
Median number of days in hospital (Q1-Q3)	10 (8-12)	8 (7-10)
Median number of days to restart of chemotherapy (Q1-Q3)	33 (28-41)	30 (25-41)

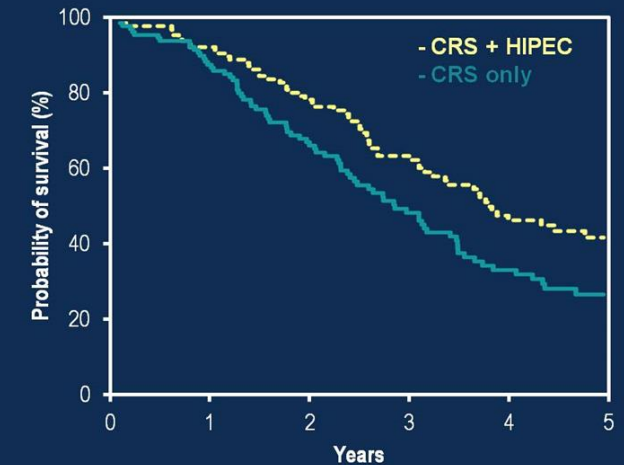
RFS
Median RFS, mo
Hazard Ratio (95% CI)

Recurrence-free Survival



RFS	CRS+HIPEC n=122	CRS only n=123
Median RFS, months	14.2	10.7
Hazard Ratio (95% CI)	0.68 (0.51–0.89)	

Overall Survival



OS	CRS+HIPEC n=122	CRS only n=123
Median OS, months	45.7	33.9
Hazard Ratio (95% CI)	0.67 (0.48–0.94)	

CRS and HIPEC : the timepoint Recurrence

Ann Surg Oncol (2015) 22:1570–1575
DOI 10.1245/s10434-014-4157-9

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – GYNECOLOGIC ONCOLOGY

Cytoreductive Surgery and HIPEC in Recurrent Epithelial Ovarian Cancer: A Prospective Randomized Phase III Study

J. Spiliotis, MD, PhD¹, E. Halkia, MD, PhD^{1,2}, E. Lianos, MD³, N. Kalantzi, MD⁴, A. Grivas, MD³, E. Efstathiou, MD¹, and S. Giannacopoulos, MD²

TABLE 2 Survival by disease stage

Mean survival	Stage III _c survival (months)	Stage IV survival (months)
HIPEC	26.9	26.4
Non-HIPEC	14.2	11.9

HIPEC hyperthermic intraperitoneal chemotherapy

→ Sample size calculation ?

→ Randomization process ?

→ HIPEC: pt-sensitive 100 mg and paclitaxel 175 mg
plt-resistant doxorubicin 35 mg and
(paclitaxel 175 mg or mitomycin 15 mg) 60 min

CRS and HIPEC : the timepoint Recurrence

Secondary Cytoreduction and Carboplatin Hyperthermic Intraperitoneal Chemotherapy for Platinum-Sensitive Recurrent Ovarian Cancer: An MSK Team Ovary Phase II Study

Oliver Zivanovic, MD¹; Dennis S. Chi, MD¹; Qin Zhou, MS¹; Alexia Iasonos, PhD¹; Jason A. Konner, MD¹; Vicky Makker, MD¹;

Journal of Clinical Oncology*

Zivanovic et al

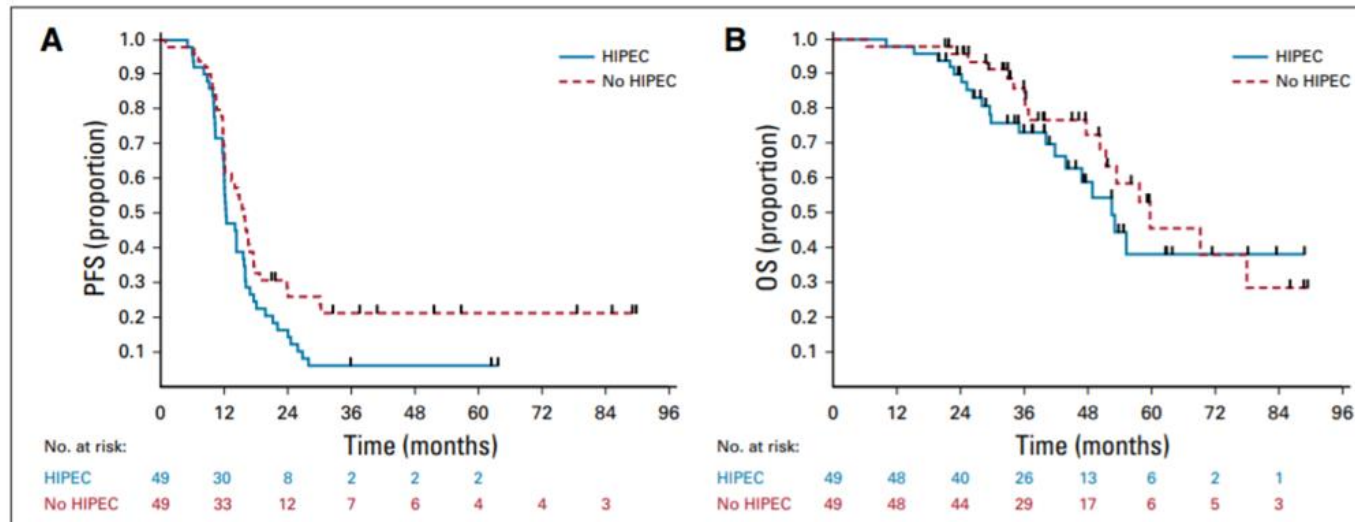


FIG 3. (A) PFS by treatment arm. Kaplan-Meier survival plots of PFS. (B) OS by treatment arm. Kaplan-Meier survival plots of OS. HIPEC, hyperthermic intraperitoneal chemotherapy; OS, overall survival; PFS, progression-free survival.

Phase II

Interval Carboplatin HIPEC

Results

- HIPEC vs no HIPEC
- DFS 12,3 vs 15,7
- OS 52,5 vs 59,7

No survival benefit to HIPEC

Patient Selection and Timing of HIPEC in Ovarian Cancer

- Interval CRS+HIPEC (cddp 75 ou 100) : Clear trend of survival benefit
- Frontline and recurrent settings : No benefit

We aim : From operability + resectability → operability + resectability + **predictive Biomarkers** (**transcriptomic signature, HR status, TME features**)

We need research to :

- find strong biomarkers to predict good responders
- Best combinaison with targeted therapy (Parpi, bevacizumab, immunotherapy). « **thinking synergistic effect** »
- Find the temperature/dose/molecule-»goal »