Algoritmo di trattamento delle pazienti con neoplasia ovarica nel 2019

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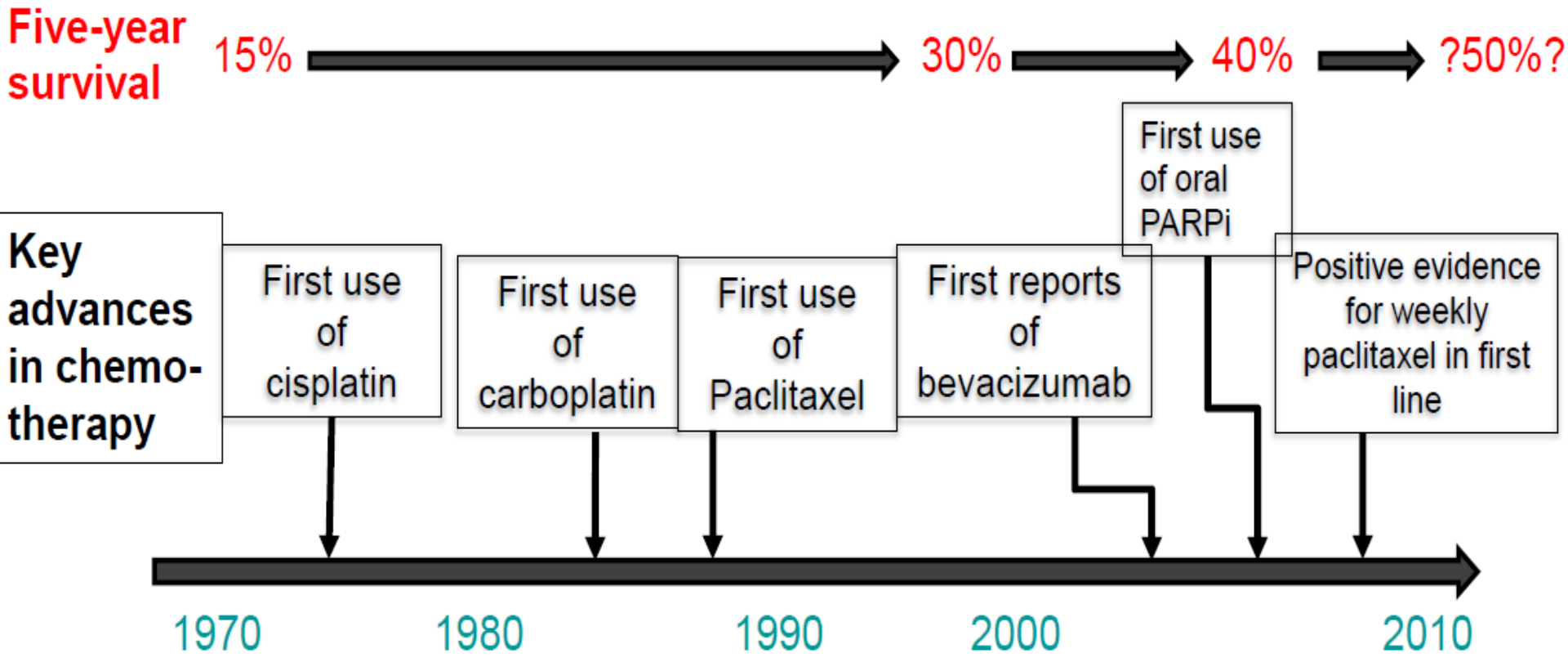
Unmet needs in ovarian cancer

- Still the biggest killer among gyn malignancies
- Despite high response rate, majority of patients will relapse
- **First line treatment mostly unchanged over the past 20 years**
- Multiple chemotherapy lines allows prolongation of survival without decreasing mortality
- Precision medicine far behind compared to other malignancies

Progress in the Management of Ovarian Cancer: Evolution Over 40 Years

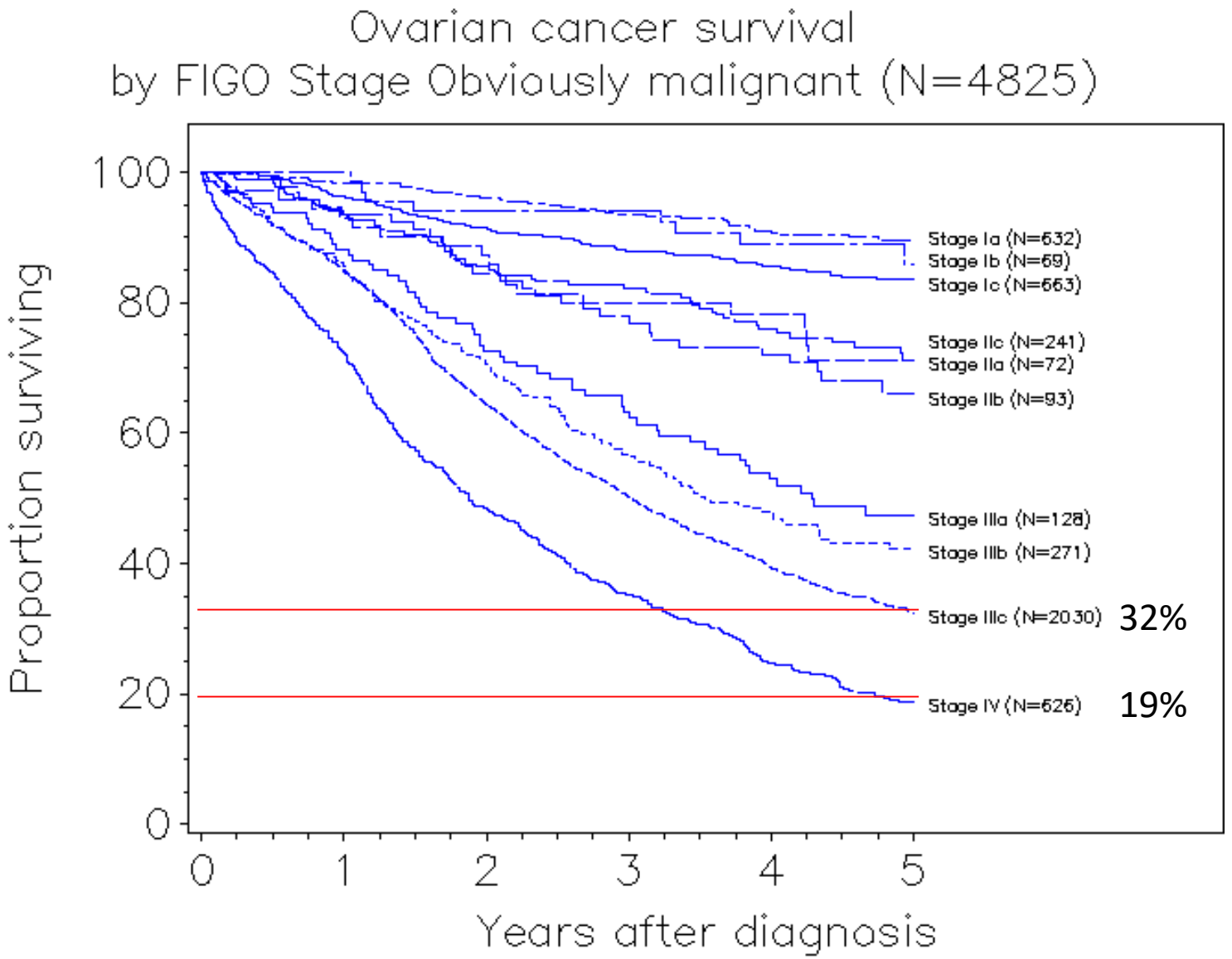


I numeri del cancro dell'ovaio in Italia

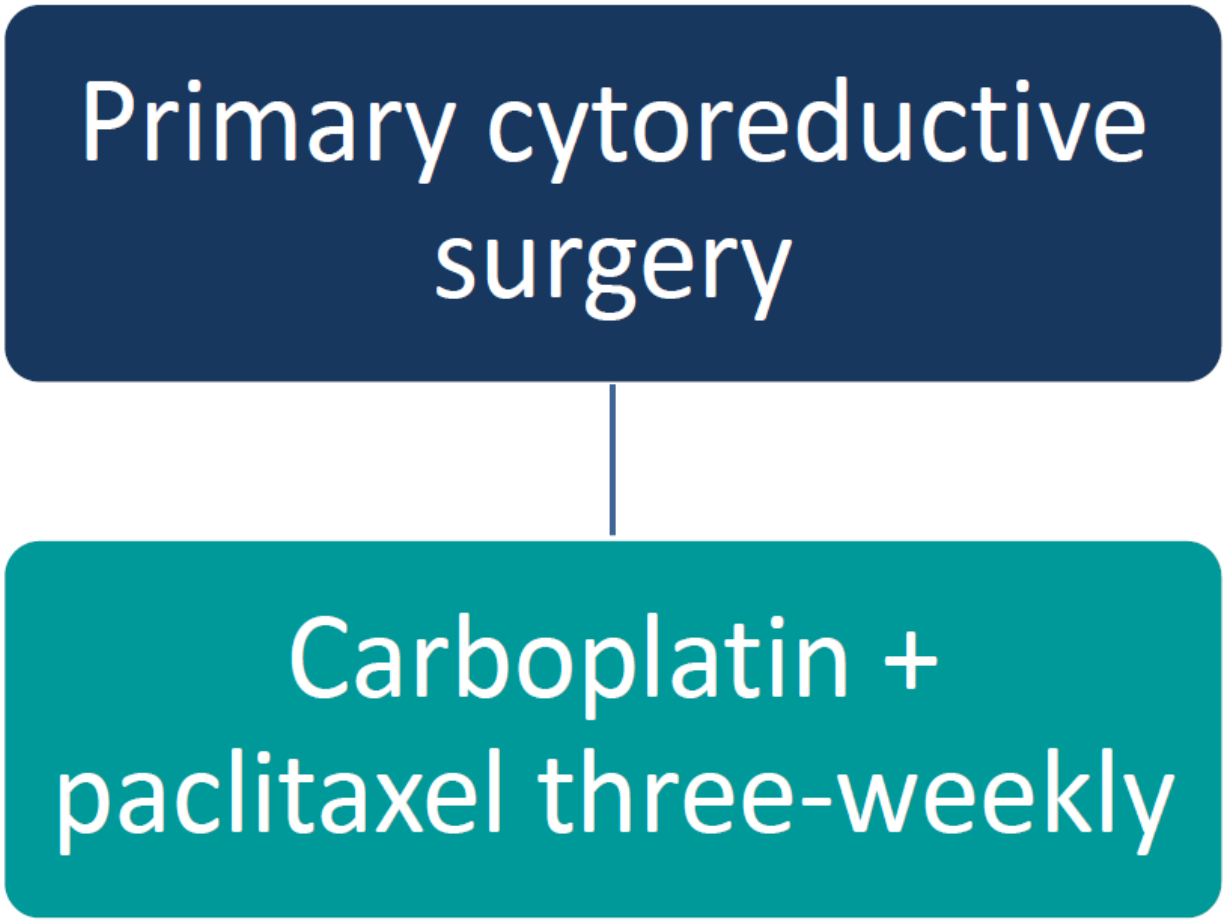
nuovi casi/anno	**5.200**
guarisce	**<1/3**
decessi/anno	**3.200**
sopravvivenza a 5 anni	**39%**

AIRTUM/AIOM 2017

26th FIGO Annual Report
Carcinoma of the Ovary: 5-yr Survival by Stage



Ovarian cancer: first line treatment algorithm



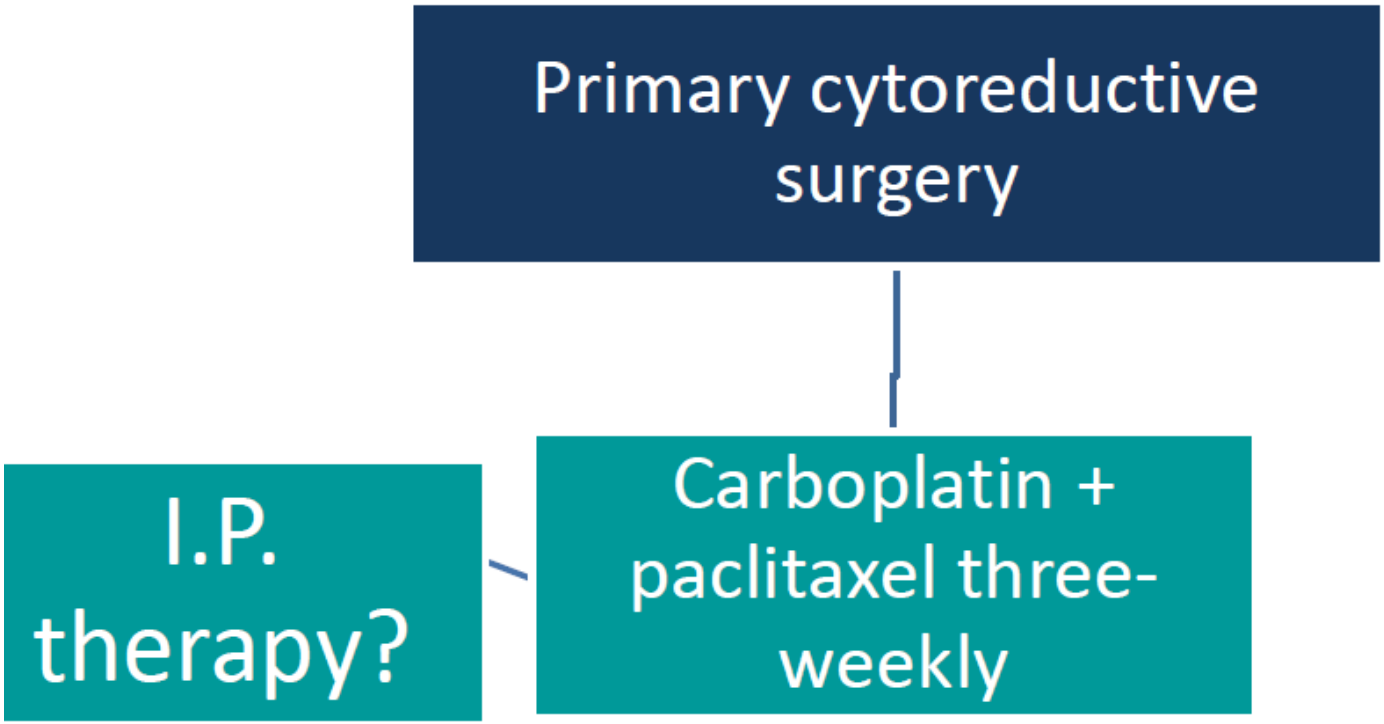
Can we choose among chemotherapy regimens

- Substitution of paclitaxel by other drug.
  - SCOTROC, MITO-2

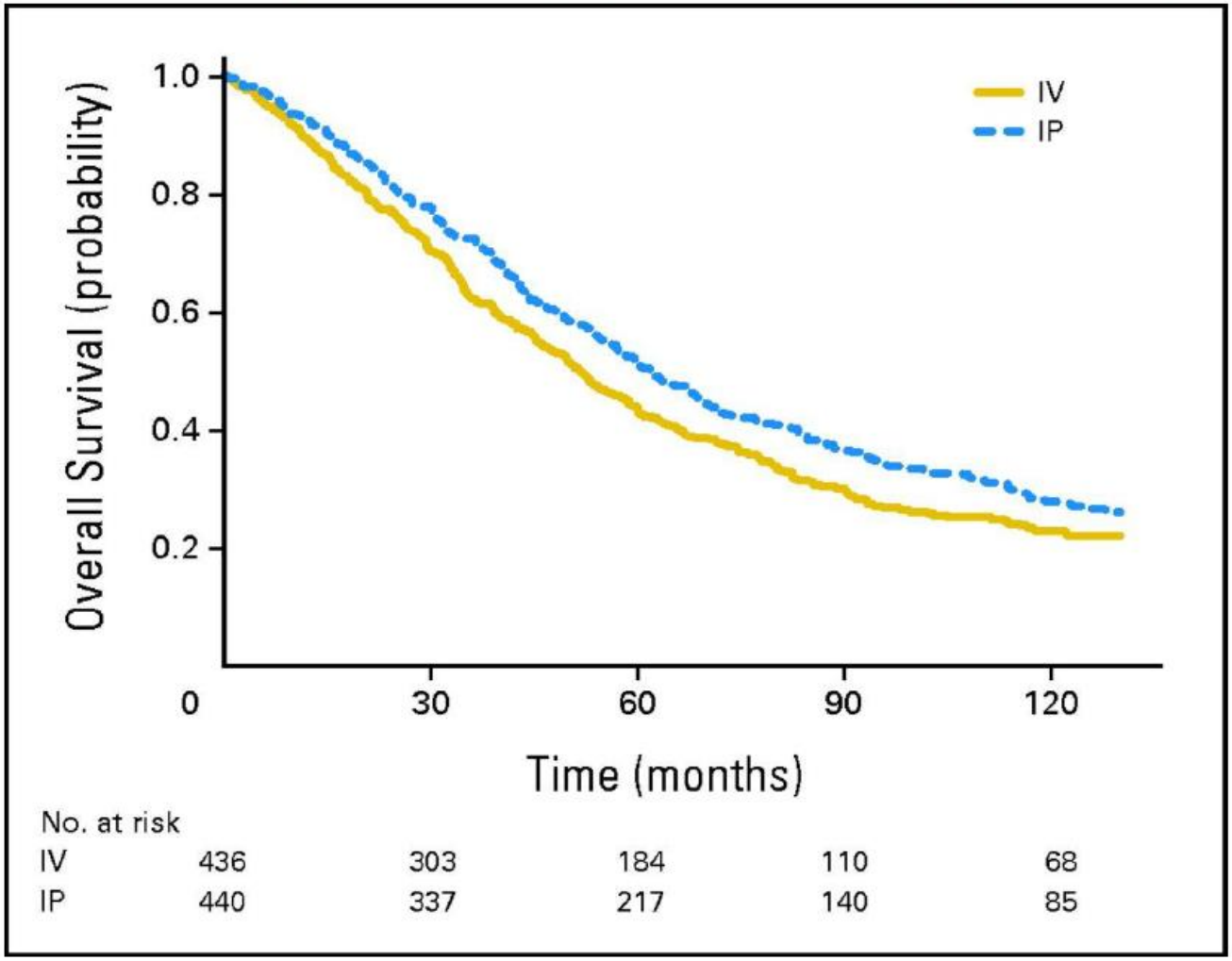
- Addition of a third drug.
  - 6 GCIG trials…≈ 11,000 patients

Nothing looks better than Carboplatin/Paclitaxel

Can we choose the route of administration?

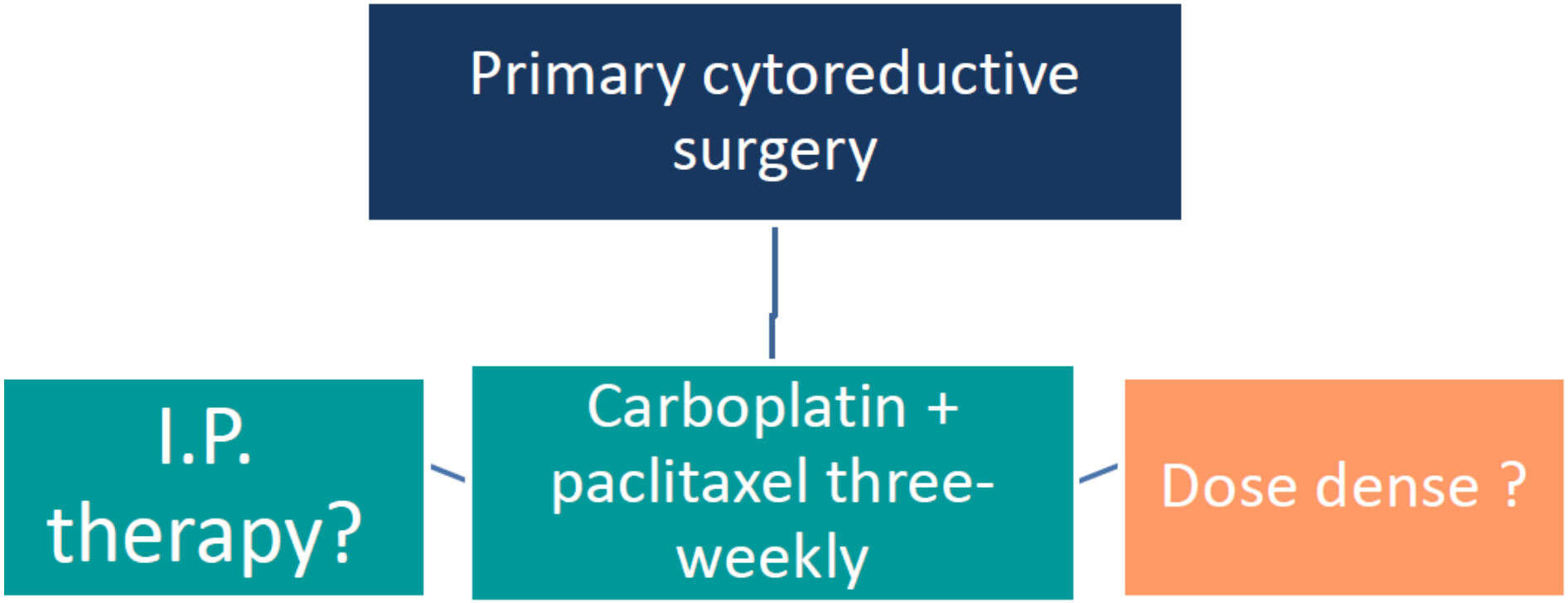


Long-term overall survival of patients treated with intravenous (IV) versus intraperitoneal (IP) chemotherapy (P = .04).



Devansu Tewari et al. JCO doi:10.1200/JCO.2014.55.9898

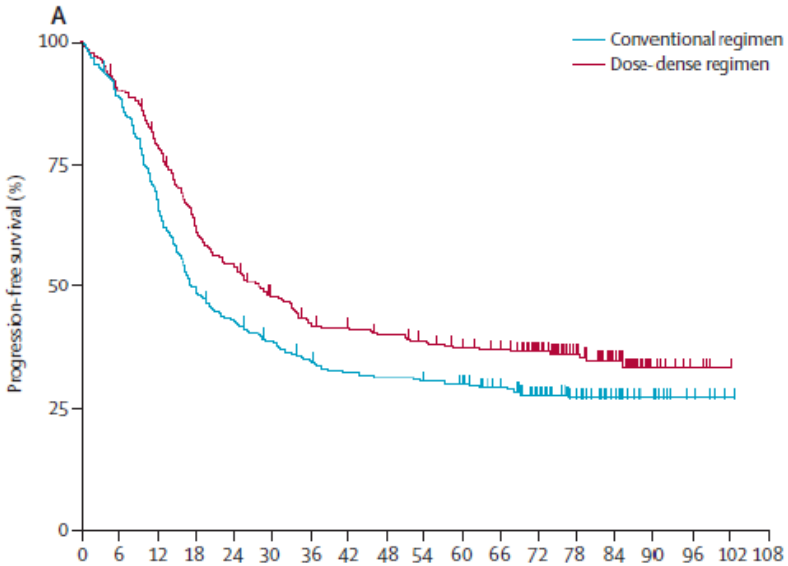
Can we change schedule?



First line Dose dense in ovarian cancer

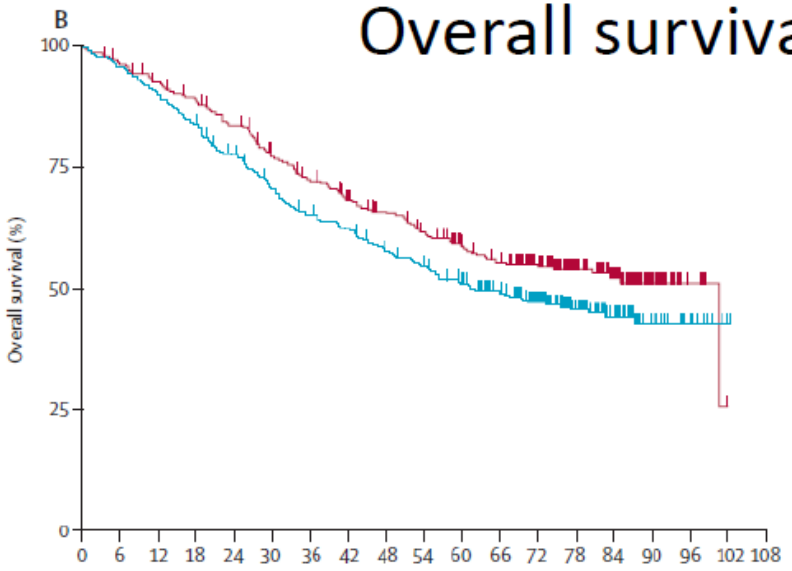
JGOG-3016

PFS



Median PFS
28.2 months vs 17.5 months
(HR 0.76, 95% CI 0.62–0.91; p=0.0037).

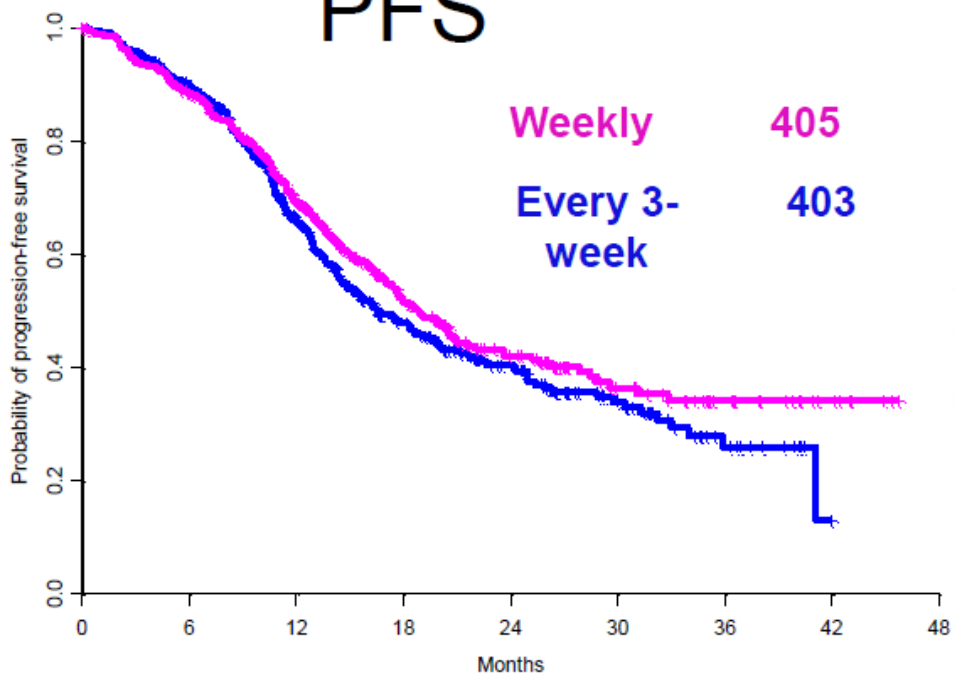
Overall survival

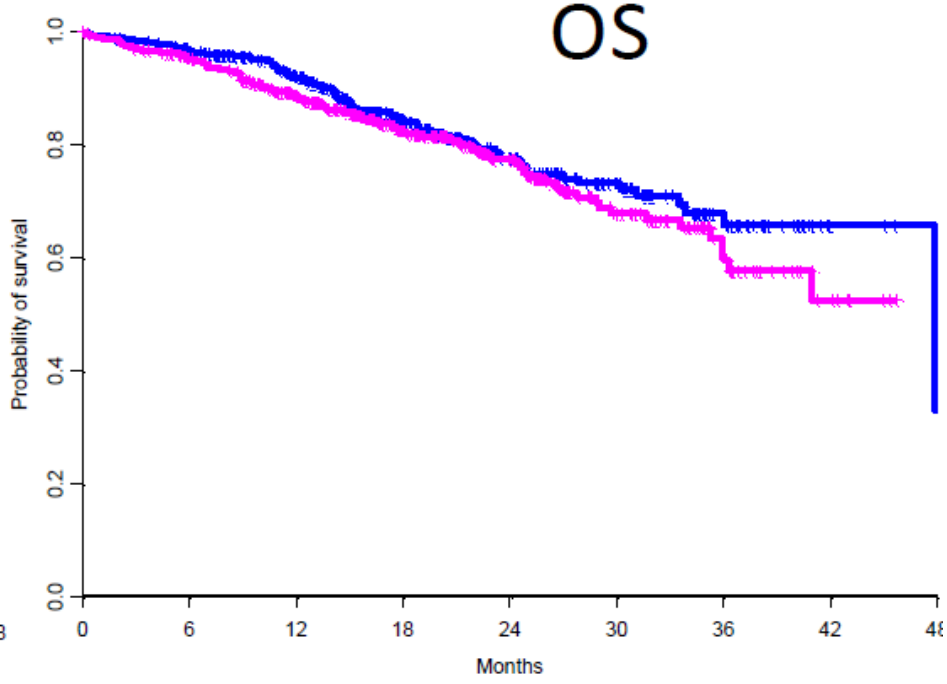


Median overall survival was
100.5 vs 62.2 months
(HR 0.79, 95% CI 0.63–0.99; p=0.039).

*Noriyuki Katsumata et al .**Lancet Oncol 2013; 14: 1020–26***

First line Dose dense in ovarian cancer
MITO 7





Median PFS 18.8 vs 16.5
Log-rank test p = 0.18
Unadjusted HR: 0.88 (0.72 – 1.06)

Median OS n.a. vs 47.9
Log-rank test p = 0.24
Unadjusted HR: 1.20 (0.88 – 1.63)

Presented by: S.Pignata

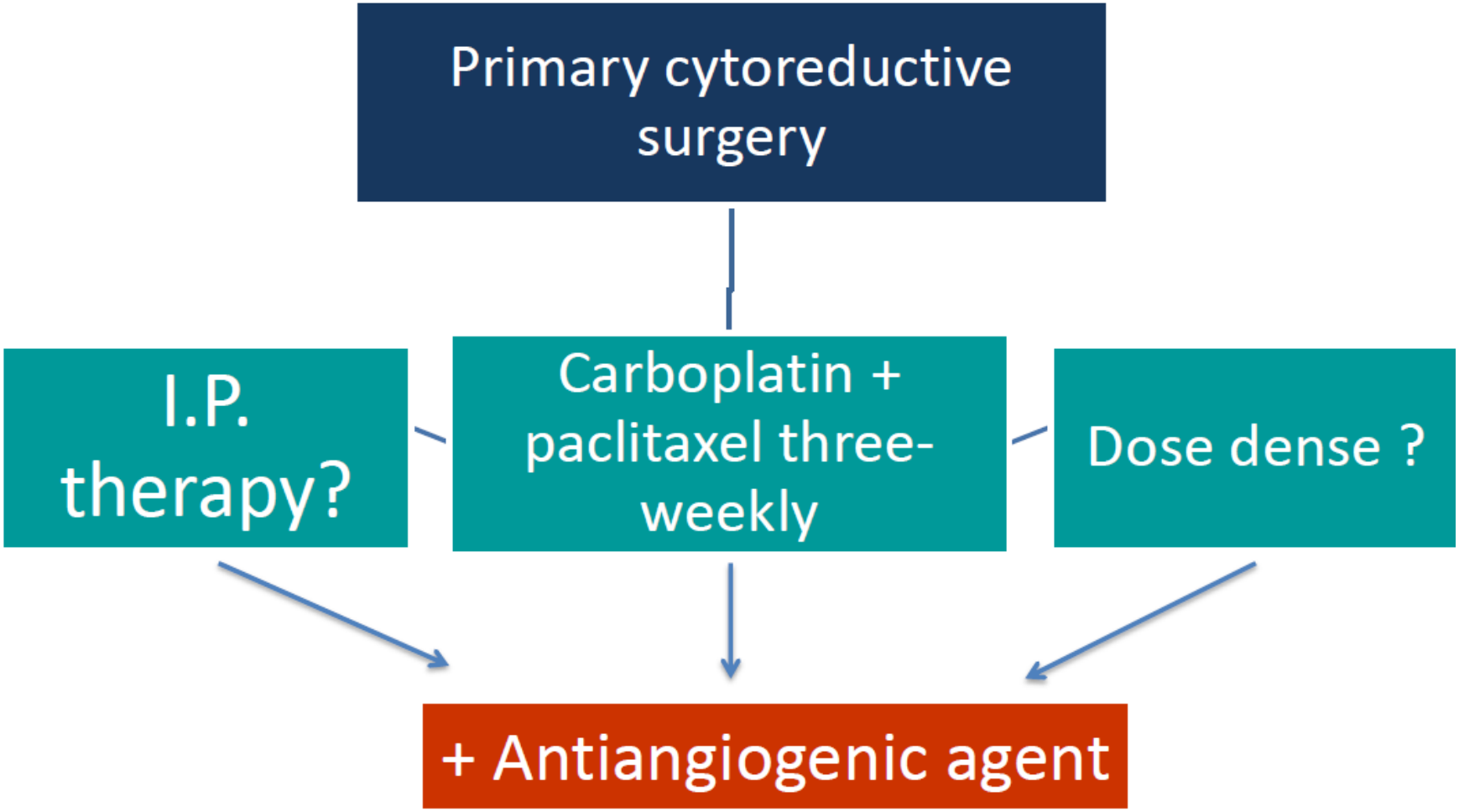
Pignata et al. Lancet Oncol. 2014 Apr;15(4):396-405

Ovarian cancer: first line treatment algorithm

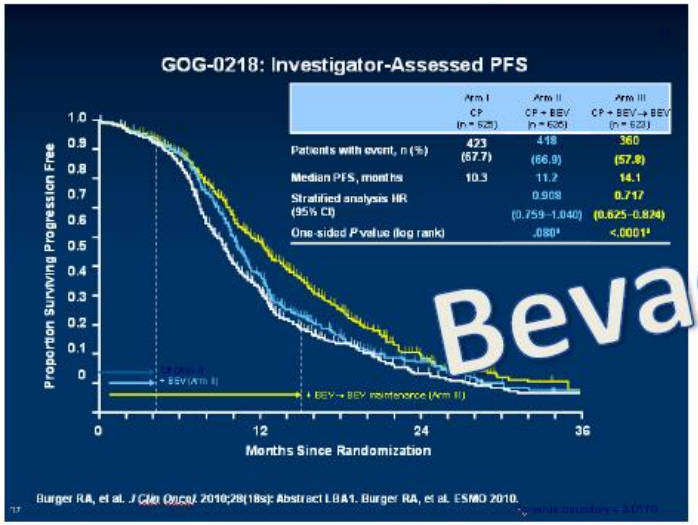
Do we have any choice?

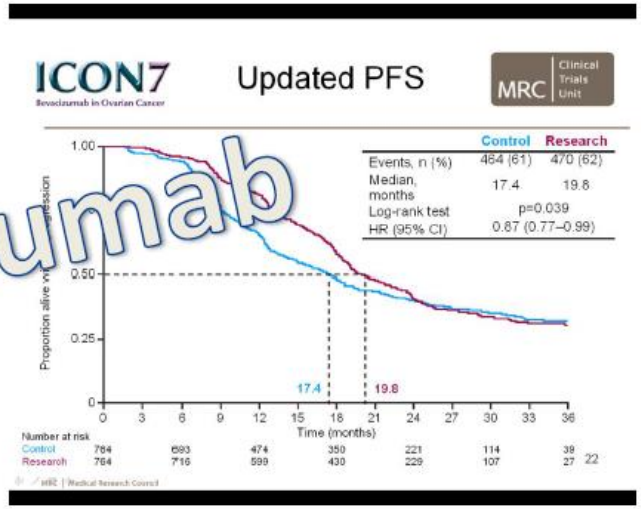
Targeted Therapy

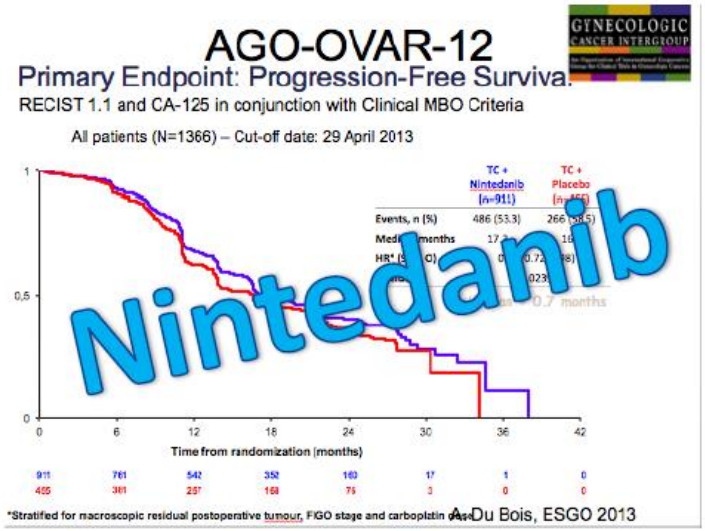
Can we add any targeted agent?

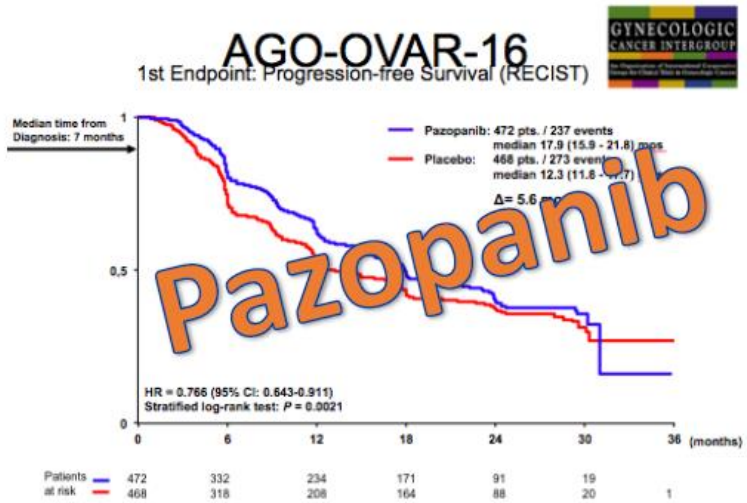


Four positive trials with antiangiogenic agents in front line









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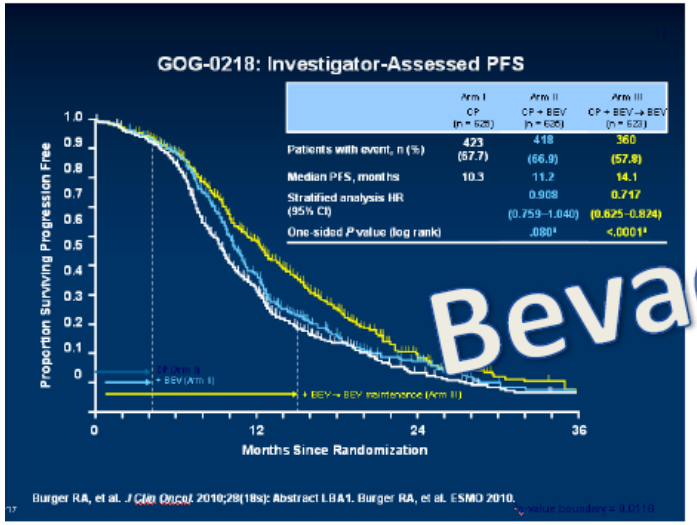
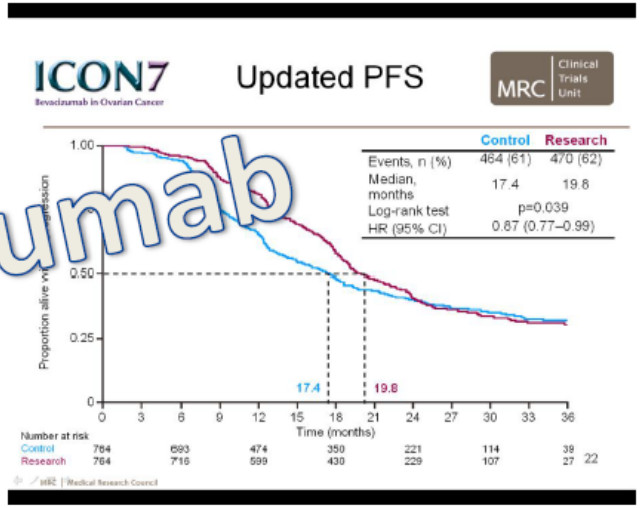
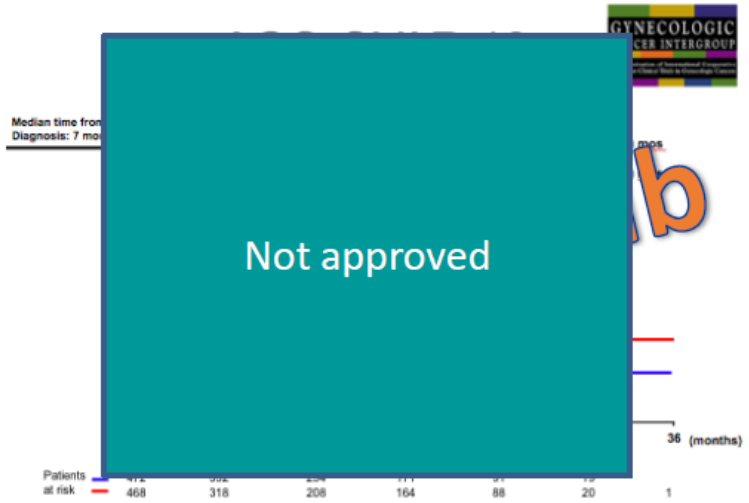
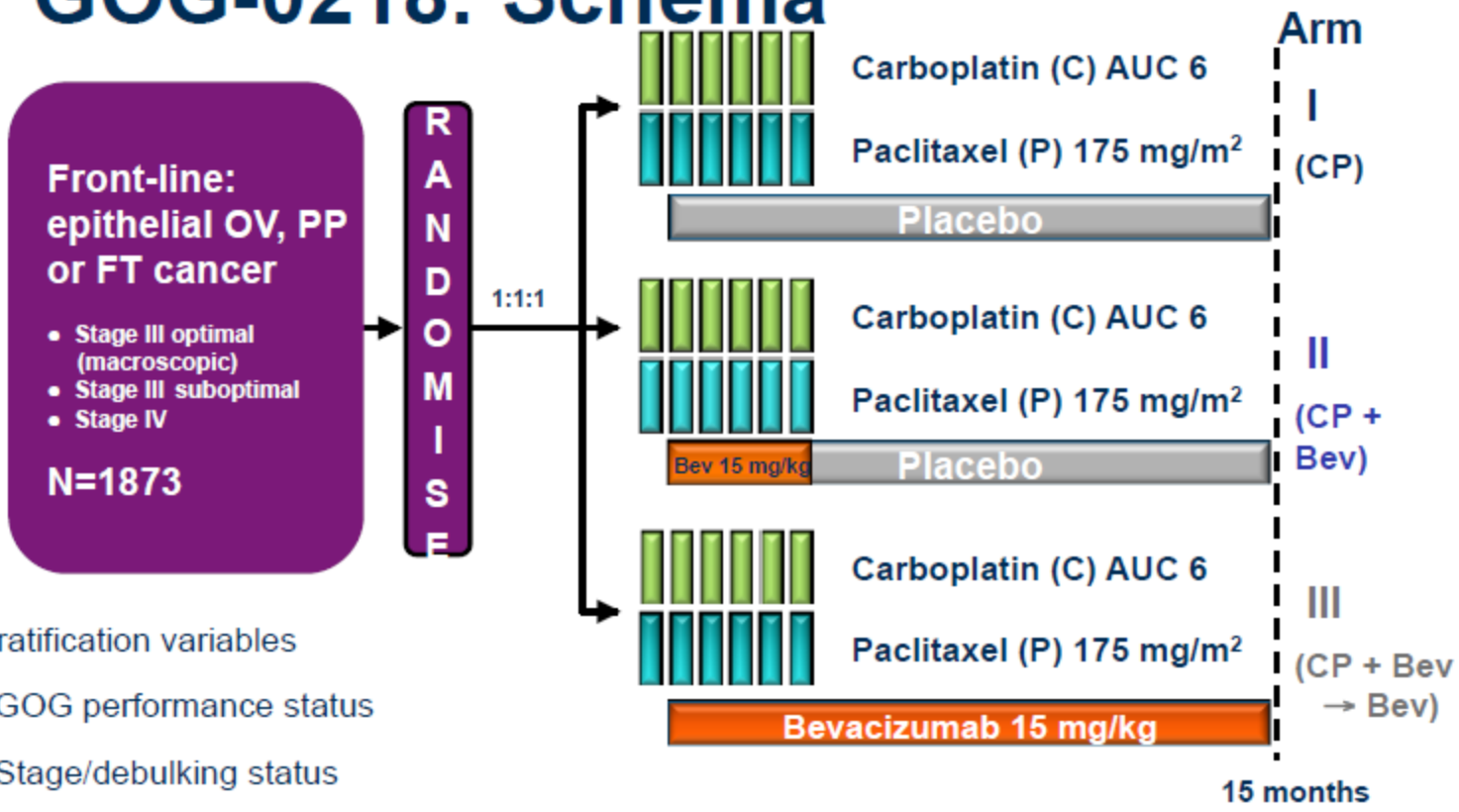




Bevacizumab



GOG-0218: Schema

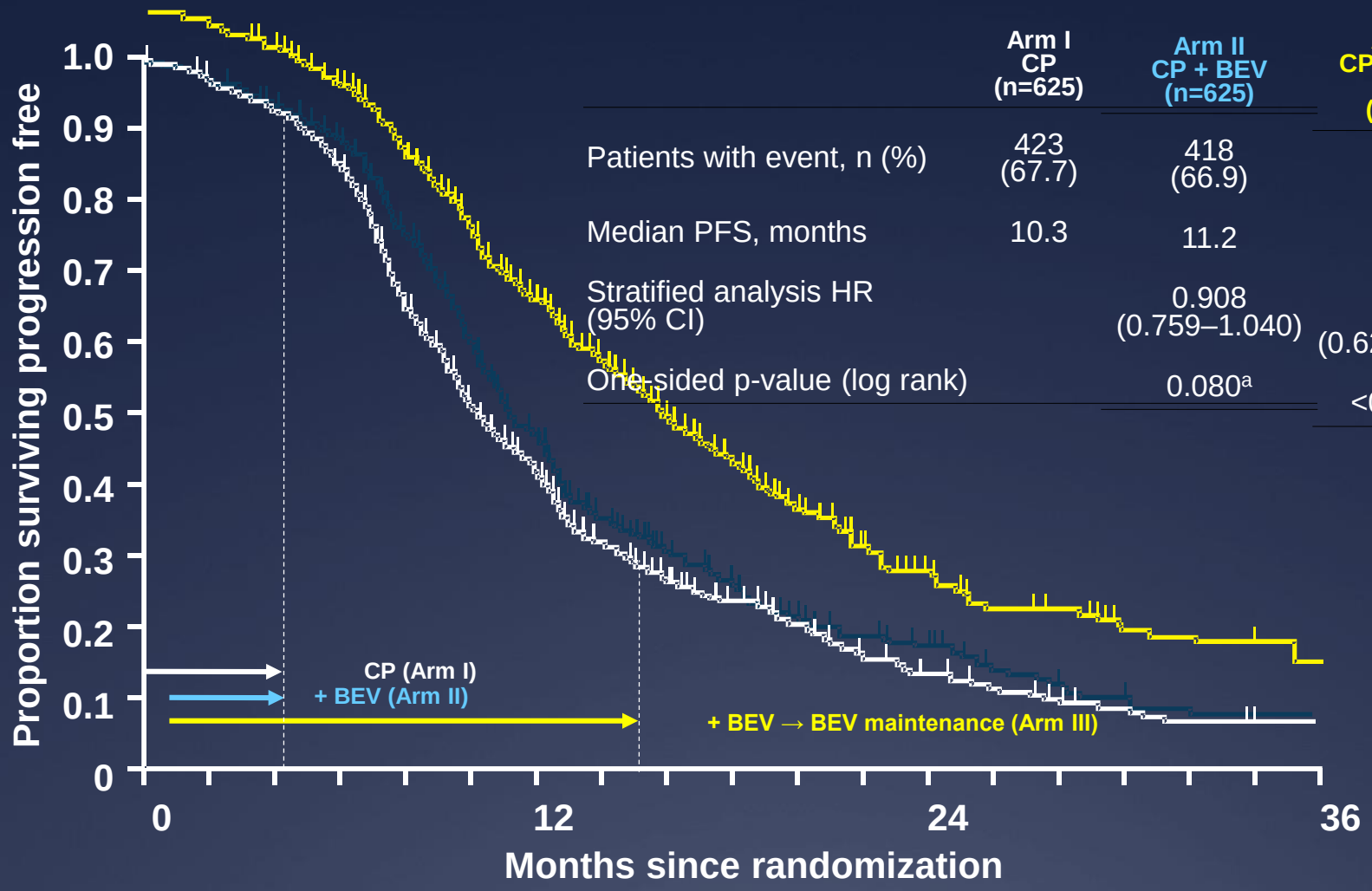


- Stratification variables
  - GOG performance status
  - Stage/debulking status

OV = ovarian; PP = primary peritoneal
FT = fallopian tube; Bev = bevacizumab

Burger et al. ASCO 2010

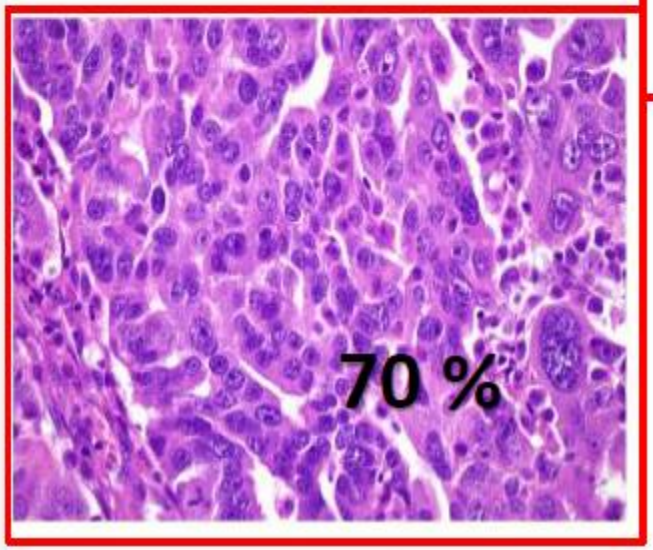
GOG-0218: Investigator-Assessed PFS



	Arm I CP (n=625)	Arm II CP + BEV (n=625)	Arm III CP + BEV → BEV (n=623)
Patients with event, n (%)	423 (67.7)	418 (66.9)	360 (57.8)
Median PFS, months	10.3	11.2	14.1
Stratified analysis HR (95% CI)		0.908 (0.759–1.040)	0.717 (0.625–0.824)
One-sided p-value (log rank)		0.080[a]	<0.0001[a]

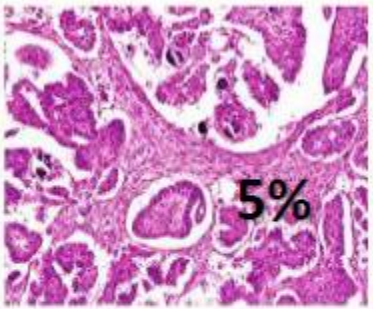
[a]p-value boundary = 0.0116

Ovarian cancer is not a single disease

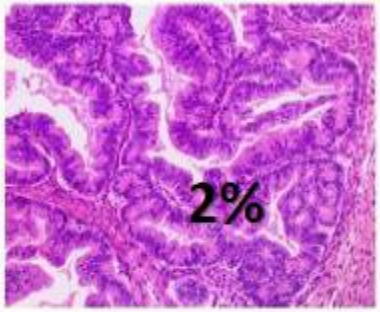


High-grade serous ovarian cancer

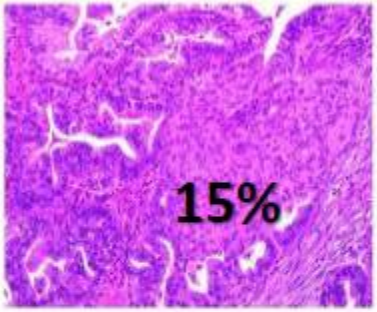
- *TP53*: encodes a protein that regulates the cell cycle
- *BRCA1* and *BRCA2*: encode proteins that are involved in genome protection



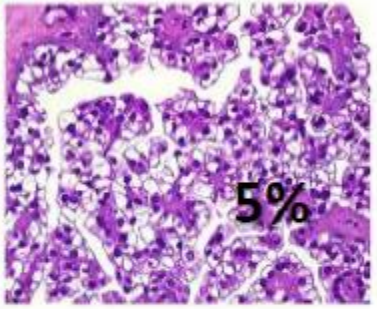
Low-grade serous
BRAF; KRAS



Mucinous carcinoma
KRAS



Endometrioid carcinoma
PTEN (low grade); *TP53*; *BRCA1/2*



Clear cell carcinoma
PTEN; *PIK3CA*; *ARID1A*

Other subtypes

Romero I et al. Endocrinology 2012; 153: 1593-1602

Recent Recommendations on *BRCA* Testing

- **NCCN (National Comprehensive Cancer Network)**

  February 2014

  Epithelial ovarian cancer at any age

- **SGO (Society of Gynecology Oncology)**

  March 2014

  Women diagnosed with epithelial ovarian, tubal, and peritoneal cancers should be considered for genetic counseling and testing, even in the absence of a family history

Raccomandazioni per l'implementazione del test BRCA nei percorsi assistenziali e terapeutici delle pazienti con carcinoma ovarico

A cura del Gruppo di Lavoro AIOM – SIGU – SIBIOC – SIAPEC–IAP

Maria Angela Bella, Ettore Capoluongo, Paola Carrera, Claudio Clemente, Nicoletta Colombo, Laura Cortesi, Gaetano De Rosa, Maurizio Genuardi, Stefania Gori, Valentina Guarneri, Antonio Marchetti, Paolo Marchetti, Nicola Normanno, Barbara Pasini, Sandro Pignata, Carmine Pinto, Paolo Radice, Enrico Ricevuto, Antonio Russo, Pierosandro Tagliaferri, Pierfrancesco Tassone, Mauro Truini, Liliana Varesco

Luglio 2015

Sulla base di queste evidenze, anche se attualmente il test BRCA è formalmente necessario come test predittivo per l'indicazione alla terapia con il PARP-inibitore, è consigliabile considerare l'invio al test BRCA sin dal momento della diagnosi per tutte le pazienti con diagnosi di carcinoma epiteliale ovarico non mucinoso e non borderline, di carcinoma delle tube di Fallopio e di carcinoma peritoneale primitivo, per completare la fase diagnostica molecolare, in previsione di un eventuale utilizzo terapeutico e per favorire l'accesso ad una consulenza genetica oncologica pre-test nell'ambito dei percorsi di prevenzione. La proposta all'esecuzione del

SOLO-1

- **Olaparib maintenance therapy in patients with newly diagnosed advanced ovarian cancer following platinum-based chemotherapy**

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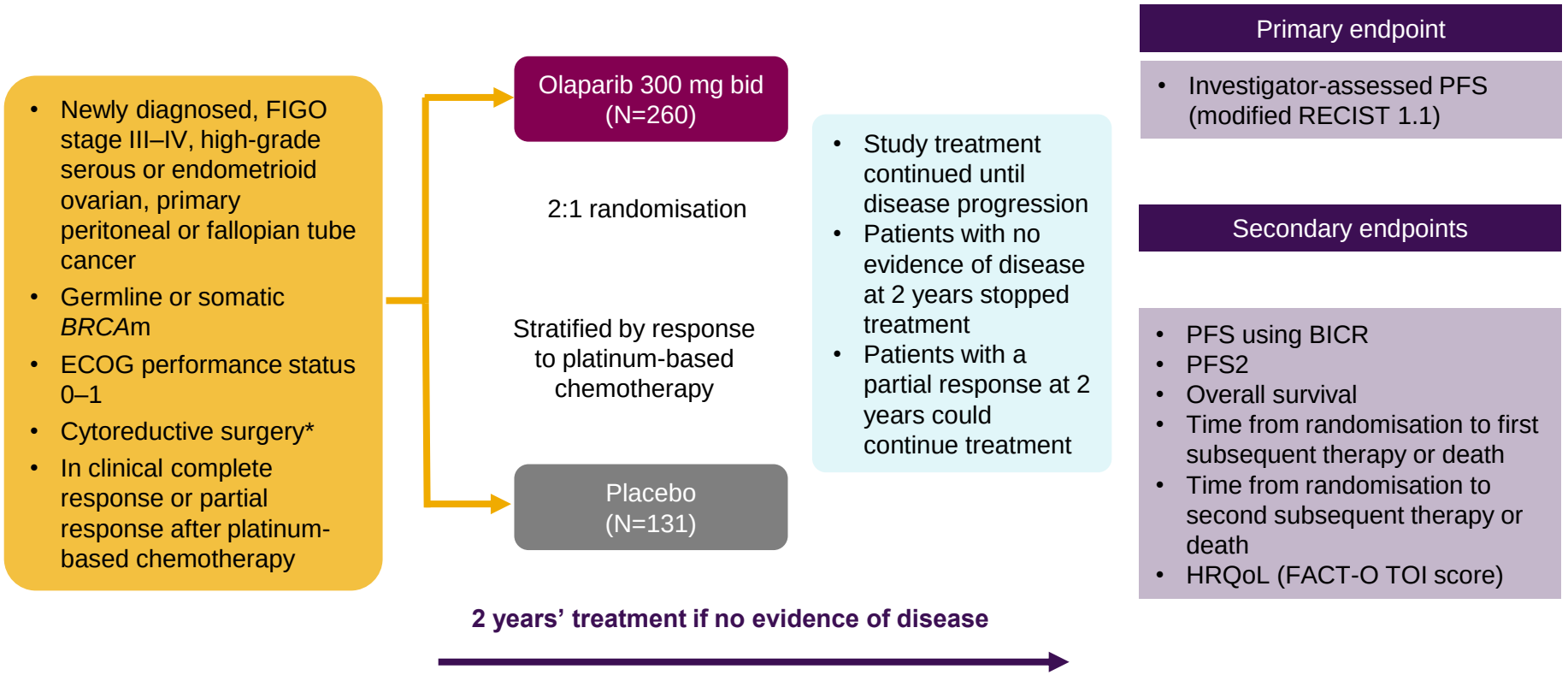
SOLO-1 is the first Phase III trial to investigate maintenance therapy with a PARP inhibitor in newly diagnosed ovarian cancer

SOLO-1 is a global randomised multicentre placebo controlled Phase III study



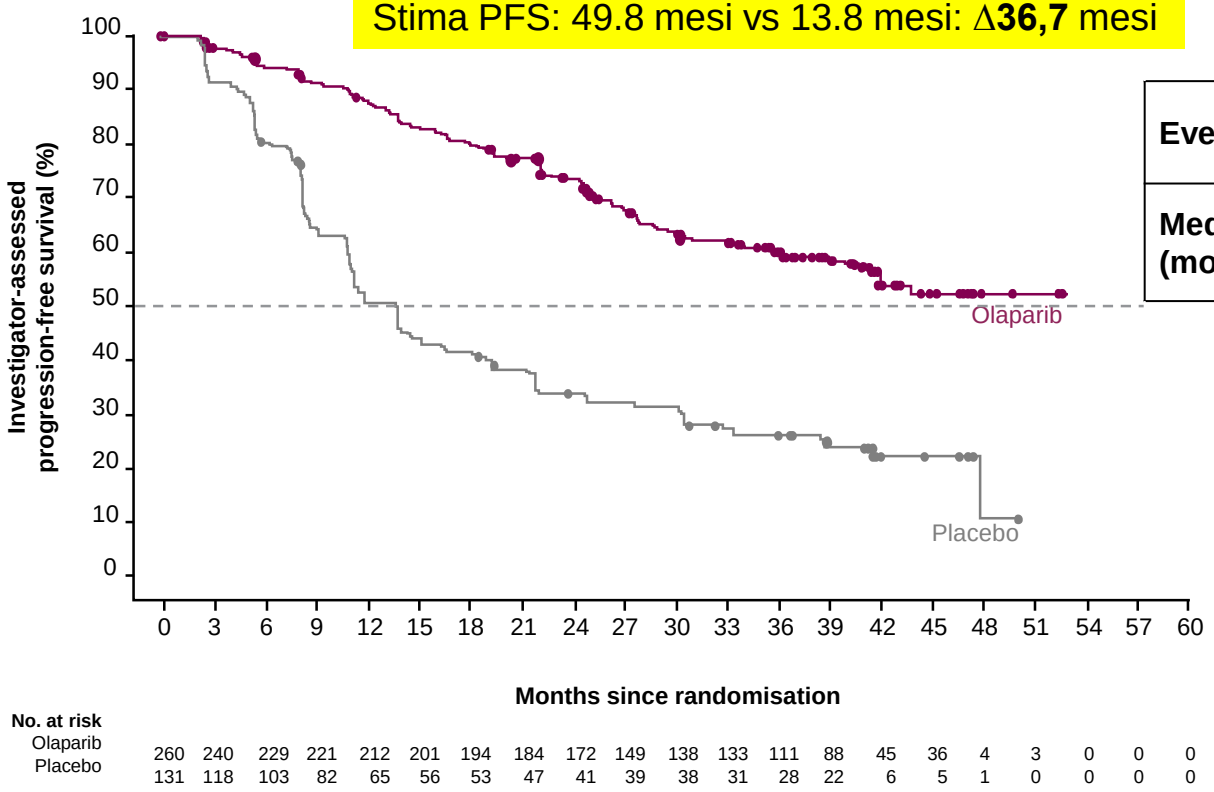
*Upfront or interval attempt at optimal cytoreductive surgery for stage III disease and either biopsy and/or upfront or interval cytoreductive surgery for stage IV disease
BICR = blinded independent central review; ECOG = Eastern Cooperative Oncology Group; FACT-O = Functional Assessment of Cancer Therapy – Ovarian Cancer; FIGO = International Federation of Gynecology and Obstetrics; HRQoL = health-related quality of life; PFS = progression-free survival; PFS2 = time to second progression or death; RECIST = Response Evaluation Criteria in Solid Tumours; TOI = Trial Outcome Index; PARP = poly (ADP-ribose) polymerase; *BRCA*m = *BRCA* gene mutation

https://clinicaltrials.gov/ct2/show/NCT01844986 (accessed October 2018)

Olaparib reduced the risk of progression or death by 70% vs. placebo[1]

*After a median follow-up of **41 months**, the median **PFS had not been reached** in the olaparib arm (vs. 13.8 months in the placebo arm)[1]*

Stima PFS: 49.8 mesi vs 13.8 mesi: Δ**36,7** mesi



	Olaparib	Placebo
Events, N (%)	102 (39.2)	96 (73.3)
Median PFS (months)	NR	13.8
	HR=0.30 95% CI: 0.23, 0.41 p<0.001	

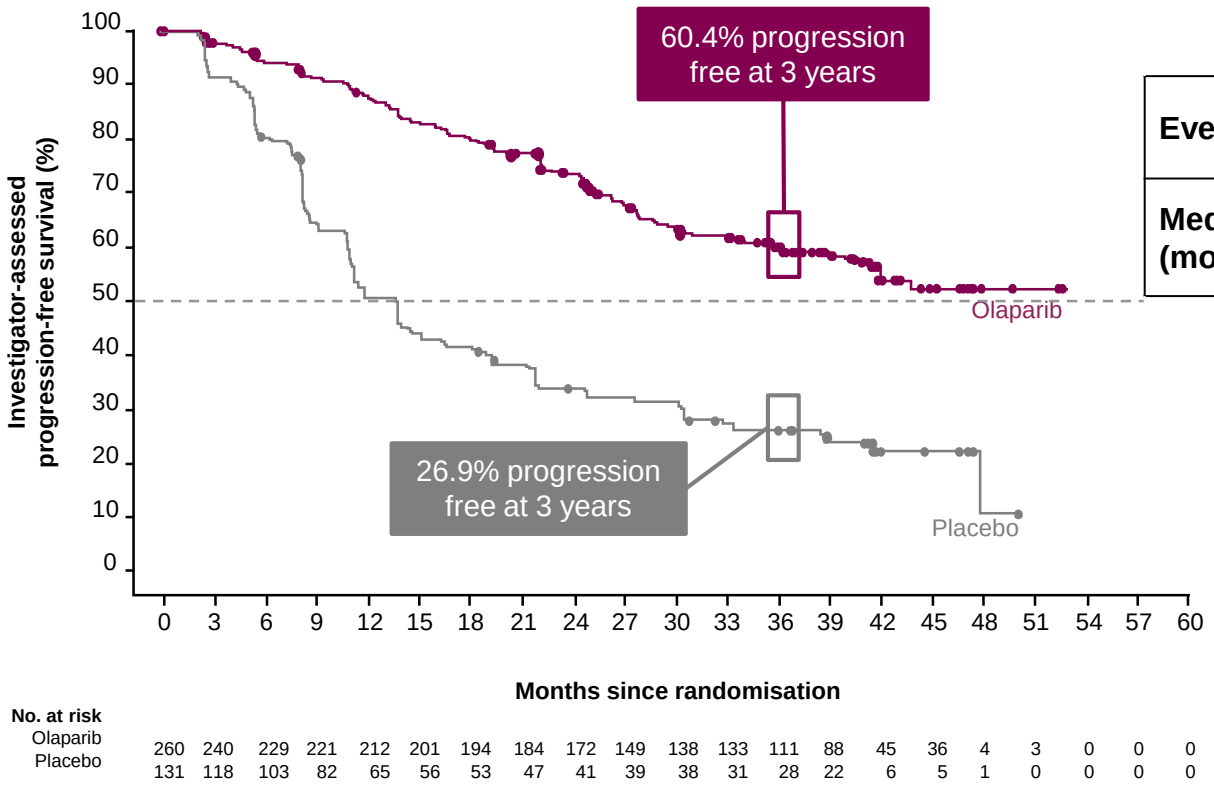
Primary endpoint: investigator-assessed PFS

DCO: May 2018; Median FU: olaparib, 40.7 months placebo, 41.2 months
Analysis was performed after 198 progression events had occurred (in 50.6% of patients)
PFS = progression-free survival; DCO = data cut-off; HR = hazard ratio; CI = confidence interval

1. Moore K et al. N. Engl. J. Med. (2018) ePub ahead of print; 2. Moore K et al. Oral presentation LBA7_PR, ESMO (2018)

Olaparib reduced the risk of progression or death by 70% vs. placebo[1]

*A **3 anni** solo il **40%** delle pazienti trattate con olaparib ricade, contro **il 70%** delle pazienti trattate con placebo*



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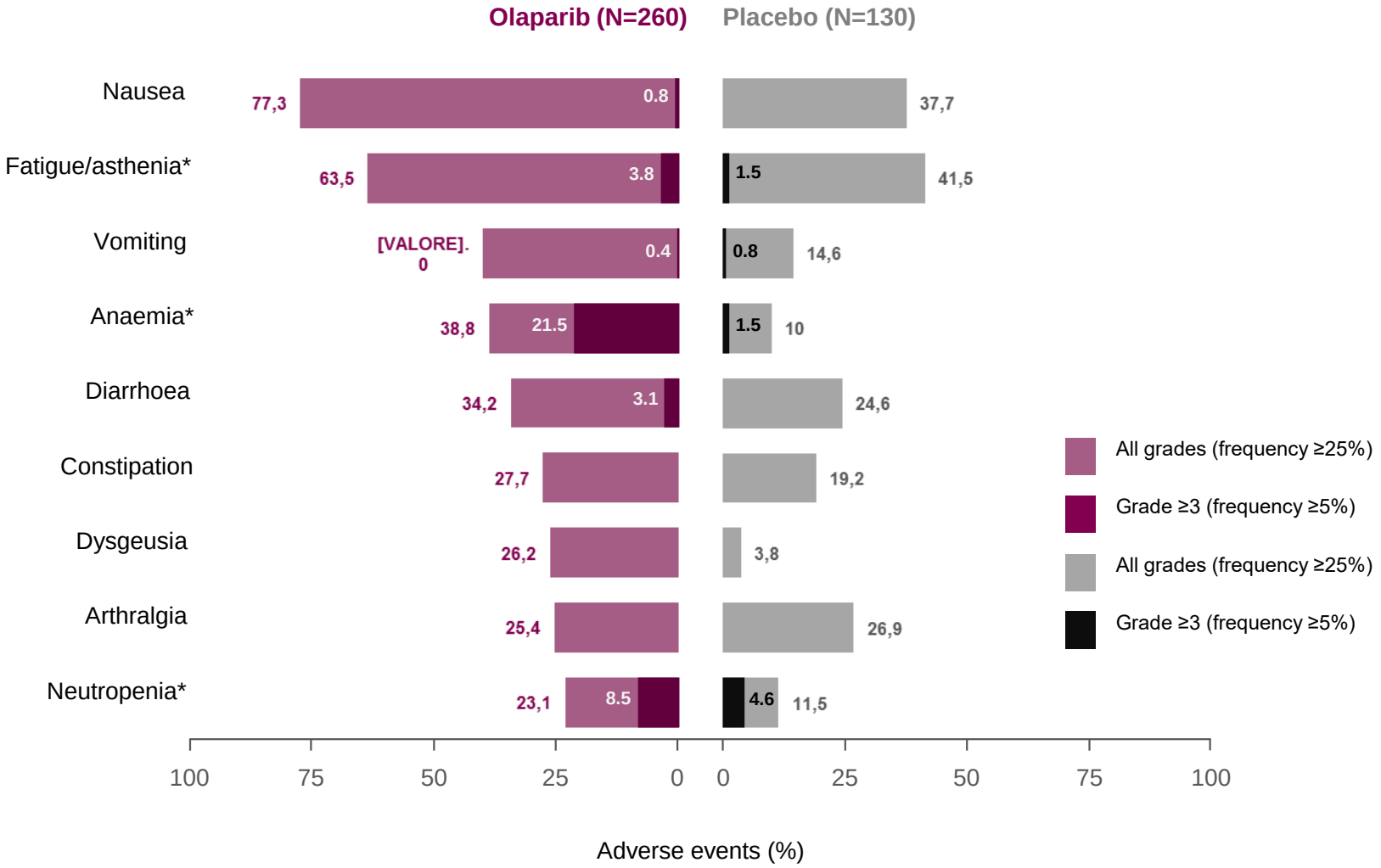
Adverse events were mostly mild or moderate in the olaparib arm[1,2]

Grade ≥3 AEs occurred in 39% of patients in the olaparib arm vs. 19% in the placebo arm

	Olaparib (N=260)	Placebo (N=130)
Median duration of treatment, months (range)	24.6 (0-52.0)	13.9 (0.2-45.6)
Any AE, N (%)	256 (98.5)	120 (92.3)
Any AE of CTCAE Grade ≥3, N (%)	102 (39.2)	24 (18.5)
Any SAE, N (%)	54 (20.8)	16 (12.3)

DCO: May 2018
A serious adverse event (SAE) is defined as any untoward medical occurrence that at any dose. results in death, is life-threatening. requires inpatient hospitalisation or causes prolongation of existing hospitalisation
AE = adverse event; CTCAE = Common Terminology Criteria for Adverse Events; DCO = data cut-off; SAE = serious adverse event
1. Moore K et al. N. Engl. J. Med. (2018) ePub ahead of print; 2. Moore K et al. Oral presentation LBA7_PR, ESMO (2018)

The most common AEs reported in patients on olaparib in SOLO-1 were gastrointestinal disturbances, fatigue and anaemia



*Grouped term
AE = adverse event

1. Moore K et al. Oral presentation LBA7_PR, ESMO (2018)

Conclusions

Maintenance olaparib led to a substantial, unprecedented improvement in PFS in patients with newly diagnosed, advanced ovarian cancer and a BRCAm, with a difference in median PFS estimated to be in the region of 3 years[1,2]

A 70% reduction in risk of disease progression or death was observed for olaparib vs. placebo-treated patients (HR 0.30; p<0.001)[1]

- After a median follow up of 41 months, median PFS was not reached on the olaparib arm vs. 13.8 months for placebo with PFS at 3 years: 60.4% vs. 26.9% for olaparib vs placebo[1]

A reduction in the risk of second progression or death was observed demonstrating that olaparib maintenance does not diminish the benefit conferred by subsequent therapy[1]

The safety profile is consistent with previous olaparib data with most AEs being mild or moderate in severity and generally not leading to dose reduction or permanent discontinuation[1]

There was no decrease in HRQoL from baseline for olaparib-treated patients over the 24-month treatment period and no clinically important differences in HRQoL compared with placebo-treated patients[1]

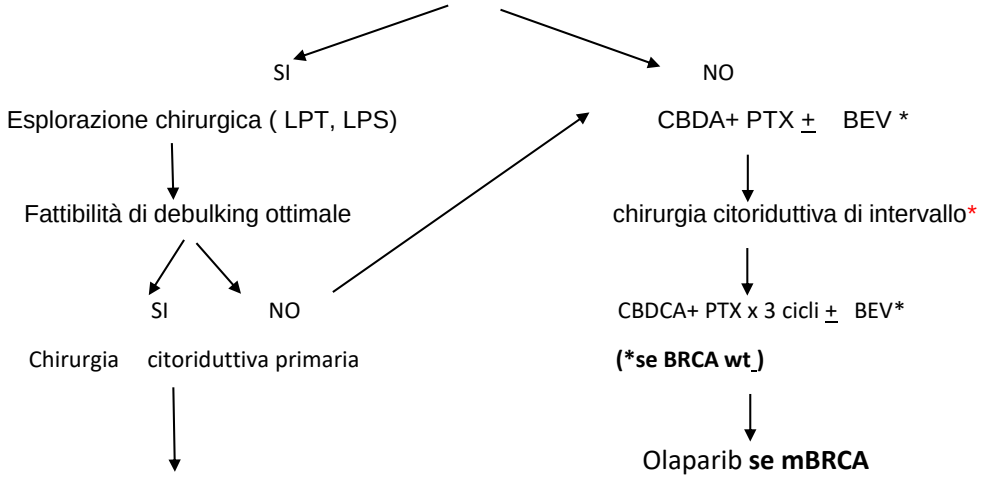
PFS = progression-free survival; AE = adverse event; HRQoL = health-related quality of life; HR = hazard ratio; *BRCA*m = *BRCA* gene mutation

1. Moore K et al. N. Engl. J. Med. (2018) ePub ahead of print; 2. Moore K et al. Oral presentation LBA7_PR, ESMO (2018)

Algoritmo di trattamento del carcinoma ovarico avanzato alla diagnosi

A) Valutazione clinica , radiologica ed anestesiologica :

Le condizioni generali della paziente sono compatibili con chirurgia citoriduttiva anche aggressiva e la diffusione di malattia fa ritenere possibile un debulking ottimale

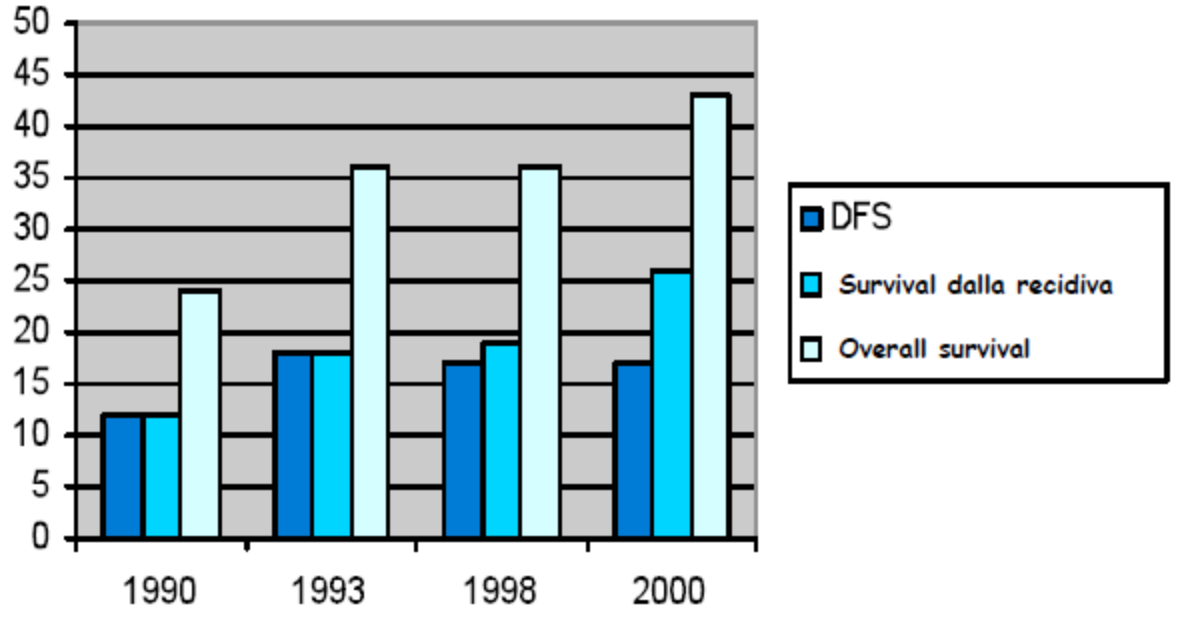


(BEV se BRCA wt in mantenimento;

olaparib **se mBRCA**)

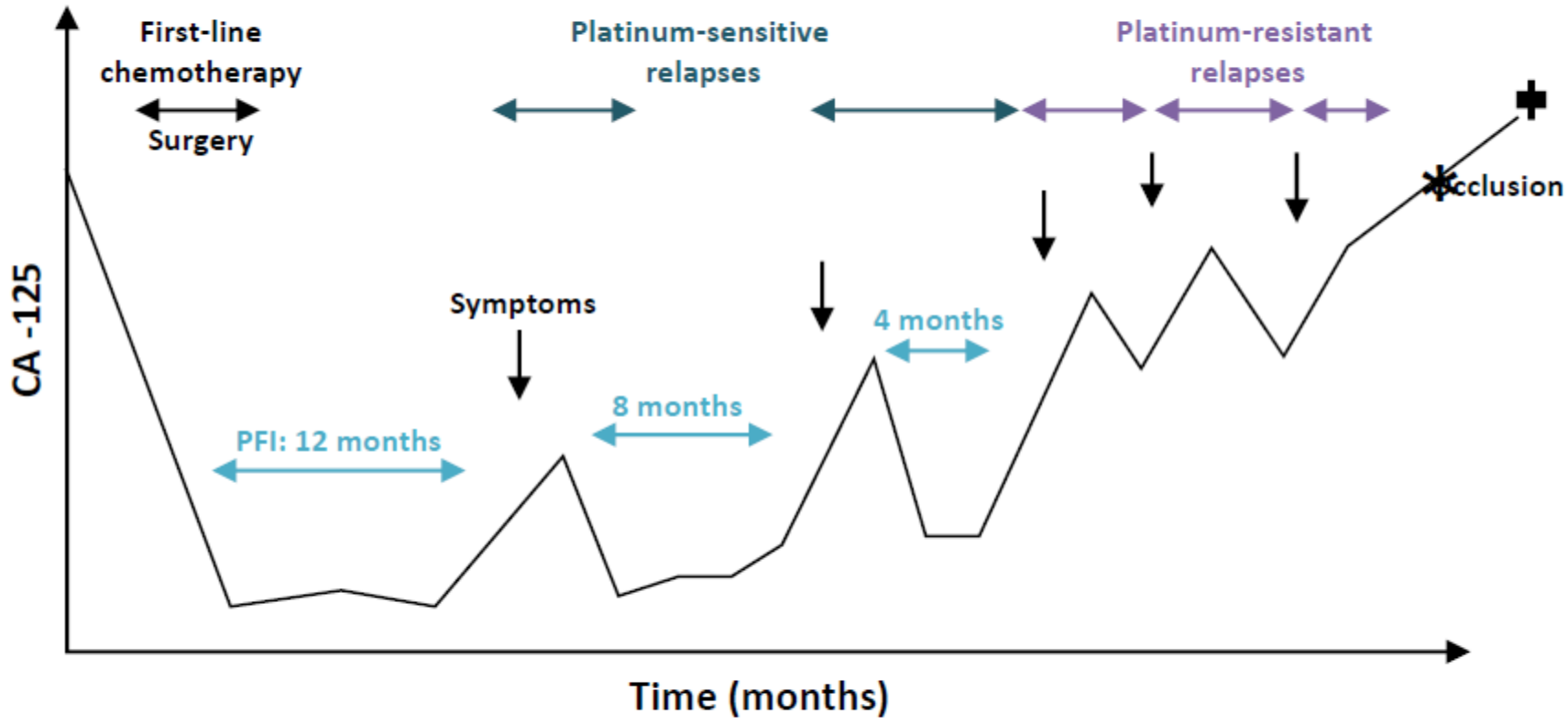
#solo se risposta a NACT e citoriduzione ottimale possibile

Survival a 5 anni migliorata per il migliore trattamento della **recidiva**



Prima linea	**Cisplatino Ciclo.**	**Cisplatino Taxolo**	**Carboplatino Taxolo**	**Carboplatino Taxol/+ terzo farmaco**

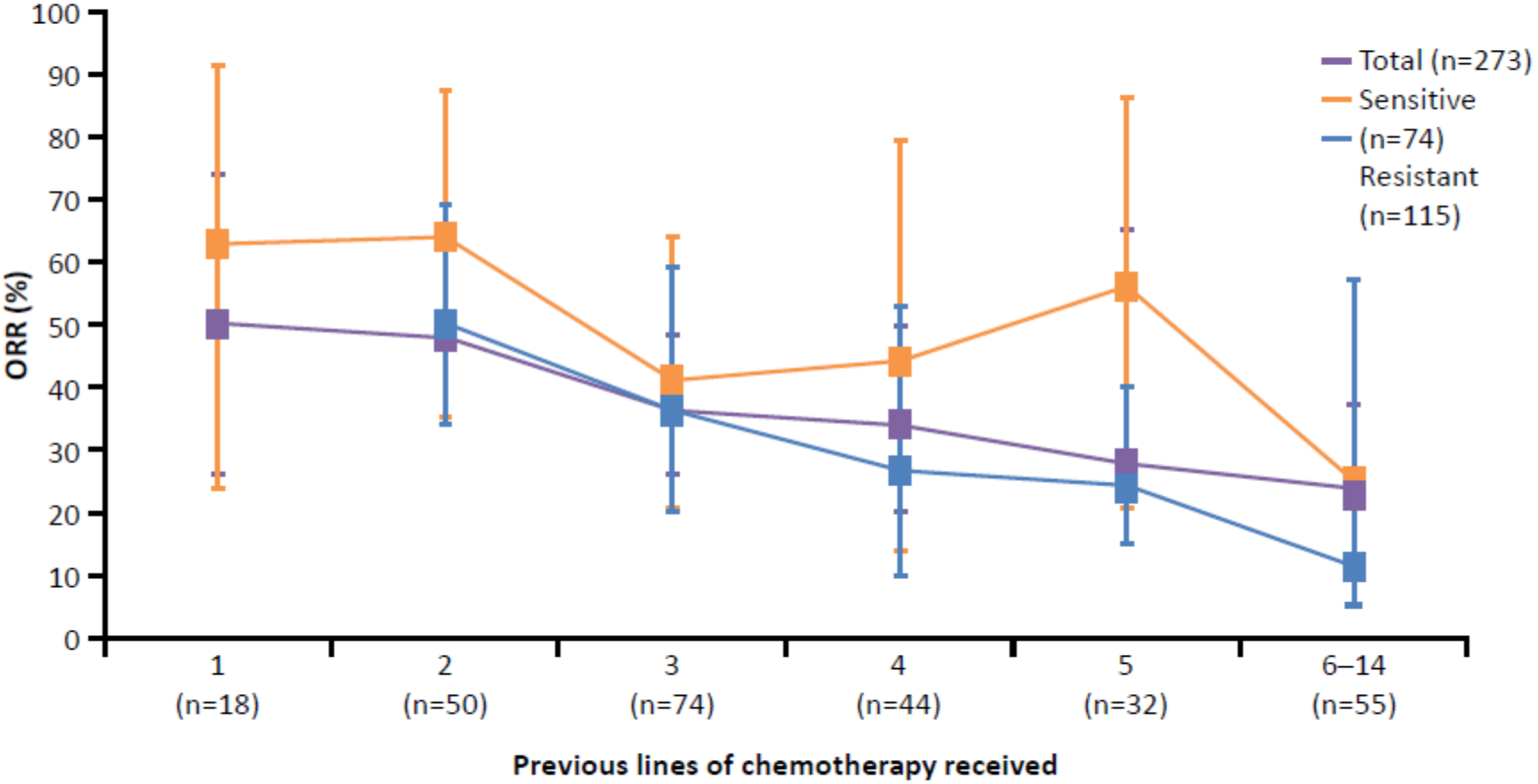
Advanced ovarian cancer: A 'chronic' disease with multiple relapses



PFI: platinum-free interval or duration of disease control without chemotherapy.

du Bois a, Pfisterer J. Zentralbl Gynakol. 2004;126:312-4.

Response to treatment in patients with ovarian cancer declines with increasing disease recurrence



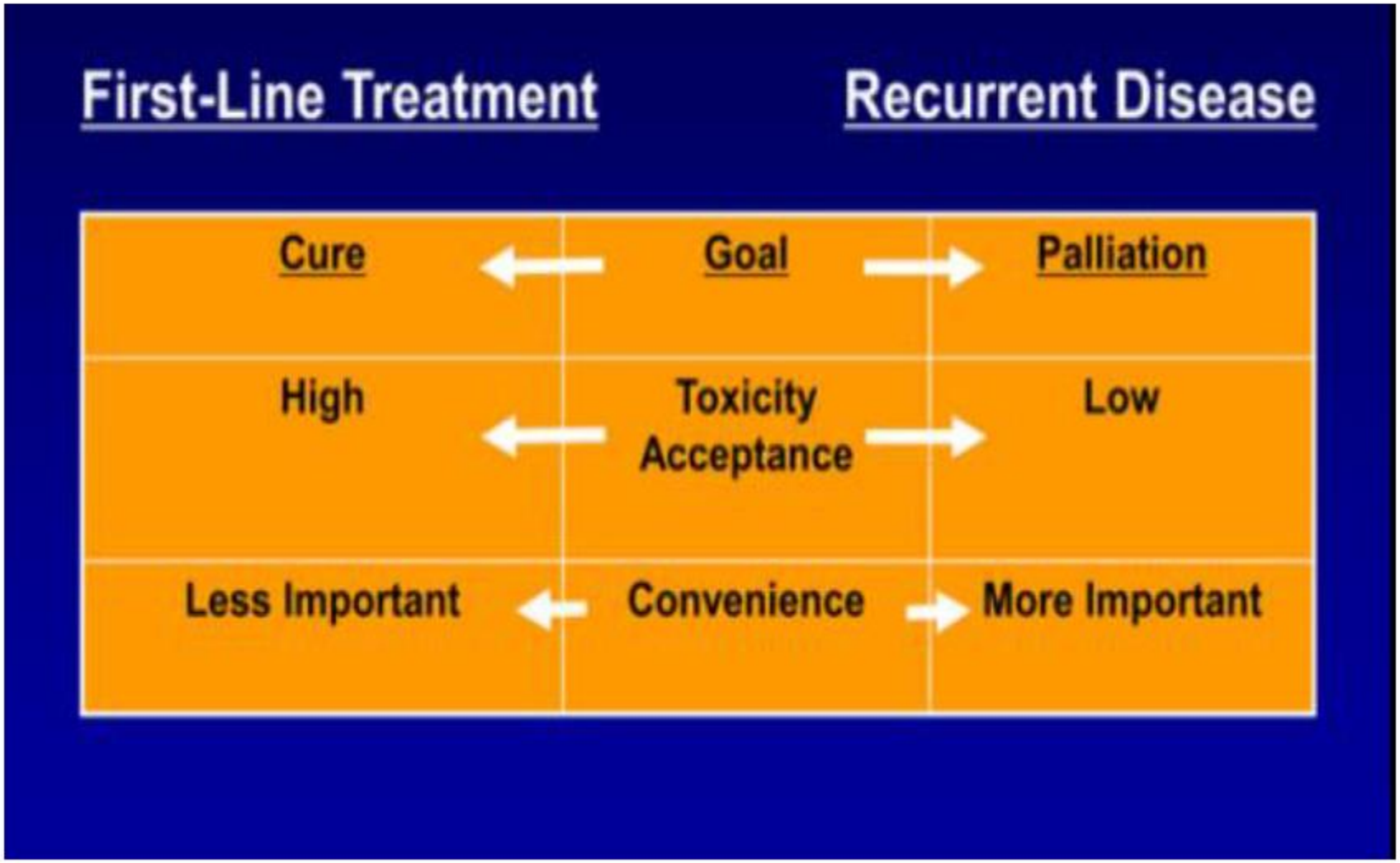
N numbers show total population; confidence lines represent 95% CIs for total population.
CI, confidence interval; ORR, overall response rate.

du Bois a, Pfisterer J. Zentralbl Gynakol. 2004;126:312-4.

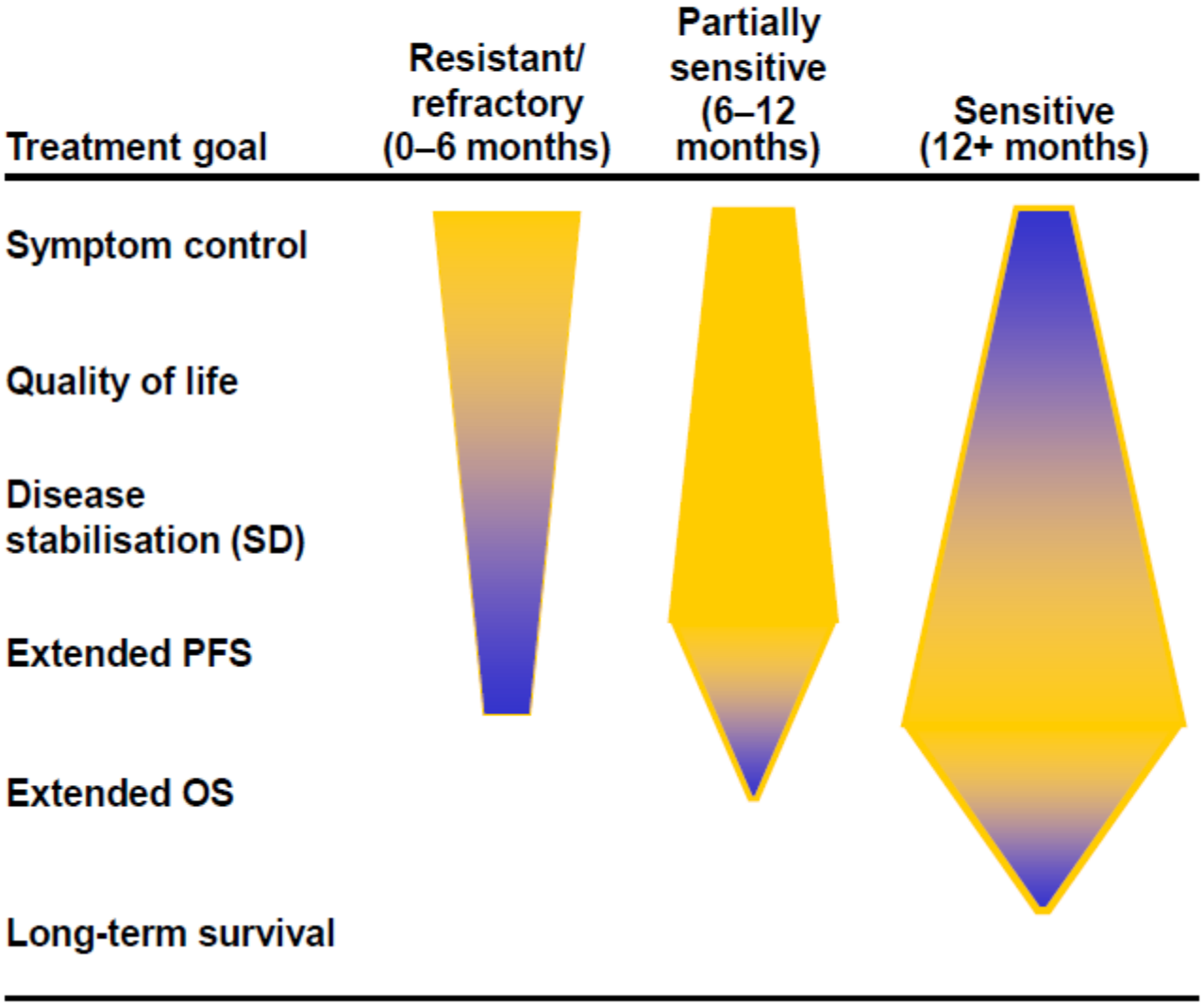
Recurrent Ovarian Cancer

- 50-90% of patients with advanced ovarian cancer will have a relapse in less than 5 years depending on:
  - the FIGO stage at diagnosis,
  - use of neo-adjuvant chemotherapy and
  - residual disease after upfront cytoreductive surgery.

Treatment Considerations

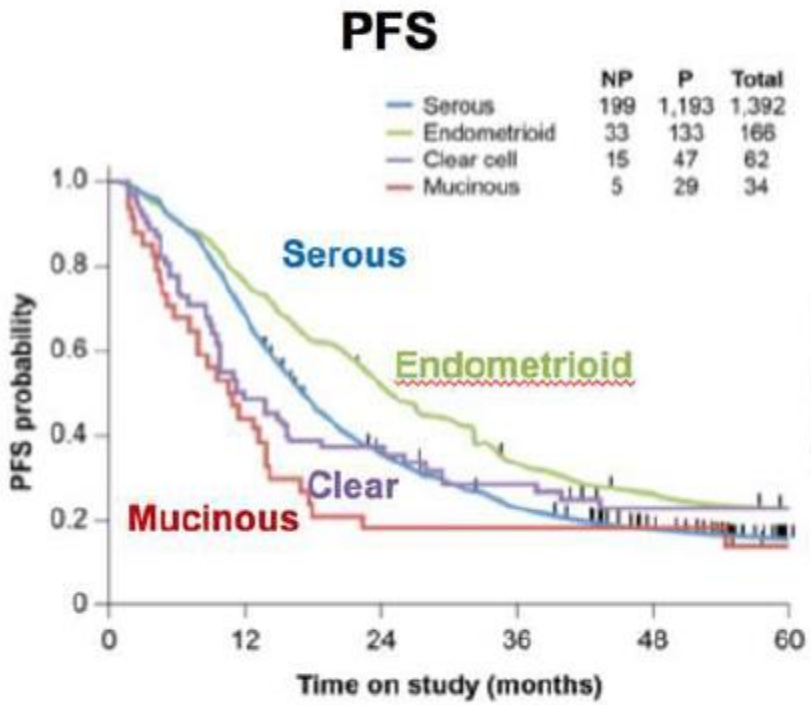


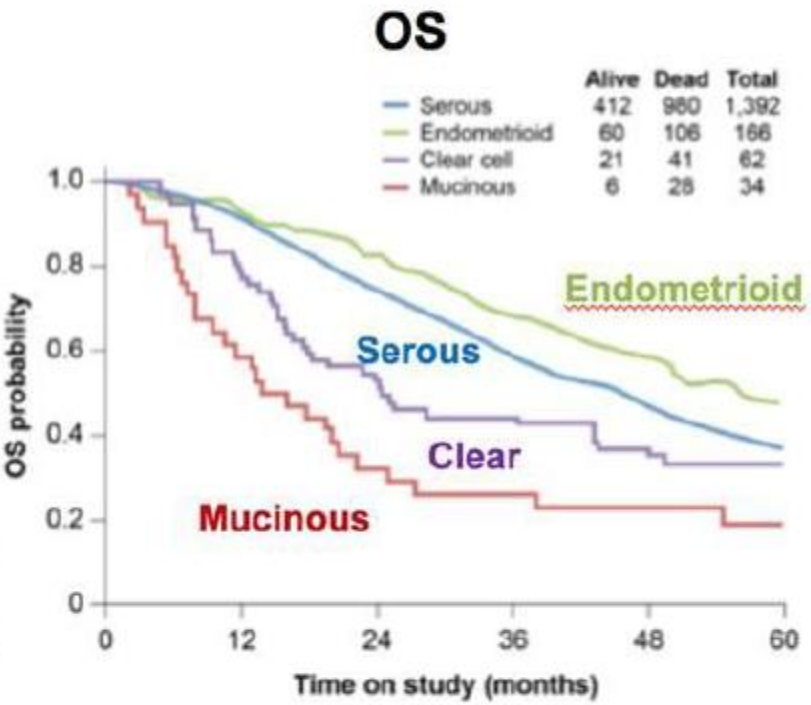
Weighting of treatment goals and expectations in recurrent ovarian cancer



Ovarian Cancer - not one disease
Outcome depends on histiotype

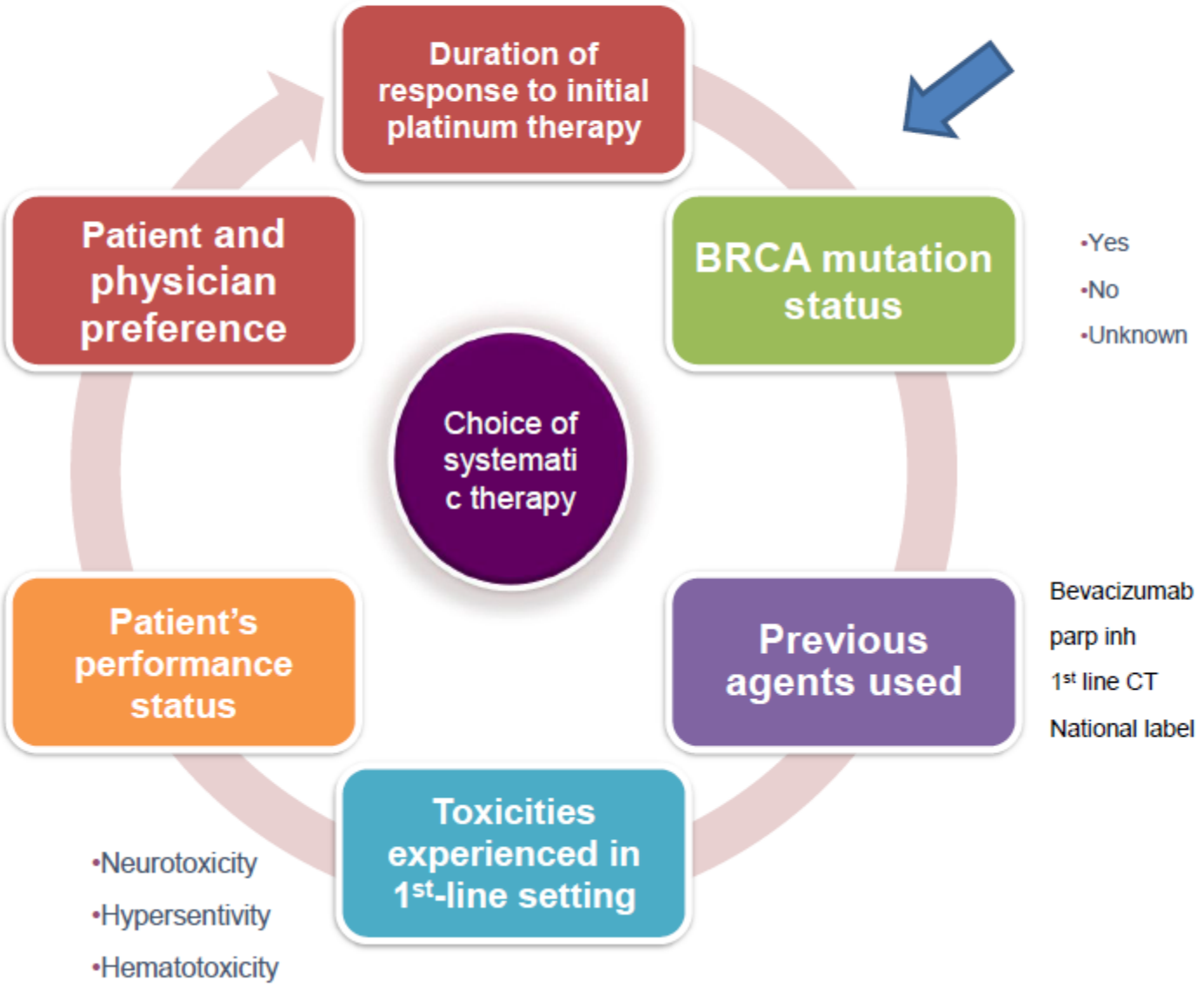
(GOG Trials #111, 114, 132, 152, 158, 172)





Winter WE III, et al. J Clin Oncol 2007;25:3621–7.

Systematic Treatment, Decisional factors
How to treat patient?



Bevacizumab in ovarian cancer: four pivotal trials

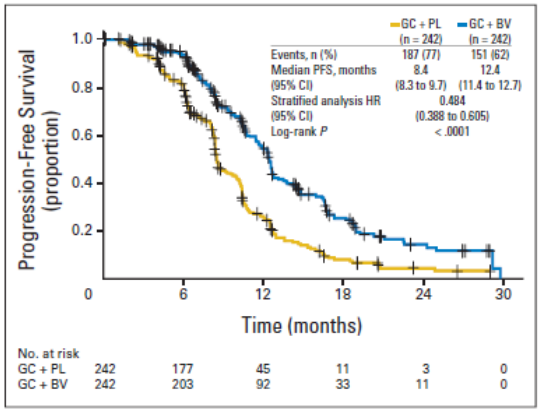
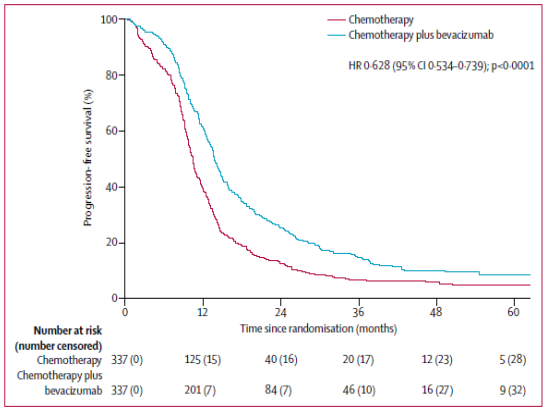
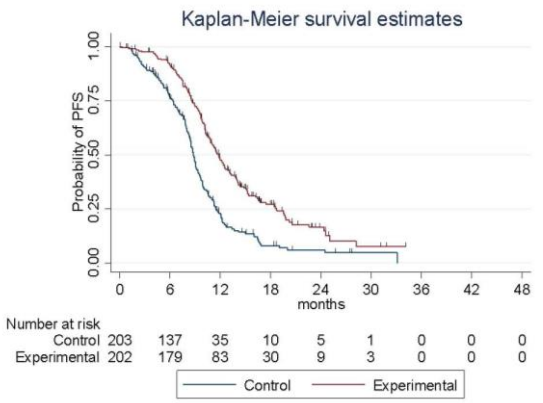
	Trial	Chemotherapy	Bevacizumab	PFS HR
First line				
	GOG-0218[1] (n=1873)	Paclitaxel Carboplatin	Concurrent and maintenance 15 mg/kg q3w (3-arm placebo)	0.72
	ICON7[2] (n=1528)	Paclitaxel Carboplatin	Concurrently only 7.5 mg/kg q3w (2 arm)	0.81
Second line				
Platinum resistant	Aurelia[3] (n=361)	Caelyx Topotecan Paclitaxel	Concurrent 10 mg/kg q2w (2 arm)	0.48
Platinum sensitive	OCEANS[4] (n=484)	Gemcitabine Carboplatin	Concurrent 15 mg/kg q3w (2 arm)	0.48

NO predictive biomarkers

1. Burger et al. N Engl J Med 2011
2. Perren et al. N Engl J Med 2011
3. Pujade-Laurain et al. J Clin Oncol 2012
4. Aghajanian et al. J Clin Oncol 2012

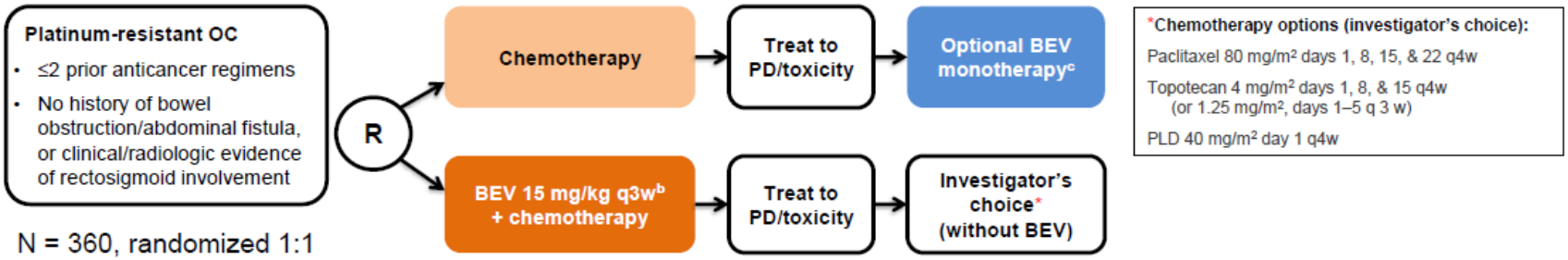
Efficacy of bevacizumab in recurrent ovarian cancer

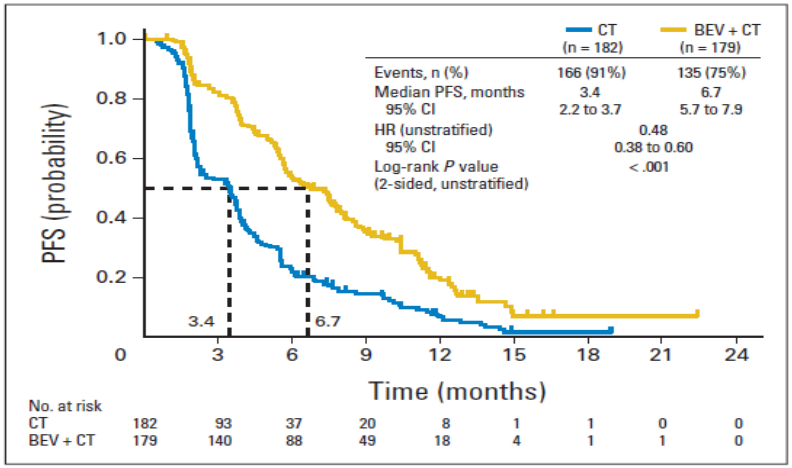
- **PRIMARY ENDPOINT: PFS**

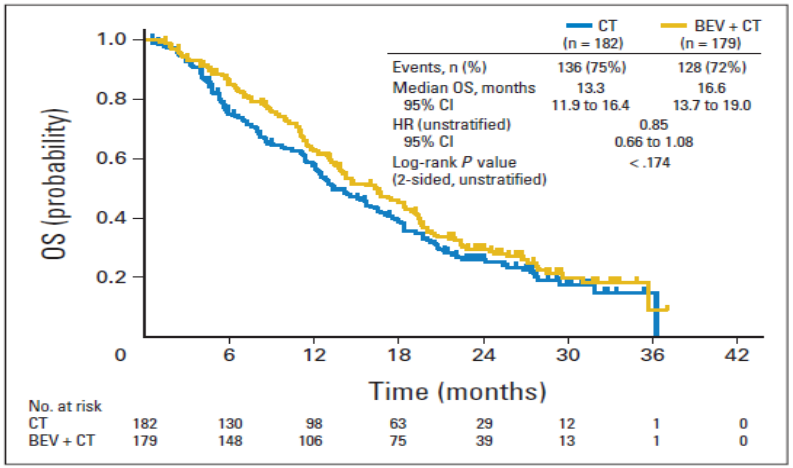
OCEANS[1]	GOG-213[2]	MITO-16[3]
		
12.4 vs 8.4 months **HR 0.48 (95% CI: 0.39-0.60)**	**13.8 vs.10.4 months** **HR 0.63 (95% CI: 0.53-0.74)**	**11.8 vs 8.8 months** **HR 0.51 (95% CI: 0.41-0.65)**

1. Aghajanian C, et al. *J Clin Oncol* 2012;30:2039-2045; 2. Coleman et al. *Lancet Oncology* 2017;18:779-791;
3. Pignata S, et al. *J Clin Oncol* 2018;36:(suppl; abstr 5506)

AURELIA: Bevacizumab in platinum-resistant ovarian cancer







Pujade-Lauraine E, et al. *J Clin Oncol 2014; 32(13): 1302-08*

Platinum is not an option
(formerly platinum-resistant)

- Definition by GCIG:
  - Short TFIp (minimum < 6 m) based on symptomatic relapse or RECIST criteria.
  - Progression on therapy.
  - Platinum allergy.
- Treatment in control arm can include a non-platinum drug as a single agent or in combination.

- Chemotherapy options:
  - Single agent: weekly paclitaxel, PLD, Topotecan, gemcitabine…
  - Combination: Trabectedine-PLD*
- Expected OS is usually short, around 12 months
- **Main objectives of treatment:**
  - QoL
  - Toxicity
  - Control of symptoms

5th OCCC of the GCIG: Recurrent Disease. Ann Oncol. 2016 Dec 19

*If TFIp > 6 months

Active Single-Agents in Recurrent Ovarian Cancer

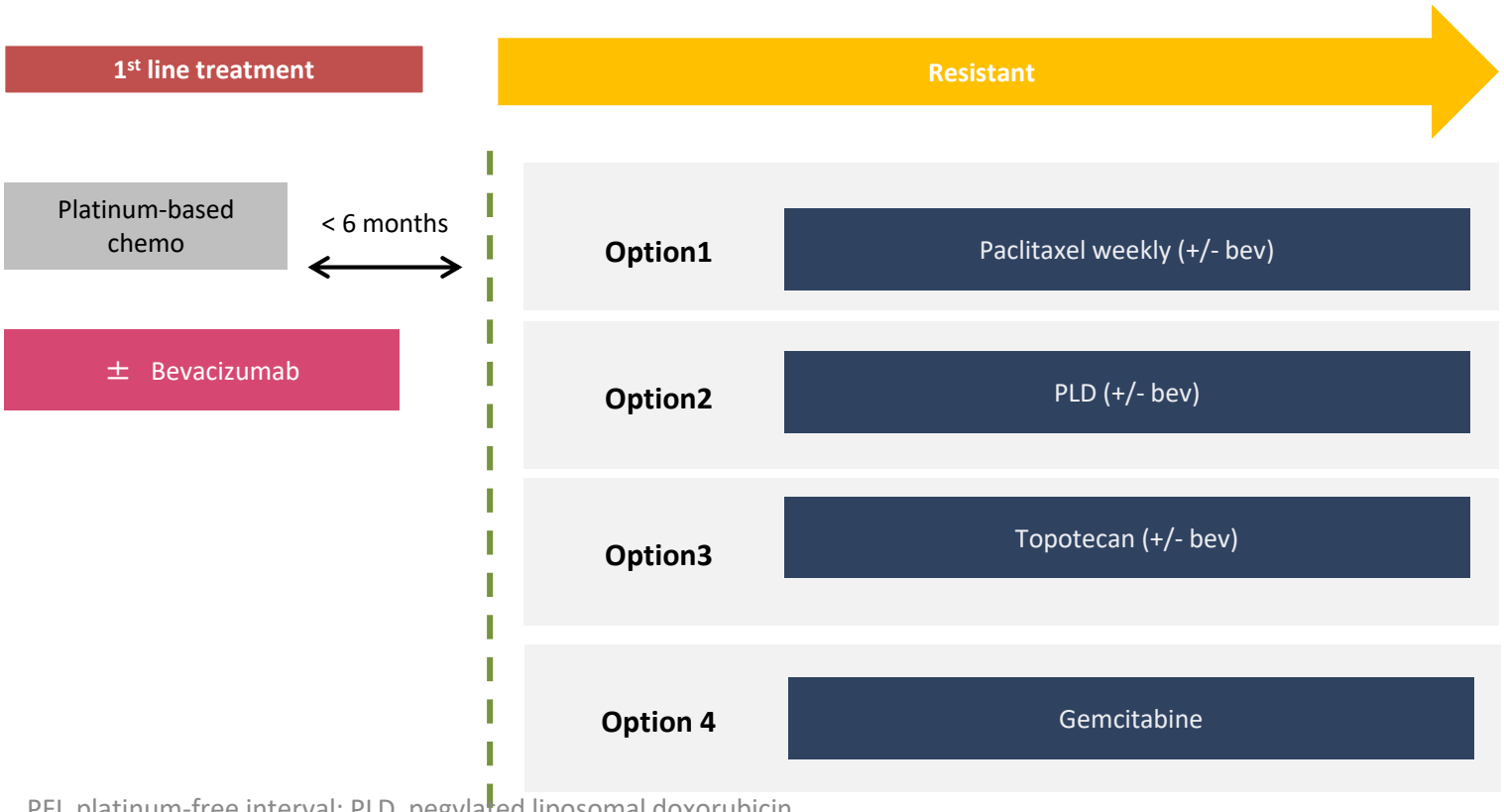
Agent	Response Rates		Patient Tolerance/QoL Issues
	Platinum-Sensitive	Platinum-Resistant	
PLD	28%	12-16%	HFS, mucositis
Paclitaxel	20-45%	7-17%	Alopecia, peripheral neuropathy, arthralgias/myalgias
Etoposide	34%	27%	Alopecia, GI toxicity
Gemcitabine	34%	13-19%	Flu-like constitutional symptoms, hepatic dysfunction, dyspnea
Yondelis	36%	7-16%	Transaminases elevation, Asthenia, GI toxicity
Vinorelbine	29%	15-19%	Constipation, nausea, peripheral neuropathy
Topotecan	33%	12-19%	Asthenia, alopecia, schedule

Armstrong et al. *The Oncologist*. 2002;7:20-28; Herzog. *Clin Cancer Res*. 2004;10:7439-7449.

Randomized phase III trials of chemotherapy combinations vs single agent in platinum refractory/resistant ovarian cancer

Author	N pts	Drugs	RR (%)	PFS (median)	OS (median)	Note
Buda 2004	212	PTX vs PTX+EPI	46.9 37.4	6.0 m 6.0 m	14.0 m 12.0 m	Increased toxicity in the combination arm
Bolis 1999	81	PTX vs PTX+EPI	17.1 34.2	NR NR	18 10 (2-year OS)	Increased toxicity in the combination arm
Sehouli 2008	502	TPT vs TPT+ VP 16 vs TPT +GEM	27.8 36.1 31.6	7.0 m 7.8 m 5.3 m	17.2 m 17.8 m 15.2 m	Increased toxicity in the combination arm
Vergote 2010	125	PLD vs CAN+PLD	12.3 8.3	3.7 m 5.6 m	NR NR	Increased toxicity in the combination arm
Monk 2010	242	PLD vs PLD + ET743	12.2 13.4	4.0 m 3.7 m	12.4 m 14.2 m	Increased toxicity in the combination arm
Lortholary 2012	165	PTX w vs CBDA + PTX w vs TPT w	35 37 39	3.7 m 4.8 m 5.4 m	19.9 m 15.2 m 18.6 m	Increased toxicity in the combination arm

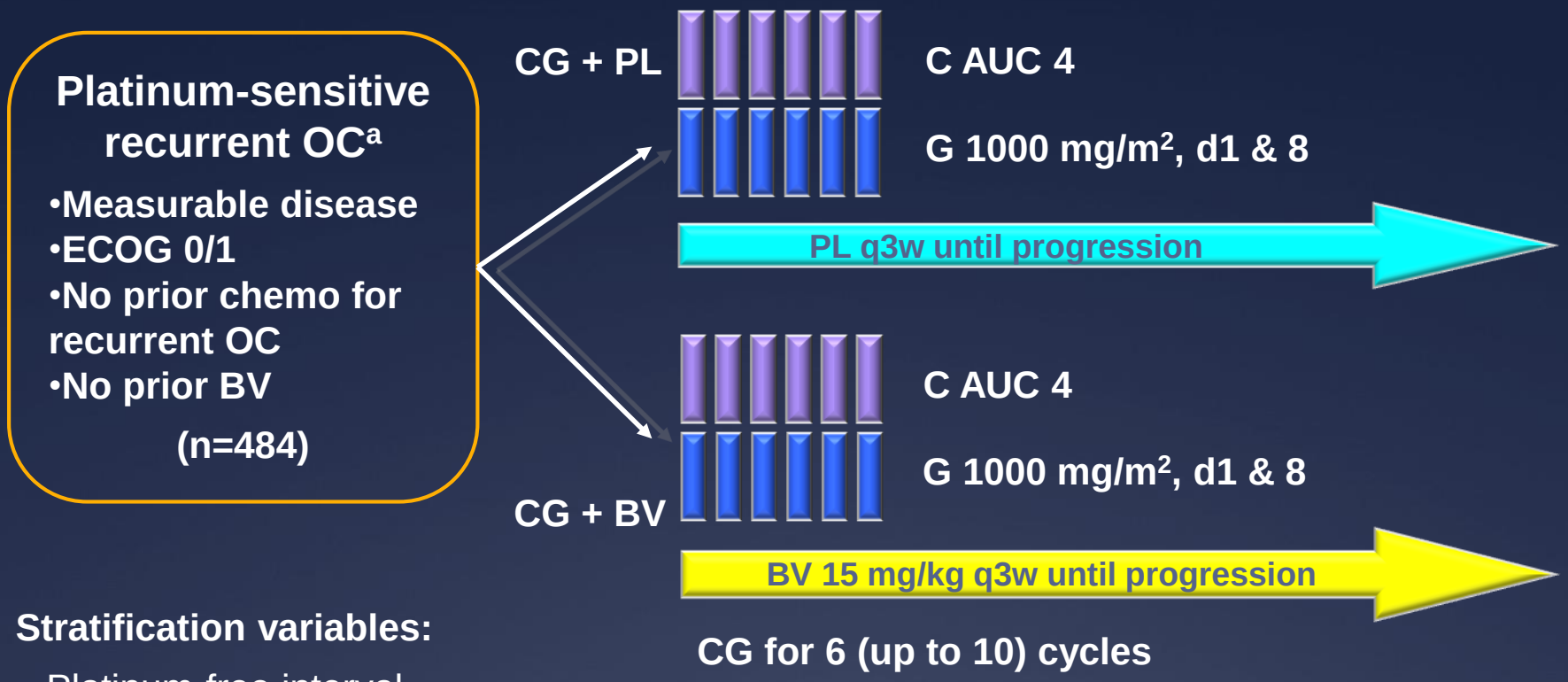
Treatment options for platinum-resistant ovarian cancer



PFI, platinum-free interval; PLD, pegylated liposomal doxorubicin

Ledermann J et al. 2013. Newly diagnosed and relapsed epithelial ovarian carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology, 24 (Supplement 6): vi24–vi32.

OCEANS: Study schema



Stratification variables:

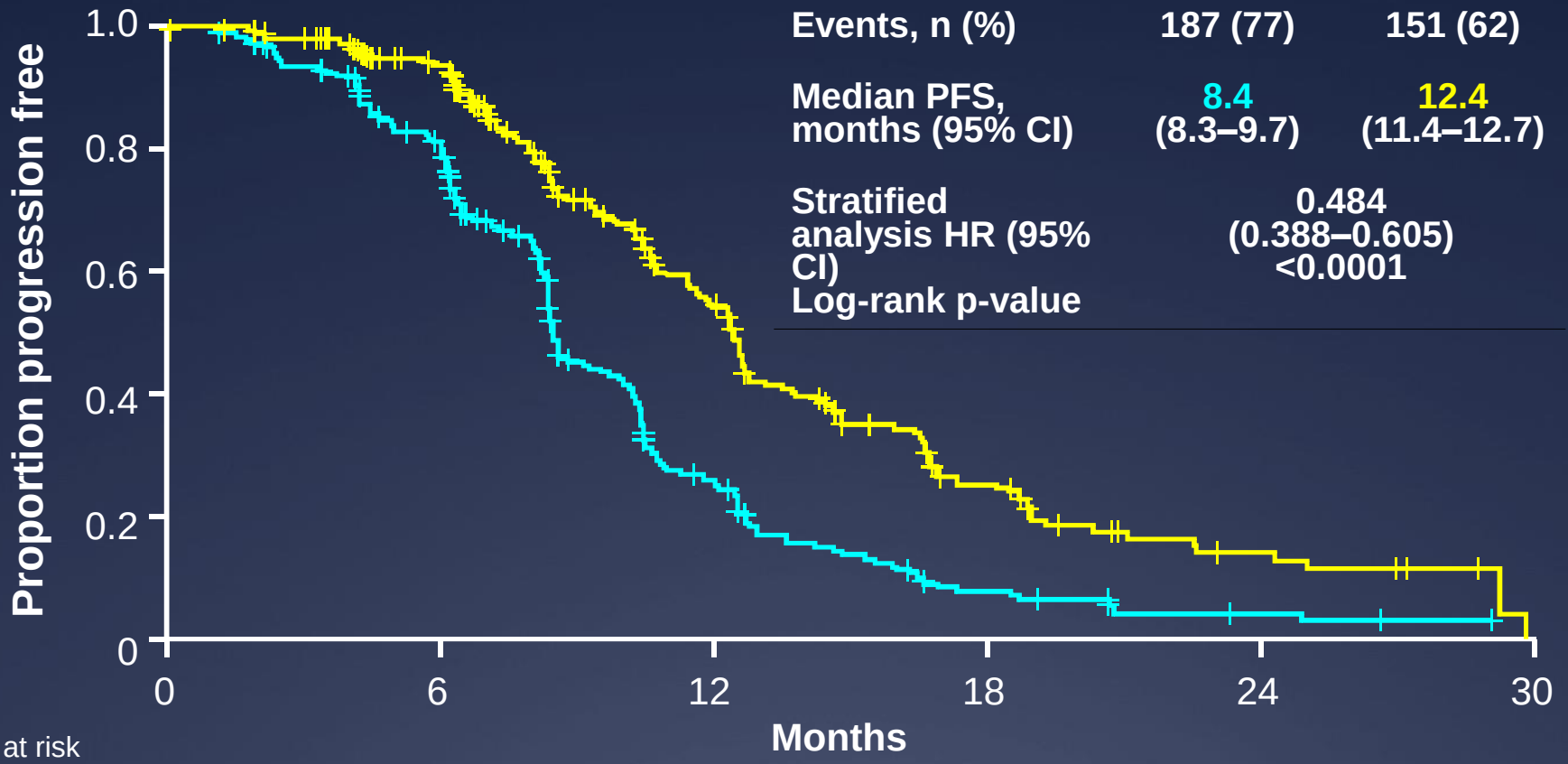
- Platinum-free interval (6–12 vs >12 months)
- Cytoreductive surgery for recurrent disease (yes vs no)

BV = bevacizumab; PL = placebo

[a]Epithelial ovarian, primary peritoneal, or fallopian tube cancer

OCEANS: Primary analysis of PFS

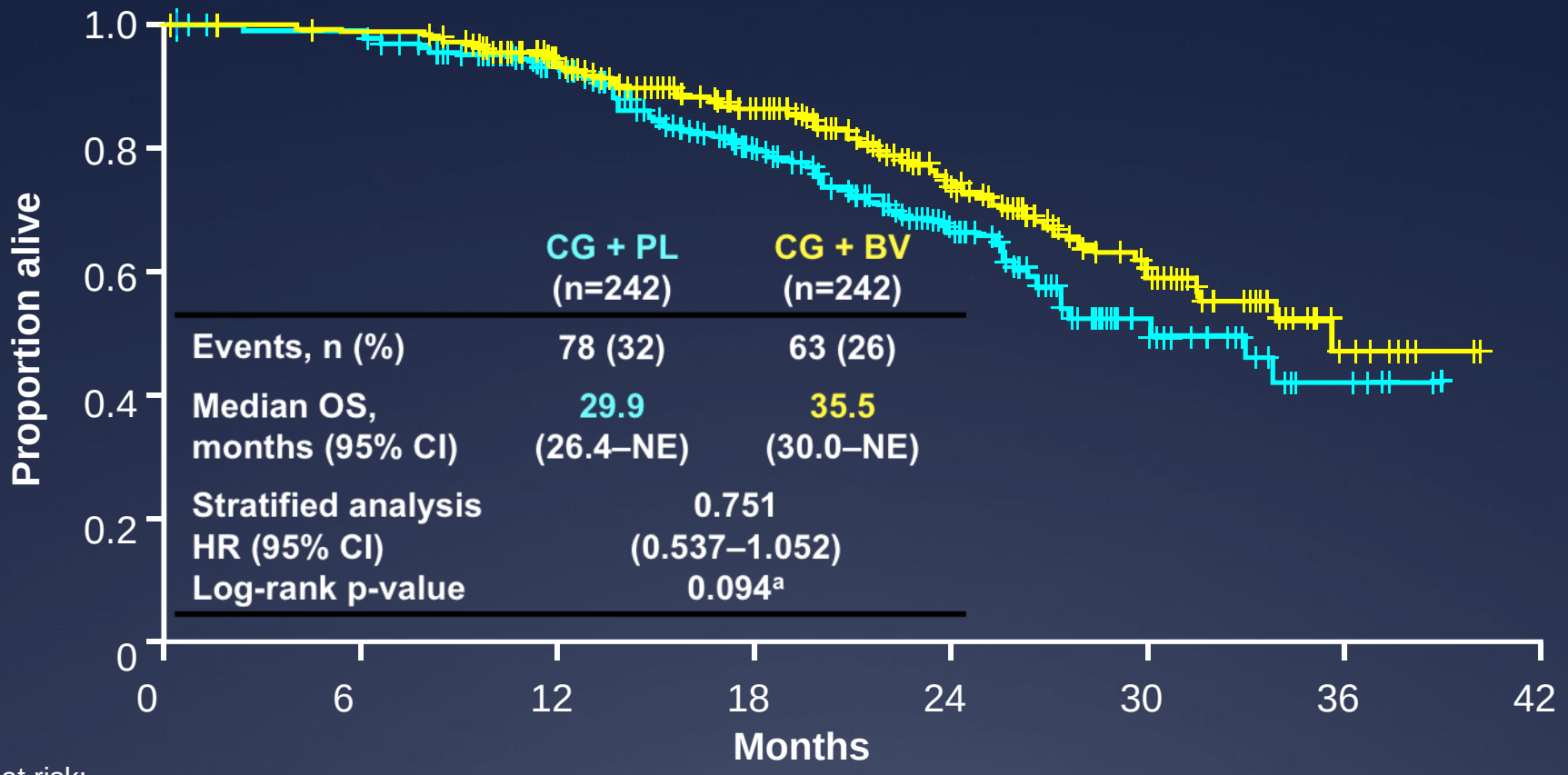
	CG + PL (n=242)	CG + BV (n=242)
Events, n (%)	187 (77)	151 (62)
Median PFS, months (95% CI)	8.4 (8.3–9.7)	12.4 (11.4–12.7)
Stratified analysis HR (95% CI)	0.484 (0.388–0.605)	
Log-rank p-value	<0.0001	



No. at risk

CG + PL	242	177	45	11	3	0
CG + BV	242	203	92	33	11	0

OCEANS: Interim OS



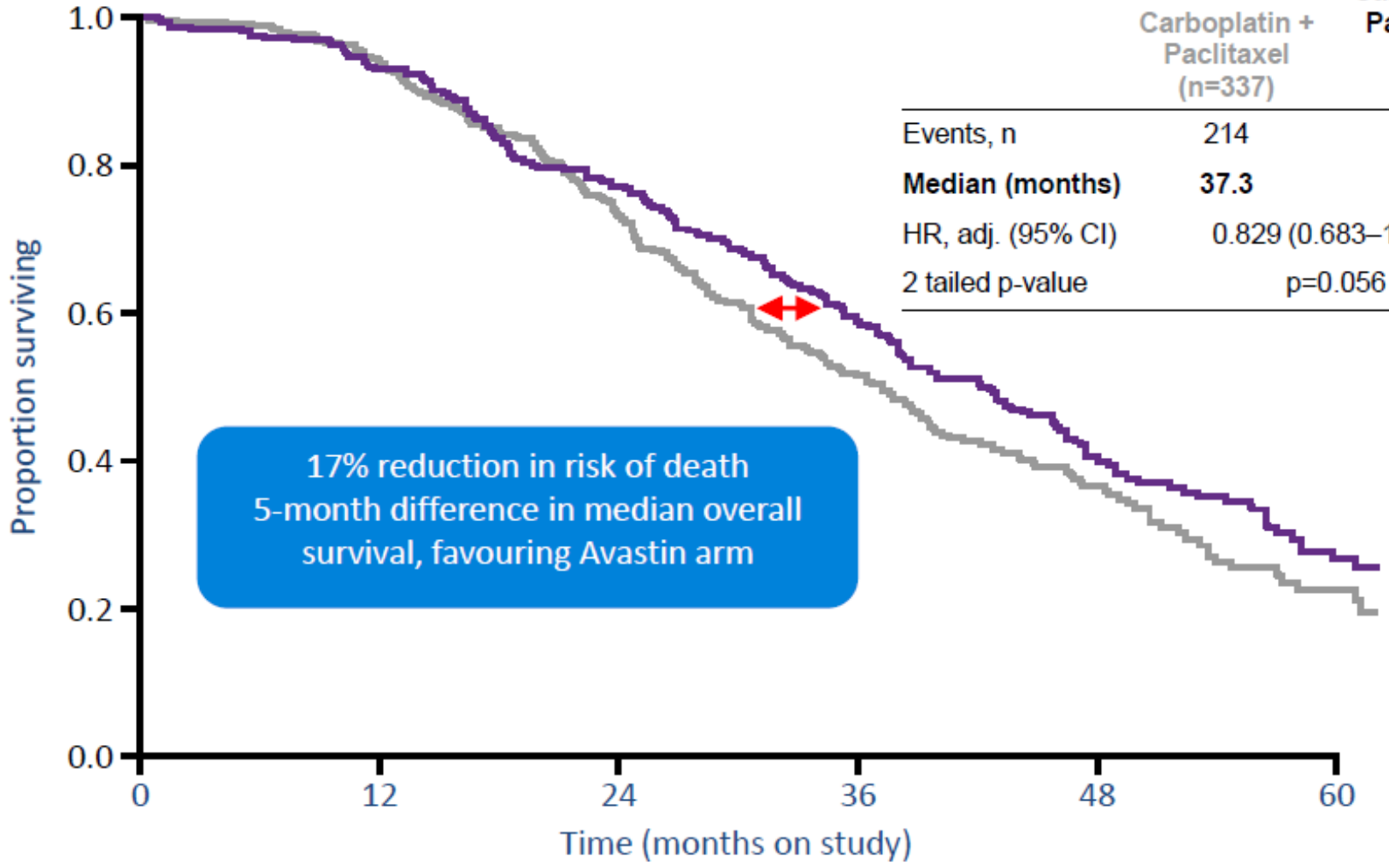
No. at risk:

CG + PL	242	235	195	131	77	26	8	0
CG + BV	242	238	200	146	82	42	8	0

NE = not estimable

[a]p-value does not cross pre-specified boundary of 0.001

GOG-0213: primary analysis of OS



	Carboplatin + Paclitaxel (n=337)	Carboplatin + Paclitaxel + Avastin (n=337)
Events, n	214	201
Median (months)	**37.3**	**42.2**
HR, adj. (95% CI)	0.829 (0.683–1.005)	
2 tailed p-value	p=0.056	

- Coleman, et al. SGO 2015 (Abstract 3)

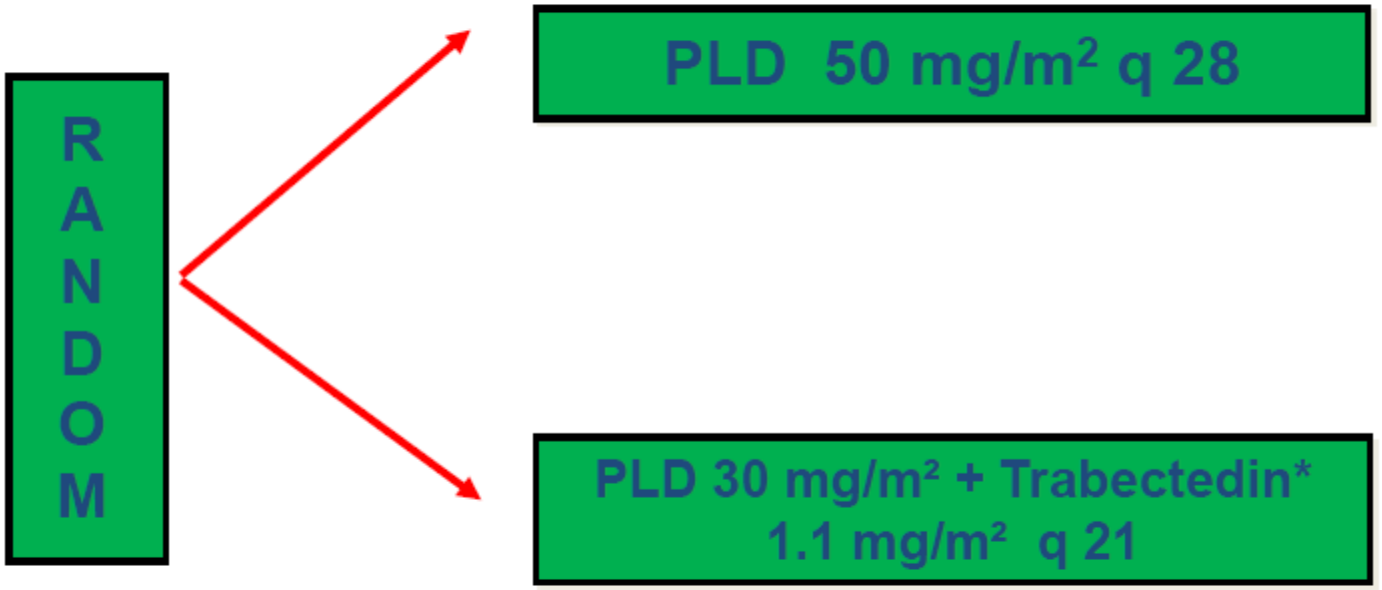
Trabectedin Plus Pegylated Liposomal Doxorubicin in Recurrent Ovarian Cancer

Bradley J. Monk, Thomas J. Herzog, Stanley B. Kaye, Carolyn N. Krasner, Jan B. Vermorken, Franco M. Muggia, Eric Pujade-Lauraine, Alla S. Lisyanskaya, Anatoly N. Makhson, Janusz Rolski, Vera A. Gorbounova, Prafull Ghatage, Mariusz Bidzinski, Keng Shen, Hextan Yuen-Sheung Ngan, Ignace B. Vergote, Joo-Hyun Nam, Youn Choi Park, Claudia A. Lebedinsky, and Andrés M. Poveda

VOLUME 28 · NUMBER 19 · JULY 1 2010

JOURNAL OF CLINICAL ONCOLOGY

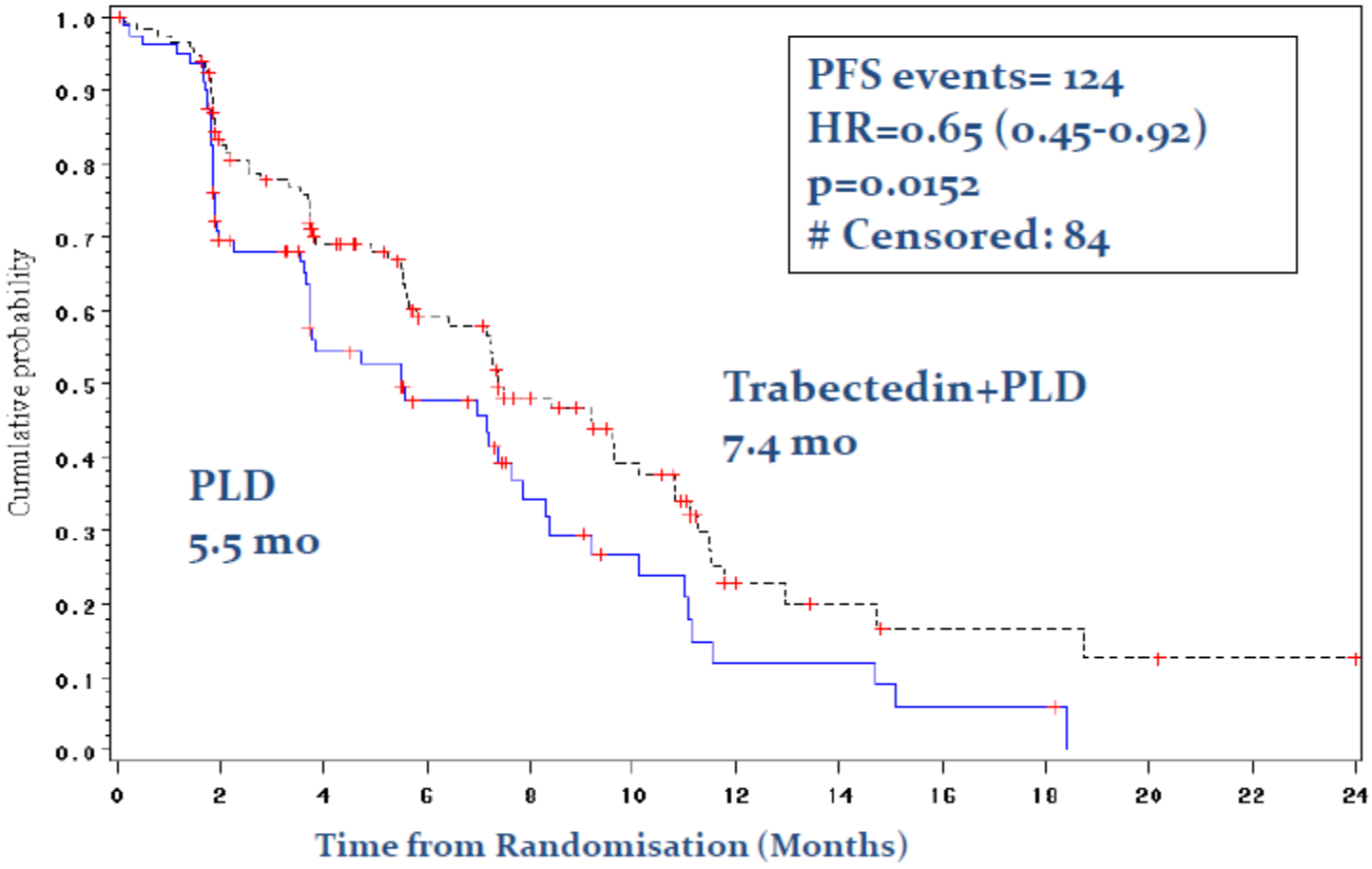
ORIGINAL REPORT



672 patients

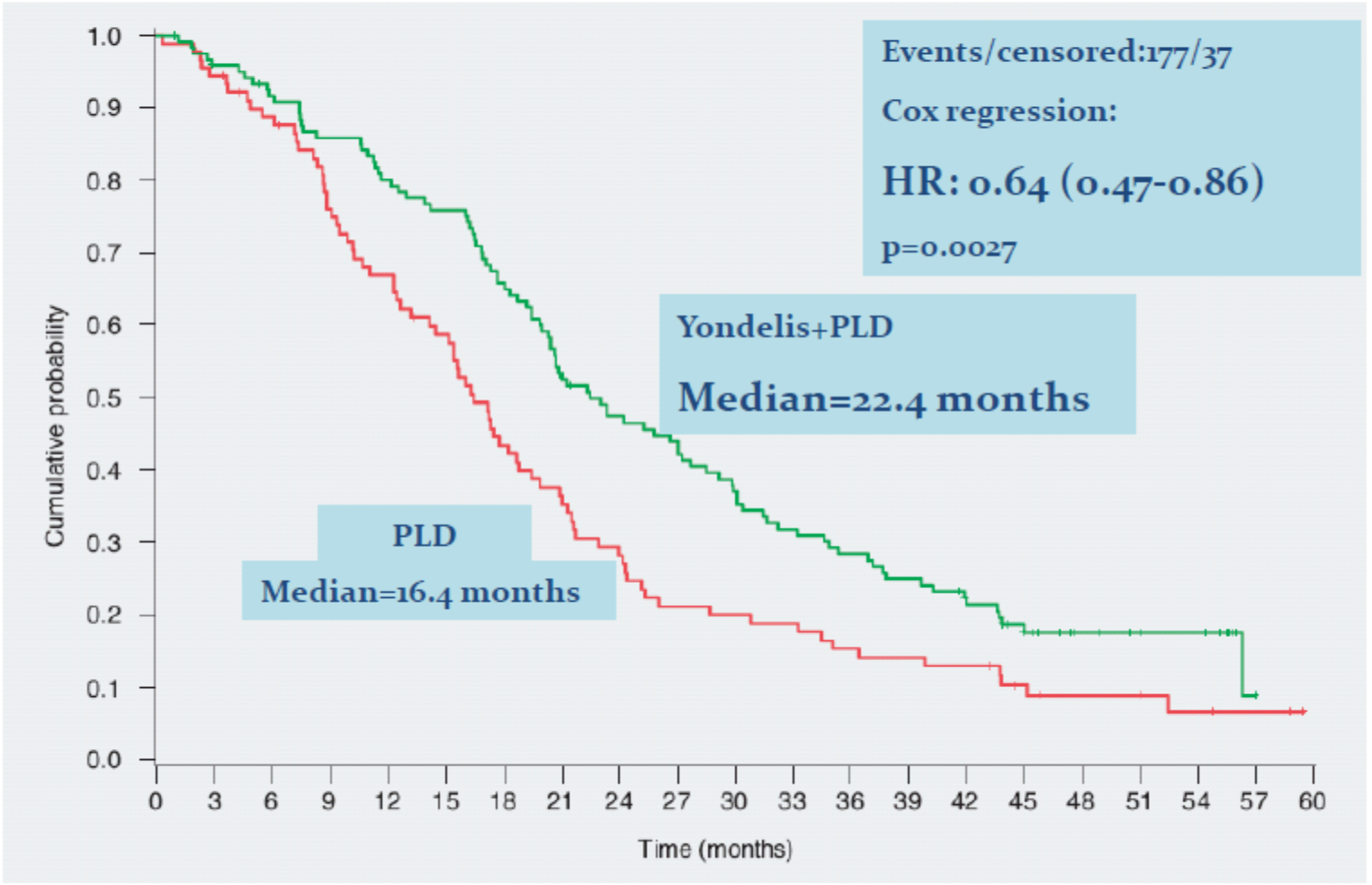
	PLD		PLD+ET743	
Platinum-free interval, months*				
< 6	117	35	115	35
6 to < 12	91	28	123	37
≥ 12	122	37	95	29

Trabectedin-PLD PFS – Intermediate Sensitivity (PFI 6-12 mo)



PFI = Platinum Free Interval

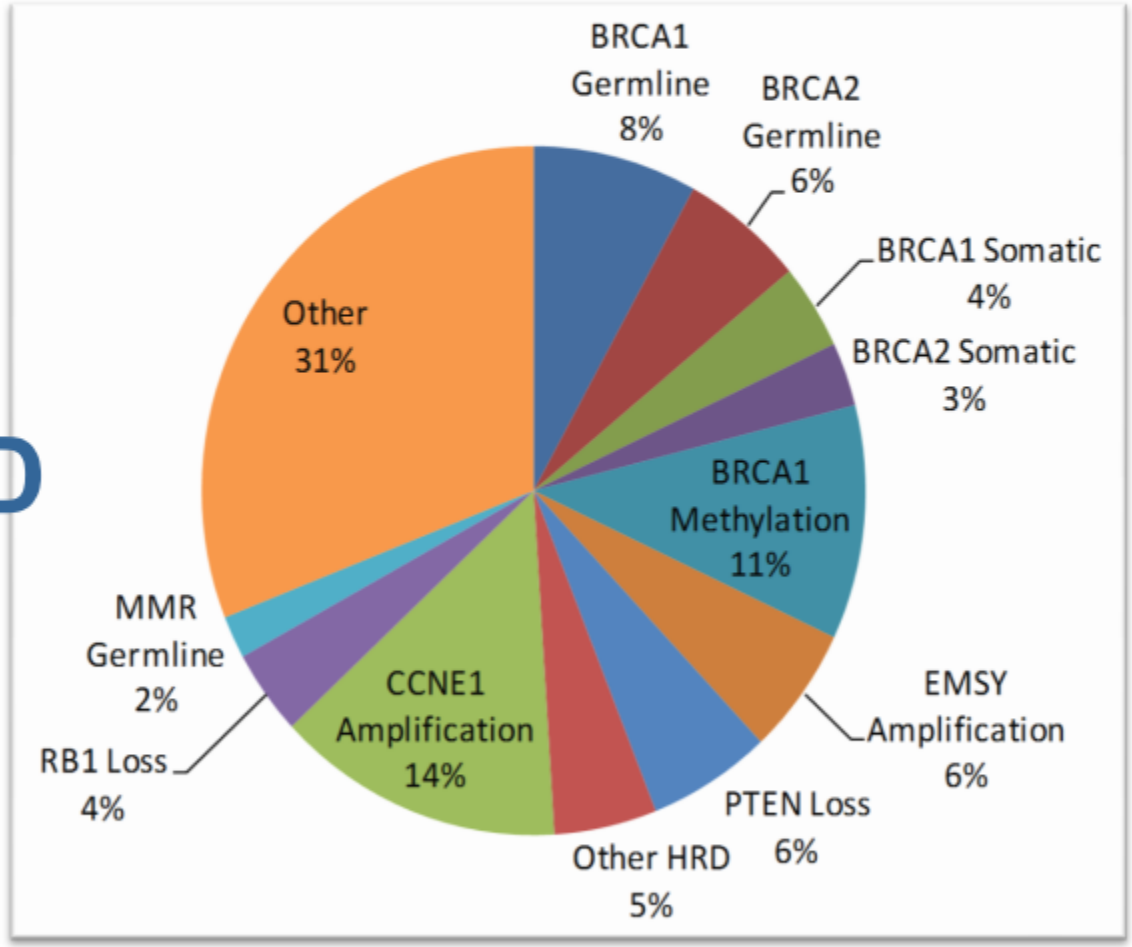
Role of Yondelis+PLD in PPS Ovarian Cancer: OS data



Monk BJ et al. J Clin Oncol. 2011:29(suppl):abstr 5046.
Sehouli J, Gonzalez A. Ann Oncol 2011. Epub 2011 Jul 6. DOI: 10.1093/annonc/mdr321

High grade serous ovarian cancer: Potential benefit of PARP inhibition in 50%

Not HRD



HRD

Cancer Genome Atlas Research Network. *Nature*. 2011;474(7353):609-615.

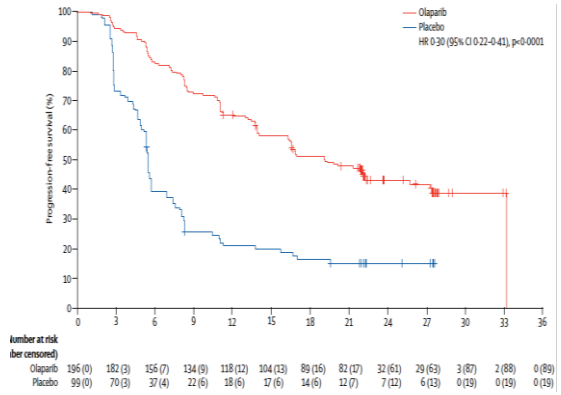
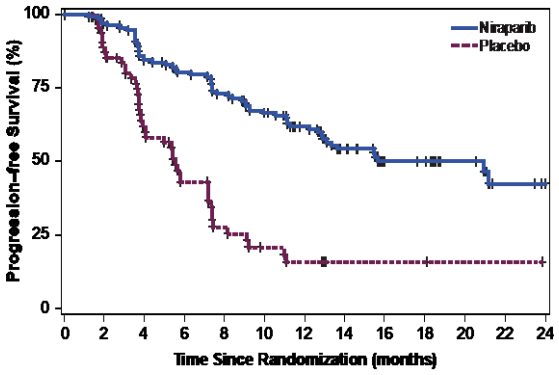
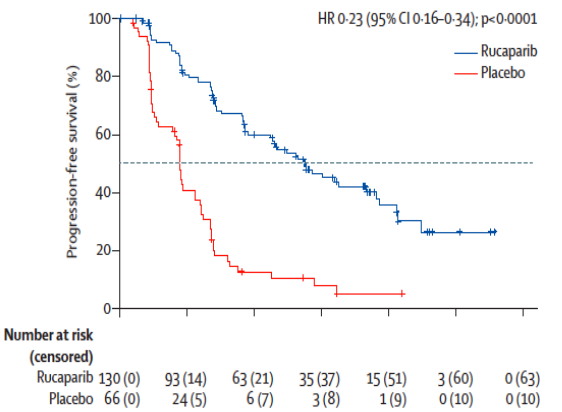
Phase III trials with PARP inhibitors

Recruiting:

- SOLO 1 and 2 (olaparib)
  - Randomised maintenance trials in first line and platinum-sensitive recurrent *BRCA*m ovarian cancer
- NOVA (niraparib)
  - Randomised maintenance trial following platinum-based chemotherapy in *BRCA*m and *BRCA*wt high-grade serous cancer
- ARIEL 3 (rucaparib)
  - Randomised maintenance trial following platinum-based chemotherapy in *BRCA*m and *BRCA*wt high-grade serous cancer with companion diagnostic

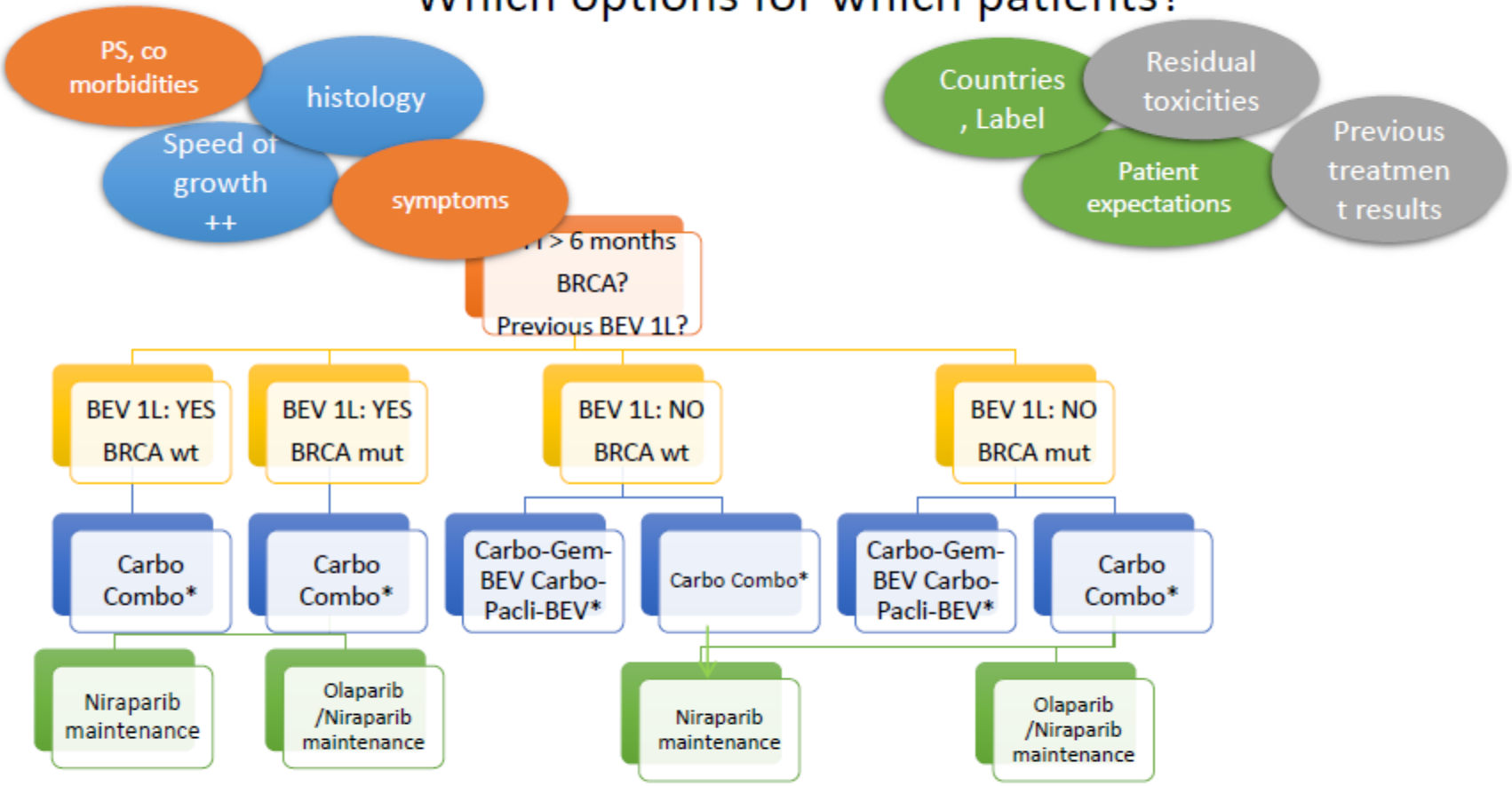
Efficacy of PARP inhibitors in BRCAm patients

PRIMARY ENDPOINT: PFS

SOLO-2 - g*BRCA*m[1]	NOVA – g*BRCA*m[2]	ARIEL-3- *BRCA*m[3]
		
19.1 vs 5.5 months HR 0.30 (95% CI: 0.22-0.41)	21.0 vs. 5.5 months HR 0.27 (95% CI: 0.17-0.41)	16.6 vs 5.4 months HR 0.23 (0.16-0.34)

1. Pujade-Lauraine E, et al. *Lancet Oncology* 2017;18:1274-1284; 2. Mirza MR, et al. *N Engl J Med* 2016;375:2154-164; 3. Coleman RL, et al. *Lancet* 2017;390:1949-1961

Systemic therapy for patienst with TFIp > 6 months
Which options for which patients?



*Platinum is an option? Consider non-platinum combination with trabectedin-PLD if platinum is not an option

Platine sensitive relapse
Bev or not bev? Parpi or not parpi?

Pro Bev

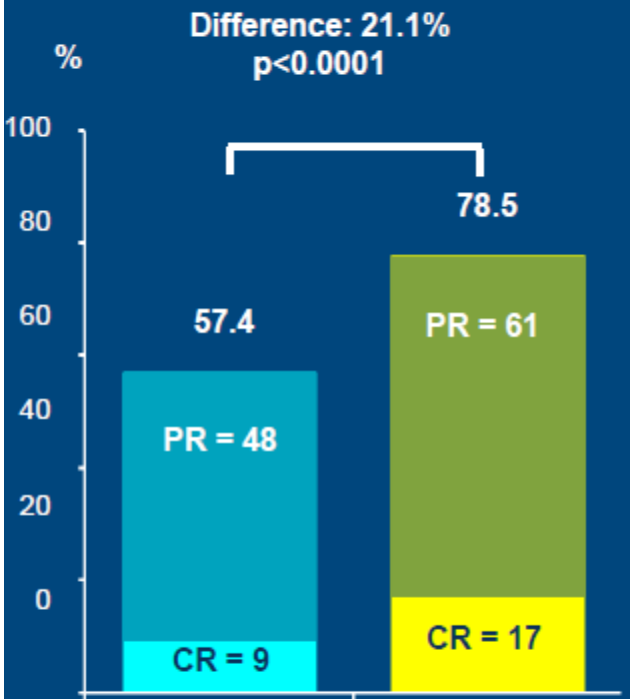
- No medical contraindication.
- No Bev before
- 1st sensitive relapse
- Independently of PFI
  - < 6 months: AURELIA
  - > 6 months: OCEANS
- No mBRCA (tumor/germ line)
- Highly progressive, ascites, symptoms, need for a quick and High RR

Pro Parpi

- mBRCA (somatic or germ line)
- BRCA unknown, high grade carcinoma (waiting for the BRCA testing)
- Last CT with platine
- Highly sensitive to platine (long PFI)
- Bev before
- > 1st relapse
- No symptoms, no ascites

Highly progressive, ascites, symptoms ….

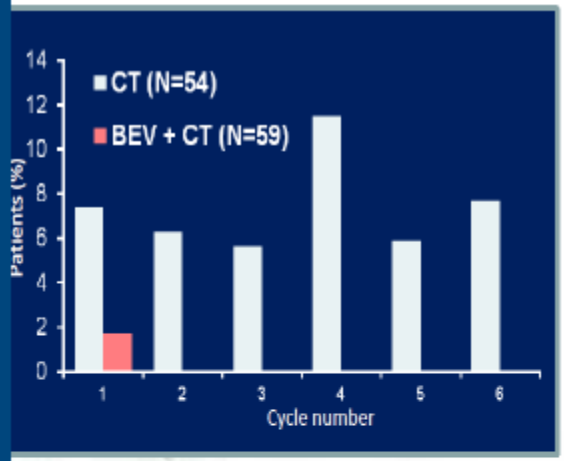
OCEANS: Objective response



Duration of response	CG + PL (n=139)	CG + BV (n=190)
Median, months	7.4	10.4
HR (95% CI)	0.534 (0.408–0.698)	
p<0.0001		

AURELIA : RR & Parencentesis

Paracentesis in subgroup with ascites



Primary hypothesis : improvement in abdominal/GI symptoms (≥15%)

Responders: **44.0% vs 4.1%**

39.9% difference

[95% CI 23.9–55.9]).

C Aghajanian, JCO 2012; E Pujade Lauraine, JCO 2014

PRESENTED AT: ASCO Annual '11 Meeting

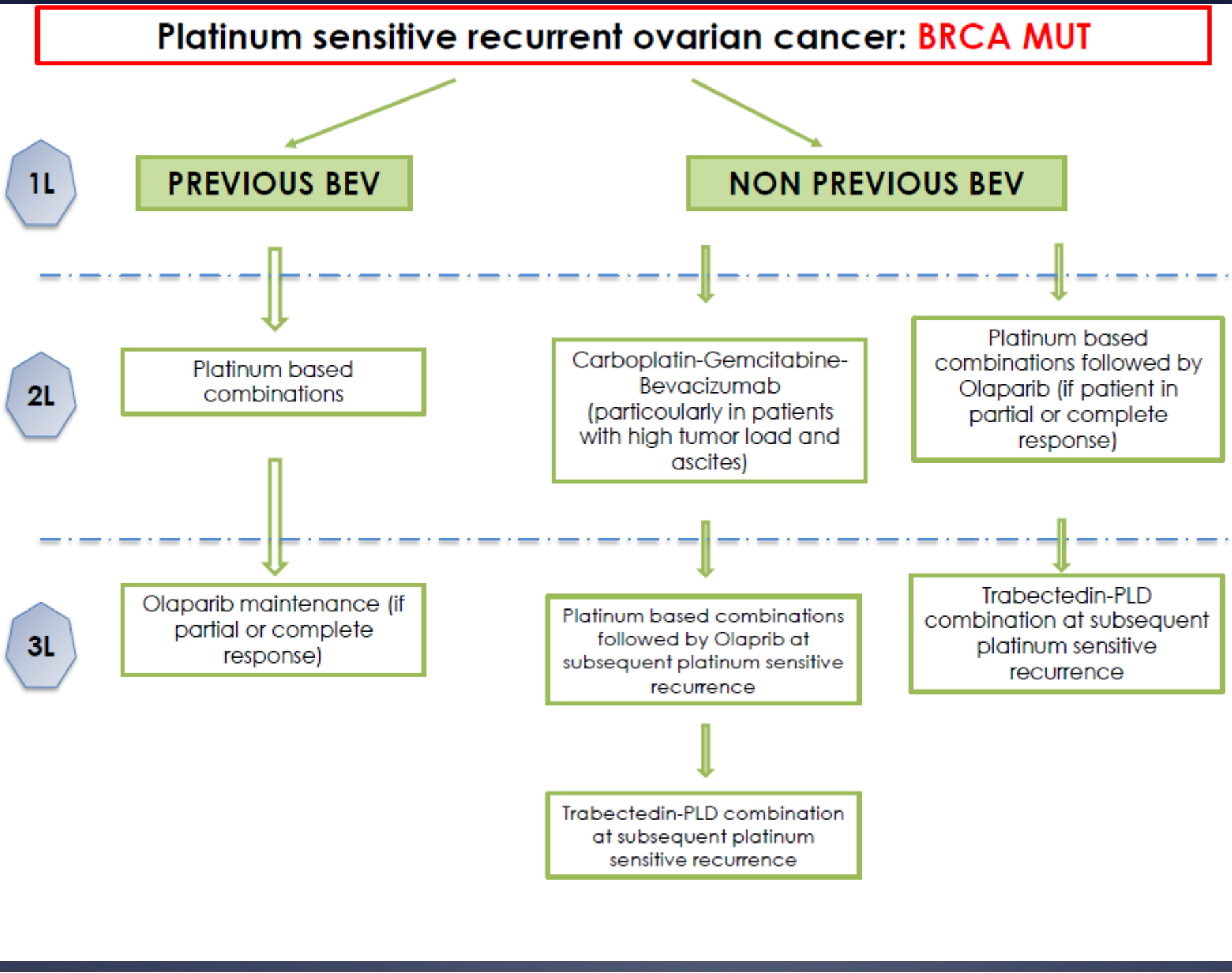
Platine sensitive relapse
Bev or not bev? Parpi or not parpi?

Pro Bev

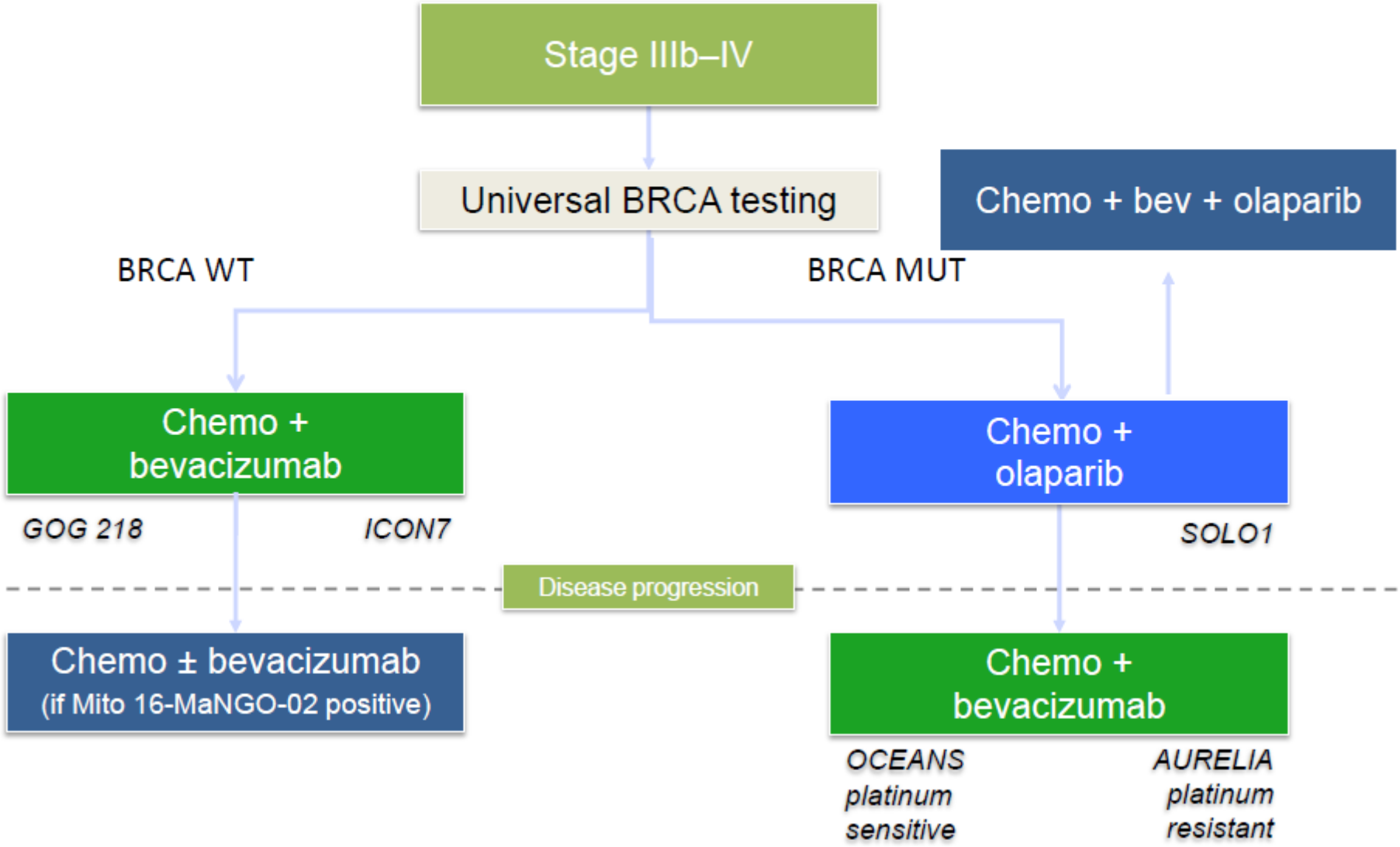
- No medical contraindication.
- No Bev before
- 1st sensitive relapse
  - Independently of PFI
    - < 6 months: AURELIA
    - > 6 months: OCEANS
- Highly progressive, ascites, symptoms, need for a quick and High RR
- No mBRCA tumor/germ line
- Favor ≠ HGSC

Pro Parpi

- mBRCA (somatic or germ line)
- BRCA unknown, high grade carcinoma (waiting for the BRCA testing)
- Last CT with platinum
- Highly sensitive to platinum (long PFI)
- Bev before
- > 1st relapse
- No symptoms, no ascites


Platinum sensitive recurrent ovarian cancer: BRCA MUT
1L
PREVIOUS BEV
NON PREVIOUS BEV
2L
Platinum based combinations
Carboplatin-Gemcitabine-Bevacizumab (particoularly in patients with high tumor load and ascites)
Platinum based combinations followed by Olaparib (if patient in partial or complete response)
3L
Olaparib maintenance (if partial or complete response)
Platinum based combinations followed by Olaprib at subsequent platinum sensitive recurrence
Trabectedin-PLD combination at subsequent platinum sensitive recurrence
Trabectedin-PLD combination at subsequent platinum sensitive recurrence

Looking at the future: Ovarian cancer treatment algorithm



Conclusioni

- BEVACIZUMAB è l'unico antiangiogenetico approvato per il trattamento del tumore ovarico sia in prima linea che nella recidiva sia platino-SENSIBILE che platino-RESISTENTE;

- OLAPARIB: nuovo farmaco con meccanismo d'azione diverso approvato sia come terapia di MANTENIMENTO nelle pazienti platino-SENSIBILI che abbiano risposto ad una precedente terapia con carboplatino e taxolo come terapia di mantenimento dopo una prima linea a base di platino;

- Niraparib e Rucaparib efficaci indipendentemente dallo stato di BRCA;

- Diversi profili di tossicità

Conclusioni

- BRCA is the first molecular biomarker for a target therapy in OC
- More patients can benefit further to germilene mutated (BRCA somatic, HRD)
- BRCA can also help in chemotherapy choice
- BRCA germile tested in all patients also for prevention

Ovarian cancer: conclusions

- Treatment according to histotype is the future!

- Antiangiogenic agents and parp inhibitors are changing the natual history of ovarian cancer disease, immunotherapy the raising star at the orizon?

- The best treatment algorytm is the one which allows patients to receive all the available and effective treatment options.

- Treatment algorytm will deeply change in the next 5 years