



# Impact of Prior PARPi on Surgery Outcomes: Challenge beyond SOC-1 Trial

**Tingyan Shi, MD PhD**

Dep. Gynecologic Oncology,  
Zhongshan Hospital, Fudan University  
Ovarian Cancer Institute, Fudan University

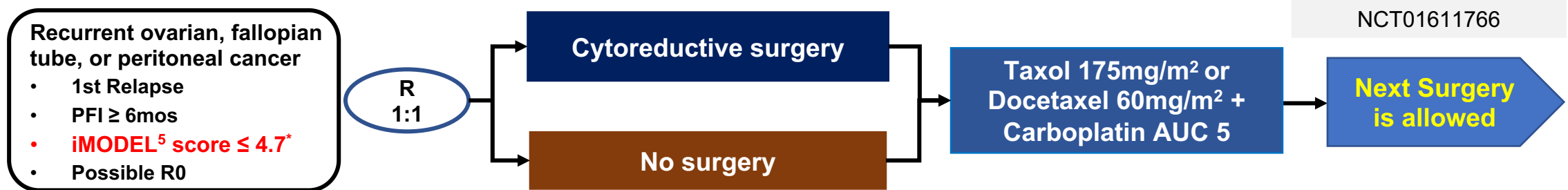


# Conflict of interest



**I have no disclosure.**

- **Ongoing debate:** OS benefit of secondary cytoreduction (SCR) in patients with platinum-sensitive, relapsed ovarian cancer
- DESKTOP III<sup>1</sup> showed a benefit of PFS and OS among patients assigned to undergo SCR, which contradicted to that of the GOG-0213<sup>2</sup>
- **SOC-1: planned interim analysis<sup>3</sup>** after 129 PFS events
  - > presented at ASCO 2020 and showing a significant PFS benefit for surgery
- **Final OS analysis: database closure JUN 30<sup>th</sup> 2023** after 210 of 209 planned events in a hierarchical testing<sup>4</sup>



\*If PI and Co-PI reach consensus that the recurrent tumor detected by PET/CT could be completely resected, the index of CA125 could be scored as 0.

**Co-Primary endpoint:** PFS, OS

**Secondary endpoints:** TFSa<sup>†</sup>, QoL, TFST, TSST, Safety

**Randomization strata:** Centers, iMODEL score, residual disease, enrolled in SUNNY trial<sup>6</sup>

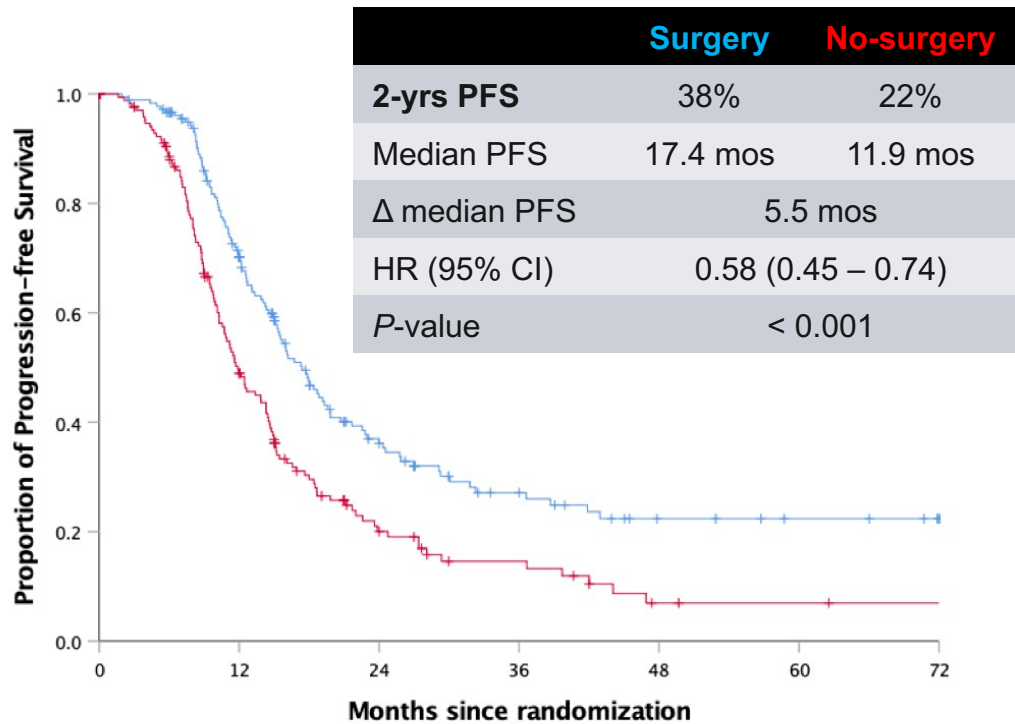
**Open:** JUL 2012

**Close:** JUN 2019

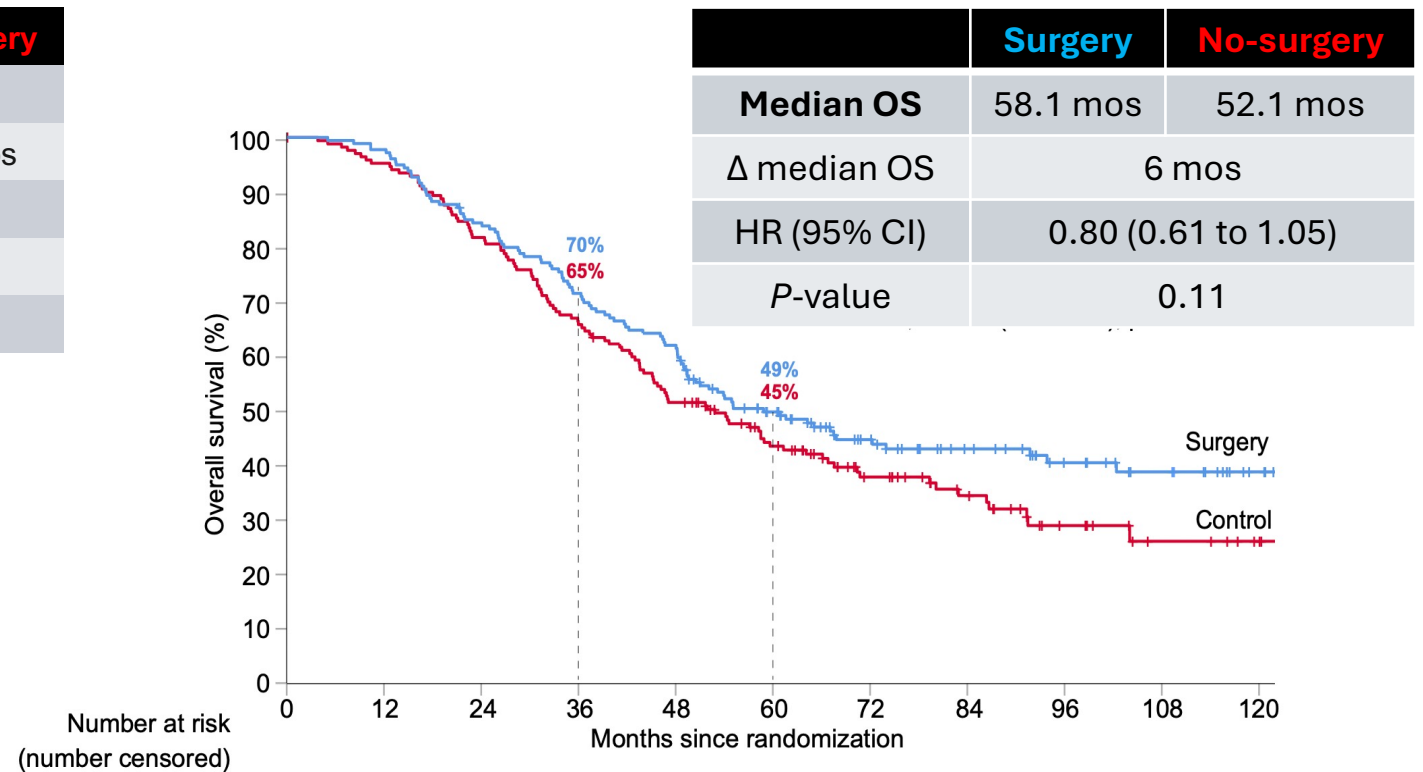
**Target:** 356 pts

<sup>1</sup>Harter P, et al. *N Engl J Med* 2021;385:2123-2131; <sup>2</sup>Coleman RL, et al. *N Engl J Med* 2019;381:1929-1939; <sup>3</sup>Shi T, et al. *The Lancet Oncol* 2021; 22:439-49; <sup>4</sup>Jiang R, et al. *Nat Med*. 2024;30:2181-2188; <sup>5</sup>Tian WJ, et al. *Ann Surg Oncol* 2012,19:597-604; <sup>6</sup>Jiang R, et al. *J Gynecol Oncol*. 2020;31(5):e86.

# SGOG SOC-1: primary endpoints – PFS & OS



No. at risk	0	12	24	36	48	60	72
Surgery	182	115	45	25	14	11	8
No-surgery	175	75	21	11	3	2	1



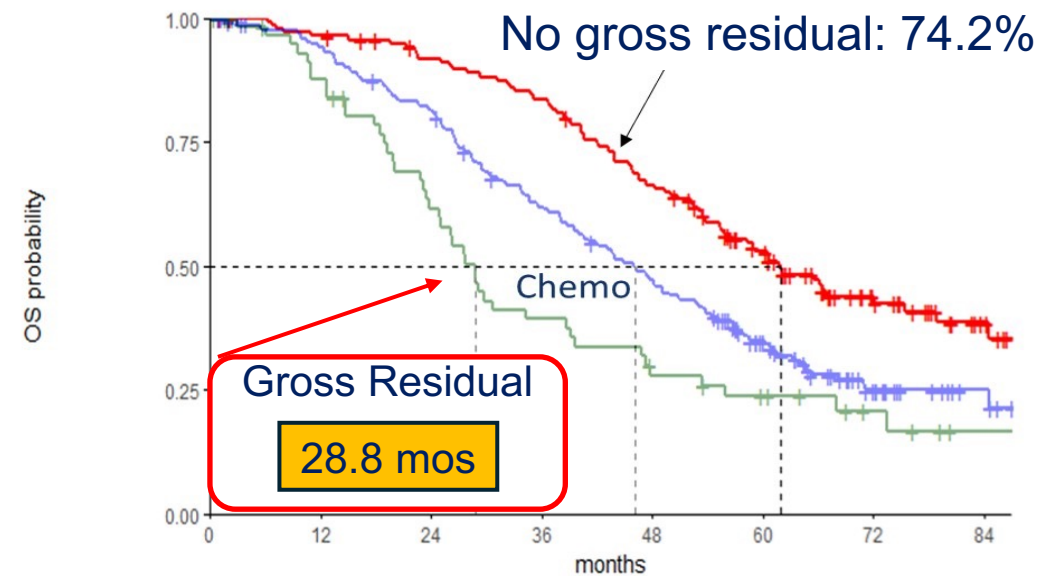
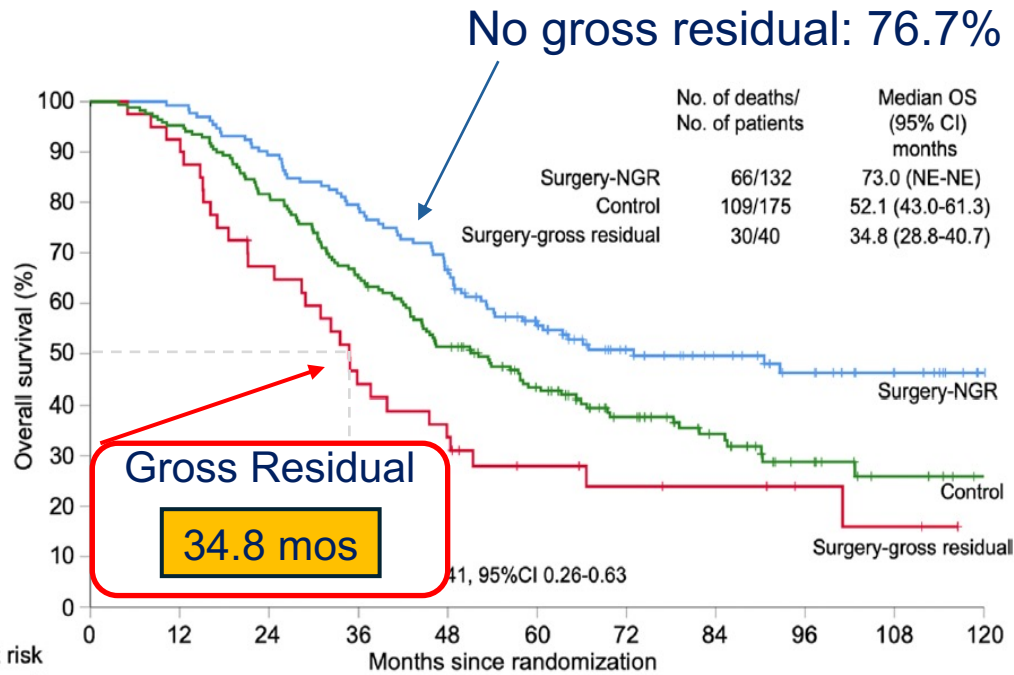
Number at risk (number censored)	0	12	24	36	48	60	72	84	96	108	120
Surgery	182 (0)	175 (3)	150 (1)	127 (0)	110 (0)	78 (11)	54 (17)	40 (12)	28 (10)	21 (6)	11 (10)
Control	175 (0)	161 (6)	138 (0)	112 (0)	86 (1)	63 (11)	41 (15)	29 (9)	15 (10)	7 (7)	3 (4)

# Impact of Gross Residual disease at Surgery on OS



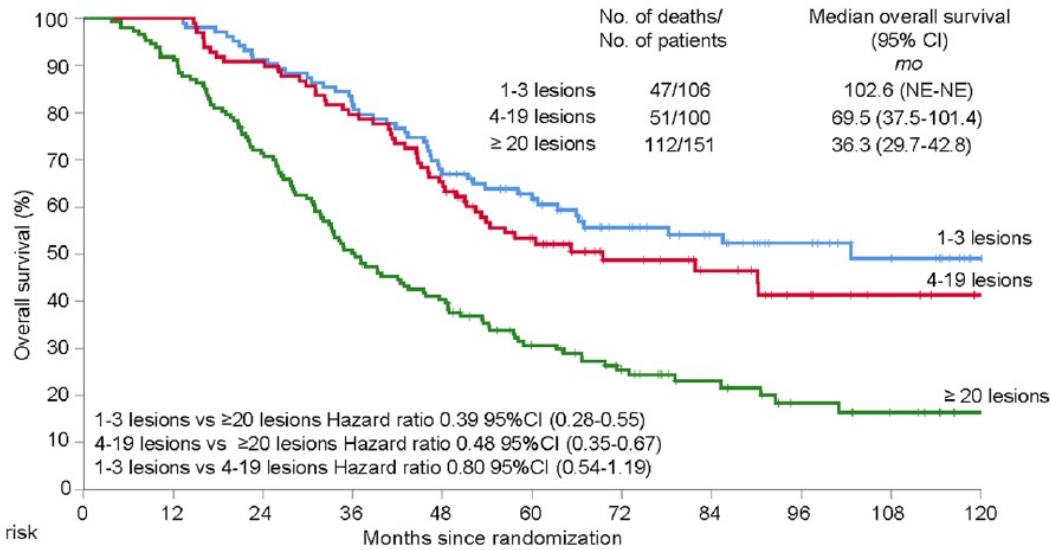
## SOC-1

## Desktop III



# Impact of relapsed lesions on OS

SOC-1



Numbers of Lesions	Median OS (mos)	HR (95% CI)	Complete resection
1 to 3	102.6	0.39 (0.28 to 0.55)	(55/59) 93%
4 to 19	69.5	0.48 (0.35 to 0.67)	(33/40) 83%
≥20	36.3	1	(44/73) 60%

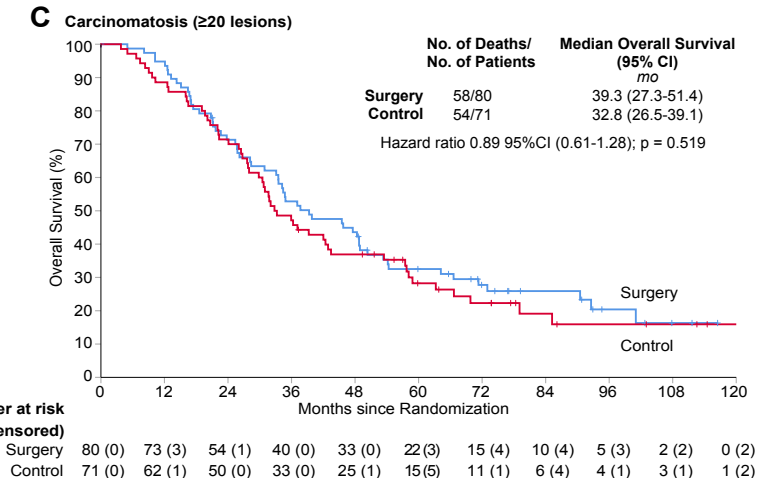
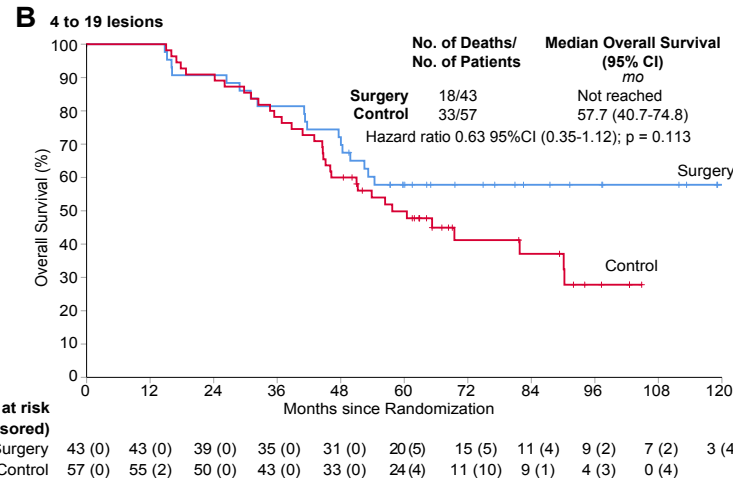
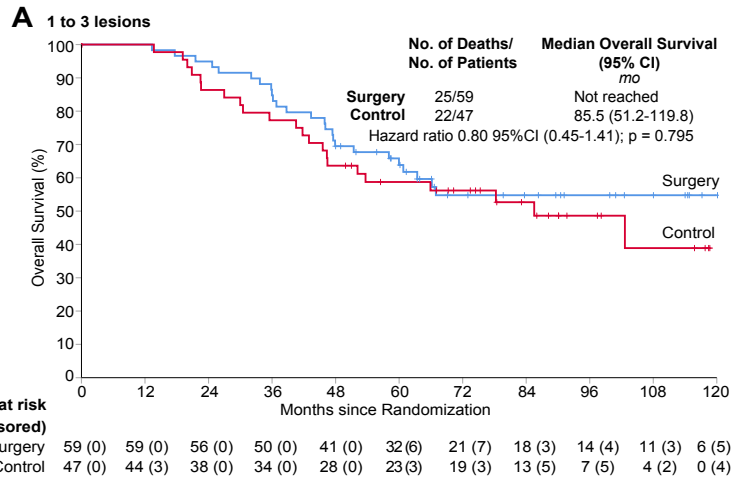
\* The number of relapsed lesions have been evaluated by Image (PET-CT).

# Impact of relapsed lesions on OS – SOC-1

## 1-3 lesions

## 4-19 lesions

## >=20 lesions



Numbers of Lesions	Median OS (mos) Surgery vs. Control	HR (95% CI)
1 to 3	NR vs. 85.5	0.80 (0.45 to 1.41)
4 to 19	NR vs. 57.7	0.63 (0.35 to 1.12)
>=20	39.3 vs. 32.8	0.89 (0.61 to 1.28)

- No gross residual disease comes to the best prognosis, while patient with residual disease is worse than those with chemo only.
- More the relapsed lesions, poorer the prognosis.
- Patients may benefit from surgery when oligoprogression ( $\leq 3$  lesions) or localized (4-19 lesions) relapse **(HR 0.69, 95% CI 0.46-1.03)**.

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**KEYPOINT: NGR, Localized lesions for secondary cytoreduction**

# Three selection criteria for NGR at surgery

## (1) MSKCC criteria

Recommendation for Secondary Cytreduction Based on Disease-free Interval, the Number of Recurrence Sites, and Evidence of Carcinomatosis

DFI	Single Site	Multiple Sites: No Carcinomatosis	Carcinomatosis
6–12 Mo	Offer SC	Consider SC	No SC
12–30 Mo	Offer SC	Offer SC	Consider SC
>30 Mo	Offer SC	Offer SC	Offer SC

DFI: disease-free interval; Mo: months; SC: secondary cytreduction.

## (2) AGO criteria

**Patients with disease-free-interval > 6 months, informed consent, and:**

- good performance status (ECOG = 0)
- no residuals after primary surgery (if unknown FIGO stage I/II initially)
- No or small volume of ascites (estimation: < 500 ml)

## (3) iMODEL score

Impact factors	Scoring <sup>a</sup>					
	0	0.8	1.5	1.8	2.4	3.0
FIGO stage	I/II	III/IV				
RD after primary surgery <sup>b</sup>	0		>0			
PFI (months)	≥16				<16	
ECOG performance status <sup>b</sup>	0–1				2–3	
CA125 at recurrence (U/ml)	≤105				>105	
Ascites at recurrence <sup>b</sup>	Absent					Present

*FIGO* International Federation of Gynecology and Obstetrics, *RD* residual disease, *PFI* Progression-free interval, *ECOG* Eastern Cooperative Oncology Group

<sup>a</sup> Low-risk: ≤4.7; high-risk: >4.7

<sup>b</sup> The Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) score system

Chi DS, *Cancer* 2005; 1933-1939

Harter P, *Ann Surg Oncol*. 2006; 13(12):1702-10.

Tian WJ,.. Zang R. *Ann Surg Oncol*. 2012; 19(2):597-604.

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## (1) MSKCC criteria

Recommendation for Secondary Cytoreduction Based on Disease-free Interval, the Number of Recurrence Sites, and Evidence of Carcinomatosis

DFI	Multiple Sites: No	
	Single Site	Carcinomatosis
6–12 Mo		
12–30 Mo		
>30 Mo		

DFI: disease-free interval

**No evidence on selection criteria with Prior PARPi**

## (2) AGO criteria

**Patients with disease-free-interval > 6 months, informed consent, and:**

- **good performance status (ECOG = 0)**
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## (3) iMODEL score

Impact factors	Scoring <sup>a</sup>					
	0	0.8	1.5	1.8	2.4	3.0
FIGO stage	I	II	III	IV	V	VI
CA125 at recurrence (U/ml)	≤105	>105				
Ascites at recurrence <sup>b</sup>	Absent			Present		

FIGO International Federation of Gynecology and Obstetrics, RD residual disease, PFI Progression-free interval, ECOG Eastern Cooperative Oncology Group

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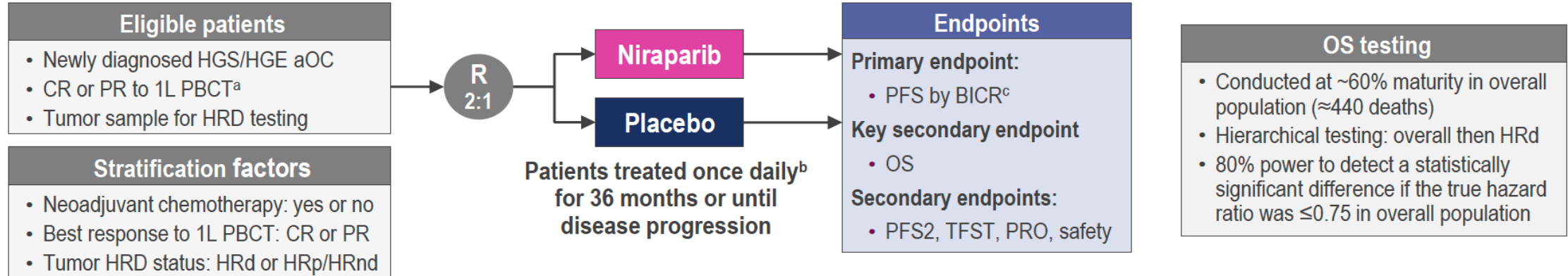
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# Recurrent lesion pattern after prior PARPi



## PRIMA trial



# Recurrent lesion pattern after prior PARPi

## PRIMA

Niraparib

314 pts with Niraparib and no evidence of lesions at baseline

190 pts, 1<sup>st</sup> relapse

		Overall (n = 190)
Median number of new lesions, n (IQR)		1.0 (1.0–2.0)
Number of new lesion(s), n (%)		
1	96 (50.5)	93.2% 1~3 lesions
2	53 (27.9)	
3	28 (14.7)	
4	9 (4.7)	
5	3 (1.6)	
> 5	1 (0.5)	

Control

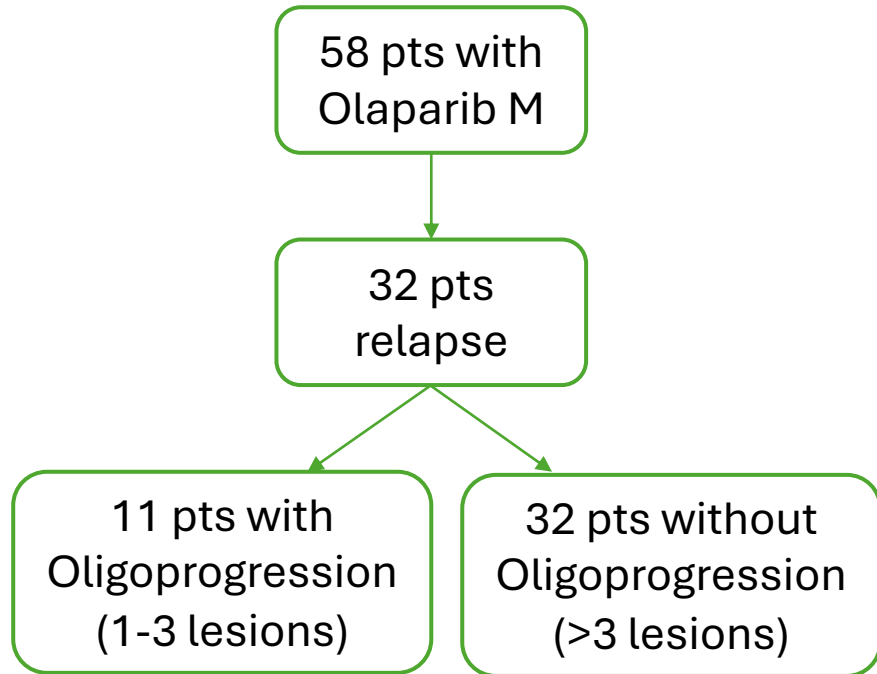
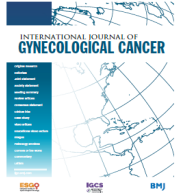
172 pts without evidence of lesions at baseline

116 pts, 1<sup>st</sup> relapse

		Overall (n = 116)
Number of new lesion(s), n (%)		
1	62 (53.4)	88.7% 1~3 lesions
2	26 (22.4)	
3	15 (12.9)	
4	7 (6.0)	
5	3 (2.6)	
> 5	3 (2.6)	

# Recurrent lesion pattern after prior PARPi

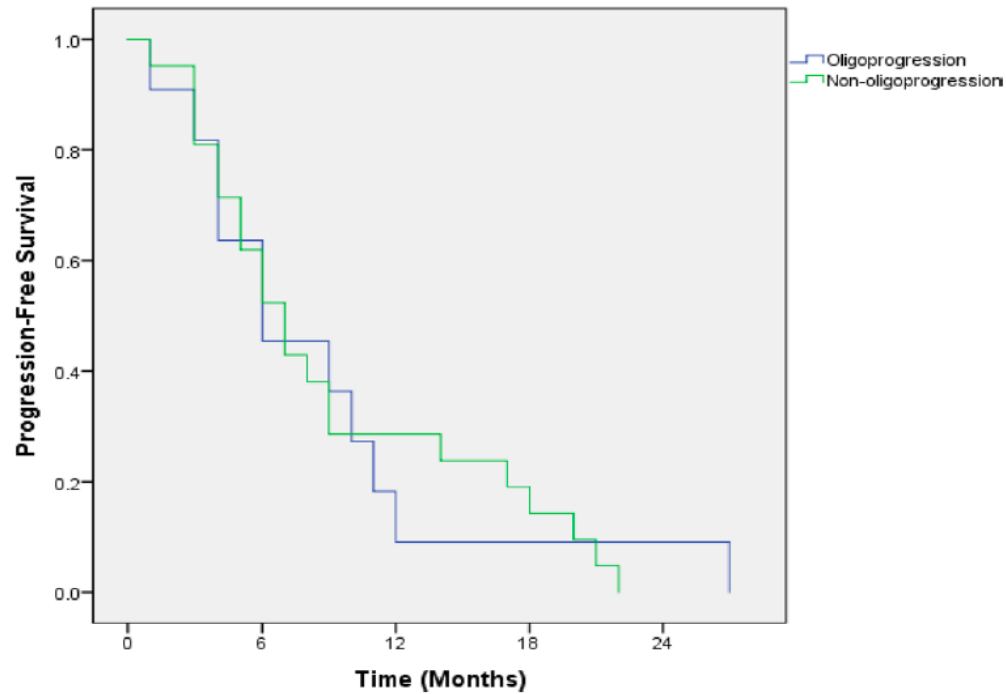
## Evaluation of patterns of progression on poly (ADP-ribose) polymerase inhibitor (PARPi) maintenance in ovarian cancer: a cross-sectional study



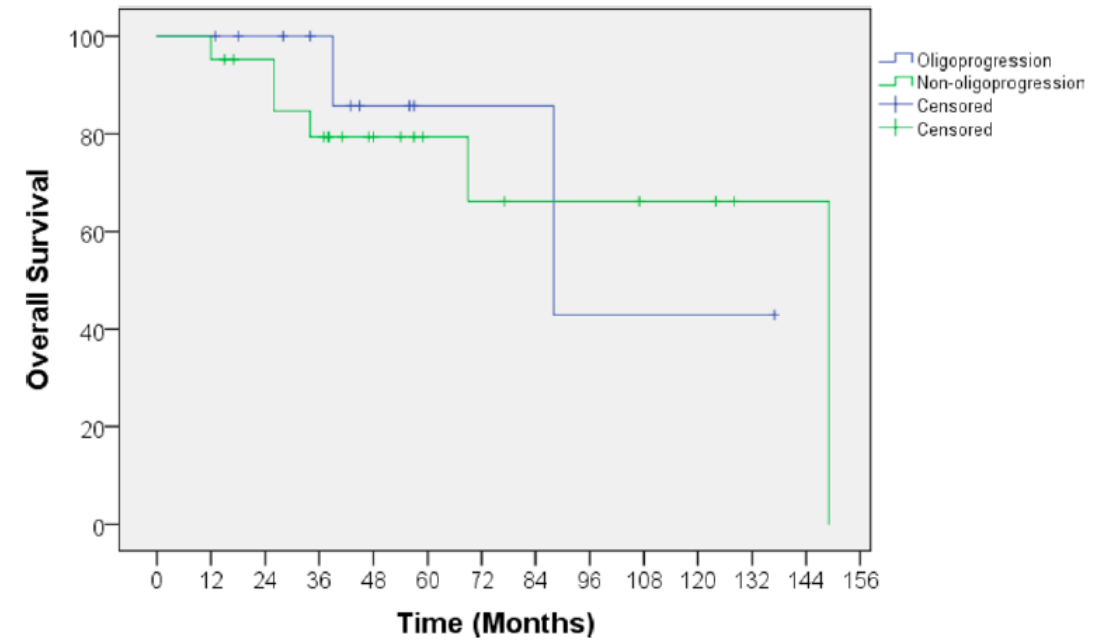
Characteristic	Entire population (n=32)	Patients with oligoprogression (n=11)	Patients without oligoprogression (n=21)	P value
BRCA mutation status				0.487
BRCA1 mutation	13 (40%)	4 (36.3%)	9 (42.8%)	
BRCA2 mutation	6 (19%)	3 (27.2%)	3 (14.1%)	
No BRCA mutation	10 (31.2%)	4 (36.3%)	6 (28.6%)	
Other (BRIP1, CHK2, other HRD)	3 (9%)	–	3 (14.2%)	
Chemotherapy lines prior to PARPi (median, IQR)	2 (1, 2.75)	2 (1, 3)	2 (1, 2.75)	0.78
Total chemotherapy lines (median, IQR)	3 (2, 4.75)	3 (2, 4)	3 (2, 5)	0.762
Months on PARPi				0.324
0–5	16 (50%)	4 (36.3%)	12 (57.1%)	
6–10	8 (25%)	4 (36.3%)	4 (19%)	
11–15	3 (9%)	2 (18.1%)	1 (4.7%)	
16–20	3 (9%)	0 (0%)	3 (14.2%)	
>20	2 (6%)	1 (9%)	1 (4.7%)	
CA125 (units) level at time of PARPi initiation (median, IQR)	17 (11, 85)	15 (8, 27)	22 (11, 157)	0.128

# Recurrent lesion pattern after prior PARPi

## PFS



## OS

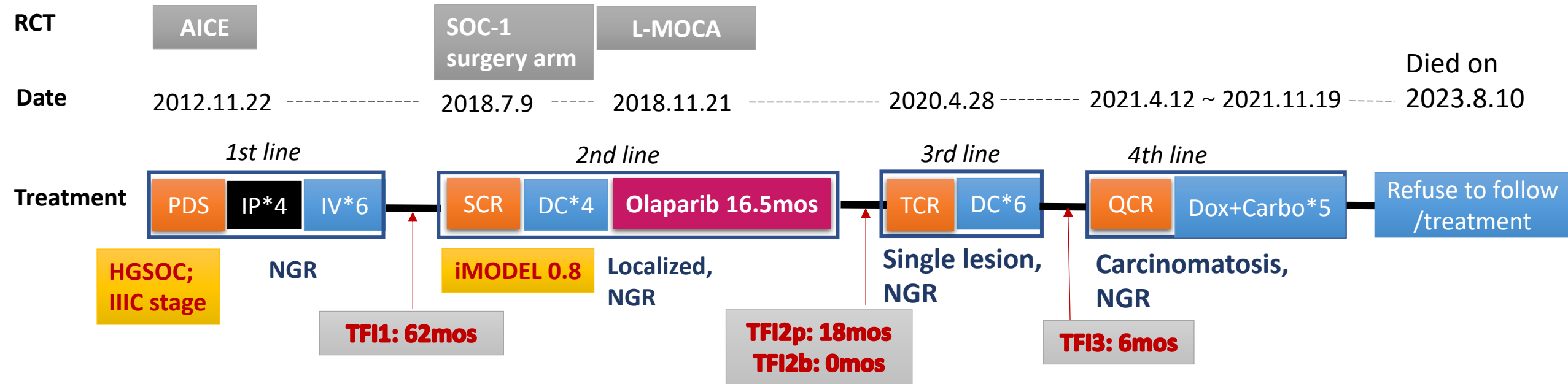


- One-third of patients on PARPi maintenance experienced oligoprogression ( $\leq 3$  sites).
- No significant differences in PFS or OS between  $\leq 3$  sites and  $> 3$  sites.

# Case

**XZY**, 56-year-old  
g/sBRCA1/2(-), Olaparib 16.5mos

CA125 at diagnosis 772U/ml  
1<sup>st</sup> R CA125 6.9U/ml  
2<sup>nd</sup> R CA125 5U/ml  
3<sup>rd</sup> R CA125 11.1U/ml



**1<sup>st</sup> Progression after PARPi M: Single lesion, No benefit from NGR**

**2<sup>nd</sup> Progression after PARPi M: Carcinomatosis, poor prognosis**

**OS: 10y 8.5m**

TFI1: 62m

TFI2: 18m

TFI3: 6m

TFI4: resistance

# Impact of Prior PARPi on Surgery Outcomes: Challenge beyond SOC-1 Trial



- No evidence on selection criteria of SCR after Prior PARPi.
- Different from non-target setting, recurrent ovarian cancer patients after prior PARPi might not benefit from complete resection, when oligoprogression, even single lesion relapse.



# Thanks!

tyshi80@163.com