MSKCC-AGOI Tumor Board Series

Ovarian Cancer Tumor Board: MSKCC and Tata Medical Center, Kolkata

25th March 2022

Memorial Sloan Kettering Cancer Center

TATA MEDICAL CENTER

Tata Medical Center, Kolkata

Dr. Jaydip Bhaumik
Consultant & Head
Dept. of Gynae-Oncology
TMC-K

Dr. Anik Ghosh
Consultant
Dept. of Gynae-Oncology
TMC-K

Dr. Joydeep Ghosh
Consultant
Dept. of Medical Oncology
TMC-K

Dr. Subhashree Rout
DrNB Trainee
Dept. of Gynae-Oncology
TMC-K

TATA MEDICAL CENTER

Tata Medical Center, Kolkata presents:

Case # 2: Platinum sensitive recurrent serous carcinoma of the ovary

Presentation & Primary Treatment

54yr, P1, ECOG 2
Medical Comorbidities: hypothyroidism

Presented to TMC-K for a second opinion on her cancer management.

Clinical Summary :

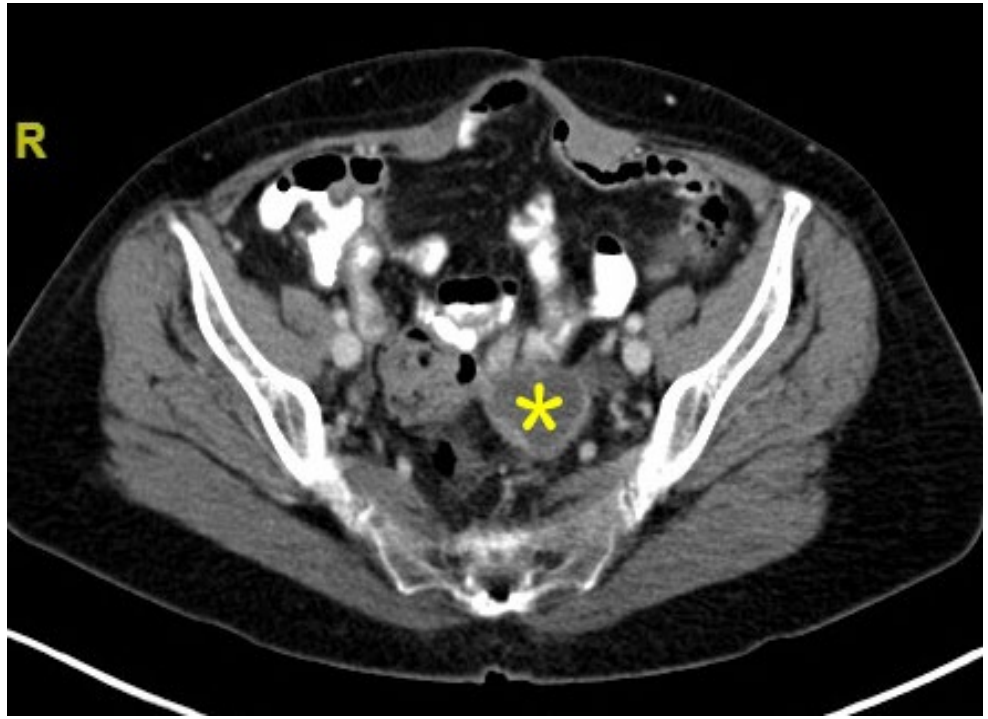
- 2014: (49yrs)- TLH-BSO for endometriosis. No malignancy.
- 2019: Evaluated for dysuria, constipation and bleeding PR → Underwent laparotomy (Gross R2 resection)
- Procedures: a. B/L ureteric DJ stenting, b. Pelvic mass excision, c. Sigmoid colectomy with end-end anastomosis and covering loop ileostomy
  - *HPE- HG Serous CA Ovary*
  - Received neoadjuvant carboplatin + paclitaxel Q3 weeks times 2

Primary Treatment- Details

- TMC-K MDT decided to continue chemotherapy and proceed with IDS after C3/4. Provision for HIPEC could be considered as FIGO stage IIIc was suspected
- End of 2019: IDS+HIPEC (100mg/m2 cisplatin over 90min) performed. PCI-7, CC-0 Procedures performed: En-bloc total pelvic peritonectomy with a cuff of vagina, b/l parietal peritonectomy, total omentectomy, b/l diaphragmatic peritonectomy
- 2 cycles of adjuvant carboplatin + paclitaxel completed early 2020
- Ileostomy closure in mid 2020
- Germline Testing: Negative for BRCA1/2 pathogenic mutations

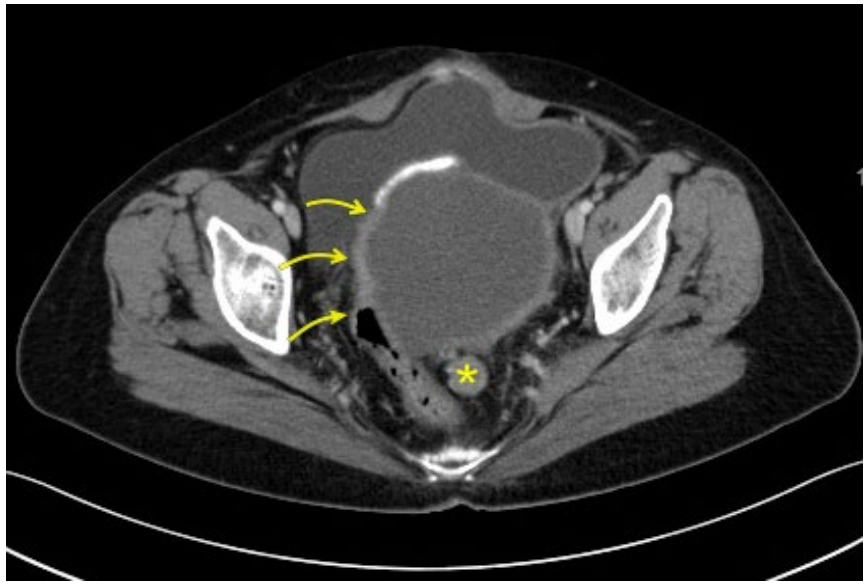
Follow Up- Details

Date	CA-125	Action Taken
Fall 2020	23	Observation
End 2020	41	Reassessed in 2 weeks
End 2020	41	CT: 35mm cystic lesion at vault- unlikely to be recurrence. Recommend close observation



Follow Up- Details

Early 2021	51	Asymptomatic. Nil on clinical examination → F/U
Mid 2021	64	CT: 10cm pelvic mass with a 2cm meso-rectal node. Mass densely abuts the ureter and bladder trigone → FNA node → HG Serous CA



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Recurrence Treatment- Details

- MDT Decision- TFIp 14mo + resectable disease (ECOG 0, no ascites/peritoneal disease/CC-0 at primary surgery) → Secondary Cytoreduction

- Patient unwilling- anticipates u/l or b/l ureteric resection/reimplant or permanent urinary diversion along with 'repeat' bowel resection

- Received 6x liposomal doxorubicin + carboplatin → Completed End of 2021 (Few delays due to chemo-toxicity)

Recurrence Treatment- Response and the road ahead …

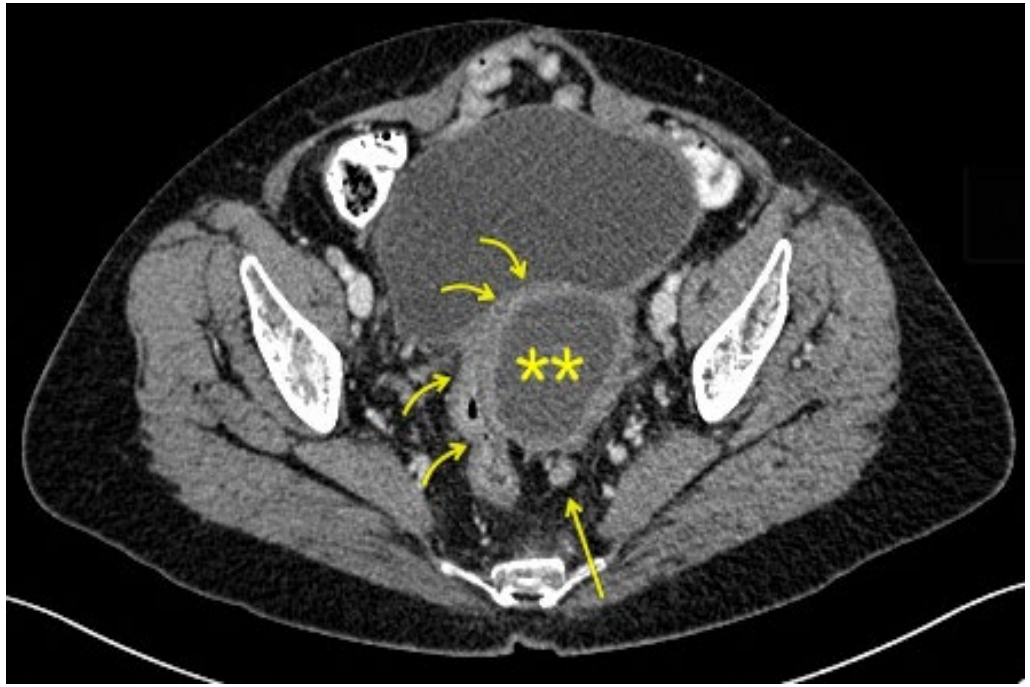
Response: Stable disease

CA125- 79

CT- Moderate HDUN, Pelvic lesion with solid components- decreased from before. Mesorectal node- 10mm. No ascites, no peritoneal disease

Patient now wishes to explore the option of a surgical resection.

She experiences significant vaginal discharge and constipation.



Questions for Poll

1. Would you consider surgical resection at this time point?

2. If yes, to the above – would you proceed even if trigone is involved and permanent urinary diversion is needed?

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Questions for Poll

3. Would you consider repeat HIPEC?

4. Would you consider HRD assay?

Panel Discussion

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ASSOCIATION OF GYNAECOLOGIC ONCOLOGISTS OF INDIA
AWARENESS
DETECTION
CURE
WE CARE
1991

TATA MEDICAL CENTER

Case #2: Heated intraperitoneal chemotherapy for ovarian cancer

Presented by Dr. Aaron Praiss

Memorial Sloan Kettering Cancer Center

ASSOCIATION OF GYNAECOLOGIC ONCOLOGISTS OF INDIA
AWARENESS
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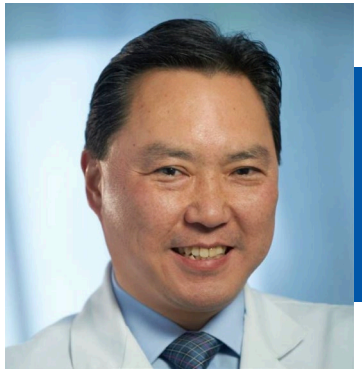


Dennis S. Chi, MD
Moderator
Head, Ovarian Cancer Surgery

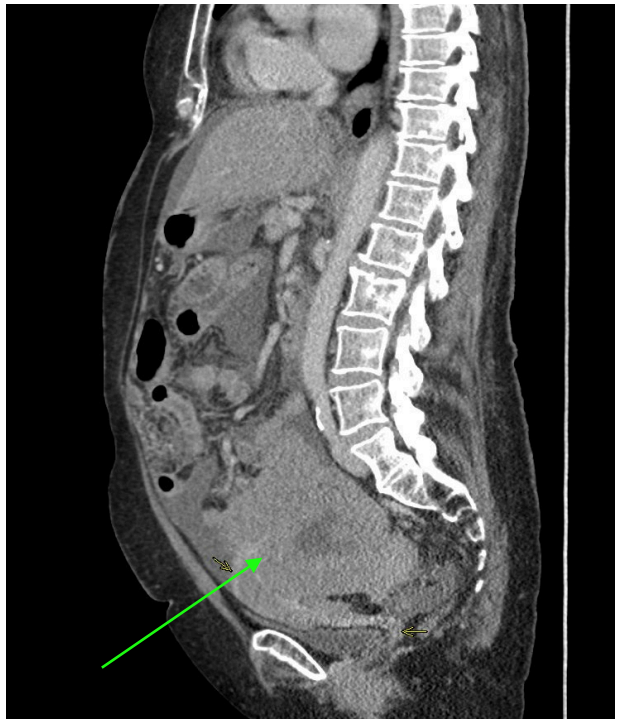
Roisin O'Cearbhaill, MD
Research Director
Gynecologic Medical Oncology

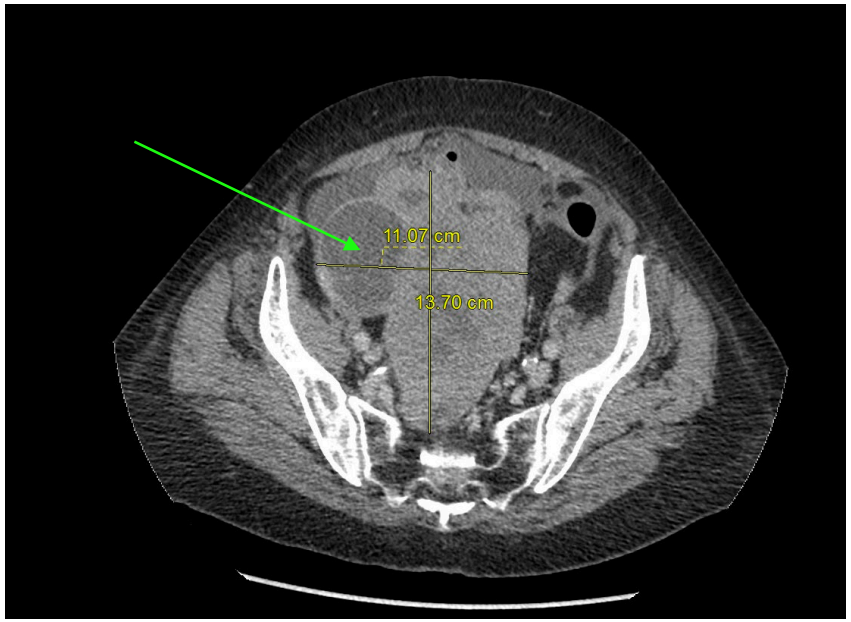
Herman Chui, MD
Gynecologic Pathology and Laboratory Medicine

Aaron Praiss, MD
Gynecologic Oncology Fellow

74-year-old with a history of left breast DCIS, presenting with bloating and increasing abdominal girth

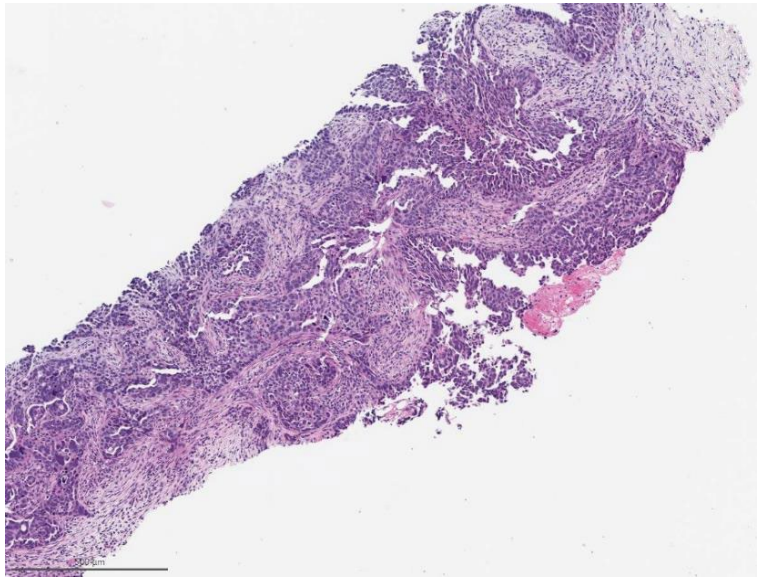
- 2021: CT C/A/P

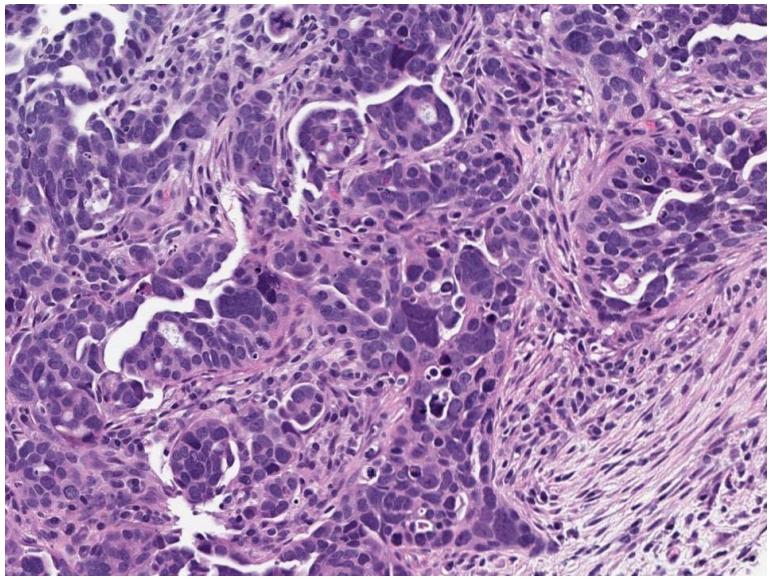




74-year-old with high grade serous ovarian cancer

- 2021: CT guided biopsy of pelvic nodule





Immunohistochemistry:

- CK7: positive
- PAX8: positive
- WT-1: positive
- P53: aberrant

Tumor markers:

CA-125 = 4,323

CEA = 2.2

Serous carcinoma, high grade

MSKCC Resectability score 2.0

Radiographic findings

Clinical factors

	Present		Category Score if Yes	Patient Score
	Yes	No		
1) Root of SB mesentery lesions	☐	☐	4	
2) Lesser sac lesion ≥1cm	☐	☐	2	
3) GB fossa (between GB and liver) **or left inter-segmental fissure** (fissure for the ligamentum venosum)	☐	☐	2	
4) Ascites (moderate to large in volume)	☐	☐	2	
5) Diffuse SB angulation and/or tethering OR diffuse SB serosal disease	☐	☐	1	
6A) Suprarenal retroperitoneal LN(s) ≥1 cm in SA (or <1 cm in SA but rounded, heterogeneous, or irregular borders). Plus **6B) Supra-diaphragmatic LN(s)** (>0.5 cm in SA)	☐	☐	1	
7) GH ligament or porta hepatis lesion(s) and/or LNs (implants or node(s) >1 cm in SA (or ≤1 cm in SA but rounded, heterogeneous, or irregular borders). If portocaval node(s) >1.5 cm in SA or (≤1.5 cm in SA but loss of oblong shape and/or heterogeneity)	☐	☐	1	
8) LUQ lesion(s) = splenic hilum, splenic ligaments or gastrocolic ligament	☐	☐	1	
	Yes	No		
Age ≥60 years	☐	☐	1	
CA-125 ≥600 U/mL	☐	☐	1	
ASA ≥3	☐	☐	1	
			TOTAL PREDICTIVE VALUE SCORE =	

Suidan et al, Gyn Onc. 2014.
Suidan et al. Gyn Onc. 2017.
Straubhar et al. Gyn Onc. 2020.

MSKCC Resectability score 2.0

+ GB fossa
+ ascites

+ LUQ lesions

Age ≥60 years old

CA-125 value ≥600U/mL

American society of anesthesiology score ≥3

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	Yes	No		
Age ≥60 years	☐	☐	1	1
CA-125 ≥600 U/mL	☐	☐	1	1
ASA ≥3	☐	☐	1	1
TOTAL PREDICTIVE VALUE SCORE =				

Suidan et al, Gyn Onc. 2014.
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MSKCC Resectability score 2.0

Table 4
Outcomes of primary debulking surgery based upon the RS2 model[a].

Total predictive score	Total patients n (%)	Complete gross resection n (%)	Gross residual disease n (%)
0–2	76 (31)	70 (92)	6 (8)
3–5	82 (33)	64 (78)	18 (22)
6–8	45 (18)	27 (60)	18 (40)
≥9	46 (18)	27 (59)	19 (41)

RS2 model: Resection Score Model 2 [12].

[a] The higher the RS2 predictive score, the higher the likelihood of not achieving a complete gross resection.

Suidan et al, Gyn Onc. 2014.
Suidan et al. Gyn Onc. 2017.
Straubhar et al. Gyn Onc. 2020.

Audience Poll Question:

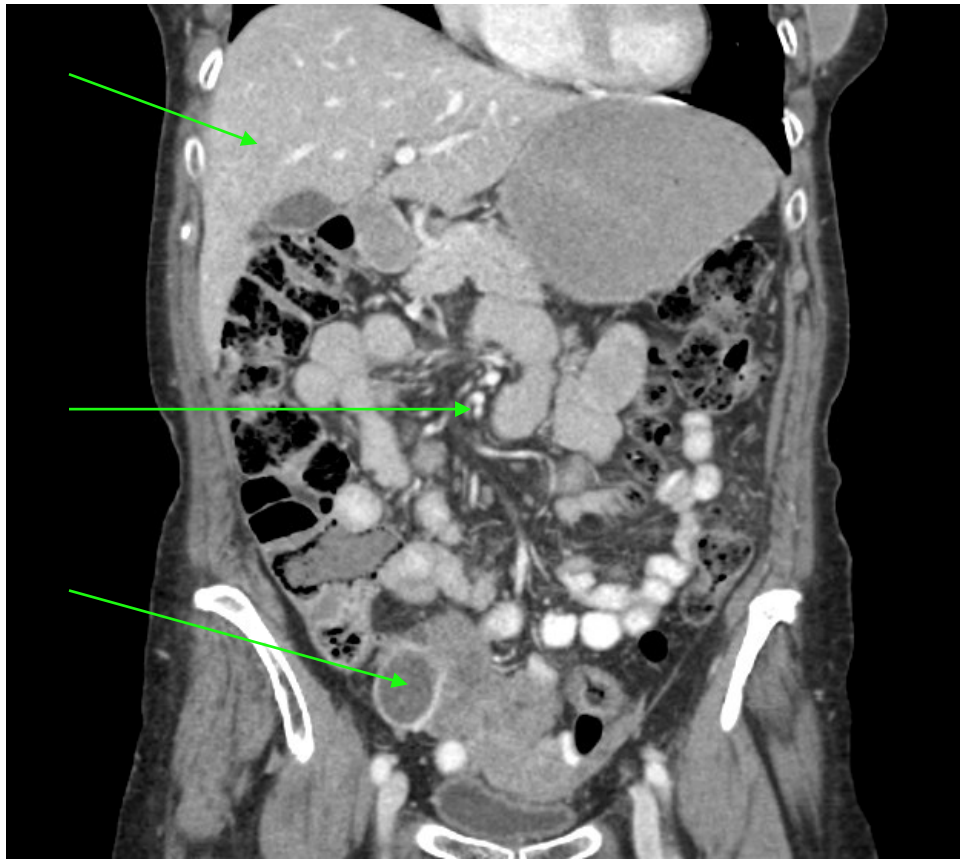
How would you proceed with this case of presumed stage III HGSOC?

- Imaging findings: cystic adnexal lesion, nodularity of mesentery and peritoneum, ascites, pelvic lymphadenopathy
- CA-125: 4,323
- MSKCC Resectability score 2.0 = 8

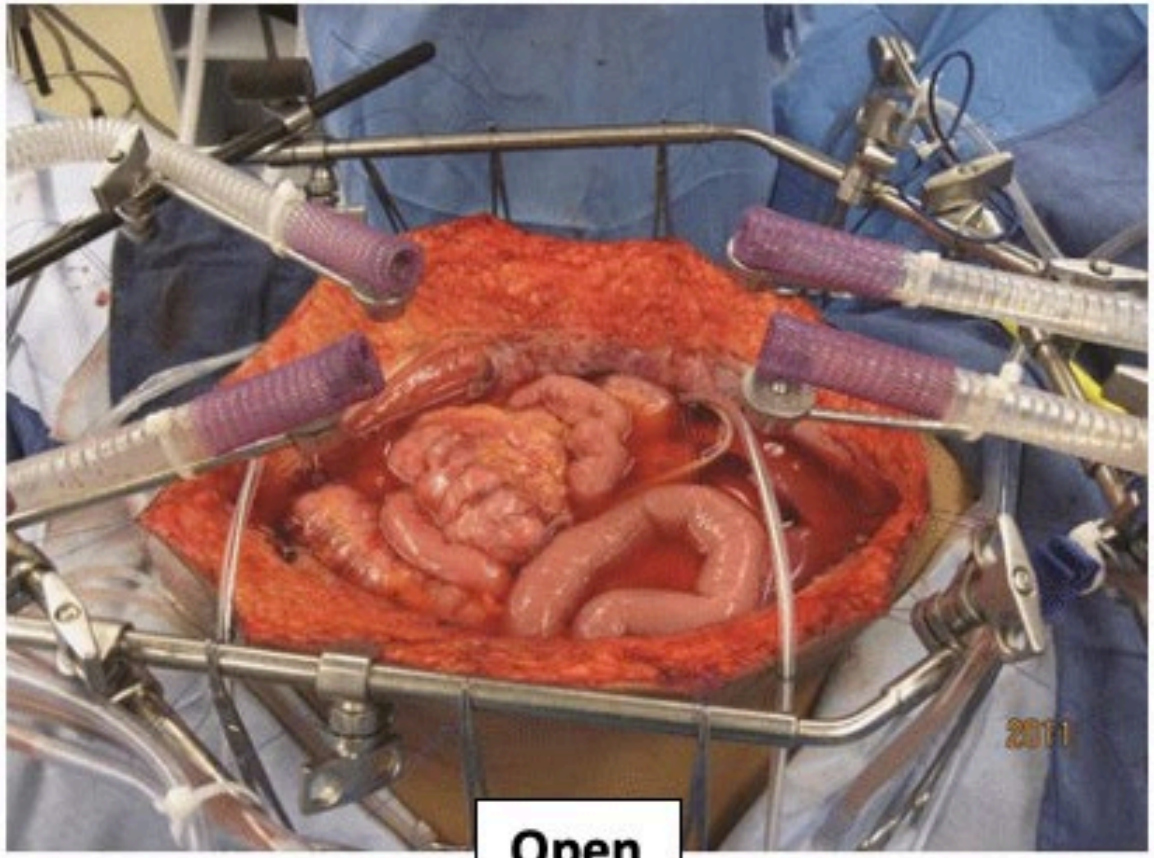
1. **Primary cytoreductive surgery**
2. **Neoadjuvant chemotherapy**

74-year-old with high grade serous ovarian cancer

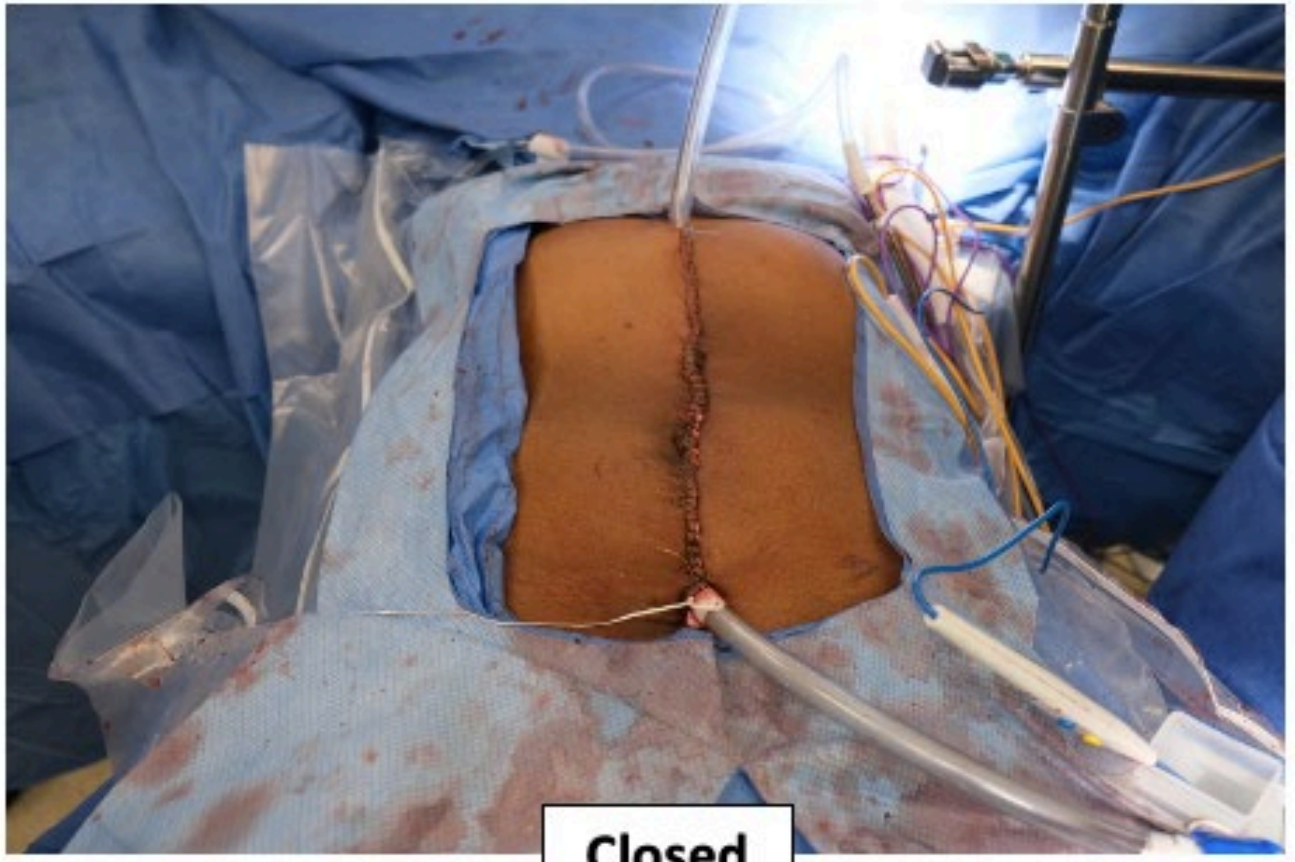
Before



After



Open



Closed

Interval cytoreductive surgery:

- Laparotomy
- Modified posterior exenteration
- Primary end-to-end rectal anastomosis
- Small bowel resection with reanastomosis
- Mobilization of splenic flexture, splenectomy
- Radical peritonectomy
- Heated intraperitoneal chemotherapy (cisplatin 100mg/m^2)
- Complete gross resection (0mm)

Somatic tumor profiling: MSK *IMPACT*

"Integrated Mutation Profiling of Actionable Cancer Targets"
Targeted Next Generation Sequencing (NGS)

Memorial Hospital For Cancer & Allied Diseases
Molecular Diagnostics Service, Department of Pathology
1275 York Avenue New York, NY, 10065
Tel: (212) 639-8280 | Fax: (212) 717-3515

MSK-IMPACT Testing Report

Somatic alterations detected in this sample:

Gene	Type	Alteration	Location	Additional Information		
Mutations						
TP53	Missense Mutation	E286K *(c.856G>A)*	exon 8	MAF: 75.2%		
BCOR	Frameshift Deletion	K607Afs*58 *(c.1818_1830del)*	exon 4	MAF: 42.7%		
KMT2C	Nonsense Mutation	R4690* *(c.14068C>T)*	exon 54	MAF: 5.8%		
MST1R	Missense Mutation	A971P *(c.2911G>C)*	exon 12	MAF: 40.3%		
Copy Number Alterations						
MYC	Whole gene	Amplification	8q24.21	FC: 2.1		
RAD21	Whole gene	Amplification	8q24.11	FC: 2.1		
Structural Variants						
ARID1A	Deletion	c.5125-417_c.5474del	exon 20	4		a
SPOP	Inversion	c.897:SPOP_chr17:g.47672459inv	exons 9 - 10			b

The power of MSK *IMPACT*

Cancer Gene Exons
All protein-coding exons of 505 genes

- Actionable mutations
- Targets of investigational agents
- Frequent mutations in cancer
- Cancer susceptibility genes

Cancer Gene Introns
70 introns of 20 rearranged genes

Non-coding Regions

- TERT promoter
- Microsatellites
- >1000 common SNPs

Memorial Sloan Kettering Cancer Center

Germline testing

Family history:

- Mother: breast cancer age 50
- Brother: prostate cancer
- Sister: stomach cancer
- Maternal grandmother: breast cancer
- Maternal first cousin: breast cancer

Variants Detected:
BRCA2 (NM_000059) c.8982_8985dupAGAT (p.Leu2996Argfs*23), Heterozygous, Pathogenic

1. Breast Ovarian Cancer Panel (ATM,BARD1,BRCA1,BRCA2,BRIP1,CHEK2,PALB2,RAD51C,RAD51D)

RESULTS:
Positive. Pathogenic variant detected in BRCA2.

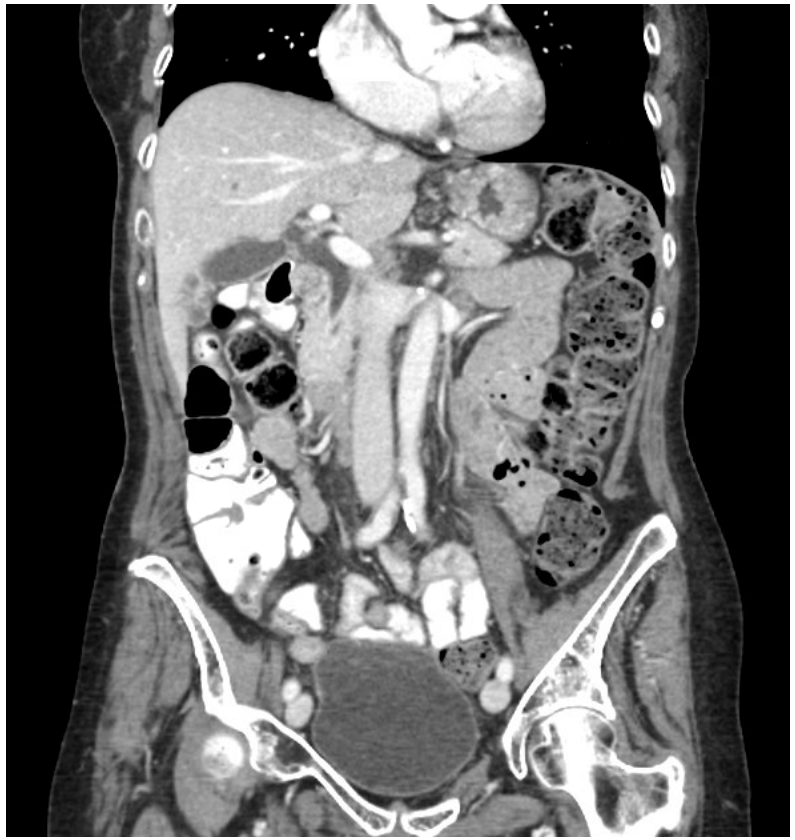
Audience Poll Question:

What systemic therapy would you consider for this patient after neoadjuvant chemotherapy followed by interval cytoreductive surgery with cisplatin HIPEC?

1. **Carboplatin/paclitaxel**
2. **Carboplatin/paclitaxel and bevacizumab**
3. **Carboplatin/paclitaxel, bevacizumab, and PARPi**
4. **Carboplatin/paclitaxel, and PARPi**
5. **PARPi alone**

74-year-old with a *BRCA2* mutation and stage IIIC high grade serous ovarian cancer

- Neoadjuvant chemotherapy x 3 cycles
- Interval cytoreductive surgery + HIPEC
- Adjuvant chemotherapy x3 cycles
- Maintenance bevacizumab
- Briefly treated with Olaparib
- Remains NED



Most recent CT

Q&A

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