Medical and Research Publications
International Open Access

**Case Report** **Journal of MAR Oncology (Volume 5 Issue 1)**

# Solitary Lesser Sac Deposit of Recurrent Ovarian Cancer mimicking GIST: A Case Report from a tertiary care Centre with Review of Literature

Supratim Bhattacharyya *

**Corresponding Author: Supratim Bhattacharyya,**

**Copy Right:** © 2022 Supratim Bhattacharyya, This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Received Date: December 14, 2022**

**Published Date: January 01, 2023**

***Abstract***

*Recurrence following completion of first line therapy is a common problem with advanced epithelial ovarian cancer. In most instances, the recurrence is along the peritoneal lining and multiple. The treatment options of recurrent ovarian cancer (ROC) include secondary cytoreduction in selective patients, systemic chemotherapy and biological therapy. The long term survival outcomes of ROC have improved over the last decade owing to introduction of anti VEGF agents, and PARP inhibitors to standard systemic chemotherapy. Herein, we report a case of recurrent epithelial ovarian cancer with a long platinum free interval presenting to us in HCG Cancer Hospital, Bangalore, with a lesser sac deposit mimicking gastrointestinal stromal tumor (GIST). To the best of our knowledge, this is the first reported case of a solitary lesser sac deposit of recurrent ovarian cancer. We reviewed the literature for incidence of solitary recurrence of ovarian cancer with special emphasis on those masquerading as GIST. We also looked into the etiology of pathological transformation from well differentiated to undifferentiated ovarian cancer on recurrent setting, the role of cancer stem cells in histological transformation, and explored the nuances of treatment options of recurrent ovarian cancer with uncommon presentation as in our case.*

***Keywords:*** *Recurrent ovarian cancer, Solitary metastasis, GIST, Undifferentiated cancer, Case report*

## Introduction

Epithelial Ovarian Cancer (EOC) is the third most common gynaecological malignancy, affecting over 200,000 women per year (1,2). But the mortality rate of EOC is highest among all of the gynaecological malignancies, as over two thirds of the cases present as advanced disease (3, 4). Approximately 70- 80 percent patients with International Federation of Gynecology and Obstetrics (FIGO) stage III- IV disease present with recurrent disease within 5 years following completion of first line therapy (5, 6). Although the scope of secondary cytoreduction for these patients remains guarded, it seems those with a limited volume of disease with longer platinum free interval (PFI) and without ascites benefit the most from such extensive resection(7- 9). For the rest of patients who are unsuitable for secondary cytoreduction, systemic therapy in form of cytotoxic chemotherapy and targeted agents remain the treatment of choice, with an aim of improving disease related symptoms and quality of life, delay progression, and possibly to prolong survival, particularly in patients with platinum sensitive recurrence. Ovarian cancer typically spreads along the peritoneal lining and a solitary deposit of ovarian cancer in lesser sac is rather a very uncommon finding in recurrent setting. Hence, a MEDLINE search was conducted for all English language literature. To the best of our knowledge, this is the first reported case of a solitary lesser sac deposit of recurrent ovarian cancer.

## Case Report

The patient is a 60 years old lady diagnosed with stage IIIC ovarian cancer 7 years back and underwent primary chemotherapy with Carboplatin and Paclitaxel 3 weekly for 6 cycles, followed by interval cytoreductive surgery (CRS) which revealed left ovarian mass adherent to uterus, omental caking adherent to transverse colon, and multiple right hemidiaphragm deposits. The PCI score was 15. Complete cytoreduction to an extent of CC0 was obtained including hysterectomy and bilateral salpingo-oophorectomy, total parietal peritonectomy, greater and lesser omentectomy, bilateral pelvic lymphadenectomy, infra-renal para aortic lymphadenectomy followed by hyperthermic intra peritoneal chemotherapy (HIPEC) with Cisplatin 100 mg/m2 and Paclitaxel 175 mg/ m2 for 60 minutes at 42.5 C using open technique. Final histopathological report revealed high grade serous carcinoma, ypT3bN0. The patient received 3 cycles of adjuvant chemotherapy with Carboplatin and Paclitaxel 3 weekly, thereafter. CA 125 at presentation was 117 U/ml which came down to normal value following completion of first line therapy. She was disease free and on follow up since then.

From September 2021 she started having upper abdominal discomfort and bloating sensation. PET CT revealed a metabolically active smooth walled encapsulated solid cystic lesion of size 8.1x 6.7 cm adherent to the posterior wall of antrum of stomach, extending to the first part of duodenum, abutting the head of pancreas, with signs of significant neo-vascularisation and SUVmax of 8.6. There was no disease elsewhere. Upper GI endoscopy showed thickened and edematous mucosa of pyloric antrum with features of extraluminal compression from posterior wall. Serum CA 125 was 25 U/ml. There was strong suspicion of the mass to be a Gastrointestinal Stromal Tumor (GIST) on PET/CT and UGI endoscopy. USG guided core needle biopsy of the mass revealed no evidence of malignancy. Considering the hypervascular nature of the mass, a decision was taken in favour of angio-embolisation, followed by diagnostic laparoscopy and guided biopsy within 24 hours of embolisation. There was a concern of bowel injury while creating pneumoperitoneum owing to the previous history of CRS and HIPEC using midline laparotomy incision. After reviewing the PET CT images and discussing with radiologists about the possible sites of adhesion, a plan was made for left upper quadrant entry using Veress needle with a higher than usual preset CO2 pressure of 15 mm of Hg. After creation of pneumoperitoneum, a 5mm port was placed 2 cm below the umbilicus in the midline after gently sweeping the adhesion away. This port was used for 30 degree telescope. Under vision two 5mm ports were placed in right and left flank respectively. Adhesiolysis was done. There was no evidence of disease in the greater sac. Lesser sac was entered. A mass of size approximately 8x7 cm was found to be arising from the posterior wall of pyloric antrum and first part of duodenum, adhered to the pancreatic head. The mass was encapsulated, seemingly solid cystic in nature, having prominent overlying blood vessels. The gross appearance of the mass was that of a GIST. Under vision, an 18 G trucut biopsy needle was advanced through an epigastric stab incision into the mass, multiple passes were made until retrieving adequate tissue for histology and immunohistochemistry (IHC).

The biopsy report revealed an undifferentiated carcinoma of ovarian origin. IHC revealed tumor cells focally positive for PanCK, S100, and PAX8. They were negative for SMA, CD34, CD117, p16, WT1, CK7, CD10, and CA125. There was of low probability for MSI-H. PD-L1 was less than 1%. The treatment options, including secondary cytoreductive surgery, second line chemotherapy with platinum re-challenge, anti VEGF therapy, and hormonotherapy were discussed in multidisciplinary tumor board. The location of the tumor was such that secondary CRS would require a pancreaticoduodenectomy at the least. Considering the morbidity of such an extensive procedure in the recurrent setting of ovarian cancer, decision was made to continue with second line chemotherapy with or without stereotactic body radiation therapy (SBRT) and re-assessment of response after completion. She is still under treatment.

## Discussion

This case is worth reporting as it challenges us with several atypical findings and makes us question ourselves about the management protocol of such a rare presentation of a relatively common disease. There are several aspects of this case that are worth discussing in depths, such as

1. How commonly does a recurrent ovarian cancer present as a solitary upper abdominal deposit?

2. What is the incidence of finding an undifferentiated histology in recurrent setting of a differentiated ovarian cancer and what are the implications of the same?

3. How commonly recurrent ovarian cancers mimic GIST clinically?

4. What are the treatment options of such a case of platinum sensitive recurrent ovarian cancer?

We tried to find out a correlation of our case, considering it's rarity, to the above mentioned broad headings in the following segment.

### 1. How commonly does a recurrent ovarian cancer present as a solitary upper abdominal deposit?

Fifty-five percent of the first relapse of ovarian cancer are found at the pelvis or abdomen (10). Other recurrent sites include retroperitoneal nodes, liver or spleen, brain, and bone. Isolated solitary upper abdominal recurrence in the setting of recurrent ovarian cancer is rare and the literature support is sparse. Minagawa et al. was the first to report isolated splenic metastasis in a case of recurrent ovarian cancer (11). Farias-Eisner et al. subsequently reported a series of four cases where all had solitary splenic parenchyma metastasis and were treated with secondary cytoreduction and splenectomy (12). Togami et al. reported a case of solitary recurrence of ovarian cancer in round ligament (13). We believe that lesser sac worked as a sanctuary site for recurrence in our patient, since it probably was not explored during interval CRS, iterating the importance of systematic exploration of all intra-abdominal sites (specially peripancreatic, retroduodenal, and the tail of pancreas) during any CRS procedure for advanced stage ovarian cancer.

**2. What is the incidence of finding an undifferentiated histology in recurrent setting of a differentiated ovarian cancer and what are the implications of the same?**

The concept of histological transformation from differentiated to undifferentiated ovarian cancer following repeated chemotherapy challenge is believed to derive from the existence and contribution of cancer stem cells (CSC). CSCs possess tumorigenic and self renewal potential. It is also widely recognised that CSCs have the potential to differentiate into several different mature neoplastic cell lineages upon activation and deactivation of different signalling pathways. If a signalling pathway is terminated or weakened by external influence, such as chemotherapy and radiation, it's function is replaced by a different pathway, essentially leading to transformation of tumor histology (14). This concept was also supported by Bapat SA et al. who addressed the evolution of tumor genotype and phenotype under selective pressure of pre operative chemotherapy, radiation, and targeted therapy (15). The effect of CSCs has been documented in several malignancies, including head and neck squamous cell carcinoma, lung cancer, breast cancer, pancreatic cancer, stomach cancer, rectal cancer and others. CSCs have been identified in ovarian cancer by the expression of CD44, c-Kit, and CD133 (16). It is believed that epithelial tumors, germ cell tumors, sex cord stromal tumors, and other tumors may originate from ovarian CSCs and with repeated external insult to tumor by different therapeutic strategies, a differentiated tumor may turn into an undifferentiated one. Huang et al. reported a case of adenocarcinoma of ovary transformed into undifferentiated small cell carcinoma following eight cycles of chemotherapy and radiation (17). Besides, high grade serous carcinoma of ovary is known to display solid, pseudo- endometrioid, transitional cell- like (SET) patterns, and solid, transitional, endometrioid, and mucin-like (STEM) patterns (18). Hence extensive histological and immunohistochemical analyses is mandated for any known high grade serous ovarian cancer revealing discordant histology.

The prognosis and therapeutic implications of CSCs in ovarian cancer is an area of active research with an ever growing landscape. It is generally recognised that the presence of CSCs confers chemoresistance, and increase the likelihood of recurrence in ovarian cancer (19, 20). A meta-analysis by Liu et al. reported a negative association between the expression of aldehyde dehydrogenase (ALDH) by IHC in CSCs and the survival (21). In this meta-analysis of 1,258 patients from 7 studies, high ALDH expression was associated with poor overall survival (OS) and disease free survival (DFS). Similar results were also noted in another meta analysis by Ruscito et al. that showed high levels of ALDH1 expression to correlate with worse OS and progression free survival (PFS) in ovarian cancer (22). The therapeutic efficacy of Metformin has been explored lately in this subgroup of patients. A phase II study by Brown et al.

concluded that tumors treated with Metformin had a 2.4 fold decrease in ALDH+ CD133+ CSCs and increased sensitivity to cisplatin ex vivo (23).

However, we should also give consideration to a second primary tumor in any patient of ovarian cancer displaying discordant histology and having a very prolonged platinum free interval, especially when the tumor is solitary and located at an uncommon site. This emphasises the importance of an adequate tissue biopsy and IHC before embarking upon a definitive treatment.

**3. How commonly recurrent ovarian cancers mimic GIST clinically?**

Although GIST arising from pelvic cavity may simulate gynaecological malignancy, the opposite is not very common. Epithelial ovarian cancer typically spreads along the peritoneal surface, and it is rather rare to find an isolated visceral peritoneal deposit in absence of disease elsewhere in the peritoneal cavity. In our case, the solitary site, size, encapsulated nature of the deposit supported the clinical diagnosis of GIST. Similar case was reported by Kang et al. who found a transmural lesion along gastric antrum which was later found out to be a metastatic deposit from primary ovarian cancer following resection (24). Hence it is necessary to have an individualistic approach to each such patient with attention to the past history of malignancy, treatment received, biopsy and immunohistochemical report with the clinico- radiological findings before reaching a final diagnosis.

**4. What are the treatment options of such a case of platinum sensitive recurrent ovarian cancers?**

Recurrent Ovarian Cancer (ROC) is a widely heterogeneous entity and the treatment options are also varied from surgical to medical management. Surgical option in platinum sensitive ROC in form of secondary CRS followed by chemotherapy has been prospectively compared with chemotherapy alone in three randomised trials, including DESKTOP III, SOC 1, and GOG 213. The prospective AGO-DESKTOP III trial recruited patients with platinum sensitive ROC and a positive AGO score to randomise between surgery followed by chemotherapy, or chemotherapy alone. In the final analysis, patients undergoing surgery showed a significant progression free survival (PFS), overall survival (OS), and median time to start of first subsequent therapy (TFST) benefit. This benefit was exclusively confined to patients having a complete resection (CR), emphasising the importance of optimised patient selection for surgery and of high volume centre to achieve CR (25). The PFS benefit of secondary CRS in platinum

sensitive ROC was also shown in SOC 1 trial, the OS data, however, is not yet mature(26). The GOG 213 trial incorporated Bevacizumab along with chemotherapy, but the trial failed to demonstrate survival benefit of secondary CRS over chemotherapy alone arm (27).

For patients with platinum sensitive and yet unresectable ROC, treatment options include systemic chemotherapy with or without Bevacizumab. Platinum based combinations (Carboplatin/ PLD, Carboplatin/ Paclitaxel, Carboplatin/ Gemcitabine) is associated with better PFS, OS compared to non-platinum or platinum single agent treatments in this population (28, 29). Bevacizumab in combination with chemotherapy in platinum sensitive ROC has been approved on the basis of two randomised phase III studies, GOG-213 and OCEANS. While the GOG-213 study showed a non statistically significant OS advantage of 5 months on adding Bevacizumab to chemotherapy, in the OCEANS trial the Bevacizumab containing arm demonstrated a better objective response rate, a longer PFS, with no difference in OS (30, 31). Olaparib has been approved as maintenance therapy after platinum response in ROC patients harbouring a somatic or germline BRCA mutation after SOLO-2 phase III trial (32, 33). Similarly the results of phase III ENGOT-OV16/ NOVA study and ARIEL2 study led to approval of Niraparib and Rucaparib, respectively, as maintenance therapy in platinum sensitive BRCA mutated ROC (34, 35).

The role of SBRT has recently been evaluated in retrospective, multicentre MITO RT1 study. It concludes the safety and efficacy of SBRT in patients with metastatic persistent ROC and identifies the clinical and treatment parameters to predict local control and complete response (36).

The efficacy of hormonotherapy in form of Tamoxifen and Aromatase Inhibitors (e.g., Letrozole) in ROC is not very clear, and is probably independent of platinum sensitivity. The limited data from retrospective studies indicate a significantly longer duration of response with letrozole than tamoxifen in ER+ high grade ROC (37).

Our patient falls in an unusual clinical circumstance where the complete resection appears to be feasible as per radiological findings, but would require nothing less than a pancreaticoduodenectomy. The selection of patient for such a morbid surgical procedure in the setting of ROC is however not well defined and probably best left to the decision of multidisciplinary tumor board. It was our decision to subject the patient to platinum re-challenge with/ without SBRT and re-evaluate to assess clinical response before taking up for complete resection. However the literature support for or against this policy is lacking.

## Conclusion

The treatment approach of ROC has evolved significantly in recent years. The indications of surgical cytoreduction as well as personalised therapy options including anti angiogenic agents, PARP inhibitors, and hormonotherapy have been standardised. However, in rare circumstances as reported in this case, the clinical decision making probably relies finally on the experience and judgment of the multidisciplinary team, in a tertiary care centre with modern facilities, tailored for the patient, and aimed at the best possible patient outcome.

## References

1. Openshaw MR, Fotopoulou C, Blagden S, et al. The next steps in improving the outcomes of advanced ovarian cancer. Women's Health 2015;11(3):355367.

2. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380(9859):2095–2128.

3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin 2019;69(1):7–34.

4. SEER Cancer Statistics Factsheets. Ovary Cancer. Bethesda, MD: National Cancer Institute. http://seer.cancer.gov/statfacts/html/ovary.html4A.

5. Bookman MA, Okamoto A, Stuart G, et al. Harmonising clinical tri- als within the Gynecologic Cancer InterGroup: consensus and unmet needs from the Fifth Ovarian Cancer Consensus Conference. Ann Oncol. 2017;28:30-35.

6. Wilson K, Pujade-Lauraine E, Aoki MR, et al. Fifth Ovarian Cancer Consensus Conference of the Gynecologic Cancer InterGroup: recur- rent disease. Ann Oncol. 2017;28:727-732.

7. Al Rawahi T, Lopes AD, Bristow RE, et al. Surgical cytoreduction for recurrent epithelial ovarian cancer. Cochrane Database Syst Rev 2013;2:CD008765.

8. Takahashi A, Kato K, Matsuura M, et al. Comparison of secondary cytoreductive surgery plus chemotherapy with chemotherapy alone for recurrent epithelial ovarian, tubal, or peritoneal

carcinoma: a propensity scorematched analysis of 112 consecutive patients. Medicine 2017;96(37):e8006.

9. Bogani G, Tagliabue E, Signorelli M, et al. A score system for complete cytoreduction in selected recurrent ovarian cancer patients undergoing secondary cytoreductive surgery: predictors- and nomogram-based analyses. J Gynecol Oncol 2018;29(3):e40.

10. Ushijima K: Treatment for recurrent ovarian cancer-at first relapse. J Oncol 2010:497429.

11. Minagawa, Y., Kanamori, Y., Ishihara, H., Morishita, K., Kigawa, J., Ito, T., et al. Solitary metastatic ovarian carcinoma of the spleen: A case report, Asia-Oceania J. Obstet. Gynaecol. 17(1), 45-48 (1991).

12. Farias-Eisner R, Braly P, Berek JS. Solitary recurrent metastasis of epithelial ovarian cancer in the spleen. Gynecol Oncol. 1993 Mar;48(3):338-41. doi: 10.1006/gyno.1993.1059. PMID: 8462900.

13. Togami, S., Kato, T., Oi, T. et al. A rare case of recurrent ovarian cancer presenting as a round ligament metastasis. World J Surg Onc 9, 144 (2011). https://doi.org/10.1186/1477-7819-9-144

14. Fu W, Madan E, Yee M and Zhang H: Progress of molecular targeted therapies for prostate cancers. Biochim Biophys Acta 1825: 140-152, 2012.

15. Bapat SA, Mali AM, Koppikar CB and Kurrey NK: Stem and progenitor-like cells contribute to the aggressive behavior of human epithelial ovarian cancer. Cancer Res 65: 3025-3029, 2005.

16. López J, Valdez-Morales FJ, Benítez-Bribiesca L, Cerbón M and Carrancá AG: Normal and cancer stem cells of the human female reproductive system. Reprod Biol Endocrinol 11: 53, 2013.

17. Huang ZP, Liu XJ, Zou BX, Shen Q, Zhao T: Ovarian cancer transformation from adenocarcinoma to undifferentiated small cell carcinoma: A case reportOncol Lett. 2015 May; 9(5): 2230–2232.

18. Hatano Y, Tamada M, Asano N, Hayasaki Y, Tomita H, Morishige KI, Hara A. High-grade serous ovarian carcinoma with mucinous differentiation: report of a rare and unique case suggesting transition from the "SET" feature of high-grade serous carcinoma to the "STEM" feature. Diagn Pathol. 2019 Jan 12;14(1):4. doi: 10.1186/s13000-019-0781-9. PMID: 30636633; PMCID: PMC6330567.

19. Vochem R, Einenkel J, Horn LC, Ruschpler P. Bedeutung der Tumorstammzellhypothese für das Verständnis des Ovarialkarzinoms [Importance of the tumor stem cell hypothesis for understanding

ovarian cancer]. Pathologe. 2014 Jul;35(4):361-70. German. doi: 10.1007/s00292-014-1910-6. PMID: 24992976.

20. Shi YY, Jiang H. Prognostic role of the cancer stem cell marker CD44 in ovarian cancer: a meta-analysis. Genet Mol Res. 2016 Aug 12;15(3). doi: 10.4238/gmr.15038325. PMID: 27525945.

21. Liu S, Liu C, Min X, Ji Y, Wang N, Liu D, Cai J, Li K. Prognostic value of cancer stem cell marker aldehyde dehydrogenase in ovarian cancer: a meta-analysis. PLoS One. 2013 Nov 25;8(11):e81050. doi: 10.1371/journal.pone.0081050. PMID: 24282568; PMCID: PMC3839885.

22. Ruscito I, Darb-Esfahani S, Kulbe H, Bellati F, Zizzari IG, Rahimi Koshkaki H, Napoletano C, Caserta D, Rughetti A, Kessler M, Sehouli J, Nuti M, Braicu EI. The prognostic impact of cancer stem-like cell biomarker aldehyde dehydrogenase-1 (ALDH1) in ovarian cancer: A meta-analysis. Gynecol Oncol. 2018 Jul;150(1):151-157. doi: 10.1016/j.ygyno.2018.05.006. Epub 2018 May 10. PMID: 29753392.

23. Brown JR, Chan DK, Shank JJ, Griffith KA, Fan H, Szulawski R, Yang K, Reynolds RK, Johnston C, McLean K, Uppal S, Liu JR, Cabrera L, Taylor SE, Orr BC, Modugno F, Mehta P, Bregenzer M, Mehta G, Shen H, Coffman LG, Buckanovich RJ. Phase II clinical trial of metformin as a cancer stem cell-targeting agent in ovarian cancer. JCI Insight. 2020 Jun 4;5(11):e133247. doi: 10.1172/jci.insight.133247. PMID: 32369446; PMCID: PMC7308054.

24. Kang WD, Kim CH, Cho MK, Kim JW, Lee JS, Ryu SY, Kim YH, Choi HS, Kim SM. Primary epithelial ovarian carcinoma with gastric metastasis mimic gastrointestinal stromal tumor. Cancer Res Treat. 2008 Jun;40(2):93-6. doi: 10.4143/crt.2008.40.2.93. Epub 2008 Jun 30. PMID: 19688055; PMCID: PMC2697489.

25. Du Bois A, Vergote I, Ferron G et al. A randomized controlled phase III study evaluating the impact of secondary cytoreductive surgery in recurrent ovarian cancer: AGO DESKTOP III/ENGOT ov20. J Clin Oncol 2017; 35(Suppl): abstr #5501.

26. Shi T, Zhu J, Feng Y, Tu D, Zhang Y, Zhang P, Jia H, Huang X, Cai Y, Yin S, Jiang R, Tian W, Gao W, Liu J, Yang H, Cheng X, Zang R. Secondary cytoreduction followed by chemotherapy versus chemotherapy alone in platinum-sensitive relapsed ovarian cancer (SOC-1): a multicentre, open-label, randomised, phase 3 trial. Lancet Oncol. 2021 Apr;22(4):439-449. doi: 10.1016/S1470-2045(21)00006-1. Epub 2021 Mar 8. PMID: 33705695.

27. Coleman RL, Spirtos NM, Enserro D, Herzog TJ, Sabbatini P, Armstrong DK, Kim JW, Park SY, Kim BG, Nam JH, Fujiwara K, Walker JL, Casey AC, Alvarez Secord A, Rubin S, Chan JK, DiSilvestro P, Davidson SA, Cohn DE, Tewari KS, Basen-Engquist K, Huang HQ, Brady MF, Mannel RS. Secondary Surgical Cytoreduction for Recurrent Ovarian Cancer. N Engl J Med. 2019 Nov 14;381(20):1929-1939. doi: 10.1056/NEJMoa1902626. PMID: 31722153; PMCID: PMC6941470.

28. Parmar MK, Ledermann JA, Colombo N et al. ICON and AGO Collaborators. Paclitaxel plus platinum-based chemotherapy versus conventional platinum-based chemotherapy in women with relapsed ovarian cancer: the ICON4/AGO-OVAR-2.2 trial. Lancet 2003; 361: 2099–2106.

29. Pfisterer J, Plante M, Vergote I et al. Gemcitabine plus carboplatin compared with carboplatin in patients with platinum-sensitive recurrent ovarian cancer: an intergroup trial of the AGO-OVAR, the NCIC CTG, and the EORTCGCG.JClinOncol2006;24: 4699–4707.

30. Coleman RL, Brady MF, Herzog TJ et al. Bevacizumab and paclitaxelcarboplatin chemotherapy and secondary cytoreduction in recurrent, platinum-sensitive ovarian cancer (NRG Oncology/Gynecologic Oncology Group study GOG-0213): a multicentre, open-label, randomised, phase 3 trial. Lancet Oncol 2017; 18: 779–791.

31. Aghajanian C, Goff B, Nycum LR et al. Final overall survival and safety analysis of OCEANS, a phase 3 trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent ovarian cancer. Gynecol Oncol 2015; 139: 10–16.

32. Ledermann J, Harter P, Gourley C et al. Olaparib maintenance therapy in patients with platinum-sensitive relapsed serous ovarian cancer: a preplanned retrospective analysis of outcomes by BRCA status in a randomised phase 2 trial. Lancet Oncol 2014; 15: 852–861.

33. Pujade-Lauraine E, Ledermann JA, Penson RT et al. Treatment with olaparib monotherapy in the maintenance setting significantly improves progression-free survival in patients with platinum-sensitive relapsed ovarian cancer: Results from the phase III SOLO2 study. 2017 Society of Gynecologic Oncologists Annual Meeting. Abstract LBA2. Presented March 14, 2017.

34. Mirza MR, Monk BJ, Herrstedt J et al. Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer. N Engl J Med 2016; 1375: 2154–2164.

35. Swisher EM, Lin KK, Oza AM et al. Rucaparib in relapsed, platinumsensitive high-grade ovarian carcinoma (ARIEL2 Part 1): an international, multicentre, open-label, phase 2 trial. Lancet Oncol 2017; 18: 75–87.

36. Macchia G, Lazzari R, Colombo N, Laliscia C, Capelli G, D'Agostino GR, Deodato F, Maranzano E, Ippolito E, Ronchi S, Paiar F, Scorsetti M, Cilla S, Ingargiola R, Huscher A, Cerrotta AM, Fodor A, Vicenzi L, Russo D, Borghesi S, Perrucci E, Pignata S, Aristei C, Morganti AG, Scambia G, Valentini V, Jereczek-Fossa BA, Ferrandina G. A Large, Multicenter, Retrospective Study on Efficacy and Safety of Stereotactic Body Radiotherapy (SBRT) in Oligometastatic Ovarian Cancer (MITO RT1 Study): A Collaboration of MITO, AIRO GYN, and MaNGO Groups. Oncologist. 2020 Feb;25(2):e311-e320. doi: 10.1634/theoncologist.2019-0309. Epub 2019 Oct 10. PMID: 32043791; PMCID: PMC7011643.

37. George, A., McLachlan, J., Tunariu, N. et al. The role of hormonal therapy in patients with relapsed high-grade ovarian carcinoma: a retrospective series of tamoxifen and letrozole. BMC Cancer 17, 456 (2017). https://doi.org/10.1186/s12885-017-3440-0