

Name of candidate:

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### **Case A: Ovarian cancer**

Patientin, geboren 1965, geschieden, 2 Kinder, 1 Bruder. Arbeitet als Krankenpflegerin

Persönliche Anamnese: unauffällig.

Familienanamnese: Mutter an Ovarialkarzinom erkrankt, Grossmutter und Tante mütterlicherseits an Brustkrebs erkrankt

Medikamente und Risikoverhalten: keine Medikamente, keine Noxen.

**Aktuelles Leiden und Befunde:** Vor 5 Monate unauffällige gynäkologische Untersuchung. Aktuell seit einigen Wochen vermehrtes Völlegefühl. Vor zwei Wochen den Hausarzt wegen zunehmendem Umfangs des Abdomens aufgesucht. Der Hausarzt veranlasst eine CT-Untersuchung mit Nachweis von Aszites und Verdacht auf Peritonealkarzinose.

Im klinischen Untersuch findet der Hausarzt ein balloniertes Abdomen und eine nicht-reponierbare Resistenz inguinal links. Der Hausarzt führt eine Ascitespunktion durch und überweist Ihnen die Patientin.

Labor: CA-124 1154 IU/l, CEA und CA-15-3 im Normbereich.

Zytologiebefund aus der Aszitespunktion: Adenokarzinom vereinbar mit Ovarialkarzinom

Inform the candidate about the content of the exam:

- Presentation of the case, what do you know and how does he/she summarize the situation.
- Questions about further investigations needed
- Questions about possible treatments / treatment strategies
- Questions about side effects of treatments
- Questions about psychosocial and economic aspects
- Questions about important clinical studies on the subject

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	Question / Task	Expected Answers	Answer given: 1 point for each correct answer given	Points reached
	Ask the candidate to summarize the case: <ul style="list-style-type: none"> <li>- history</li> <li>- patient's complains</li> <li>- results of investigations</li> <li>- suspected diagnosis</li> </ul>	<ul style="list-style-type: none"> <li>- Abdominal distension and nodal mass in left groin</li> <li>- CT scan reveals ascites and is highly suspicious for peritoneal metastases</li> <li>- high CA-125 and low CEA</li> <li>- Cytology: poorly differentiated carcinoma, compatible with ovarian origin</li> <li>- Ovarian cancer, probably FIGO III B</li> <li>- Family history of cancer with possible BRCA-1/2 mutation</li> </ul>		...../6
<b>A CT-scan was performed Invite the candidate to scroll through the CT-images on the desktop computer.</b>				
	Comment the CT-scan	<ul style="list-style-type: none"> <li>- Ascites</li> <li>- Peritoneal nodules</li> <li>- Pelvic mass</li> <li>- Mass in the left groin</li> <li>- No pleural effusion</li> <li>- No liver metastasis</li> </ul>		...../4
	How would you proceed?	<ul style="list-style-type: none"> <li>- Present the case at the TB</li> <li>- Discuss immediate surgery versus chemo before surgery (Chorus trial, Lancet May 2015 und Vergote NEJM 2010)</li> <li>- Discuss genetic counseling</li> <li>-</li> </ul>		...../3

	Question / Task	Expected Answer	Answer given: 1 point for each correct answer given	Points reached
	<p>Ask about appropriate situations for chemo first</p> <p>When do you apply chemo first?</p>	<ul style="list-style-type: none"> <li>- Very extensive tumor dissemination at diagnosis (FIGO IIIC, IV)</li> <li>- Poor performance status</li> <li>- Low albumin level</li> <li>- Chorus trial may change practice to start with 3 cycle of chemo (reduced overall side effects; lower death rate; shorter stay in hospital)               <ul style="list-style-type: none"> <li>o EORTC 55971 same topic</li> </ul> </li> </ul>		...../3
	<p>At the TB immediate surgery was recommended.</p> <p>What is the goal of surgery and why?</p>	<ul style="list-style-type: none"> <li>- Total macroscopic tumor clearance with no gross residual disease</li> <li>- Prognosis is associated with residual disease.</li> </ul>		...../2
	<p>Surgery was performed with residual multifocal peritoneal implants &lt; 5mm.</p> <p>Peritoneal mets were up to 4 cm in diameter.</p> <p>How would you classify the disease according to FIGO stage</p>	<ul style="list-style-type: none"> <li>- FIGO III C (peritoneal mets&gt;2cm)</li> </ul>		...../1
	<p>If chemo is given first, which regimen would you propose</p>	<ul style="list-style-type: none"> <li>- Platinum based , eg carboplatin/paclitaxel q3wk for 3 cycles followed by interval debulking</li> </ul>		...../1

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<p><b>Next information to the candidate:</b> Histology of definitive surgery: High-grade serous carcinoma</p>				
	<p>Name distinct subtypes of ovarian cancer Which one is the most frequent?</p>	<p>Epithelial origin in ~90% of cases</p> <ul style="list-style-type: none"> <li>- Serous low-grade and high-grade</li> <li>- Serous is most frequent (~80%)</li> <li>- Endometrioid</li> <li>- Mucinous</li> <li>- Clear cell</li> <li>- Transitional cell (Brenner)</li> <li>- Mixed epithelial tumors</li> <li>- Undifferentiated/unclassified</li> </ul> <p>Borderline tumors (low-grade tumors) Carcinosarcoma Sex cord stromal tumors</p>		<p>...../4</p>
	<p>We call it “ovarian cancer”. According to accumulating evidence, which organ is most probably the true origin of high-grade serous ovarian and peritoneal cancer?</p>	<ul style="list-style-type: none"> <li>- Majority of high-grade serous ovarian and so called “primary peritoneal cancer” originate in the fimbria of the fallopian tube and metastasize to the ovaries and the peritoneal cavity.</li> </ul>		<p>...../1</p>

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	What is the role of BRCA-1 and BRCA-2 in ovarian cancer?	<ul style="list-style-type: none"> <li>- Approximately 10-15 % of all ovarian cancers have an identifiable germ line mutation, eg BRCA1 or 2 (somatic mutation in the tumor even more common)</li> <li>- BRCA-1: lifetime risk of developing ovarian cancer ~40 % and breast cancer 50-80%</li> <li>- BRCA-2: life-time risk for ovarian cancer 10-20% and breast cancer ~45 %</li> <li>- Carrier develops disease 10 years earlier</li> </ul>		...../4
	What is the biological function of BRCA 1 and BRCA 2?	<ul style="list-style-type: none"> <li>- Tumor suppressor gens</li> <li>- Involved in DNA repair</li> </ul>		...../1
<p><b>Next information to the candidate:</b>            After <u>up-front surgery</u> with maximum debulking and residual disease &lt; 5mm, the patient's situation is discussed at the TB.</p>				
	Would you recommend further treatment and what kind of therapy?	<ul style="list-style-type: none"> <li>- Yes, adjuvant chemotherapy</li> <li>- Platinum based doublet (usually carboplatin) and paclitaxel for 6 cycles</li> </ul>		...../2

	Question / Task	Expected Answer	Answer given: 1 point for each correct answer given	Points reached
	Do you know methods/strategies to improve outcome of first line platinum/paclitaxel chemotherapy?	<ul style="list-style-type: none"> <li>- Dose-dense regimen with weekly paclitaxel results in better PFS and OS</li> <li>- Intraperitoneal delivery of chemo (in CH not frequently used)</li> <li>- Addition of bevacizumab for 1 year in high-risk patients according to ICON-7 definition (stage III suboptimal debulked &gt; 1cm; stage IV, non-operated patients) improved median OS by 9.4 months (in CH on-label)</li> <li>- Maintenance with several agents does not improve survival (except for olaparib in platinum sensitive relapse, Ledermann NEJM 2012)</li> </ul>		...../3
	Discuss side effect of chemotherapy with carboplatin/paclitaxel	<ul style="list-style-type: none"> <li>- Alopecia</li> <li>- Hematological toxicities</li> <li>- Neutropenia and infections</li> <li>- Polyneuropathy</li> <li>- Fatigue</li> <li>- Hypersensitivity reaction to paclitaxel <u>during infusion</u> (IgE mediated? Cremophor induced release of histamine)</li> <li>- Hypersensitivity reaction to carboplatin usually after multiple infusions. <ul style="list-style-type: none"> <li>o Rapid desensitization possible</li> </ul> </li> </ul>		...../5

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	<p>Suppose the patient is not a nurse but a <u>professional violin player</u> and suffers from <u>diabetes</u>. How would you incorporate this information in your treatment proposal ?</p>	<ul style="list-style-type: none"> <li>- Discuss avoiding paclitaxel (ICON-3 trial)</li> <li>- Substitute paclitaxel with docetaxel (same efficacy, significantly less <u>neuropathy</u>. <i>Scotroc trial</i>)</li> </ul>		<p>...../2</p>
	<p>PFS and OS of 1<sup>st</sup>-line carboplatin/paclitaxel?</p>	<ul style="list-style-type: none"> <li>- ICON-7 standard arm:               <ul style="list-style-type: none"> <li>o PFS overall ~1 ½ years</li> <li>o OS overall ~ 5 years</li> </ul> </li> <li>- Scotroc trial (<u>carbo/paclitaxel</u> vs carbo/docetaxel)               <ul style="list-style-type: none"> <li>o PFS overall 15 months</li> <li>o OS at 2 y: 69 %</li> </ul> </li> </ul>		<p>...../2</p>
<p><b>After 6 cycles of chemotherapy the patient has a few questions</b></p>				
	<p>At surgery residual multifocal peritoneal implants &lt; 5mm were left. Should we do a 2<sup>nd</sup> look operation?</p>	<ul style="list-style-type: none"> <li>- No, 2<sup>nd</sup> look surgery has never shown an impact on survival.</li> </ul>		<p>...../1</p>
	<p>If 2<sup>nd</sup> look is not performed, how do you define CR at the end of chemo?</p>	<ul style="list-style-type: none"> <li>- CT scan without any visible mass</li> <li>- CA-125 within normal range</li> </ul>		<p>...../2</p>

	Question / Task	Expected Answer	Answer given: 1 point for each correct answer given	Points reached
	<p>The patient (a nurse) argues that detecting a rising CA-125 without symptoms and restarting treatment would prolong her life.</p> <p>Is there any phase III evidence for counseling your patient?</p>	<ul style="list-style-type: none"> <li>- A British phase III study found that second-line therapy based on elevated CA 125 compared with treatment begun on clinical evidence of relapse showed no OS advantage of early CA 125-directed retreatment.</li> <li>- Treatment was delayed by a median of 4.8 months with no detriment to OS</li> <li>- Measuring CA-125 without any other evidence of relapse compromised QoL due to more chemotherapy</li> <li>- On the other hand not measuring CA-125 might miss surgically resectable recurrence. <ul style="list-style-type: none"> <li>o Ongoing trials are evaluating if surgery for relapse improves survival</li> </ul> </li> </ul>		...../3
<p><b>4 months after the end of chemotherapy the patient has again abdominal distension and a CA-125 level of 375 IU/l. CT-scan reveals ascites and multiple peritoneal nodes.</b></p>				
	<p>Would you restart a platinum-based chemotherapy?</p>	<ul style="list-style-type: none"> <li>- No, relapse is less than 6 months since end of 1<sup>st</sup>-line chemo. Chance of response to platinum based chemo is small.</li> <li>- By definition the patient has platinum-resistant disease.</li> </ul>		...../1



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	Does BRCA mutation status impact on your decision?	<ul style="list-style-type: none"><li>- PARP-Inhibitor (Olaparib) has shown promising activity even in platinum-resistant disease (ORR ~45%)</li><li>- Currently (september 2015) not licensed in CH (but available )</li></ul>		...../1
	Which drugs would you discuss in a platinum-resistant disease?	<ul style="list-style-type: none"><li>- Clinical trial</li><li>- Paclitaxel</li><li>- Topotecan</li><li>- Pegylated liposomal Doxorubicin</li><li>- Gemcitabine</li> <li>- Add Bev to chemo (Aurelia Trial) improves PFS by 3 months but without gain in OS (~14months). In CH off-label and not covered by insurance.</li></ul>		...../3

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	Question / Task	Expected Answer	Answer given	Points reached
	Topics of examiners choice	Questions:		...../5
Total points achieved				...../60

A minimum of 39 points (65% of 60 points) must be achieved to pass the exam.

Examiners: Name:.....

Name:.....

Date of examination:.....