**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 finden 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
**Name of candidate:**

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| Ask the candidate to summarize the case:                                      | - Abdominal distension and nodal mass in left groin  
- CT scan reveals ascites and is highly suspicious for peritoneal metastases  
- High CA-125 and low CEA  
- Cytology: poorly differentiated carcinoma, compatible with ovarian origin  
- Ovarian cancer, probably FIGO III B  
- Family history of cancer with possible BRCA-1/2 mutation | ..../6                                                |
| A CT-scan was performed                                                        | **Invite the candidate to scroll through the CT-images on the desktop computer.**                                                                                                                                 |                                                     |
| Comment the CT-scan                                                            | - Ascites  
- Peritoneal nodules  
- Pelvic mass  
- Mass in the left groin  
- No pleural effusion  
- No liver metastasis                                      | ..../4                                                |
| How would you proceed?                                                         | - Present the case at the TB  
- Discuss immediate surgery versus chemo before surgery (Chorus trial, Lancet May 2015 und Vergote NEJM 2010)  
- Discuss genetic counseling                                                                                                                                 | ..../3                                                |
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| Ask about appropriate situations for chemo first                              | - Very extensive tumor dissemination at diagnosis (FIGO IIIC, IV)  
- Poor performance status  
- Low albumin level  
- Chorus trial may change practice to start with 3 cycle of chemo (reduced overall side effects; lower death rate; shorter stay in hospital)  
  - EORTC 55971 same topic                                                                                                                |                                                                                                     | ....../3        |
| When do you apply chemo first?                                                | - Total macroscopic tumor clearance with no gross residual disease  
- Prognosis is associated with residual disease.                                                                                               |                                                                                                     | ....../2        |
<p>| At the TB immediate surgery was recommended.                                  | - FIGO III C (peritoneal mets&gt;2cm)                                                                                                                                                                               |                                                                                                     | ....../1        |
| Surgery was performed with residual multifocal peritoneal implants &lt; 5mm.     | - Platinum based, eg carboplatin/paclitaxel q3wk for 3 cycles followed by interval debulking                                                                                                                   |                                                                                                     | ....../1        |
| how would you classify the disease according to FIGO stage                     |                                                                                                                                                                                                                 |                                                                                                     |                |
| If chemo is given first, which regimen would you propose                       |                                                                                                                                                                                                                 |                                                                                                     |                |</p>
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<td><strong>Next information to the candidate:</strong> Histology of definitive surgery: High-grade serous carcinoma</td>
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| Name distinct subtypes of ovarian cancer Which one is the most frequent? | Epithelial origin in ~90% of cases  
- Serous low-grade and high-grade  
- Serous is most frequent (~80%)  
- Endometrioid  
- Mucinous  
- Clear cell  
- Transitional cell (Brenner)  
- Mixed epithelial tumors  
- Undifferentiated/unclassified  
Borderline tumors (low-grade tumors)  
Carcinosarcoma  
Sex cord stromal tumors | | |
<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? | - 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. | | ....../1 |</p>
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<td>What is the role of BRCA-1 and BRCA-2 in ovarian cancer?</td>
<td>- 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)   - BRCA-1: lifetime risk of developing ovarian cancer ~40 % and breast cancer 50-80%   - BRCA-2: life-time risk for ovarian cancer 10-20% and breast cancer  ~45 %   - Carrier develops disease 10 years earlier</td>
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<td>What is the biological function of BRCA 1 and BRCA 2?</td>
<td>- Tumor suppressor gens   - Involved in DNA repair</td>
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<td><strong>Next information to the candidate:</strong></td>
<td><strong>After up-front surgery</strong> with maximum debulking and residual disease &lt; 5mm, the patient’s situation is discussed at the TB.</td>
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<td>Would you recommend further treatment and what kind of therapy?</td>
<td>- Yes, adjuvant chemotherapy   - Platinum based doublet (usually carboplatin) and paclitaxel for 6 cycles</td>
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| Do you know methods/strategies to improve outcome of first line platinum/paclitaxel chemotherapy? | - Dose-dense regimen with weekly paclitaxel results in better PFS and OS  
- Intraperitoneal delivery of chemo (in CH not frequently used)  
- Addition of bevacizumab for 1 year in high-risk patients according to ICON-7 definition (stage III suboptimal debulked > 1cm; stage IV, non-operated patients) improved median OS by 9.4 months (in CH on-label)  
- Maintenance with several agents does not improve survival (except for olaparib in platinum sensitive relapse, Ledermann NEJM 2012)                                                                                                                                                                                                                      | ....../3                                                                                               |                |
| Discuss side effect of chemotherapy with carboplatin/paclitaxel               | - Alopecia  
- Hematological toxicities  
- Neutropenia and infections  
- Polyneuropathy  
- Fatigue  
- Hypersensitivity reaction to paclitaxel during infusion (IgE mediated? Cremophor induced release of histamine)  
- Hypersensitivity reaction to carboplatin usually after multiple infusions.  
  - Rapid desensitization possible                                                                                                                                                                                                                                                                  | ....../5                                                                                               |                |
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| Suppose the patient is not a nurse but a professional violin player and suffers from diabetes. How would you incorporate this information in your treatment proposal? | - Discuss avoiding paclitaxel (ICON-3 trial)  
- Substitute paclitaxel with docetaxel (same efficacy, significantly less neuropathy. Scotroc trial)                                                                 |                                                                                                 | ....../2       |
| PFS and OS of 1\textsuperscript{st}-line carboplatin/paclitaxel?               | - ICON-7 standard arm:  
  - PFS overall ~1 ½ years  
  - OS overall ~ 5 years  
- Scotroc trial (carbo/paclitaxel vs carbo/docetaxel)  
  - PFS overall 15 months  
  - OS at 2 y: 69 %                                                                 |                                                                                                 | ....../2       |

**After 6 cycles of chemotherapy the patient has a few questions**

| At surgery residual multifocal peritoneal implants < 5mm were left. Should we do a 2\textsuperscript{nd} look operation? | - No, 2\textsuperscript{nd} look surgery has never shown an impact on survival.                                                                 |                                                                                                 | ....../1       |
| If 2\textsuperscript{nd} look is not performed, how do you define CR at the end of chemo? | - CT scan without any visible mass  
- CA-125 within normal range                                                                 |                                                                                                 | ....../2       |
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| The patient (a nurse) argues that detecting a rising CA-125 without symptoms and restarting treatment would prolong her life. Is there any phase III evidence for counseling your patient? | - 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.  
  - Treatment was delayed by a median of 4.8 months with no detriment to OS  
  - Measuring CA-125 without any other evidence of relapse compromised QoL due to more chemotherapy  
  - On the other hand not measuring CA-125 might miss surgically resectable recurrence.  
  o Ongoing trials are evaluating if surgery for relapse improves survival |                                                                                                                                             | ....../3                  |

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.

| Would you restart a platinum-based chemotherapy? | - No, relapse is less than 6 months since end of 1st-line chemo. Chance of response to platinum based chemo is small.  
  - By definition the patient has platinum-resistant disease. |                                                                                                           | ....../1                  |
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<td>Does BRCA mutation status impact on your decision?</td>
<td>- PARP-Inhibitor (Olaparib) has shown promising activity even in platinum-resistant disease (ORR ~45%)&lt;br&gt;- Currently (september 2015) not licensed in CH (but available)</td>
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<tr>
<td>Which drugs would you discuss in a platinum-resistant disease?</td>
<td>- Clinical trial&lt;br&gt;- Paclitaxel&lt;br&gt;- Topotecan&lt;br&gt;- Pegylated liposomal Doxorubicin&lt;br&gt;- Gemcitabine&lt;br&gt;- Add Bev to chemo (Aurelia Trial) improves PFS by 3 months but without gain in OS (~14 months). In CH off-label and not covered by insurance.</td>
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A minimum of 39 points (65% of 60 points) must be achieved to pass the exam.

Examiners: Name:…………………………         Name:………………………………

Date of examination:……………………

SGMO Facharztprüfung FMH  31.10.15         V.04.10.15