Name of candidate:

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 Hausazrt 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:

	Question / Task	Expected Answers	Answer given: 1 point for each correct answer given	Points reached
	Ask the candidate to summarize the case: - history - patient's complains - results of investigations - suspected diagnosis	- 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

Name of candidate:

	Question / Task	Expected Answer	Answer given: 1 point for each correct answer given	Points reached
	Ask about appropriate situations for chemo first When do you apply 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) o EORTC 55971 same topic		……/3
	At the TB immediate surgery was recommended. What is the goal of surgery and why?	- Total macroscopic tumor clearance with no gross residual disease - Prognosis is associated with residual disease.		……/2
	Surgery was performed with residual multifocal peritoneal implants < 5mm. Peritoneal mets were up to 4 cm in diameter. How would you classify the disease according to FIGO stage	- FIGO III C (peritoneal mets>2cm)		……/1
	If chemo is given first, which regimen would you propose	- Platinum based , eg carboplatin/paclitaxel q3wk for 3 cycles followed by interval debulking		……/1

Name of candidate:

	Question / Task	Expected Answer	Answer given: 1 point for each correct answer given	Points reached
	Next information to the candidate: Histology of definitive surgery: High-grade serous carcinoma			
	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		……/4
	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

Name of candidate:

	Question / Task	Expected Answer	Answer given: 1 point for each correct answer given	Points reached
	What is the role of BRCA-1 and BRCA-2 in ovarian cancer?	- 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		……/4
	What is the biological function of BRCA 1 and BRCA 2?	- Tumor suppressor gens - Involved in DNA repair		……/1
	Next information to the candidate: After **<u>up-front surgery</u>** with maximum debulking and residual disease < 5mm, the patient's situation is discussed at the TB.			
	Would you recommend further treatment and what kind of therapy?	- Yes, adjuvant chemotherapy - Platinum based doublet (usually carboplatin) and paclitaxel for 6 cycles		……/2

Name of candidate:

	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?	- 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. o Rapid desensitization possible		……/5

Name of candidate:

	Question / Task	Expected Answer	Answer given: 1 point for each correct answer given	Points reached
	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 1st-line carboplatin/paclitaxel?	- ICON-7 standard arm: o PFS overall ~1 ½ years o OS overall ~ 5 years - Scotroc trial (carbo/paclitaxel vs carbo/docetaxel) o PFS overall 15 months o 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 2nd look operation?	- No, 2nd look surgery has never shown an impact on survival.		……/1
	If 2nd 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

Name of candidate:

	Question / Task	Expected Answer	Answer given: 1 point for each correct answer given	Points reached
	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

Name of candidate:

	Question / Task	Expected Answer	Answer given: 1 point for each correct answer given	Points reached
	Does BRCA mutation status impact on your decision?	- PARP-Inhibitor (Olaparib) has shown promising activity even in platinum-resistant disease (ORR ~45%) - Currently (september 2015) not licensed in CH (but available)		……/1
	Which drugs would you discuss in a platinum-resistant disease?	- Clinical trial - Paclitaxel - Topotecan - Pegylated liposomal Doxorubicin - Gemcitabine - 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.		……/3

Name of candidate:

	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:…….