Clinical decision making in advanced ovarian and advanced/recurrent endometrial cancers

A touchROUNDTABLE sponsored by GSK

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Welcome and Introduction

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Expert panel

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Agenda

Open and introductions	5 mins	Prof. Jalid Sehouli (chair)
1 **PRESENTATION:** Individualising treatment decisions in advanced ovarian cancer	5 mins	Prof. Shibani Nicum
2 **PANEL DISCUSSION :** Individualising treatment decisions in advanced ovarian cancer	20 mins	All faculty
3 **PRESENTATION :** Managing individualised treatment in advanced/recurrent endometrial cancer	5 mins	Prof. Nicole Concin
4 **PANEL DISCUSSION :** Managing individualised treatment in advanced/recurrent endometrial cancer	20 mins	All faculty
Close	5 mins	All faculty

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Faculty disclosures

Prof. Jalid Sehouli

- Institutional research funding from AstraZeneca, Pfizer, Roche; advisory and speaker honoraria from Abbvie, AstraZeneca, Clovis, GSK, Novocure, Roche and Tesaro; travel expenses from AstraZeneca, Merck, GSK, Roche and Tesaro; and peer-reviewed research funding from AstraZeneca, GSK, MSD and Roche.

Prof. Nicole Concin

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Faculty disclosures

Prof. Shibani Nicum

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Ms. Lynn Buckley

- Consulting, advisory and speaker honorarium from AstraZeneca, Clovis and GSK.

Presentation: Individualising treatment decisions in advanced ovarian cancer

Prof. Shibani Nicum

Ovarian cancer presentation and initial decision making

Overview

- 87% of cases are stage III/IV at diagnosis.[1]
- High-grade serous ovarian cancer is the most common type.[1]
- Treatment options include surgery, chemotherapy and adjuvant therapy.[2,3]
- Biomarker testing informs prognosis and treatment decisions.[1,4]

Initial decision considerations

Patient characteristics - fitness of patients and importance of prehabiliation for surgery.

Molecular testing - when/how to collect samples for molecular testing, and which test to perform.

Treatment response - outcomes from surgery/chemotherapy i.e. RECIST and CA-125.

Timing - when should clinical decisions be made and how does the patient contribute to this?

1 Lisio MA, et al. *Int J Mol Sci.* 2019;20(4):952; 2. Lheureux S, et al. *Lancet*. 2019;393(10177):1240-1253; 3. Colombo N, et al. *Ann Oncol.* 2019;30(5):672-705; 4. Miller RE, et al. *Ann Oncol.* 2020;31(12):1606-1622.
CA-125, Cancer antigen 125; RECIST, Response Evaluation Criteria in Solid Tumors.

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Surgical decision making

Surgical decisions

- Primary vs interval debulking.[1]
  - Resectability – R0.
- Influencing factors:[2–4]
  - Patient fitness for surgery.
    - Performance status.
    - Comorbidities.
  - Patient choice.

Fitness for surgery

Prehabiliation

- Poor functional capacity is a risk factor for morbidity and mortality post-surgery.[3]
- Prehabilitation includes physical interventions, nutritional counselling and psychological support.[3]

Surgery aftercare

- Enhanced Recovery After Surgery (ERAS) results in clinical improvements for patients.[5]

1. Lheureux S, et al. *Lancet*. 2019;393(10177):1240-1253; 2. Makar AP, et al. *Oncologist*. 2016;21(6):745-54; 3. Miralpeix E, et al. *Int J Gynecol Cancer*. 2019;29(8):1235-1243; 4. Colombo N, et al. *Ann Oncol.* 2019;30(5):672-705; 5. Nelson G, et al. *Int J Gynecol Cancer.* 2019;29(4):651-668.

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Treatment selection

Treatment selection

- Carboplatin ± paclitaxel chemotherapy followed by maintenance therapy.[1,2]
- **Maintenance bevacizumab**: anti-VEGF treatment improves:
  - PFS in advanced stage patients.[1]
  - OS in patients at high risk of progression.[3]
- **Maintenance PARPi:** can be considered for all patients, with the magnitude of benefit based on *BRCA* mutation and HRd status.[4,5]

Biomarkers

- ***BRCA* mutations** occur in 18–22% cases and predict response to PARPi treatment and disease prognosis.[4,6]
- **HRd** is present in 50% of patients and is associated with improved response to PARPi therapy and disease prognosis.[4,5,7]

1. Lheureux S, et al. *Lancet*. 2019;393(10177):1240-1253; 2. Ledermann JA, et al. *Ann Oncol.* 2013;24(6):vi24-vi32; 3. Martin AG, et al. *Gynecol Oncol.* 2019; 152(1): 53–60; 4. Miller RE, et al. *Ann Oncol.* 2020;31(12):1606-1622; 5. Colombo N, et al. *Ann Oncol.* 2019;30(5):672-705; 6. Huang J, et al. *Cancer Biomark*. 2010; 8(0): 231–251; 7. Takaya H, et al. *Sci Rep*. 2020;10(1):2757.
HRd, homologous recombination deficiency; PFS, progression-free survival; OS, overall survival; PARPi, Poly-ADP ribose inhibitor; VEGF, vascular endothelial growth factor.

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Managing treatment and empowering patients

Common PARPi AEs[1]

- Anaemia (44–50%).
- Thrombocytopenia (14–61%).
- Nausea (74–76%).
- Increased creatinine (11–15%).
- Fatigue (59–69%).

Common bevacizumab AEs[2]

- Hypertension (26%).
- Neutropenia (28%).
- Mucocutaneous bleeding (37%).
- Thromboembolic events (11%).

Patient empowerment

- Empowering patients increases satisfaction with care, adherence and care outcomes.[3]
- HCPs play a key role in empowering patients, increasing their motivation to adhere with treatment.[3]
- Providing patients with information on AEs may improve AE management and manage expectations for daily living.[4]

1. LaFargue CJ, et al. *Lancet Oncol*. 2019;20(1):e15-e28; 2. Perren TJ, et al. *N Engl J Med.* 2011;365(26):2484-2496;
3. Jørgensen CR, et al. *Qual Health Res.* 2018;28(2):292-304; 4. Simacek K, et al. *Cancer Nurs.* 2017;40(5):E17-E27.
AE, adverse event.; HCP, healthcare practitioner; PARPi, Poly-ADP ribose inhibitor.

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Presentation: Managing individualised treatment in advanced/recurrent endometrial cancer

Prof. Nicole Concin

Endometrial cancer presentation and initial decision making

Overview

- The most common cancer of the female genital tract and has increased in incidence over time.[1,2]
- Surgery is recommended in early stage disease.[3]
- ESGO/ESTRO/ESP guidelines recommend biomarker testing at diagnosis.[3]
- Biomarker testing has led to new treatment options for advanced/recurrent disease.[3]

Initial decision considerations

Patient characteristics – how do you ensure fitness for active treatment

Molecular testing - when/how to collect samples for molecular testing

Previous treatment – what impact does previous treatment have

1. Faria SC, et al. *Semin Ultrasound CT MR.* 2019;40(4):287-294; 2. Constantine GD, et al. *J Womens Health (Larchmt).* 2019;28(2):237–243; 3. Concin N, et al. *Int J Gynecol Cancer.* 2021;31(1):12-39.
ESG, European Society of Pathology; ESGO, European Society of Gynaecological Oncology; ESTRO, European SocieTy for Radiotherapy and Oncology.

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Biomarker and systemic treatment options

Biomarkers

- **MSI-H/MMRd:** intermediate prognosis and indicate tumors, which may respond to ICI treatment.[1]
- **NSMP**: intermediate prognosis and tumors are frequently ER/PR positive.[1]
- ***TP53* abnormal**: group with a poor prognosis, often HGS/HG endometrioid.[1]
- ***POLE***: indicates good prognosis and a group who could avoid treatment.[1,2]
- **Hormone receptor status:** may indicate tumors responsive to hormone treatment.[2]

Treatment options

- In advanced/recurrent disease, standard options include surgery, chemotherapy and radiotherapy.[2]
- ICI are indicated in patients with MSI-high/MMRd tumors.[1,2]
    - ICI combined with a TKI has demonstrated a 36% response rate.[1]
- Hormone therapy is sometimes indicated, although there are no universally accepted factors to predict response.[2]

1. van den Heerik ASVM, et al. *Int J Gynecol Cancer. Published Online First: 01 January, 2020. doi 10.1136/ijgc-2020-001822*; 2. Concin N, et al. *Int J Gynecol Cancer.* 2021;31(1):12-39.

dMMR, mismatch repair deficiency; ER, estrogen receptor; HG, high grade; HGS, high-grade serous; ICI, immune checkpoint inhibitors; MSI, microsatellite instability; NSMP, no specific molecular profile; POLE, DNA polymerase epsilon; PR, progesterone receptor; TKI, tyrosine kinase inhibitor.

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Managing AEs and patient support

Immune-related AEs[1,2]

- Fatigue (28–48%).
- Dermatological (14–24%).
- Diarrhoea (26–30%).
- Increased AST (15–27%).
- Pneumonitis (1%).
- Although low in frequency, due to the multi-system potential of ICI-related AEs, a multidisciplinary team approach is recommended for management.[3]

Patient support

- **Proactively** providing patients with information on potential ICI AEs, and **early** reporting facilitate immediate medical intervention to manage AEs.[4]
- **Continuous evaluation** and **patient empowerment** via a personalised survivorship plan including information, lifestyle education and prevention of secondary malignancies facilitates positive long-term outcomes.[5]

1. Jemperli. 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761174s000lbl.pdf (accessed December 2021); 2. Keytruda. 2014. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/125514Orig1s054lbl.pdf (accessed December 2021); 3. Londoño MC, et al. *Cancers (Basel).* 2020;12(11):3446; 4. Myers G. *Curr Oncol.* 2018;25(5):342-347; 5. Concin N, et al. *Int J Gynecol Cancer.* 2021;31(1):12-39. AE, adverse event; ALA, alanine transaminase; AST, aspartate transaminase; ICI, immune checkpoint inhibitors.

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