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Global Perspectives in Gynecologic Malignancies (ESMO 2022)

Saturday, September 24, 2022

Report Contents

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Meeting Snapshot

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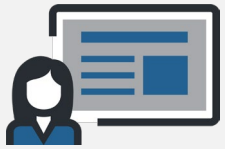
VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
September 24, 2022



DISEASE STATE AND DATA PRESENATIONS
by key experts

INSIGHTS REPORT
including postmeeting analyses and actionable recommendations

PANEL: Key experts in gynecologic cancer
- 4 from US
- 3 from Europe

GYNECOLOGIC MALIGNANCY-SPECIFIC DISCUSSIONS on latest research updates, therapeutic advances, and their application in clinical decision-making

Panel Consisting of 4 US and 3 European Gynecologic Cancer Experts

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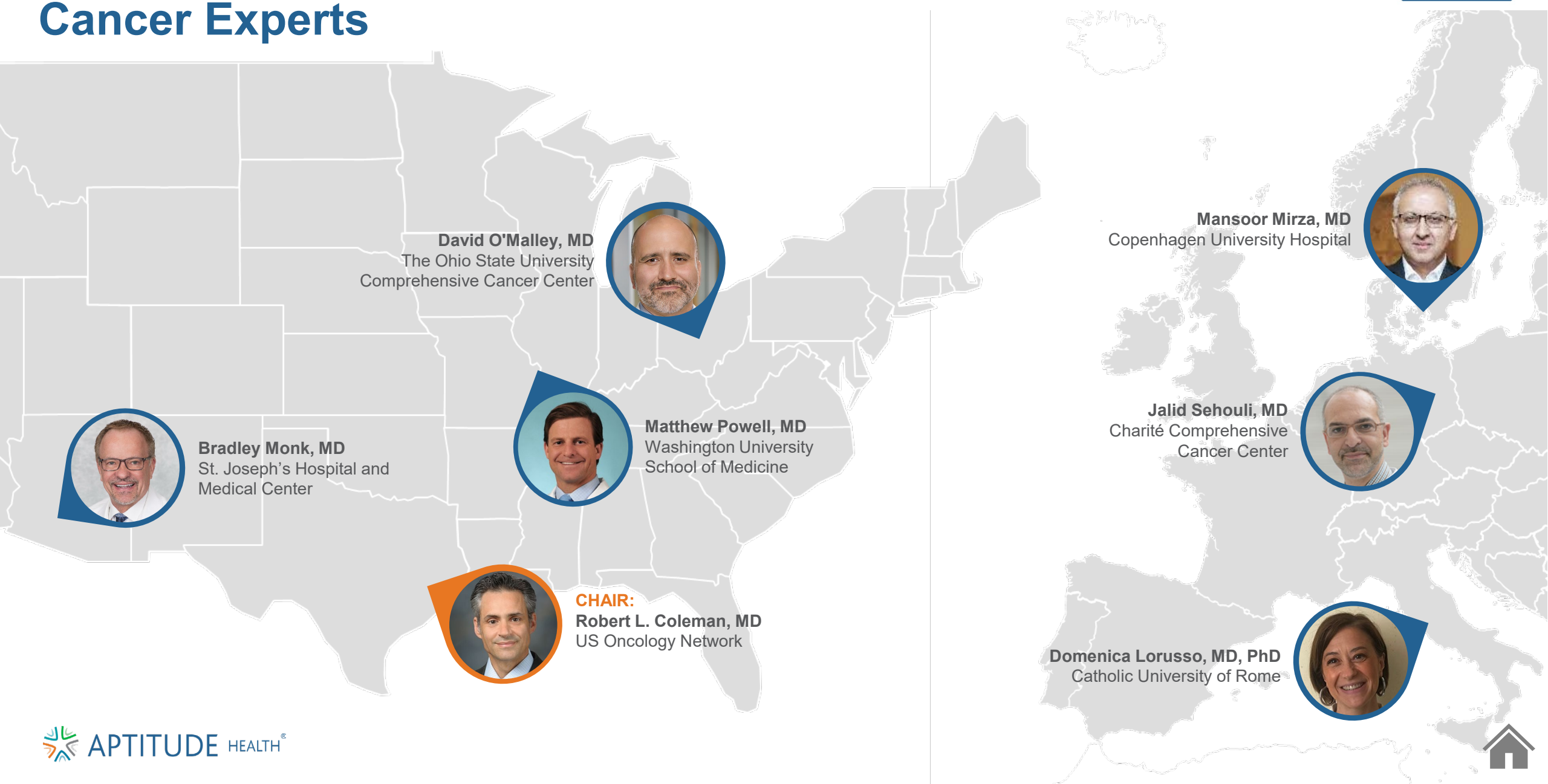

David O'Malley, MD
The Ohio State University
Comprehensive Cancer Center

Bradley Monk, MD
St. Joseph's Hospital and
Medical Center

Matthew Powell, MD
Washington University
School of Medicine

CHAIR:
Robert L. Coleman, MD
US Oncology Network

Mansoor Mirza, MD
Copenhagen University Hospital

Jalid Sehouli, MD
Charité Comprehensive
Cancer Center

Domenica Lorusso, MD, PhD
Catholic University of Rome

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Meeting Agenda (1/2)

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Time (EST)	Topic	Speaker/Moderator
8.00 AM – 8.05 AM	**Welcome and Introductions**	Robert L. Coleman, MD
8.05 AM – 8.15 AM	**Early-Stage Ovarian Cancer**	David O'Malley, MD
8.15 AM – 8.30 AM	*Key Questions and Discussion*	Robert L. Coleman, MD
8.30 AM – 8.35 AM	*Key Takeaways*	David O'Malley, MD
8.35 AM – 8.50 AM	**Advanced Ovarian Cancer: First-Line Therapy**	Mansoor Mirza, MD
8.50 AM – 9.00 AM	**Advanced Ovarian Cancer: Optimal Maintenance Therapy – What Do We Know Today?**	Bradley Monk, MD
9.00 AM – 9.30 AM	*Key Questions and Discussion*	Robert L. Coleman, MD
9.30 AM – 9.35 AM	*Key Takeaways*	Mansoor Mirza, MD, and Bradley Monk, MD
9.35 AM – 9.55 AM	**Advanced Ovarian Cancer: Treatment Strategies in the Relapsed Setting**	Jalid Sehouli, MD, PhD
9.55 AM – 10.25 AM	*Key Questions and Discussion*	Robert L. Coleman, MD
10.25 AM – 10.30 AM	*Key Takeaways*	Jalid Sehouli, MD, PhD
10.30 AM – 10.40 AM	Break	

Meeting Agenda (2/2)

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Time (EST)	Topic	Speaker/Moderator
10.40 AM – 10.55 AM	**Advanced Endometrial Cancer: Current Treatment and Future Directions**	Matthew Powell, MD
10.55 AM – 11.20 AM	*Key Questions and Discussion*	Robert L. Coleman, MD
11.20 AM – 11.25 AM	*Key Takeaways*	Matthew Powell, MD
11.25 AM – 11.40 AM	**Advanced Cervical Cancer: Current Treatment and Future Directions**	Domenica Lorusso, MD, PhD
11.40 AM – 12.00 PM	*Key Questions and Discussion*	Robert L. Coleman, MD
12.00 PM – 12.05 PM	*Key Takeaways*	Domenica Lorusso, MD, PhD
12.05 PM – 12.10 PM	**Closing and Wrap-up**	Robert L. Coleman, MD

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Early-Stage Ovarian Cancer

Early-Stage Ovarian Cancer

Presented by David O'Malley, MD

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Adjuvant therapy in early-stage EOC: A history lesson

Fertility-sparing surgery (FSS), the removal of only 1 ovary and preservation of the uterus, is clearly safe in borderline/low malignant tumors

Key Takeaways: Early-Stage Ovarian Cancer (1/3)

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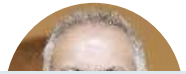
Adjuvant, platinum-based chemotherapy is justified in early-stage OC that is at high risk of recurrence

Although tumor histology plays a role in the success of chemotherapy, expert opinion is that a risk-vs-



Key Takeaways: Early-Stage Ovarian Cancer (2/3)

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Adjuvant, platinum-based chemotherapy is justified in early-stage OC that is at high risk of recurrence (cont.)

- However, experts commented that fully staged, nonserous, stage I EOC may be given 3 cycles of chemotherapy

Key Takeaways: Early-Stage Ovarian Cancer (3/3)

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Several questions/unmet needs are still open in early-stage ovarian cancer, and more trials are needed to provide answers (cont.)

BRCA mutation is the predictive biomarker for efficacy of PARPi

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Advanced Ovarian Cancer: First-Line and Maintenance Therapy

Advanced Ovarian Cancer: First-Line Therapy

Presented by Mansoor Mirza, MD

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Currently available first-line therapy in advanced ovarian cancer

Integration of PARPi into the front line has changed the treatment of ovarian cancer and has identified new unmet needs. The 3 major

1. Chan JK, et al. *Gynecol Oncol*. 2010;116:301-306.

Advanced Ovarian Cancer: First-Line Therapy

Presented by Mansoor Mirza, MD

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Efficacy of PARPi is seen in all populations

Efficacy of PARPi is highest in *BRCA*m followed by *BRCA*wt HRD populations. Modest efficacy is observed in *BRCA*wt HRP populations

Advanced Ovarian Cancer: Optimal Maintenance Therapy

Presented by Bradley Monk, MD

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Currently available maintenance options in the first-line setting

Frontline maintenance options available for advanced EOC

Key Takeaways: Advanced Ovarian Cancer – First Line and Maintenance (1/3)

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Experts think it is important to know in each case the better starting point for optimal outcomes: surgery or neoadjuvant chemotherapy

One of the major decisions experts must make in treating ovarian cancer is surgery or neoadjuvant chemotherapy

Key Takeaways: Advanced Ovarian Cancer – First Line and Maintenance (2/3)

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Genetic testing in advanced OC is a topic of active discussion (cont.)

Novel biomarkers (*RAD51C* or *RAD51CD*) as predictors of PARP

Dr O'Malley:

Key Takeaways: Advanced Ovarian Cancer – First Line and Maintenance (3/3)

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Experts consider frontline maintenance a must for all high-grade OC (cont.)

Use of PARPi and bevacizumab

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Advanced Ovarian Cancer: Treatment Strategies in the Relapsed Setting

Advanced Ovarian Cancer: Treatment Strategies in the Relapsed Setting

Presented by Jalid Sehouli, MD

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Management of recurrent OC

Recurrence of OC is common and is one of the greatest treatment challenges

Key Takeaways: Advanced Ovarian Cancer – Relapsed Setting (1/2)

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Clinical trial is the first choice of experts for a patient who has experienced relapse

Key Takeaways: Advanced Ovarian Cancer – Relapsed Setting (2/2)

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Preference of therapy for a patient who has experienced platinum-sensitive

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Advanced Endometrial Cancer: Current Treatment and Future Directions

Advanced Endometrial Cancer: Current Treatment and Future Directions (1/3)

Presented by Matthew Powell, MD

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Use of molecular subtyping to drive management of EC

The journey of EC from prognostic to predictive biomarkers has been incredible

Advanced Endometrial Cancer: Current Treatment and Future Directions (2/3)

Presented by Matthew Powell, MD

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Current and future perspectives in the management of advanced EC

Various modalities for endometrial cancer include antiangiogenic agents, EGFR targeting, mTOR/PI3K/AKT inhibitors, immunotherapy,

Advanced Endometrial Cancer: Current Treatment and Future Directions (3/3)

Presented by Matthew Powell, MD

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Current and future perspectives in the management of advanced EC (cont.)

Key Takeaways: Advanced Endometrial Cancer (1/3)

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Current treatment paradigms in EC

Unfortunately, more patients are being diagnosed with high-risk endometrial cancer, due to an aging

Key Takeaways: Advanced Endometrial Cancer (2/3)

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Immunotherapy in the frontline setting

The future looks interesting with the appearance of IO in the frontline and the disappearance of radiation

Key Takeaways: Advanced Endometrial Cancer (3/3)

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Hormonal therapy

Experts acknowledged that endocrine therapy plays a role in the treatment paradigm of EC, especially in the subgroup where

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Advanced Cervical Cancer: Current Treatment and Future Directions

Advanced Cervical Cancer: Current Treatment and Future Directions (1/3)

Presented by Domenica Lorusso, MD, PhD

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Recurrent or metastatic disease presents an area of high unmet clinical need

CC remains a major public health problem, with >58,000 new cases every year. There is a need for better drugs for treatment of recurrent CC

Advanced Cervical Cancer: Current Treatment and Future Directions (2/3)

Presented by Domenica Lorusso, MD, PhD

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The future of clinical research is dedicated to exploring ADCs and dual combination of immunotherapy

Recurrent or metastatic cervical cancer has been an unmet clinical need for decades, and ADCs will play a major role for

Advanced Cervical Cancer: Current Treatment and Future Directions (3/3)

Presented by Domenica Lorusso, MD, PhD

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The future of clinical research is dedicated to exploring ADCs and dual combination of immunotherapy (cont.)

> Cadonilimab is a next-generation, first-in-class, humanized bispecific antibody-drug candidate targeting PD-1 and CTLA-4 simultaneously. A

Key Takeaways: Advanced Cervical Cancer (1/3)

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Immunotherapy is changing the history of CC management

Experts test for PD-L1 in most of their patients, except patients with early-stage disease. FDA approval of the KEYNOTE-826 regimen

Key Takeaways: Advanced Cervical Cancer (2/3)

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Treatment options for women with PD-L1–positive recurrent or metastatic CC remain limited

The recent approval of tisotumab vedotin by the FDA partially addresses the unmet need for patients with PD-L1–positive recurrent or

Key Takeaways: Advanced Cervical Cancer (3/3)

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Upcoming trials in CC management

The future management strategy for CC will depend on the results of the KEYNOTE-A18 trial, which will determine whether

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Abbreviations

Abbreviations

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- ADC, antibody-drug conjugate
- AKT, protein kinase B
- AUC, area under the concentration-time curve
- *BRCA*, breast cancer susceptibility gene
- CC, cervical cancer
- CDK4/6, cyclin-dependent kinase 4/6
- CPS, Combined Positive Score
- CR, complete response
- CT, chemotherapy
- CTLA-4, cytotoxic T-lymphocyte antigen 4
- EC, endometrial cancer
- EGFR, epidermal growth factor receptor
- EMA, European Medicines Agency
- EOC, epithelial ovarian cancer
- ESMO, European Society for Medical Oncology
- FDA, US Food and Drug Administration
- FIGO, International Federation of Gynecology and Obstetrics
- FSS, fertility-sparing surgery
- FTC, fallopian tube cancer
- g*BRCA*, germline *BRCA*
- GCIG, Gynecological Cancer InterGroup
- HER2, human epidermal growth factor receptor 2
- HPV, human papillomavirus
- HR, hazard ratio
- HRD, homologous recombination deficiency
- HRP, homologous recombination proficiency
- IHC, immunohistochemistry
- IO, immunotherapy
- LAG3, lymphocyte-activation gene 3
- m, mutant
- MMR(d/p), mismatch repair (deficiency/proficiency)
- mTOR, mechanistic target of rapamycin
- MRD, minimal/measurable disease
- MSI(-H), microsatellite instability (high)
- NGS, next-generation sequencing
- NK, natural killer
- NSMP, no specific molecular profile
- OC, ovarian cancer
- ORR, overall response rate
- OS, overall survival
- PARPi, poly(ADP-ribose) polymerase inhibitor
- PD-L1, programmed cell death protein 1 ligand 1
- PFS, progression-free survival
- PI3K, phosphoinositide 3-kinase
- PPC, primary peritoneal cancer
- PR, partial response
- PVR, poliovirus receptor
- QOL, quality of life
- RT, radiotherapy
- SOC, standard of care
- STIC, serous tubal intraepithelial carcinoma
- t*BRCA*, tumor *BRCA*
- T-DM1, trastuzumab emtansine
- TIGIT, T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains
- TILs, tumor-infiltrating lymphocytes
- TMB, tumor mutational burden
- wt, wild-type

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