



EPICS

Global Perspectives in Gynecologic Malignancies (ESMO 2022)

Saturday, September 24, 2022

Content	Slide
Meeting Snapshot	3 
Faculty Panel	4 
Meeting Agenda	5 
Key Insights and Strategic Recommendations	7 
Early-Stage Ovarian Cancer	9 
Advanced Ovarian Cancer: First-Line and Maintenance Therapy	14 
Advanced Ovarian Cancer: Treatment Strategies in the Relapsed Setting	21 
Advanced Endometrial Cancer: Current Treatment and Future Directions	25 
Advanced Cervical Cancer: Current Treatment and Future Directions	32 

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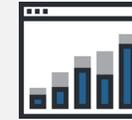
VIRTUAL CLOSED-DOOR ROUNDTABLE



DATE:
September 24, 2022



**DISEASE STATE AND
DATA PRESENTATIONS**
by key experts



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



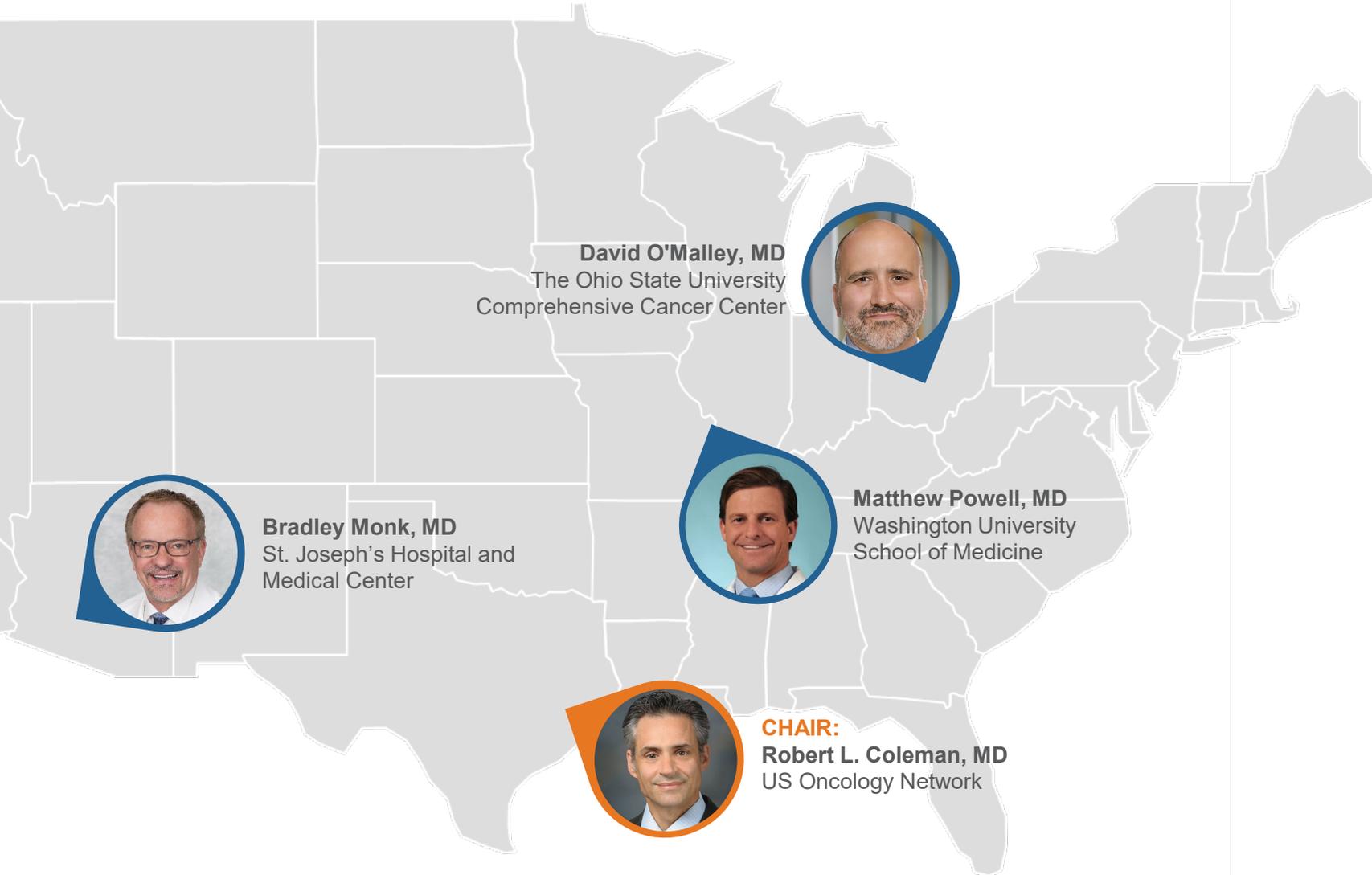
PANEL: Key experts in
gynecologic cancer
> 4 from US
> 3 from Europe



**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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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	<i>Key Questions and Discussion</i>	Robert L. Coleman, MD
8.30 AM – 8.35 AM	<i>Key Takeaways</i>	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	<i>Key Questions and Discussion</i>	Robert L. Coleman, MD
9.30 AM – 9.35 AM	<i>Key Takeaways</i>	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	<i>Key Questions and Discussion</i>	Robert L. Coleman, MD
10.25 AM – 10.30 AM	<i>Key Takeaways</i>	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	<i>Key Questions and Discussion</i>	Robert L. Coleman, MD
11.20 AM – 11.25 AM	<i>Key Takeaways</i>	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	<i>Key Questions and Discussion</i>	Robert L. Coleman, MD
12.00 PM – 12.05 PM	<i>Key Takeaways</i>	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

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

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

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-



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

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



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

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

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. PARPi in platinum-based regimens

Platinum-based regimens with PARPi have shown improved overall survival compared to platinum-based regimens without PARPi in advanced ovarian cancer.

2. PARPi in platinum-free regimens

PARPi in platinum-free regimens have shown improved overall survival compared to platinum-free regimens without PARPi in advanced ovarian cancer.

3. PARPi in maintenance therapy

PARPi in maintenance therapy have shown improved overall survival compared to maintenance therapy without PARPi in advanced ovarian cancer.





Advanced Ovarian Cancer: First-Line Therapy

Presented by Mansoor Mirza, MD

Efficacy of PARPi is seen in all populations

Efficacy of PARPi is highest in *BRCAm* followed by *BRCAw*t HRD populations. Modest efficacy is observed in *BRCAw*t HRP populations

Key Message 1: PARPi efficacy is highest in *BRCAm* populations, followed by *BRCAw*t HRD populations, and modest efficacy is observed in *BRCAw*t HRP populations.

Key Message 2: PARPi efficacy is highest in *BRCAm* populations, followed by *BRCAw*t HRD populations, and modest efficacy is observed in *BRCAw*t HRP populations.

Key Message 3: PARPi efficacy is highest in *BRCAm* populations, followed by *BRCAw*t HRD populations, and modest efficacy is observed in *BRCAw*t HRP populations.





Advanced Ovarian Cancer: Optimal Maintenance Therapy

Presented by Bradley Monk, MD

Currently available maintenance options in the first-line setting

Frontline maintenance options available for advanced EOC

PARP Inhibitors

• Olaparib, niraparib, rucaparib

• Indicated for BRCA1/2-mutated advanced EOC

• Improves progression-free survival (PFS) compared to placebo

Anti-angiogenic Agents

• Bevacizumab

• Improves PFS compared to placebo

• Commonly used in combination with chemotherapy

Other Maintenance Options

• Hormonal therapy (tamoxifen, aromatase inhibitors)

• Immunotherapy (checkpoint inhibitors)

• Targeted therapy (MEK inhibitors, CDK4/6 inhibitors)

Key Considerations

• Patient characteristics (BRCA status, performance, comorbidities)

• Clinical trial enrollment

• Supportive care (anti-nausea, pain management)



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

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

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



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

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



Dr O'Malley:

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

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



Use of PARPi and bevacizumab

PARPi

• PARPi is indicated for maintenance treatment in patients with advanced ovarian cancer who have not received prior platinum-based chemotherapy.

• The most commonly used PARPi is olaparib.

Bevacizumab

• Bevacizumab is indicated for maintenance treatment in patients with advanced ovarian cancer who have not received prior platinum-based chemotherapy.

• The most commonly used bevacizumab formulation is 10 mg/kg.

Key Takeaways

- PARPi and bevacizumab are important components of frontline maintenance therapy for advanced ovarian cancer.
- These agents are used in combination with platinum-based chemotherapy.
- Maintenance therapy is essential for improving overall survival in advanced ovarian cancer.

References

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2. [Faded reference text]

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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

Management of recurrent OC

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

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

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

Key Takeaway 1: Clinical Trial is the First Choice

For patients with advanced ovarian cancer who have experienced relapse, the first choice of experts is to enroll in a clinical trial. Clinical trials offer access to new treatments and are often the best chance for a patient to receive the most advanced care available. Experts should discuss the benefits and risks of clinical trials with their patients and help them make an informed decision.

Key Takeaway 2: Multidisciplinary Approach

Advanced ovarian cancer is a complex disease that requires a multidisciplinary approach to treatment. Experts should work together to develop a treatment plan that takes into account the patient's overall health, the extent of the disease, and the patient's preferences. This may include surgery, chemotherapy, targeted therapy, and radiation therapy.

Key Takeaway 3: Supportive Care

Supportive care is an important part of the treatment of advanced ovarian cancer. Experts should provide patients with information about the available options for managing symptoms and side effects. This may include pain management, anti-nausea medications, and nutritional support. Supportive care can help improve the patient's quality of life and make it easier for them to tolerate their treatment.

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

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

Platinum-sensitive relapsed disease

Platinum-based therapy is preferred for platinum-sensitive relapsed disease. Carboplatin is preferred over cisplatin due to its lower toxicity profile. Paclitaxel is preferred over docetaxel. Combination therapy with carboplatin and paclitaxel is preferred over single-agent therapy.

Platinum-resistant relapsed disease

Non-platinum-based therapy is preferred for platinum-resistant relapsed disease. Liposomal doxorubicin is preferred over conventional doxorubicin. Gemtuzumab is preferred over other anti-CD22 antibodies. Combination therapy with liposomal doxorubicin and gemtuzumab is preferred over single-agent therapy.

Platinum-refractory relapsed disease

Platinum-based therapy is preferred for platinum-refractory relapsed disease. Carboplatin is preferred over cisplatin. Combination therapy with carboplatin and paclitaxel is preferred over single-agent therapy.

Platinum-sensitive relapsed disease

Platinum-based therapy is preferred for platinum-sensitive relapsed disease. Carboplatin is preferred over cisplatin. Paclitaxel is preferred over docetaxel. Combination therapy with carboplatin and paclitaxel is preferred over single-agent therapy.

Platinum-resistant relapsed disease

Non-platinum-based therapy is preferred for platinum-resistant relapsed disease. Liposomal doxorubicin is preferred over conventional doxorubicin. Gemtuzumab is preferred over other anti-CD22 antibodies. Combination therapy with liposomal doxorubicin and gemtuzumab is preferred over single-agent therapy.

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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

Use of molecular subtyping to drive management of EC

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

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

Presented by Matthew Powell, MD

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,

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

Presented by Matthew Powell, MD

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

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Key Takeaways: Advanced Endometrial Cancer (1/3)

Current treatment paradigms in EC

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

Diagnosis and Staging

Endometrial cancer is the most common gynecologic malignancy in the United States. The incidence has increased significantly over the past few decades, particularly in older women. The most common histologic type is endometrioid adenocarcinoma. Staging is based on the FIGO system, which takes into account the extent of the tumor, lymph node involvement, and distant metastasis.

Treatment

The primary treatment for endometrial cancer is surgery, which typically involves a total hysterectomy with bilateral salpingo-oophorectomy. In some cases, lymph node dissection and omentectomy may be performed. Adjuvant therapy, such as radiation and chemotherapy, is used to reduce the risk of recurrence and improve survival. The choice of treatment depends on the stage and risk factors of the cancer.

Prognosis and Follow-up

The prognosis for endometrial cancer is generally good, especially for early-stage disease. However, high-risk endometrial cancer, which is often diagnosed in older women, has a poorer prognosis. Regular follow-up is essential to monitor for recurrence and manage any side effects from treatment.

Key Takeaways: Advanced Endometrial Cancer (2/3)

Immunotherapy in the frontline setting

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

KEY TAKEAWAY 1
The future looks interesting with the appearance of IO in the frontline and the disappearance of radiation

KEY TAKEAWAY 2
The future looks interesting with the appearance of IO in the frontline and the disappearance of radiation

KEY TAKEAWAY 3
The future looks interesting with the appearance of IO in the frontline and the disappearance of radiation

Key Takeaways: Advanced Endometrial Cancer (3/3)

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

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

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

Presented by Domenica Lorusso, MD, PhD

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

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

Presented by Domenica Lorusso, MD, PhD

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

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Key Takeaways: Advanced Cervical Cancer (1/3)

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

KEYNOTE-826
Phase III trial comparing KEYTRUDA (pembrolizumab) plus chemotherapy to chemotherapy alone in advanced cervical cancer. The study showed a statistically significant improvement in overall survival for the immunotherapy group.

PD-L1 Testing
Most experts test for PD-L1 in advanced cervical cancer patients. The presence of PD-L1 expression is associated with better outcomes in immunotherapy treatment.

Management
Immunotherapy is becoming a standard part of the management for advanced cervical cancer, particularly for patients with PD-L1 expression. The KEYNOTE-826 regimen is a key example of this approach.

Key Takeaways: Advanced Cervical Cancer (2/3)

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

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

Key Takeaway 1: [Blurred text]

Key Takeaway 2: [Blurred text]

Key Takeaway 3: [Blurred text]

Key Takeaways: Advanced Cervical Cancer (3/3)

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

KEYNOTE-A18
Phase III, Randomized, Controlled Trial
Comparing Pembrolizumab + Chemotherapy vs. Chemotherapy
in Advanced Cervical Cancer

KEYNOTE-826
Phase III, Randomized, Controlled Trial
Comparing Pembrolizumab + Chemotherapy vs. Chemotherapy
in Cervical Cancer

KEYNOTE-858
Phase III, Randomized, Controlled Trial
Comparing Pembrolizumab + Chemotherapy vs. Chemotherapy
in Cervical Cancer

KEYNOTE-859
Phase III, Randomized, Controlled Trial
Comparing Pembrolizumab + Chemotherapy vs. Chemotherapy
in Cervical Cancer

KEYNOTE-860
Phase III, Randomized, Controlled Trial
Comparing Pembrolizumab + Chemotherapy vs. Chemotherapy
in Cervical Cancer

KEYNOTE-861
Phase III, Randomized, Controlled Trial
Comparing Pembrolizumab + Chemotherapy vs. Chemotherapy
in Cervical Cancer

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Abbreviations

Abbreviations

- > 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
- > *gBRCA*, 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
- > *tBRCA*, 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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