



EPICS

Global Perspectives in Gynecologic Malignancies at ESMO 2021

22 September 2021

FULL REPORT

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VIRTUAL CLOSED-DOOR ROUNDTABLE



DATE:
22 September 2021



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



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



PANEL: Key experts in
gynecologic oncology
> 4 from US
> 4 from Europe



**GYNECOLOGIC CANCER-
SPECIFIC DISCUSSIONS** on
therapeutic advances and
their application in clinical
decision-making

Panel Consisting of 4 US and 4 European Gynecologic Cancer Experts

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



Leslie Randall, MD, MAS
Virginia Commonwealth
University Health
Massey Cancer Center



Ursula Matulonis, MD
Dana-Farber Cancer
Institute



Mansoor Mirza, MD
Copenhagen University
Hospital



Jonathan Ledermann, MD
Cancer Research UK
London and UCL Cancer
Trials Centre



**Christina Fotopoulou,
MD, PhD**
Imperial College London



Nicoletta Colombo, MD, PhD
European Institute of Oncology



CHAIR:
Robert Coleman, MD
FACOG, FACS
US Oncology Network



Meeting Agenda (1/2)

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Time (EDT)	Topic	Speaker/Moderator
9.00 AM – 9.05 AM	Welcome, Introductions, and Meeting Objectives	Robert Coleman, MD, FACOG, FACS
9.05 AM – 9.20 AM	First-Line Treatment and Maintenance Therapy for Advanced Ovarian Cancer	Christina Fotopoulou, MD, PhD
9.20 AM – 9.45 AM	Key Questions and Topics for Discussion	Robert Coleman, MD, FACOG, FACS
9.45 AM – 9.50 AM	Key Takeaways	Christina Fotopoulou, MD, PhD; Robert Coleman, MD, FACOG, FACS
9.50 AM – 10.05 AM	Treatment Strategies for Relapsed Ovarian Cancer	Mansoor Mirza, MD
10.05 AM – 10.30 AM	Key Questions and Topics for Discussion	Robert Coleman, MD, FACOG, FACS
10.30 AM – 10.35 AM	Key Takeaways	Mansoor Mirza, MD Robert Coleman, MD, FACOG, FACS
10.35 AM – 10.50 AM	Current Treatment and Future Directions for Advanced Endometrial Cancer	Ursula Matulonis, MD
10.50 AM – 11.15 AM	Key Questions and Topics for Discussion	Robert Coleman, MD, FACOG, FACS
11.15 AM – 11.20 AM	Key Takeaways	Ursula Matulonis, MD; Robert Coleman, MD, FACOG, FACS



Meeting Agenda (2/2)

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Time (EDT)	Topic	Speaker/Moderator
11.20 AM – 11.25 AM	Break	
11.25 AM – 11.40 AM	Advanced Cervical Cancer: Current and Future Treatment in First Line	David O'Malley, MD
11.40 AM – 12.05 PM	Key Questions and Topics for Discussion	Robert Coleman, MD, FACOG, FACS
12.05 PM – 12.10 PM	Key Takeaways	David O'Malley, MD; Robert Coleman, MD, FACOG, FACS
12.10 PM – 12.25 PM	Recurrent Cervical Cancer: Current and Future Treatments	Leslie M. Randall, MD, MAS
12.25 PM – 12.50 PM	Key Questions and Topics for Discussion	Robert Coleman, MD, FACOG, FACS
12.50 PM – 12.55 PM	Key Takeaways	Leslie M. Randall, MD, MAS; Robert Coleman, MD, FACOG, FACS
12.55 PM – 1.00 PM	Conclusion and Wrap-up	Robert Coleman, MD, FACOG, FACS



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GLOBAL PERSPECTIVES



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First-Line Treatment and Maintenance Therapy for Advanced Ovarian Cancer



Global Perspectives in Gynecologic Malignancies – ESMO 2021

(1/3)

Presented by Christina Fotopoulou, MD, PhD

Current Landscape of Frontline Ovarian Cancer

Ovarian cancer has seen recent changes in systemic treatments

STAGE POPULATION

1. 2019-2020: 200,000 patients with ovarian cancer, 150,000 with early-stage disease, 50,000 with advanced disease. 100,000 patients with early-stage disease, 50,000 with advanced disease. 100,000 patients with early-stage disease, 50,000 with advanced disease. 100,000 patients with early-stage disease, 50,000 with advanced disease.

STAGE POPULATION

2. 100,000 patients with early-stage disease, 50,000 with advanced disease. 100,000 patients with early-stage disease, 50,000 with advanced disease. 100,000 patients with early-stage disease, 50,000 with advanced disease.

KEY POINT CONCLUSIONS

1. 100,000 patients with early-stage disease, 50,000 with advanced disease. 100,000 patients with early-stage disease, 50,000 with advanced disease. 100,000 patients with early-stage disease, 50,000 with advanced disease.





Global Perspectives in Gynecologic Malignancies – ESMO 2021

(2/3)

Presented by Christina Fotopoulou, MD, PhD

PARP Inhibitors

PARP inhibitors have shown strong efficacy as maintenance therapy, both alone or in combination with bevacizumab

STUDY POPULATION

1. 1000 patients with BRCA1/2 mutation, advanced ovarian cancer, after platinum-based chemotherapy. 500 patients received PARP inhibitor (olaparib) and 500 patients received placebo. The primary endpoint was overall survival (OS). The median OS was 13.4 months in the olaparib group and 11.7 months in the placebo group. The hazard ratio (HR) for OS was 0.77 (95% CI 0.63-0.94). The p-value was 0.016.

RESULTS

2. 1000 patients with BRCA1/2 mutation, advanced ovarian cancer, after platinum-based chemotherapy. 500 patients received PARP inhibitor (olaparib) and 500 patients received placebo. The primary endpoint was overall survival (OS). The median OS was 13.4 months in the olaparib group and 11.7 months in the placebo group. The hazard ratio (HR) for OS was 0.77 (95% CI 0.63-0.94). The p-value was 0.016.

KEY TAKEAWAYS

3. PARP inhibitors have shown strong efficacy as maintenance therapy, both alone or in combination with bevacizumab.





Global Perspectives in Gynecologic Malignancies – ESMO 2021

(3/3)

Presented by Christina Fotopoulou, MD, PhD

Choice of First-Line Therapy

When choosing frontline therapy, advisors are strongly guided

Immunotherapy

Immunotherapy has not yet demonstrated efficacy in ovarian



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Key Insights: First-Line and Maintenance Therapy for Advanced Ovarian Cancer

Approaches to Biomarker Testing in Ovarian Cancer

Testing Algorithms

Experience with biomarker testing in ovarian cancer varies between countries, and between institutions within the same country

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Frontline Therapy

Most advisors would prefer to use PARP inhibitors in the first line and

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Dr Ledermann:

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Treatment Strategies for Relapsed Ovarian Cancer



Treatment Strategies for Relapsed Ovarian Cancer (1/3)

Presented by Mansoor Mirza, MD

Landscape of Platinum-Sensitive, Relapsed Ovarian Cancer

More patients now live with ovarian cancer as a chronic disease, due to recent advancements in treatment

Chemotherapy

The addition of the novel antiangiogenic drug, bevacizumab (BVZ), to the platinum-based chemotherapy regimen has been shown to be a significant benefit for the platinum-sensitive population of relapsed ovarian cancer (RSC).

- Patients who received platinum-based chemotherapy with bevacizumab and antiangiogenic therapy in the platinum-sensitive population had significantly better overall survival (OS) compared to patients who received platinum-based chemotherapy without bevacizumab.
- The addition of bevacizumab to platinum-based chemotherapy in the platinum-sensitive population was associated with a statistically significant improvement in OS compared to platinum-based chemotherapy without bevacizumab.

Targeted Therapy in Platinum-Sensitive RSC

There are clinical trials with the aim to "build up" the platinum-based chemotherapy regimen by adding targeted therapy to address improved results from chemotherapy.

- The addition of an anti-HER2 drug (trastuzumab, TDM) may provide the necessary chemotherapy cell death required by the activity of TDM in the platinum-sensitive population, as shown in the MARIAN study. The addition of trastuzumab to platinum-based chemotherapy in platinum-sensitive RSC was associated with a statistically significant improvement in OS compared to platinum-based chemotherapy without TDM.
- The use of novel targeted therapies (TDM) may increase chemotherapy, hormonal therapy, immunotherapy, and targeted therapy (TDM) use in platinum-sensitive RSC. Research is continuing with novel and existing targeted therapy. Clinical responses, suggesting that TDM can be effective in building up a team.





Treatment Strategies for Relapsed Ovarian Cancer (2/3)

Presented by Mansoor Mirza, MD

Sequencing Therapy in the Relapsed Setting

Restrictions on reuse of bevacizumab and PARP inhibitors has led to limited options for treatment in relapsed disease

Bevacizumab

The addition of the vascular endothelial growth factor (VEGF) inhibitor bevacizumab to the platinum-based chemotherapy regimen has been shown to improve overall survival in patients with relapsed ovarian cancer (R2OC).

- Patients who received bevacizumab with platinum-based chemotherapy and anti-metastatic agents in the adjuvant setting had significantly better overall survival, progression-free survival, and time to treatment failure compared to patients who received platinum-based chemotherapy alone.
- The addition of bevacizumab to platinum-based chemotherapy is not recommended in patients who have received bevacizumab in the adjuvant setting.

PARP Inhibitors

There are clinical trials with the aim to "test out" the timing of PARP inhibitor use to increase effectiveness in patients with relapsed disease from chemotherapy.

- The addition of an anti-metastatic drug (metastatic agent) may provide the necessary chemotherapy and anti-metastatic agents to the extent of PARP inhibition, as shown in the BRCA1/2 study. The addition of bevacizumab to platinum-based chemotherapy in patients with relapsed disease is not recommended with PARP inhibitors.
- The use of bevacizumab with platinum-based chemotherapy and anti-metastatic agents may increase overall survival and progression-free survival in patients with relapsed disease. However, the addition of bevacizumab to platinum-based chemotherapy is not recommended in patients who have received bevacizumab in the adjuvant setting.





Treatment Strategies for Relapsed Ovarian Cancer (3/3)

Presented by Mansoor Mirza, MD

Immunotherapy

Immunotherapy has not yet shown efficacy in relapsed ovarian

Immunotherapy

The addition of the immune checkpoint inhibitor (ICI) to the chemotherapy regimen may increase the immunogenicity of a chemotherapy regimen. The addition of immune checkpoint inhibitors (ICIs) to relapsed ovarian cancer (ROC) patients with disease progression with chemotherapy and immunotherapy combination in the adjuvant and first-line setting is being evaluated. ICIs, including pembrolizumab, nivolumab, ipilimumab, and atezolizumab, have been used in combination with chemotherapy in patients with ROC. The addition of pembrolizumab to first-line chemotherapy in ROC patients with disease progression with chemotherapy and immunotherapy combination in the adjuvant and first-line setting is being evaluated. The addition of pembrolizumab to first-line chemotherapy in ROC patients with disease progression with chemotherapy and immunotherapy combination in the adjuvant and first-line setting is being evaluated.

ADCs

Folate receptor alpha-targeted ADCs have shown interesting

Folate receptor alpha-targeted ADCs

There are clinical trials with the aim to "boost up" the tumor killing potential by increasing immunogenicity to address resistance to chemotherapy. The addition of an antibody drug conjugate (ADC) may provide the necessary immunogenic cell death required for the activity of ICI in the ICI+ population, as shown in the IMMU-100 trial. The addition of immunotherapy to ICI+ population is being evaluated. The use of immune checkpoint inhibitors (ICIs) may increase immunogenicity, immunogenicity, immunogenicity, and increase ICI response rates. Pembrolizumab is combined with capecitabine and irinotecan in relapsed ovarian cancer patients, suggesting that ICI+ can be effective in treating ROC.



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Key Insights: Relapsed Ovarian Cancer

Sequencing Drugs in Platinum-Sensitive Relapse

Treatment of Platinum-Sensitive Ovarian Cancer

Advisors anticipate increased use of bevacizumab in the relapsed setting with the uptake of PARP inhibitors in the first line

KEY TAKEAWAYS

- Advisors anticipate increased use of bevacizumab in the relapsed setting with the uptake of PARP inhibitors in the first line
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ADVISOR COMMENTARY

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Advisors anticipate increased use of bevacizumab in the relapsed setting with the uptake of PARP inhibitors in the first line

PARP Inhibitor Reuse

PARP inhibitors could potentially be reused in some patients, on

Choice of PARP Inhibitor

> Advisors generally feel that all 3 available PARP inhibitors have

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Emerging Therapies for Platinum-Resistant Disease

Advisors feel ADCs will be game-changers for ovarian cancer

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Rebiopsy After Relapse

The BRIDGEROCK study in the UK found a shift in genomic



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Current Treatment and Future Directions for Advanced Endometrial Cancer



Endometrial Cancer (1/4)

Presented by Ursula Matulonis, MD

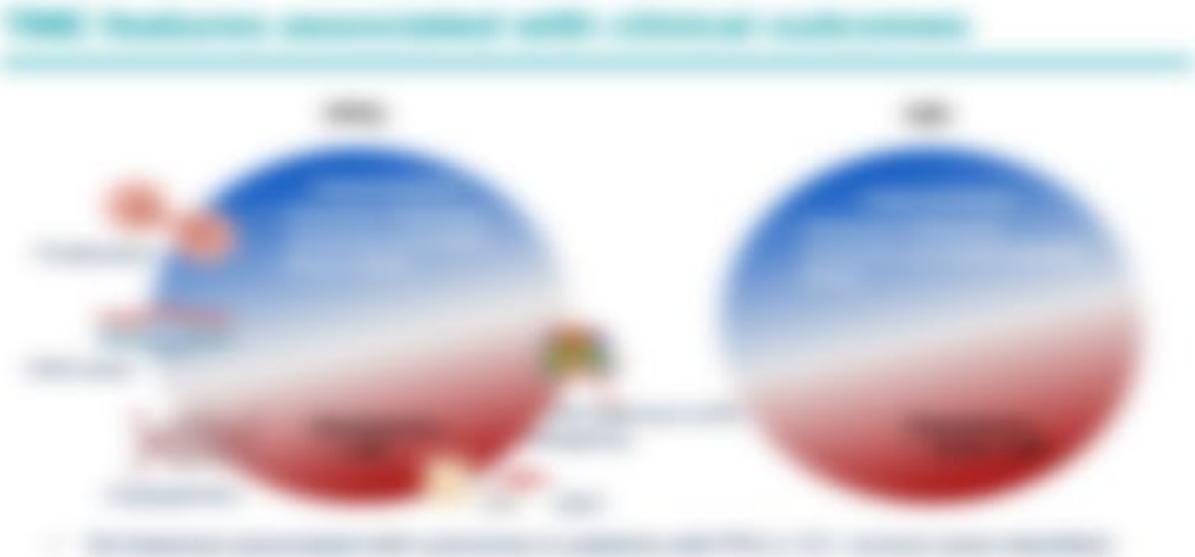
Landscape of Advanced Endometrial Cancer in 2021

Incidence of endometrial cancer in the US and worldwide is

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Molecular Subtyping of Endometrial Tumors

Molecular subtypes are used when making treatment decisions





Endometrial Cancer (2/4)

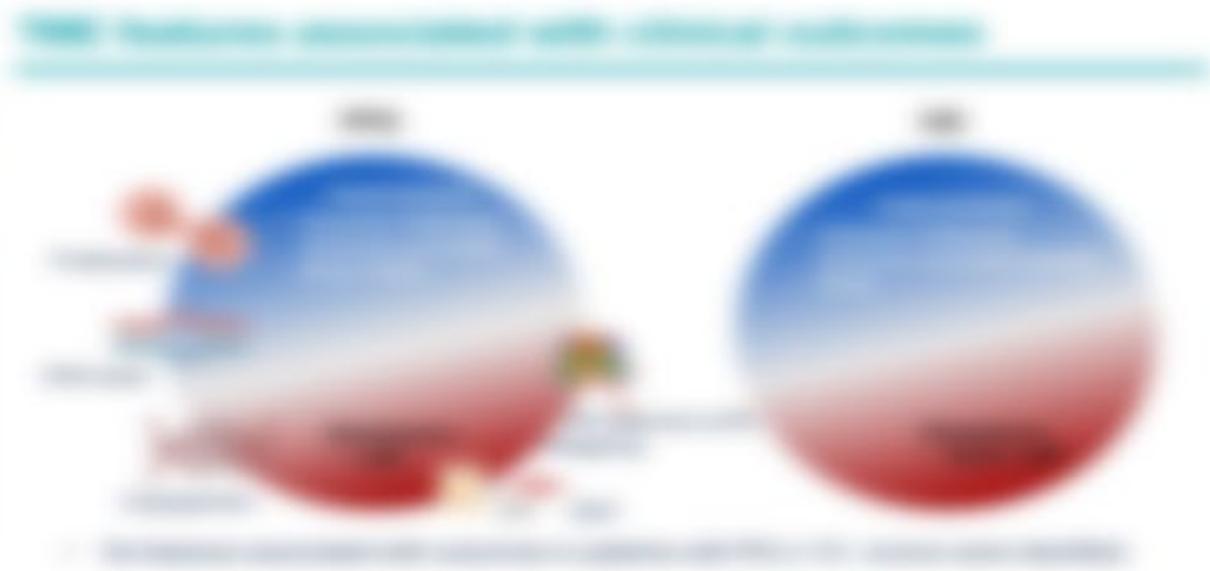
Presented by Ursula Matulonis, MD

HER2-Targeted Approaches

Trastuzumab may play a role in treating patients with HER2-

Trastuzumab + Carboplatin-Paclitaxel

Overall survival vs. Trastuzumab, advanced USPC





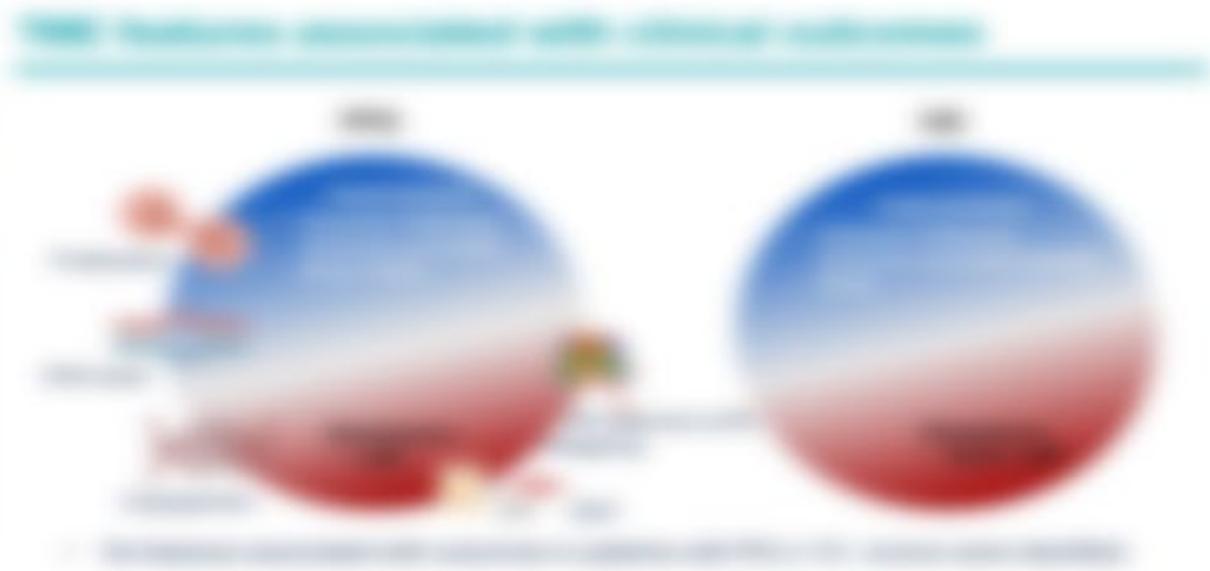
Endometrial Cancer (3/4)

Presented by Ursula Matulonis, MD

Pembrolizumab + Lenvatinib (KEYNOTE-775)

The phase III KEYNOTE-775 study demonstrated that pembro +

KEYNOTE-775: PFS by BICR





Endometrial Cancer (4/4)

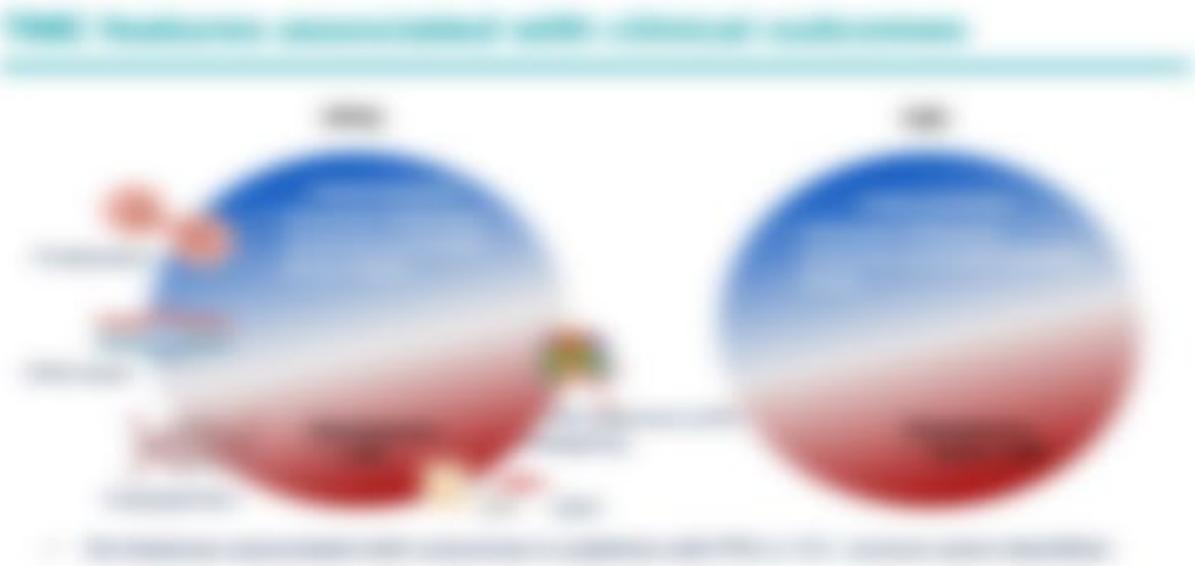
Presented by Ursula Matulonis, MD

Wee1 Inhibitors

Wee1 inhibitors have shown promising results in patients with

CDK4/6 Inhibitors

Early data suggest the combination of a CDK4/6 inhibitor + AI is



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Key Insights: Advanced Endometrial Cancer

Molecular Characterization

Advisors agreed that molecular characterization is an important part of patient workup in endometrial cancer

Molecular Classification of Endometrial Cancer (The Cancer Genome Atlas)



Evolving Treatment Landscape of Advanced Endometrial Cancer

Frontline Immunotherapy

Ongoing trials are investigating the addition of IO to frontline chemotherapy. However, advisors question whether carboplatin-

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Advanced Cervical Cancer: Current and Future Treatment in First Line



First-Line Advanced, Metastatic Cervical Cancer: Current and Future Treatment (2/3)

Presented by David O'Malley, MD

KEYNOTE-826

KEYNOTE-826 is a phase III, randomized, controlled trial comparing pembrolizumab plus platinum-based chemotherapy with placebo plus chemotherapy in patients with advanced, metastatic cervical cancer. The primary endpoint is overall survival (OS). Secondary endpoints include progression-free survival (PFS), objective response rate (ORR), and quality of life. The trial is currently ongoing and has not yet reached its primary endpoint.

- Pembrolizumab plus chemotherapy is superior to placebo plus chemotherapy in terms of OS in patients with advanced, metastatic cervical cancer.
- Pembrolizumab plus chemotherapy is superior to placebo plus chemotherapy in terms of PFS, ORR, and quality of life.
- The overall survival benefit is maintained in patients with PD-L1 expression.



Timeline of FDA Approvals for HER2+ Breast Cancer

Year	Drug	Indication
2012	Trastuzumab	HER2+ Breast Cancer
2013	Trastuzumab emtansin	HER2+ Breast Cancer
2015	Trastuzumab deruxtecan	HER2+ Breast Cancer
2017	Trastuzumab	HER2+ Breast Cancer (Adjuvant)
2018	Trastuzumab	HER2+ Breast Cancer (Neoadjuvant)
2019	Trastuzumab	HER2+ Breast Cancer (Adjuvant)
2020	Trastuzumab	HER2+ Breast Cancer (Adjuvant)
2021	Trastuzumab	HER2+ Breast Cancer (Adjuvant)





First-Line Advanced, Metastatic Cervical Cancer: Current and Future Treatment (3/3)

Presented by David O'Malley, MD

Additional Trials of Frontline Immunotherapy

Emerging Therapies

In addition to KEYNOTE-826, several other trials are moving

LN-145 TIL therapy received Breakthrough Therapy designation

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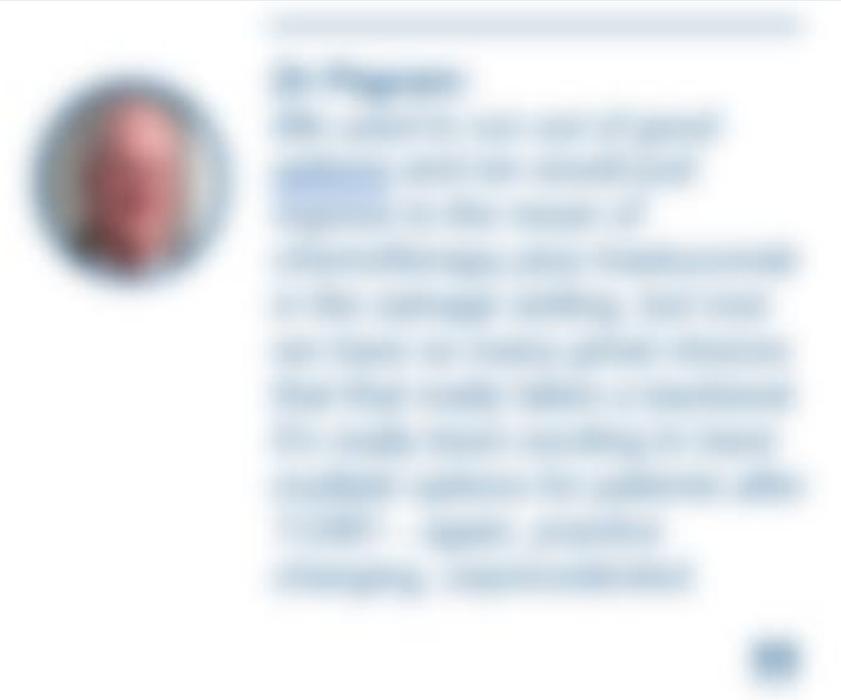


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Key Insights: First-Line Treatment of Advanced Cervical Cancer

KEYNOTE-826 Results

Advisors are excited about the results of KEYNOTE-826, and see adding pembrolizumab to frontline treatment as the new standard of care



The Role of PD-L1 Status in Frontline Cervical Cancer

PD-L1 Status in KEYNOTE-826

Although KEYNOTE-826 was positive for all-comers, advisors

The Future Role of PD-L1 Testing

The PD-L1-low population was underpowered in KEYNOTE-826,

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Recurrent Cervical Cancer: Current and Future Treatments



Recurrent Cervical Cancer and the Evolving Therapeutic Landscape (2/3)

Presented by Leslie Randall, MD, MAS

Tisotumab Vedotin

Accelerated approval for tisotumab vedotin (TV) is significantly changing the cervical cancer treatment landscape; TV has shown

STUDY POPULATION

Phase 1b study, 100 patients with recurrent, locally advanced or metastatic cervical cancer. 50 patients received TV (100 mg q2w) and 50 patients received best supportive care (BSC). Primary endpoint: overall survival (OS). Secondary endpoints: progression-free survival (PFS), quality of life (QoL), and safety.

RESULTS

OS was significantly improved in the TV group compared to the BSC group (HR: 0.58, 95% CI: 0.38-0.88, p=0.008). PFS was also significantly improved in the TV group (HR: 0.45, 95% CI: 0.28-0.73, p=0.001). QoL was significantly improved in the TV group. Safety profile was acceptable.

KEY CONCLUSIONS

TV significantly improved OS and PFS compared to BSC in patients with recurrent, locally advanced or metastatic cervical cancer. TV is a promising treatment option for this population.





Recurrent Cervical Cancer and the Evolving Therapeutic Landscape (3/3)

Presented by Leslie Randall, MD, MAS

TILs

LN-145 autologous TILs received FDA Breakthrough Therapy

STUDY POPULATION

Phase 1 study of LN-145 autologous TILs in patients with recurrent cervical cancer. The study included 20 patients with recurrent cervical cancer who had received prior treatment with platinum-based chemotherapy and radiation therapy. The patients were treated with LN-145 autologous TILs and followed up for 24 weeks. The study showed that LN-145 autologous TILs were well tolerated and induced an immune response in all patients. The study also showed that LN-145 autologous TILs were effective in treating recurrent cervical cancer, with a response rate of 50%.

RESULTS

LN-145 autologous TILs were well tolerated and induced an immune response in all patients. The study also showed that LN-145 autologous TILs were effective in treating recurrent cervical cancer, with a response rate of 50%.

KEY TAKEAWAYS

LN-145 autologous TILs are a promising treatment option for recurrent cervical cancer. The study showed that LN-145 autologous TILs were well tolerated and induced an immune response in all patients. The study also showed that LN-145 autologous TILs were effective in treating recurrent cervical cancer, with a response rate of 50%.

Other Emerging Therapies

Recurrent treatment options are moving toward combination IO

RESPONSE RATES IN RECURRENT CERVICAL CANCER

RESPONSE RATES IN RECURRENT CERVICAL CANCER

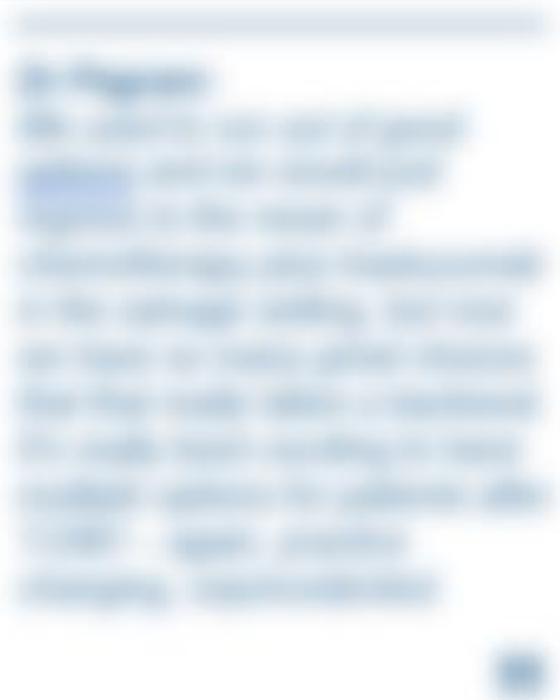
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Key Insights: Recurrent Cervical Cancer

Sequencing in Recurrent Cervical Cancer

Sequencing After Frontline IO

> With advisors anticipating adoption of IO in frontline therapy, those



Treatment Approaches in Recurrent Cervical Cancer

Tisotumab Vedotin

Advisors were divided on the necessity of ocular assessment

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HPV-Based Approaches

Advisors feel we need to do a better job utilizing the preventive

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