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Global Perspectives in Gynecologic Malignancies at ESMO 2021

22 September 2021

FULL REPORT

Report Contents

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Meeting Snapshot

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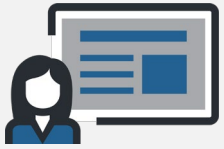
VIRTUAL CLOSED-DOOR ROUNDTABLE

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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Ursula Matulonis, MD
Dana-Farber Cancer Institute

Mansoor Mirza, MD
Copenhagen University Hospital

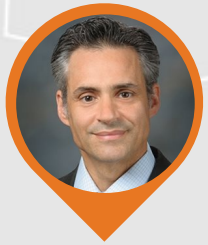
David O'Malley, MD
The Ohio State University Comprehensive Cancer Center

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

Christina Fotopoulou, MD, PhD
Imperial College London

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

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 PM – 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

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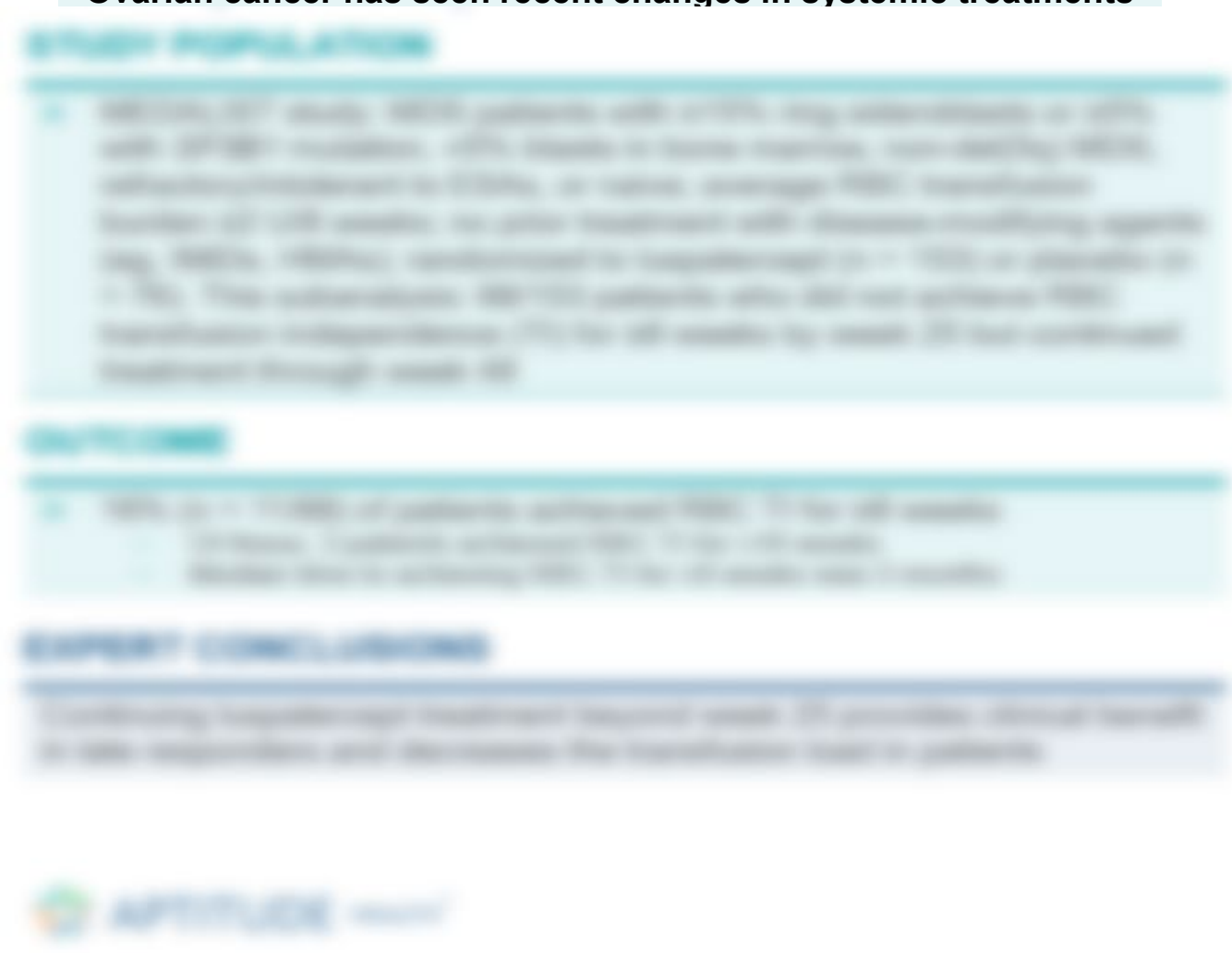
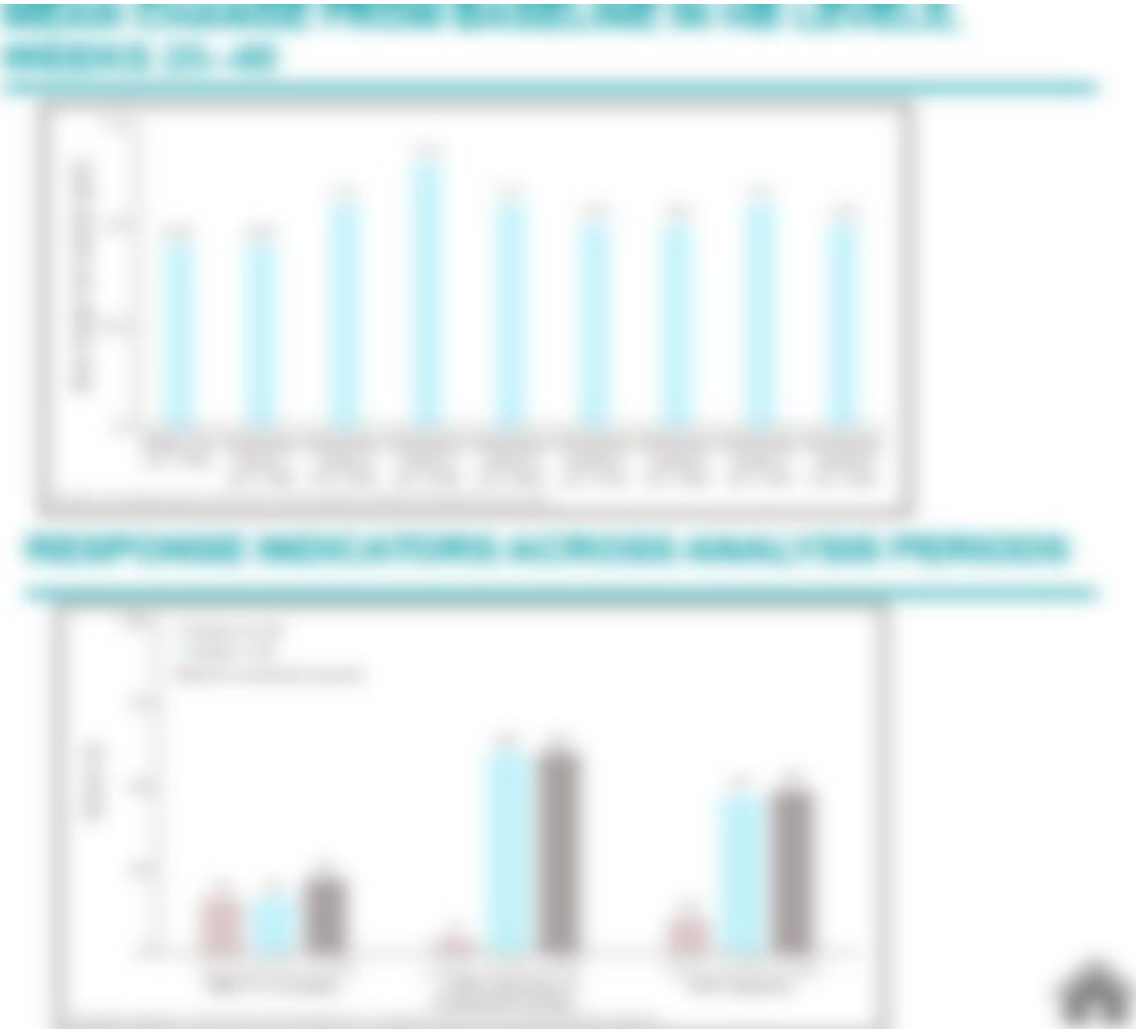
Current Landscape of Frontline Ovarian Cancer

Ovarian cancer has seen recent changes in systemic treatments





Global Perspectives in Gynecologic Malignancies – ESMO 2021 (2/3)

Presented by Christina Fotopoulou, MD, PhD

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PARP Inhibitors

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

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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

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Testing Algorithms

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

Expert Perspectives on the Frontline Setting

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Frontline Therapy

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

“

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

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Landscape of Platinum-Sensitive, Relapsed Ovarian Cancer

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

[redacted]

[redacted]

Treatment Strategies for Relapsed Ovarian Cancer (2/3)

Presented by Mansoor Mirza, MD

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Sequencing Therapy in the Relapsed Setting

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

[redacted]

[redacted]

*Presented at ESMO 2021.

Treatment Strategies for Relapsed Ovarian Cancer (3/3)

Presented by Mansoor Mirza, MD

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Immunotherapy

Immunotherapy has not yet shown efficacy in relapsed ovarian

ADCs

Folate receptor alpha-targeted ADCs have shown interesting

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Key Insights: Relapsed Ovarian Cancer

Sequencing Drugs in Platinum-Sensitive Relapse

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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

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PARP Inhibitors in Platinum-Sensitive Relapse

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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

Rebiopsy and Platinum-Resistant Disease

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Emerging Therapies for Platinum-Resistant Disease

Advisors feel ADCs will be game-changers for ovarian cancer

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

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Landscape of Advanced Endometrial Cancer in 2021

Incidence of endometrial cancer in the US and worldwide is

Molecular Subtyping of Endometrial Tumors

Molecular subtypes are used when making treatment decisions

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dMMR, mismatch repair deficient; MSI-H, microsatellite instability-high; TMB, tumor mutation burden.

Endometrial Cancer (2/4)

Presented by Ursula Matulonis, MD

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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

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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

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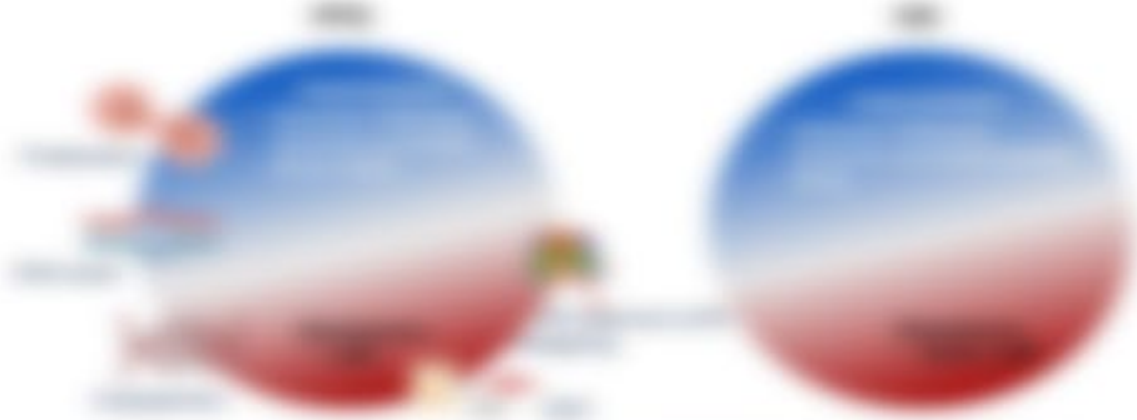
Wee1 Inhibitors

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 in Endometrial Cancer

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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)

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Evolving Treatment Landscape of Advanced Endometrial Cancer

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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 (1/3)

Presented by David O'Malley, MD

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Current Frontline Treatment Landscape

The addition of bevacizumab to frontline chemotherapy has helped to further increase survival in cervical cancer

- [illegible] for HER2+ mBC between 2019-2020, dramatically expanding options and improving outcomes for patients
- National Comprehensive Cancer Network (NCCN) guidelines recommend a CLEOPATRA-like regimen including a taxane, trastuzumab, and pertuzumab for first-line therapy, and T-DM1 for second-line therapy
  - Newer agents or regimens such as trastuzumab deruxtecan, tucatinib plus trastuzumab and capecitabine, neratinib plus capecitabine, and margetuximab, are recommended in the third line and beyond
  - Trastuzumab deruxtecan is preferred post T-DM1 for patients with visceral metastases
  - The tucatinib triplet is preferred post T-DM1 for patients with CNS metastases

Timeline of FDA Approvals for HER2+ Breast Cancer

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[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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						[illegible]

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1985 1997 2005 2009 2013

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

Presented by David O'Malley, MD

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KEYNOTE-826

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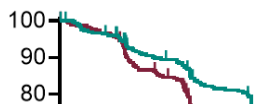

KEYNOTE-826: All-Comer PFS

12-mo rate (95% CI)
44.7% (38.8-50.4)

Timeline of FDA Approvals for HER2+ Breast Cancer

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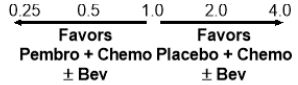

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*Presented at ESMO 2021.

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

Presented by David O'Malley, MD

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Additional Trials of Frontline Immunotherapy

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

Emerging Therapies

LN-145 TIL therapy received Breakthrough Therapy designation

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*Presented at ESMO 2021.

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Key Insights: First-Line Treatment of Advanced Cervical Cancer

KEYNOTE-826 Results

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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

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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 (1/3)

Presented by Leslie Randall, MD, MAS

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Treatment Landscape of Recurrent Cervical Cancer

Chemotherapy options for recurrent cervical cancer have

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

Presented by Leslie Randall, MD, MAS

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Tisotumab Vedotin

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

STUDY POPULATION

OUTCOMES

EXPERT CONCLUSIONS

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

Presented by Leslie Randall, MD, MAS

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TILs

LN-145 autologous TILs received FDA Breakthrough Therapy

Other Emerging Therapies

Recurrent treatment options are moving toward combination IO

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Key Insights: Recurrent Cervical Cancer

Sequencing in Recurrent Cervical Cancer

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Sequencing After Frontline IO

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

Treatment Approaches in Recurrent Cervical Cancer

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Tisotumab Vedotin

Advisors were divided on the necessity of ocular assessment

HPV-Based Approaches

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

APTITUDE HEALTH®

US Headquarters
5901-C Peachtree Dunwoody Road NE
Suite 200, Atlanta, GA 30328, US

EU Headquarters
Wilhelmina van Pruisenweg 104
2595 AN The Hague, the Netherlands

aptitudehealth.com