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EPICS

EPICS: Breast Cancer in 2022 and Beyond

April 22 and 23, 2022

Report Contents

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Meeting Snapshot

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VIRTUAL CLOSED-DOOR ROUNDTABLE

DATES:
April 22 and 23, 2022

DISEASE-STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in breast cancer

> 10 from the US

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

Panel Consisting of 10 US Breast Cancer Experts

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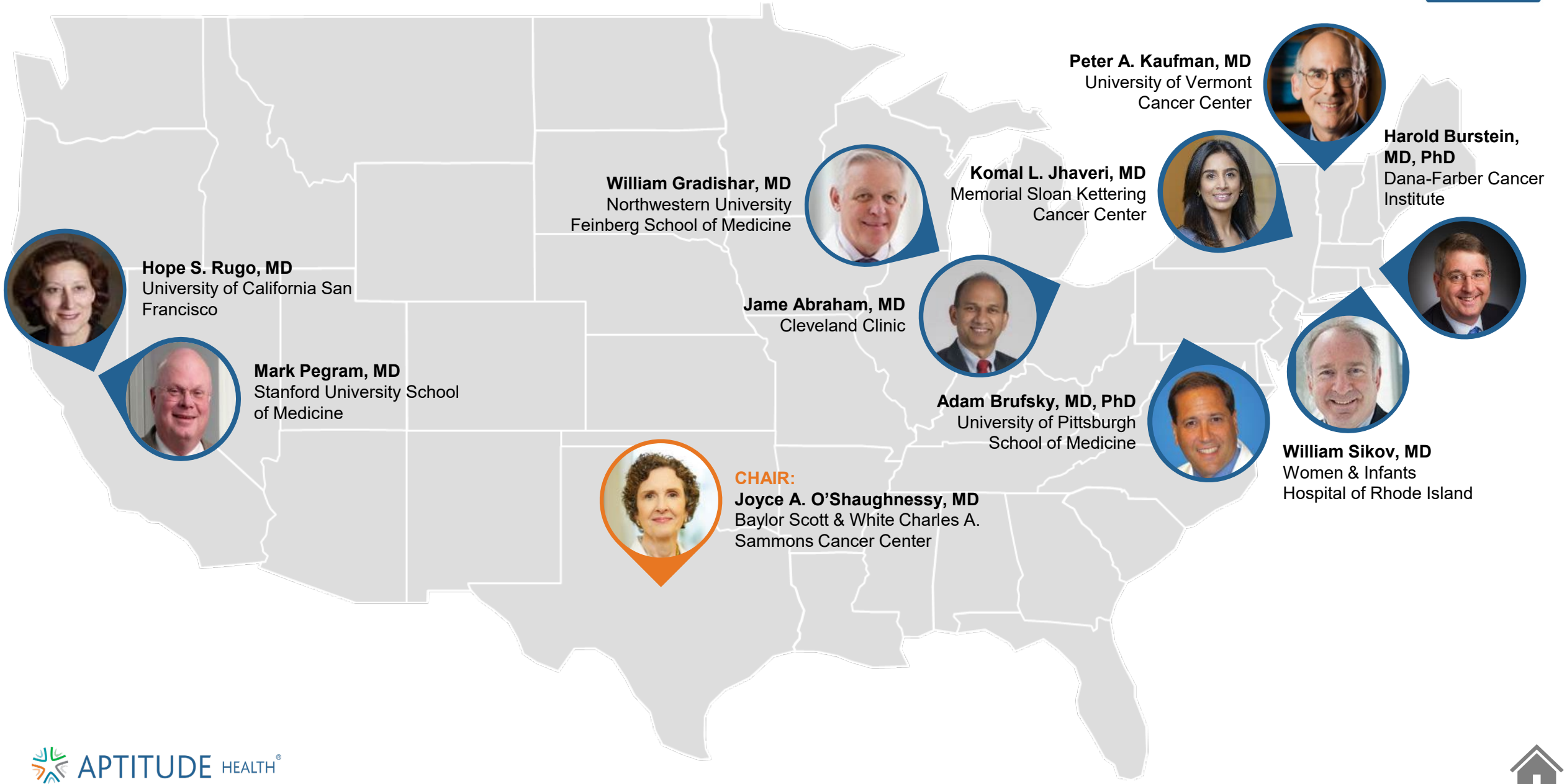

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Meeting Agenda: Day 1 – Friday, April 22, 2022

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Time	Topic	Speaker/Moderator
4.00 PM – 4.10 PM	Welcome and Introductions	Joyce O'Shaughnessy, MD
4.10 PM – 4.30 PM	Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer	William Sikov, MD
4.30 PM – 4.55 PM	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
4.55 PM – 5.00 PM	Summary and 3 Key Takeaways	William Sikov, MD
5.00 PM – 5.20 PM	New Standards in HER2+ Early Breast Cancer	William Gradishar, MD
5.20 PM – 5.55 PM	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
5.55 PM – 6.00 PM	Summary and 3 Key Takeaways	William Gradishar, MD
6.00 PM – 6.15 PM	BREAK	
6.15 PM – 6.35 PM	Maximizing Potential Targeting of HER2 in HER2+ and HER2-Low ABC	Mark Pegram, MD
6.35 PM – 7.15 PM	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
7.15 PM – 7.20 PM	Summary and 3 Key Takeaways	Mark Pegram, MD
7.20 PM – 7.30 PM	Standard and Emerging Strategies for High-Risk Early-Stage Triple-Negative Breast Cancer	Jame Abraham, MD
7.30 PM – 7.50 PM	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
7.50 PM – 7.55 PM	Summary and 3 Key Takeaways	Jame Abraham, MD
7.55 PM – 8.00 PM	Wrap-up and Overview of Day 2 Activities	Joyce O'Shaughnessy, MD

Meeting Agenda: Day 2 – Saturday, April 23, 2022

EPICS

Time	Topic	Speaker/Moderator
10.00 AM – 10.05 AM	Introduction and Review Agenda for Day 2	Joyce O'Shaughnessy, MD
10.05 AM – 10.20 AM	Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer	Hope Rugo, MD, FASCO
10.20 AM – 10.50 AM	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
10.50 AM – 10.55 AM	Summary and 3 Key Takeaways	Hope Rugo, MD, FASCO
10.55 AM – 11.10 AM	Therapeutic Horizons in HR+ Advanced Breast Cancer	Komal L. Jhaveri, MD, FACP
11.10 AM – 11.50 AM	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
11.50 AM – 11.55 AM	Summary and 3 Key Takeaways	Komal L. Jhaveri, MD, FACP
11.55 AM – 12.10 PM	BREAK	
12.10 PM – 12.20 PM	Therapeutic Horizons in HR+ Early Breast Cancer	Harold Burstein, MD, PhD, FASCO
12.20 PM – 12.40 PM	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
12.40 PM – 12.45 PM	Summary and 3 Key Takeaways	Harold Burstein, MD, PhD, FASCO
12.45 PM – 12.55 PM	Old and New Targets in Breast Cancer	Peter Kaufman, MD
12.55 PM – 1.20 PM	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
1.20 PM – 1.25 PM	Summary and 3 Key Takeaways	Peter Kaufman, MD
1.25 PM – 1.55 PM	General Discussion: Future Directions in Breast Cancer Treatment	Adam Brufsky, MD, PhD, FACP
1.55 PM – 2.00 PM	Conclusions and Wrap-up	Joyce O'Shaughnessy, MD

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Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer

Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer (1/2)

Presented by William Sikov, MD

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Genetic testing in BC

Extending use of genetic testing in BC

Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer (2/2)

Presented by William Sikov, MD

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Genomic testing is recommended by ASCO in early BC

STUDY POPULATION

OUTCOME

EXPERT CONCLUSIONS

Discussion: Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer (1/4)

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Genetic testing is extending in BC

Experts extend genetic testing beyond NCCN guideline recommendations to include patients with BRCAness in

Discussion: Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer (2/4)

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Genetic testing (cont), next-generation sequencing

Discussion: Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer (3/4)

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Ki67 testing

Discussion: Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer (4/4)

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Genomic testing in eBC

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New Standards in HER2+ Early BC

New Standards in HER2+ Early BC

Presented by William Gradishar, MD

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Anti-HER2 treatment is SOC

> Trastuzumab-containing regimens improved patient outcomes,

Optimizing treatment in HER2+ eBC

> The KATHERINE trial established 1 year of adjuvant T-DM1 as

Discussion: New Standards in HER2+ Early BC (1/3)

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Dual HER2 blockade plus chemotherapy

Dual anti-HER2 blockade (trastuzumab-pertuzumab) plus chemotherapy has become the standard clinical

Discussion: New Standards in HER2+ Early BC (2/3)

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Novel adjuvant approaches

T-DM1 is SOC for patients with residual disease after neoadjuvant therapy on the basis of the KATHERINE

Discussion: New Standards in HER2+ Early BC (3/3)

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Recurrence in 1L

Sequencing strategies are evolving for patients with recurrent disease after (neo)adjuvant therapy

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Maximizing Potential in HER2+ and HER2-Low ABC

Maximizing Potential in HER2+ and HER2-Low ABC (1/3)

Presented by Mark Pegram, MD

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Current treatment landscape

> Current treatment approaches in HER2+ mBC are based on CNS involvement and previous treatment responses

- [illegible] 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 regimen is preferred post T-DM1 for patients with CNS metastases

Maximizing Potential in HER2+ and HER2-Low ABC (2/3)

Presented by Mark Pegram, MD

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HER2+ mBC with brain mets

> On the basis of the HER2CLIMB study, tucatinib combination has

Attempted coup to dethrone CLEOPATRA in the frontline

> THP is SOC in frontline, on the basis of the CLEOPATRA trial

Maximizing Potential in HER2+ and HER2-Low ABC (3/3)

Presented by Mark Pegram, MD

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Second and later lines in HER2+ mBC

> T-DXd showed extraordinary results in DESTINY-Breast03 with

HER2-low

> HER2-low patients showed HER2 FISH– results but expressed +

Discussion: Evolving Standards of Care in HER2+ mBC (1/5)

EPICS

Current treatment landscape and treatment sequencing

Current standard approaches include a CLEOPATRA-like regimen (taxane-trastuzumab-pertuzumab) in 1L, and T-DXd and tucatinib

- [illegible] 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

Discussion: Evolving Standards of Care in HER2+ mBC (2/5)

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Refining usage of available treatments

Margetuximab is an efficacious alternative to trastuzumab; however, its activity is dependent on Fc

Timeline of FDA Approvals for HER2+ Breast Cancer

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Discussion: Evolving Standards of Care in HER2+ mBC (3/5)

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Assessment and treatment of patients with active or stable brain mets

On the basis of the DB-03 results, more experts use MRI to screen patients for possible brain mets, to

- [illegible] 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
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Timeline of FDA Approvals for HER2+ Breast Cancer

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

Discussion: Evolving Standards of Care in HER2+ mBC (4/5)

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Future developments: Combinations vs sequencing

Experts are impressed by the observed PFS benefit in the DESTINY-Breast03 trial and discussed the

Discussion: Evolving Standards of Care in HER2+ mBC (5/5)

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A new class in BC: HER2-low

Identification of HER2-low patients may be a challenge for some institutions

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Dr Kaufman:
IHC for this low-level HER2 overexpression is really a less-

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Standard and Emerging Strategies for High-Risk Early-Stage TNBC

Standard and Emerging Strategies for High-Risk Early-Stage TNBC

Presented by Jame Abraham, MD

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Current standards of (neo)adjuvant TNBC treatment

> In KEYNOTE-522, the addition of pembrolizumab to neoadjuvant

Open questions in eTNBC

> The optimal usage of available treatments in early TNBC

Discussion: Standard and Emerging Strategies for High-Risk Early-Stage TNBC (1/4)

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Chemotherapies in neoadjuvant TNBC

Chemotherapy with paclitaxel plus anthracycline is SOC in early TNBC; next step for more-intensive

Timeline of FDA Approvals for HER2+ Breast Cancer

Discussion: Standard and Emerging Strategies for High-Risk Early-Stage TNBC (2/4)

EPICS

Pembrolizumab is a new standard in high-risk (neo)adjuvant TNBC

Pembrolizumab in combination with neoadjuvant platinum-based chemotherapy and as monotherapy in the adjuvant setting is a new

Discussion: Standard and Emerging Strategies for High-Risk Early-Stage TNBC (3/4)

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Adjuvant olaparib is a new standard for patients with *BRCA* mutation

Experts are impressed with the survival data in the OlympiA trial with olaparib maintenance for

Timeline of FDA Approvals for HER2+ Breast Cancer

Discussion: Standard and Emerging Strategies for High-Risk Early-Stage TNBC (4/4)

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The future of early TNBC treatment

Experts discussed the potential of new treatments with ADCs, novel CDK4/6 inhibitors, and AKT

Timeline of FDA Approvals for HER2+ Breast Cancer

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Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer

Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer (1/4)

Presented by Hope Rugo, MD, FASCO

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TNBC classification

> TNBC is a collection of heterogeneous diseases. Intrinsic

PARPi in TNBC

> The OlympiAD and EMBRACA trials showed a significant PFS

Schettini et al, NPJ Breast Cancer 2021

N=673 N=701 N=325

Luminal A Luminal B HER2-enriched Basal-like Normal-like

Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer (2/4)

Presented by Hope Rugo, MD, FASCO

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Immune checkpoint inhibitors

- Pembrolizumab added to chemotherapy showed survival

ADCs in TNBC (1/2)

- Sacituzumab govitecan, an anti-TOPO2 ADC with irinotecan

Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer (3/4)

Presented by Hope Rugo, MD, FASCO

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ADCs in TNBC (2/2)

- In the DAISY trial, T-DXd showed impressive response rates in

AKTi and novel CDK4/6i in TNBC

- TNBC has alterations in PIK3CA/AKT1/PTEN pathway and

Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer (4/4)

Presented by Hope Rugo, MD, FASCO

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AR as target in TNBC

> Androgen receptor-targeted therapies are under investigation in

The biomarker hunt

> A broad range of TNBC biomarkers are shown in the biomarker

Discussion: Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer (1/2)

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PD-L1 testing, chemotherapies in mTNBC

PD-L1 testing and NGS are generally ordered for TNBC patients; streamlined testing is needed for

Discussion: Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer (2/2)

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Standard approaches in mTNBC

Chemotherapy with pembrolizumab followed by pembrolizumab maintenance is the standard 1L regimen for patients with PD-L1+ mTNBC

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Therapeutic Horizons in HR+ Advanced Breast Cancer

Therapeutic Horizons in HR+ Advanced Breast Cancer (1/3)

Presented by Komal L. Jhaveri, MD, FACP

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Clinical pathway for treatment of HR+, HER2– mBC

> CDK4/6i in combination with ET is the standard first-line

Key data summary from CDK4/6i trials

> Each of the currently available CDK4/6i has been prospectively shown to

Therapeutic Horizons in HR+ Advanced Breast Cancer (2/3)

Presented by Komal L. Jhaveri, MD, FACP

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Key data summary from PI3Ki trials

> Multiple studies targeting the PI3K/mTOR pathway have shown mPFS of

Resistance mechanisms to CDK4/6i and/or ET

> Resistance to CDK4/6 inhibition and/or ET presents a

Therapeutic Horizons in HR+ Advanced Breast Cancer (3/3)

Presented by Komal L. Jhaveri, MD, FACP

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Ongoing research

> Novel combinations with CDK4/6i are currently being studied in HR+, HER2– advanced disease

Discussion: Therapeutic Horizons in HR+ Advanced Breast Cancer (1/3)

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CDK4/6 inhibitors

CDK4/6i plus ET are first-line SOC for most patients with HR+ metastatic disease

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Discussion: Therapeutic Horizons in HR+ Advanced Breast Cancer (2/3)

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CDK4/6 inhibitors (cont.)

The post-CDK4/6 space is heterogeneous, and treatment of patients who

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Discussion: Therapeutic Horizons in HR+ Advanced Breast Cancer (3/3)

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ER-targeting agents including oral SERDs

Experts highlighted the importance of efficacious treatment for patients with ET-refractory disease. Novel treatments targeting ER,

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Therapeutic Horizons in HR+ Early Breast Cancer

Therapeutic Horizons in HR+ Early Breast Cancer (1/2)

Presented by Harold Burstein, MD, PhD, FASCO

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Neoadjuvant therapy: Chemotherapy vs ET

> Neoadjuvant chemotherapy confers the highest advantages in

Incorporation of genomic assays into HR+ BC

> The 21-gene Oncotype DX Recurrence Score is the most widely

Therapeutic Horizons in HR+ Early Breast Cancer (2/2)

Presented by Harold Burstein, MD, PhD, FASCO

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Adjuvant therapy: Optimal treatment duration of ET

> Traditionally, the standard treatment for adjuvant ET was 5 years, but multiple studies now suggest that patients with early-stage HR+ BC,

Discussion: Therapeutic Horizons in HR+ Early Breast Cancer (1/2)

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(Neo)adjuvant treatment for HR+ BC

ER+ BC is the most heterogeneous among all BC subtypes and requires a great deal of individualized decision-

Discussion: Therapeutic Horizons in HR+ Early Breast Cancer (2/2)

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Role of adjuvant CDK4/6 inhibition

While the positive results from the monarchE trial are encouraging, the conflicting results from other adjuvant CDK4/6i trials raise questions

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Old and New Targets in Breast Cancer

Old and New Targets in Breast Cancer (1/2)

Presented by Peter A. Kaufman, MD

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Oral taxanes

> Development of cytotoxic agents remains important in the

Functionally activating *HER2* mutations as therapeutic targets

> *HER2* mutations in the absence of gene amplification or protein overexpression

Old and New Targets in Breast Cancer (2/2)

Presented by Peter A. Kaufman, MD

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ADCs

> ADCs are changing the treatment of relapsed BC, and are

Vaccines

> Vaccines show promise, but remain in development

Discussion: Old and New Targets in Breast Cancer (1/2)

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Ongoing developments

Data with oral taxane look interesting

Discussion: Old and New Targets in Breast Cancer (2/2)

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DESTINY-Breast04 and TROPICS-2

Experts look forward to the detailed findings of DESTINY-

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Future Directions in Breast Cancer Treatment

Discussion: Future Directions in Breast Cancer Treatment (1/2)

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Remaining gaps: (Neo)Adjuvant setting

Better diagnostic tools are needed in early-stage disease, especially in TNBC and high-risk HR+ tumors, to better identify and stratify patients

Discussion: Future Directions in Breast Cancer Treatment (2/2)

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Remaining gaps: Metastatic setting

While there have been huge therapeutic advances in the metastatic setting, particularly in HER2+ BC, a high unmet need for better

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*CASES: Aptitude Health Community Access via Scientific Exchange Series. CASES programs are regional peer-to-peer educational and data-collection events where 10–15 oncologists and hematologists from community practices along with leading scientific experts gather to discuss data on distinct clinical care patterns and market issues that drive treatment decisions. Insight reports are then developed to reflect these discussions that yield a wealth of information about community practices.

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