EPICS

Breast Cancer in 2023 and Beyond

Friday, May 19, 2023, 2.00 PM – 6.00 PM CDT
Saturday, May 20, 2023, 8.00 AM – 12.00 PM CDT

Chair: Joyce O'Shaughnessy, MD
Texas Oncology – Baylor Scott & White Charles A. Sammons Cancer Center

Faculty:

Peter A. Kaufman, MD	University of Vermont Cancer Center
Hope S. Rugo, MD	UCSF Helen Diller Family Comprehensive Cancer Center
William Sikov, MD	Women & Infants Hospital of Rhode Island
Heather McArthur, MD, MPH	University of Texas Southwestern Medical Center
Peter Beitsch, MD	Dallas Surgical Group
Banu Arun, MD	University of Texas MD Anderson Cancer Center
Kelly McCann, MD, PhD	UCLA Medicine

AGENDA

Day 1

Time (CDT)	Topic	Presenter
2.00 PM – 2.10 PM (10 min)	**Welcome and Introductions**	Joyce O'Shaughnessy, MD
2.10 PM – 2.25 PM (15 min)	**Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer** • Current standards: ER/PgR, HER2, *BRCA1/2*, *PIK3CA*, PD-L1, *ESR1*, Ki67(?) • Investigational biomarkers (eg, *PALB2*, HRD) • Prognostic and predictive genomic assays • NGS • ctDNA, CTCs, etc	William Sikov, MD
2.25 PM – 2.50 PM (25 min)	**Key Questions and Topics for Discussion** • Which biomarkers do you consider standard to test for (and which do you test for) – In early-stage breast cancer? – In advanced/metastatic disease? • Do you use prognostic/predictive gene expression assays to make decisions about chemotherapy (in aBC or neoadjuvant)? Extended adjuvant endocrine therapy? In which patients? • How has the availability of therapy for HER2-low mBC changed testing paradigms for HER2?	Joyce O'Shaughnessy, MD

	– Does HER2 testing methodology need to evolve to become more quantitative? – What are the implications of a HER2 IHC >0, <1 category? – Do you retest if results come back "negative"? What will you do in the future for IHC 0 patients? • When do you test for *ESR1* and *PIK3CA* mutations? If NGS is performed at diagnosis, do you retest after endocrine therapy? • Is there still a role for assessing Ki67 in patients with ER+, HER2– early BC in light of the recent label change for abemaciclib? • Are there any other biomarkers that have shown promise or are close to being ready for routine clinical use? Are there any emerging markers of CDK4/6 inhibitor resistance? • How does NGS testing fit into your practice? When and where do you use it? • Aside from testing for *PIK3CA* mutations in ctDNA, are there any other routine uses for ctDNA or CTC testing at this time? Where do you see these technologies being used in the future? – Is there a role for ctDNA/CTC MRD monitoring for surveillance in early-stage disease? What about late-stage disease? • Which of your HR+, HER2– patients do you test for g*BRCA*? (What are the triggers for g*BRCA* testing – diagnosis, patient profile, tumor type [eg, TNBC])? • Are there other gene mutations in which you consider using a PARP inhibitor (eg, *PALB2*, s*BRCA*m, PTEN)? Why or why not?	
2.50 PM – 2.55 PM (5 min)	**Summary and 3 Key Takeaways**	
2.55 PM – 3.10 PM (15 min)	**The Changing Landscape of HER2+ Early Breast Cancer** • Current adjuvant and neoadjuvant options, including patient selection – Dual targeting of HER2 (APHINITY) – Extended adjuvant therapy (ExteNET) – Residual disease (KATHERINE) – De-escalation (APT, ATEMPT) • Identifying appropriate patients for adjuvant and neoadjuvant treatment • Ongoing trials (eg, CompassHER2 RD, DESTINY-Breast05, eMonarcHER [enrollment suspended after 1 yr, results expected 2024])	Joyce O'Shaughnessy, MD

3.10 PM – 3.35 PM (25 min)	**Key Questions and Topics for Discussion**
	• What has changed in the management of early-stage HER2+ breast cancer over the past year?
	• What criteria do you use to estimate recurrence risk in patients with HER2+ early-stage breast cancer?
	  – Is the HER2DX assay ready for prime time?
	• Is neoadjuvant therapy now the standard for most patients?
	  – When do you go directly to surgery followed by adjuvant therapy?
	  – If you do not use neoadjuvant therapy, do you typically use an APHINITY or ExteNET adjuvant approach?
	• For patients with residual disease at highest risk for recurrence, do you consider extending adjuvant therapy with neratinib following T-DM1?
	• Is adjuvant therapy necessary if a patient achieves a pCR with neoadjuvant therapy?
	  – How would you treat a patient with high-risk disease who achieves a pCR with neoadjuvant therapy?
	• What is your treatment approach for patients with low-risk HER2+ breast cancer? When do you use a de-escalated approach, and what is your preferred regimen?
	  – Do all patients with early-stage HER2+ BC receive HER2-targeted therapy? If not, how do you make this decision?
	• Where do you see the future for stage II–III HER2+ breast cancer? How do you see your (neo)adjuvant approaches changing in the next 2–3 years?
	  – How do you think results from ongoing trials investigating novel agents such as tucatinib, T-DXd, and/or CDK4/6 inhibitors could impact paradigms for early-stage disease?
		Joyce O'Shaughnessy, MD

3.35 PM – 3.40 PM (5 min)	**Summary and 3 Key Takeaways**	
3.40 PM – 3.55 PM (15 min)	BREAK	

3.55 PM – 4.10 PM (15 min)	**Maximizing Potential Targeting of HER2 in HER2+ mBC**
	• Current algorithm(s) with available agents
	  – Trastuzumab, pertuzumab, T-DM1, T-DXd, tucatinib, neratinib, margetuximab
	  ▪ Data in CNS metastases
	• Optimal patient selection and sequencing
	  – Cancer aggressiveness
	  – Brain metastases
	  – Comorbidities
	• Investigational drugs and combinations
	  – ADCs: SYD985, RC48-ADC (disitamab vedotin)
		Kelly McCann, MD, PhD

	– Pyrotinib, poziotinib – CDK4/6 inhibitors – Immune checkpoint inhibitors – PI3K inhibitors	
4.10 PM – 4.35 PM (25 min)	**Key Questions and Topics for Discussion** • How has the management of HER2+ mBC changed over the past year? How do you see it continuing to evolve? • Where do the recently approved agents fit into the treatment algorithm? – How have the results of the DESTINY-Breast03 trial impacted the algorithm? Is T-DXd now the preferred second-line option? Where does T-DM1 fit now? – Does the algorithm change if the patient has brain metastases? ▪ Do emerging data with T-DXd in patients with CNS involvement influence your decision, or is tucatinib still preferred on the basis of HER2CLIMB? ▪ What are your thoughts on the Flatiron real-world data with tucatinib in patients with HER2+ brain mets? ▪ Has the introduction of tucatinib changed your threshold for imaging for brain metastases? ▪ How do you manage leptomeningeal metastases? – Where does margetuximab fit into your algorithm? ▪ Do you test to determine if patients are low-affinity CD16A allele carriers? – Where do other TKIs (eg, neratinib and lapatinib) fit? Is there still a role for these agents? – How does the potential for toxicities such as ILD or diarrhea influence your treatment choices? How do you prevent, monitor for, and/or manage these toxicities? ▪ Are there any factors that may identify patients at greater risk for developing ILD? • How has the use of HER2-targeted agents in the (neo)adjuvant setting affected the incidence of metastatic disease? Has the proportion of de novo HER2+ mBC vs recurrent cases changed? If so, how do you think this will impact the development of new therapies for metastatic disease? And what are the differences in the way you treat de novo cases vs recurrent cases? • As current HER2-targeted therapies move to the adjuvant setting, how will this impact the algorithms for patients with metastatic disease? – What DFI would influence you to avoid or reuse an agent already used for early-stage disease? • How do you treat patients with HER2+, HR+ mBC?	Joyce O'Shaughnessy, MD

	– Which patients receive hormonal therapy in addition to HER2 therapy? And in which lines? – What role do you see for CDK4/6 inhibitors in this setting? Will this be a first-line approach, or reserved for second line or beyond? • What is your opinion of the investigational agents and/or combinations for HER2+ mBC? Which are you most excited about? How may efficacy vs toxicity shape the future landscape with new agents? Where do you see these new agents fitting into the treatment paradigm? – Is there room for new HER2-targeted ADCs? ▪ What is your perception of the TULIP results, and where SYD985 might fit if approved? – Is there space for new HER2-targeted TKIs?	
4.35 PM – 4.40 PM (5 min)	**Summary and 3 Key Takeaways**	
4.40 PM – 4.55 PM (15 min)	**Clinical Implications of HER2-Low Breast Cancer** • Targeting HER2 in HER2-low, *HER2*-nonamplified breast cancer – T-DXd (DESTINY-Breast04, DEBBRAH, DAISY) ▪ T-DXd plus IO (BEGONIA) – Other investigational HER2-targeted agents ▪ SYD985 ▪ RC48-ADC (disitamab vedotin) ▪ ARX788	Banu Arun, MD
4.55 PM – 5.15 PM (20 min)	**Key Questions and Topics for Discussion** • How have the DESTINY-Breast04 data and subsequent approval of T-DXd for HER2-low mBC changed paradigms in breast cancer management? – Is HER2-low now a recognized disease entity, and how is it being treated? – Where does T-DXd fit into the algorithms with regard to other conventional agents for HR+ or TN mBC? What patient/disease characteristics determine when T-DXd is adopted into the treatment algorithm? After how many lines of endocrine therapy should T-DXd be used? – For what duration will T-DXd be administered (to response and then switch to endocrine therapy, to PD, or other)? • Is there sufficient precision in current lab testing to reliably distinguish between differences in low-level HER2 expression? Does this differ between academia and community? • Is there any difference in T-DXd efficacy on the basis of HER2 expression level (1+ vs 2+)? • Do PATH reports provide a breakdown of IHC score (0, 1+, 2+/ISH–) or further detail such as percentage of membrane staining?	Joyce O'Shaughnessy, MD

	• If a patient initially had HER2– early-stage breast cancer, should HER2 be retested if they recur with metastatic disease? Does a rescore of archival tissue or a rebiopsy typically happen in this clinical scenario? – Is there any role for T-DXd in HER2 IHC 0 or IHC >0, <1 mBC? – What is your perspective on DB-06? If DB-06 data showed actionability in IHC >0, <1 population, do you see a role for T-DXd in this population (what would be your clinical approach)? Would existing IHC 0 scores be retested to determine if IHC >0, <1? Would you consider this category an extension of "HER2-low," or how would you clinically define? • What are the next steps to further improve treatments for HER2-low breast cancers? What combinations should be investigated?	
5.15 PM – 5.20 PM (5 min)	**Summary and 3 Key Takeaways**	
5.20 PM – 5.35 PM (15 min)	**Standard and Emerging Strategies for High-Risk, Early-Stage, Triple-Negative Breast Cancer** • PARP inhibitors – (Neo)adjuvant trials in *BRCA*m breast cancers • Immunotherapy-chemotherapy combinations – (Neo)adjuvant data (KEYNOTE-522, NeoPACT, I-SPY 2, IMpassion031, NeoTRIPaPDL1) – Implications of GeparNuevo, GeparDouze, KEYNOTE-242 (SWOG) • Neoadjuvant platinum data • Adjuvant chemotherapy and/or immunotherapy for patients with residual disease (CREATE-X) • Investigational strategies (eg, sacituzumab govitecan)	Heather McArthur, MD, MPH
5.35 PM – 5.55 PM (20 min)	**Key Questions and Topics for Discussion** • How do you assess risk in patients with early-stage TNBC? – Is intensification of systemic therapy always necessary, or are there some patients with "low-risk" disease for whom systemic therapy may be de-escalated or even omitted? • What types of genomic or molecular testing do you routinely perform for your patients with early-stage TNBC? – *BRCA*? PD-L1/CPS score? MSI? HRD? Other? – Whom do you test? Whom do you not test? Why or why not? – If you test for PD-L1 and MSI in early stage, why? What would trigger you to test at early stage?	Joyce O'Shaughnessy, MD

	– What are the barriers/challenges of testing at the community level? What strategies would you suggest to improve testing in the community? • How have the OlympiA and KEYNOTE-522 trials changed treatment paradigms for early-stage TNBC? – Is preoperative pembro now standard for all patients with early-stage TNBC? ▪ Are there patients in whom you WOULD NOT use preop pembro? Why? ▪ For patients who achieve a pCR, do you always continue with adjuvant pembro? – In which patients with g*BRCA*m TNBC do you use adjuvant olaparib (rather than pembro)? Is there any role for olaparib in preoperative regimens? – For a patient with high-risk *BRCA*m TNBC with residual disease, would you consider both adjuvant olaparib and pembrolizumab? – For a patient with high-risk *BRCA* WT TNBC with residual disease, would you consider both adjuvant pembrolizumab and capecitabine? • Do you see a potential role for sacituzumab govitecan, T-DXd, or other ADCs in earlier-disease settings? – What opportunities and challenges will exist for ADCs in TNBC early-disease setting? • How concerned are you about AEs associated with agents in the early-stage curative setting, such as potentially long-term irAEs? Do you monitor and/or manage AEs differently in early-stage vs metastatic disease? – What are the implications for drug development in this setting? • What other new agents or approaches to the treatment of high-risk early-stage TNBC are you most enthusiastic about? • What are the future roles for radiation therapy plus IO (and/or other systemic therapies) for patients with residual disease? What is the approach (eg, which agents, used in combination or sequentially)?	
5.55 PM – 6.00 PM (5 min)	**Summary and 3 Key Takeaways**	
6.00 PM	**Wrap-up and Overview of Day 2 Activities**	Joyce O'Shaughnessy, MD

Day 2

Time (CDT)	Topic	Presenter
8.00 AM – 8.05 AM (5 min)	**Introduction and Review Agenda for Day 2**	Joyce O'Shaughnessy, MD
8.05 AM – 8.20 AM (15 min)	**Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer** • Emerging biomarker-based subtypes within TNBC • PARP inhibitors (olaparib, talazoparib, other investigational PARPi) – Metastatic trials only in g*BRCA*m BC (OlympiAD, EMBRACA, BROCADE3) – PARP inhibitors beyond g*BRCA*m breast cancers – Combinations with immunotherapy • Immunotherapy-chemotherapy combinations (pembrolizumab) – PD-L1/CPS scoring • ADCs – Sacituzumab govitecan (approved) – Ladiratuzumab vedotin, datopotamab deruxtecan (investigational) • Investigational approaches – IO-IO (NIMBUS) – PI3K/AKT inhibitors (ipatasertib, capivasertib) – CDK4/6 inhibitors (trilaciclib) – AR+: androgen receptor-signaling inhibitors	William Sikov, MD
8.20 AM – 8.50 AM (30 min)	**Key Questions and Topics for Discussion** • What types of genomic or molecular testing do you routinely perform for your patients with TNBC? – *BRCA*? PD-L1/CPS score? MSI? HRD? Other? – Do you perform this testing for all patients with mTNBC? – What are the barriers/challenges to this testing in the community? – What strategies would you suggest to improve testing in the community? • For patients with g*BRCA*m mTNBC, where do you place PARP inhibitors in your treatment algorithm? – How do you choose between platinum agents and PARP inhibitors for *BRCA*m mTNBC? – Do you use PARP inhibitors in patients with either somatic *BRCA* mutations or other mutations in DNA repair pathways? ▪ Is HRD testing useful in selecting patients for PARPi therapy? • For patients who are PD-L1+/CPS ≥10, where does immunotherapy fit into the treatment algorithm? – How do you decide which cytotoxic agent to pair with pembrolizumab?	Joyce O'Shaughnessy, MD

	– How would you treat a patient with g*BRCA*m, PD-L1+ mTNBC? • How has the introduction of sacituzumab govitecan changed the treatment algorithm? In which patients, and when do you use this agent? • What are your thoughts on other investigational ADCs? – What ADC combinations are of greatest interest to you? • What are your thoughts on the prospects for capivasertib and the ongoing CAPItello-290 trial in light of the negative IPATunity130 trial? • What new agents or approaches to the treatment of TNBC are you most enthusiastic about? – What are your thoughts on the potential of AR inhibitors or CDK inhibitors? – How do you envision the treatment landscape evolving in the next 3–5 years?	
8.50 AM – 8.55 AM (5 min)	**Summary and 3 Key Takeaways**	
8.55 AM – 9.05 AM (10 min)	**Therapeutic Horizons in HR+ Early Breast Cancer** • Neoadjuvant therapy • Adjuvant therapy – CDK4/6 inhibitors (monarchE, PALLAS, PENELOPE-B, NATALEE) – PARPis (OlympiA) • Duration of neo/adjuvant treatment	Peter A. Kaufman, MD
9.05 AM – 9.25 AM (20 min)	**Key Questions and Topics for Discussion** • What role do gene expression assays play in your decisions about – When to use adjuvant chemotherapy? On the basis of the results of the RxPONDER and ADAPT trials, do you use these assays in node-positive HR+ breast cancer? – When do you use extended adjuvant endocrine therapy? – Which gene expression assay(s) do you use most frequently, and do they differ by purpose/setting? • What is the expected impact of NATALEE on the treatment landscape in early HR+ breast cancer? • How does the difference in study populations for NATALEE (ie, inclusion of a broader population in HR+, HER2– eBC that includes stage II/III node positive or node negative [for stage IIA N0, an additional high-risk factor is needed: either grade 3 or grade 2+, high Ki67, or high genomic risk]) vs monarchE (ie, node-positive, high-risk, HR+, HER2– eBC) affect your perception of the activity of the respective SERDs?	Joyce O'Shaughnessy, MD

	• How do the durations of therapy in NATALEE (3 years) vs monarchE (2 years) affect your perception of these agents in eBC? • How do you interpret the conflicting results from monarchE vs PALLAS and PENELOPE-B vs NATALEE? – Do you routinely use abemaciclib for high-risk patients? ▪ How do you define high risk? Ki67 ≥20? Clinical criteria? Has the label change influenced your recommendations? – How important are OS data? – Will adjuvant use of abemaciclib impact your use of CDK4/6 inhibitors in the metastatic setting? How would the DFI influence treatment choice? Would you re-treat with CDK4/6i (same or different) in combination with AI or fulvestrant? – How do you view the future role of hormone monotherapy vs CDK4/6i-hormone combination in eBC? How will they be used, and what patients would need escalation of treatment with a CDK4/6i in addition to ET? – How might the NATALEE readout change your perception of this class, and how would it affect the treatment landscape? • How does the approval of olaparib for adjuvant treatment of g*BRCA* patients with eBC impact your current practice? – To what extent do the OlympiA OS data impact g*BRCA* testing in HR+ breast cancer, or patient hesitancy to get g*BRCA* testing in your current practice? • For high-risk g*BRCA* HR+, HER2– patients, how do you choose between adjuvant olaparib or abemaciclib? Would you ever consider using both? • What are other promising novel treatment approaches in the adjuvant and neoadjuvant HR+ setting? • How might oral SERDs potentially fit into the treatment of HR+ early-stage breast cancer in the future? – What are good trial designs to evaluate oral SERDs for early HR+ BC?	
9.25 AM – 9.30 AM (5 min)	**Summary and 3 Key Takeaways**	
9.30 AM – 9.45 AM (15 min)	**Break**	
9.45 AM – 10.00 AM (15 min)	**Therapeutic Horizons in HR+ Advanced Breast Cancer** • Established standards	Hope S. Rugo, MD

	– AIs, fulvestrant, tamoxifen – CDK4/6 inhibitors (and latest data) – Everolimus – Alpelisib (*PIK3CA* mutated) – PARP inhibitors (g*BRCA*m) • Recent additions to the armamentarium – T-DXd (HER2 low) – Elacestrant, camizestrant – Sacituzumab govitecan • Investigational drugs and regimens – AKT inhibitors (capivasertib, ipatasertib) – Other oral SERDS – ADCs – CDK7 inhibitors, samuraciclib – AURKA inhibitors – CPI-CDK4/6 combinations – Androgen receptor signaling inhibitors (enobosarm) • Other ER-targeted agents (SERMs, SERCAs, PROTACs)	
10.00 AM – 10.40 AM (40 min)	**Key Questions and Topics for Discussion** • What is your current treatment strategy for HR+, HER2– mBC? – Do all patients receive CDK4/6 inhibitors first line? If not, which patients would not receive these agents? Would prior use of a CDK4/6 inhibitor for early stage affect your use in the metastatic setting? – What is your preferred combination partner for CDK4/6 inhibitors? ▪ Does menopausal status influence your decision? – Which data drive/influence your decision? Do you perceive differences in efficacy between CDK4/6 inhibitors in the metastatic setting? ▪ Do data from the adjuvant setting influence your perception of differential efficacy? ▪ How does RWE, such as the OS data from P-REALITY X, factor into your therapy decisions? – What is the impact of sites of metastases on treatment selection? Bone, visceral, CNS? – What are your thoughts on the RIGHT Choice trial results? Is CDKi-endocrine therapy preferable in all patients? If not, when would you still use chemotherapy? – Are there any promising biomarkers to predict sensitivity or resistance to CDK4/6 inhibitors?	Joyce O'Shaughnessy, MD

	• What treatment should patients receive once their disease progresses on a CDK4/6 inhibitor? – Do you consider continuing CDK inhibition beyond progression with a switch of endocrine agent? What are your thoughts on the MAINTAIN and PACE data? – Do you test all patients with HR+ mBC for *PIK3CA* mutations? Do you test tumor tissue or ctDNA (or both)? ▪ Where does alpelisib-fulvestrant fit into your algorithm for *PIK3CA*m tumors? ▪ What is your impression of capivasertib on the basis of CAPItello-291? If approved, where would this agent fit into your algorithm? Which patients and when? ▪ What differences do you perceive between alpelisib and capivasertib? If both were available, which would you choose for a patient with *PIK3CA*m HR+ mBC? What are your thoughts on *PIK3CA*m vs AKT pathway alterations? – What are the options for patients with *PIK3CA* WT cancers? How frequently do you use everolimus? • Does *ESR1* mutation status offer any guidance to treatment choices? What are your perspectives on a ctDNA-guided switch strategy (eg, PADA-1, SERENA-6)? • Do you think *ESR1* testing will be critical for treatment selection in patients with ER+ mBC? – Is *ESR1* mutation testing available in your practice? How often is it requested? – In your perspective, what will be the feasibility of testing *ESR1*m sequentially with Guardant360 in clinical practice? • What are your impressions of the EMERALD and SERENA-2 results with oral SERDs? – Do you now test all patients with HR+, HER2– mBC for *ESR1* mutations? And when do you test? – Where does elacestrant fit into your algorithm for patients with *ESR1*m, HR+ mBC? Do you consider it a replacement for fulvestrant? Or an additional agent? – Where might other oral SERDs fit in the mBC setting? – What are your thoughts on the divergent results from the phase III trials with the other oral SERDs that have reported so far? ▪ Do you perceive any clinically relevant differences between the new SERDs on	

	the basis of the data so far? Or are the differences related to trial designs? • What are your thoughts on the TROPiCS-02 data? – Where does sacituzumab fit into your algorithm for HR+ mBC? – For patients with HER2-low, HR+ mBC, how do you sequence T-DXd and sacituzumab govitecan? • Where do PARP inhibitors fit for patients with HR+, g*BRCA*m mBC? • What are the most promising novel approaches? – Novel targets beyond CDK4/6 inhibitors? – Combinations of CDK inhibitors with other targeted agents? – Next-generation CDK inhibitors? – SERCAs and PROTACs? • Do you see any potential role for immunotherapy? Are there any promising strategies to make "cold" breast cancers "hot"?	
10.40 AM – 10.45 AM (5 min)	**Summary and 3 Key Takeaways**	
10.45 AM – 10.55 AM (10 min)	**Old and New Targets in Breast Cancer** • Cytotoxic chemotherapy – Anthracyclines, liposomal irinotecan, microtubule-targeted agents, antimetabolites, platinums, *nab*-paclitaxel – Novel cytotoxics (OPE, tesetaxel) • *HER2*m breast cancer – Neratinib • HER3 – Anti-HER3 mAbs, bispecifics, and ADCs • Other immunotherapeutic approaches (vaccines, OPT-822/OPT-821 vaccine, bispecific mAbs, and IDO inhibitors, nelipepimut-S)	Peter A. Kaufman, MD
10.55 AM – 11.20 AM (25 min)	**Key Questions and Topics for Discussion** • With the introduction of ADCs and targeted agents, do you foresee the role of conventional cytotoxics diminishing? Or will these be with us for the foreseeable future? – Is there any future for the investigational oral taxanes (OPE and tesetaxel)? • Do you perform genomic testing to identify patients with *HER2* mutations? If a *HER2* mutation is identified, do you offer neratinib or another HER2-targeted TKI? – What are your thoughts on results from the SUMMIT trial? – Should other TKIs and/or combinations be tested?	Joyce O'Shaughnessy, MD

	• What is your impression of the data with HER3-targeted agents to date? How do you see this investigational approach evolving? How should these agents be developed? • What other emerging targets are you most interested in? Where would these fit in the treatment armamentarium?	
11.20 AM – 11.25 AM (5 min)	**Summary and 3 Key Takeaways**	
11.25 AM – 11.55 AM (30 min)	**General Discussion: Future Directions in Breast Cancer Treatment** • What are the major areas of unmet need in breast cancer? Directions for research? • Are there any major differences in clinical practice between the community and academic settings? – Relevant differences in practice patterns? – Biomarker testing? – Knowledge/education gaps? – How can we improve uptake of novel treatment and/or testing approaches in the community setting? • What do you consider the biggest challenge in treating breast cancer in 2023? • How do you see the treatment of breast cancer evolving over the next 5 years? Ten years? • Do you have advice or suggestions for future clinical trial development? • Drug pricing – how do you see this evolving? • What is the importance of RWE, QOL analyses, and PROs? How useful are these data when making treatment decisions?	Joyce O'Shaughnessy, MD
11.55 AM – 12.00 PM (5 min)	**Conclusions and Wrap-up**	Joyce O'Shaughnessy, MD