APTITUDE HEALTH®

EPICS

BREAST CANCER IN 2021 AND BEYOND

Chair: Joyce O'Shaughnessy, MD

Virtual Meeting Part 1 – April 28, 2021

Time (CDT)	Topic	Speaker/Moderator
10.30 AM – 10.40 AM	Welcome and Introductions	Joyce O'Shaughnessy, MD
10.40 AM – 10.55 AM	**Evolving Paradigms in HER2+ MBC** • Available agents – Trastuzumab (IV and SC) and biosimilars, pertuzumab (IV and SC), T-DM1, lapatinib – Recently approved agents: trastuzumab deruxtecan, neratinib, tucatinib, margetuximab • Investigational approaches – Novel TKIs: pyrotinib, poziotinib – Novel ADCs: SYD985 – Combinations with ▪ CDK4/6 inhibitors ▪ Immune checkpoint inhibitors ▪ PI3K inhibitors • Optimal patient selection and sequencing • Special populations, including brain metastases, HR+/HER2+	Bill Gradishar, MD
10.55 AM – 11.40 AM	**Key Questions and Topics for Discussion** • How has the management of HER2+ breast cancer changed over the past year? How do you see it continuing to evolve? Integration of new agents? • What are the most exciting drugs/clinical trials? • Where do the recently approved agents fit into the treatment algorithm? – Does the algorithm change if the patient has brain metastases? – Has the introduction of tucatinib changed your threshold for imaging for brain metastases? – Are you testing if patients are low-affinity CD16A allele carriers? – 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? • What is the clinical relevance of new SC formulations?	All

	• As current HER2-targeted therapies move to the adjuvant setting, how will you treat patients with metastatic disease? • How do you manage HER2+/HR+ patients? – 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? – For your first-line HER2+/HR+ patients, what percentage of the time do they receive chemo as part of the regimen? For which patient types would you skip the chemo? – What are other potential treatment combinations for HER2+/HR+ disease? – Which patients receive hormonal therapy in addition to HER2 therapy? And in which lines? • What is your opinion of the investigational agents for HER2+ MBC? Is any agent more promising than another? How may efficacy vs toxicity shape the future landscape with new agents? Where do you see these new agents fitting into the treatment paradigm? • How are biosimilars impacting treatment patterns? Are clinicians adopting these alternative agents for all approved indications, or just the indication in which a trial was conducted? • Impact of COVID-19 pandemic	
11.40 AM – 11.45 AM	**Summary and 3 Key Takeaways**	
11.45 AM – 12.00 PM	**Individualizing Therapy for 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) • Assessing risk of recurrence in early breast cancer • Ongoing trials (eg, CompassHER2 RD, DESTINY-Breast05, eMonarcHER)	Mark Pegram, MD
12.00 PM – 12.35 PM	**Key Questions and Topics for Discussion** • What is your current standard of care for neoadjuvant therapy for HER2+ breast cancer? – Are there additional patients who would benefit from neoadjuvant therapy who do not receive it today? How do we ensure these patients receive appropriate treatment? – Do all patients receive trastuzumab-containing therapy? If not, how do you make this decision?	All

	– Have you incorporated pertuzumab into the neoadjuvant setting, or do you prefer trastuzumab-chemo alone? – Are there any patients for whom you consider adjuvant, rather than neoadjuvant, therapy? In what settings are you using an APHINITY or ExteNET adjuvant approach? • How do you assess risk of recurrence for HER2+ disease? – How do you manage a patient with high-risk disease who achieves a pCR with neoadjuvant therapy? – How do you manage a patient with very high-risk disease with residual disease after neoadjuvant therapy? Is there any role for further extension of adjuvant therapy after T-DM1? • What is your management approach for patients with low-risk HER2+ breast cancer? When do you use a de-escalated approach, and what is your preferred regimen? • 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 does use of HER2-targeted regimens in the (neo)adjuvant setting impact your treatment of metastatic disease and how is this changing? • Impact of COVID-19 pandemic	
12.35 PM – 12.40 PM	**Summary and 3 Key Takeaways**	
12.40 PM – 12.50 PM	BREAK	
12.50 PM – 1.05 PM	**Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer** • Biomarker testing and subtypes • PARP inhibitors (olaparib, talazoparib, other investigational PARPi) – Metastatic trials only (OlympiAD, EMBRACA, BROCADE3) – *BRCA*-mutated breast cancers – PARP inhibitors beyond g*BRCA*-mutated breast cancers – Combinations with immunotherapy • Immunotherapy/chemotherapy combinations (atezolizumab, pembrolizumab) – PD-L1/CPS+ – Metastatic data only (IMpassion130/131 and KEYNOTE-355, single-agent trials)	Priyanka Sharma, MD

	• ADCs: sacituzumab govitecan (approved), ladiratuzumab vedotin (investigational) • Investigational approaches – PI3K/AKT inhibitors (ipatasertib, capivasertib) – Novel cytotoxics (OPE, tesetaxel) – AR+: androgen receptor-signaling inhibitors – CDK4/6 inhibitors (trilaciclib)	
1.05 PM – 1.45 PM	**Key Questions and Topics for Discussion** • What types of genomic or molecular testing are you routinely doing for your patients with TNBC? – BRCA? PD-L1/CPS score? MSI? HRD? Other? – Do you do this testing for all patients with metastatic TNBC? – What strategies would you suggest to improve testing in the community? • For patients with g*BRCA*-mutated mTNBC, where do you place PARP inhibitors in your treatment algorithm? – How do you choose between platinum agents and PARP inhibitors for *BRCA*-mutated mTNBC? – Does platinum chemotherapy add benefit for other TNBC subtypes? – Are you using 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 paradigm? – Which PD-(L)1 test do you utilize most? – How do you explain the differences between atezolizumab and pembrolizumab in combination with standard paclitaxel? Are you comfortable using cytotoxics other than *nab*-paclitaxel? Does this influence your choice of ICI? – How would you manage a patient with g*BRCA*-mutated, PD-L1+ mTNBC? • How has the introduction of sacituzumab govitecan changed the treatment algorithm? In which patients and when are you using this agent? – Is TROP2 biomarker testing important for patient selection for sacituzumab? – What ADC combinations are of greatest interest to you? – What are your thoughts on other investigational ADCs?	All

	• How do you interpret the results of the IPATunity130 trial, and what can we learn from this trial for the design of future trials and the development of other new targeted agents? – Thoughts on capivasertib and the ongoing CAPItello-290 trial? • What is your perception of the investigational oral taxanes (OPE and tesetaxel)? Where would these agents fit into the algorithm if approved? • How do you view the potential of AR inhibitors in TNBC? • What are your thoughts on the strategy of using CDK4/6 inhibitors for TNBC? • What other new agents or approaches to the treatment of TNBC are you most enthusiastic about? • Impact of COVID-19 pandemic	
1.45 PM – 1.50 PM	**Summary and 3 Key Takeaways**	
1.50 PM – 2.00 PM	Wrap-up and Overview of Day 2	Joyce O'Shaughnessy, MD

Virtual Meeting Part 2 – May 3, 2021

Time (CDT)	Topic	Speaker/Moderator
9.30 AM – 9.35 AM	Introduction and Review of Agenda	Joyce O'Shaughnessy, MD
9.35 AM – 9.45 AM	**Standard and Emerging Strategies for High-Risk Early Stage Triple-Negative Breast Cancer** • PARP inhibitors – Ongoing (neo)adjuvant trials in *BRCA*-mutated breast cancers (OlympiA, I-SPY2, BRE09-146, BrighTNess, PARTNER) • Immunotherapy-chemotherapy combinations (atezolizumab, pembrolizumab) – Neoadjuvant data (I-SPY2, KEYNOTE-522, IMpassion031, NeoTRIPaPDL1) • Neoadjuvant platinum data • Adjuvant chemotherapy for patients with residual disease (CREATE-X) – Investigational strategies	Hope Rugo, MD, FASCO
9.45 AM – 10.05 AM	**Key Questions and Topics for Discussion** • What types of genomic or molecular testing are you routinely doing for your patients with early stage TNBC? – BRCA? PD-L1/CPS score? MSI? HRD? Other?	All

	– What strategies would you suggest to improve testing in the community? • Do you see a role at the current time for either PARP inhibitors or immune checkpoint inhibitors in earlier disease settings outside of a clinical trial? • Do you see a potential role for sacituzumab govitecan or other ADCs in earlier disease settings? • How do you manage patients with early stage TNBC? How frequently is neoadjuvant therapy used? Do you recommend additional adjuvant chemotherapy to patients with residual disease? • What other new agents or approaches to the treatment of high-risk early stage TNBC are you most enthusiastic about? • Impact of COVID-19 pandemic	
10.05 AM – 10.10 AM	**Summary and 3 Key Takeaways**	
10.10 AM – 10.20 AM	**Novel Targets in Breast Cancer** • Targeting HER2 in HER2-low, HER2-nonamplified breast cancer – Trastuzumab deruxtecan, SYD985 • *HER2*-mutated breast cancer – Neratinib • HER3 – Anti-HER3 mAbs, bispecifics, and ADCs	Sara Tolaney, MD, MPH
10.20 AM – 10.40 AM	**Key Questions and Topics for Discussion** • How do you define “HER2 low”? How are you currently managing HER2-low patients? • What are your thoughts on preliminary data with HER2-targeted ADCs (trastuzumab deruxtecan, SYD985) in this population? – Would you consider use of a HER2-targeted ADC outside of a clinical trial? • Do you do genomic testing to identify patients with *HER2* mutations? If a *HER2* mutation is identified, do you offer neratinib or another HER2-targeted TKI? • 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?	All
10.40 AM – 10.45 AM	**Summary and 3 Key Takeaways**	
10.45 AM – 11.00 AM	**Evolving Treatments and New Developments in HR+ Metastatic Breast Cancer**	Peter Kaufman, MD

	• Current standards – AIs, tamoxifen – CDK4/6 inhibitors (palbociclib, ribociclib, abemaciclib) – PI3K pathway and mTOR inhibitors (eg, alpelisib, everolimus) – PARP inhibitors (*BRCA*-mutated MBC) • Investigational combination regimens incorporating targeted agents – PI3K/AKT inhibitors (buparlisib, pictilisib, taselisib, capivasertib, ipatasertib) – SERDs and SERCAs: RAD1901, SAR439859, GDC-9545, AZD9833, LY3484356, rintodestrant, H3B-6545, and others – AURKA inhibitors – ICI-CDK4/6 combinations – Androgen receptor agonists – ADCs: sacituzumab govitecan	
11.00 AM – 11.30 AM	**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? – What is your preferred combination partner for CDK4/6 inhibitors? – Does menopausal status influence your decision? – What is the typical duration of treatment? – What is the impact of sites of metastases on treatment selection? Bone, visceral, CNS? – How does prior treatment in the adjuvant setting influence choice of endocrine partner? • How are you selecting between available CDK4/6 inhibitors? Do you personalize your selection on the basis of patient factors (eg, disease burden, comorbidities, age, metastatic site), or use the same agent in every patient? Are they interchangeable? In specific settings? • Can RWE data on CDK4/6 be useful in your treatment decision-making process? What kind of data? – Where can RWE supplement RCTs? • What treatment should patients get once their disease progresses on CDK4/6 inhibitors? – Do you test all patients with HR+ MBC for *PIK3CA* mutations? Are you testing tumor tissue or ctDNA?	All

	– Where does alpelisib/fulvestrant fit into your algorithm for *PIK3CA*-mutated tumors? – What are the options for patients with *PIK3CA* wild-type cancers? – Where do PARP inhibitors fit for patients with HR+ g*BRCA*-mutated MBC? – Would you consider rechallenge with the same CDK4/6i with a different endocrine partner, or with a different CDK4/6 inhibitor at a later time? • Are there any promising biomarkers to predict sensitivity or resistance to CDK4/6 inhibitors? • Does *ESR1* mutation status offer any guidance to treatment choices? • What are your thoughts on the novel oral SERDs (and SERCAs) in development, and the design of ongoing phase III trials? – How would you integrate these agents if approved? What would it take for them to replace fulvestrant? – Do you perceive any clinically relevant differences between the new SERDs on the basis of the data so far? – What are your thoughts on the design of the ongoing phase III trials? • 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 • Do you see any potential role for immunotherapy? • Impact of COVID-19 pandemic	
11.30 AM – 11.35 AM	**Summary and 3 Key Takeaways**	
11.35 AM – 11.50 AM	**Break**	
11.50 AM – 12.05 PM	**Evolving Paradigms in HR+ Early Breast Cancer** • Gene expression assays for predicting recurrence risk and/or benefit from extended adjuvant therapy – Node-negative patients – Node-positive patients • Duration of (neo)adjuvant treatment • CDK4/6 inhibitors in the adjuvant setting (monarchE, PALLAS, PENELOPE-B)	Joyce O'Shaughnessy, MD
12.05 PM – 12.30 PM	**Key Questions and Topics for Discussion** • What role do gene expression assays play in your decisions about	All

	– When to use adjuvant chemotherapy? On the basis of the results of the RxPONDER and ADAPT trials, are you using these assays in node-positive HR+ breast cancer? – When to use extended adjuvant endocrine therapy? • Which gene expression assay(s) do you use most frequently, and do they differ by purpose/setting? • How do you interpret the conflicting results from monarchE vs PALLAS and PENELOPE-B? – Are CDK4/6 inhibitors ready for routine use in the adjuvant setting? If so, in which patients? If not, what additional data are needed? – Will (neo)adjuvant use 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 CDK-hormone combination in EBC? How would they be used differently? • How do you determine whether to use neoadjuvant chemotherapy? How do you anticipate your use changing over the next 5 years? Why, and what factors may influence this? How will this anticipated change in use vary by disease stage? • What are other promising novel treatment approaches in the adjuvant and neoadjuvant HR+ setting? • What are good trial designs to evaluate oral SERDs for early HR+ BC? • Impact of COVID-19 pandemic	
12.30 PM – 12.35 PM	**Summary and 3 Key Takeaways**	
12.35 PM – 12.40 PM	Conclusions and Wrap-up	Joyce O'Shaughnessy, MD