San Antonio Breast Cancer Symposium 2021 Conference Review™

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In this review:

Abbreviations used in this review:

BC = breast cancer; **BMI** = body mass index; **CI** = confidence interval; **HER2** = human epidermal growth factor receptor-type 2; **HR** = hazard ratio; **HoR** = hormone receptor; **IDFS** = invasive disease-free survival; **mTOR** = mechanistic target of rapamycin; **OFS** = ovarian function suppression; **OS** = overall survival; **PBS** = Pharmaceutical Benefits Scheme; **PD-L1** = programmed death-ligand 1; **PFS** = progression-free survival; **RR** = rate ratio; **SWOG** = Southwest Oncology Group; **T-DXd** = trastuzumab deruxtecan; **TRAE** = treatment-related adverse event.

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Welcome to our review of the San Antonio Breast Cancer Symposium (SABCS)

held in December 2021 in San Antonio, Texas, USA. SABCS 2021 was a hybrid meeting, catering for both onsite and virtual meeting attendees, and provided state-of-the-art information on the experimental biology, aetiology, diagnosis, prevention, and therapy of breast cancer and premalignant breast disease. Dr Belinda Kiely has chosen and reviewed 10 studies that she believes will be of particular interest to local practitioners with an interest in breast cancer.

We hope you find this conference review interesting and the content useful in your clinical practice.

Kind Regards,

Dr Janette Tenne

Editor

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GS2-07: Updated results from a phase 3 randomized clinical trial in participants (pts) with 1-3 positive lymph nodes (LN), hormone receptor-positive (HR+) and HER2-negative (HER2-) breast cancer (BC) with recurrence score (RS) ≤ 25 randomized to endocrine therapy (ET) +/- chemotherapy (CT): SWOG S1007 (RxPONDER)

Authors: Kalinsky KM et al.

Summary: This *post hoc* analysis of data from the randomised clinical phase III SWOG S1007 RxPONDER trial examined invasive disease-free survival (IDFS) and distant disease-free survival (DDFS) in 4984 women with 1-3 positive lymph nodes (LN), who had hormone receptor-positive and HER2-negative breast cancer with recurrence score <25 randomised to endocrine therapy with or without chemotherapy. Over a median follow-up of 6.1 years there were 553 IDFS events, post-menopausal women had no IDFS or DDFS benefit from chemotherapy. However, in premenopausal women, a 5-year absolute benefit of chemotherapy was observed for IDFS of 5.9% and DDFS of 3.3% and the distant recurrence-free interval was improved for all recurrence score values <25 (absolute improvement 2.3% for recurrence scores of 0-13 and 2.8% for recurrence scores of 14-25). Overall, 12.4% (n = 206) of pre-menopausal women had micro-metastases (pNmi; diameter 0.2-2 mm) with a trend for chemotherapy benefit (HR 0.44; CI 0.18-1.08). Only 17.2% of premenopausal endocrine therapy recipients underwent ovarian function suppression (OFS) in the first 2 years and there was no IDFS benefit of OFS (HR 0.88; 95% CI 0.47-1.63). The majority (58.9%) of premenopausal women receiving endocrine therapy stopped having periods within the first 24 months, and IDFS improved numerically compared to continued regular periods (HR 1.48; 95% CI 0.92-2.40). In premenopausal women receiving chemotherapy followed by endocrine therapy, 80.8% stopped having periods within the first 24 months and had a numerically improved IDFS (HR 1.56; 95% CI 0.85-2.86).

Comment: With a median 6-year follow-up this update confirms the benefit of chemotherapy regardless of recurrence score in premenopausal women with 1-3 positive nodes (including micro-metastases). Only 9% of the pre-menopausal women received OFS (16% in the endocrine therapy alone group) so we do not know whether chemotherapy has a benefit independent of chemotherapy-induced menopause. Only 2.9% of participants were <40 years of age and given the worse outcomes seen in very young women, gene expression profiling should not be performed. It is possible OFS plus aromatase inhibitor is just as effective as chemotherapy in women over 40 with "genomic low risk" tumours and involved nodes, but in the absence of data we should discuss chemotherapy with all premenopausal women with node-positive cancers. A trial randomising premenopausal women with node-positive, "genomic low-risk" cancers to OFS plus endocrine therapy with or without chemotherapy is needed.

Reference: Cancer Res. 2022;82(4 Suppl):GS2-07

Abstract

GS1-08: CCTGMA.32, a phase III randomized double-blind placebo controlled adjuvant trial of metformin (MET) vs placebo (PLAC) in early breast cancer (BC): Results of the primary efficacy analysis (clinical trials.gov NCT01101438)

Authors: Goodwin PJ et al.

Summary: This US randomised, double-blind, placebo-controlled phase III clinical trial assessed the use of adjuvant metformin in 3649 patients with early breast cancer without diabetes. Among 2533 oestrogen receptor/progesterone receptor-positive patients (mean age 52.7 years; mean BMI 28.8 kg/m^2), any grade ≥3 toxicity did not differ between metformin and placebo recipients (21.7% vs 18.7%). Over a median follow-up of 96.2 months, there were 465 IDFS events (234 metformin, 231 placebo, 76% due to breast cancer). In receptor/progesterone receptor-positive recipients, there was no difference between metformin and placebo in IDFS (HR 1.01; 95% CI 0.84-1.21) or OS (HR 0.89; 95% CI 0.64-1.23).

Comment: Following observational studies suggesting metformin may be associated with better breast cancer outcomes, this prospective randomised trial sought to determine if 5 years of metformin improves outcomes in non-diabetic women with early breast cancer. Overall, there was no difference in IDFS or OS in hormone receptor-positive and -negative populations. An exploratory analysis in 620 patients with HER2-positive cancers found metformin was associated with improved IDFS and OS. Metformin was well tolerated with no cases of lactic acidosis. Based on these data, metformin should not be recommended for non-diabetic patients as a treatment for breast cancer. Importantly, metformin did not cause worse breast cancer outcomes, so it remains a safe treatment for patients with breast cancer and diabetes or insulin resistance, where it can also assist with weight loss. The HER2-positive results are intriguing and require further research. A similar trial evaluating the role of aspirin in early breast cancer (ABC trial) recently reported no IDFS benefit for aspirin.

Reference: Cancer Res. 2022;82(4 Suppl):GS1-08
Abstract

GS1-07: Adjuvant palbociclib in HR+/HER2- early breast cancer: Final results from 5,760 patients in the randomized phase III PALLAS trial

Authors: Gnant M et al.

Summary: The multinational, randomised, open-label, phase III PALLAS trial assessed addition of palbociclib to adjuvant endocrine therapy versus endocrine therapy alone in 5761 patients with hormone receptor-positive HER2-negative (HoR+/HER2-) early breast cancer (median age 52 years; 17.6% stage IIA, 82.1% stages IIB/III). A prespecified interim analysis crossed the futility threshold, so 349 on-treatment palbociclib recipients were transferred to follow-up. After a median follow-up of 31 months, 516 IDFS events had occurred and the 3-year IDFS rate did not differ between treatments; palbociclib plus adjuvant endocrine therapy 89.3% (95% CI 87.8-90.6) versus endocrine therapy alone 89.4% (95% CI 88.0-90.7; HR 0.96; 95% CI 0.81-1.14). Grade 3 and 4 neutropenia was the most common adverse event with palbociclib (61.9% and 0.4%). Overall, 42% of palbociclib recipients discontinued treatment early, 28.2% due to adverse events.

Comment: This final analysis with 31 months' follow-up confirmed no benefit from adding 2 years of adjuvant palbociclib to endocrine therapy. This is different to the monarchE trial where 2 years of adjuvant abemaciclib improved IDFS at 3 years by 5%. The reason for the different results in these 2 trials is unknown. The PALLAS population was lower risk and the number of patients who discontinued palbociclib early was high (45%). However, no benefit from palbociclib was seen in the high-clinical-risk or >70% palbociclib dose intensity subgroups. Differences in the structures of the drugs themselves and the continuous dosing schedule of abemaciclib (vs intermittent dosing of palbociclib) may be more important in the early stage compared to the advanced-stage setting. No trial has shown an OS benefit for adjuvant CDK4/6 inhibitors and longer follow-up is needed. The optimal duration of adjuvant CDK4/6 inhibition is to be determined and we await results from the Natalee trial evaluating 3 years of adjuvant ribociclib.

Reference: Cancer Res. 2022;82(4 Suppl):GS1-07
Abstract

GS2-04: Aromatase inhibitors versus tamoxifen in pre-menopausal women with estrogen receptor positive early stage breast cancer treated with ovarian suppression: A patient level meta-analysis of 7,030 women in four randomised trials

Authors: Bradley R et al.

Summary: This meta-analysis of 4 randomised controlled trials (ABCSG XII, SOFT, TEXT and HOBOE), included data from 7030 pre-menopausal women with oestrogen receptor-positive breast cancer receiving OFS or ablation and an aromatase inhibitor or tamoxifen for 3 or 5 years. Overall, the annual recurrence rate was 21% lower with an aromatase inhibitor versus tamoxifen (RR 0.79; 95% 0.69-0.90; p = 0.0005). The main benefit from aromatase inhibitors was observed from 0-4 years (RR 0.68; 99% CI 0.58-0.80), with no further benefit between 5-9 years (RR 0.98; 99% 0.73-1.32), and limited data after year 10. Five-year absolute risk of breast cancer recurrence was lower by 3.2% in aromatase inhibitor recipients versus tamoxifen recipients (6.9% vs 10.1%; p = 0.0005). Distant recurrence was reduced by aromatase inhibitors (RR 0.83; 95% CI 0.71-0.97; p = 0.02), there was no difference in breast cancer mortality. Aromatase inhibitors appeared to be ineffective in N4+ disease. More bone fractures occurred in aromatase inhibitor recipients (5.0% vs 3.8%; p = 0.02). Few non-breast cancer deaths occurred (0.9% vs 0.7%; RR 1.30; 95% CI 0.75-2.25), and endometrial cancer was rare (0.2% vs 0.3%).

Comment: OFS plus aromatase inhibitor reduces the risk of recurrence by 21% (absolute benefit 2.8%) and risk of distant recurrence by 17% (absolute benefit 1.9%) compared with OFS plus tamoxifen. The main benefit was in years 0-4, suggesting the importance of starting the aromatase inhibitor therapy early. The relative risk reduction was regardless of node status, age, tumour grade and histological subtype. An unexpected finding was that aromatase inhibitor therapy was no better than tamoxifen in the 729 women with ≥4 positive lymph nodes, but given this was a small subgroup and not seen in trials of post-menopausal women I would not make much of it. There was no effect on breast cancer mortality or OS, but this will require longer follow-up. The small benefits of aromatase inhibitors need to be balanced against increased toxicity, especially arthralgia, sexual dysfunction, and osteoporosis. Starting with OFS plus aromatase inhibitors in high-risk patients and switching to tamoxifen if not tolerated is a good approach.

Reference: Cancer Res. 2022;82(4 Suppl):GS2-04
Abstract

GS2-05: Randomized comparison of adjuvant aromatase inhibitor exemestane (E) plus ovarian function suppression (OFS) vs tamoxifen (T) plus OFS in premenopausal women with hormone receptor-positive (HR+) early breast cancer (BC): Update of the combined TEXT and SOFT trials

Authors: Regan MM et al.

Summary: This update report provides data after a median 13-year follow-up of the TEXT and SOFT randomised controlled trials comparing 5 years of adjuvant exemestane plus OFS versus tamoxifen plus OFS and optional chemotherapy in premenopausal women with HoR-positive early breast cancer. In total there were 953 disease-free survival (DFS) events and 473 deaths and outcomes for exemestane plus OFS (n = 2346) continued to be better than tamoxifen plus OFS (n = 2344) including 12-year DFS (80.5% vs 75.9%; 4.6% improvement HR 0.79; 95% CI 0.70-0.90), invasive breast cancer-free interval (improved 4.1%) and distant recurrence-free interval (improved 1.8%). OS was 90.1% with exemestane plus OFS versus 89.1% with tamoxifen plus OFS (HR 0.93; 95% CI 0.78-1.11). There was an emerging OS benefit for exemestane plus OFS versus tamoxifen plus OFS in patients with HER2-negative tumours who received chemotherapy in both trials. In patients with HER2-negative tumours, 12-year DFS was improved by 7.4% and OS was improved by 2.7% in patients with pN1a disease, and by 10.6% and 4.5% in patients with tumours >2 cm.

Comment: Compared to tamoxifen alone, there is a significant improvement in OS at 12 years with OFS (2.3% with tamoxifen, 2.6% with exemestane). The absolute benefit of OFS is greatest in women at highest risk including age <35 years, ≥4 positive lymph nodes and those requiring chemotherapy. It is reassuring that tamoxifen alone remains an effective treatment for women with low-risk cancers, especially those not requiring chemotherapy where OS at 12 years is 95.8%. In women with HER2-negative cancers who received chemotherapy, OFS plus exemestane is more effective than OFS plus tamoxifen (3.3% improvement in OS at 12 years). In contrast, in HER2-positive cancers, OFS plus tamoxifen is more effective; however, this subgroup was small and not all received trastuzumab. The benefits of OFS are small and must be balanced against side effects and quality of life, both of which impact treatment adherence and reduce efficacy. Better measures to reduce the side effects of endocrine therapy are urgently needed to improve treatment adherence.

Reference: Cancer Res. 2022;82(4 Suppl):GS2-05
Abstract

GS1-01: KEYNOTE-522 study of neoadjuvant pembrolizumab + chemotherapy vs placebo + chemotherapy, followed by adjuvant pembrolizumab vs placebo for early-stage TNBC: Event-free survival sensitivity and subgroup analyses

Authors: Schmid P et al.

Summary: The randomised controlled KEYNOTE-522 study examined the effect of pembrolizumab plus chemotherapy versus placebo plus chemotherapy followed by adjuvant pembrolizumab versus placebo in 1174 patients with early-stage triple-negative breast cancer. This prespecified sensitivity and subgroup analyses assessed the robustness and consistency of the primary outcome analysis which demonstrated an improvement in event-free survival (EFS). Over a median follow-up of 39.1 months, the benefit of neoadjuvant pembrolizumab plus chemotherapy followed by adjuvant pembrolizumab was generally consistent with the primary EFS results across five sensitivity analyses including alternate censoring rules (HR 0.64; 95% CI 0.48-0.84), new anticancer therapy for metastatic disease considered an EFS event (HR 0.63; 95% CI 0.48-0.82), positive margin at last surgery removed from EFS definition (HR 0.65; 95% CI 0.50-0.85), positive margin at last surgery and second primary malignancy removed from EFS definition (HR 0.63; 95% CI 0.48 - 0.84), and second breast malignancy included in EFS definition (HR 0.63; 95% CI 0.48 - 0.82). This benefit was generally consistent across patient subgroups including those defined by nodal involvement, disease stage, menopausal status, and HER2 status.

Comment: Adding pembrolizumab to chemotherapy significantly improved 3-year EFS by 8%. Similar benefits were seen regardless of stage and node status. With PD-L1 expression not differentiating responders from non-responder's, research is needed to find a biomarker to identify patients most likely to benefit. Although there is no OS benefit yet, it is expected given pembrolizumab significantly reduced distant recurrences. Adding immunotherapy to chemotherapy is becoming standard of care internationally for patients with high-risk stage II and III triple-negative cancers. Without PBS reimbursement, use in Australia will be very limited. There are several important unanswered questions, including the need for adjuvant immunotherapy for patients achieving complete pathological response, need for all 4 chemotherapy agents when immunotherapy is used, optimal integration of immunotherapy with post-neoadjuvant capecitabine and olaparib for patients with residual disease, benefit of pembrolizumab in *BRCA* mutation carriers, long-term side effects of immunotherapy, and the impact of immunotherapy on fertility.

Reference: Cancer Res. 2022;82(4 Suppl):GS1-01
Abstract

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Independent commentary by Dr Belinda Kiely

Dr Belinda Kiely is a medical oncologist who sub-specialises in breast cancer. She is a Staff Specialist at Concord and Campbelltown hospitals in Sydney.

GS2-06: Taxane with anthracycline versus taxane without anthracycline: An individual patient-level meta-analysis of 16,500 women with early-stage breast cancer in 13 randomised trials

Authors: Braybrooke J et al.

Summary: This patient-level meta-analysis of data from 13 randomised controlled trials including 16,500 participants examined the use of taxane chemotherapy with or without anthracycline, in particular the docetaxel-cyclophosphamide regimen in women with early-stage breast cancer. Anthracycline and taxane combination therapy lowered rates of breast cancer recurrence by 18% (RR 0.82; 95% CI 0.75-0.90; $p < 0.0001$) versus a taxane schedule without anthracycline; absolute reduction in 10-year recurrence of 3.1% (95% CI 1.4-4.8). The 10-year breast cancer mortality risk was reduced by 1.8% (RR 0.85; 95% CI 0.75-0.95; $p = 0.006$). Proportional reduction in recurrence was greatest with concurrent anthracycline plus docetaxel-cyclophosphamide versus docetaxel-cyclophosphamide (RR 0.66; 95% CI 0.55-0.79; $p < 0.0001$). With sequential anthracycline and docetaxel versus the higher cumulative taxane dose docetaxel-cyclophosphamide regimen there was no significant benefit from anthracycline (RR 0.93; 95% CI 0.80-1.07). Across a number of sub-group analyses, anthracycline and taxane chemotherapy benefits persisted throughout years 0-1, 2-4 and 5-9. Reductions in recurrence were observed in oestrogen receptor-positive and -negative disease.

Comment: These results are thought-provoking. Overall, adding anthracycline to taxane reduced 10-year recurrence risk by 2.5% and breast cancer mortality by 1.6%. The relative benefit was seen regardless of oestrogen receptor or nodal status, although the absolute benefit was larger in oestrogen receptor-negative cancers. The benefit of anthracyclines was greatest when given concurrently with taxane (e.g., docetaxel, doxorubicin and cyclophosphamide [TAC] x 6). There was no benefit when sequential anthracycline-taxane was compared to taxane without anthracycline. It was surprising to see no increase in deaths from cardiovascular disease or leukaemia, the main concerns with anthracyclines. Very few of the included trials used dose-dense chemotherapy so we do not know how dose-dense sequential anthracycline-taxane compares to concurrent anthracycline-taxane. High rates of toxicity, especially febrile neutropaenia and colitis, make most oncologists reluctant to prescribe TAC. The findings also suggest that 4 to 6 cycles of docetaxel-cyclophosphamide are a good alternative to sequential anthracycline-taxane for lower-risk cancers, especially oestrogen receptor-positive cancer.

Reference: Cancer Res. 2022;82(4 Suppl):GS2-06
Abstract

GS2-02: Elacestrant, an oral selective estrogen receptor degrader (SERD), vs investigator's choice of endocrine monotherapy for ER+/HER2- advanced/metastatic breast cancer (mBC) following progression on prior endocrine and CDK4/6 inhibitor therapy: Results of EMERALD phase 3 trial

Authors: Bardia A et al.

Summary: The multicentre, international, open-label, randomised controlled phase III EMERALD trial tested the use of the oral selective oestrogen receptor degrader (SERD) elacestrant versus standard of care (fulvestrant or aromatase inhibitor) in 447 postmenopausal women with oestrogen receptor-positive/HER2-negative advanced/metastatic breast cancer who had progressed on endocrine therapy plus cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors. Risk of progression or death was reduced by 30% with elacestrant (HR 0.697, 95% CI 0.552-0.88; $p = 0.0018$), and there was a 45% reduction in risk of progression or death in a subgroup of 228 patients with *ESR1* mutations (HR 0.546; 95% CI 0.387-0.768; $p = 0.0005$). At 12 months, the PFS rate was 22.32% (95% CI 15.24-29.40) with elacestrant versus 9.42% (95% CI 4.02-14.81) with standard of care, and 26.76% (95% CI 16.17-37.36) versus 8.19% (95% CI 1.26-15.12) in the *ESR1* mutation subgroup. A prespecified interim OS analysis suggested a trend in favour of elacestrant (HR 0.751; 95% CI 0.542-1.038; $p = 0.0821$) and in the *ESR1* mutation subgroup (HR 0.592; 95% CI 0.361-0.958; $p = 0.0325$). Common (>10%) TRAEs for elacestrant versus standard of care included nausea (25.3% vs 8.7%), vomiting (11% vs 2.6%), and fatigue (11% vs 7.9%). TRAEs leading to discontinuation occurred in 6.3% versus 4.4% of patients; grade ≥3 TRAEs were 7.2% versus 3.1%, mainly nausea (2.1% vs 0.9%).

Comment: This proof of concept study has established oral SERDs as an active treatment option in oestrogen positive breast cancer, especially in tumours that have developed *ESR1* mutations. A substantial number of patients had no response to elacestrant or investigator's choice endocrine therapy and progressed within 8 weeks, demonstrating that after first-line CDK4/6 inhibitors, many cancers are no longer sensitive to endocrine therapy, especially single-agent endocrine therapy. Methods to identify patients most likely to respond to oral SERDs are needed, especially given a proportion of patients remained progression free beyond 12 months. Nausea and vomiting (predominantly low grade) were more frequent with elacestrant than fulvestrant. While this trial, in itself, is not practice changing, given the simple oral administration and improved activity compared to fulvestrant, oral SERDs are likely to replace fulvestrant in the future. Studies evaluating oral SERDs in the early and advanced settings are ongoing, including combination therapies with CDK4/6 inhibitors and mTOR inhibitors.

Reference: Cancer Res. 2022;82(4 Suppl):GS2-02
Abstract

GS1-02: Final results of KEYNOTE-355: Randomized, double-blind, phase 3 study of pembrolizumab + chemotherapy vs placebo + chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer

Authors: Cortes J et al.

Summary: This analysis of data from the randomised controlled KEYNOTE-355 examined the effect of pembrolizumab plus chemotherapy versus placebo plus chemotherapy in subgroups of triple-negative breast cancer patients identified by additional combined positive score (CPS) cut-offs. Among 847 patients with measurable disease at 44 month's follow-up, HRs for OS were 0.73 (95% CI 0.55-0.95) in the CPS ≥10 subgroup, 0.86 (95% CI 0.72-1.04) in the CPS ≥1 subgroup, and 0.89 (95% CI 0.76-1.05) in the overall intent-to-treat population; for PFS, HRs were 0.66 (95% CI 0.50-0.88), 0.75 (95% CI 0.62-0.91), and 0.82 (95% CI 0.70-0.98), respectively. OS results in CPS 1-9 patients had similar efficacy for pembrolizumab plus chemotherapy and placebo plus chemotherapy; however, results in the CPS 10-19 and CPS ≥20 subgroups identified a benefit with pembrolizumab.

Comment: This final analysis confirms the role of immunotherapy in the first-line treatment of advanced triple-negative breast cancer that is PD-L1 positive (38% of patients in KEYNOTE-355 were PD-L1 positive CPS ≥10). Of note 78% received chemotherapy that was from a different class to what they received in the adjuvant setting. The 6.9-month improvement in OS in the PD-L1 CPS ≥10 subgroup is clinically meaningful but with the median OS less than 2 years in all patients, we are still a long way from the approximate 5-year median OS times seen for ER-positive and HER2-positive advanced breast cancers. This highlights the need for more effective treatments for triple-negative breast cancer. We also need effective treatments for the 60% of patients with PD-L1 negative cancers and for those relapsing within 6 months of completing adjuvant therapy. It will also become important to learn how to treat patients who relapse after (neo)adjuvant immunotherapy.

Reference: Cancer Res. 2022;82(4 Suppl):GS1-02
Abstract

GS1-05: Datopotamab deruxtecan in advanced/metastatic *HER2*- breast cancer: Results from the phase 1 TROPION-PanTumor01 study

Authors: Krop I et al.

Summary: The multicentre, open-label, phase I TROPION-PanTumor01 study tested datopotamab deruxtecan, a humanised anti-TROP2 IgG1 monoclonal antibody conjugated to a topoisomerase I inhibitor payload, in 43 previously treated patients with triple-negative breast cancer. Over a median duration of treatment of 2.8 months and median follow-up of 3.9 months, 38 patients were evaluable for response, in whom the objective response rate (ORR) was 39% (15 partial responses); disease control rate was 84%. Median time to response was 1.35 months for 12 confirmed partial responses. All-cause TEAEs of any grade occurred in 95% of patients with grade ≥3 TEAEs in 35% of patients; there were 2 grade 4 events. The most common TEAEs of any grade (≥30%) and grade ≥3 included nausea (58%; 0%), stomatitis (53%; 9%), alopecia (35%), vomiting (35%; 2%), and fatigue (33%; 7%). Serious TEAEs occurred in 5 patients (12%).

Comment: Datopotamab deruxtecan is an antibody-drug conjugate in which a Trop2 antibody (like sacituzumab) is attached to the potent Topo 1 inhibitor deruxtecan (like T-DXd). In this heavily pre-treated cohort (median 3 prior metastatic therapies, 43% prior immunotherapy), the response rate was 34%, very similar to the 35% response rate for sacituzumab in the ASCENT trial. The responses seem durable with median duration of response not reached with 7.6 months median follow-up. The main side effects are nausea and stomatitis, with low rates of neutropenia and diarrhoea, which are the main side effects of sacituzumab. A phase III trial is planned, but it is exciting to see another potentially active drug for advanced triple-negative breast cancer. Work is needed to determine predictors of response and the best way to sequence and combine immunotherapy, chemotherapy and antibody-drug conjugates in advanced and early-stage triple-negative breast cancers.

Reference: Cancer Res. 2022;82(4 Suppl):GS1-05
Abstract

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