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MEETING REPORT

Part 1 – Highlights of the San Antonio Breast Cancer Symposium 2023

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1. Introduction

The annual SABCS combines the principles of multidisciplinary management with the basic science underlying pathobiological processes in breast cancer. The 46th meeting was held at the Henry B Gonzales Convention Centre in downtown San Antonio, TX, USA on 5–9 December 2023. The symposium delivers a range of presentations covering basic, translational and clinical sciences. Important trials that are potentially practice changing are often presented as late breaking news and published concurrently or shortly thereafter. This is the first of a two-part report highlighting important presentations and focuses on topics relating to breast cancer screening, completion axillary lymph node dissection for positive sentinel nodes after primary surgery or neoadjuvant chemotherapy (NACT) and omission of regional nodal radiation. The second part will cover issues relating to pregnancy after breast cancer in BRCA mutation carriers, CDK 4/6 inhibitors for early and advanced breast cancer and immunotherapy with checkpoint inhibitors for breast cancer.

1.1. Breast cancer screening

Current guidelines for radiological surveillance after a breast cancer diagnosis in women aged ≥50 years recommend annual mammography for 5 years with reversion to triennial mammograms within the National Health Service Screening programme thereafter [1]. The frequency of imaging is not stratified based on recurrence risk. Surveillance policies for other countries are variable and unspecified in terms of frequency and duration of follow-up mammography. There are cost implications in the context of an aging population and more intensive surveillance with annual mammography potentially has a negative psychological impact from generation of heightened patient anxiety. Janet Dunn (Clinical Trials Unit, University of Warwick, UK) presented results of the MAMMO-50 trial that evaluated less frequent mammography in women aged ≥50 years who were 3 years from curative breast surgery. The trial recruited more than 5000 women aged between 55 and 75 years among whom 87% had invasive cancer. Women were randomly allocated to annual or less frequent mammography; those undergoing breast conserving surgery (BCS) had 2 yearly mammograms while mastectomy patients had 3 yearly imaging. There were dual primary end points of breast cancer specific survival and cost–effectiveness with recurrence-free interval (RFI) and overall survival (OS) as secondary end points. No difference in breast cancer specific survival was observed between annual (98.1%) and less frequent (98.3%) cohorts at a median follow-up of 5.7 years (HR: 0.92; 95% CI: 6.4–1.32) – this represented 8.7 years since curative surgery. Furthermore, there were no significant differences in the secondary outcomes of RFI and OS with almost identical rates of RFI at 5 years for annual and less frequent mammography (94.1 and 94.5%, respectively [HR: 1; 95% CI: 0.81–1.24]). Compliance rate for the less frequent cohort was just 69% compared with 83% for the annual cohort but results were similar after sensitivity analysis of the compliant population. Thus less frequent was declared non inferior to annual mammography with these results considered potentially practice changing. Mammography schedules should be stratified based on risk profile with less frequent imaging for women at lower risk of recurrence.

1.2. Surgical treatment of breast cancer

It remains unclear whether omission of completion axillary lymph node dissection (ALND) is safe for mastectomy patients with macrometastases in 1 or 2 sentinel nodes after primary surgery. The Z0011 trial [2] excluded mastectomy patients and the IBCSG 23-01 trial [3] included 9% of patients with mastectomy and only those with micrometastatic disease. The proportion of mastectomy patients was slightly higher in the SINODAR-ONE trial (22%) and results of the POSNOC trial are

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awaited [4,5]. There is lingering uncertainty whether mastectomy patients can avoid completion ALND if not in receipt of chest wall radiation that captures the lower axillary nodes. The international multicenter SENOMAC trial was launched in 2015 and recruited patients from 67 sites in five countries [6]. The trial aimed to clarify the role of ALND in BCS or mastectomy patients both of whom received radiotherapy and was complementary to the AMAROS trial [7]. A total of 2539 patients with one or two nodal macrometastases were enrolled with almost two-thirds undergoing BCS and a third mastectomy. Of note, this trial recruited T1–3N0 patients, although T3 tumors constituted only 5.8% of the trial population and most patients (85%) had a single positive sentinel node. The SENOMAC trial randomized patients to either standard treatment with ALND ($n = 1204$) or not ($n = 1335$). The majority of patients had irradiation of nodal fields irrespective of whether standard (88.4%) or intervention (89.9%) arm. The primary outcome was OS at 5 years with a non-inferiority margin of 2.5% for omission of ALND. Jana de Boniface (Karolinska Institute, Stockholm, Sweden) presented results of the prespecified secondary outcome measure of RFS. There was no difference in RFS at a median follow-up of 47 months between standard (87.7%) or intervention (89.7%) groups (HR: 0.89; 95% CI: 0.66–1.19) with 8 and 7% RFS events, respectively. Moreover, non inferiority was upheld on sensitivity analysis ($p < 0.001$) and these results for RFS were similar in subset analyses of key subgroups including age (<65 vs >65 years), stage (T1/T2 versus T3), number of nodes (1 vs 2 with macrometastases), tumor type (lobular versus non-lobular) and type of surgery. Results of SENOMAC suggest that nodal irradiation may be equally effective as ALND but a definitive answer will be provided by the POSNOC trial. It was emphasized during discussion that longer follow-up is essential as most tumours were luminal and have the potential to recur after 15–20 years. Patients should be informed of the relative risks and benefits for ALND and axillary radiotherapy and it was commented that few patients having primary surgery have ≥4 positive nodes and hence benefit from newer forms of systemic therapies such as CDK 4/6 inhibitors.

The significance of micrometastases [ypN1mi] and/or isolated tumor cells (ITCs) [ypN0i] in sentinel nodes after NACT remains unclear with some evidence for worse disease-free survival for ypNmi and ypN0i compared with ypN0 [8]. Randomized clinical trials have failed to confirm the need for ALND when ITCs are the only focus of residual tumor burden in sentinel nodes after NACT for clinically node negative (cN0) or positive disease (cN1). This is partly due to the small number of patients in these categories. Although patients with ITCs represent only 1.5% of all cN1 patients undergoing NACT, the current treatment recommendation is usually completion ALND. All studies to-date have collectively shown an incidence for nonsentinel lymph node involvement in this setting of about 37%. The ICARO study led by the Oncoplastic Breast Consortium is a retrospective multi-institutional collaboration across 60 sites on four continents and aimed to collect real-world data on outcomes for NACT with residual ITCs. This methodology permits rapid accrual of data relating to routine clinical practice and fortuitously this study included large numbers of patients ($n = 583$) treated with or without completion ALND. A similar number of patients underwent BCS and mastectomy with comparable proportions with or without ALND according to operation type ($p = 0.13$). Additional positive nodes were found in 30% of patients undergoing ALND and these were most commonly further ITCs (18%) but also micrometastases (7%) and macrometastases (5%). Axillary recurrence was analyzed as an isolated event or combined with local and distant for no-ALND and ALND groups. There were no significant differences in rates of either isolated (1.1 vs 1.7% ($p = 0.7$)) or combined (4.6 vs 4.1% ($p = 0.8$)) axillary recurrence at 5 years between groups. Moreover, there were no differences in rates of any invasive recurrence between no-ALND and ALND groups at 5 years (19 vs 16%, respectively [$p = 0.13$]). The presenter Giacomo Montagna (Memorial Sloan Kettering Cancer Centre, New York, NY, USA) acknowledged limitations of the study relating to its retrospective nature, short median duration of follow-up (3.2 years) and lack of standardization of pathological assessment. Despite ICARO being non randomized without provision of level I evidence, it was a large study and these results were considered practice changing and supported omission of routine ALND in patients with residual ITCs following NACT for cN0 or cN1 disease. Nonetheless, due to limited duration of follow-up, outcomes for this group of patients undergoing de-escalation of axillary surgery for residual nodal disease should be carefully audited. The role of radiotherapy in this group of patients remains unclear and is unlikely to be resolved by results of the NSABP B-51 study for which the pN0 category includes patients with ITCs who are likely to be simply classified as pN0 without qualification.

1.3. Regional nodal radiation therapy

Results of the NSABP B-51 trial were also presented at SABCS2023; this seminal trial aimed to determine whether chest wall and regional nodal irradiation (RNI) post mastectomy or addition of RNI to breast radiotherapy post lumpectomy decreases invasive breast cancer recurrence in patients converting from clinically node positive (cN1) to pathologically node negative

(ypN0) after NACT [9]. There are concerns that omission of RNI will increase rates of recurrence but patients themselves are keen to avoid radiotherapy whenever possible. Eleftarios Mamounas (NRG Breast Oncology, CA, USA) presented results of the NSABP B-51 that recruited 1641 patients who had completed at least 8 weeks of chemotherapy before BCS or mastectomy. Half the patients were randomized to chest wall irradiation and RNI or whole breast irradiation and RNI after BCS with the other half allocated to observation only without RNI. The primary end point of this trial was invasive breast cancer-free interval and secondary end points included loco-regional and distant RFI, disease-free survival and OS. Fewer recurrence events were reported ($n = 172$) than were expected and this prompted a time-driven interim analysis at a median follow-up of 59.5 months. It is noteworthy that baseline features were remarkably well matched between the two groups including racial and ethnic groupings. A similar percentage of patients remained free of invasive breast cancer recurrence in the no RNI (91.8%) versus RNI (92.7%) groups (HR: 0.88; 95% CI: 0.6–1.29). Moreover, there were comparable results for all the aforementioned secondary outcomes with no significant differences between no RNI and RNI groups at 5 years. It was conceded that limitations on statistical analysis were inevitable due to fewer breast cancer recurrences than anticipated when designing the trial and longer term follow-up is essential for definitive conclusions on outcomes of the trial. However, Mamounas concluded that these interim results were an opportunity for de-escalation of radiotherapy at a time of improved systemic therapies that include CDK 4/6 inhibitors, immunotherapy and a range of antibody-drug conjugates. There is greater reliance in contemporary practice on more effective systemic therapies for locoregional control of disease with avoidance of toxicities from radiation therapy.

Author contributions

Both authors (JR Benson and I Jatoi) have contributed significantly to this manuscript in terms of conception, execution and interpretation of data. JR Benson has written the manuscript that has been critically reviewed by I Jatoi and both authors agree to publication of this article in Future Oncology. Likewise, both JR Benson and I Jatoi have reviewed and agreed all versions of the article before submission and will review the final version that is accepted for publication and agree to any changes introduced at the proofing stage. Moreover, both JR Benson and I Jatoi agree to take responsibility and be accountable for the contents of the article and to share responsibility to resolve any questions raised about the accuracy or integrity of the published work.

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JR Benson was on the Planning Committee and I Jatoi the Executive Committee for the above meeting. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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