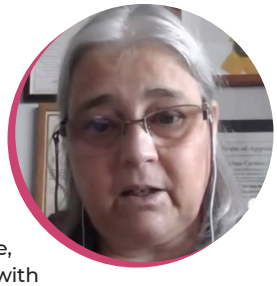
Highlights from Europa Donna's **Metastatic Breast Cancer Advocacy Webinar 2023**

16 June 2023

Europa Donna – The European Breast Cancer Coalition held its 6th annual Metastatic Breast Cancer (MBC) Advocacy Webinar for people with this disease to keep them up to date on MBC and equipped with advocacy strategies. **A focus of the day was the Coalition's new MBC awareness campaign** #TheCancerCurrency **highlighting the true value of the lives of five Europa Donna advocates living with MBC throughout Europe.** Three of these women participated in the webinar, which included 57 people from 27 countries across three continents. Among the attendees were women with MBC or early breast cancer and almost all were advocates wanting to learn more about this as yet incurable form of breast cancer and the unique needs of those with the disease. Some said they found attending the webinar empowering and a reminder of their advocacy goals, saying: "knowledge is empowerment". Others expressed the wish for the MBC advocacy voice to resonate as loudly as that for early breast cancer, and for it to be widely understood that having MBC affects all aspects of a person's life, from daily activities, family, and social interactions to work and finances. In this light, sessions by expert speakers addressed the latest treatments, emotional support, and the right to work for women with MBC.

In the conference opening, **Europa Donna CEO Marzia Zambon** shared her enthusiasm for the new MBC awareness campaign that will continue across the year and beyond. It involves a "cancer currency" in the form of specially designed bank notes featuring the five Europa Donna advocates living with MBC, from five different countries, who volunteered to share their stories. The campaign aims to show that life with MBC, despite being incurable, has value. It brings attention to the fact that those living with this disease have been underrecognised, underrepresented and undervalued for too long. The women in the campaign videos demonstrate why this must change. Some 30% of women diagnosed with early breast cancer will go on to have advanced or metastatic disease.



About MBC and Treatment and Research for HER2+ MBC

Leading the science discussion, **Fatima Cardoso**, Director of the Breast Unit in Champalimaud Clinical Centre in Lisbon, Portugal and President of the ABC Global Alliance, provided an introduction to MBC and the latest treatment for HER2+ MBC. Breast cancer itself has many shapes and forms, from hormone dependent to triple negative (ie, with no targetable receptors for therapy). Advanced breast cancer (ABC) comprises both breast cancer that is locally advanced and inoperable (stage 3) and MBC, where cancer has spread to distant sites, such as bone, lung or liver (stage 4). In developed countries, the disease is advanced at diagnosis in 10-15% of cases compared with 50-60% in developing countries. In its earlier forms, breast cancer may be curable in some 70% of cases. MBC is mainly incurable, although treatment can improve survival, delay progression and control symptoms. **The aim of treatment is, if not to cure, to make it a chronic disease, ie, where people live long term with therapy, although this has yet to be achieved.** Any choice of treatment should take into account patient preferences as well as the patient, disease and tumour characteristics. The main challenges lie in identifying which patients may benefit most from a therapy (ie, precision medicine), and eventual resistance of the tumour to therapy. It remains unclear why some patients with MBC remain relatively symptom-free on therapy while others perish.

HER2+ MBC

On the topic of HER2+ MBC, the current drug strategies targeting this type of MBC make it the MBC subtype with the longest survival, at more than 5 years. Unless there are contraindications, **patients should be offered anti-HER2 therapy early and it should be continued during later therapy, even if there is disease progression – this is a change of paradigm**. Trastuzumab was the first anti-HER2 therapy. In studies published as far back as 2001, a combination of this drug and chemotherapy (CT) led to a significant improvement in overall survival (OS) and other outcomes compared with CT alone. One of the first forms of immunotherapy, this drug was generally well tolerated, except for rare cardiac effects which are generally reversible. Next on the scene was pertuzumab, another anti-HER2 therapy blocking different areas of the HER2 receptors and used in combination with trastuzumab as a "dual blockade". The CLEOPATRA study, based on about 8 years of follow-up, confirmed an OS advantage of about 30% with the addition of pertuzumab. Then came the first antibody drug conjugate (ADC), trastuzumab emtansine (T-DM1), which uses the trastuzumab antibody "as a bus" to transport CT inside the tumour cell, making it more targeted and less toxic. In later lines of therapy, it has an OS benefit of 3 months over physicians' choice of therapy and in the second-line setting, it showed a 6-month survival benefit over lapatinib plus capecitabine. It can lead to decreased platelets, liver toxicity and fatigue, but is generally well tolerated. Next was trastuzumab deruxtecan (T-DXd), a form of CT, which delivers even more CT into the tumour cell and surrounding cells. The DESTINY trial showed a 12.7-month OS benefit with this therapy over trastuzumab or lapatinib plus capecitabine. Compared with T-DM1, it showed a 7.5% improvement in OS at 24 months, when median OS had not yet been reached for either therapy. The most common adverse effects were nausea, fatigue and vomiting, some of which can be curtailed through preventive therapy, but importantly, rare cases of fatal lung disease can occur. Lastly, as a later-line option, the tyrosine kinase inhibitor tucatinib combined with trastuzumab and capecitabine led to a median 4.5 month increase in OS vs trastuzumab plus capecitabine in heavily pre-treated patients. It has more side effects, but preventive therapy can address them. An advantage of this therapy is that it can cross the blood-brain barrier and reach the brain in order to treat brain metastases. In conclusion, **Dr Cardoso said that for HER2+ MBC, trastuzumab is a must-have, pertuzumab is very important to have, and T-DM1, T-DXd and tucatanib are good to have, and emphasised that is it crucial to keep blocking the HER2 pathway even after the disease has progressed several times**. She also discussed the ABC Global Alliance, with 93 member countries, a large number via Europa Donna. As guidelines and multidisciplinary care have led to improvements in early breast cancer outcomes over the years, it aims to achieve the same for MBC. Its main achievement is the biannual ABC Consensus Conference where international guidelines on how to optimally manage this disease are developed and published, with strong participation of patients and patient advocates. The Alliance also holds yearly awareness campaigns, with a recent one focusing on returning to work after an ABC diagnosis (see more at: www.abcglobalalliance.org).

Treatment and Research for ER+/HER2– MBC

Covering treatment and research for oestrogen receptor-positive (ER+)/HER2– MBC, **Alexandru Eniu**, Medical Oncologist and Chief Physician at the Hôpital Riviera-Chablais in Rennaz, Switzerland, emphasised that to improve survival, the full continuum of care is required: from screening and early detection to therapy for early breast cancer and access to the newest MBC therapies. In recent decades, advances in therapies for MBC have increased survival – this sends a strong political message in favour of access to new therapies. He urged Europa Donna to keep up its advocacy work to this end. In terms of therapy**, he said that in cases of ER+/HER2– tumours, endocrine therapy (ET) is the preferred approach and should be continued in multiple lines without CT, unless needed.** The main hurdle is to delay endocrine resistance for as long as possible. To do so, the standard of care is a combination of ET and a CDK4/6 inhibitor, which increases OS and at least maintains quality of life (QoL). This has changed the lives of many patients, he said. The ABC guidelines recommend this combination for newly occurring or recurrent MBC, as first- or second-line therapy for post-menopausal women, and in combination with an LHRH agonist for pre-menopausal women, and men. Anti-CDK4/6 therapy delays the time to first CT by about 1 year and in second-line therapy, it decreases the risk of death by 30% vs ET alone. These therapies are better tolerated than CT; however, they can cause low white blood cell counts and altered liver function tests, but QoL is maintained. There are as yet no additional biomarkers to indicate which patients may benefit most from a CDK4/6 inhibitor or an mTOR inhibitor, which is the next step when endocrine resistance occurs. Dr Eniu also mentioned elacestrant, a selective oestrogen receptor degrader, as studies show it is effective in patients previously treated with a CDK4/6 inhibitor, an important finding given the increased exposure to these therapies. An ADC, sacituzumab govitecan, which targets Trop-2, has shown progression-free survival (PFS) and OS advantages compared with CT. Likewise, T-DXd has shown a PFS benefit in ER+ MBC and in HER2-low (tumours that do not surpass the threshold to be classified as HER2+) with about a 50% lower risk of disease progression and death than with CT. These newer treatments are costly, however. **Dr Eniu highlighted the "financial toxicity" that some patients experience when health systems do not cover MBC therapies and patients pay out of pocket**. This can lead to bankruptcy, which in turn is associated with a higher risk of early death. What is more, there is a shortage of many medicines that are considered essential (eg, tamoxifen, cisplatin) due to lack of supply, not due to lack of resources. **In conclusion, ABC guidelines recommend that several ETs (tamoxifen, aromatase inhibitors and fulvestrant) are must-haves; CDK4/6 inhibitors are important to have; mTOR inhibitors and PI3KCA inhibitors are good to have; the place of ADC is to be determined; and several CT agents are must haves.** It is important to decrease symptoms for as long as possible with the fewest side effects.

Treatment and Research for Triple Negative MBC

Javier Cortés, Head of the International Breast Cancer Center (IBCC) of Barcelona in Spain focused on triple-negative metastatic breast cancer (TNMBC), which expresses none of the receptors commonly found in breast cancer and has the worst outcome. There is an ongoing quest for targetable biomarkers for therapy. In the meantime, taxane-based CT remains the backbone for triple-negative breast cancer (TNBC). However, in those with BRCA1/2 mutations a platinum-based CT (carboplatin) shows a better response than docetaxel. **TNBC is a target for immunotherapy because it has a high mutation rate, lymphocyte infiltration and expresses PD-L1, a protein involved in immune responses**. PD-L1 expression can be higher in certain sites, such as in lymph nodes or skin. ABC guidelines recommend assessing PD-L1 in metastatic tissue if immune checkpoint inhibitors are available. These plus CT are the preferred first-line option for PD-L1+ tumours due to the better PFS vs some types of CT alone. OS results differed according to the CT type used. A combination of atezolizumab and nab-paclitaxel may also be a first-line option for PD-L1+ TNMBC. **There is also research into blocking the AKT pathway, which is activated in some 35% of TNBCs. PARP inhibitors are a targeted approach for patients with BRCA mutations. The ABC guidelines prefer these over CT due to their benefit for PFS, QoL and their toxicity profile.** Starting from second-line, ADCs that deliver drugs into the cell are options for all TNBC. Sacituzumab govitecan targets Trop-2 – overexpressed in many cancers and linked to poor overall survival – and shows a PFS and OS benefit (5.4 months) compared with physicians' choice of therapy. This is the ABC guideline preference for those with two or more previous lines of therapy, alongside early management of side effects. Studies are under way for other ADCs targeting Trop-2, HER3 or LIV-1. Some 55% of patients who would be considered HER2– can be classified as HER2-low. T-DXd has shown a benefit in PFS and OS in patients with TNMBC and HER2-low. In conclusion, Dr Cortes said that he believes that triple-negative is no longer "negative", and if one looks carefully, it will be positive for a marker which may be targeted now or in the future.

Emotional Support for MBC Patients and Caregivers

Maria Die Trill, from the Cancer Center, Psycho-Oncology, Clínica Universidad de Navarra, Madrid Site in Spain, said that people with a cancer recurrence may experience fear, grief and uncertainty, citing an early study showing that 78% found a recurrence more upsetting than the original diagnosis. MBC is the focus of fewer studies because of the difficulty of doing research in vulnerable groups. Four main forms of support can help people with MBC: 1) education, which can reduce feelings of helplessness and confusion by providing information and correcting misconceptions, and ultimately decreasing anxiety; 2) individual psychotherapy to reduce distress and improve coping, mood and QoL; 3) cognitive behavioural therapy, with strategies to identify and restructure thoughts to improve emotional well-being and functioning; and 4) group interventions, such as support groups led by professionals. **Much of the unmet need in MBC lies in lack of communication skills in health-care providers (HCPs), including difficulties in discussing risk assessment, treatment failures and end of life.** HCPs require training in essential communication skills to improve collaborative decision-making and patients' QoL as well as their own. The International Psychooncology Society **calls for psychosocial cancer care to be a universal human right**, for the psychosocial domain to be integrated into routine care, and for distress to be measured as an additional vital sign. Such distress assessment is already a requirement in some health systems. All of this can contribute to patient empowerment, a process that helps people gain control over their lives and increases their capacity to act on issues that are important to them. Those who feel empowered understand their medical condition and how they might improve it through lifestyle changes, for example. They feel capable of making informed decisions and participating in a treatment discussion. They take responsibility for their health and seek medical help when they need it. This can be achieved through health literacy, participating in their own care and in other health initiatives. The webinar itself is an example of education and support. Dr Die Trill added that families of people with MBC must not be forgotten. It is important for psychosocial support to be provided throughout the MBC continuum to help everyone cope with a disease that affects the entire household and beyond.

Working with Advanced Cancer

Barbara Wilson, founder of Working with Cancer in the United Kingdom, covered the rights of cancer patients to return to work as a lifelong **"right to be remembered"**, especially given that 50% of the population will be diagnosed with cancer in their lifetime. The European Code of Cancer Practice, a manifesto by a team of cancer patients, advocates and cancer professionals, calls for patients to be able to return to work and a normal life. Yet challenges remain. MBC treatment often causes life-changing side effects, such as brain fog and fatigue. Employers may not understand that such side effects can fluctuate. Uncertainty about periods of wellness and changing treatment plans can make a standard working week almost impossible. Nonetheless, many people can and want to continue to work and must receive the necessary support to do so. The workplace itself presents other challenges, such as inflexible policies or hours, ignorance about cancer, and stigma involving poor communication. A 2021 survey of 1241 working-age cancer survivors, including 28% with breast cancer, showed **that those with advanced or MBC received less support from their employers than those with early disease. Many experienced bullying and many worried about being a burden to colleagues.** To address these challenges, there are three main points to advocate for: 1) Make returning to work with cancer a lifelong right for anyone who has had an advanced cancer diagnosis (eg, via phased return to work, flexible hours, open communication, time off for medical appointments, no discrimination); 2) Employers should know and follow best practice; 3) Make working with cancer a valid clinical outcome (ie, treatment will enable a patient to work successfully). With this in mind, in collaboration with some reference cancer centres in the US, UK and France, Ms Wilson's organisation is a major partner in a campaign, the "Working with Cancer Pledge" campaign, which so far over 600 companies have signed, declaring that they will take charge with concrete steps to help abolish the stigma and insecurity that exist for people with cancer in the workplace. The campaign was launched by a major communications group at the 2023 World Economic Forum in Davos. For more on this colossal campaign, see: https://workingwithcancerpledge.com.

Advocating Effectively: Tips and Tricks

Europa Donna's Policy and Research Officer **Martina Fontana** provided tips for advocating effectively, to help MBC advocates use what they learned in the webinar to call for change. It is important to **develop a plan with a clear objective, to have solid, evidence-based and independent data** to support it. This includes statistics on MBC, expenditure figures, existence of guidelines and breast centres in your country/region, for example. Next is to find partners to help advance your aims, and to create a skilled team. Know who to approach, from scientists and health committees to political leaders, and contact them, stating your case precisely and concisely and be prepared to answer questions. Build and maintain relationships with policymakers whose job it is to represent us. Evaluate the results and do not give up: persistence, patience and persuasion.

Amplifying the Outreach of the Europa Donna MBC Campaign: #TheCancerCurrency

Two talks focused on Europa Donna's new MBC #TheCancerCurrency campaign and spreading the word. This campaign, launched two days before the webinar, aims to show that the life of each person with MBC has value – they must not be given up on. **Those living with MBC have been left underfunded, undertreated and underserved, even though their lives still hold immense value. Their lives are as important as anyone with another cancer type and have a socioeconomic value**. The campaign is targeting policymakers, who can make positive change happen for people with this disease, as well as the general public who need improved awareness of this disease and can in turn help the message reach the policymakers. The campaign itself involves a series of five banknotes – by the same designer as United States $50 and $100 notes – each inscribed with the stories of five women living for over 5 years with MBC. People are asked to share the currency found on www.thecancercurrency.com via social media and the shares will be tallied over the year to come. The statistics gathered globally can be presented to policymakers to influence improvements for MBC care. The webinar included talks from some of the women who participated in the campaign and what participation has meant to them.

MBC is an advocacy priority for Europa Donna, which began holding annual MBC conferences and training in 2017 to address the unmet needs of people with MBC. There is a special MBC section on the Coalition website which houses key advocacy information on this topic, including MBC video testimonials.

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