LBCA Patient Advocate Report – San Antonio Breast Cancer Symposium (SABCS) 2025

Kirstin Spencer – LBCA / METUP UK / ICPV

Attending the **San Antonio Breast Cancer Symposium (SABCS) 2025** supported by the LBCA travel grant was profoundly meaningful to me, both personally and professionally, as a patient living with metastatic lobular breast cancer and as an advocate representing the breast cancer community internationally.

- **Thoughts about what I learned**

SABCS is exciting because it is one of the few global conferences where cutting-edge breast cancer science, clinical practice, and patient advocacy can truly intersect. The microbiologists can answer questions and researchers are thinking 'out of the box' all united to find solutions to the plethora of questions and issues arising from the disease.

SABCS 2025 reinforced how rapidly the treatment landscape is evolving, while also highlighting persistent gaps for lobular disease. Many sessions focused on endocrine resistance, novel targeted therapies, and biomarker-driven approaches - areas of particular relevance to lobular breast cancer. However, there was limited lobular-specific data presented and this underscored why continued advocacy is essential. Being present in these spaces matters deeply. It is where inspired communication begins to translate into better science.

Participating as a patient advocate panellist was both engaging and thought-provoking. Being invited to contribute alongside clinicians and researchers sends a powerful message: **patient experience is not an "add-on" to scientific discussion, but a vital source of insight** that can meaningfully shape research priorities, trial design, and clinical decision-making.

For the Alamo Breast Cancer Foundation advocate program supported by the American Association for Cancer Research, I was one of three patient advocates on the panel discussing 'Optimising Communication to Facilitate and Demystify Patients' involvement in Research". The panel also included two experienced oncologists, Fatima Cardoso and Mariana Chavez. Together we highlighted various aspects of the topic and there was a striking contrast in trial experience between myself (having contributed to trial design and patient input initiatives, since my metastatic diagnosis in 2021) failing to access any clinical trials and in contrast, my fellow panellist participating in sixteen trials.

This disparity starkly illustrates the reality of trial access for patients, regardless of the country they live in. Opportunities may depend on specific hospitals or individual oncologists, rather than patient need or eligibility alone. Patients spoke to me about their trial experience and these conversations also reflected a huge disparity in trial access. Following this, in conversations with several pharmaceutical companies, I enquired how trial sites are selected. The response was candid: companies tend to work with sites and clinicians they already know and trust. This no doubt may shape trial access in ways that can inadvertently exclude many patients.

As oestrogen is the predominant driver of much breast cancer - **including the vast majority of invasive lobular breast cancers (ILC)** - the consequences of oestrogen inhibition deserve close scrutiny. Lobular disease is characteristically highly oestrogen-receptor–driven, often for prolonged periods, and yet ultimately demonstrates distinctive patterns of endocrine resistance and metastatic

spread. Understanding the biological differences between selective oestrogen receptor modulators (SERMs) and degraders (SERDs) therefore feels especially relevant for patients with lobular breast cancer.

The viral reactivation of dormant HER2 tumour cells I found very interesting, linking acute inflammation with an awakening and proliferation response from tumour cells and raised cytokine Interleukin 6 levels. Glucocorticoid (stress) hormone levels can influence immune function, inflammation, metabolism, and cellular signalling pathways, highlighting that these wider influences may affect how tumours progress and metastasise. This served as a reminder that cancer can be a whole-body disease, and that both the tumour ecosystem and its micro and macro environments must be considered, which leads me to the work of Donald McDonnell and his team, looking at extrinsic actions of oestrogen modulators.

I very much appreciated Professor McDonnell's candid acknowledgement that aggressive ESR1-mutated disease is, in many cases, **a consequence of prior endocrine treatments**. This is something I am painfully aware of as a patient and advocate, particularly in lobular breast cancer where long-term endocrine pressure is common and resistance often emerges later but more insidiously. It reinforces the importance of looking beyond media headlines and interrogating the biology beneath, especially for tumour types that are under-represented in trials yet heavily exposed to endocrine therapies.

I was fascinated by the emerging evidence that **oestrogens can suppress interferon immune pathway signalling** - through effects on cytokine release and JAK–STAT - mediated gene expression - leading to immune modulation and pathogen inhibition. These findings may have implications for immune checkpoint blockade strategies and potentially for the immunomodulatory effects of radiotherapy even for lobular breast cancer, which is typically considered immunologically "cold".

Equally compelling was the discussion of oestrogen induced efferocytosis impacting immuno-suppression and also how some endocrine therapies can positively influence natural killer (NK) cell activity, delaying progression and visceral metastases. Given the tendency of invasive lobular breast cancer to metastasise to visceral organs, peritoneum, gastrointestinal tract and bone marrow, the observation that oestrogen can reduce NK cell activity - and that knocking out the oestrogen receptor on NK cells alters this - may be particularly relevant. The suggestion that future work may explore knocking out the oestrogen receptor on CAR-T cells raises important questions about whether immunotherapeutic strategies could be tailored for highly endocrine-driven cancers such as ILC. Notably, the finding that **fulvestrant suppresses NK cell activity in a manner similar to oestrogen itself was striking** and potentially concerning in this context.

The discussion around SERDs action in the brain held me spellbound. Lobular breast cancer is well recognised for its propensity to metastasise to unusual and difficult-to-detect sites, including the vital barrier of the meninges, which surround and protect the central nervous system (CNS) - comprising the brain and spinal cord. It can sometimes (along with other oestrogen driven breast cancers) also metastasise to the brain. The possibility that some SERDs cross the blood–brain barrier - and may promote stronger, oestrogen-independent tumour growth within the brain - feels highly relevant, particularly in later lines of treatment. The contrast between camizestrant, which appears not to cross the blood–brain barrier, and Imlunestrant, which does, highlights the need for **far greater nuance in drug selection** for patients at risk of CNS involvement.

While inhibiting oestrogen remains central to controlling tumour growth in lobular (and oestrogen positive breast cancers of no specific type), the caution raised around oestrogen suppression potentially reprogramming the sympathetic nervous system in the hypothalamus - with downstream effects on tumour behaviour - is sobering. For a lobular subtype already associated with late recurrence, diffuse growth, and potential CNS involvement, these findings underline the risks of assuming that deeper oestrogen suppression is always better.

From second line onwards should we be wary of targeting the oestrogen receptor? Professor McDonnell's conclusion was that truly **precision-based approaches** are needed to identify **which patients will benefit from SERDs** strongly resonated with me. For lobular breast cancer in particular, this presentation reinforced the urgent need to move beyond one-size-fits-all endocrine strategies and to better understand how prolonged oestrogen manipulation shapes both tumour biology and metastatic behaviour, including the troubling potential of ILC to spread to the meninges.

On a personal level, attending SABCS while living with advanced disease carried significant emotional weight. Conferences like this are a reminder that **while science advances, patients are living — and dying — in the present**. I had intended to attend alongside my friend, mentor, and colleague Joanne Taylor of METUP UK and ABC Diagnosis, but she became increasingly unwell over the summer and died from metastatic breast cancer just weeks before the conference. In the lead-up to SABCS, I found myself speaking at her funeral and advocating in Westminster, a stark juxtaposition that underscored the reality behind the data and discussions.

The cumulative loss of people to this disease is profoundly challenging, compounded by the sudden, searing pain of losing those with whom we have shared deep personal and professional connections. Yet being in the room - contributing meaningfully, continuing to hold the torch, and representing those who have died and those who may never have the opportunity to attend - was both humbling and motivating. It reaffirmed why advocacy matters, even when the personal cost is high.

- **My experience networking with other patient advocates.**

Equally important were the informal conversations or 'networking' - with researchers, clinicians, pharmaceutical companies and fellow advocates - that happen between sessions. These discussions often provide the clearest insight into emerging ideas, future trials, and where patient input could have the greatest impact. The ability to listen to and communicate with other patient advocates is one of the most valuable aspects of attending conferences and participating in panels.

I was able to reconnect with my Project LEAD colleagues and continue to develop networking opportunities and invaluable support. This can be both scientific and practical advice. On this occasion, those connections directly informed one of my projects in the UK, where recruiting representation from all the communities we aim to include can be challenging.

A particularly meaningful part of the conference were two meetings around a dinner and a breakfast. The first was a special dinner and then hosted privately in a beautiful house for lobular breast cancer patient advocates, generously hosted by Dr. John Doski, whose wife died from lobular breast cancer. The setting created a rare and valuable space away from the intensity of the conference programme, allowing for quieter reflection and more authentic connection. Sharing such delicious food in such an intimate environment allowed an opportunity for advocates and researchers to make connections and speak with each other more informally which can be missed or more difficult to achieve in formal scientific settings. Hearing a researcher speak about his work in this context - grounded not only in data but in shared purpose and personal loss - deepened understanding on both sides.

The Patient Advocate breakfast that LBCA hosted with Dr Jason Mouabbi, a specialist in Lobular Breast Cancer, was enlightening and fun. It offered a rare opportunity for patients to access a specialist and ask questions in a safe informal and friendly space. The events served to remind me that progress in research is driven as much by relationships, trust, and lived experience as it is by science itself.

The Patient Advocate lounge created a safe and honest hub to share lived experiences, compare challenges, and validate concerns that can otherwise feel isolating. Speaking with advocates from different hospitals, countries, and health systems helps me better understand where inequities in care

and trial access persist, and reassures me that many of the barriers faced are systemic rather than individual. These relationships also provide ongoing peer support and strengthen collective confidence to speak openly and constructively to advance patient experience of breast cancer.

- **How I will use this experience and new knowledge to advance ILC advocacy in future.**

I have already enjoyed reading the research from Christos Sotiriou's laboratory led by Professor Laurence Buisseret and wrote Patient Advocate Letter in Support of a Phase II Randomised Trial of Neoadjuvant Inavolisib, Letrozole and Ribociclib Compared to Letrozole and Ribociclib in Early-Stage Lobular Breast Cancer and wrote a patient advocate letter of support for a proposal focusing on advancing treatment strategies for ILC through a novel neoadjuvant combination targeting PI3K, ER and CDK 4/6 pathways. The enhanced PI3K pathway of activity in ILC, independent of PIK3CA mutation status, reflects an important target to better control lobular tumour biology. It is encouraging for lobular breast cancer patients to see robust laboratory findings translated into a trial designed specifically for this sub type. Additionally, the research ensures **patients' contributions lead to better understanding and better treatments in the future.** This is done by collecting tumour and blood samples at multiple time points reflecting a **commitment to learn from every participant** and **begin to understand why treatments work for some people and not for others**. All cancer patients consistently express a desire for research that moves beyond short-term outcomes and contributes to more personalised and effective treatment options for those who follow.

The continued development of **Lasofoxifene** in Elaine III (Sermonix pharmaceuticals teaming up with Athira Pharma) is also something I would like to explore and see if the large phase III trials planned have capacity to separate lobular from NST breast cancer. However, outside of the upcoming Elaine III trials compassionate access to this drug seems to be the only alternative pathway.

I am also a GRASP mentor and enjoyed many posters, mentoring on two the week after SABCS. One that especially held my attention was an **intratumoral injection** of Zeta-BC-003 which provided a radiographic complete response with no skeletal related events (SRE's) in 9 patients (13 lesions) and is the first non-palliative treatment reducing SRE risk, decreasing pain, ceasing MBC lesion activity, reconstituting trabecular bone, and increasing quality of life. An **unexpected finding** was that **both bisphosphonate and CDK4/6 inhibitor therapies were ineffective at preventing progressive lesions** in superior and inferior adjacent and non-adjacent vertebrae. Overall survival has not been reported yet.

The second poster was on longitudinal genomic profiling of circulating DNA in metastatic ILC and NST. It addressed a critical gap for people living with metastatic invasive lobular breast cancer by using longitudinal ctDNA data to show how tumour fraction, copy number changes (including chr11q13.3 amplification) and ESR1 mutation status reflect real-world disease progression and treatment resistance over time. **For patients, this work highlights the promise of liquid biopsy as a less invasive, more responsive way to monitor disease and guide conversations about treatment effectiveness**. I felt that this work supported the case for lobular-specific research and personalised monitoring strategies for people living with advanced disease. Strengthening the link between these molecular findings and how they could be used in routine care would help translate this work into meaningful benefit for patients. **You've got to love science!**

- **SABCS event advice.**

Firstly, **plan, plan, plan**, right down to advocate meet ups and evening appointments because once you are there you are swept up in a whirlwind of science and opportunity. One night I had several dinners to attend and felt akin to the 'Vicar of Dibley' at Christmas…

Secondly, I have noticed that conversations with oncologists can differ markedly from those with researchers and laboratory scientists. As an inquisitive and responsible patient advocate - one who is actively seeking truth - I try to look beyond published headlines and conference soundbites. This includes exploring emerging or unpublished data where possible, examining what sits beneath the presentation of new drugs and treatment pathways, and paying close attention to post hoc analyses and feedback from real-world patient populations.

These deeper explorations often reveal a more complex picture than is presented on the main stage. Navigating this landscape can feel like an exhilarating jungle, where **curiosity and critical thinking are essential**. It has also taught me not to be overly influenced by reputation alone. High-profile voices play an important role in advancing the field, but they may also operate **within constraints that shape how openly uncertainties, limitations, or challenges can be discussed**. Maintaining space for honest, nuanced dialogue is therefore crucial if we are to truly serve patients' best interests.

Thank you to LBCA

I am deeply grateful to the **Lobular Breast Cancer Alliance (LBCA)** for supporting my attendance. Their commitment to ensuring lobular patient voices are present at major scientific meetings is critical. This support enabled me not only to learn, but to actively contribute and voice some lobular breast cancer perspectives. The science allows me to bring knowledge and hope back to the wider patient community and specifically informs my drug approval meetings, research and policy involvement which I hope should provide patients with real world benefit.

In summary, SABCS 2025 was not just a conference I attended — it was a space where the voices of breast cancer patients more broadly, were heard. Continued investment in patient advocate participation is essential if future breast cancer research is to be inclusive, relevant, and truly patient-centred.