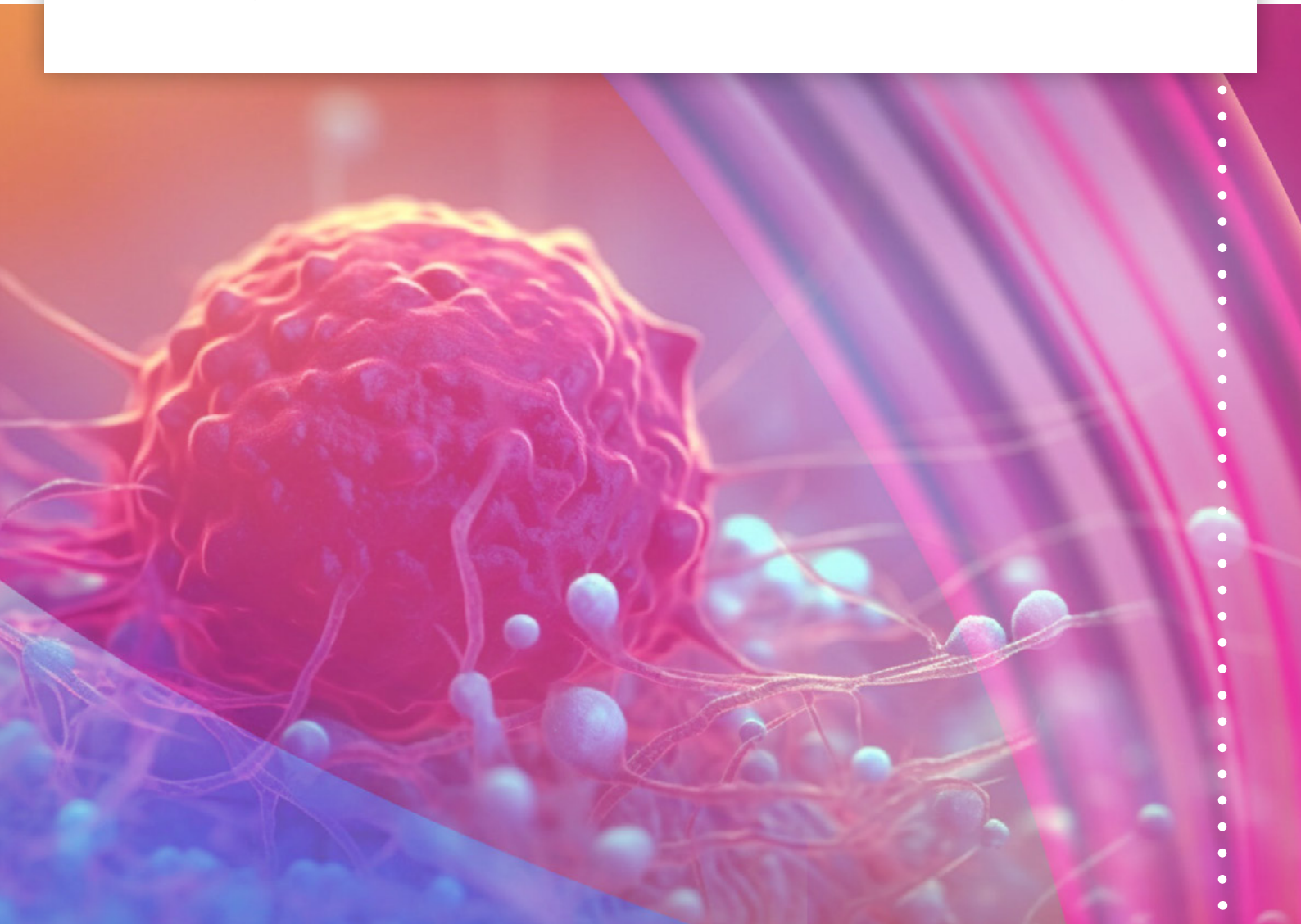
CANCER PATIENTS EUROPE

New Biomarkers in Metastatic Breast Cancer & Awareness on ESR1 and Liquid Biopsy: **Analysis of a European Patient Survey**



New Biomarkers in Metastatic Breast Cancer & Awareness on ESR1 and Liquid Biopsy: **Analysis of a European Patient Survey**

CONTENTS

Breast Cancer in Europe

Breast cancer continues to be the most common female cancer in the EU, with an incidence of **29.4%** of all cancers in women. It is the leading cause of cancer deaths in women in the EU (**16.7%, 138,000**). Though **breast cancer** fatalities in the EU have declined from **17.9/100,000** in **2002** to a predicted **14.9/100,000** in **2022**, there still exists a big gap between Eastern and Western EU countries, with an elevated incidence in the West but higher death rates in the East[1].

Breast cancer is the most common cancer in EU women, with metastatic cases, especially ER+/HER2-, driving high mortality due to ESR1 mutations that cause resistance to standard treatments.

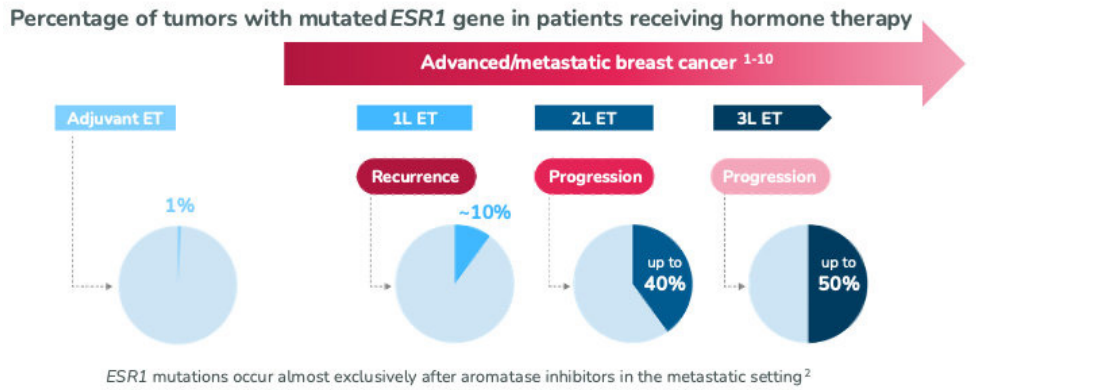
What is Metastatic Breast Cancer

Metastatic Breast Cancer (mBC), also referred to as **advanced breast cancer** (ABC), occurs when the cancer spreads from the initial tumor and forms other tumors in different parts of the body. During initial diagnosis, 5-10% of all breast cancer patients are metastatic, and 20-30% of patients diagnosed with early-stage breast cancer initially, will eventually progress to the **metastatic stage**. The **ER+/HER2-subtype** is the most common in mBC (68%)[3], and the median survival of mBC patients is nearly 3 years[4,5].

Current standard treatment for mBC patients

The **European Society for Medical Oncology (ESMO)** guidelines **recommend** the **endocrine-based (hormone) therapy (HT)** as the preferred first-line option for women with **ER+/HER2- mBC** cancer[6]. However, almost **1 in 2 patients** with **ER+ mBC develop** resistance to hormone therapy, **allowing** progression of the disease, due to mutations on **ESR1 (Estrogen receptor 1)**, the target for the hormone treatment. **ESR1-mutated ER+/HER2- mBC is** associated with **poorer outcomes**[7]. Tumors with **ESR1 mutations are more difficult to treat**[8].

ESR1 Mutations Develop During Hormone Therapy*



ESR1 mutations occur almost exclusively after aromatase inhibitors in the metastatic setting[2]

National treatment guidelines recommend routine blood testing for *ESR1* mutations at each worsening of ER+/HER2- metastatic breast cancer in patients receiving hormone therapy[11]

ESR1, estrogen receptor gene; ESR1 -mut, mutated *ESR1*; ET=endocrine (hormone) therapy
*Hormone therapy in the first line is typically given in combination with a CDK 4/6 inhibitor.

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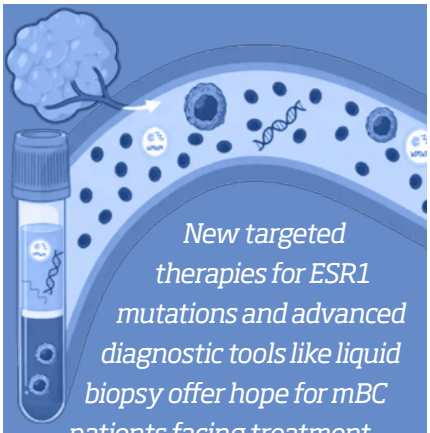
New advances for mBC treatment and diagnosis

Despite the **delay** with combined therapy, **HT resistance** will **appear** in most cases, complicating the next options of treatments. A new **targeting drug** has now been **developed** directly targeting the **ESR1 mutation**. This therapy **provides** a new promising alternative to mBC patients, consistent with the clinical guidelines to **use** after other treatment options and before **moving** on to chemotherapy. Along with new therapies, the application in mBC of blood diagnostic tools (**liquid biopsy**) is **essential**. **Treatment guidelines recommend** routine blood testing for **ESR1 mutations** at each worsening and progression of **ER+/HER2- metastatic breast cancer** in patients receiving hormone therapy[9].



New targeted therapies for ESR1 mutations and advanced diagnostic tools like liquid biopsy offer hope for mBC patients facing treatment resistance, but greater awareness and routine testing are urgently needed to ensure access to these breakthroughs.

ESR1 mutations are **subclonal** and **heterogeneous** within the tumor, hence not all of them will be **detected** in a tissue biopsy. **Blood-based ctDNA** is considered the preferred testing methodology[10]. Archival tissue from primary tumor should not be used to identify **ESR1 mutations**, as **ESR1-mutations** develop mainly during treatment with aromatase inhibitors.[9] This is a great example of how new **advanced therapies** are tightly linked to the use of new **diagnostic techniques** and **genetic analysis methods**[11].

Cancer Patients Europe continues campaigning to support Breast Cancer patients and in particular metastatic Breast Cancer patients.

CPE has already previously **developed** a campaign (**my Cancer my Concern**) to **create awareness** about the use of **personalised medicine** and **genetic analysis** to improve **Breast Cancer** patients' livelihoods. Now, **CPE** is promoting a new initiative directed towards **metastatic Breast Cancer** patients, to **create awareness** about new **therapeutical advances** that can **give** new hope when other treatment options fail[12]. Patients should **ask** their **HCPs (Health Care Providers)** for an **ESR1 test** at every progression in the **metastatic setting**, if not detected previously[13].

SURVEY ANALYSIS

This **survey** was initiated and promoted by **CPE** and **aimed** to tackle the **interest** of a group of **Breast Cancer patients** (**metastatic Breast Cancer**) with an incurable and resilient disease. The goal was to **create awareness** and **improve** the level of information that these patients have regarding new **advances**, using **biomarkers**, that bring better **therapeutic** and **diagnostic options**. By **raising awareness** and **spreading** the latest information to the patients, it will **help** to **combat** the burden presented by the tumor's resistance to current treatments and the **side-effects** of current treatment; ultimately **giving** them **hope** for a better **quality of life**.

Advisory Board

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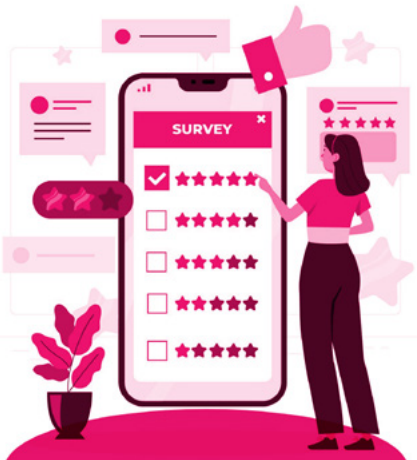


The CPE survey aimed to raise awareness and gather insights from metastatic breast cancer patients across five European countries, focusing on their knowledge of new treatments, biomarkers, and liquid biopsy as critical tools in improving patient care.

Methodology

The **survey** was **designed** by **CPE** as a **42-question questionnaire**, **reviewed** and **approved** by the **Advisory Board**. The questionnaire was **disseminated** by **CPE**, local **patient organisations** and **individuals** in five European countries: **France**, **Spain**, **Italy**, **UK**, and **Germany**.

Structure and target population The **survey** was **intended** to obtain information and **create awareness** among **breast cancer patients** about new **innovative therapies** and **diagnostic tools**, and in particular the mutated **ESR1** and the use of **liquid biopsy** for **genetic detection**. The survey is divided in five sections: **Demographics** and

treatment background; **Awareness** and **information sources**; **Knowledge** and **perception** of **ESR1**; **Biopsy preferences** and **awareness**; **Treatment preferences**. The channels used to **distribute** the survey included: **Social media** (**Facebook**, **Instagram**), **CPE newsletter** (delivered to **breast cancer patient associations**).

Results

The **survey** was available for a **six-week period**. There was a total of **1268 respondents** across the five participant countries: **UK: 205; Germany: 161; Spain: 237; Italy: 364; France: 301.**

- Almost **100%** (**99.9**) **self-identified** as **women**. **54% diagnosed** with **metastatic Breast Cancer (mBC)** and **59%**with an **ER+/HER2- subtype**. **43%** were **ER+/HER2-** and **mBC patients** (the **target population** for **ESR1 mutant diagnostic** and **therapeutic new advances**).

- **67%** of the respondents were between the range of **50-69 years old**.

The survey reveals a significant lack of awareness among metastatic breast cancer patients about biomarker testing and liquid biopsy, with many unaware of their ESR1 mutations and the potential of new targeted therapies.

Key Findings

The **survey** shows obvious signs of a **lack of information** about the use and analysis of **biomarkers** and their importance for the use of new **targeted therapies**:

- **70%** of total respondents **did not know** the markers they had been tested for and **75%** had not **discussed** biomarker testing with their **oncologists**.

- **70%** of **ER+/HER2- mBC** respondents were **unaware** of the role of **ESR1 mutations** in tumor resistance to hormone therapy.

- Only **16%** of **ER+/HER2- mBC patients** that **answered**, were aware of new drugs targeting mutant **ESR1**. Even in the countries where **anti-ESR1 drugs** are available, awareness is very limited (**24% in Germany**; **22% UK**) in the **target community**.

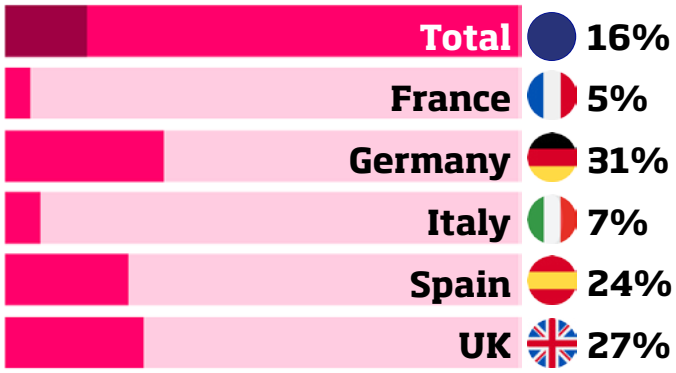
- Only **23%** of **ER+/HER2- mBC respondents** in **Germany** had been tested for **ESR1 mutations** (in the total of the five countries only **12%**). We have to consider that almost **50%** of **mBC with the ER+/HER2- subtype** that follow hormone therapy **develop ESR1 mutations**.

- There is an overall **lack of knowledge** about the new uses of **liquid biopsies** in **cancer diagnosis**. **53%** of respondents **did not know** that cancers **release DNA** to the bloodstream and **a 60%** had no information that **liquid biopsy** can **detect** that **cell-free DNA**. Almost **30%** of the respondents **did not trust** the use of **liquid biopsy** to test their tumor and that may be due to the fact that **60%** (of the total) **did not know** that **liquid biopsy** can give **reliable information** about the type of their cancer.

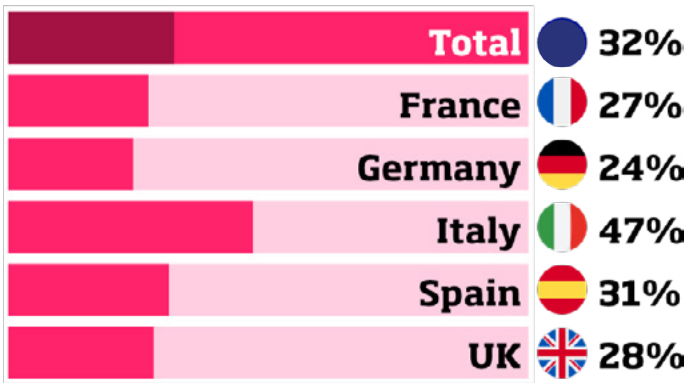
Country variations

Nevertheless, there are some interesting **variations** amongst the **participant countries**:

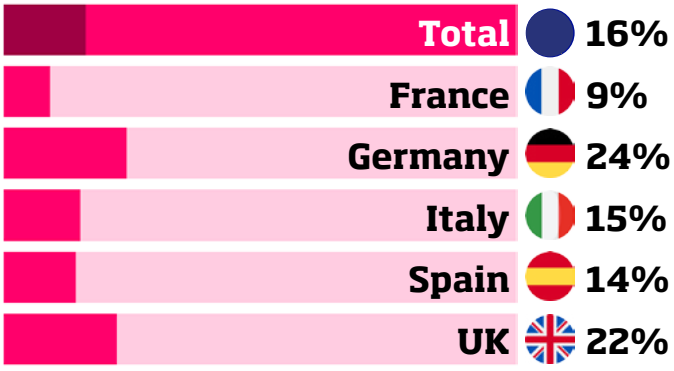
Awareness about the importance of **ESR1 mutations** in **mBC ER+/HER2-**:



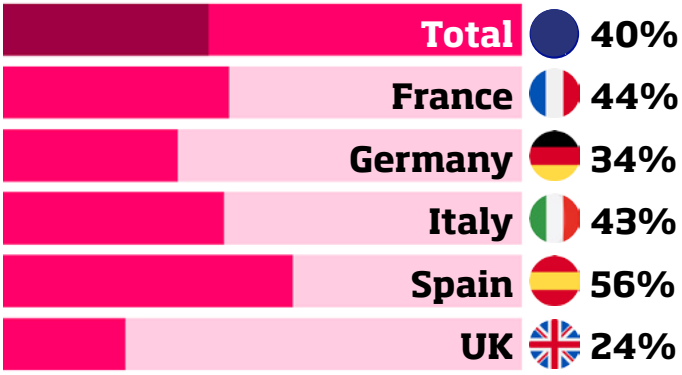
Waiting time for biomarkers test results (more than 2 weeks):



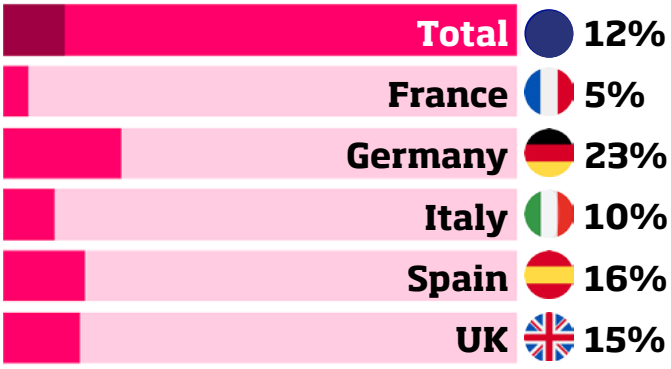
Awareness about **drugs targeting ESR1 mutations**:



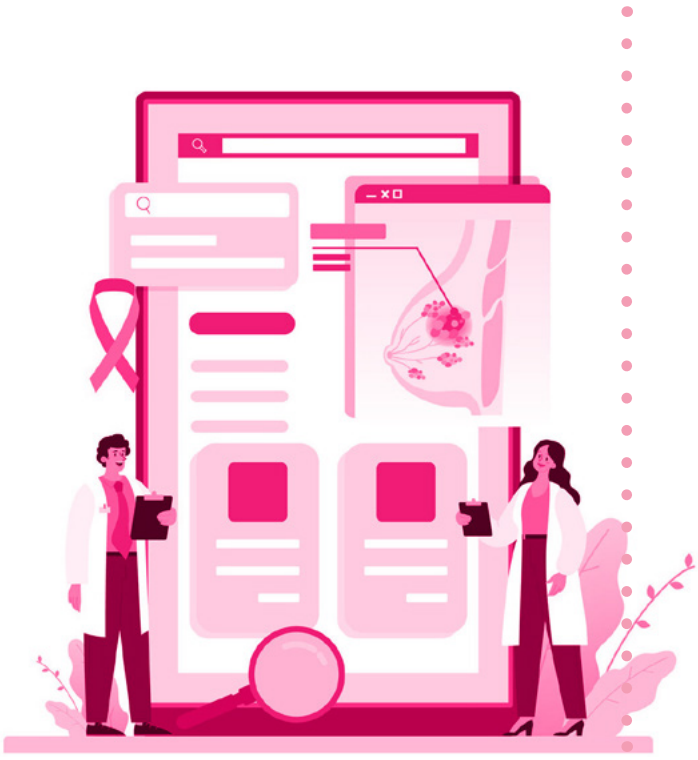
Use of liquid biopsy for diagnosis of the cancer



ESR1 Mutations:



There are some **differences** amongst the **participant countries**, mostly related to the **guidelines** that every country uses about the **testing** of **markers (ESR1)** and the type of **diagnostic tool** chosen (**liquid biopsy**).



CALL TO ACTION

The **results** from this **survey** show a significant **gap** between the incredible **development** in new **therapeutical** and **diagnostic solutions** during the last years and the time they reach the **cancer patients**. New, more specific **drugs**, are **addressing** the needs for those **cancer patients** that had limited **treatment options**. **Advanced therapies** give not only **hope** to **extend the life** of those **patients**, but also **offer** the possibility of less severe **side effects**, and thus, an **improvement** of the **quality of life**. A proper **profiling** of the **patient** and **tumor genetic status** is absolutely necessary to **select** the most advanced and proper **therapy** for **patients**. **Detection** of specific **mutations** and other **genetic markers** are now possible with the use of less invasive and more accessible **diagnostic tools** such as **liquid biopsy**. A proper **information** about the possibilities of these new **advances** is needed for **cancer patients**, but also for **clinicians** in order to make the **best** out of them.

For policy makers

The **absence** of a common **standard** for **healthcare** in the **EU** results in huge **gaps** of the time when new **advanced therapies** can be **accessible** to all **cancer patients**. New **legislation** at **European level** such as the new **HTA regulation** can help to reduce the **inequalities** in accessing highly developed **therapeutical** and **diagnostic tools**. In addition, even in those **countries** of the **EU** where **advanced therapies** are **faster** and more readily **available**, differences in the **standards** in terms of **application** create **disparities** and **inequalities**. This is the case for **mBC patients**, resulting in **reduced solutions** when the tumor becomes **resistant** to the standard **hormonal therapy**. A **homogenisation** of the **protocols** and **guidelines** are necessary regarding the use of new **testing tools** across **EU health systems**. To ensure the **accessibility** for all **patients**, **biomarker testing** needs to be properly **funded** by the **health systems**, considering the **reimbursement** of **treatment** and **testing**, as they need to be **used together**.

A common EU standard for cancer care is urgently needed to reduce disparities in access to advanced therapies and diagnostic tools, ensuring all patients benefit from timely, life-saving treatments.

For healthcare professionals

Guidelines and **recommendations** about the **implementation** of new **therapeutical options** and **diagnostic tools** can only be successful with the active **support** of the **healthcare community**. Proper and continuous **updates** about the new available **therapeutical options** and their **potential** are needed for **clinical professionals**. In addition, there is a need to improve the way that **information** is **disseminated** to **cancer patients**. Giving **mBC patients** easily digestible **information** pertaining to their options will allow them to **participate** in their own **treatment's decisions**. A well-informed **mBC patient** is not only more **receptive** to a new **treatment** but can also provide better

Healthcare providers must stay updated on new treatments and diagnostic tools, ensuring mBC patients receive timely, accurate information to actively participate in treatment decisions and improve their outcomes.

feedback to the **clinical staff** to improve the **implementation** and **use** of **therapies** and **diagnostic solutions**. **Differences** in standard decisions on **biomarker testing** should also be **homogenised**. Testing for **ESR1** is very different amongst the participant **countries**. Some **healthcare systems** consider it only useful as any **drug** is available. However, other **countries** consider the test as a **prognostic factor** (to early detection of treatment resistance) to **preview** and **foster decision** on **treatment changes** even if the specific **drug** is not available. A general **compromise** using **scientific evidence** within the **clinical community** should be arranged at **European level** to create a **framework** where all **patients** in the **EU** can access the best **treatments** and the best **quality** of their lives.

For patient associations

Healthcare professionals are the main source of **information** for **cancer patients**. However, this can be limited by the **clinician knowledge** and sometimes it may reach the **patient** too late. For that reason, **cancer patient associations**should provide a closer avenue for the **patients** allowing them to access **reliable** and up-to-date **information** about the new **therapies** and **diagnostic possibilities**. **Cancer patient associations** can create **awareness** in the **cancer patient community** to reduce **toxic sources** that may induce **mistrust** and **unwillingness** towards the use of **advanced medications**. For **mBC patients**, better **information** about **drugs** that can **overcome** the **resistance** of their **cancer** to the standard **treatment**, will give them a **faster access** to the new **therapies**. Detailed and easy to understand **explanations** of the **potential** and **reliability** of new **diagnostic tools**, their **use** and their **application** can also create **trust** and facilitate the **patient's acceptance**.

Cancer patient associations must bridge the information gap, providing mBC patients with clear, reliable updates on new therapies and diagnostics, empowering them to access the best possible care.

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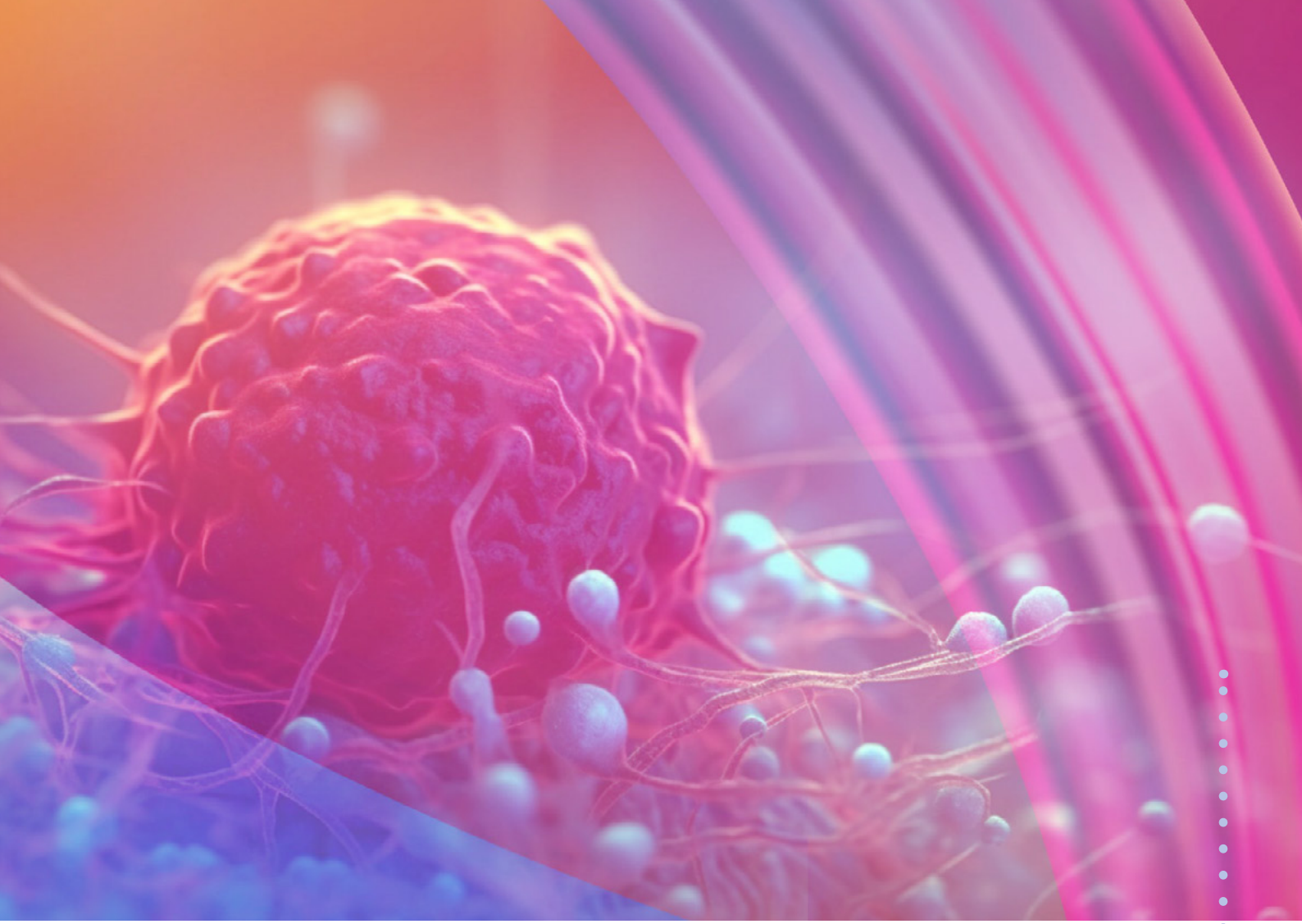

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