

Meaningful Goals in the Management of mBC

This global landmark primary research study was commissioned by Pfizer Inc. to understand the goals of mBC treatment, beyond clinical outcomes.

Patient Perspectives and Emotions Along the mBC Care Continuum

- ▼ Patient outlook varies considerably over the disease continuum, as changing perspectives and emotions strongly impact the patient's overall disease experience
- ▼ While news of disease progression affects patients differently, most experience a significant negative emotional impact

Goals of Treatment in mBC

- ▼ Patients with mBC have several treatment goals beyond survival alone, which may differ depending on disease stage and environment
- ▼ Patients' understanding of delaying disease progression and survival are similar; both ultimately mean to patients staying alive as long as possible
- ▼ While physicians hope to ultimately increase survival, they also strongly consider delaying disease progression as a relevant goal in 1L; however, goals may shift as patients progress to 2L

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The Impact of Physician and Patient Interactions on Goals

- ▼ Interaction with physicians is a key influencer on patient satisfaction, emotional experience, and management goals
- ▼ Physicians are not always comfortable communicating with patients about mBC, but both physicians and patients recognize the value and importance of discussing treatment preferences and goals; nevertheless, neither is initiating the conversation

Introduction

The *Global Status of Advanced/Metastatic Breast Cancer 2005 — 2015 Decade Report*, published in March 2016, details the most comprehensive analysis to date of the global advanced and metastatic breast cancer (mBC) landscape over the past decade. This first-of-its-kind report revealed both areas of improvement and substantial gaps in care, needs for access to resources and support, and gaps in treatment outcomes for women with mBC.

Key findings from the Patient Care Perspectives section of the *Global Decade Report* highlighted the requirement for further insights into the decision-making process between patients and physicians regarding goals of treatment throughout the mBC continuum. To investigate further, and to inform recommendations for improvements, this global landmark primary research study was commissioned by Pfizer Inc. to understand the goals of mBC treatment, beyond clinical outcomes alone, and to compare patient and physician perspectives. The findings described here discuss the meaningful goals of managing mBC and related unmet needs, from both patient and physician perspectives. With varying access to treatments, the patient journey may be very different for HR+, HER2+, and TNBC.* The research in this report did not differentiate between these, and thus all molecular subtypes have been included. Additional insights from an international expert committee inform the interpretation of these research findings and have shaped a series of key recommendations based on clinical experience.

Findings from this research address three distinct themes:

1. **Patient Perspectives and Emotions Along the mBC Care Continuum** reviews how the emotional experience and outlook of the patient evolves over the course of the disease, with specific focus on disease progression.

2. **Goals of Treatment in mBC** shares patient and physician perspectives on their goals of treatment and how these differ throughout lines of therapy. Patient and physician views on delaying disease progression are discussed in the context of patient benefit.
3. **The Impact of Physician and Patient Interactions on Goals** considers the value of patient and physician communication and how this impacts overall patient experience, outlook, and goals.

This initiative aims to highlight the treatment goals that are meaningful to patients with mBC, and how these goals change with patients' outlook as the disease progresses, as well as interactions between patients and their physicians, who may have different treatment goals.

Methods

Both quantitative and qualitative primary research was conducted with more than 500 respondents across 10 countries. Both physicians managing patients with mBC and patients themselves were included within the research (Figure 1 and Figure 2).

Qualitative research completed with physicians in prior research helped frame questions in the quantitative physician survey.

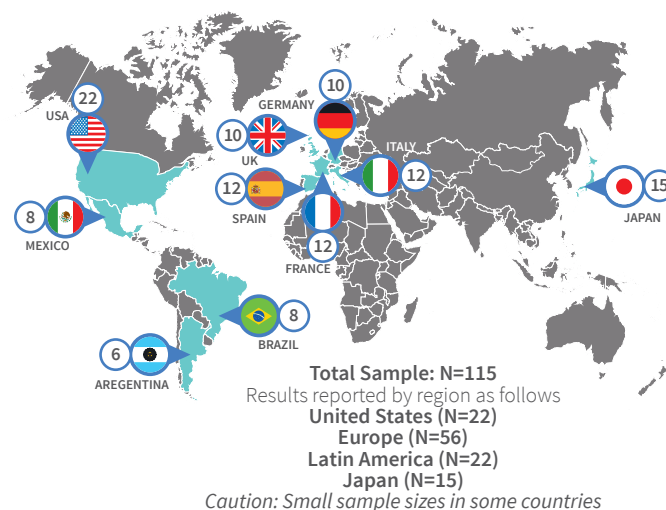
Additional information on this research methodology and details regarding respondents can be found in the Appendix.

Research Objectives:

- ▼ Understand patient and physician goals in relation to the management of mBC
- ▼ Determine the value of delaying disease progression and what that means for patients
- ▼ Establish how disease progression is assessed, communicated, explained, and monitored by both physicians and patients
 - Identify the relative importance of delaying disease progression from a physician's perspective and how they perceive patients view this
- ▼ Gain an insight into the interactions between doctors and their patients, and identify any disconnects that exist in these communications
 - Includes how physicians communicate with patients regarding the management of mBC
- ▼ Identify the physician's perspective on the goals of patients when managing their mBC

Figure 1. Global Overview of Patient Respondents

Interviews conducted **via phone/in person**
 Lasting **60 mins** (45 mins in Japan)
 Research conducted between **October 2015 and March 2016**

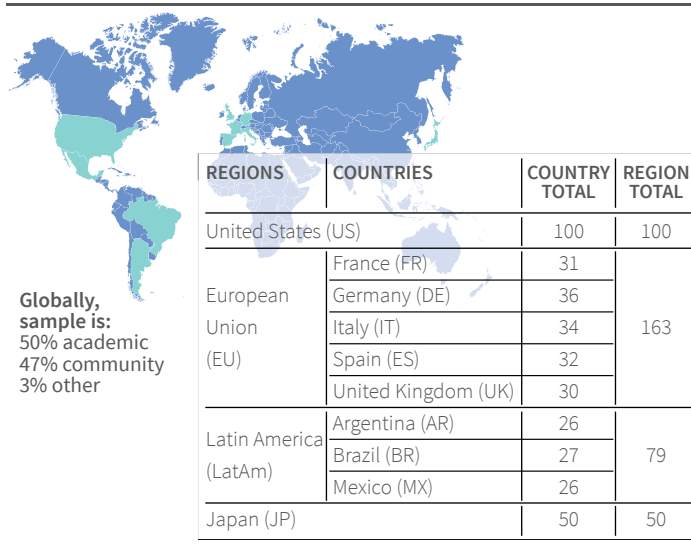


Note: A variety of patients were enrolled with different cultural and socio-economic statuses which should be considered when interpreting results.

Figure 2. Global Overview of Physician Respondents

Sample:
N=392 Oncologists and Gynecologists (DE only)
 treating mBC patients

Methodology:
 45-minute
 online survey
 February 17, 2016–March 11, 2016



1. Patient Perspectives and Emotions Along the mBC Care Continuum

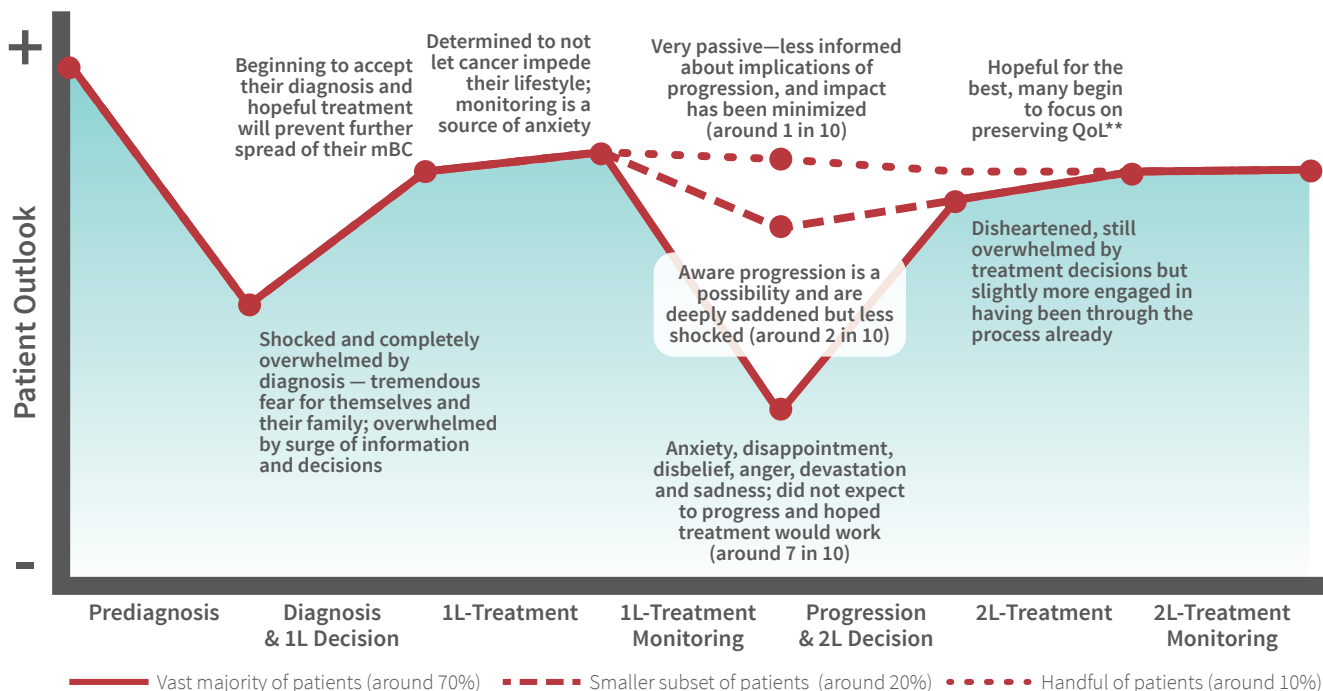
- ▼ Patient outlook fluctuates throughout the disease continuum as lines of treatment progress
 - ▶ Evolving emotions and perspectives influence personal goals of treatment
- ▼ Patient perspectives surrounding mBC and its impact are varied
 - ▶ Some patients have misperceptions that could impact the overall experience of living with the disease
- ▼ The news of disease progression has a significant negative emotional impact on the majority of patients
 - ▶ Many patients feel they are not sufficiently prepared by their healthcare team for news of disease progression. Patients express feelings of anxiety, disappointment, disbelief, anger, devastation, and sadness

1.1 Patient outlook fluctuates considerably over time; perspectives and emotions play a strong role in the overall disease experience.

The course of mBC, from the time of initial diagnosis through to end-of life care, is different for every patient. Although some patients may live for many years with the disease, median survival is estimated to be 2 to 3 years.¹ Patient outlook fluctuates throughout the disease continuum as lines of treatment progress, and these evolving emotions and perspectives can influence personal goals of treatment (Figure 3). At the time of diagnosis, patients experienced shock and fear, often feeling completely overwhelmed by the information they were given and the decisions they are required to make. After each line of treatment (1L or 2L*), trends showed that patient outlook generally improved with increased acceptance of diagnosis and hope that treatments would delay further disease progression. News of progression can have a substantial impact on patient outlook; many experienced feelings of anger, disappointment, and disbelief, resulting in a negative impact on outlook, sometimes even more so than at diagnosis.

Figure 3. Patient Emotions Are Varied Throughout the Care Continuum

Summary of Qualitative Patient-Reported Research



Please note that this research was qualitative in nature, and therefore only estimated percentages of patients expressing these outlooks can be provided.

¹ Weide R, Feiten S, Friesenhahn V, et al. Metastatic breast cancer: prolongation of survival in routine care is restricted to hormone-receptor- and Her2-positive tumors. Springerplus. 2014;3:535.


*1L — first-line treatment, 2L — second-line treatment

**QoL — Quality of Life

1.2 Patient perspectives surrounding mBC and its impact are varied, highlighting some misperceptions that could impact the overall experience of living with the disease.

Globally, almost a quarter of patients reported that they believe mBC to be curable; however, strong regional variation was observed (vide infra). Twenty-two percent and 41% of patients in the EU and Latin America, respectively, believed mBC is curable, while 18% and 21% of patients in the US and Japan, respectively, were neutral about this belief. When stratified, 28% of patients in later lines of treatment (3L+*) agreed with the statement “mBC is curable,” compared with 19% in 1L and 20% in 2L, which may be due to the smaller population size of 3L+ patients. Of *de novo* mBC patients, 32% believed that the disease was curable, compared with 20% of patients with recurrent disease†.

Experts expressed surprise that patients in their third line of treatment still believed the disease to be curable.



Approximately half of patients across countries believed that mBC can be managed for many years. Forty-nine percent of patients remained hopeful that both their disease and quality of life (QoL) could be managed for some time; however, only 27% of patients in the US held this view†.

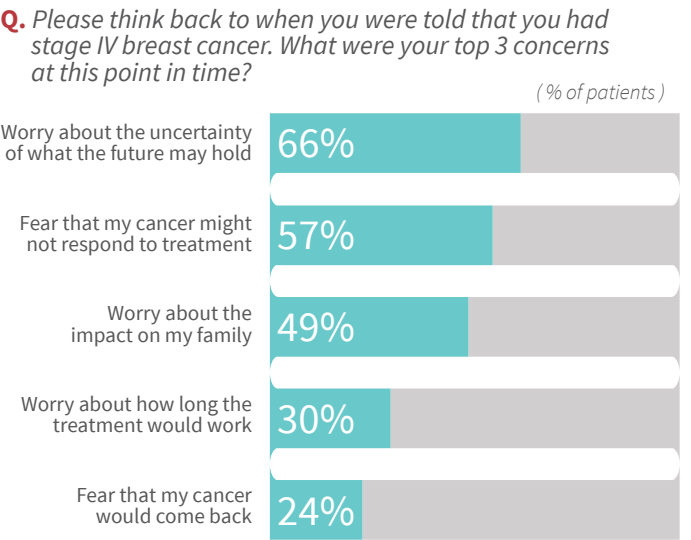
Alongside emotions, patient concerns across the course of their disease also influence personal treatment and management goals. Both concerns and fears changed as patients moved from initial diagnosis through to 1L-Treatment, ranging from a focus on cancer outlook and treatment response to the impact on their family (Figure 4).

The most prominent patient concerns at the time of initial mBC diagnosis related to uncertainty of what the future might hold (particularly dominant in the US at 91%†), fears that the cancer may not respond to treatment, and worries about the impact of the diagnosis on the patient’s family. In Japan, while the top concern remained consistent with the other countries, worries regarding the length of time a treatment would be effective was a more prominent concern at diagnosis than in other countries (53%†). Although patients continued to endure many of the initial concerns experienced at diagnosis; as 1L-Treatment was initiated, concerns shifted towards the impact of treatment and its effectiveness. Fear that the cancer might not respond to treatment was reported as the biggest concern in the 1L setting across countries (Figure 4).

*3L — third line treatment (or third-line)
† — Data on File

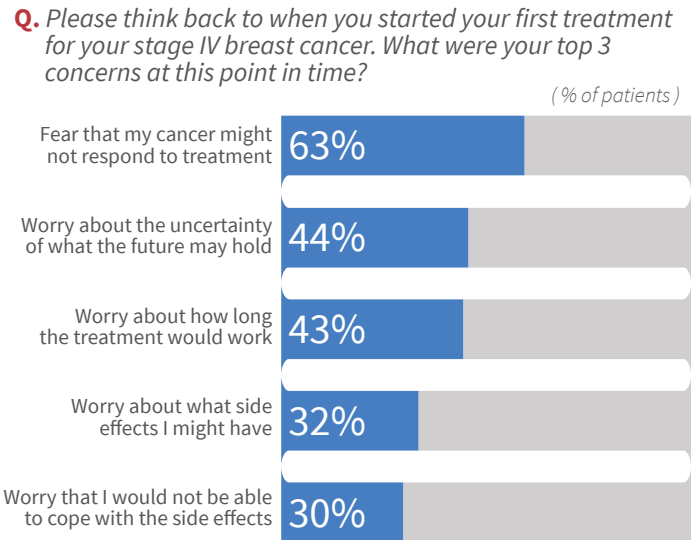
Figure 4. Top 3 Patient Concerns at mBC Diagnosis and at 1L-Treatment Initiation (Patient Reported)

Diagnosis



Base: All respondents: US (22), EU (56), LatAm (22), JP (15).
Please enter a 1, 2, and 3 in the yellow column below to indicate your top 3 concerns; Worry about what side effects I might have: US 9%, EU 21%, LatAm 9%, JP 27%; Worry about the number of treatment options left: US 5%, EU 13%, LatAm 27%, JP 20%; Worry that I may not be able to work anymore: US 14%, EU 7%, LatAm 9%, JP 33%; Worry that I would not be able to cope with the side effects: US 0%, EU 9%, LatAm 14%, JP 13%; Fear that experiencing symptoms like pain or cough may be a sign of cancer getting worse: US 9%, EU 7%, LatAm 5%, JP 13%.
Note: The top 5 concerns reported are based on respondents selecting their top 3 concerns.

1L-Treatment



Base: All respondents: US (22), EU (56), LatAm (22), JP (15).
Please enter a 1, 2, and 3 in the yellow column below to indicate your top 3 concerns; Worry about the number of treatment options left: US 0%, EU 13%, LatAm 18%, JP 20%; Worry that I may not be able to work anymore: US 0%, EU 4%, LatAm 14%, JP 13%; Fear that experiencing symptoms like pain or cough may be a sign of cancer getting worse: US 5%, EU 5%, LatAm 5%, JP 0%.
Note: The top 5 concerns reported are based on respondents selecting their top 3 concerns.

“As you move into treatment, focus increases on expectations of efficacy and side effects, however, this can be fairly subjective; those patients who may have experienced previous issues with side effects ask again what to expect, for those who haven’t had previous issues with side effects... they are less likely to raise this.”



Across the US, EU, and Latin America, surveyed physicians indicated that patients’ greatest concern at 1L-Treatment initiation was fear of dying from their disease; however, in Japan, physicians indicated that patients communicate that their greatest fear relates to side effects that may occur. Another major concern cited in Japan was the financial burden of treatment; this was a much lower concern in other regions[†].

1.3 Although news of disease progression affects patients differently, the vast majority experience a significant negative emotional impact.

The impact of disease progression places the largest emotional burden on most patients, increasing uncertainty and significantly changing outlook (Figure 5). The prospect of a new, unknown treatment is challenging for patients; there are uncertainties relating to how they will cope, whether it will work, and how long for. Patients worry that changing treatments means there are fewer options in reserve, and that the side effects from this new treatment may impact their daily lives. Additionally, feelings

of despair that all efforts made at 1L were in vain and guilt that patients may have done something wrong to cause the disease to progress were reported[†].

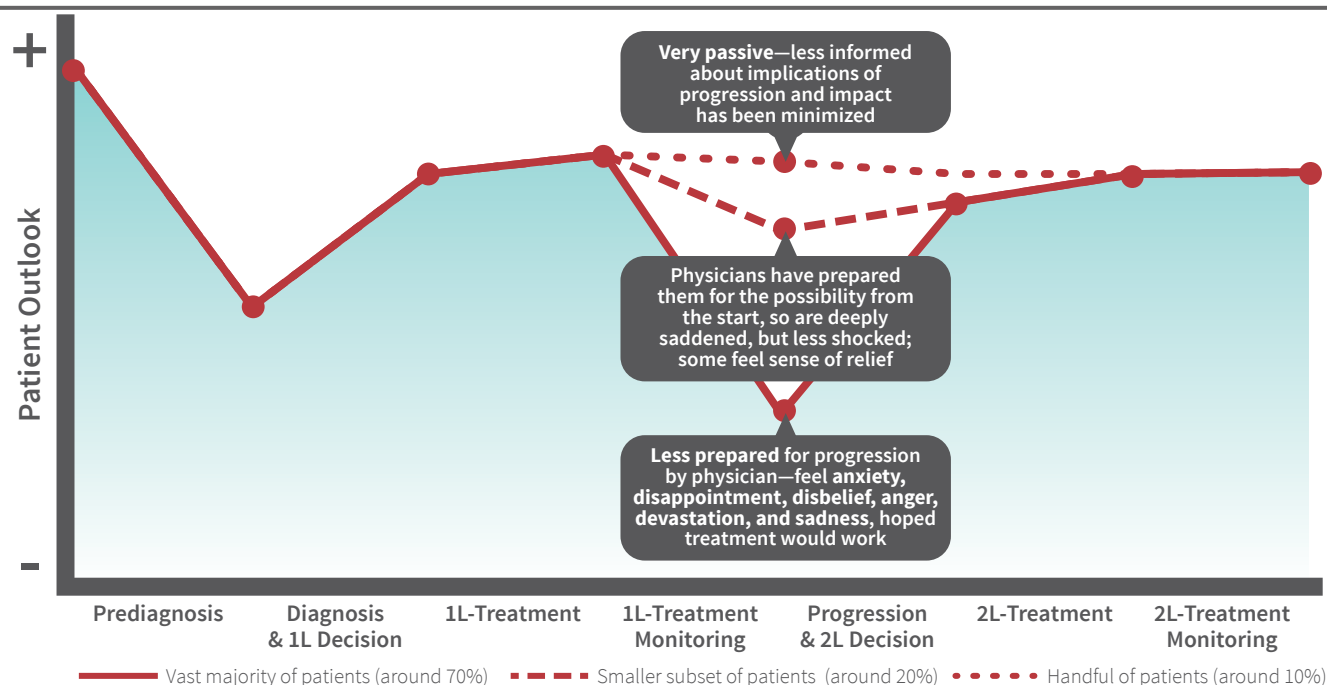
When receiving news of disease progression, those patients with a significantly decreased outlook felt they had not been sufficiently prepared by their healthcare team (Figure 5). However, a majority of patients across all regions reported that they understand what progression means (Latin America 59%, Japan 73%, EU 74%, and US 83%) and that accepting news of progression can be emotionally difficult[†].

“Patients most likely to be impacted by a diagnosis of progression to 2L-Treatment are those who had more indolent forms of the disease and longer disease-free survival on adjuvant therapy prior to 1L-Treatment.”



Following progression, with the initiation of 2L-Treatment, higher levels of variation relating to patient concerns were observed between regions. However, the majority expressed worries about the future and fear that the cancer may not respond to treatment in their top 3 concerns, a similar pattern as seen at diagnosis. Worry about how long the treatment would work was more prominent and increased compared with diagnosis across all countries, especially in Latin America and Japan (24% increase and 17% increase, respectively). Worry about side effects and whether they would be able to cope with them were both top

Figure 5. While Patients React in a Number of Ways, Many Express Feelings of Anxiety, Disappointment, and Disbelief Upon Receiving the News of Disease Progression



Please note that this research was qualitative in nature, and therefore only estimated percentages of patients expressing these outlooks can be provided.

[†]<http://www.mhlw.go.jp/file/06-Seisakujouhou-10800000-Iseikyoku/0000056917.pdf>
[†] — Data on File

3 concerns relating to progression and 2L-Treatment, neither of which were in the top 3 concerns at diagnosis across all countries. Worries about treatment efficacy and side effects took greater precedence over worries about the impact on the patient's family, which dropped in all countries compared with those at diagnosis, indicating that the impact of the news of progression may mean patients become more focused on their own well-being than those around them. Patients in Japan had the highest level of concern about the treatment working and side effects, relative to other countries, but did not, however, specifically worry as much about the potential impact of disease progression on their family (47% stated this was a top 3 concern at diagnosis, 0% at progression), possibly due to cultural differences (see Appendix 5.3, Figure 20).

“Japanese patients, especially female patients, do have concerns about their family, but try not to involve family in the early course of relapsed disease, and solve their health problems on their own. There is stigma associated with Japanese mothers and wives bothering their children and husband. This attitude may also be influenced by what is communicated by physicians at the time of recurrence and how patients understand it.”



The emotions of patients with mBC fluctuate over the disease continuum, with a big negative impact on outlook at diagnosis and to a greater extent with news of progression. Patient concerns in different regions are more aligned at diagnosis and initiation of 1L-Treatment, but diverge at the initiation of 2L-Treatment, with Japan differing the most from the other regions. At progression, a patient's negative outlook and emotions are reflected in the change in their concerns. Understandably, concerns at the news of disease progression focus more around side effects of treatment and patients are more aware of the effects treatment can have on their well-being and daily life. In the following section, the treatment goals of patients with mBC will be discussed, taking into consideration the relative patient emotions and perspectives throughout the disease continuum.

2. Goals of Treatment in mBC

- ▼ Patients with mBC have several treatment goals beyond survival alone
 - Treatment goals differ depending on line of treatment and country
- ▼ Patients' understanding of delaying disease progression and survival are similar
 - Ultimately, both translate to patients as staying alive as long as possible
- ▼ Physicians' treatment goals differ between first- and second-line treatment settings
- ▼ Physicians recognize the benefits of delayed disease progression
 - Specifically, both are related to increased quality and quantity of life

Patient perspectives

2.1 Patients with mBC have several treatment goals beyond survival alone, which differ depending on line of treatment and cultural country.

At the initiation of 1L-Treatment, patients' priority goals focused on living as long as possible and delaying the progression of cancer; however, as the disease advances, maintaining the ability to carry out daily activities increases in importance.

The primary goals for patients at both 1L- and 2L-Treatment stage were to live as long as possible, and they cited delaying disease progression as an equally important goal at all stages of the care continuum (Figure 6). In 2L, delaying disease progression increased in importance among the top 3 treatment goals.

As the disease progresses, and patients undergo 2L-Treatment, maintaining the ability to carry out day-to-day activities also increased with importance. This was particularly true for patients in Latin America, who at 2L valued maintaining the ability to carry out daily activities with equal importance as living as long as possible, an increase of 26% from 1L (Figure 7). Across countries, patients consistently said that they were “determined to continue living as normal,” a sentiment particularly important in Japan. These trends could be linked to the changes in emotional outlook of the patient and levels of acceptance along the care continuum (Figure 3).

Despite these general trends in patients' treatment goals at a global level, definite variances can be seen between countries. For example, in the US, 91% of patients identified “living as long as possible” as one of their top 3 goals in 1L (Figure 7).

Figure 6. Top 3 Goals of 1L- and 2L-Treatment (Patient Reported)

Q. What were your top 3 goals for this treatment?

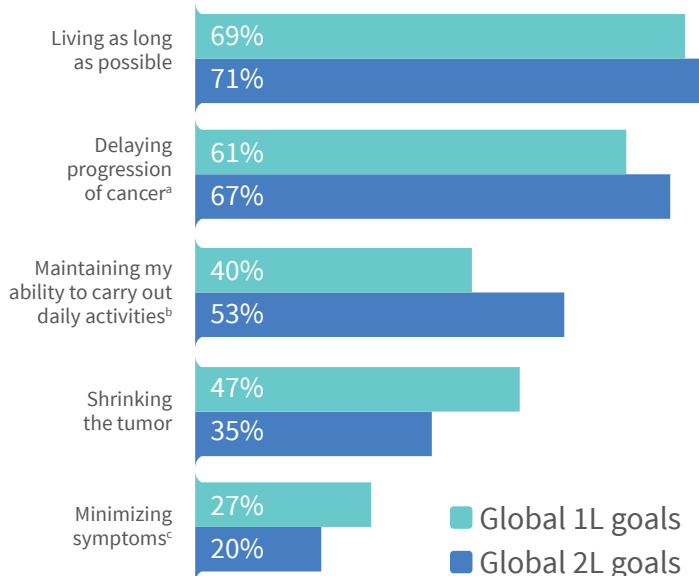


Figure Notes:

^acould also be thought of as spending as long as possible on this treatment;

^bsuch as work or looking after family;

^ceg, pain, tiredness, other symptoms due to your breast cancer

Base: All respondents: US (18), EU (42), LatAm (17), JP (10)

Please enter a 1, 2, and 3 in the yellow column below to indicate your top 3 goals of treatment; Avoiding chemotherapy: US 25%, EU 11%, LatAm 22%, JP 27%; Ensuring side effects are manageable: US 19%, EU 21%, LatAm 6%, JP 18%; Having oral treatment: US: 0%, EU 3%, LatAm 0%, JP 0%; Other: US 0%, EU 3%, LatAm 0%, JP 9%

“Maintaining the ability to carry out daily activities” was also a consistent top goal of patients alongside “living as long as possible.”

The Japanese external expert noted that in Japan, patients are more likely to communicate their uncertainty regarding side effects as a concern; this may be because of cultural communication barriers that make side effects easier to discuss than other personal aspects of disease, prognosis, and treatment expectations.



When asked to prioritize, patients generally felt that controlling cancer took precedence over side effects. The exception was Japan, where many patients either disagreed or had neutral/mixed opinions regarding this and expressed a particularly strong aversion to chemotherapy.

“We have to accept side effects. If I am sick, I will take a pill for sickness, if I have bone pain I will take an anti-inflammatory drug. Otherwise the therapy doesn't do anything.” (Patient, Italy)



The external US experts felt that this number (91%) was high and cautioned against physicians setting unrealistic expectations with patients, yet they agreed that directionally it was acceptable.



The external EU experts stated that the patient's own experience with chemotherapy would also heavily influence decisions (and responses). Side effects experienced during chemotherapy elicit strong emotions from patients, and this is one of the reasons why the practice of screening and selecting patients for targeted therapy has increased.



However, by 2L, fewer US patients saw this as their top priority (Figure 7). In comparison, living as long as possible and delaying disease progression increased in EU respondents between 1L- and 2L-treatment. In Japan, patients felt that other factors, beyond extending life alone, were important, in comparison to other regions, specifically “delaying progression of cancer,” which was the most important treatment goal for both 1L- and 2L-treatment.

Globally, the impact of treatment on QoL was considered important but made treatment choices difficult for patients. Almost all patients voiced feelings of internal conflict when weighing durability of treatment against adverse events. Many patients, in all regions except Japan, agreed that having a treatment that controls cancer for longer was most important regardless of side effects. Previous experience or perception of side effects with chemotherapy may result in a reluctance to accept, or even refusal of treatment, especially in Germany or Japan (see Appendix 5.3, Figure 20). The language used to describe side effects and their impact may shape patients' perceptions.

“In Japan there is a tradition of finding beauty in transience, an awareness of impermanence as described by “mono no aware,” a transient gentle sadness (or wistfulness) at their passing as well as a longer, deeper gentle sadness about this state being the reality of life. Hence culturally, Japanese patients may not demonstrate the ‘fighting’ that may be apparent elsewhere, which can affect their decision-making and treatment goals.”



Figure 7. Top 3 Goals of Treatment (1L & 2L) by Region (Patient Reported)

Q. Please think back to the drug treatment you received after your breast cancer came back or continued to grow.
What were your top 3 goals for this treatment?

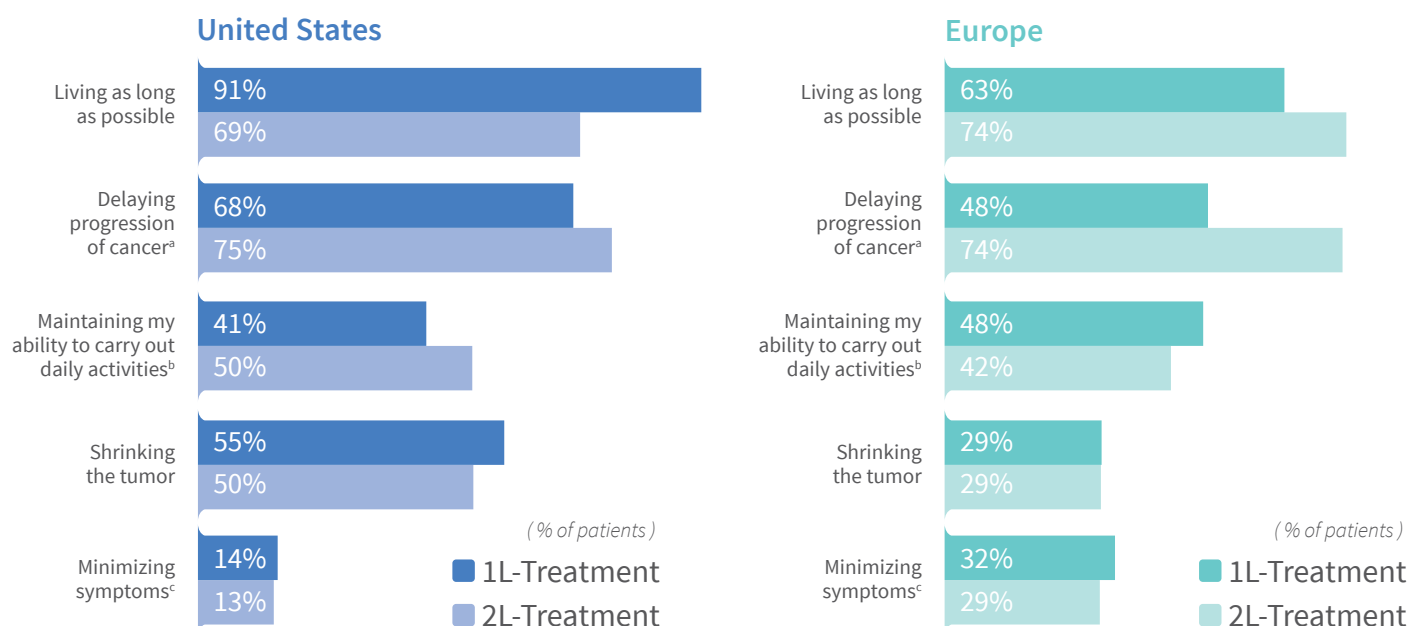


Figure Notes: ^acould also be thought of as spending as long as possible on this treatment; ^bsuch as work or looking after family; ^ceg, pain, tiredness, other symptoms due to your breast cancer

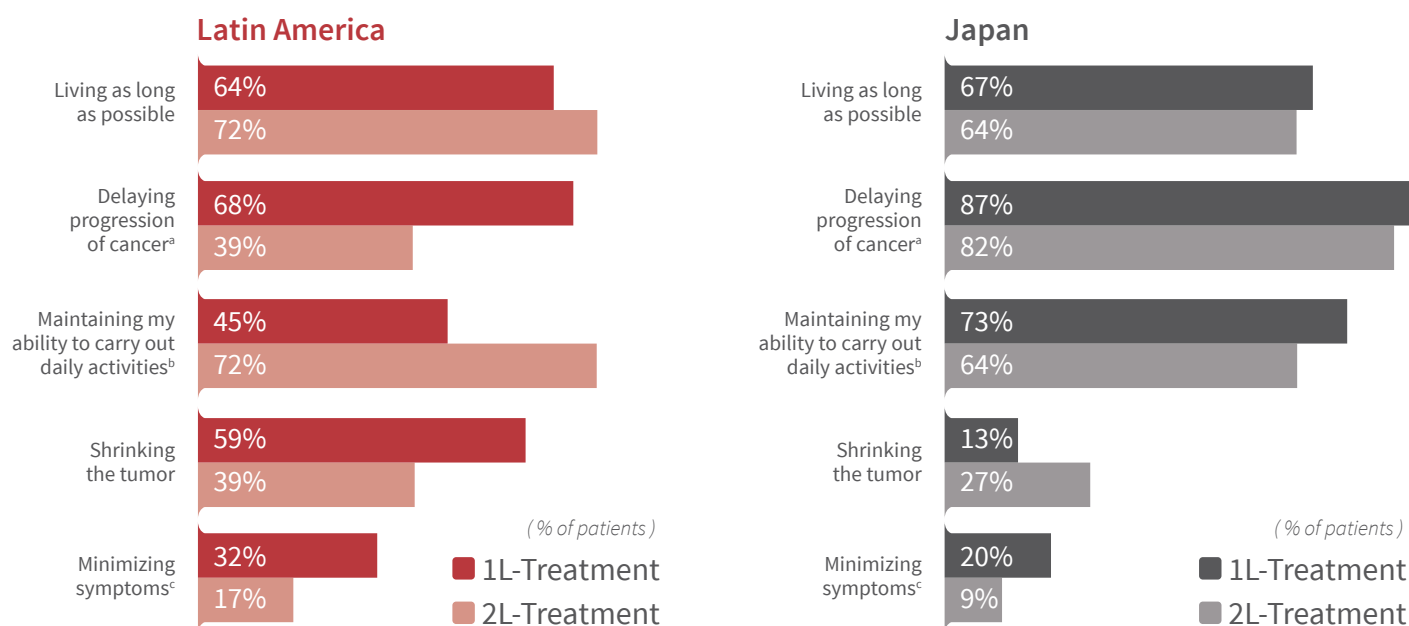


Figure Notes: ^acould also be thought of as spending as long as possible on this treatment; ^bsuch as work or looking after family; ^ceg, pain, tiredness, other symptoms due to your breast cancer

Base: All respondents: US (18), EU (42), LatAm (17), JP (10).

Please enter a 1, 2, and 3 in the yellow column below to indicate your top 3 goals of treatment; Avoiding chemotherapy: US 25%, EU 11%, LatAm 22%, JP 27%; Ensuring side effects are manageable: US 19%, EU 21%, LatAm 6%, JP 18%; Having oral treatment: US: 0%, EU 3%, LatAm 0%, JP 0%; Other: US 0%, EU 3%, LatAm 0%, JP 9%.

2.2 Patients' understanding of delaying disease progression and survival are similar; ultimately, both translate to patients as staying alive as long as possible.

Findings demonstrated that patients interpreted the concept of delaying disease progression more readily than “survival.” Despite physicians categorizing delaying disease progression and living as long as possible as separate goals, patients had an understanding that delaying disease progression ultimately means staying alive as long as possible.

“Delaying disease progression is a way to extend life expectancy.” (Patient, Spain)



Patients interpreted delaying disease progression as “not getting worse,” “maintaining quality of life,” and “maintaining treatment options” and understood that they will remain on a treatment as long as it continued to control the cancer. Most patients understood that different individuals respond in different ways, and the goal is to find the most appropriate treatment patient by patient. Most, but not all, understood that treatment may need to be changed at some point. Findings suggested that survival was rarely discussed directly with patients, as life expectancy is unknown and patients prefer to live in hope rather than discuss their prognosis[†].

“We always know we can’t be cured; however, by reducing the size of the tumors, we have more chance of extending our lives and the first one (delaying disease progression) is almost the same as the second one (overall survival), because by reducing it (the size of the tumor), you have more chance of extending your life.” (Patient, Argentina)



Physicians also recognized that patients understood delaying disease progression in several ways and use language that is reflective of this, such as, “stopping the cancer spreading,” “stabilizing the cancer,” and “stopping the cancer from getting worse.” Scientific language was rarely used in conversations between physicians and patients[†].

The external experts noted that when defining “progression” in the survey, it was not defined as symptomatic progression or progression based on clinical assessment, which could affect how patients interpret what it means. When explaining delaying disease progression in practice, experts generally tend to focus more on phrases such as “not getting worse,” “maintaining quality of life,” and “maintaining treatment options,” but noted that patients do ask about survival. Many patients may not ask about survival because of their fears about the future, while others prefer to know to be able to plan.



Physician Perspectives

2.3 When physicians consider treatment goals and decisions in the first-line setting, increased overall survival is not the only factor evaluated.

While, similarly to patients, physicians reported ultimately hoping to increase the survival time of their patients when making 1L-Treatment decisions, they also strongly consider delaying disease progression as a relevant goal alongside a multitude of other factors (Figure 8). Approximately two-thirds of physician goals, based on an allocation of 100 points across different categories, focused on factors beyond survival and delaying progression when making treatment decisions. Symptom relief and maintaining symptom-free time were also of importance. Consideration of side-effect profiles for available therapies, determining the aggressiveness of the treatment strategy, and deciding when to switch treatments were all evaluated during the physician’s treatment decision and when setting management goals.

“I want my patients to have more time. And that’s what my patients want as well.” (Physician, Germany)



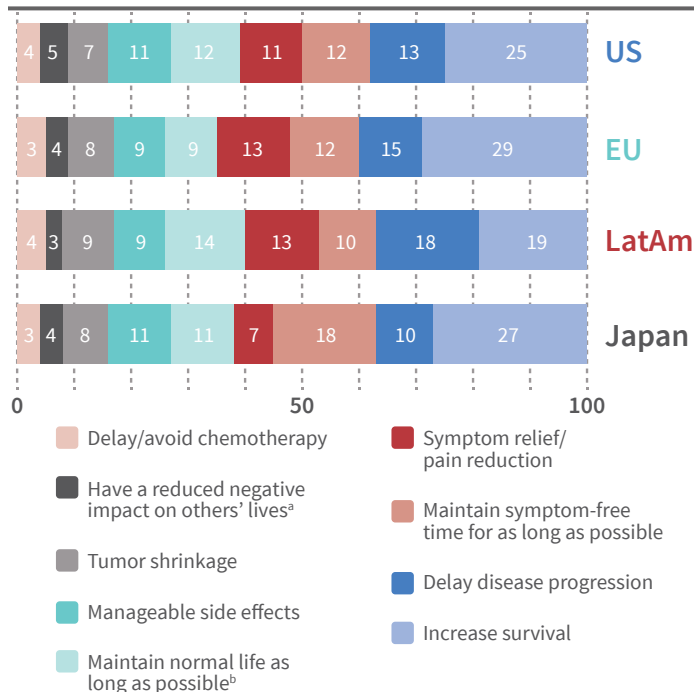
“Quality of life matters much more than the number of months I can offer a patient — what good is living longer if you aren’t actually having a good life?” (Physician, United States)



External experts commented on the prioritization of overall survival. They felt that this demonstrated a trend toward talking about survival in a mBC population; however, despite limited evidence to support this, experts considered stopping or delaying disease progression to be a more realistic goal.



Figure 8. Relative Importance of 1L mBC Treatment Physician Goals: Point Allocation (0–100) — Mean Scores (Physician Reported)



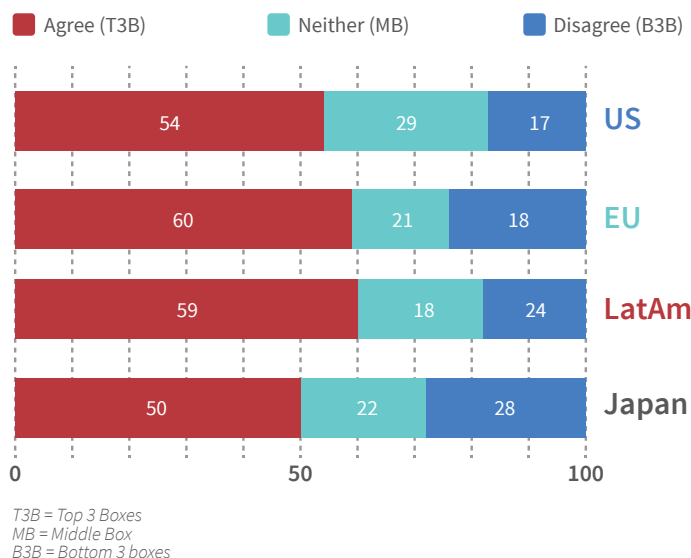
Base: All respondents US (100), EU (163), LatAm (79), JP (50); C5/C6/C7. Below are the goals you selected when initiating 1L-treatment for [SUBTYPE] mBC patients. We are now interested in understanding how important each goal is. You will have 100 total points; please use any number from 1 to 100 to represent the importance of each. Assign more points to a goal that you consider more important and fewer points to a goal that you consider less important. You must assign at least 1 point to each of the listed goals; Note: ^aHave a reduced negative impact on others' lives (eg, family, friends, you, nursing staff, etc); ^bMaintain normal life as long as possible compared to life prior to mBC; >5 points not shown.

2.4 Physicians acknowledge that goals shift between 1L and 2L therapy management of mBC.

More than half of physician respondents across the 4 regions agreed that their goals in 2L differed from those in 1L (Figure 9); furthermore the subtype of breast cancer would also influence management goals, particularly in patients with triple negative breast cancer (TNBC).

Figure 9. 2L-Treatment Physician Goals: Differences with 1L — By Region (Physician Reported)

Q. My goals in 2L-Treatment differ from those in 1L-Treatment



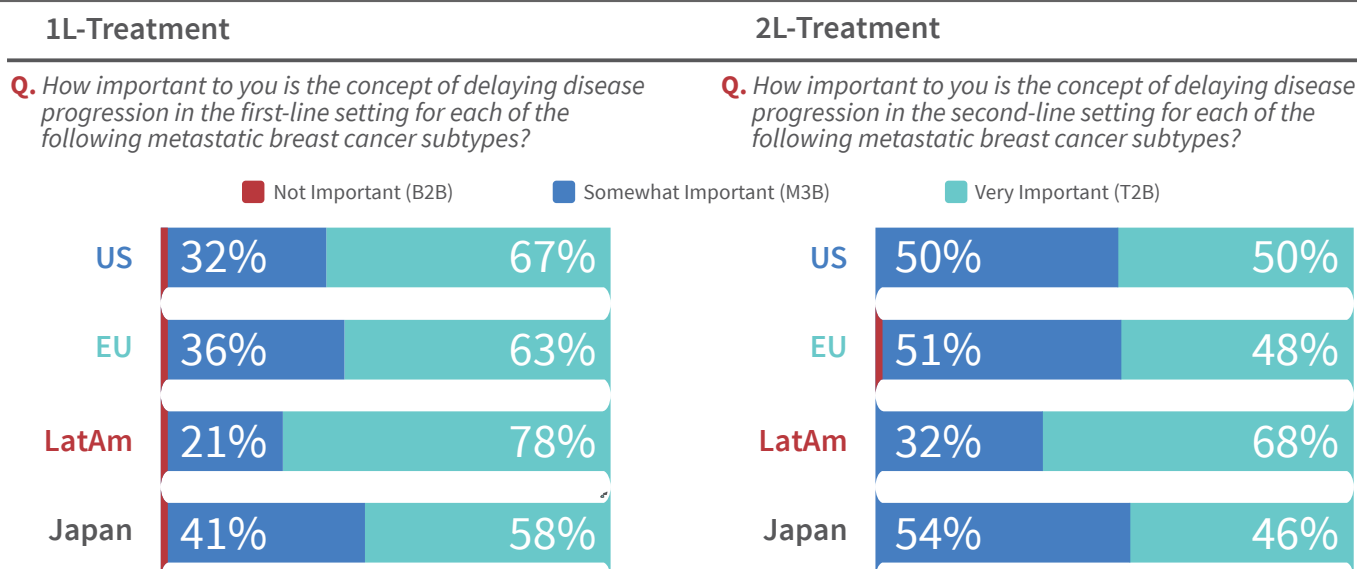
When considering delaying disease progression as a treatment goal specifically, physicians reported this as a “very important” goal in the 1L setting. To both physicians and their patients, this was especially prominent in Latin America. Across all countries, as patients progress to 2L, the relative importance of delaying disease progression decreased as physician focus shifts to symptom control and quality of life. Physicians could feel somewhat torn between accepting side effects or prioritizing quality of life; in Latin America, physicians placed more importance on quality of life than quantity.

The physician views on delaying disease progression in the 2L setting were contrary to patient reported perspectives in the US and EU, where it was viewed by patients as slightly more important in the 2L setting (Figure 7). The shift in patient perspective could be attributable to readjustment of perspectives and emotions that immediately follows news of progression.

The external experts agreed that mBC treatment goals change between 1L- and 2L-Treatment. The importance of delaying disease progression decreases as patients progress, with symptom management and quality of life increasing in priority. In addition, the benefit of delaying disease progression is less in 2L.



Figure 10: Importance of Delaying Disease Progression in 1L- & 2L-Treatment (Physician Reported)



Note: Asked by subtype, average across subtypes shown

Base: All respondents: US (100), EU (163), LatAm (79), JP (50)
 Note: 7= "Extremely important to me", 1= "Not at all important to me"
 T2B = Top 2 Boxes
 MB = Middle Box
 B2B = Bottom 2 boxes

Base: All respondents: US (100), EU (163), LatAm (79), JP (50)
 Note: 7= "Extremely important to me", 1= "Not at all important to me"
 T2B = Top 2 Boxes
 MB = Middle Box
 B2B = Bottom 2 boxes

2.5 Physicians recognize the benefits of delayed disease progression in clinical practice, specifically related to increased quality and quantity of life.

When asked to rank statements that described what the benefits of delaying disease progression were, physicians selected "maintaining a better quality of life for a longer time" and "the ability to help patients live longer" as the top 2 benefits across all regions (Figure 11). Latin American physicians additionally felt the possibility of delaying chemotherapy (in HR+/HER2- patients) was also an important benefit.

External experts discussed how realistic "living longer" was as a benefit and preferred to consider "living well" as a more appropriate expectation.



Experts did not expect that "helping patients live longer" would be rated so highly and had anticipated that being able to "delay chemotherapy (for HR+/HER2- patients)" would be given a greater priority across all regions.



Figure 11: Benefit of Delaying Disease Progression for mBC Patients (Physician Reported)

Q. What is the real-world benefit of increased progression free survival in mBC for you, the clinician, in treating metastatic breast cancer?

| | US | EU | LatAm | Japan |
|---|-----|-----|-------|-------|
| Able to help patients maintain a better quality of life for longer time | 65% | 72% | 86% | 58% |
| Able to help patients live longer | 66% | 63% | 65% | 62% |
| Delay chemotherapy (for HR+/HER2- patients) | 44% | 43% | 58% | 36% |
| Means my patients are more content | 34% | 45% | 32% | 48% |
| Makes me feel like I am doing a better job | 40% | 40% | 39% | 20% |
| It is a statistical measure that gives me greater confidence in treatment decision making | 34% | 22% | 33% | 20% |
| Allows me to compare treatment options | 24% | 18% | 24% | 26% |
| Do not have to share news of progression with patients | 22% | 20% | 13% | 12% |
| Fewer treatment decisions | 18% | 13% | 16% | 16% |
| Purely statistical and nothing else* | 3% | 2% | 0% | 6% |

>50% of physicians

30%-50% of physicians

Note: Responses came from a pre-determined list for physicians to select from

Base: All respondents: US (100), EU (163), LatAm (79), JP (50).

E1. What is the real-world benefit of increased progression free survival in mBC for you, the clinician, in treating metastatic breast cancer?

Note: *Mutually exclusive. Other: US 0%, EU 1%, LatAm 3%, JP 0%.

3. The Impact of Physician and Patient Interactions on Goals

- ▼ Physicians reported varying degrees of comfort when communicating with patients about their disease
 - US physicians report a far greater level of comfort when communicating with patients
- ▼ Both physicians and patients recognize the value and importance of discussing treatment goals and preferences
 - Neither patient nor physician is initiating this conversation
- ▼ Levels of patient satisfaction with their medical team vary between regions

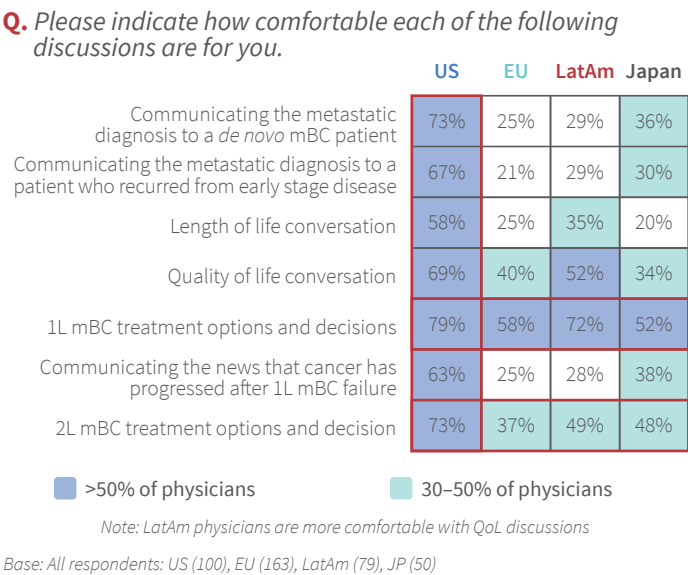
3.1 Varying degrees of comfort exist among physicians when communicating with patients about their disease.

Communication between physicians and patients can naturally be difficult, irrespective of which stage in the disease continuum discussions occur. The interaction between a patient and his or her physician does however play a critical role influencing the patient experience and can impact both emotional outlook and treatment goals. Physician feedback demonstrated varying levels of comfort when holding difficult discussions with patients. When asked to rate various types of patient discussions, physicians reported very low levels of comfort specifically in delivering the news of a diagnosis of mBC (*de novo* or recurrent) across all regions except the US. Few physicians in Latin America, EU, and Japan felt comfortable communicating a diagnosis of mBC to patients, compared with much higher levels of comfort in the US (73%). This pattern was also reflected in comfort levels when discussing the news of cancer progression and 2L-Treatment options and decisions. Across all regions, physicians felt most comfortable discussing 1L-Treatment options.

External experts felt feedback could be very subjective based on most recent physician experiences and highlighted the delicate balance required for all discussions with mBC patients. Experts were surprised at the variation of level of comfort among regions and agreed that this difference may be explained by the quality of training received or the type of physician practice, leading to greater confidence on the part of the US physicians. Knowing how to communicate a diagnosis (and also prognosis) is challenging, and variability across patient backgrounds, educational perspectives, and where they are in the disease continuum, makes it difficult to determine what to communicate.



Figure 12: Comfort with Types of Discussions with mBC Patients (Physician Reported)



Several factors were prioritized as contributing to the difficulty in delivering news of a diagnosis of mBC. A lack of patient understanding about mBC and the amount of time physicians have with the patient to discuss the diagnosis were 2 key factors. Especially given the fact that the delivery of a diagnosis of mBC and the conversation regarding treatment options often occurs during the same visit, physicians reported this was the case for almost half of patients. Other factors that physicians felt contributed to the difficulty in communicating a diagnosis were level of prior relationship the physician had with the patient and, particularly in the EU and Japan, the lack of effective treatment options available.

Figure 13: Factors that Contribute to the Difficulty of the Communication Regarding a Diagnosis of mBC (Physician Reported)

Q. Please select any of the below that contribute to the difficulty of the communication of the mBC diagnosis.

| | US | EU | LatAm | Japan |
|---|-----|-----|-------|-------|
| Patient's lack of understanding of what mBC is | 46% | 39% | 35% | 46% |
| Time/length of the visit | 30% | 40% | 43% | 30% |
| Prior relationship with patient ^a | 40% | 38% | 35% | 20% |
| Lack of effective treatment options | 29% | 31% | 19% | 38% |
| Language barrier ^b | 25% | 29% | 9% | 18% |
| Guilt I feel that the patient has progressed to mBC | 25% | 12% | 4% | 8% |
| Lack of training aimed at how to communicate mBC diagnosis to patient | 14% | 14% | 6% | 12% |
| I do not personally find the mBC diagnosis difficult | 22% | 18% | 27% | 20% |

 >40% of physicians  30%–40% of physicians

Base: All respondents: US (100), EU (163), LatAm (79), JP (50).

^aPrior relationship with patient (i.e., telling early stage patient that disease is now metastatic) Other: US 1%, EU 0%, LatAm 4%, JP 0% ^bLanguage barrier (i.e., I am not able to communicate with patient in language she is familiar with);

External experts were surprised that the amount of time needed with patients had not been rated higher. They also considered that the practice setting may contribute to physician comfort with communicating a difficult diagnosis. Pressure from the hospital or lack of reimbursement regarding time spent were factors highlighted by experts, and the amount of time spent with patients is expected to be rated higher in the future. Those who practice individually may not have the peer resources to manage this communication, in contrast to those who practice in a communal setting.



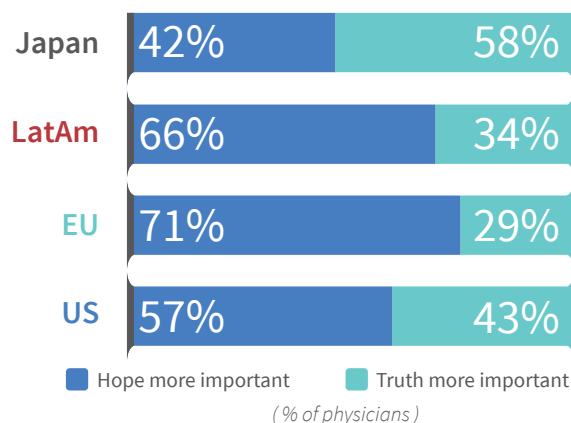
In most countries, physicians tend to value hope more than truth when discussing a diagnosis of mBC. The results appeared to indicate that hope was reported as particularly more important to physicians in EU and Latin American countries, while in Japan physicians prefer to be more truthful (Figure 14).

External experts noted that hope and truth are not mutually exclusive so did not necessarily agree with this finding. A lot of truth and honesty is being conveyed in practice and this has improved over the years, without diminishing hope.



Figure 14: Delivery of mBC Diagnosis: More Important to Convey Truth vs. Hope (Physician Reported)

Q. While we understand that the following statements may not be mutually exclusive, please select the one which is more important to you when delivering a diagnosis of mBC.



Base: All respondents: US (100), EU (163), LatAm (79), JP (50).

Note: Full options as follows: "Conveying the truth of the situation irrespective of how difficult the truth is," "Conveying hope to the patient so they can remain motivated for the battle ahead (ie, treatment)."

When relaying a diagnosis of mBC, physicians prefer to use neutral language rather than making definitive statements. The most common phrases reported when discussing a diagnosis include "spread to other organs" and "metastatic." Physicians in Latin America were more likely to describe the disease as a "recurrence" and highlight that the disease is "controllable" with a possibility of "getting better," whereas in the US, "incurable" was used more frequently than in other countries across all types of mBC. Language used during a diagnosis conversation also differed depending on the type of disease the patient has, with more hopeful language being used with HR+/HER2- and HER2+ subtypes in most countries. In conversations with patients with TNBC specifically, physicians may convey different messages around diagnosis, treatment options, and prognosis compared to other metastatic subtypes. Physicians were less likely to tell patients with metastatic TNBC that they could live for many years and maintain a good quality of life, preferring to remain vague regarding the number of treatment options available[†].

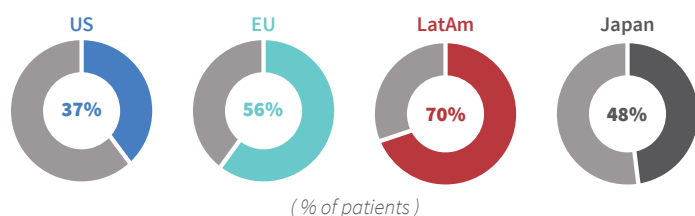
There was great variation in the percentage of physicians who had received training on how to discuss a diagnosis of mBC (Figure 15). Despite the fact that few US physicians reported having received specific training in this area, they demonstrated the greatest levels of comfort in delivering the news of a diagnosis of mBC across all regions.

External experts from different regions discussed this and felt comfort levels were actually likely to be more cultural than based on level of training received; however, physicians also recognize that many patients do not walk away retaining all information that is shared with them following this often emotionally overwhelming conversation.



Figure 15: Percentage of Physicians Who Have Received Training on Communicating a Terminal Oncology Diagnosis (Physician Reported)

Q. Have you ever had training — either while in school or as continuing education — on how to communicate the news of a terminal oncology diagnosis?



Base: All respondents: US (100), EU (163), LatAm (79), JP (50).

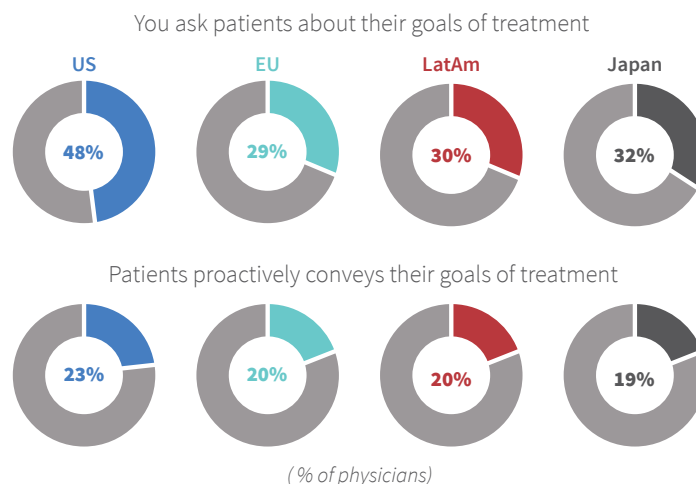
“In Japan we have a 2-day intensive ‘Palliative Care Training Program,’ including basic communication skills training, which is mandated to all physicians who belong to designated cancer centers nationwide. There is also an advanced communication skill program, but only a limited number of (interested) oncologists have received it.”



3.2 Both physicians and patients recognize the value and importance of discussing preference and treatment goals; however, neither is initiating the conversation.

There are varying degrees to which physicians and patients would like to discuss treatment goals and actually initiate a conversation. Physicians agreed to some extent that it is important to hear the treatment goals and preferences of the patient (EU 40%, Japan 46%, Latin America 56%, US 61%). However, by their own admission, only one-third of physicians in the EU, Latin America and Japan, and under half of the physicians in the US, asked the patient directly about their goals of treatment (Figure 16). In contrast, physicians did not feel that the patient proactively discusses their management goals; in fact, this happened less often than did the doctor requesting this information from patients[†].

Figure 16: Physicians Perspective on Their Conversations with Patients about Treatment Goals (Physician Reported)



Overall, the vast majority of patients surveyed did not feel that the patient’s goals were receiving much discussion beyond the implicit desire to stay alive. Language is centered on “stabilizing the tumor” with little discussion on the side effects or wider patient goals of treatment, such as wanting more good days rather than just more days. This limited discussion may result in the patient being uncertain about what to expect from their treatment and does not equip them with the knowledge or the forum to be able to evaluate and discuss their treatment goals. In the EU specifically, patients felt that they were not encouraged to discuss their views on the management of treatment, with only 37% encouraged to do so by their doctor. Because of this lack of discussion, patients feel their treatment decisions remain in the hands of the physician, with the physician holding the majority of influence on the final treatment decision in both 1L and 2L[†].

Neither patients nor physicians are effectively initiating conversations about patient goals, and potentially less than 50% of physicians are communicating 1L goals and preferences to patients. Older patients generally are often not as engaged in these discussions, as younger patients who may bring many opinions to the discussion. Some external experts indicated that they do not ask what patients want from treatment, but rather they outline goals about stopping or delaying progression. They felt that it may be difficult to ask patients to express their goals for therapy when they haven’t had time to fully process the impact of a cancer diagnosis.



One factor that may contribute to the limited influence patients feel they have on treatment decision making is the varying degree to which patients understand a diagnosis of mBC. Many patients agreed that it is easy to understand the initial mBC diagnosis, but between 20%–36% of patients disagreed, with a lower understanding of the implications highlighted in Mexico and Germany. However, upon reflection, patients described feeling so overwhelmed at the diagnosis that it was difficult for them to absorb and retain information. Patients did not recall exactly what they were told, because it was “a blur.” In fact, in the EU and Latin America, a proportion of patients still believed that their disease was curable (22% and 41%, respectively)[†].

3.3 Patient levels of satisfaction with their medical team, specifically their physicians, vary, especially between regions.

Interaction with physicians is a key influencer on patient satisfaction, emotional experience, and ultimately, management goals. Many patients with mBC had mixed opinions, or disagreed that they had enough emotional support from their doctors. The highest number of patients who felt they did receive emotional support was seen in Latin America (67%)[†], where words of “hope” were used more in patient conversations. Overall, despite feeling the need for further emotional support, results of the quantitative research showed that patients agreed that they have enough time with the doctor to discuss the questions they have about their disease, treatments, and feelings[†]. This is contrary to physicians who believed they don’t have enough time with patients during their visit (Figure 17). However, further discussions determined that some patients do feel particularly frustrated, stating that doctors can be dismissive of patients, eg, offering limited explanations, only giving information if the patient asks, or spending limited time with patients[†].

Patients cited that physician approach plays a major role in their experience along the care continuum. The greatest satisfaction was seen where medical teams were identified as caring, empathetic, and reassuring, and patients in the care of these teams felt more protected and hopeful. Where patients were dissatisfied with their medical teams, descriptors such as cold, distant, insensitive, and dismissive were used. These dramatic differences highlight the critical role that healthcare professionals have in ensuring effective emotional support is provided alongside medical care throughout the management of mBC. Conceptually, Figure 18 highlights the impact levels of “realism” and “empathy” on patient outlook.

External experts commented that the upper right quadrant should be where the oncology community strives to reach with patients.


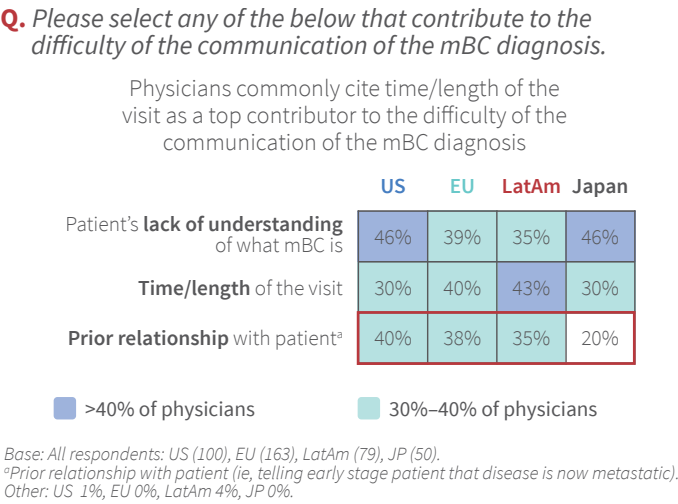


Figure 17. Quantitative Research Suggests That Patients and Doctors Have Different Perceptions Regarding the Amount of Time Spent Discussing a Diagnosis of mBC (Physician and Patient Reported)



The majority of patients say they get enough time with their doctor to ask the questions they need about their disease, treatment, and feelings

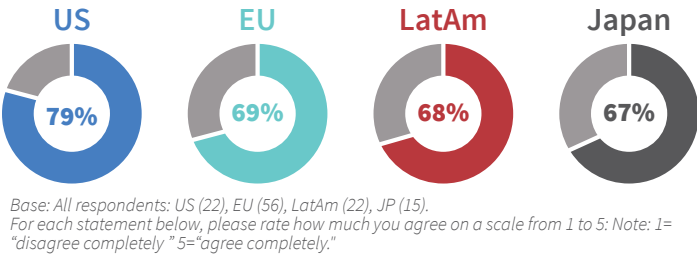
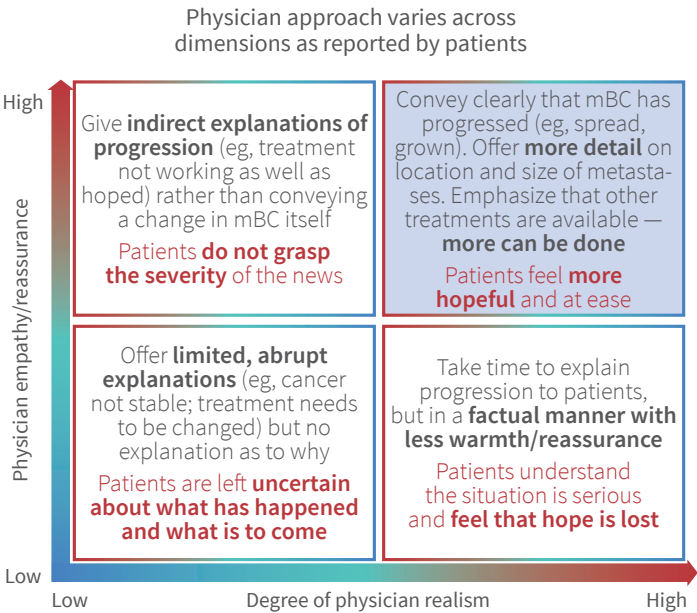


Figure 18: Physician Interaction Plays a Critical Role in Supporting Patients Emotionally Through Their Disease



† — Data on File

This research highlights an intrinsic link among how the physician delivers news, tone and terminology used, and how a patient feels about their disease, prognosis, goals, and decisions that need to be made. Those receiving clear detailed explanations of the stage of their disease, possible treatment options, and optimism were left with a more hopeful, accepting outlook.

External experts agreed that physicians need to feel empowered to support their patients on a personal level, within a multidisciplinary setting if possible, in order to ensure patients with mBC have the best possible emotional experience and outlook during the course of their disease.



4. Recommendations:

- ▼ Highlight the importance of delaying disease progression, especially at diagnosis and in earlier lines of treatment, where it was an important goal for both patients and physicians
- ▼ Increase healthcare professional proactive behavior towards discussing patient mBC management goals, using clear and detailed language around the disease and treatments available
- ▼ Improve patient education about mBC to empower patients to consider, voice, and support their management goals
- ▼ Provide support networks of multidisciplinary healthcare professionals, such as nurse navigators, whom patients can rely on and access throughout the care continuum
- ▼ Balance the focus on delaying disease progression and improving overall survival with quality of life and life goal discussions
- ▼ Shift focus of managing mBC from “endpoints” to “outcomes.” It is important to promote patient-physician communication about the value of life and realistic goals
- ▼ Improve physicians’ comfort levels around discussing a diagnosis or progression of mBC, including management options
- ▼ Encourage patients to develop social networks with other mBC patients to increase their sense of community
- ▼ Provide scripts to physicians showing examples about how to convey both truth and hope to patients across the mBC care continuum

5. APPENDIX

5.1 Methods

All research was carried out through interviews with patients and physicians. All data interpretation reflects trends and insights. In some cases, respondent groups were small, and it is possible that there are variations in different regions that were not captured in the survey responses. No statistical analysis for significance has been conducted.

5.2 Qualitative and Quantitative Research with Physicians

Physicians were recruited through opt-in healthcare databases using an online methodology. For their participation in the survey, respondents were given honoraria payments. Japan was the single exception; respondents were paid in points which can be redeemed for a variety of medical texts, equipment, accessories, etc. in accordance with local compliance regulations.

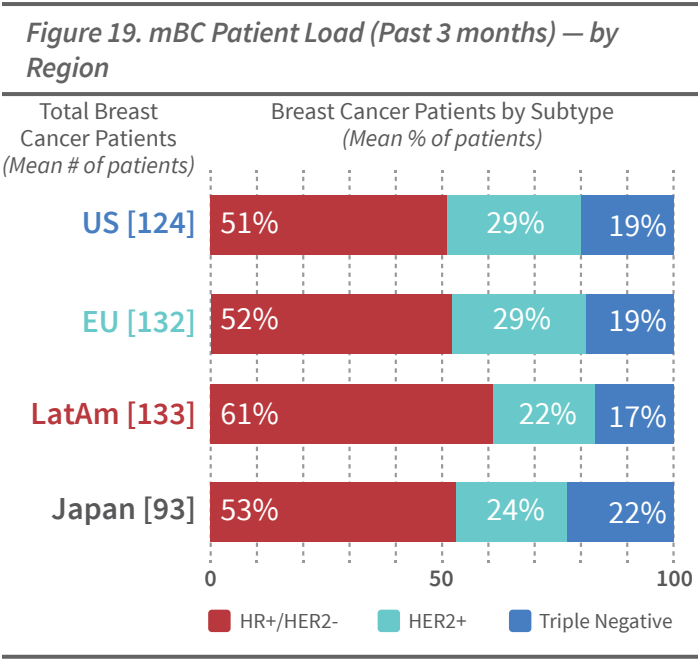
The inclusion criteria were the following:

- ▼ Specialty in oncology, gynecology (Germany and France only) or radiation oncology, surgical oncology, breast/mammary surgery (Japan only)
- ▼ Board certified in oncology (US only)
- ▼ Practicing oncology for 3–30 years (4–30 in the UK only)
- ▼ Grade of consultant or specialist registrar (EU only)
- ▼ Spend a minimum of 65% of professional time in direct patient care
- ▼ Treat a minimum of 50 total cancer patients in the past 3 months (30 in Japan only)
- ▼ Treat a minimum of 15 mBC patients in the past 3 months (5 in Japan only)
- ▼ Personally initiate treatment for breast cancer patients and have active involvement in the decision-making process both at initiation and throughout treatment (moderately to highly involved)

A total of 392 oncologists (and gynecologists in Germany only) treating patients with mBC undertook a 45-minute online survey fielded from February–March 2016. The number of participating physicians from each country is shown in Figure 1. Findings from a small qualitative study further informed development of the quantitative survey.

Physicians represented the specialties of medical oncology/ oncology, hematology, breast/mammary surgeon (JP), radiation oncology (JP), surgical oncology (JP), clinical oncology (UK), or gynecology (DE). Physicians had an average of between 10 and 19 years in practice, with a mean of 87%–93% of their time currently

spent in direct patient care. The number and types of breast cancer patients seen by the physicians in the 3 months prior to being surveyed is detailed in Figure 19.



Physicians surveyed mainly worked in a hospital-based setting, apart from in the US where most of the respondents were from an office or clinic-based practice.

5.3 Qualitative and Quantitative Research with Patients

Patients were recruited using a range of methods. These included utilization of panels and databases, referrals from patients (patients referring other patients), referrals from physicians, and referrals from support groups or networks. All molecular subtypes (HR, HER2, and TNBC) were included (Table 1). For their participation in the survey, respondents were given honoraria payments in compliance with local regulations.

The inclusion criteria were the following:

- ▼ Females patients only
- ▼ Diagnosed with stage IV* breast cancer in the last 5 years
- ▼ Had ever received drug treatment (targeted treatment, endocrine treatment or chemotherapy) for their stage IV* breast cancer
- ▼ Not a physician, nurse, or other type of healthcare professional

A total of 115 patients with mBC (38% *de novo* and 67% recurrent) were given a pre-task of rating their level of agreement with statements about beliefs around mBC treatment and relationships with doctors, followed by a 45- to 60-minute in-person or phone interview conducted between October 2015 and March 2016.

*For purposes of this paper, stage IV breast cancer includes metastatic, advanced, and secondary diseases.

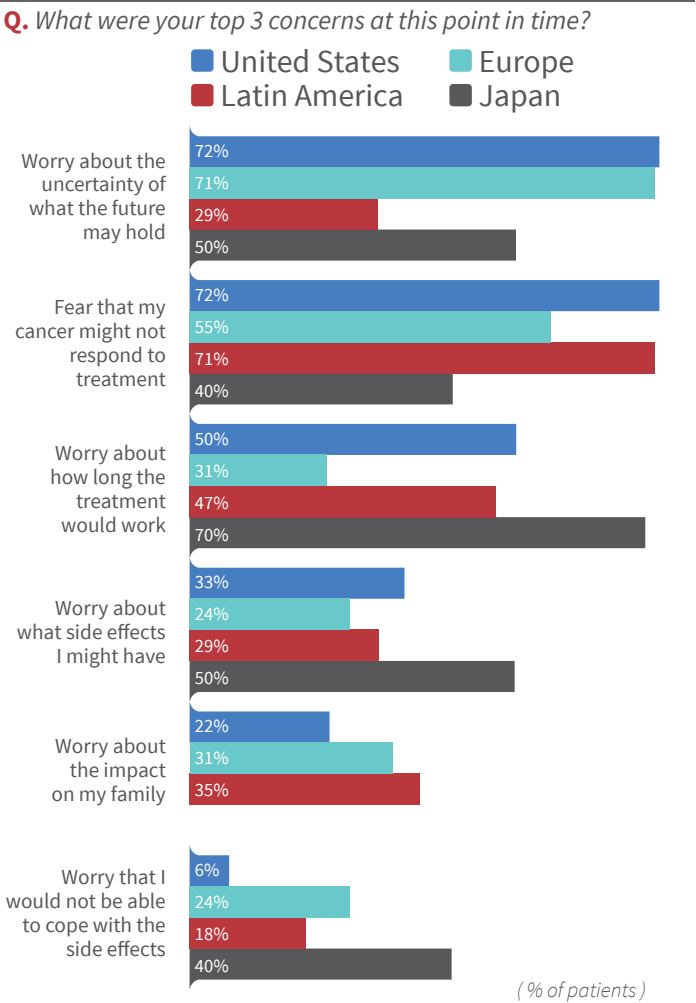
Patients’ time since mBC diagnosis ranged from less than 1 year to 5 years, with a mean of 2 to 3 years. The majority of patients (78%) were on second-line (2L) treatment or later.

Patients’ ages ranged between 30 and 70+ years. Sixty-three percent of patients interviewed had received their mBC diagnosis up to 2 years previously, while 37% had been living with this diagnosis for 2.3 years (mean). The number of participating patients from each country is shown in Figure 1.

Table 1. Molecular Subtype of Patient Respondents (Self-Reported)

| SUBTYPE | PERCENT OF PATIENTS WITH SUBTYPE |
|-----------|----------------------------------|
| HR+ HER2- | 46% |
| HR- HER2- | 33% |
| HER2+ | 21% |
| Unsure | 1% |

Figure 20. Top 3 Concerns: Progression (by Region) (Patient Reported)



Base: All respondents: US (18), EU (42), LatAm (17), JP (10)
Please think back to when you changed your treatment because your stage IV breast cancer came back or continued to grow. Please enter a 1, 2, and 3 in the yellow column below to indicate your top 3 concerns; Worry about the number of treatment options left: US 28%, EU 10%, LatAm 18%, JP 30%; Fear that cancer would come back: US 11%, EU 17%, LatAm 24%, JP 10%; Fear that experiencing symptoms like pain or cough may be a sign of cancer getting worse: US 6%, EU 21%, LatAm 12%, JP 10%; Worry that I may not be able to work anymore: US 0%, EU 12%, LatAm 12%, JP 0%