

Clinician Update

HR+/HER2- Breast Cancer

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The path to shared decision-making *starts with you*

Distilling complex treatment options is a critical job for clinicians. Here's how to help patients absorb information and make informed choices.

“Breast cancer is a very difficult diagnosis to digest,” says Madiha A. Gilani, MD, director of Hematology Oncology Services at Penn Medicine Radnor and a clinical associate professor of Hematology-Oncology. “Patients handle it in varying ways, from denial, to going into ‘fix-it mode’ and pushing through, to not knowing how they’ll navigate this life-changing information.”

As a clinician, you're at the helm of helping patients wade through this often-shocking news—and that includes facilitating their understanding of complex treatment decisions, says Dr. Gilani. Following is expert-backed advice and best practices for guiding an open dialogue with patients and caregivers so they can better navigate medical therapy.

Learn about your patient

One challenge as a clinician is, simply put, to read the room. “For me, I try to understand my patient’s personality,” says Dr. Gilani. “Where are they starting off in their knowledge and understanding of their diagnosis, and where do I need to meet them?” From there, she explains:

- type of breast cancer, stage and what that means
- what their scans show, including genetics or oncotype reports, when applicable
- treatment recommendation, plus evidence with data/research to support why this treatment is applicable to the patient and features of their cancer
- how treatment can be tailored to their specific needs

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“This journey is long, and it’s important that the patient feels comfortable with their oncologist...”

—Madiha A. Gilani, MD

Put the emphasis on personalization

Treatment decisions are complicated, and patients may not express their personal preferences and needs—or even understand that they matter. Though the goal of clinicians is to provide standard of care and guideline-based therapy, patients may not always be able (or willing) to adhere to the guidelines exactly as written, says Dr. Gilani.

You may need to tweak the approach or adjust the schedule based on factors like age, support or an upcoming life event. “This journey is long, and it’s important that the patient feels comfortable and able to have a free, frank and straightforward dialogue. The goal is to enable a shared decision together as much as possible,” she adds.

Evelyn Taiwo, MD, hematologist/oncologist at Weill Cornell Medicine and New York-Presbyterian Brooklyn Methodist Hospital, agrees. “Whatever phase of cancer a patient is in—early to metastatic—it’s important for patients to know they’re part of the treatment decision-making process. Treatment is not something that’s just done to them.”

Knowing who your patient is ensures this happens. Dr. Taiwo recalls a patient who was a violin player, so it was important to choose a regimen that limited neuropathy side effects. Another patient was an actress, and she needed to consider how treatment would affect her physical appearance. Quality of life (QoL) continues to be a critical consideration for talking to your patients about their treatment and what they can expect—and that’s across all stages of breast cancer.

In one survey of patients with



ER+/HER2- mBC, 68% said that QoL was the most or a very important factor for making a treatment decision based on risks, as it affects their mental state, career, relationships, daily tasks and finances.¹

Assess your patient’s understanding

“One of the biggest challenges for many patients is the narrative that comes with a breast cancer diagnosis,” says Dr. Taiwo. “There is a lot of fear, as well as grappling with one’s mortality.” In addition, loss of control over their body and life is a frightening prospect. Dr. Taiwo stresses that at the time of diagnosis, community primary care professionals become critical partners in distilling initial information. She adds that if there’s already a built-in layer of trust between doctor and patient, that’s valuable.

When your patient first sees you, it’s important to realize they may have no knowledge of their cancer, and you may be the first person they’re seeing. “I don’t assume the patient knows everything. I want to make sure the patient and I are on the same page and that they understand why I am suggesting a certain treatment,” says Dr. Gilani.

Patients should leave an appointment with a clear understanding of their treatment plan:

- What I am going to go through
- What this treatment will do to me
- Why I really need this treatment
- How the treatment will impact my life, job and family
- How much this treatment will cost

“These are challenging thought processes that exist



beyond the specifics of treatment,” says Dr. Gilani.

Agree on goals

Breast cancer staging affects patient communication, notes Dr. Gilani. “When we’re speaking with someone who has a curable disease, the conversation is different vs. when speaking with a patient who has an incurable cancer.” Patient reactions often rest on prognosis, whether they have an early breast cancer or metastatic diagnosis. “How they’re taking in the information is different,” she says.

With curative breast cancer, Dr. Gilani approaches the conversation by describing the disease as a challenge—but a challenge that exists for a limited period of time. “There is light at the end of the tunnel, and it’s our goal to get there,” she says. With metastatic disease, the overall goal is not

a cure but to turn their cancer into a chronic illness, and treatment will be indefinite.

She notes: “As long as we can, for as long as our treatment allows, we want to be able to keep the cancer under control.”

Encourage a support team

“I’m always grateful when a patient has a family member or another care person with them who’s in a position to listen and take in information on treatment options and have another discussion later with them,” says Dr. Gilani. Overall, support is an often-overlooked factor in a patient’s ability to navigate treatment decisions.

“Breast cancer is such a significant burden the patient faces, and asking about mental health is extremely important. It’s also often an unmet need,” contin-

ues Dr. Gilani. Indeed, research in the *Journal of Clinical Medicine* shows that mental health support is a growing and important part of precision oncology that, when paired with advanced therapies, promotes treatment adherence and tolerance, QoL and overall survival.²

Monitor the patient’s internet research

Whether it’s through social media or ping-pong Dr. Google, patients learn information on breast cancer treatment and care online, which can be both a help and hindrance in conveying information on treatment options. One survey from the Breast Cancer Research Foundation found that patients rely on a mix of information from search engines, social media, AI tools and their clinicians.³ Problem is, this online information commonly directly contradicts their doctor, the research revealed.

As a clinician, you can work with this. “I’m very appreciative when patients come to talk to me about what they’ve researched,” says Dr. Gilani. This can open up a conversation to clear up confusion or conflicting information as well as manage expectations. She says it’s the clinician’s job to help a patient analyze what they’ve read. “Our role is to guide, support and help patients get the right kind of information.”

Preemptively discuss side effects

A multicountry study found almost half of patients with early breast cancer reported receiving information on a specific side effect—only after they experienced that side effect. And nearly as many said they got insufficient



or no information on side effects from their clinicians at all.⁴ Proactive communication is key as you talk to patients about treatment options and recommendations.

For side effects with a 10% higher risk, Dr. Taiwo will discuss these with her patient. Anything that is rare (less than 1% odds), not relevant and won't otherwise change their overall treatment trajectory may not be discussed, though she says this is patient dependent. Talking about potential negative side effects can overload patients with information. "There's a skill in knowing your patient," says Dr. Taiwo.

A patient's ability to trust their clinician with an honest assessment of the ins and outs of treat-

ment increases the likelihood that they will stay in contact with you via phone, email portal or another in-person appointment, when challenges occur that could hinder adherence, explains Dr. Gilani. "Treatment is only as good as a patient can tolerate. And if they can't tolerate it, there's no point, so I always need patients to communicate with me honestly."

Invite second opinions

Early breast cancer or metastatic disease is a stressful diagnosis. That's where encouraging a second opinion comes in. "I offer the option of seeking out a second opinion before a patient even asks," says Dr. Taiwo. One potential concern among

patients is that this second opinion will delay treatment. And while it does increase the time from diagnosis to treatment, the timing remains within Commission on Cancer standards.⁵

It's important to let patients know that you support those efforts—and that you'll be happy to care for them if that's what they'd like, explains Dr. Taiwo. "Some people need to hear the same thing over and over again to buy into treatment. And we need that buy-in." ●

—by Jessica Migala

IMPROVING BREAST CANCER HEALTH LITERACY

About 9 in 10 adults in the US have limited health literacy.⁶ In the breast cancer space, this becomes more challenging as breast cancer treatment has become increasingly complex and individualized, notes research. As such, clinicians need to convey medical information with care.

Keep treatment conversations at a 6th to 8th grade comprehension level, unless a patient themselves elevates the conversation, advises Weill Cornell Medicine hematologist and oncologist Evelyn Taiwo, MD. Deep dives into exact mechanisms of drugs or clinical trial findings aren't required and, in general, simpler is better. This aligns with the National Institutes of Health's own plain language initiative.⁷ While this initiative focuses on medical communication through writing, the overall message is that plain language and clear communication is not dumbing down your message or talking down to someone—it is a recipe for providing clear, effective communication. The result? Patients who can make informed treatment decisions.⁸

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Ending undertreatment, *enhancing quality of life*

The oncology community is increasingly recognizing the value of symptomatic breast cancer treatment in improving patient quality of life. A multifaceted approach that prizes clear communication can help smooth their cancer journeys.

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“Quality of life is literally the most important goal when managing a patient with breast cancer,” says Cassidy Lockwood, RN, an oncology nurse at Smilow Cancer Hospital, Yale New Haven Health. “It is our duty to take that objective seriously.” That perspective reflects a broader shift in oncology care toward prioritizing symptom management alongside disease control. Consider, recent studies indicate that a significant number of patients with early-stage breast cancer (eBC) may be undertreated for symptoms, and a 2024 analysis found that 12.97% (62 out of 478) of patients with eBC were undertreated—meaning they did not receive recommended therapeutic interventions such as appropriate surgery or radiation therapy that could have managed their cancer or its symptoms.¹

“QUALITY OF LIFE IS LITERALLY THE MOST IMPORTANT GOAL WHEN MANAGING A PATIENT WITH BREAST CANCER.”

—Cassidy Lockwood, RN

Today, both the American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) recognize the need to minimize suffering for patients with breast cancer and have developed recommendations to help guide symptomatic cancer treatment.^{2,3}

“At each visit, the oncology team should ask questions that

capture both disease impact and overall wellness,” says Naoto T. Ueno, MD, PhD, director of the University of Hawai‘i Cancer Center. “Emphasizing the importance of assessing physical symptoms, psychosocial status and cognitive condition helps clinicians feel capable of delivering comprehensive care tailored to each patient’s needs.” You and your oncology team can make a tremendous difference in patient quality of life (QoL) by:

Recognizing progression patterns

Although each patient’s experience is unique, says Dr. Ueno, clinicians often observe recurring phases in how breast cancer progresses. These usually include slowly progressing “smoldering” disease; a “gradual” pattern that is stable at first but then can turn symptomatic; a “rapid” course characterized by

ic treatment is needed at any given point, says Dr. Ueno (see sidebar on p. 9). But while patterns may be guideposts, he warns that they are not a cookbook. “The four progression patterns are best thought of as a practical lens rather than fixed boxes,” he adds. “They help clinicians judge timing: when to lean more on symptom control, when to push rehabilitation and when to shift toward planning.”

Carrying out a symptom assessment

Because symptom burden can change throughout treatment, symptomatic care should begin at the first visit and continue throughout the disease course, Lockwood and Dr. Ueno emphasize. That means maintaining a rapport with the patient, asking key questions at each visit to tease out the disease’s specific impact and then devising a tailored treatment plan, Dr. Ueno says. It also means tracking treatment and keeping all oncology care team members informed on treatment decisions and progress, visit by visit.

One approach for gauging physical symptoms is to “go from head to toe,” Lockwood suggests. “Start by asking, ‘Do you have any eye issues?’ Then ask, ‘Do you have any nasal or nose issues?’ and just keep working your way down,” she says. “Many patients have so much on their minds that prompting them with head-to-toe questions gets the best responses. You ask the patient about each part of the body, and the patient of-

ten says, ‘I do have an issue with that; I forgot about it until you asked.’”

Regardless of the approach, each symptom assessment needs to include two critical questions:

1. What symptom is bothering you most right now?
2. What symptom or adverse treatment effect do you find intolerable?

“This is very important to discuss,” says Lockwood. “Often patients think they just need to grin and bear their symptoms but opening that dialogue can enable patients to feel more comfortable discussing them.” Dr. Ueno also suggests asking the following questions during the visit:

- How has your breast cancer or treatment affected your daily activities?
- Can you eat, sleep, move around and rest the way you need to?
- Are you having pain, shortness of breath, nausea, constipation, fatigue or trouble sleeping?
- What matters most to you now in terms of treatment and QoL?
- How is your mood, stress level or anxiety?
- Are you feeling overwhelmed, depressed or worried about the future?
- Are there new concerns from family or caregivers that we should address?

Targeting common symptoms

Once problems have been identified, the next step is im-

plementing targeted interventions. Following are strategies to proactively manage some of the most common breast cancer-related symptoms:²

Pain. Narcotic or non-narcotic pain relievers are appropriate based on the patient’s pain tolerance and pain scale self-rating, says Lockwood, who stresses the importance of gauging the patient’s proclivity or aversion toward use of narcotics or controlled substances before prescribing a pain reliever.

Patient lifestyle is another consideration, Lockwood adds, as “some patients might be in their 70s or 80s, retired and at home most of the day, while another patient is aged 35 years with three kids and taking care of children while the spouse or partner is at work. It’s important to look at each patient individually and listen to their subjective statements about their pain.”

Nausea/GI symptoms. Urge patients to eat smaller, more frequent meals and consider referral to a dietitian, Dr. Ueno advises. Also suggest prophylactic use of anti-nausea agents, Lockwood adds.

Insomnia. Interventions range from light exercise, relaxation and stress reduction techniques to improving sleep hygiene and, if appropriate, using supplements like melatonin, magnesium and chamomile tea, both experts note.

Fatigue. Fatigue can be particularly challenging because it often stems from both the disease

PHASES OF BREAST CANCER METASTASIS

Metastasis in breast cancer can generally be classified into four distinct phases, says Naoto T. Ueno, MD, PhD, director of the University of Hawai‘i Cancer Center:

1. Smoldering disease tends to unfold slowly, often over years, with relatively little symptom burden. At this phase, Dr. Ueno suggests a “steady and anticipatory” course of symptomatic treatment that includes education; routine follow-up; guiding the patient toward self-management, exercise and healthy eating; and occasional advance care planning discussions.

2. Gradual progression usually starts with a stable period and then becomes more symptomatic. Maintenance treatment is appropriate early in the course, Dr. Ueno says, “but as symptoms build, care should pivot to active symptom control, closer coordination and a clearer structure around follow-up.”

3. Rapid progression. Patients are symptomatic early, and the window for maintaining QoL is shorter, Dr. Ueno notes. The priority is relief first: Get symptoms under control, reassess frequently, support the patient’s caregivers and have goals-of-care conversations sooner rather than later.

4. De novo poor-condition. From the initial diagnosis of metastasis, patients present with challenging conditions, Dr. Ueno says. “These patients often have limited reserve at diagnosis, so supportive care needs to be built in from day one—tight symptom control, attention to function and starting palliative care early as part of routine management, rather than a later step.”



COMMUNICATING AS A TEAM

Symptomatic treatment of mBC requires a team effort, and keeping colleagues in the loop is critical. “I support multidisciplinary, phase-based care, so communication needs to be explicit and ongoing rather than ad hoc,” says Naoto T. Ueno, MD, PhD, of the University of Hawai‘i. He suggests summarizing each visit with your team using this basic template:

1. Current phase: stable or acute
2. Top 2 concerning symptoms
3. Functional change since last visit
4. Psychosocial or caregiver issues
5. Specific action requested from palliative care, nursing, social work, physical/occupational therapists, dietitian or psychology professionals

Another tactic for the entire oncology team is to meet once or twice weekly and “run the list,” suggests Cassidy Lockwood, RN, of Yale New Haven Health. “We sit together and review every patient that was seen that day, what the updates are, what we’re doing for that patient and what we’re changing to ensure we’re all on the same page about what’s going on,” she notes.

Also important: “Involve caregivers in treatment discussions and align treatment plans with the patient’s goals,” says Dr. Ueno. “Especially when advance care planning or life-sustaining treatment decisions are relevant.”

and its treatment, Lockwood notes, adding that reducing the dose or modifying treatment frequency might alleviate tiredness. Alternatively, low-intensity exercise can help increase a patient’s energy and significantly reduce fatigue, as can a rehabilitation/physical therapy course and changes in daily routine to conserve energy, Dr. Ueno notes.⁶ In rare cases, a stimulant medication might be offered to counter fatigue, Lockwood notes, again taking patient preference and phase of metastasis into consideration.

Monitoring emotional wellness

Physical symptoms are only part of the picture. Gauging a patient’s emotional state is particularly important, both experts say, as depression, anxiety and psychological distress are common among patients with breast cancer at any stage, and those rates tend to be slightly higher among patients with metastatic breast cancer.^{5,7,9} Common breast cancer-related symptoms such as pain, appetite loss and dyspnea may increase the risk of a depressive disorder, as can deficits in physical and emotional function.⁹

“Sometimes we forget that mental health is as important as physical health for patients with a breast cancer diagnosis, whether early breast cancer or metastatic breast cancer,” says Lockwood. “Whether projected survival is for two years or 10 years, that’s a very daunting place to be mentally.” What’s more, she explained that the ef-

fect of an emotional disorder is dangerously reciprocal: Depressive and anxiety disorders have been shown to increase the risk of breast cancer recurrence and mortality by about one-third.^{4,10} By contrast, alleviating depression and anxiety symptoms may decrease recurrence/mortality risk and extend disease-free survival.^{11,12}

These findings underscore the need to watch for warning signs of depression and anxiety—and to ask about these disorders at each visit, both experts say. But don't force the conversation, Lockwood warns, as some patients may become angry and defensive when questioned about their mental health. "If a patient tells us, 'I don't want you to ask me this every time,' that is 100% okay," Lockwood suggests. "It's the patient's body, so we can respect that." But, she adds, you can still monitor the mental health of a patient with breast cancer with these gentle but effective techniques:

Hand patients a brief mental health screening questionnaire every 60 to 90 days, then give them a flexible timeframe for completing it. The short-form Patient Health Questionnaire, Generalized Anxiety Disorder questionnaire, or NCCN Distress Thermometer are quick and effective tools,

Dr. Ueno says. Again, metastatic phase should dictate the monitoring approach, with ongoing surveillance and psychological support for patients at the smoldering or gradual-progression phases, and regular screening and prompt referral to and integration with mental health services for rapid-progression or de novo-phase patients, he adds.

Ask patients about psychosocial issues, for example, "Are you having trouble affording food or paying bills?" "These issues can pile up to increase risk for a mental health problem," Lockwood says.

Establish and continue to build a rapport. This way you can gain your patient's trust over time, and the patient will begin feeling more comfortable and open up about fears and frustrations toward their breast cancer, says Lockwood, who considers this approach "the best way to talk to patients about depression and anxiety."

Ultimately, the oncology team plays a central role in helping patients maintain comfort, function and QoL throughout their cancer journey. "There's no need for these patients to suffer," Lockwood says. "We have so many tools and supportive treatments at our disposal that can help." ●

—by Pete Kelly

"AT EACH VISIT, THE ONCOLOGY TEAM SHOULD ASK QUESTIONS THAT CAPTURE BOTH DISEASE IMPACT AND OVERALL WELLNESS."

—Naoto T. Ueno, MD, PhD

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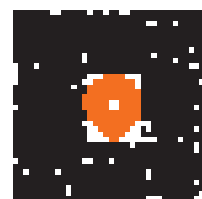
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In patients with ABC, a majority of cases (70%) cited KISQALI as a top KISQALI option as a monotherapy or combined with ET. In patients with mBC, a majority of cases (43%) cited KISQALI as a top KISQALI option as a monotherapy.

Most patients with ABC, a majority of cases (70%) cited KISQALI as a top KISQALI option as a monotherapy or combined with ET. In patients with mBC, a majority of cases (43%) cited KISQALI as a top KISQALI option as a monotherapy.

For more information, visit <https://www.kisqali-hop.com> or contact your local KISQALI representative for more information on the latest data.



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• **How to use the book:** This book is designed to be used in a variety of ways. It can be used as a textbook for a course in statistics, as a reference for students and professionals, or as a self-study guide. The book is organized into chapters that cover the basic concepts and methods of statistics, and each chapter includes exercises and problems to reinforce the material. The book is written in a clear and concise style, and it includes many examples and diagrams to help illustrate the concepts. The book is suitable for students at the undergraduate and graduate levels, and it is also a valuable resource for professionals in a wide range of fields.

1. *Journal of the American Medical Association*, 2000; 284: 2689-2695.

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1. *Chlorophyll a* and *Chlorophyll b* were determined by the method of Lichtenthal and Whistler (1973). The total chlorophyll content was determined by the method of Arar and Cook (1980). The carotenoid content was determined by the method of Lichtenthal and Whistler (1973). The total carotenoid content was determined by the method of Arar and Cook (1980). The total protein content was determined by the method of Lowry et al. (1951). The total lipid content was determined by the method of Bligh and Dyer (1959). The total carbohydrate content was determined by the method of Dubois and Gilles (1950). The total nucleic acid content was determined by the method of Burton (1956). The total ash content was determined by the method of AOAC (1990). The total moisture content was determined by the method of AOAC (1990). The total dry matter content was determined by the method of AOAC (1990). The total organic acid content was determined by the method of AOAC (1990). The total alkaloid content was determined by the method of AOAC (1990). The total saponin content was determined by the method of AOAC (1990). The total tannin content was determined by the method of AOAC (1990). The total flavonoid content was determined by the method of AOAC (1990). The total phenol content was determined by the method of AOAC (1990). The total terpenoid content was determined by the method of AOAC (1990). The total steroid content was determined by the method of AOAC (1990). The total glycoside content was determined by the method of AOAC (1990). The total alkaloid content was determined by the method of AOAC (1990). The total saponin content was determined by the method of AOAC (1990). The total tannin content was determined by the method of AOAC (1990). The total flavonoid content was determined by the method of AOAC (1990). The total phenol content was determined by the method of AOAC (1990). The total terpenoid content was determined by the method of AOAC (1990). The total steroid content was determined by the method of AOAC (1990). The total glycoside content was determined by the method of AOAC (1990).

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1. **Identify the main idea of the passage.**
 2. **Identify the supporting details.**
 3. **Identify the author's purpose.**
 4. **Identify the author's tone.**
 5. **Identify the author's bias.**
 6. **Identify the author's point of view.**
 7. **Identify the author's audience.**
 8. **Identify the author's style.**
 9. **Identify the author's structure.**
 10. **Identify the author's language.**

It is important to note that the above results are based on the assumption that the data are stationary. If the data are non-stationary, the results may be biased. Therefore, it is important to test for stationarity before conducting the regression analysis.

1. The first step in the process is to identify the problem. This involves gathering information about the situation and understanding the needs of the stakeholders involved.

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POLYMER LETTERS

1. *Journal of the American Medical Association*, 2000; 284: 2689-2695.

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1. The first step in the process is to identify the problem or issue that needs to be addressed. This involves gathering information and understanding the context of the problem.

1. *Chlorophyll a* and *Chlorophyll b* were determined by the method of Arar and Collins (1971) using a Shimadzu 1601 UV-Visible Spectrophotometer. The concentration of chlorophyll was expressed in $\mu\text{g mL}^{-1}$.

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The following table shows the results of the regression analysis for the dependent variable "Number of children in the household" (N = 1,000). The independent variables are "Age of the head of household" and "Gender of the head of household". The dependent variable is "Number of children in the household".

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1. *Phragmites* spp.

Date	Description	Debit		Credit	
		Amount	Account	Amount	Account
1998-01-01	Balance				
1998-01-05	Deposited			100.00	100.00
1998-01-10	Withdrawal	50.00	50.00		
1998-01-15	Deposited			25.00	25.00
1998-01-20	Withdrawal	25.00	25.00		
1998-01-25	Deposited			75.00	75.00
1998-01-30	Withdrawal	75.00	75.00		
1998-02-05	Deposited			100.00	100.00
1998-02-10	Withdrawal	100.00	100.00		
1998-02-15	Deposited			150.00	150.00
1998-02-20	Withdrawal	150.00	150.00		
1998-02-25	Deposited			200.00	200.00
1998-02-28	Balance				
1998-03-01	Balance				

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1. **Introduction**

DATE		DESCRIPTION		AMOUNT		BALANCE	
1/1/01		OPENING BALANCE				100.00	
1/15/01		PAYROLL		50.00		150.00	
2/1/01		RENT		200.00		350.00	
2/15/01		PAYROLL		50.00		400.00	
3/1/01		RENT		200.00		600.00	
3/15/01		PAYROLL		50.00		650.00	
4/1/01		RENT		200.00		850.00	
4/15/01		PAYROLL		50.00		900.00	
5/1/01		RENT		200.00		1100.00	
5/15/01		PAYROLL		50.00		1150.00	
6/1/01		RENT		200.00		1350.00	
6/15/01		PAYROLL		50.00		1400.00	
7/1/01		RENT		200.00		1600.00	
7/15/01		PAYROLL		50.00		1650.00	
8/1/01		RENT		200.00		1850.00	
8/15/01		PAYROLL		50.00		1900.00	
9/1/01		RENT		200.00		2100.00	
9/15/01		PAYROLL		50.00		2150.00	
10/1/01		RENT		200.00		2350.00	
10/15/01		PAYROLL		50.00		2400.00	
11/1/01		RENT		200.00		2600.00	
11/15/01		PAYROLL		50.00		2650.00	
12/1/01		RENT		200.00		2850.00	
12/15/01		PAYROLL		50.00		2900.00	
1/1/02		RENT		200.00		3100.00	
1/15/02		PAYROLL		50.00		3150.00	
2/1/02		RENT		200.00		3350.00	
2/15/02		PAYROLL		50.00		3400.00	
3/1/02		RENT		200.00		3600.00	
3/15/02		PAYROLL		50.00		3650.00	
4/1/02		RENT		200.00		3850.00	
4/15/02		PAYROLL		50.00		3900.00	
5/1/02		RENT		200.00		4100.00	
5/15/02		PAYROLL		50.00		4150.00	
6/1/02		RENT		200.00		4350.00	
6/15/02		PAYROLL		50.00		4400.00	
7/1/02		RENT		200.00		4600.00	
7/15/02		PAYROLL		50.00		4650.00	
8/1/02		RENT		200.00		4850.00	
8/15/02		PAYROLL		50.00		4900.00	
9/1/02		RENT		200.00		5100.00	
9/15/02		PAYROLL		50.00		5150.00	
10/1/02		RENT		200.00		5350.00	
10/15/02		PAYROLL		50.00		5400.00	
11/1/02		RENT		200.00		5600.00	
11/15/02		PAYROLL		50.00		5650.00	
12/1/02		RENT		200.00		5850.00	
12/15/02		PAYROLL		50.00		5900.00	
1/1/03		RENT		200.00		6100.00	
1/15/03		PAYROLL		50.00		6150.00	
2/1/03		RENT		200.00		6350.00	
2/15/03		PAYROLL		50.00		6400.00	
3/1/03		RENT		200.00		6600.00	
3/15/03		PAYROLL		50.00		6650.00	
4/1/03		RENT		200.00		6850.00	
4/15/03		PAYROLL		50.00		6900.00	
5/1/03		RENT		200.00		7100.00	
5/15/03		PAYROLL		50.00		7150.00	
6/1/03		RENT		200.00		7350.00	
6/15/03		PAYROLL		50.00		7400.00	
7/1/03		RENT		200.00		7600.00	
7/15/03		PAYROLL		50.00		7650.00	
8/1/03		RENT		200.00		7850.00	
8/15/03		PAYROLL		50.00		7900.00	
9/1/03		RENT		200.00		8100.00	
9/15/03		PAYROLL		50.00		8150.00	
10/1/03		RENT		200.00		8350.00	
10/15/03		PAYROLL		50.00		8400.00	
11/1/03		RENT		200.00		8600.00	
11/15/03		PAYROLL		50.00		8650.00	
12/1/03		RENT		200.00		8850.00	
12/15/03		PAYROLL		50.00		8900.00	
1/1/04		RENT		200.00		9100.00	
1/15/04		PAYROLL		50.00		9150.00	
2/1/04		RENT		200.00		9350.00	
2/15/04		PAYROLL		50.00		9400.00	
3/1/04		RENT		200.00		9600.00	
3/15/04		PAYROLL		50.00		9650.00	
4/1/04		RENT		200.00		9850.00	
4/15/04		PAYROLL		50.00		9900.00	
5/1/04		RENT		200.00		10100.00	
5/15/04		PAYROLL		50.00		10150.00	
6/1/04		RENT		200.00		10350.00	
6/15/04		PAYROLL		50.00		10400.00	
7/1/04		RENT		200.00		10600.00	
7/15/04		PAYROLL		50.00		10650.00	
8/1/04		RENT		200.00		10850.00	
8/15/04		PAYROLL		50.00		10900.00	
9/1/04		RENT		200.00		11100.00	
9/15/04		PAYROLL		50.00		11150.00	
10/1/04		RENT		200.00		11350.00	
10/15/04		PAYROLL		50.00		11400.00	
11/1/04		RENT		200.00		11600.00	
11/15/04		PAYROLL		50.00		11650.00	
12/1/04		RENT		200.00		11850.00	
12/15/04		PAYROLL		50.00		11900.00	
1/1/05		RENT		200.00		12100.00	
1/15/05		PAYROLL		50.00		12150.00	
2/1/05		RENT		200.00		12350.00	
2/15/05		PAYROLL		50.00		12400.00	
3/1/05		RENT		200.00		12600.00	
3/15/05		PAYROLL		50.00		12650.00	
4/1/05		RENT		200.00		12850.00	
4/15/05		PAYROLL		50.00		12900.00	
5/1/05		RENT		200.00		13100.00	
5/15/05		PAYROLL		50.00		13150.00	
6/1/05		RENT		200.00		13350.00	
6/15/05		PAYROLL		50.00		13400.00	
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7/15/05		PAYROLL		50.00		13650.00	
8/1/05		RENT		200.00		13850.00	
8/15/05		PAYROLL		50.00		13900.00	
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10/15/05		PAYROLL		50.00		14400.00	
11/1/05		RENT		200.00		14600.00	
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1/1/06		RENT		200.00		15100.00	
1/15/06		PAYROLL		50.00		15150.00	
2/1/06		RENT		200.00		15350.00	
2/15/06		PAYROLL		50.00		15400.00	
3/1/06		RENT		200.00		15600.00	
3/15/06		PAYROLL		50.00		15650.00	
4/1/06		RENT		200.00		15850.00	
4/15/06		PAYROLL		50.00		15900.00	
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5/15/06		PAYROLL		50.00		16150.00	
6/1/06		RENT		200.00		16350.00	
6/15/06		PAYROLL		50.00		16400.00	
7/1/06		RENT		200.00		16600.00	
7/15/06		PAYROLL		50.00		16650.00	
8/1/06		RENT		200.00		16850.00	
8/15/06		PAYROLL		50.00		16900.00	
9/1/06		RENT		200.00		17100.00	
9/15/06		PAYROLL		50.00		17150.00	
10/1/06		RENT		200.00		17350.00	
10/15/06		PAYROLL		50.00		17400.00	
11/1/06		RENT		200.00		17600.00	
11/15/06		PAYROLL		50.00		17650.00	
12/1/06		RENT		200.00		17850.00	
12/15/06		PAYROLL		50.00		17900.00	
1/1/07		RENT		200.00		18100.00	
1/15/07		PAYROLL		50.00		18150.00	
2/1/07		RENT		200.00		18350.00	
2/15/07		PAYROLL		50.00		18400.00	
3/1/07		RENT		200.00		18600.00	
3/15/07		PAYROLL		50.00		18650.00	
4/1/07		RENT		200.00		18850.00	
4/15/07		PAYROLL		50.00		18900.00	
5/1/07		RENT		200.00		19100.00	
5/15/07		PAYROLL		50.00		19150.00	
6/1/07		RENT		200.00		19350.00	
6/15/07		PAYROLL		50.00		19400.00	
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7/15/07		PAYROLL		50.00		19650.00	
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9/15/07		PAYROLL		50.00		20150.00	
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2/1/08		RENT		200.00		21350.00	
2/15/08		PAYROLL		50.00		21400.00	
3/1/08		RENT		200.00		21600.00	
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9/15/08		PAYROLL		50.00		23150.00	
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10/15/08		PAYROLL		50.00		23400.00	
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11/15/08		PAYROLL		50.00		23650.00	
12/1/08		RENT		200.00		23850.00	
12/15/08		PAYROLL		50.00		23900.00	
1/1/09		RENT		200.00		24100.00	
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2/1/09		RENT		200.00		24350.00	
2/15/09		PAYROLL		50.00		24400.00	
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6/15/09		PAYROLL		50.00		25400.00	
7/1/09		RENT		200.00		25600.00	
7/15/09		PAYROLL		50.00		25650.00	
8/1/09		RENT					

[illegible]

Date		Time			
Location		Weather			
Observer		Remarks			
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13	14	15	16	17	18
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the 1990s, the number of people in the world who are illiterate has increased from 1.2 billion to 1.5 billion. The number of illiterate people in the world is projected to increase to 1.7 billion by the year 2015. The number of illiterate people in the world is projected to increase to 1.7 billion by the year 2015.

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Abstract The purpose of this study was to determine the effect of a 12-week training program on the physical fitness of 100 male and 100 female students. The program was designed to improve cardiovascular endurance, muscular strength, and flexibility. The results showed that the program had a significant positive effect on all three components of physical fitness. The students who participated in the program showed a significant increase in their cardiovascular endurance, muscular strength, and flexibility compared to the control group. The program was found to be effective in improving the physical fitness of both male and female students.

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Teaching patients to be *smarter* about AI

Experts offer strategies for using chatbots effectively, evaluating the answers and ensuring patients understand when AI isn't enough.

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A Artificial intelligence (AI) is revolutionizing oncology care.

At the same time, it's also changing how patients with cancer, including early-stage breast cancer (eBC) and metastatic breast cancer (mBC), search for information about their diagnosis, treatment options, tests and symptoms. AI-driven consumer chatbots show promise for equipping patients with knowledge that can help them advocate for their preferences and communicate more effectively with their care teams, says Robert Wachter, MD, professor and chair of the Department of Medicine at the University of California San Francisco and author of *A Giant Leap: How AI Is Transforming Healthcare and What That Means for Our Future*.¹ “The latest versions of AI tools—particularly the new health chatbots—are much better than they were just two to three years ago,” notes Dr. Wachter. “For understanding what their diagnosis, treatment and lab results mean and for suggesting questions patients can ask at their next appointment, AI can be much more helpful than a standard internet search.”

Many people already rely on chatbots to learn more about their cancer. In a 2025 survey of 1,000 U.S. oncologists, half of respondents said their patients were using AI. About 10% of clinicians thought AI helped patients understand options and ask better questions. But 38% were concerned about misinformation and confusion stemming from AI search results, and 8% said AI searches could cause patient anxiety and worry.²

“AI could help patients with breast cancer understand basic principles about their condition and about treatments,” says Michelle E. Melisko, MD, a breast medical oncology specialist at the University of California San Francisco Health and clinical professor of medicine in the Division of Hematology and Oncology at UCSF who is studying AI for patient education in breast cancer. “But my colleagues and I have also seen patients finding information that’s not right for them or information that they misunderstand because they don’t have the foundation to interpret what they’re reading.”

The pitfalls and potential: what the evidence shows

AI tools aimed at finding medical information are evolving rapidly. In 2026, chatbots became available that focus exclusively on health topics; some allow patients to personalize searches by uploading their electronic medical records. Meanwhile, researchers such as Dr. Melisko are testing specialized, experimental patient education chatbots called Retrieval-Augmented Generation (RAG) Large Language Models (LLMs) that are trained on information that’s peer-reviewed, guideline-based and authored by experts.

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Recent research illustrates where AI can help—and where it can fall short—in cancer care, highlighting opportunities for healthcare providers to guide and educate patients. A summary of notable findings:

- **False and harmful responses:** A 2025 analysis found that 6% to 40% of chatbot answers to cancer-related questions contained false or medically harmful information.³
- **Varying levels of accuracy:** Another evaluation asked a widely used chatbot 100 common questions about mBC. Thirty-one answers were highly accurate, 42 were accurate but not comprehensive, 22 were partially accurate and five were entirely inaccurate.⁴ Also concerning: a Harvard University study that evaluated chatbot responses to treatment questions for breast, lung and prostate cancer found that 34% included recommendations that were not in line with current National Comprehensive Cancer Network (NCCN) guidelines.⁵
- **Training AI improved output:** An assessment of 122 women with breast cancer found that those who used an AI chatbot trained on guide-



line-based and peer-reviewed data felt more knowledgeable and more empowered than patients who received standard of care alone.⁶

- **Oncologists' answers still rated more highly.** In a 2025 study, physicians and patients evaluated responses

from oncologists and from chatbots about cancer symptoms, tests and medical decisions.⁷ Patients rated oncologists' answers higher than AI-generated responses for empathy, accuracy and trustworthiness when it came to making medical decisions.

“FOR SUGGESTING QUESTIONS PATIENTS CAN ASK AT THEIR NEXT APPOINTMENT, AI CAN BE MUCH MORE HELPFUL THAN A STANDARD INTERNET SEARCH.”

—Robert Wachter, MD

AI and breast cancer care: five messages for patients

With more patients using chatbots to research cancer information, clinicians need to set expectations early—especially for patients who may overesti-



mate AI's ability to recommend treatments or interpret test results. "Medicine is an art," Dr. Melisko says. "Oftentimes our choices are not black and white, but must balance many things that are unique to a patient's medical history, symptoms and preferences. AI doesn't have that context or relationship with a patient." Oncologists can help steer them in the right direction by offering this advice:

1. Use it to learn the basics.

AI is great at explaining foundational information about eBC and mBC, tumor biology, how metastasis works and

treatments, Dr. Melisko says. "I think patients can use AI to educate themselves about their disease state and familiarize themselves with terms that their oncologist, surgeon and radiologist might use," she says. "AI could really help there because these things are true across the board for patients." Patients could use AI at any point in their cancer journey—from diagnosis through treatment—to better understand the basics about their cancer stage, test results, treatment options and symptoms, among other topics.

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PATIENT PERSPECTIVE: *using AI for self-advocacy*

Diagnosed with mBC in 2015, Adiba Zeito uses AI as her own personal research assistant to support self-advocacy with her care team. "I'm more prepared and more confident going into medical appointments," she says. "I have the knowledge to ask the right questions and understand medical terms."

Zeito, whose professional career included executive positions at Silicon Valley tech firms, is also the founder of the AICANcer Patient Advocacy Group—a nonprofit foundation aimed at bringing patient perspectives into the adoption of AI technology in oncology to reduce bias and ensure access and security. The group, Zeito says, also aims to help cancer patients make effective use of AI to research their own condition.

"A lot happens when you're a patient with stage IV cancer," Zeito says. "There's no remission. You learn to live with it. For me, the toughest part is chronic pain due to metastasis to my spine and radiation treatments that have caused mobility and nerve issues."

For her personal AI research, Zeito avoids inaccurate and potentially harmful responses by asking search tools to provide citations and depending on the question, to use only peer-reviewed research, advice from physicians who treat a condition she's investigating (such as bone health) and/or information from respected medical organizations. She then goes to original sources to fact-check the information.

Zeito advises against using AI for information such as treatment doses and interactions. "Your care team has a historic record of everything that's happened to you medically. You can rely on them for that information." She may include pertinent information about her own health in a search—such as her age and cancer stage, but she advises against uploading health records and reports. "Patient data is valuable currency in the AI world," she says. "It should be secure and protected at all times."



2. Remember: AI doesn't know the whole picture.

The American Medical Association (AMA) advocates for telling patients to avoid using AI to find information in a medical emergency and instead call 911.⁸ “The patient should trust their own internal compass when it comes to emergencies,” Dr. Wachter says.

Also emphasize that an AI search will not encompass all the information that oncologists and other care team members use when making treatment decisions. “If you’ve known a patient with breast cancer for years and know one of the patient’s priorities is not losing their hair to treatment and that they’ve struggled with

constipation, those things will factor into treatment choices,” Dr. Melisko says. “AI responses can look definitive but may be missing important information your doctor knows.”

3. Ask for sources and compare chatbots.

AI can “sound confident—even when it’s wrong,” warns



Illustration AI-generated using Midjourney

“I HAVE SEEN PATIENTS FINDING INFORMATION THAT’S NOT RIGHT FOR THEM...WITHOUT THE FOUNDATION TO INTERPRET WHAT THEY’RE READING.”

—Michelle E. Melisko, MD

the AMA. Patients may be able to increase AI accuracy by prompting a chatbot to provide citations—and they should double-check the information in cited sources.

Dr. Wachter suggests that patients check responses by asking the same question to different chatbots because results can vary. For example, in a 2026 study researchers posed 23 common questions to recent versions of Gemini and ChatGPT about skin effects of radiation for breast cancer.⁹ Radiation therapists rated Gemini higher for clinical details and empathetic tone, and the information was found to align with an 11th-grade reading level. ChatGPT, on the other hand, scored higher on directness and accessibility, corresponding to an 8th-grade reading level.

4. The question matters as much as the answer.

How patients structure AI prompts can lead to answers that are seemingly incorrect or don’t apply to them. “If someone’s bringing in information from an AI search that doesn’t seem accurate, I’ll ask them to bring in the question they asked,” Dr. Melisko says.

“They can write the questions down or just take a screenshot. If we know what they’ve searched, we can explain why the answer isn’t right.”

5. Think twice before sharing personal information.

While providing specific health details may yield more personalized responses from AI, it also hands sensitive patient information over to companies that aren’t legally obligated to abide by the HIPAA privacy and security rules that govern healthcare.

“I think AI can provide better answers when it has a patient’s past history for context,” Dr. Wachter says. “The disadvantage is the patient needs to give AI permission to have their personal information. AI companies promise to keep personal data private, but sometimes there are breaches.” Patients can also decide how much or how little personal data they’ll type into a search question, he adds. The AMA recommends that patients do not include identifying details, such as their name, address, contact information or account numbers.⁸ ●

—by Sari Harrar

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PATIENT: SOFIA, 40, WAS AN ACTIVE PREMENOPAUSAL WOMAN WITH A PRIOR HISTORY OF MILD ASTHMA.

“Sofia remains active on adjuvant therapy”



PHYSICIAN:

Dionisia Quiroga, DO, PhD, FASCO

Breast Medical Oncologist, Assistant Professor of Medicine, Ohio State University Comprehensive Cancer Center, James Cancer Hospital & Solove Research Institute, Columbus, OH

History:

Sofia was unmarried and working as a school teacher. During a routine exam, her gynecologist felt a left breast lump in September 2023. A mammogram and ultrasound revealed an irregular mass measuring 2.5 cm. Biopsy of this mass showed hormone receptor HR+/HER2- invasive ductal carcinoma of the left breast. Sofia underwent left mastectomy and sentinel lymph node biopsy in November 2023. Surgical pathology confirmed a 2.5 cm tumor (estrogen receptor 100%, progesterone receptor 95%, HER2 IHC 0) with 2 of 3 lymph nodes positive for carcinoma. CT scans of her chest, abdomen, pelvis and a nuclear bone scan showed no signs of residual disease or distant metastatic disease.

During Sofia's visit with me, we discussed that since she was premenopausal with pT2 pN1a disease, I would recommend adjuvant chemotherapy. She proceeded with 4 cycles of docetaxel and cyclophosphamide. She received adjuvant radiation therapy to her left axilla. At a follow-up, she felt nervous about her cancer diagnosis, particularly due to her young age. She stated that she wanted to be “as proactive as possible” in preventing recurrence. Sofia also wanted to stay active, continuing to work and travel with her boyfriend, which were important priorities for her.

Treatment:

We discussed that the cornerstone of adjuvant HR+ breast cancer treatment is endocrine therapy (ET). Based on SOFT/TEXT trial data, I advised ovarian suppression, e.g., every 4-week goserelin injections. We also discussed the need for tamoxifen or an aromatase inhibitor. I explained the side effects (SE) of each, after which she opted for anastrozole daily.

I also spoke with her about the NATALEE trial. I explained the study found that patients who were randomized to 3 years of ribociclib with ET were less likely to have recurrence than those who received ET alone.

We discussed the SEs of both therapies, e.g., for ET, potential joint pain, bone thinning, vasomotor symptoms, vaginal dryness and other sexual SE, and for ribociclib, fatigue, QTc prolongation (monitored for initially with EKGs), liver and kidney function changes, cytopenias and nausea. We reviewed monitoring with bloodwork. Per NATALEE design, we discussed starting her on 400 mg ribociclib, lower than the 600 mg starting dose for

metastatic disease. We also spoke about taking it 21 days on, 7 days off but continuing anastrozole every day. Sofia was very interested in this therapy and started on ribociclib with ET. She experienced mild neutropenia and grade 2 fatigue, which decreased to grade 1 fatigue after her first two cycles. She also had vaginal dryness, which we treated with moisturizers and vaginal DHEA. Her nocturnal hot flashes were notable but improved with gabapentin every night.

As of today, Sofia remains on ribociclib/ET and plans to finish all 3 years of treatment. At this time, there are no signs of cancer recurrence. Throughout treatment she has remained active and is planning an autumn trip to France with her boyfriend.

Considerations:

This case reflects the expanding role of adjuvant systemic therapy in HR+/HER2- early-stage breast cancer. While ET remains the foundation, additional options—including CDK4/6 inhibitors for appropriate high-risk patients, consistent with current ASCO, NCCN and ESMO guidance—have further reduced the risk of recurrence. The key is identifying those most likely to derive meaningful benefit from treatment escalation. Also important: Decisions about adjuvant therapy require shared decision-making with patients, balancing the potential for long-term risk reduction with AE, QoL and patient priorities.



NEW!

KOL ON DEMAND VIDEO
Scan here for more insight on Sofia's case.

History:

Ellen, an attorney, married with 2 children, presented to our clinic with a 2-month history of persistent lower back pain, fatigue and unintentional weight loss of 17.6 lbs. Physical exam revealed that she had tenderness over the lumbar spine but no palpable breast masses or lymphadenopathy. Initial blood work showed elevated alkaline phosphatase (ALP) at 250 U/L (normal range: 44-147 U/L), suggesting possible bone involvement, while other markers like CA 15-3 were mildly raised at 45 U/mL (normal <30 U/mL).

Staging CT scan of her chest, abdomen and pelvis, along with a bone scan, revealed multiple lytic lesions in the lumbar vertebrae and pelvis, consistent with stage IV metastatic breast cancer (mBC) [T2NOMI]. No visceral metastases were noted in her liver or lungs. Mammography and ultrasound of both breasts identified a 2.5 cm irregular mass in the right upper outer quadrant, suspicious for malignancy (BI-RADS 5). A core needle biopsy confirmed invasive ductal carcinoma, grade 2, with strong estrogen receptor (ER) positivity (90%), progesterone receptor (PR) positivity (70%), and HER2 negativity by immunohistochemistry and FISH. Her ECOG performance status was 1, reflecting good functional capacity despite symptoms.

Treatment:

Given Ellen's metastatic HR+ disease, I discussed first-line therapy with ribociclib in combination with letrozole. She agreed and began ribociclib 600 mg orally once daily for 21 days, followed by a 7-day break in a 28-day cycle, while letrozole was administered continuously at 2.5 mg daily. Zoledronic acid 4 mg IV every

4 weeks was added for bone metastases to prevent skeletal-related events.

Therapy began in March 2023. A baseline ECG showed normal QTc interval (420 ms), and complete blood count (CBC) was within normal limits. Monitoring during the first two cycles included CBC to watch for neutropenia, a common ribociclib side effect. In cycle 1, the patient experienced grade 3 neutropenia (absolute neutrophil count [ANC] $0.8 \times 10^9/L$), managed with dose interruption for 7 days until recovery to grade 1. She also reported mild fatigue and nausea, controlled with supportive care (ondansetron and rest). Her liver function tests remained stable, with no significant transaminitis.

By cycle 3, imaging (CT and bone scan) showed stable disease with partial sclerosis of bone lesions, indicating response. By this cycle Ellen was feeling better and returned to work. CA 15-3 decreased to 28 U/mL, and ALP normalized. The patient tolerated subsequent cycles well. ECG monitoring every 3 months confirmed no QTc prolongation (>500 ms). Her adherence was excellent, supported by patient education on the importance of the 3-week-on/1-week-off schedule to mitigate cumulative toxicity.

At 24 months (March 2025), restaging scans showed partial response with >30% reduction in

the primary tumor size and further healing of bone metastases. PFS was ongoing at 33 months (December 2025), exceeding the median of 25.3 months reported in MONALEESA-2.

Ellen's QoL improved significantly, with resolution of back pain and her return to part-time work. No new metastases emerged, and she remains on therapy without progression.

Considerations:

This case illustrates the efficacy of first-line ribociclib in extending PFS while preserving QoL, particularly in bone-dominant disease. Subgroup analyses from MONALEESA-2 confirm benefits across age groups and metastatic sites. Compared to chemotherapy, ribociclib offers fewer severe toxicities (e.g., less alopecia and neuropathy), making it preferable for patients without the need for urgent symptom control. Extended follow-up in the MONALEESA trials show OS benefit.

Ellen's case underscores ribociclib's role as a cornerstone first-line therapy in HR+/HER2-advanced breast cancer, balancing efficacy with tolerability. Multidisciplinary care, including supportive care and regular monitoring, is key to success. This approach delays progression and aligns with patient-centered care, minimizing the burden of more aggressive regimens. ●

PATIENT: ELLEN, 58, HAD HYPERTENSION AND NO FAMILY HISTORY OF BREAST CANCER.

“Her back pain resolved and QoL improved”



PHYSICIAN:

Adam M. Brufsky, MD, PhD

*Oncologist
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dard practice to identify actionable genomic alterations, including *PIK3CA*, *ESR1* and AKT pathway alterations, that can guide the use of targeted therapies. These alterations contribute to tumor growth and endocrine resistance, and their identification enables a more personalized treatment approach.

For patients with *PIK3CA*-mutated disease, the PI3K inhibitors alpelisib and imatinib are approved in combination with endocrine therapy following progression on prior endocrine therapy, including a CDK4/6 inhibitor. For tumors harboring *ESR1* mutations, the oral selective estrogen receptor degraders (SERDs) elacestrant and imlunestrant provide effective targeted treatment options after progression on endocrine therapy. And for tumors with AKT pathway alterations, capivasertib, an AKT inhibitor, is approved in combination with endocrine therapy following progression on prior endocrine therapy.

These biomarker-driven therapies have expanded treatment options and show the importance of routine molecular testing in metastatic HR+/HER2- breast cancer. Importantly, unlike germline or most somatic driver alterations, *ESR1* mutations are acquired during treatment as a mechanism of resistance to aromatase inhibitors. Consequently, repeat molecular testing with ctDNA at the time of disease progression is recommended to detect newly acquired *ESR1* mutations and to optimize subsequent treatment selection.

Advanced diagnostic tools

Q: How do you integrate genomic assays and molecular profiling into treatment selection and sequencing?

A: In early-stage disease, the 21-gene Oncotype DX Recurrence Score (RS) assay is performed in patients with T1-3, N0-1 breast cancer to provide prognostic information and to predict the potential benefit from adjuvant chemotherapy in reducing the risk of distant recurrence. In node-negative disease, the prospective TAILORx trial demonstrated that postmenopausal women with an RS of 0-25 derived no significant benefit from adjuvant chemotherapy, whereas those with an RS of 26-100 experienced a clear benefit.

Among premenopausal women, a modest benefit from chemotherapy was observed for those with intermediate RS values (16-25). In patients with node-positive (N1) disease, the

prospective RxPONDER trial similarly demonstrated that postmenopausal women with an RS of 0-25 did not benefit from adjuvant chemotherapy, whereas premenopausal women derived benefit regardless of RS, likely reflecting, at least in part, the effects of ovarian function suppression.

Recently, based on results of the OPTIMA study, the Prosigna assay can be utilized to help decision making regarding the benefit of chemotherapy in tumors that are 3.0 cm or larger or that have up to 9 positive nodes.

Another clinically useful genomic assay in early-stage HR+/HER2- breast cancer is the Breast Cancer Index (BCI), an 11-gene assay that provides both prognostic information regarding the risk of late recurrence and predictive information regarding the likelihood of benefit from extended adjuvant endocrine therapy beyond five years. In the metastatic setting, comprehensive molecular profiling of tumor tissue and/or circulating tumor DNA (ctDNA) has become stan-

Q

A

Insights on managing HR+/HER2- breast cancer

Treatment considerations

Q: How do you monitor for disease progression and treatment toxicity?

A: Monitoring for disease progression and treatment-related toxicity in patients with breast cancer requires an individualized approach that integrates clinical assessment, laboratory testing and imaging while minimizing unnecessary testing, patient burden and anxiety. The cornerstone of surveillance is a thorough history and physical examination. Changes in symptoms often provide the earliest indication of disease progression and should guide the need for additional diagnostic evaluation. For example, new or worsening bone pain may suggest osseous metastases; headaches, visual disturbances, dizziness or seizures may raise concern for central nervous system involvement; cough, dyspnea or chest pain may indicate pulmonary metastases; and abdominal pain, bloating, early satiety or changes in bowel habits may be suggestive of hepatic or peritoneal disease. The emergence of new symptoms or a significant change in existing symptoms should prompt further evaluation.

Laboratory assessment plays an important role in monitoring for disease progression. New elevations in liver function tests may indicate hepatic involvement, while worsening cytopenias may reflect bone marrow infiltration, treatment-related

toxicity or other underlying pathology requiring further investigation. Imaging remains the gold standard for assessing treatment response and disease progression in the mBC setting.

Routine clinical assessment is equally important for identifying treatment-related toxicities and facilitating early intervention. Common adverse effects include fatigue, alopecia, nail changes, arthralgias, bone pain, peripheral neuropathy, stomatitis, nausea and diarrhea. Serial laboratory monitoring is also essential for detecting hematologic abnormalities and organ dysfunction associated with systemic therapies.

Importantly, surveillance strategies should balance the need for timely detection of disease progression and treatment toxicity with the goal of minimizing unnecessary testing and scan-related anxiety. Rather than performing routine imaging at fixed intervals for all patients, surveillance should be individualized based on tumor biology, treatment response, disease trajectory and the patient's symptoms and preferences, thereby promoting high-value, patient-centered care.

Individualizing treatment

Q: When would a patient switch from endocrine therapy to chemotherapy?

A: For HR+/HER2- mBC, endocrine therapy remains the preferred treatment for

most patients because of its efficacy, favorable toxicity profile and ability to preserve QoL. The transition from endocrine-based therapy to chemotherapy is generally reserved for patients with endocrine-refractory disease, those who have exhausted available endocrine and biomarker-directed treatment options or those with rapidly progressive disease for whom a timely response is needed. Chemotherapy is also indicated in the setting of visceral crisis, where the primary goal is achieving rapid disease control.

Selection of a chemotherapy regimen should be individualized based on several clinical factors. Prior systemic therapy, including agents used, toxicities and duration of response to previous treatment, is an important consideration. Patient-related factors are equally important. Performance status, age, comorbidities, pre-existing toxicities, organ function and patient goals all influence the choice. Patient preferences matter, too, such as oral versus intravenous therapy, treatment frequency, anticipated adverse effect profiles and impact on QoL. Ultimately, treatment decisions should balance disease control with preservation of QoL, ensuring that therapy is aligned with each patient's clinical status, goals and preferences. ●

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Clinician Update

DECISION TOOL

Considerations for CDK4/6 inhibitor therapy

While CDK4/6 inhibitors combined with endocrine therapy have transformed outcomes for many patients with HR+/HER2- breast cancer, selecting the most appropriate option extends beyond guideline recommendations. Disease characteristics, toxicity profile, comorbidities and patient preferences all play an important role. To support shared decision-making, keep in mind the following considerations.

FACTORS TO CONSIDER WHEN INDIVIDUALIZING THERAPY:

Patient-specific factors such as:

- Age
- Menopausal status
- Presence of comorbidities, such as kidney/liver dysfunction and cardiovascular or gastrointestinal disorders

For early-stage breast cancer:

- Number of involved lymph nodes and tumor grade and size
- Pregnancy/family planning and work schedule

For metastatic breast cancer:

- Metastatic site(s)
- Frailty

Treatment-related factors such as:

- Response to prior therapies (if applicable)
- Tolerability of common SEs such as nausea, diarrhea, fatigue and neutropenia
- Ease of dosing and dose reduction
- Cost, scheduling and access to treatment



Source: National Cancer Institute at the National Institutes of Health ([cancer.gov](https://www.cancer.gov)).