

ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

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A Patient's Perspective on Long-Term Toxicities Associated With Cancer Treatment



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H&O What are the challenges in measuring long-term toxicities among patients with cancer?

PS Many toxicities occur throughout cancer care and cancer treatment. During active treatment, there are many possible short-lived toxicities, like nausea, vomiting, and hair loss. Long-term toxicities may arise during the treatment course, but can last for a long time afterward or arise many years later. Long-term toxicities are likely more common than expected because they are not typically measured. More research is needed to determine the prevalence of long-term toxicities. Once a patient ends active treatment, he or she visits the doctor less often. The patient may transition from treatment with an oncologist to a primary care physician, who may not recognize the connection between current ailments and previous cancer treatment.

Patients often wonder when life will get back to normal. It is important to measure long-term toxicities in order to inform patients of what to expect and how long it may be before they feel like they did before treatment. For example, there may be a side effect that persists beyond active treatment but will eventually resolve after 2 years. It is helpful for patients to be aware of this possibility, as well as the management options, particularly if the side effect could significantly impact their daily living.

H&O What are some examples of long-term toxicities?

PS There are many different kinds of long-term toxicities. They differ according to the type of cancer and even

the subtype of cancer, as well as the disease stage and type of treatment. As an example, I became a survivor of breast cancer at the age of 40. The treatment put me into menopause; I went from completely premenopausal to completely postmenopausal in 4 months. There were short-term and long-term effects. Issues with bone health run in my family, but mine started when I was 40 years old rather than 60 years old. I also developed hypothyroidism at age 40 rather than age 60. Hormonal therapies can also have a profound impact on the entire body in both women and men. Hormonal therapies are associated with many different types of side effects. Patients are now receiving hormonal therapy for 5 to 10 years, whereas in the past they were commonly treated for 2 to 5 years, so they are dealing with side effects for a longer period. More research is needed to assess the association between hormonal therapies and side effects like hot flashes, bone pain, and joint pain.

Peripheral neuropathy is another long-term toxicity that can be associated with certain cancer treatments used in breast cancer and other cancers. Patients can have different experiences with peripheral neuropathy; it is not known how it will manifest in each case. In some cases, it improves after treatment ends. In other cases, it can persist for years or even indefinitely. Peripheral neuropathy is not just tingling in the toes and fingers. It is numbing, and it can affect fine motor skills. Persistent peripheral neuropathy can be debilitating, particularly in a patient whose career depends on fine motor skills. It can also disrupt sleep. I have heard patients ask, "How do I get to sleep with my feet on fire?" It is necessary to better capture the impact of these types of events.

There are other severe effects that can arise long after treatment. For example, lung disease has been associated with radiation, and heart disease has been linked to certain cancer treatments. Several of my friends have developed esophageal cancer, acute myeloid leukemia, and endometrial cancer even 20 years after treatment for an earlier cancer.

There are also psychosocial needs that must be addressed. Anxiety, depression, fear of recurrence, and body image issues can remain with the patient for a long time after treatment ends.

H&O Should the possibility of long-term toxicities help guide treatment selection?

PS When discussing treatment options, physicians should inform patients of a drug's possible side effects. In some cases, a patient might prefer certain treatments based on their toxicity profiles. For example, an athlete might choose to avoid a treatment with lung-related side effects. I know a potter who experienced difficulty with antihormonal therapy because of associated bone pain. A patient's lifestyle will dictate which particular adverse events are particularly troublesome. It is essential to know the patient's priorities regarding treatment-related toxicities.

H&O What are some ways to improve the management of long-term toxicities?

PS When a patient receives a cancer diagnosis and begins treatment, he or she does not know what to expect. The patient might not know whether to report a particular ailment. It may not be possible for a physician to foresee all of the possible adverse events that might develop. Therefore, it is important for the physician to initiate an open-ended conversation, during which the patient can talk about any health-related changes since treatment began. It is important for the physician to understand how a side effect is impacting a patient's daily life. For example, a patient may report sleep disturbances. Further questioning might reveal that the cause is peripheral neuropathy.

There is no consistent process to identify treatment-related long-term adverse events. Patient questionnaires can be used to assess toxicity during treatment, when many adverse events occur. It would be helpful to administer patient questionnaires even after completion of the treatment course. They could be tailored for use in the post-treatment space. A questionnaire allows the patient's voice to be heard.

There should be a system in place for patients to report toxicities. Patients vary in their feelings of empowerment, and it should not be their responsibility to initiate a conversation about what they are experiencing.

There also needs to be a continuation of care that incorporates supportive self-management after active treatment ends. It is not enough to just provide instructions to patients. The support can consist of regular monitoring or other interventions. The physician cannot see patients forever, so there should be some way to support them after treatment has ended.

Patients should be aware that there are services available to them. Regular exercise and a healthy diet are common recommendations, but often there is no one to help patients implement these changes. With a continuum of care, it would be easier to gather information on how patients are feeling and which long-term effects might be associated with certain treatments.

It is important for the physician to understand how a side effect is impacting a patient's daily life.

H&O How can clinical trials more effectively assess long-term toxicities?

PS There is a survey for patients to report their symptoms—the Patient-Reported Outcomes, Common Terminology Criteria for Adverse Events (PRO-CTCAE)—which is used to assess toxicity during treatment. With the PRO-CTCAE, the patient can provide information regarding the severity, frequency, and impact of adverse events. However, the PRO-CTCAE is not usually used to assess long-term toxicities. Assessment of long-term toxicities would benefit from a unique set of questions. A questionnaire could begin with a broad question like, “Do you have anything to report, yes/no?” If the answer is yes, the next question could be, “Do you want to go through these questions, yes/no?” The next questions could be tailored toward long-term toxicities rather than short-term toxicities, in order to identify what really matters to patients.

H&O How can patient-reported outcome (PRO) measures improve drug development?

PS I strongly support the use of PROs in drug development. After drugs are approved by the US Food and Drug

Administration (FDA) and move into use in the general population, sometimes there is a lack of information regarding how patients felt and functioned during treatment. This information can be important to patients who might receive the drug. PROs are a component of many clinical trials now, but it is not clear how the information is used. It is important to bring this information back to physicians and patients so that it can help guide treatment selection.

The FDA is trying to inform patients about the applications of PROs. More can be done to help patients understand the relevance of PROs. Communication that allows patients to understand long-term side effects is important. The difficulties inherent in this type of communication are exemplified by our experience during the COVID-19 pandemic. Statements by scientists can be misinterpreted. It can be challenging to provide clear, nuanced information to the public.

Patient questionnaires and PRO measurements should be used early in the drug development process. These assessments tend to be relegated to phase 3 clinical trials. However, waiting until phase 3 means that some important questions might be omitted because information was not gathered during earlier evaluation. Targeted questions in smaller, phase 1/2 trials would allow more precise, meaningful measurements of PROs in phase 3 trials.

H&O Are there other ways that the drug development process can better accommodate the patient's needs?

PS Including patients in all aspects of drug development is key. I am a patient advocate for several clinical trial groups, including the Alliance for Clinical Trials in Oncology at the National Cancer Institute's National Clinical Trials Network. It is essential to obtain patient

input early in the development of a new drug. PROs and other endpoints should measure what matters to patients.

Clinical trials are becoming more complicated and increasingly more burdensome for patients. When designing a clinical trial, investigators should ensure that everything they ask the patient to do is necessary and streamlined. For example, it may be possible to combine all the blood draws into one visit. Is it absolutely essential for the patient to visit the clinic to provide another urine sample? There are ways to make the process more patient-centered across the entire continuum of clinical trials and drug development.

Unfortunately, in many cases, patients are consulted after the trial design has already been established, perhaps to provide insight into why accrual is low. At this point, it may be too late to fix any problems. Patients, particularly those with the disease being studied, can provide valuable information to improve trial design.

Disclosure

Ms Spears participates in advisory committees at Pfizer.

Suggested Readings

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