Malnutrition ‘almost epidemic’ among patients with advanced cancer

Malnutrition is one of the most common — and most serious — side effects of cancer and its treatment. The condition affects up to 80% of patients depending on tumor type and stage, according to NCI, and is responsible for nearly one in five cancer-related deaths.

“Malnutrition is very widespread — almost epidemic,” David Jennings II, MSN, RN, AGPCNP-BC, oncology nurse practitioner at Levine Cancer Institute at Carolinas HealthCare System and a HemOnc Today Editorial Board member, told HemOnc Today. “Almost everyone I see is either malnourished or at very high risk for being malnourished. We in the oncology community should be more proactive in identifying and managing at-risk patients.”

Despite its prevalence, malnutrition remains one of the least researched and most undertreated cancer-related adverse events.

“As little as a 5% drop in weight can predict shorter survival. When physicians ask dieticians to intervene on behalf of patients with severe weight loss — used as a diagnostic criterion for malnutrition — often little can be done to reverse the condition’s course. “Nutritionists and oncologists need to be locked in the same room and collaborate to provide a treatment plan that will benefit patients who have very high risk for poor cancer outcomes because they are malnourished,” Vickie Baracos, PhD, professor of palliative care medicine and a lead researcher in oncology and metabolism at University of Alberta in Canada, told HemOnc Today. “These providers’ fundamental approaches to dealing with someone at nutritional risk are completely different.”

HemOnc Today spoke with oncology care providers about the importance of monitoring for malnutrition ‘almost epidemic’ among patients with advanced cancer

No action is being taken until the malnutrition gets very bad. Leaving it until then is completely missing the opportunity for effective intervention. — VICKIE BARACOS, PHD

Very few patients are visibly malnourished, according to Vickie Baracos, PhD. “Although [oncologists] may recognize their patients are losing weight, they may not see that as an imminent challenge to their well-being, even though the weight-losing cancer patient has a terrible prognosis,” she said.

Failed confirmatory trial raises questions about atezolizumab for advanced urothelial cancer

The future of atezolizumab as second-line treatment for urothelial cancer is in question after results of a confirmatory trial indicated the agent failed to extend survival.

A phase 2 study showed atezolizumab (Tecentriq, Genentech) — a monoclonal antibody designed to bind with PD-L1 — improved tumor response rate and duration of response compared with chemotherapy among patients with locally advanced or metastatic urothelial carcinoma who progressed after prior chemotherapy.

Based on these data, the FDA last year granted accelerated approval to atezolizumab for use in the second-line setting. The drug became the first FDA-approved anti–PD-L1 therapy, as well as the first drug approved to treat bladder cancer since 1998.

However, Genentech last month announced the confirmatory randomized phase 3 IMvigor211 trial — designed to convert the accelerated approval to full approval — failed to meet its primary endpoint. “Will the FDA continue to grant approval to atezolizumab for this space?” Terence Friedlander, MD, assistant professor of oncology at Memorial Sloan Kettering Cancer Center, told HemOnc Today.

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BY THE NUMBERS

HPV vaccination confers high degree of protection against oral infections

- Vaccinated participants
  - 0.11%
  - 1.64%
  - 4.74%
- Unvaccinated participants
  - 3.98%  

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malnutrition in patients diagnosed with cancer, best practices for prevention, assessment and management; how patients’ nutritional needs evolve during treatment and in the survivorship phase; and the impact diet and nutrition may have on cancer outcomes.

‘Part of the cancer experience’

Depending upon tumor type, up to 80% of patients with cancer experience significant involuntary weight loss, defined as at least 10% of total body weight lost within 6 months. This often is associated with treatment interruption, infections, hospital readmission and early mortality, according to a study published in Journal of Oral and Maxillofacial Pathology.

Many oncologists overlook weight loss as an early indicator for malnutrition, which occurs when individuals do not get enough calories or consume the appropriate amount of key nutrients.

“There is a certain level of tolerance,” Declan Walsh, MD, MSc, chair of the Department of supportive oncology at Levine Cancer Institute, told HemOnc Today. “Clinicians will say, ‘Well, of course you’re not eating properly, you have cancer.’ In other words, it is just accepted as being part of the cancer experience.”

Patients’ weight at diagnosis also may lead clinicians to overlook malnutrition, Walsh said. NIH data show 60% of American adults are overweight or obese. “Because of the obesity epidemic, somebody could present to a physician having lost 15% of their pre-diagnosis body weight and are at serious nutritional risk,” Walsh said. “But they look OK, because they were so overweight before they got cancer and they do not have the traditional cachectic appearance.”

Monitoring involuntary weight loss in combination with BMI has been standard to determine malnutrition among patients with cancer. Clinicians also should monitor patients’ muscle mass to detect sarcopenia — or low muscle mass — and cancer-related malnutrition.

“If you stand at the front door of a cancer center anywhere in North America — even in an advanced-disease, metastatic setting — you’d be hard-pressed to find even 1% or 2% of patients who are visibly malnourished,” Baracos said. “This lends itself to the conclusion by most oncologists that they have other things more important to worry about. Although they may recognize their patients are losing weight, they may not see that as being an imminent challenge to their well-being, even though the weight-losing cancer patient has a terrible prognosis.”

Weight loss and BMI can independently predict cancer survival.

A study by Martin and colleagues — published in 2015 in Journal of Clinical Oncology — showed that weight-stable patients with a BMI at or above 28 survived nearly five times longer (20.5 months; 95% CI, 17.9-23.9) than those who lost 15% or more of their body weight and received a BMI of 22 or less (4.3 months; 95% CI, 4.1-4.6).

“That paper showed that — regardless of whether your starting body weight is large, medium or small — weight loss is still highly associated with mortality,” Baracos said.

This issue is “the elephant in the room in cancer care,” Walsh said.

“We know that being cachectic leads to worse outcomes from surgery, more side effects from chemotherapy or radiation therapy, and a serious impairment in life expectancy,” he said. “Lack of attention to this is a significant issue.”

Several factors contribute to weight loss among patients with cancer. These include tumor location, surgery, chemotherapy, radiation and stress. Treatment side effects — such as nausea, vomiting, diarrhoea, anorexia, mouth sores, difficulty swallowing, taste changes and poor appetite — also play a role.

“Malnourished patients are often unable to withstand the rigorous and aggressive treatments that best treat the cancer, and that may mean they have to reduce doses or take breaks from treatment,” Rachael Lopez, MPH, RD, clinical research dietitian for surgical oncology and cancer immunotherapy at the NIH Clinical Center, told HemOnc Today. “This ultimately leads to a suboptimal treatment plan, which translates to poor cancer outcomes.”

Patients with head and neck cancers who undergo surgery around their esophagus, mouth or nasal cavity can have difficulty eating and swallowing. Those with solid tumors who require radiation can experience painful symptoms such as mucositis and esophagitis.

“Radiation therapy can destroy taste buds and salivary glands, which changes the pH of your mouth,” Jennings said. “Patients with lung cancer who undergo radiation are at similar risk. Depending on the size and location of the radiation field, their gastrointestinal health can be at risk, and pain and reflux symptoms can occur. These are all factors that discourage patients from eating.”

Chemotherapeutic agents such as carboplatin and cisplatin are platinum based, often producing a metallic taste in a patient’s mouth. For that reason, Jennings said he encourages those patients not to eat with metal forks and spoons.

Improved monitoring

Adults routinely lose muscle at a rate of 0.3% per year as part of the normal aging process. However, patients with cancer may lose 3.3% of muscle each year.

Sarcopenia can occur 10 to 25 times faster among patients who receive chemotherapy or radiation, Baracos said. Patients who require bone marrow transplant plants can experience even greater losses of muscle mass.

“It’s like aging 10 years in 1,” Baracos said. “One of the big issues is that no action is being taken until the malnutrition gets very bad. Leaving it until then is completely missing the opportunity for effective intervention.”

Despite the consequences of late action, muscle loss and other effects of malnutrition often go unaddressed.

“Oftentimes when people are referred to a dietician, it is already late in the game,” Walsh said. “By the time malnutrition is obvious, it may already be too late to do something about it.”

Low-fiber dietary guidelines for patients with cancer undergoing surgery, or who have diarrhea, cramping or trouble digesting food

EAT

DO NOT EAT

PROTEIN

All beans, nuts, peas, legumes and legumes, processed meats, hard, cheese, custard or pudding, and tough meats with gristle

Milk, chocolate milk, buttermilk and milk drinks, yogurt without seeds or granules, sour cream, cheese and cottage cheese, custard or pudding, ice cream and frozen desserts, and cream sauces, soups and casseroles

DAIRY

Ice cream with nuts, and more than a small amount of dairy

All raw or dried fruits; and prune juice, all beans; potatoes with skin; all beans; peas, corn, cabbage, broccoli, all beans; potatoes with skin; all beans; peas, corn, cabbage, broccoli, cauliflower, broccoli sprouts and greeen, and served with lean meats and vegetables

CEREALS & GRAINS

Brown or wild rice; whole grains, tender cuts of meat and ground meat; tender, well-cut fresh or canned vegetables without seeds, stems or skins; tender, well-cut fresh or canned vegetables without seeds, stems or skins; tender or canned fruit without seeds or skin; small amounts of well-cooked beans, steamed or clear peas, and small amounts of soft cereals or bran muffins

White bread, pastries, French toast, plain white rolls and white bread, toast, proteins, crackers and matzoh, plant-based white rice, and cereals without whole grains, added fiber, seeds, sauces or others, white bread toast; white bread toast; white bread toast; white bread toast; white bread toast

VEGETABLES

Soft, steamed or canned fruit without seeds or skin; small amounts of well-cooked beans, steamed or clear peas, and small amounts of soft cereals or bran muffins

VEGETABLES

Fruits

All raw or dried fruits; berries, and prune juice, peas, and raisins

However, measuring muscle loss can be one piece of the puzzle in identifying risk for malnutrition early on. Before 2007, clinicians often determined malnutrition by a patient’s weight in relation to his or her height. Over the past decade, cancer centers have identified additional markers, such as caloric intake, body fat, muscle mass, fluid accumulation and grip strength.

At NIH, it is standard for a registered dietician to screen each inpatient for nutrition risk and to follow-up with a nutrition assessment and plan for each patient found to be at risk. In outpatient centers, tools such as the Nutrition Risk Screening 2002 (NRS 2002) survey, a validated five-question survey, can be used at diagnosis and during each outpatient visit to assess for nutrition risk.

“NRS 2002 is one screening tool to catch people before they’ve lost 20% of their body weight, or before they’ve lost so much lean body mass that they are unable to perform their activities of daily living,” Lopez said. Clinicians at Levine Cancer Institute assess patients with a validated malnutrition screening tool. “The electronic survey alerts the nutrition department if a patient is at risk. “It puts the patient on the nutritionists’ radar,” Jennings said. “They can contact the physician and be proactive about it instead of waiting until malnutrition becomes problematic during treatment.”

Many cancer centers have adopted the use of CT to measure muscle loss in patients with cancer.

“All you’re really doing is putting body weight under a different lens and quantifying the muscle and fat tissues,” Baracos said. “It is a paradigm change. [Previous-]ly, all we ever asked was how much patients weighed and how tall they were. Using diagnostic imaging to reveal the exact composition of a person’s body is regarded as a gold standard.”

Toxicity vs. nutrition
Metabolic changes also may drive cancer-associated malnutrition, meaning it can only be partially reversed by conventional nutritional support. Negative energy balance and skeletal muscle loss due to metabolic derangements — such as insulin resistance and systemic inflammation — can lead to malnutrition, according to European Society for Parenteral and Enteral Nutrition guidelines issued last year.

The biggest source of debate is that there is well-documented evidence that if patients are malnourished during their treatment, their treatment is less effective. Losing too much muscle can only be partially reversed by conventional nutrition support, which limits the ability to “beat” cancer. There is some implication that the immune system also is compromised due to malnutrition, which further adds to the reason to continue to swallow during treatment.

However, caring for patients who have such bad metabolic dysfunction,” Collins Champ, MD, radiation oncologist at UPMC—Cancer Center and co-author of several studies on malnutrition in patients with cancer, told HemOnc Today. “Those are the cases that are extremely difficult and, frankly, we have no solution.”

“Having those patients eat more and more calories does not work because they have such bad metabolic dysfunction,” Collins Champ, MD, radiation oncologist at UPMC—Cancer Center and co-author of several studies on malnutrition in patients with cancer, told HemOnc Today. “Those are the cases that are extremely difficult and, frankly, we have no solution.”

Oncologists and nutritionists often debate the toxicity of treatments and their impact on patients already at risk for malnutrition. Chemotherapy dosing is frequently based on overall body weight, not lean tissue. Although researchers in France are comparing dosing in patients with varying body compositions, there are many unknowns.

“Theoretically, if the amount of che...Cover Story continues on page 16

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POINT / COUNTER

Do the benefits of a feeding tube outweigh the risks for a malnourished patient with cancer treated with curative intent?

POINT

Nutrition intervention should be considered a critical supportive measure in the overall oncology strategy.

Malnutrition — suspected to occur in 40% to 80% of patients with cancer — can negatively affect response to treatment; increase treatment-related toxicity; interrupt treatment plan schedules; extend hospital stays; impair muscle function; and decrease performance status, immune function, quality of life and OS.

Patients’ physiological response to the cancer and the effects of treatment can lead to malnutrition. Other circumstances include reduced food intake, altered in normal absorption and utilization of nutrients, and increased metabolic needs. Cancers — particularly those involving the alimentary canal — may place stress on the body due to impaired organ function, increased nutrient losses, and treatment-related toxicities that impact nutritional status.

There are no definitive guidelines for starting nutrition support; however, the decision to use enteral nutrition support (ENS) is relatively simple for a malnourished patient who is undergoing treatment for curative disease but unable to meet nutrition needs orally for 7 or more days.

Consistent with National Comprehensive Cancer Network Guidelines, clinicians should consider nutrition support for a patient with life expectancy of months or years. Guidelines and recommendations from the European Society for Parenteral and Enteral Nutrition, Academy of Nutrition and Dietetics, American Society of Parenteral and Enteral Nutrition, and the Dietitians of Australia also recommend initiation of nutrition intervention for malnourished patients or those expected to experience difficulties with eating.

Methods of nutrition support depend on the presence or absence of a functioning gut, treatment plans, nutritional deficits, quality of life and prognosis. If a patient is unable to meet nutritional needs through oral intake and the gut is functional, clinicians should consider a gastrostomy or jejunostomy tube. For short-term support of 3 weeks or less, clinicians can place a nasogastric, -duodenal or -jejunal tube after consideration of patient discomfort, possible mucosal erosion and concern for the tube in the treatment field. Also, patients with esophageal cancer who receive neoadjuvant treatment and need nutrition support may require placement of a nasogastric feeding tube to prevent disruption or compromise of the future surgical site.

Barriers may include lack of expertise in ENS management, patient dissatisfaction, cancer for long-term tube feeding dependency and swallowing dysfunction after treatment. Enlisting the services of an interprofessional team that includes a registered dietitian nutritionist and speech language pathologist can help overcome management challenges and improve nutritional outcomes.

ENS is not only a viable option for management of malnutrition in patients being treated for curable cancer; it can significantly benefit aspects of quality of life during a difficult process.

COUNTER

Feeding tubes can lead to poor quality of life, especially for patients with head and neck cancer.

Feeding tubes play a critical role in maintaining positive nitrogen balance during cancer therapy. Most oncologists agree that placing them to optimize nutrition is a critical step in successful cancer therapy. However, placement of a percutaneous endoscopic gastrostomy (PEG) tube is a surgical procedure and, as such, carries inherent risk.

Feeding tubes can play a critical role in maintaining positive nitrogen balance during cancer therapy. Most oncologists agree that placing them to optimize nutrition is a critical step in successful cancer therapy. However, placement of a percutaneous endoscopic gastrostomy (PEG) tube is a surgical procedure and, as such, carries inherent risk. A large meta-analysis showed a procedure-related morbidity of 9.4% and mortality of 0.53%. Most series report morbidity rates ranging from 9% to 17%, although major complications occur in only 1% to 3% of cases.

When weighing the benefits and risks of enteral nutrition support is crucial for patients with head and neck cancer, because the treatments we administer — particularly the combinations of chemotherapy and radiation therapy — result in significant mucositis and swallowing-related difficulties. It has been a debate in our field for many years as to how beneficial it is to give patients a feeding tube to maintain their weight compared with encouraging them to continue to swallow during treatment.

There has been literature supporting both sides of the argument. However, we have learned that — in head and neck cancer in particular, and possibly in other malignancies — the continued exercise of the pharyngeal musculature and tongue musculature during therapy results in better swallowing outcomes after treatment. High doses of radiation therapy to the head and neck damage the muscles of the throat and weaken a patient’s ability to recover. We have taken the approach of having a feeding tube there as a safety valve, but doing very aggressive speech and swallowing therapy during treatment and after treatment to maintain optimal swallowing after therapy.

The biggest source of debate is that there is well-documented evidence that if patients are malnourished during their treatment, their treatment is less effective. Losing too much weight during therapy may affect a patient’s ability to recover from treatment. There is some implication that the immune system also is compromised due to malnutrition, which limits the ability to “beat” cancer. There is overwhelming evidence that malnutrition is correlated with poorer cancer outcomes. The balancing act is maintaining a patient’s weight while still dealing with the significant side effects from the tumor, which are long-lasting and can negatively affect quality of life.

In head and neck cancer, quality of life surveys after treatment show the number one predictor of a poor quality of life is a feeding tube — even more than a tracheotomy and more than fear of cancer coming back. It is not a small deal to have a feeding tube long term, so we try to make sure the patient is nourished, while also ensuring they will be able to swallow well after treatment is complete so they have optimal quality of life.

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"It’s the most common question patients ask: ‘What should I eat?’ We should have an answer, but it is an epidemiologic minefield.”

— COLIN CHAMP, MD

“ That might be medical management to improve appetite, control symptoms, or add nutritional supplements like fortified drinks that provide nutrition when people are unable to eat regular meals or tolerate solid foods,” Lopez said.

Patients who undergo stem cell transplants who are at risk for graft-versus-host disease, or those with gastric or esophageal cancer, sometimes require additional interventions.

Nutritionists may recommend enteral feeding tubes — which deliver nutrition through a tube into the gut — or parenteral feedings through IVs, Lopez said. These help prevent dose reductions and breaks from treatment.

Weighing the risks and rewards of enteral and parenteral feedings is a source of ongoing debate, Jennings said. “We should have an answer, but it is an epidemiologic minefield.”

“ In our head and neck cancer population, the utilization of feeding tubes is somewhat controversial,” Jennings said.

“ Is it worth putting the patient at risk of complications and infection with an additional surgery? Some patients easily tolerate 7 weeks of radiation therapy with concurrent chemotherapy and never use a feeding tube, and others rely heavily on it.”

It is important for clinicians to understand that patients with cancer may continue to lose weight despite the fact they have a good diet or are on nutritional support, Walsh said.

Individualized diets

Dietary recommendations and studies often provide inconsistent and conflict- ing guidance about how to stay nourished during cancer treatments and into survivorship.

“It’s the most common question patients ask: ‘What should I eat?’” Champ said.

“We should have an answer, but it is an epidemiologic minefield. The recommendations are all over the place.”

Champ and colleagues surveyed 21 National Comprehensive Cancer Network institutions. The results — published in 2013 in Nutrition and Cancer — showed only four of them provided dietary rec- ommendations for patients with cancer on their websites. Of those four, two recom- mended diets that contained food rich in carbohydrates, protein, and fat, and two recommended diets that primarily con- sisted of carbohydrate-rich foods.

“There is so much misinformation out there,” Lopez said. “ A simple internet search of ‘diet and cancer’ will bring you pages and pages of fed diets that claim to cure cancer or diets recommending expensive supplements that have not been tested. For people searching for their cure [who] want to do everything they possibly can, it is really heartbreakingly to see them spend their money on these unsearched supplements or to follow these very restrictive diets that end up making them malnourished.”

Some patients are “weeefully malnour- ished” because they refuse to eat foods with carbohydrates, Lopez said.

“We have had patients unable to go through treatments because they are on so many supplements it is interfering with their liver function and it is not safe to start chemotherapy,” she added. “They are actually setting themselves back.”

A Women’s Intervention Nutrition Study showed an association between low-fat diet and reduced recurrence among certain women with breast cancer. Long-term follow-up from that trial presented in 2014 at an Antonio Breast Cancer Symposium — showed median survival was 11.7 years in the control arm, 13.6 years among women with ER-nega- tive disease who received the dietary in- tervention (HR = 0.64, P = .045) and 14 years among women with ER/PR-nega- tive tumors who received the intervention (HR = 0.40, P = .006).

However, low-fat, “cardiac prudent” diets may not be best for all patients with cancer, Champ said.

“A diet that includes healthy fats is pro- ductive for everyone,” Champ said. “A lot of calorically dense foods that are tradition- ally sourced are nutrient-dense with min- erais and vitamins, things cancer patients need.”

Champ encourages his patients to eat healthy sources of fats like eggs from free- range chickens from local farms.

“We know eggs from those chickens have higher amounts of nutrients and vi- tamins,” he said. “I don’t tell them to not eat meat. I tell them to eat better-sourced types of meat — beef from grass-fed cows, which has higher amounts of conjugated linoleic acid and omega-3 fatty acids, which help fight breast cancer.”

American Cancer Society guidelines suggest a lower fiber diet for patients who experience diarrhea or cramping, and those who have trouble digesting food (see Table on page 14). Clinicians also may recommend this diet after certain types of cancer surgery.

Green, leafy vegetables offset toxins, can stimulate the immune system and are good for patients with cancer who are not on blood thinners, Champ said. Protein powders and medium chain triglycerides from coconut oil also are recommended to help spare muscle in patients with sar- copenia, he added.

Addressing the dietary needs of pa- tients with cancer requires an individual- ized approach, said Champ, who spends up to 90 minutes discussing food options with his patients.

“I don’t tell people to eat ‘low carb’ or ‘high carb’ or ‘low fat’ or ‘high fat,’” he said. “I go through the types of food they like and try to get them to eat the healthi- est sources of those foods. It takes quite a bit of time, and I’m not sure everyone is up for that challenge.”

Stimulating appetite

The definition of healthy eating chang- es throughout a patient’s treatment course. It can be affected by their tolerance of treatments and other chronic conditions, such as high blood pressure, high choles- terol or diabetes.

“It can be very challenging to have two-thirds of your plate filled with fruits, vegetables, whole grains and lean proteins if you are having profuse diarrhea and should be limiting those types of foods because of treatments,” Lopez said.

Patients whose appetite is suppressed because of chemotherapy or radiation may benefit from megestrol acetate or dronabinol (Marinol, AbbottVie), as well as corticosteroids such as dexamethasone or prednisone, or antidepresants such as mirtazapine (Remeron, Organon USA). However, megestrol acetate can increase the risk for blood clots or strokes, and dronabinol can increase fatigue.

“Our patients are often experi- encing treatment-related fatigue, we might not want to add a medication that would compound that problem,” Jennings said.

Simply increasing a patient’s appetite does not necessarily translate to better nu- tritional status, Walsh said.

“Earily satiety is a very unrecognized symptom, where somebody is hungry and they have a spoonful or two of food and they think they are full and cannot eat anymore,” Walsh said. “If that is the case, maybe they are off eating six meals a day instead of three.”

Other, more practical strategies can enhance a patient’s appetite during treat- ment, Lopez said. She suggested patients avoid their favorite foods when their taste buds are compromised.

“When people lose their love for their favorite food because it tastes like card- board, it can be very depressing,” Lopez said. “Occasionally a patient will say ‘ They are able to tolerate food without nausea and taste changes, I en- courage patients who can leave their hospi- tal beds to sit down at a table and that’s nicely set for a home-cooked meal with loved ones.”

Oncologists, nutritionists and dieticians agree on the need for earlier intervention by nutritionists, as well as the need for in- increased research funding to study the nu- tritional needs of patients with cancer.

“We know that patients who have bet- ter nutrition tolerate chemotherapy more easily, which leads to improved outcomes,” Jennings said. “That’s why we frequently collaborate with our dietitians and nutritio- nists. The first remedy for malnutrition is prevention, and it is too great a task to tackle on our own. It takes a multidiscipli- nary approach.”

Baracos is on a research team studying more than 17,000 cases from 17 cancer centers to produce definitive criteria for diagnosing malnutrition in patients with cancer.

More research is needed in that area, as well as more comprehensive dietary rec- ommendations for patients with specific cancers, Champ said.

“There are no good randomized stud- ies and there absolutely should be,” Champ said. “We should know more about how diet impacts survival. We do not have the answers, but if we are not pushing re- search in that direction, how are we sup- posed to get closer to providing answers?”

If we want to give doctors the right things to say to patients, we have to come up with those answers,”— by Chud Giltman

See references online at Healio.com/HemOnc.