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Senior Adult Oncology: Three Cases of Advanced Cancer in Patients of Advanced Age

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INTRODUCTION

The American Cancer Society reports that more than 60% of all cancers and 80% of cancer-related deaths in the United States occur in patients older than age 65 (1,2). Epidemiologic data show that the likelihood of developing certain cancers in older age is higher than in younger individuals, and intuitively, this stands to reason, due to physiologic factors, time for the expression and development of genetically-related cancers, and a longer range of environmental exposures. However, many cancers may be more difficult to treat in older individuals due to higher incidence of medical co-morbidities, as well as the biology of certain tumors themselves. Heterogeneous behaviors of several cancers manifest as unique situations in elderly patients across a broad spectrum, including on average, more indolent estrogen-receptor-positive breast cancers, as well as more drug-resistant acute leukemias which may arise on a background of a long history of myelodysplasia. In addition, optimum dosing and prediction of treatment toxicity remains a difficult question, as older cancer patients are not well represented in clinical trials, for which often the inclusion criteria list a maximum age of 70. Furthermore, many cancers such as hematologic malignancies, may not be able to be treated with maximum aggressiveness such as high-dose chemotherapy followed by stem cell transplant or autologous stem cell rescue as would be tolerated by younger individuals (usually under the age to 60–65). In our quest as physicians to “first do no harm” (3,4), we wrestle with our best recommendations for our elderly patients, often in the face of frail physicality and potential for increased risk of infection and iatrogenically-induced side effects and morbidity.

We present here 3 cases of advanced cancers in patients of advanced chronologic age, who also exhibit multiple medical co-morbidities. Their situations likely warrant specifically tailored treatment given their age, which would be markedly different if they presented in earlier decades of life. We pose the following clinical questions: (a) What treatments would you offer/feel comfortable offering these patients? (b) What factors are important in arriving at these decisions between and among the physician, patients, and families? (c) What

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modifications would you make to standard treatments if indicated for these particular patients?

CASE REPORTS

Case One: Metastatic Colorectal Cancer in 78-year-old with History of Stroke and Mild Dementia

The patient is a 78-year-old female with history of hypertension, stroke requiring anticoagulation 20 years ago, mild chronic obstructive pulmonary disease (COPD) with 50-pack-year smoking history, and rheumatoid arthritis, who was in her usual state of health when she noticed vague gastrointestinal symptoms, including bloating, dyspepsia, occasional episodes of nausea and vomiting, abdominal discomfort, and 20 pound weight loss over one month. Lab work showed a white count 8.49, hemoglobin 14.4, hematocrit 47.4, MCV 77.2, platelets 294, with PT slightly elevated at 12 seconds, INR 1.1, alkaline phosphatase 164 units per liter (reference range 30–126) and AST 42 units per liter with (reference range 14–36), with normal bilirubin. A CAT scan of the abdomen revealed a large mass lesion in the right lobe of the liver measuring 4.8×10.1 cm and irregularity of the wall of the transverse colon (Figure One). Alpha-fetoprotein (AFP) level was normal at 3.5 (reference range 1.6–4.5 ng per milliliter), but carcinoembryonic antigen (CEA) level was high at 135.0 ng per milliliter (with reference range 0.0–2.9). She had never had a colonoscopy prior to this, and upon undergoing the procedure, had an incomplete study secondary to cardiorespiratory difficulties; only sigmoid diverticular disease was detected. A CT-guided liver biopsy was then arranged, with fine needle aspiration showing malignant cells, consistent with adenocarcinoma, and a core biopsy further determined this as moderately differentiated adenocarcinoma with focally abundant mucin production, favoring metastasis of an adenocarcinoma such as a primary colon carcinoma. Preliminary panel of immunohistochemical stains showed no staining for cytokeratin (CK) 7, positive staining for CK 20, negative for TTF-1 and CA 125, and positive for CDX2, favoring metastatic colorectal carcinoma.

On examination, the patient is escorted by her son, who helps her ambulate with her cane. During the interview, the patient defers all questions and decision to her son. He reports he takes care of her medications as she has had short-term memory loss worsening over the last 3 years.

Case Two: Acute Myeloid Leukemia in a 74-year-old with DM and CHF

The patient is a 75-year-old female with history of type 2 diabetes, hypertension, and congestive heart failure requiring intermittent diuretics, who was evaluated by an oral maxilla-facial surgeon for frequent gum infections and osteonecrosis of the jaw requiring antibiotics. In a preoperative workup for debridement of the mandible, it was found that her white blood cell count had risen from 12,000 to 26,400 over one month's time, with a decrease in her platelet count to 35,000 to 25,000 with 3 metamyelocytes seen in the differential assessment of the peripheral blood (Figure Two). Comparison blood counts from 6 months prior showed a white count of 12.1, hemoglobin 12.9, and platelets 193.

On the examination, she complains of dyspnea on exertion, associated with a dry cough; she has never smoked. She is moderately obese. She had some mild petechiae over the distal extremities. A defect was noted in the area of 2 previous molars in the left lower jaw.

A bone marrow biopsy revealed a hypercellular marrow with 95% cellularity with left-shifted myeloid maturation with 28% blasts and promonocytes, consistent with acute myeloblastic leukemia consistent with myelomonocytic (FAB-M4) differentiation with myelodysplasia-related changes, and no evidence of promyelocytic granules or changes. The cytogenetics were normal (Figure Two). PCR showed mutation in FLT3-ITD and NPM1-4bp insertion.

The next week, her complete blood count showed WBC 52.9k/uL, hemoglobin 10.3 g/dL, and platelets count 21k/uL.

Case Three: Triple-Negative Breast Cancer in 83-year-old Wheelchair-Bound Female

The patient is an 82-year-old female with a previous history of osteoarthritis, need for lumbar laminectomy, who has limited mobility, history of hypertension or hyperlipidemia, who had presented to a surgeon, with an inflammatory breast mass associated with breast pain and redness of the skin, which she had brought to the attention to her family. A mammogram was done, which showed a large mass with suspicious microcalcifications in the outer upper quadrant of the right breast with relatively dense axillary lymph nodes. The patient underwent an excisional biopsy of the right breast mass as well as the skin, showing a $6.0 \times 4.2 \times 2.5$ cm invasive ductal carcinoma of the breast grade III with DCIS 5% to 10% of the total volume, prominent lymphatic vascular invasion and invasive carcinoma focally identified at the deep margin of the excision (Figure Three). The skin excision was negative for any Paget disease or in situ or invasive breast carcinoma. The phenotype was triple negative, 0% ER, 0% PR expression, and no HER-2/neu expression. A PET scan demonstrated multiple right axillary lymph nodes, with markedly increased hypermetabolic activities, most consistent with metastatic adenopathy, with the SUV measurements 3.5 in the skin thickening and up to 16.39 in the lymph nodes. The patient underwent a right modified mastectomy which further confirmed 6.0 cm of extensive residual invasive ductal carcinoma of the breast, grade III, extensive lymphatic vascular invasion; 14 of 16 lymph nodes were positive for metastatic carcinoma (Figure Three). The patient was re-admitted twice to the hospital for cellulitis and required IV antibiotics.

On examination, the patient had mild erythema of the healing mastectomy site, and was wheelchair-bound.

SENIOR ONCOLOGIST'S AND GERIATRIC EXPERTS' OPINIONS

The evaluation and management of the geriatric oncology patient is usually quite complex. At the time of the cancer diagnosis, these patients will frequently already have developed other comorbid illnesses such as diabetes mellitus, renal insufficiency or congestive heart failure. Additionally, this patient population is at risk for the development of geriatric syndromes such as dementia, malnutrition, osteoporosis and falls. In order to treat these comorbidities, the patients will frequently be taking multiple medications, often in excess of 4

or 5. The cancer diagnosis then adds additional physical and psychological stress to the patient.

Many elders are either over or under treated when their treatment plans are based solely on their chronologic age. Issues that need to be addressed include tolerability of treatment, benefit versus risk, life expectancy, and meeting the patient's goals. Additionally, several practical issues need to be considered at the outset. Such issues include establishing the caregiver and support system so the patient can get to their appointments, appropriately adhere to their medication regimen, obtain their medications, and accurately report side effects as they arise in order to facilitate safe, high quality care.

Finally, the patient's ability to comprehend the diagnosis and the issues surrounding treatment may be compromised for various reasons. This group of patient may have difficulty with their vision or hearing. Both numeracy and literacy may limit their understanding of the data presented to them making them heavily reliant on their caregivers for support in this process. They may suffer from some degree of cognitive impairment which will limit their ability to make decisions. The following three cases of advanced cancer in patients of advanced age clearly illustrate the issues confronting the geriatric oncology patient each day.

In **Case One**, with a 78-year-old female diagnosed with metastatic colorectal cancer, the first question to be addressed is whether this patient has a curable cancer, and if so, is she able to tolerate the necessary treatment to afford her the chance for cure. The data presented indicate a solitary mass in the liver and an abnormal appearing transverse colon (likely the source of the cancer) that was not able to be visualized during the colonoscopy due to cardio-respiratory difficulties. Biopsy of the liver appears consistent with metastatic colon cancer. Her co-morbid illnesses presented include: HTN, previous CVA necessitating anticoagulation 20 years earlier, COPD with and extensive smoking history, and rheumatoid arthritis. She currently ambulates with a cane, and by report of her son has some degree of memory loss suggesting underlying dementia. She defers all questions to him, and he is solely responsible for administering her medications indicating her dependence for at least some of her Independent Activities of Daily Living (IADL's).

Based on this information, this is the ideal patient to undergo a comprehensive geriatric assessment(CGA) to better quantify the severity of her co-morbidities and to identify and address geriatric syndromes, risks related to poly-pharmacy and safety issues related to care-giving. This assessment can provide a much more in depth assessment of functional status than performance status alone. Together, this information can then be utilized to determine the patient's life expectancy and how the cancer/cancer treatment will affect this estimation.

This information gained from a CGA can then be utilized in a discussion with the patient and family to develop a treatment plan that accurately reflects the goals. The information presented in this case would suggest that this patient is potentially frail, and may be a poor candidate for surgery (should PET scan prove no other evidence of metastasis, other than the solitary hepatic metastasis). The CGA would serve to confirm these suspicions and enable a discussion regarding the risks/benefits of palliative chemotherapy. While there is clear

evidence that palliative combination chemotherapy can prolong survival when compared to best supportive care, this benefit may not be realized in a frail patient, and may have profound deleterious effects on their quality of life (5). Age alone is not an adequate criterion to determine this patient's overall fitness.

In **Case Two**, a 75-year-old female diagnosed with Acute Myelogenous Leukemia, specific issues for elders are presented, primarily due to the aggressive nature of the disease, the frequent presence of adverse covariates (antecedent hematological disease, complex karyotype, mutations in FLT3 etc.), and the intensive treatments required in attempt to cure the disease (6). Therefore, a thorough evaluation of the patient's functional status, caregiver support, and covariate analysis is needed prior to the initiation of any therapy. Standard induction chemotherapy with Idarubicin and cytarabine (Ara C) has been associated with survival of 8–12 months in this patient population (7). The survival benefit in elders using this regimen is modest at best, and is likely overestimated in clinical trials as less fit elders were screened out of the studies (8). It is for these reasons that current NCCN guidelines recommend consideration for clinical trials in patients age 60 and above who develop AML with associated poor risk factors (9).

This patient presents with co-morbidities including hypertension, diabetes mellitus, and congestive heart failure that has required diuretic therapy. The leukemia has a normal karyotype but myelodysplastic changes noted on histological evaluation would suggest the leukemia developed in the setting of a previous myelodysplastic syndrome. We would recommend further evaluation of this patient including a Comprehensive Geriatric Assessment to better characterize her functional status, in efforts to reduce risk of toxicity if treatment is pursued. We would also recommend cardiac function evaluation including echocardiogram or MUGA scan with ejection fraction assessment.

We would suspect that with her co-morbidities, she is likely a poor candidate for anthracycline based therapy. Additionally, the presence of antecedent hematological disease in the form of myelodysplasia would suggest leukemia more refractory to standard therapy. This information needs to be clearly presented to the patient and caregiver in efforts to accurately depict the risks and limited benefit of treatment with standard induction chemotherapy and to aid them in establishing realistic goals. For these reasons we would recommend clinical trial enrollment if available, or palliative chemotherapy including either 5-azacytidine or decitabine. Transfusion support, early treatment of infections, and palliative care consultation would likely offer the most benefit.

In **Case Three**, this 82-year-old female diagnosed with triple negative breast cancer presents very difficult issues. Specifically, the presence of extensive lymphovascular invasion, and greater than 10 positive lymph nodes from the mastectomy indicate an extremely high risk for recurrence. In efforts to better define her treatment options, several factors need to be considered including the patient's goals of treatment, willingness to undergo treatment with chemotherapy, life expectancy, and a thorough assessment of true functional status and extent of caregiver support. Since the benefits of hormonal therapy and trastuzumab (Herceptin, Genetech) are likely to be marginal, the only adjuvant treatments available to potentially prevent recurrence are chemotherapy and radiation. The presence of both

hypertension and hyperlipidemia raise concern about underlying cardiovascular disease that also requires further assessment before considering which chemotherapy option to recommend. As stated, she has underlying osteoarthritis and need for lumbar laminectomy, which presumably is the cause for her immobility and need for wheelchair assistance. The compromise in her mobility therefore does not appear to be on the basis of the cancer.

We would recommend Radiation Oncology evaluation for consideration of radiation therapy in efforts to improve local control with the high number of positive lymph nodes, and consideration for combination chemotherapy with prophylactic GCSF. Palliative care consultation would also be helpful to support the patient and her family regardless of what treatment option they choose (10).

Based on the information provided, all three of these patients display some degree of functional impairment suggesting they are a least vulnerable. We would therefore recommend that each of these patients undergo a comprehensive geriatric assessment that would include evaluation by a geriatrician, pharmacist, dietician, and social worker to better characterize the risks of treatment and more clearly establish the goals of therapy and available care giving support. This information will then aid the patient, family and oncologist in the decision making process in efforts to personalize the care for each patient.

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GERIATRIC ONCOLOGISTS' EXPERT OPINION

The patient presented in **Case One** is a common manifestation of colorectal cancer in an older patient. The median age of colorectal cancer is 70 years of the age(11), and we will need to treat more and more patients with advanced colorectal disease. In this particular situation, in a patient with significant comorbidities, she unfortunately has never had a screening colonoscopy. There have been a studies which show that older patients have colonoscopies at a decreased incidence (12). There is a question of benefit of colorectal cancer screening in an older patient with significant comorbidities. One could speculate that the colonoscopy was deferred because of the patient's comorbid conditions which do limit her survival. It may have been felt that the risks of the procedure outweigh the benefits, particularly in someone with cardiovascular disease who was anticoagulated. It is

conceivable, because of her dementia, her symptoms were not evaluated appropriately and the patient was finally evaluated after overwhelming symptoms of abdominal pain and weight loss. It is interesting that her hematologic profile is within normal limits and does not show overt evidence of iron deficiency anemia. It is unfortunate that the colonoscopy could not be performed to fully evaluate this patient. However, it is clear that she has metastatic disease as evidenced by the CT scan and the biopsy.

It appears there is information that we do not have available to us. We do not know the full extent of her colonic disease because she cannot undergo a colonoscopy. We also do not know other facts about the patient, for instance, her full extent of her abilities to perform activities of daily living and instrumental activities of daily living. We are given a clue because it is stated that her son takes care of her medication. She defers decisions to him; this may be a reflection of her dementia. We also do not know her living situation, whether she lives alone (which is unlikely), lives in assisted living (which is possible), or lives with her son. I would assume also that she is not having any hemorrhage as her hemoglobin is 14.4g/dL. It is possible that her abdominal symptoms may represent an impending obstruction, though we are not given this information in this case report. I would also assume that she is probably not a good surgical candidate because of the issues with the colonoscopy, and it would place her at high risk for morbidity and mortality following surgery.

In a patient in this situation, it would be preferable to get a sense of her overall functional status by performing activities of daily living, instrumental activities of daily living, and a brief Mini-Mental Status Exam to test her memory (13). Patients with inability to perform activities of daily living, or instrumental activities of daily living, would be considered frail and would be at higher risk for toxicity and inability to complete the chemotherapy regimens (14). However, because the patient is symptomatic and may have an impending obstruction in the left colon, therapy cannot be deferred. It is stated the patient had an incomplete study, but I get a sense from her gastroenterologist and the CT scan findings, that there is a question of impending obstruction. There are some data which indicate that stenting can alleviate obstruction, and may be able to palliate the patient (15). If it is felt that this is a critical issue, I would have the patient be evaluated by a cardiologist and pulmonary physicians to see if they could optimize her comorbidities and maybe undergo the procedure, particularly if she is very symptomatic.

Assuming that stenting and/or surgery is not required to alleviate obstruction, decision has to be made regarding treatment. The patient will have to undergo treatment with a fluoropyrimidine and possible combination chemotherapy. She clearly has risk factors for increased toxicity from chemotherapy, including her comorbidity and the sense that she is in a frail condition. It has been shown, however, that older patients can benefit from chemotherapy in colorectal cancer (16,17).

The options of therapy to administer a fluoropyrimidine include bolus therapy, such as the Mayo regimen; infusional therapy, such as the de Gramont infusion; or oral therapy with capecitabine. My own preference is to use infusional therapy. The bolus regimens, particularly the Mayo Regimen and the Roswell Regimen, were found to increase toxicity in

older patients(18). I am concerned about capecitabine because of issues with compliance, the fact that dosing is somewhat erratic, and the potential interactions with anticoagulants. Infusional regimens necessitate the use of an indwelling catheter, either a MediPort catheter or possibly a PICC line; but a 48-hour infusional therapy, particularly if the patient lives with her son, would be the least toxic and give her the most chance of benefit.

The other drugs used for metastatic disease have issues regarding toxicity, which are problematic in this situation. Bevacizumab, has some activity, but the risk administering this drug in a 78-year-old woman with a history of stroke and dementia, is high. I would defer this medication if at all possible(19). I am concerned about the use of oxaliplatin. Its high incidence of neuropathy results in issues regarding gait disturbances, ambulation, and the potential exacerbation of falls. A recent paper places in doubt whether the addition of oxaliplatin or irinotecan really is of benefit (20). In some situations, if a response is required very rapidly, one may consider these medications; however, the risks of oxaliplatin as enumerated and irinotecan with its resultant diarrhea are not to be underestimated in an older patient population. The other drugs potentially of use are the EGFR receptor inhibitors, cetuximab and panitumumab. We are not given in the case report her KRAS status, though if it was KRAS wild type, these drugs can be considered, but I would not use them as first line.

Therefore, my recommendations would be to place either a MediPort catheter or PICC line and administer the de Gramont infusion regimen; to optimize her comorbidities and to get more information about her left-sided colonic regarding an impending obstruction. The other important issue is to express to the family the limitations of this treatment, particularly because of her frail state. However, I think that treatment is clearly warranted because of the symptomatic nature of her disease and the potential benefit of therapy.

In **Case Two**, the patient is a 75-year-old woman with diabetes, hypertension, and history of heart failure on diuretics, who was found to have acute FAB M4 leukemia in the setting of evaluation of osteonecrosis of the jaw. Over a 2–3 week period of time, her white count increased to 52,000, and a platelet count declined to 21,000. The treatment of acute leukemia in the elderly is one of great difficulty. Despite the advances in younger patients, there has been no significant improvement in the overall picture for older patients, particularly those with significant comorbidity in their mid to late 70s or above. While select older patients can benefit from standard treatment, they experienced greater treatment-related toxicity, lower remission rates, shorter disease-free survival times, and shorter overall survival times (21). It is felt that part of this issue is that older patients present with more unfavorable prognostic features, though it is interesting that this patient had cytogenetics of intermediate risk. The SEER data from 1988 to 2004 show approximately 20% one year overall survival for patients over the age of 65. There have been a number of studies looking at various ways of modulating treatment regimens to make it tolerable on older patients, including infusional therapy, avoiding higher doses of therapy, particularly cytosine arabinoside that has markedly increased toxicity, particularly neurotoxicity, in older patients. There have been studies looking at treatment versus supportive care that seem to favor treatment. However, when most of these studies looking at older patients, they are really talking about patients of 60 years of age or somewhat older, not 75 as this patient is.

Especially interesting is that the patient showed mutation in FLT3-IDT and NPM1-4bp insertion. NPM1 mutations were most prevalent in patients with normal karyotypes, 45.7% versus 8.5% for the abnormal karyotypes and more significantly associated with several clinical parameters including high bone marrow blast counts, high white blood cell and platelet counts, and female sex. NPM-1 alterations were associated with FLT3-IDT mutations (22). Some of the patient's with the NPM-1 mutations did have a somewhat better prognosis than have normal karyotypes. However, in this patient, the biology of her disease and the need for anti-leukemic therapy is paramount. It is possible that one can palliate her with some infusional cytosine arabinoside or other therapies, but I feel her overall prognosis and the likelihood of withstanding induction therapy is quite poor. The use of anthracyclines may be contraindicated because of her history of congestive heart failure, and then she also may not withstand the requirements of infusional therapy and the antibiotics and the stress of that. One can argue that it may be reasonable to make the attempt at treatment. But, the median survival duration remains less than one year in clinical trials. This is a patient who may not have been eligible for any clinical trials because of her comorbidity, so one would suspect that her overall survival is much lower.

The situation really requires a discussion with the patient and family to see whether palliative care should be offered instead of active therapy. If the patient has the poor performance status then, I think hospice care may be the best option for this patient.

Case Three is an 83-year-old woman with triple-negative breast cancer who is wheelchair bound. She has a previous history of osteoarthritis requiring lumbar laminectomy, limited mobility, hypertension, and hyperlipidemia. She was brought to a surgeon because of a breast mass and was found to have microcalcification in the upper outer quadrant of the right breast with relatively dense axillary nodes. She had excisional biopsy of the right breast mass showing a $6 \times 4.2 \times 2.5$ cm ductal carcinoma grade 3, with prominent lymphovascular invasion with a focally positive deep margin. The patient was triple negative. Final pathology after she underwent a right modified radical mastectomy that confirmed a 6cm lesion with 4/16 nodes positive. The patient is probably a stage IIIA and required hospitalization after the surgery.

Patients with triple negative breast cancer have a poorer prognosis than do other patients. The peak risk of recurrences are 1–3 years and the median time of the death among patients with triple negative breast cancer was shorter than with other subtypes (4.2 versus six years). Overall survival is poor with five year survival rates of 79% compared to 88.7%. Because of the advanced nature this disease at presentation, she is at very high risk for early onset of metastatic disease and mortality. Despite the fact that she is in a wheelchair, we really do not know about her overall performance status and functional status. We know she has hypertension and hyperlipidemia, but we really do not know whether she has any other cardiovascular risk factors that preclude chemotherapy such as regimens containing anthracyclines. One of the current standards for adjuvant treatment of triple-negative breast cancer in older patients is a dose-dense regimen by Citron *et al* (23). This is doxorubicin and cyclophosphamide followed by paclitaxel given every two weeks with pegfilgrastim support. If there is concern about toxicity, one can use the sequential arm of that study that showed the same overall benefit but may be more tolerable as sequential single agents.

There is also a lower incidence of anemia with that regimen. An older patient may find this kind of regimen more tolerable than to give combination chemotherapy. Before one could decide whether any chemotherapy can be given, a fuller geriatric evaluation should be undertaken to include questioning about activities of daily living, instrumental activities of daily living, and Mini Mental Status. In older patients getting chemotherapy, particularly one with a mobility disability, we have to be cautious about social support. If the patient has a toxic event, we need to be confident the patient can contact her physicians and seek medical attention as soon as possible. It is quite unreasonable to put the patient at increased risk.

In terms of other regimens that might be considered, there was a recent randomized study published by Muss et al utilizing intravenous regimens of either CMF (cyclophosphamide, methotrexate, 5-FU) , or doxorubicin, cyclophosphamide (AC) versus capecitabine (24). It was shown that the intravenous regimens were superior to the oral regimen with reasonable toxicity. The other issue that we are not aware of is the patient's laboratory evaluation. We do not know if the patient has renal insufficiency or other end-organ dysfunctions that may complicate the treatment regimen. Another study by the Early Breast Cancer Trialists Group did demonstrate a 6% absolute reduction in 10-year breast cancer mortality for women age 50–69 years old treated with CMF. It is somewhat reasonable to extrapolate that all the patients would derive the same benefit. Other trials have shown that in women with high risk, lymph node positive, hormone receptor negative tumors, the greatest reduction in recurrence is derived from more intensive anthracycline and taxane-containing chemotherapy regimens. If there is also concern about cardiovascular disease, a non-anthracycline regimen such as docetaxel and cyclophosphamide might be a potentially good choice.

Therefore, after the patient recovers from this acute episode of infection, she will need a further evaluation including cardiovascular evaluation, a brief geriatric assessment, greater understanding of her social situation and mental status before a final decision can be made. If she is otherwise fit despite her issue of being wheelchair bound due to osteoarthritis, then an adjuvant regimen certainly can be considered.

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GASTROINTESTINAL MEDICAL ONCOLOGIST'S EXPERT OPINION, Case One

Elderly patients with metastatic colorectal cancer present a unique challenge for today's community oncologist. Our aging population is making the above clinical situation in Case One more common, and unfortunately, there is a paucity of clinical trial data to guide our treatment decisions.

As with any patient, the goals of care need to be clearly defined from the beginning. She has incurable disease and discussions regarding palliative chemotherapy should be balanced with best supportive care. Regardless if she and her son choose to receive palliative chemotherapy, a living will should be completed with clear instructions for end of life care.

Despite lack of data, I do believe treatment for her malignancy could afford her a better quality of life and longevity. If the decision is made to treat her with chemotherapy, I believe this patient has several options. Capecitabine (Xeloda, Roche Pharmaceuticals), a 5-FU prodrug metabolized by the liver to its active form, has been shown to be well tolerated and effective in elderly patients. There is no creatinine listed, but assuming the GFR is above 60, Xeloda is a reasonable first option. However, caution should be taken as patients over the age of 80 years as they have an increased incidence of grade 3 and 4 adverse reactions; 62% of the 21 patients over 80 years old on Xeloda as monotherapy for breast or colon cancer experienced grade 3 or 4 adverse events. The dosing of Xeloda can be a challenge, especially in the elderly population, so a stepwise approach may be appropriate. Starting at a dose of 1gm per day (500mg BID), one week on and one off seems to be well tolerated without significant mucositis, diarrhea, hand foot syndrome or leucopenia. If this protocol is tolerated, I typically increase to 1.5 gm for the second cycle and 2gm (1gm BID) per day after third. This protocol, unlike Xeloda days 1–14 then 1 week off seems to be better tolerated. During this treatment, a CEA level can be followed to show response.

Many elderly patients are fearful of the concept of intravenous chemotherapy, but the use of oxaliplatin and irinotecan has been shown to be well tolerated with significant response rates in elderly patients with metastatic colon cancer. Still, pooled data show that there is increased hematologic toxicity with the use of oxaliplatin in the elderly population, other toxicities such as neurologic, diarrhea, nausea, vomiting, infection or overall incidence of grade 3 toxicities were similar in both younger and older groups. In addition, the relative benefit of oxaliplatin did not differ by age for response rate, time to progression, recurrence free survival or overall survival. These data do not preclude the use of oxaliplatin in treating these patients; however dose reduction may be appropriate. Typically, I start at 75mg/m² and find this dose to be well tolerated in the elderly population and would only incorporate this if the Xeloda was well tolerated. Finally, special care should be taken in patients with preexisting neuropathy or diabetes as there is increased risk of neurologic toxicity.

Finally, the use of biologic therapy should be discussed. This patient has incurable disease and her primary tumor is left intact. Her blood work reveals microcytosis indicating iron deficiency from gastrointestinal blood loss. I do not believe that the benefit of bevacizumab in this situation is worth the risk. The highest risk of perforation with bevacizumab is when

the primary tumor has not been removed as is the clinical situation here. In addition, her use of coumadin for a previous CVA further outweighs the risks versus benefits. Cetuximab, an IgG1 chimeric monoclonal antibody against epidermal growth factor receptor, has activity in KRAS/BRAF wild type colorectal patients and despite being well tolerated, in this palliative setting with a mildly demented elderly patient, I would not recommend the standard use of this product.

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HEMATOLOGIC ONCOLOGIST'S EXPERT OPINION: Case Two

The patient in Case Two is a 75 year old woman with DM, HTN, intermittent CHF of uncertain etiology, and osteonecrosis of the jaw who has been diagnosed to have acute myeloid leukemia with myelodysplasia (MDS)-related changes (possibility of antecedent MDS) and diploid cytogenetics. She also has FLT3 internal tandem duplication mutation and NPM1 mutation. Unfortunately, the combination of advanced age, FLT3-ITD, and possibly MDS-related changes as well as her comorbid conditions suggest that she has a less favorable prognosis and perhaps may not achieve long-term Leukemia-free survival with standard induction regimens using cytotoxic chemotherapy combination of cytarabine and anthracyclines. However, several recent studies have clearly suggested that leukemia-specific therapy in the older population does improve response rate, survival, and symptoms. She should clearly be offered chemotherapy or available clinical trials (preferably the latter), particularly since she seems to have a rapidly proliferative disease. Several new strategies such as clofarabine-based regimens, hypomethylating agents, and specific FLT3 kinase inhibitors are under evaluation in the older population. My suggestion would be a trial of a FLT3 kinase inhibitor plus chemotherapy (there is an ongoing INTERGROUP study of PKC412 plus cytarabine and daunorubicin induction (if she is eligible particularly with the concerning history of CHF) and if not other studies of FLT3 inhibitors such as Sorafenib or AC220.

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BREAST MEDICAL ONCOLOGIST'S EXPERT OPINION: Case Three

With our aging population, this case is becoming a fairly familiar situation in the clinic. Unfortunately though, this type of patient (**Case Three**) often encounters bias because of their chronological age. There is a misconception that breast cancer in women aged over 70 years is more indolent. However, no major differences in outcomes were seen in the older population with breast cancer when compared to stage-matched patients. Multi-variate analysis showed that age is not an independent risk factor for distance-disease free survival. Rather, it is significantly impacted by tumor size, node positivity and systemic therapy (25). Therefore, indications for mastectomy and radiotherapy should similarly be applied to this cohort. Toxicities of radiation does not appear to be higher in those over 65 years of age (26). High-risk women over 70 derived significant survival advantage from post-mastectomy radiation (27). The decision on chemotherapy though in this situation is more difficult. Not only do we deal with the age bias but the interaction of baseline comorbidities factor in to a greater degree. However, it is important to keep in mind that as with the other adjuvant modalities, older women derive the same benefit from chemotherapy as the younger population. And those with hormone negative lesions derive more absolute benefit in terms of survival. Therefore, robust elderly patients should be considered for the same systemic regimens as their younger counterparts. Anthracycline-based regimens plus/minus a taxane would be the preferred regimen. However, a doublet regimen of docetaxel and cyclophosphamide is a viable option. In the pivotal trial that demonstrated this, Jones, *et al* included patients up to 75 years old. Disease-free survival data favored both subgroups of patients stratified below or above 50 years (28).

For the above patient, there is no doubt she has a high risk disease. Although she has multiple comorbidities as would be expected in her advanced age, the main question will be whether or not these are well-controlled. It will also help if we could tease out whether her post-operative course was brought on more by her comorbidities or other factors such as very dense breast anatomy, ability to do post-op wound care, etc. I would not be quick to dismiss standard recommendations for adjuvant treatment because of the aggressive biology of her tumor. But the decision will certainly be tempered by her wishes and the result of individualized comprehensive geriatric assessment that would impact her functionality, tolerance to treatment and more importantly overall survival.

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DISCUSSION

Treatment of both solid as well as hematologic malignancies in the elderly presents a very challenging entity in cancer care. While multiple factors must be considered before embarking upon optimal therapy for any malignancy, even more specific attention to determine individual fitness in the elderly to withstand even commonly used therapy is needed. As discussed by Drs. Swartz and Chapman, standardized assessments such as done

in many multidisciplinary centers which have Senior Oncology programs may help in decision making (Figure 4)(29).

Specifically, as discussed by both Drs. Lichtman and Levitz in the example of colorectal cancer, however, chemotherapy options do exist for the elderly and even the frail (30,31). While these can dispel apprehension that otherwise indicated combination therapy could be tolerated at all in the elderly, individual treatment choice is certainly dictated by physician experience as well as the toxicity data reported in the literature (20,30). As discussed by Dr. Ravandi, older patients with AML likely have other poor risk factors, and despite historical descriptions that they may fare worse in outcome due to disease biology and individual factors (33), there do exist agents which aim toward biological targets, for which the thrust of clinical trials is key in all age groups. And in the situation of aggressive triple-negative breast cancer (TNBC) in the elderly, the quandary of aggressively attacking this specific biologic entity which has a high likelihood of systemic involvement (especially if of the basal phenotype) (34,35) versus individual tolerance, Drs. Lichtman and Chan specifically illustrated how one could evaluate all aspects of a person's presentation in order to make these decisions. There are indeed conflicting data suggesting disparate levels of survival gain (36); nevertheless, Gandhi and Verma, for example (37), do promote that age in and of itself should not deter specific breast cancer therapy, but the use of comprehensive multidisciplinary assessment in order to determine eligibility should be employed. London illustrated in her editorial that "undertreatment of the elderly may contribute to deaths of older cancer patients", and multiple aspects which may otherwise impede decisions to go forward with treatment should be weighed alongside national guidelines (38). Dr Lichtman also advocates for participation in clinical trials, by which these guidelines evolve for cancer care in not only a general sense, but now an increasingly individualized fashion in this decade (39).

I appreciate the authors participating in this excellent round-table discussion.

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Axial w/contrast

Coronal w/contrast

Figure One.

CAT scan of the abdomen with oral and intravenous contrast, showing liver in (a) axial view, and (b) coronal view. Courtesy of Dave Soltis, Advanced Imaging Specialists, Scranton, PA.

Hematopathology

Blood smear

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Cytogenetics – Karyotype

Normal Karyotype

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Figure Two.

(Panel A) Peripheral blood smear, Hematoxylin and Eosin stain, 10x magnification, showing left-shifted atypical myelomonocytic proliferation of white blood cells. (Panel B) Cytogenetic study showing normal karyotype. Courtesy of Genoptix Medical Laboratory, Inc., Carlsbad, CA.

Figure Three.

(Panel A) Hematoxylin and Eosin stain of lumpectomy specimen, at 10X magnification; **(Panel B)** Hematoxylin and Eosin stain of lumpectomy specimen, at 40X magnification; **(Panel C)** Hematoxylin and Eosin stain of mastectomy specimen, at 10X magnification, showing lymph node metastases; **(Panel D)** Hematoxylin and Eosin stain of mastectomy specimen, at 40X magnification. Immunohistochemistry (IHC) was negative for expression of estrogen receptor, progesterone receptor, or HER-2-neu expression. Courtesy of Dr. Thomas Himes, Department of Pathology, Community Medical Center, Scranton, PA.

VES-13

1. Age _____

SCORE: 1 POINT FOR AGE 75-84
3 POINTS FOR AGE ≥ 85

2. In general, compared to other people your age, would you say that your health is:

Poor,* (1 POINT)

Fair,* (1 POINT)

Good,

Very good, or

Excellent

SCORE: 1 POINT FOR FAIR or POOR

3. How much difficulty, on average, do you have with the following physical activities:

	No Difficulty	A little Difficulty	Some Difficulty	A Lot of Difficulty	Unable to do
a. stooping, crouching or kneeling?				*	*
b. lifting, or carrying objects as heavy as 10 pounds?				*	*
c. reaching or extending arms above shoulder level?				*	*
d. writing, or handling and grasping small objects?				*	*
e. walking a quarter of a mile?				*	*
f. heavy housework such as scrubbing floors or washing windows?				*	*

SCORE: 1 POINT FOR EACH * RESPONSE
IN Q3a THROUGH f. MAXIMUM OF 2
POINTS.

4. Because of your health or a physical condition, do you have any difficulty:

a. shopping for personal items (like toilet items or medicines)?

YES Do you get help with shopping?

YES * NO

NO

DONTDO Is that because of your health?

YES * NO

b. managing money (like keeping track of expenses or paying bills)?

YES Do you get help with managing money?

YES * NO

NO

DONTDO Is that because of your health?

YES * NO

Continued

□ 2001 R

c. walking across the room? USE OF CANE OR WALKER IS OK.

YES Do you get help with walking? YES * NO

NO

DONTDO Is that because of your health? YES * NO

d. doing light housework (like washing dishes, straightening up, or light cleaning)?

YES Do you get help with light housework? YES * NO

NO

DONTDO Is that because of your health? YES * NO

e. bathing or showering?

YES Do you get help with bathing or showering? YES * NO

NO

DONTDO Is that because of your health? YES * NO

SCORE: 4 POINTS FOR ONE OR MORE *
RESPONSES IN Q4a THROUGH Q4e

Cognitive Screen (3 Item Recall):

- Ask patient to immediately repeat 3 words (they should continue repeating until all 3 are remembered): ball, car, tree
- Instruct patient to remember these 3 words
- Wait 1-2 minutes, then ask patient to repeat the 3 words (no prompts): _____ ball _____ car _____ tree
(score 1 point for each correctly recalled word.)

Score: _____ / 3

(Any score less than 3/3 is abnormal and warrants more formal cognitive assessment to rule out dementia/ cognitive impairment.)

Gait Dysfunction Screen (Timed Get Up and Go):

Patient should be seated in a chair with no wheels and no arms. If an armless chair is not available, instruct the patient not to use the chair arms. Ask patient to rise from the chair, walk 3 meters, turn, walk back to the chair and sit down again. The patient should use any assistive device they normally use while walking (i.e. cane, walker).

Time: _____ seconds

(Normal is less than 10 seconds; longer time, or inability to complete the task without using the arms to rise from a chair, for instance, indicate increased risk of falls and physical frailty.)
(Podsiadlo and Richardson.. *J Am Geriatr Soc*, 39:142-8, 1991.)

Figure Four.

Example of a clinical evaluation form for Senior Oncology patients. Reference 29, Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc*. 1991;39:142-8.