NCCN Guidelines® Insights

Older Adult Oncology, Version 2.2016

Featured Updates to the NCCN Guidelines

Noam VanderWalde, MD^{1,*†}; Reshma Jagsi, MD, DPhil^{2,*†}; Efrat Dotan, MD^{3,*}; Joel Baumgartner, MD⁴; Ilene S. Browner, MD⁵; Peggy Burhenn, MS, RN⁶; Harvey Jay Cohen, MD⁷; Barish H. Edil, MD⁸; Beatrice Edwards, MD, MPH⁹; Martine Extermann, MD, PhD¹⁰; Apar Kishor P. Ganti, MD¹¹; Cary Gross, MD¹²; Joleen Hubbard, MD¹³; Nancy L. Keating, MD, MPH¹⁴; Beatriz Korc-Grodzicki, MD, PhD¹⁵; June M. McKoy, MD, MPH, JD, MBA¹⁶; Bruno C. Medeiros, MD¹⁷; Ewa Mrozek, MD¹⁸; Tracey O'Connor, MD¹⁹; Hope S. Rugo, MD²⁰; Randall W. Rupper, MD, MPH²¹; Dale Shepard, MD, PhD²²; Rebecca A. Silliman, MD, PhD, MPH²³; Derek L. Stirewalt, MD²⁴; William P. Tew, MD¹⁵; Louise C. Walter, MD²⁰; Tanya Wildes, MD²⁵; Mary Anne Bergman^{26,*}; Hema Sundar, PhD^{26,*}; and Arti Hurria, MD^{6,*}

Abstract

Cancer is the leading cause of death in older adults aged 60 to 79 years. Older patients with good performance status are able to tolerate commonly used treatment modalities as well as younger patients, particularly when adequate supportive care is provided. For older patients who are able to tolerate curative treatment, options include surgery, radiation therapy (RT), chemotherapy, and targeted therapies. RT can be highly effective and well tolerated in carefully selected patients, and advanced age alone should not preclude the use of RT in older patients with cancer. Judicious application of advanced RT techniques that facilitate normal tissue sparing and reduce RT doses to organs at risk are important for all patients, and may help to assuage concerns about the risks of RT in older adults. These NCCN Guidelines Insights focus on the recent updates to the 2016 NCCN Guidelines for Older Adult Oncology specific to the use of RT in the management of older adults with cancer.

J Natl Compr Canc Netw 2016;14(11):1357–1370

From ¹St. Jude Children's Research Hospital/The University of Tennessee Health Science Center; ²University of Michigan Comprehensive Cancer Center; ³Fox Chase Cancer Center; ⁴UC San Diego Moores Cancer Center; ⁵The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins; ⁶City of Hope Comprehensive Cancer Center; ⁷Duke Cancer Institute; ⁸University of Colorado Cancer Center; ⁹The University of Texas MD Anderson Cancer Center; ¹⁰Moffitt Cancer Center; ¹¹Fred & Pamela Buffett Cancer Center; ¹²Yale Cancer Center/Smilow Cancer Hospital; ¹³Mayo Clinic Cancer Center; ¹⁴Dana-Farber/Brigham and Women's Cancer Center; ¹⁵Memorial Sloan Kettering Cancer Center; ¹⁶Robert H. Lurie Comprehensive Cancer Center of Northwestern University; ¹⁷Stanford Cancer Institute; ¹⁸The Ohio State University Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute; ¹⁹Roswell Park Cancer Institute; ²⁰UCSF Helen Diller Family Comprehensive Cancer Center; ²¹Huntsman Cancer Institute at the University of Utah; ²²Case Comprehensive Cancer Center/University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute; ²³Consultant; ²⁴Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance; ²⁵Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine; and ²⁶National Comprehensive Cancer Network.

*Provided content development and/or authorship assistance.

†These authors contributed equally.

Please Note

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a statement of consensus of the authors regarding their views of currently accepted approaches to treatment. **The NCCN Guidelines® Insights highlight important changes to the NCCN Guidelines® recommendations from previous versions. Colored markings in the algorithm show changes and the discussion aims to further the understanding of these changes by summarizing salient portions of the NCCN Guideline Panel discussion, including the literature reviewed.**

These NCCN Guidelines Insights do not represent the full NCCN Guidelines; further, the National Comprehensive Cancer Network® (NCCN®) makes no representation or warranties of any kind regarding the content, use, or application of the NCCN Guidelines and NCCN Guidelines Insights and disclaims any responsibility for their applications or use in any way.

The full and most current version of these NCCN Guidelines are available at NCCN.org.

© National Comprehensive Cancer Network, Inc. 2016, All rights reserved. The NCCN Guidelines and the illustrations herein may not be reproduced in any form without the express written permission of NCCN.

Older Adult Oncology, Version 2.2016

NCCN: Continuing Education**Accreditation Statement**

This activity has been designed to meet the educational needs of physicians, nurses, and pharmacists involved in the management of patients with cancer. There is no fee for this article. The National Comprehensive Cancer Network (NCCN) is accredited by the ACCME to provide continuing medical education for physicians. NCCN designates this journal-based CE activity for a maximum of 1.0 *AMA PRA Category 1 Credit™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

NCCN is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

NCCN designates this educational activity for a maximum of 1.0 contact hour. Accreditation as a provider refers to recognition of educational activities only; accredited status does not imply endorsement by NCCN or ANCC of any commercial products discussed/displayed in conjunction with the educational activity. Kristina M. Gregory, RN, MSN, OCN, is our nurse planner for this educational activity.

National Comprehensive Cancer Network is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. NCCN designates this continuing education activity for 1.0 contact hour(s) (0.1 CEUs) of continuing education credit in states that recognize ACPE accredited providers. This is a knowledge-based activity. UAN: 0836-0000-16-011-H01-P

All clinicians completing this activity will be issued a certificate of participation. To participate in this journal CE activity: 1) review the learning objectives and author disclosures; 2) study the education content; 3) take the posttest with a 66% minimum passing score and complete the evaluation at <http://education.nccn.org/node/79757>; and 4) view/print certificate.

Release date: November 1, 2016; Expiration date: November 1, 2017

Learning Objectives:

Upon completion of this activity, participants will be able to:

- Integrate into professional practice the updates to NCCN Guidelines for Older Adult Oncology
- Describe the rationale behind the decision-making process for developing the NCCN Guidelines for Older Adult Oncology

Disclosure of Relevant Financial Relationships**Editor:**

Kerrin M. Green, MA, Assistant Managing Editor, *JNCCN—Journal of the National Comprehensive Cancer Network*, has disclosed that she has no relevant financial relationships.

CE Authors:

Deborah J. Moonan, RN, BSN, Director, Continuing Education, NCCN, has disclosed that she has no relevant financial relationships.

Kristina M. Gregory, RN, MSN, OCN, Vice President, Clinical Information Operations, NCCN, has disclosed that she has no relevant financial relationships.

Rashmi Kumar, PhD, Senior Manager, Clinical Content, NCCN, has disclosed that she has no relevant financial relationships.

Individuals Who Provided Content Development and/or Authorship Assistance:

Noam VanderWalde, MD, Panel Member, has disclosed that he has no relevant financial relationships.

Reshma Jaggi, MD, DPhil, Panel Member, has disclosed that she has no relevant financial relationships.

Efrat Dotan, MD, Panel Vice-Chair, has disclosed that he receives grant/research support from Pfizer Inc.

Arti Hurria, MD, Panel Chair, has disclosed that she receives consulting fees/honoraria from Boehringer Ingelheim GmbH, Carevive Systems, Inc., GTX, Inc., and sanofi-aventis U.S.; and she has received grant/research support from Celgene Corporation, GlaxoSmithKline, and Novartis Pharmaceuticals Corporation.

Mary Anne Bergman, Guidelines Coordinator, NCCN, has disclosed that she has no relevant financial relationships.

Hema Sundar, PhD, Oncology Scientist/Senior Medical Writer, NCCN, has disclosed that she has no relevant financial relationships.

This activity is supported by educational grants from AstraZeneca, Bayer Healthcare Pharmaceuticals Inc., Bristol-Myers Squibb, Clovis Oncology, Foundation Medicine, Genentech, Novartis Oncology, Otsuka America Pharmaceutical, Inc., Seattle Genetics, Inc., and Takeda Oncology; support provided by Actelion Pharmaceuticals US, Inc.; and by an independent educational grant from Astellas and Medivation, Inc.

Older Adult Oncology, Version 2.2016

DISEASE-SPECIFIC ISSUES RELATED TO AGE

Breast Cancer*

- Multiple studies have shown that older women often do not receive “standard of care” treatment, and do not do as well as younger women with the same stage of breast cancer.
- Women older than 75 years receive less aggressive treatment and have higher mortality from early-stage breast cancer than younger women.¹⁻³ Biologic as well as chronologic age should be considered in selecting treatments for older women with breast cancer.

Surgery:

- Women who do not undergo axillary lymph node (ALN) dissection, sentinel lymph node (SLN) biopsy, or ALN irradiation may be at increased risk for ipsilateral lymph node recurrence, especially if they fail to undergo standard adjuvant systemic therapy.
- In the absence of definitive data demonstrating superior survival from the performance of ALN dissection,⁴⁻⁶ in patients 65 years or older with no palpable axillary lymph nodes, performance of ALN dissection or SLN dissection may be considered optional for the following patients:
 - patients with particularly favorable tumors
 - patients for whom the selection of adjuvant systemic therapy is unlikely to be affected
 - older patients or for patients with serious comorbid conditions (See NCCN Guidelines for Breast Cancer)

Radiation Therapy:

- In patients 70 years or older, omission of radiation therapy can be considered for patients with stage I estrogen receptor-positive breast cancer who undergo a lumpectomy with negative margins and who are likely to complete 5 years of endocrine therapy. Omission of radiation therapy has been associated with a modest increased risk of local recurrence (4% vs. 1% at 5 years; 10% vs. 2% at 10 years); however, there has been no difference in OS or distant metastatic disease.^{7,8}

Primary Endocrine Therapy:

- At the current time, primary endocrine therapy should be reserved for patients who are not surgical candidates (reduced predicted life expectancy to less than 5 years).⁹

Adjuvant Therapy:

- A select group of older adults is enrolled in clinical trials. A review of CALGB studies for node-positive breast cancer demonstrated that only 8% (542/6487) of patients enrolled in cooperative group trials were 65 years and older and only 2% (159/6487) of patients were 70 years or older.¹⁰
- Older adults (65 years or older) with breast cancer enrolled in cooperative group trials of adjuvant chemotherapy derive similar benefits (disease-free survival and OS) compared to younger patients. However, older patients have an increased risk of side effects and treatment-related mortality.¹¹
- In the adjuvant treatment of breast cancer, single-agent capecitabine is inferior to either cyclophosphamide, methotrexate, and fluorouracil (CMF) or doxorubicin and cyclophosphamide (AC) in patients 65 years or older. Unplanned subset analysis suggested that the greatest difference was seen in women with hormone-receptor-negative tumors.¹¹
- The results of the randomized phase III trial (ELDA) showed that weekly docetaxel did not improve disease-free survival compared to CMF as adjuvant treatment for older women (65–79 years) with early breast cancer. Docetaxel was associated with severe nonhematologic toxicity and worse quality of life.¹²

Version 2.2016 © National Comprehensive Cancer Network, Inc. 2016. All rights reserved. The NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN®.

Continue
OAO-B
5 OF 32

NCCN Categories of Evidence and Consensus

Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise noted.

Clinical trials: NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Overview

Cancer is the leading cause of death in women and men aged 60 to 79 years.¹ More than 50% of all cancers and more than 70% of cancer-related deaths in the United States occur in patients who are 65 years or older.² It is estimated that by 2030 approximately 70% of all cancers will be diagnosed in adults aged 65 years or older.³ An aging US population and a greater life expectancy mean that cancer in older adults is becoming an increasingly common problem. Furthermore, older patients with cancer are underrepresented in clinical trials for new cancer therapies.⁴ Therefore, less evidence-based information exists to guide treatment of these patients. The challenge of managing older patients with cancer is to assess whether the expected benefits of treatment are superior to the risk in a population with decreased life expectancy and decreased tolerance to stress. There are unique issues to consider when caring for an older adult with cancer.

DISEASE-SPECIFIC ISSUES RELATED TO AGE

Metastatic Disease:

- A randomized, double-blind, placebo-controlled phase III study investigating the efficacy and safety of pertuzumab, trastuzumab, and docetaxel compared with placebo, trastuzumab, and docetaxel in patients with HER2-positive first-line metastatic breast cancer showed that the combined use of pertuzumab, trastuzumab, and docetaxel resulted in superior progression-free survival (PFS) in older patients. Patients ≥65 years treated with pertuzumab, trastuzumab, and docetaxel experienced diarrhea, neutropenia, and dysgeusia more frequently compared to patients age ≥65 years treated with placebo, trastuzumab, and docetaxel. Patients ≥65 years (in comparison with those <65 years) were more likely to experience diarrhea, decreased appetite, vomiting, fatigue, asthenia, and dysgeusia. In contrast, older adults were less likely to experience neutropenia and febrile neutropenia; however, older adults were more likely to have dose reductions and a lower number of median cycles of docetaxel, possibly explaining these findings.¹³
- A randomized, double-blind, placebo-controlled phase III study investigating the efficacy and safety of everolimus with exemestane versus exemestane plus placebo in patients with HER2-negative, hormone receptor positive breast cancer showed that treatment with everolimus plus exemestane was associated with an improvement in PFS regardless of patient age. Treatment with everolimus plus exemestane (compared to exemestane plus placebo) was associated with increased risk of stomatitis, pneumonitis, infection, rash, and hyperglycemia. Older adults had a similar adverse event profile compared to younger adults; however, older adults were more likely to experience on-treatment death. Cautious monitoring and appropriate dose reductions or interruptions for adverse event management are recommended during treatment with everolimus.¹⁴
- A recently published population-based retrospective study of patients 66 years and older who were diagnosed with stage I-III breast cancer and have been treated with trastuzumab demonstrate a CHF rate of almost 30%, which is substantially higher than the rate reported in the clinical trials. Among patients treated with trastuzumab, the rate of CHF was associated with weekly administration of trastuzumab, older age, hypertension, anthracycline use, increases in comorbidities (based on the Charlson comorbidity scale), coronary artery disease, and patients who are non-Hispanic black. Patients who did not receive trastuzumab were more likely to receive anthracycline-based treatment.¹⁵

Surveillance:

- Decisions about mammograms for older breast cancer survivors should incorporate discussions with patients about their risk of developing a recurrent or new breast cancer, the potential benefits of mammography in improving outcomes, the potential harms of mammography (including false positives and overdiagnosis/overtreatment), and patients' values and preferences.¹⁶

Some key points include:

- ▶ Breast cancer survivors continue to have an increased risk of recurrence or new primaries that is higher than the general population (the risk is about 4%–5% over 5 years).
- ▶ Regular mammograms may be helpful in finding these cancers early and improving outcomes, but mammograms also have harms, including false positives, unnecessary biopsies, and finding cancers that never would have become clinically significant in a woman's lifetime (overdiagnosis).
- There likely is no benefit to regular mammograms for older women with a life expectancy of less than 5 years. In this group, the harms of mammographic screening among asymptomatic women probably outweigh any potential benefits that the patient might experience.

Continue

Version 2.2016 © National Comprehensive Cancer Network, Inc. 2016. All rights reserved. The NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN®.

OA0-B
6 OF 32

The biologic characteristics of certain cancers and their responsiveness to therapy are different in older patients compared with their younger counterparts.⁵ In addition, older patients also have decreased tolerance to anticancer therapy. Nevertheless, advanced age alone should not be the only criteria to preclude effective treatment that could improve quality of life or lead to a survival benefit in older patients.^{6,7}

Surgery, radiation therapy (RT), chemotherapy, and targeted therapies should be considered as treatment options for all older patients who are able to tolerate curative treatment. RT can be offered either in the curative or palliative setting.^{8,9} Available data from the literature indicate that RT can be highly effective and well tolerated, so that age alone need not be a limiting factor.^{10–12} Advanced RT techniques (eg, intensity-modulated RT [IMRT], image-guided RT [IGRT], and stereotactic body RT [SBRT] or stereotactic ablative RT [SABR]) facilitate the delivery of large doses of radiation to small target

volumes while limiting the risk of radiation-induced damage to normal surrounding tissues and organs at risk (OAR).¹³ Judicious application of these techniques may also help assuage concerns about the risks of RT in older adults. Hypofractionated RT may also help improve treatment tolerability by limiting overall treatment time without compromising clinical outcomes in some patients.¹⁴

The NCCN Guidelines for Older Adult Oncology address specific issues related to the management of cancer in older adults and provide an approach to decision-making with the application of comprehensive geriatric assessment (CGA). In addition, the NCCN Guidelines for Older Adult Oncology also provide age-specific recommendations for the use of surgery, RT, chemotherapy, and targeted therapies for different cancer subtypes. These NCCN Guidelines Insights focus on recent updates to the 2016 NCCN Guidelines for Older Adult Oncology specific to the use of RT in the management of older adults with cancer.

Older Adult Oncology, Version 2.2016

(References)

Breast Cancer*

- ¹Bouchardy C, Rapiti E, Fioretta G, et al. Undertreatment strongly decreases prognosis of breast cancer in elderly women. *J Clin Oncol* 2003;21:3580-3587.
- ²Schonberg MA, Marcantonio ER, Li D, et al. Breast cancer among the oldest old: tumor characteristics, treatment choices, and survival. *J Clin Oncol* 2010;28:2038-2045.
- ³Yood MU, Owusu C, Buist DSM, et al. Mortality impact of less-than-standard therapy in older breast cancer patients. *J Am Coll Surg* 2008;206:66-75.
- ⁴Martelli G, Miceli R, Daidone MG, et al. Axillary dissection versus no axillary dissection in elderly patients with breast cancer and no palpable axillary nodes: results after 15 years of follow-up. *Ann Surg Oncol* 2011;18:125-133.
- ⁵Rudenstam CM, Zahrieh D, Forbes JF, et al. Randomized trial comparing axillary clearance versus no axillary clearance in older patients with breast cancer: first results of International Breast Cancer Study Group Trial 10-93. *J Clin Oncol* 2006;24:337-344.
- ⁶Giuliano AE, Hunt KK, Ballman KV, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. *JAMA* 2011;305:569-575.
- ⁷Hughes KS, Schnaper LA, Berry D, et al. Lumpectomy plus tamoxifen with or without irradiation in women 70 years of age or older with early breast cancer. *N Engl J Med* 2004;351:971-977.
- ⁸Hughes KS, Schnaper LA, Bellon JR, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 or older with early breast cancer: Long-term follow-up of CALGB 9343. *J Clin Oncol*. 2013;31: 2382-2387.
- ⁹Morgan JL, Reed MW, Wyld L. Primary endocrine therapy as a treatment for older women with operable breast cancer - a comparison of randomised controlled trial and cohort study findings. *Eur J Surg Oncol* 2014;40:676-684.
- ¹⁰Muss HB, Woolf S, Berry D, et al. Adjuvant chemotherapy in older and younger women with lymph node-positive breast cancer. *JAMA* 2005;293:1073-1081.
- ¹¹Muss HB, Berry DA, Cirincione CT, et al. Adjuvant chemotherapy in older women with early-stage breast cancer. *N Engl J Med* 2009;360:2055-2065.
- ¹²Perrone F, Nuzzo F, Di Rella F, et al. Weekly docetaxel versus CMF as adjuvant chemotherapy for older women with early breast cancer: final results of the randomized phase III ELDA trial. *Ann Oncol* 2015;26:675-682.
- ¹³Miles D, Baselga J, Amadori D, et al. Treatment of older patients with HER2-positive metastatic breast cancer with pertuzumab, trastuzumab, and docetaxel: subgroup analyses from a randomized, double-blind, placebo-controlled phase III trial (CLEOPATRA). *Breast Cancer Res Treat* 2013;142:89-99.
- ¹⁴Pritchard KI, Burris HA, 3rd, Ito Y, et al. Safety and efficacy of everolimus with exemestane vs. exemestane alone in elderly patients with HER2-negative, hormone receptor-positive breast cancer in BOLERO-2. *Clin Breast Cancer* 2013;13:421-432.
- ¹⁵Chavez-MacGregor M, Zhang N, Buchholz TA, et al. Trastuzumab-related cardiotoxicity among older patients with breast cancer. *J Clin Oncol* 2013;31:4222-4228.
- ¹⁶Walter LC, Schonberg MA. Screening mammography in older women: a review. *JAMA* 2014; 311:1336-1347.

*For comparison of efficacy and toxicity of various targeted therapies between younger and older patients, see Gonsalves W, Ganti AK. Targeted anti-cancer therapy in the elderly. *Crit Rev Oncol Hematol* 2011;78:227-242.

Version 2.2016 © National Comprehensive Cancer Network, Inc. 2016. All rights reserved. The NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN®.

OA0-B
7 OF 32

Breast Cancer

RT as a component of breast-conserving therapy after lumpectomy is not always necessary in selected older women with stage I breast cancer. In a study that randomized 636 women (aged ≥70 years) treated with lumpectomy for clinical stage I estrogen receptor–positive breast cancer to either tamoxifen with whole-breast RT or tamoxifen alone, locoregional recurrence was slightly higher among those who did not receive RT.^{15,16} At the median follow-up of 12.6 years, the 10-year local recurrence rates were 2% and 10%, respectively, for those who received tamoxifen with RT and those who received tamoxifen alone. However, there were no significant differences in time to mastectomy, time to distant metastasis, breast cancer–specific survival, or overall survival (OS) between the groups.¹⁶ The 10-year OS rates were 67% and 66%, respectively, and the estimated 10-year breast cancer–specific survival rates were

97% and 98%, respectively. In this study, all patients received adjuvant tamoxifen for 5 years. Results of the recently published PRIME II study led the authors to conclude that because the rate of ipsilateral recurrence is low, omission of whole-breast RT after breast-conserving surgery could be considered for some women aged 65 years or older with early-stage breast cancer.¹⁷ In this study, 1,326 women aged 65 years or older who had undergone breast-conserving surgery for early-stage, low-risk breast cancer (hormone receptor–positive, axillary node-negative, T1–T2 up to 3 cm at the longest dimension, and clear margins; either grade 3 tumors or lymphovascular invasion) and receiving adjuvant endocrine treatment were randomized to whole-breast RT and no further treatment. After median follow-up of 5 years, the ipsilateral recurrence rate was 1.3% in women assigned to whole-breast RT and 4.1% for those assigned no RT ($P=.0002$), with no difference in OS between the groups; the 5-year OS rate was 93.4% in both groups.

DISEASE-SPECIFIC ISSUES RELATED TO AGE

Central Nervous System Cancers***Glioblastoma****Surgery:**

- Patients older than 70 years with glioblastoma who are treated surgically with gross total resection achieve a greater OS than those who are treated with lesser resection. Just as in younger patients, it is difficult to be certain that this is a direct effect of the surgical procedure or a result of selection bias.^{1,2}

Adjuvant Therapy:

- Postsurgical radiation alone is effective in improving outcomes in patients older than 70 years with glioblastoma, and shorter course regimens are reasonable to consider. **Hypofractionated accelerated course RT (with the goal of completing the treatment in 2–3 weeks) is a reasonable treatment option for older patients.** Typical fractionation schedules are 34 Gy/10 fractions or 40.05 Gy/15 fractions.^{3,4}
- For anaplastic astrocytomas and glioblastomas in patients older than 64 years, temozolomide alone is non-inferior to radiation alone. Temozolomide alone produces improved event-free survival over radiation alone in tumors with a methylated promoter for the methylguanine methyltransferase gene (in an unplanned subset analysis).⁵ In patients with glioblastoma who are older than 70 years, hypofractionated RT alone over two weeks OR temozolomide alone each produce an OS benefit compared to standard fractionated radiation therapy over six weeks. This study also confirms the predictive benefit of MGMT promoter methylation status with temozolomide use.⁶
- The addition of temozolomide concurrently with radiation therapy followed by at least 6 months of adjuvant temozolomide improves survival in patients between 60 and 70 years of age.⁷
- **Hypofractionated accelerated course RT with concurrent and adjuvant temozolomide is safe in older patients, and may have comparable survival and less toxicity to standard fractionated RT with concurrent and adjuvant temozolomide.**^{8,9} **Hypofractionated accelerated course RT with concurrent and adjuvant temozolomide has been shown to be superior to hypofractionated accelerated course of RT alone in a randomized controlled trial of newly diagnosed GBM patients ≥ 65 years of age.**¹⁰

Recurrent Disease:

- In recurrent glioblastoma, bevacizumab likely improves quality of life (and possibly OS) in patients 55 years and older.¹¹

Central Nervous System Lymphoma:

- Patients older than 60 years with primary central nervous system lymphoma should be treated primarily with chemotherapy, saving radiation for palliative therapy.^{12,13}

Continue

Version 2.2016 © National Comprehensive Cancer Network, Inc. 2016. All rights reserved. The NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN®.

OA0-B
8 OF 32

The NCCN Guidelines Panel concluded that omission of RT can be considered in women aged 70 years or older with stage I estrogen receptor–positive breast cancer who undergo a lumpectomy with negative margins and who are likely to complete 5 years of endocrine therapy. Given that the PRIME study results are based on the 5-year follow-up,¹⁷ the panel concluded that currently there is not enough evidence to extrapolate these results to any patient aged 65 years or older with a life expectancy of greater than 5 years.

Central Nervous System Cancers

Surgery followed by RT in combination with concurrent and adjuvant temozolomide is the standard treatment for glioblastoma multiforme (GBM) in patients younger than 70 years.¹⁸ Recent reports from a global randomized phase III clinical trial confirmed that the addition of concurrent and adjuvant temozolomide to hypofractionated RT (40

Gy in 15 fractions over 3 weeks) is well tolerated and significantly improves OS and progression-free survival (PFS) in older patients with newly diagnosed GBM and good performance status.¹⁹ In this trial, 562 patients (aged ≥65 years) were randomized to short-course RT (40 Gy in 15 fractions over 3 weeks) either alone or in combination with concomitant temozolomide plus adjuvant temozolomide until progression or 12 cycles. The median OS and PFS for patients who received short-course RT with concurrent and adjuvant temozolomide were 9.3 and 5.3 months respectively, compared with 7.6 and 3.9 months for those who were treated with short-course RT alone ($P < .0001$).¹⁹ Patients with methylguanine DNA methyltransferase (MGMT) methylated tumors benefited the most from the addition of temozolomide to RT. Earlier reports from other investigators also suggest that the addition of temozolomide to standard RT (60 Gy) or short-course RT (40 Gy in 15 fractions over 3 weeks) can prolong survival with acceptable toxicity in older patients

Older Adult Oncology, Version 2.2016

DISEASE-SPECIFIC ISSUES RELATED TO AGE
(References)

Central Nervous System Cancers*

- ¹Martinez R, Janka M, Soldner F, Behr R, Gross. Total resection of malignant glioma in elderly patients: implications in survival. *Zentrabl Neurochir* 2007;68:176-181.
- ²Vuorinen V, Hinkka S, Farkkila M, Jaaskelainen J. Debulking or biopsy of malignant glioma in elderly people. A randomized study. *Acta Neurochir* 2003;145: 5-10.
- ³Keime-Guibert F, Chinot O, Taillandier L, et al. Radiotherapy for glioblastoma in the elderly. *N Engl J Med* 2007;356:1527-1535.
- ⁴Roa W, Brasher PM, Bauman G, et al. Abbreviated course of radiation therapy in older patients with glioblastoma multiforme: a prospective randomized trial. *J Clin Oncol* 2004;22:1583-1588.
- ⁵Wick W, Platten M, Meisner C, et al. Temozolomide chemotherapy alone versus radiotherapy alone for malignant astrocytoma in the elderly: the NOA-08 randomised, phase 3 trial. *Lancet Oncol* 2012;13:707-715.
- ⁶Malmstrom A, Gronberg B, Marosi C, et al. Temozolomide versus standard 6-week radiotherapy versus hypofractionated radiotherapy in patients older than 60 years with glioblastoma: the Nordic randomized, phase 3 trial. *Lancet Oncol* 2012;13:916-26.
- ⁷Stupp R, Hegi M, Mason W, et al. Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomized phase III study: 5-year analysis of the EORTC-NCIC trial. *Lancet Oncol* 2009;10:459-466.
- ⁸Minniti G, Scaringi C, Lanzetta G, et al. Standard (60 Gy) or short-course (40 Gy) irradiation plus concomitant and adjuvant temozolomide for elderly patients with glioblastoma: a propensity-matched analysis. *Int J Radiat Oncol Biol Phys* 2015;91(1):109-115.
- ⁹Minniti G, Lanzetta G, Scaringi C, et al. Phase II study of short-course radiotherapy plus concomitant and adjuvant temozolomide in elderly patients with glioblastoma. *Int J Radiat Oncol Biol Phys* 2012;83(1):93-99.
- ¹⁰Perry JR, Laperriere N, O'Callaghan CJ, et al. A phase III randomized controlled trial of short-course radiotherapy with or without concomitant and adjuvant temozolomide in elderly patients with glioblastoma (CCTG CE.6, EORTC 26062-22061, TROG 08.02, NCT00482677) [abstract]. *J Clin Oncol* 2016;34 (18 suppl):Abstract LBA2.
- ¹¹Nghiemphu PL, Liu W, Lee Y, et al. Bevacizumab and chemotherapy for recurrent glioblastoma: a single-institution experience. *Neurology* 2009;72:1217-1222.
- ¹²Gavrilovic I, Hormigo A, Yahalom J, et al. Long term follow-up of high-dose methotrexate-based therapy with and without whole brain irradiation for newly diagnosed primary CNS lymphoma. *J Clin Oncol* 2006;24:4570-4574.
- ¹³Zhu J-J, Gerstner ER, Engler DA, et al. High-dose methotrexate for elderly patients with primary CNS lymphoma. *Neuro Oncol* 2009;11:211-215.

*For comparison of efficacy and toxicity of various targeted therapies between younger and older patients, see Gonsalves W, Ganti AK. Targeted anti-cancer therapy in the elderly. *Crit Rev Oncol Hematol* 2011;78:227-242.

Version 2.2016 © National Comprehensive Cancer Network, Inc. 2016. All rights reserved. The NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN®.

OA0-B
9 OF 32

with GBM.²⁰⁻²³ In a phase II trial of 71 patients (≥70 years of age) with newly diagnosed GBM treated with short-course RT (40 Gy in 15 fractions over 3 weeks) in combination with temozolomide, the median OS and PFS were 12.4 and 6 months, and the 1-year OS and PFS rates were 58% and 20%, respectively.²⁰ In a retrospective matched-pair analysis of older patients with newly diagnosed GBM treated with RT alone (n=103) or in combination with concurrent and adjuvant temozolomide (n=190), the combined modality treatment prolonged survival in patients older than 70 and 75 years, respectively.²¹ In patients older than 70 years, the median survival was 7.5 and 3.2 months, respectively, for patients treated with RT and combined modality treatment ($P<.0001$). In patients older than 75 years, the corresponding median survival was 9.2 and 3.2 months ($P<.0001$), respectively. In a propensity matched analysis of 127 patients (aged ≥65 years) treated with temozolomide in combination with standard RT or short-course RT, the median OS (12 vs 12.5

months) and PFS (5.6 vs 6.7 months) were similar for both treatment groups.²² However, standard RT was associated with a significant increase in grade 2 and 3 neurologic toxicity and higher posttreatment dosing of corticosteroid. Results from another recent retrospective analysis also showed that the addition of temozolomide to standard or short-course RT resulted in similar OS in patients 65 years or older with newly diagnosed GBM.²³

Postoperative RT alone has also been shown to effectively improve clinical outcomes in older patients with GBM.^{24,25} In a randomized trial, older patients with GBM treated with surgery (≥60 years; n=100) were randomized to either standard-course RT (60 Gy in 30 fractions over 6 weeks) or an abbreviated course of RT (40 Gy in 15 fractions over 3 weeks).²⁴ The median OS was similar for both treatment groups (5.1 months for standard-course RT and 5.6 months for abbreviated-course RT). However, among those who completed RT as planned, more patients who received standard RT

DISEASE-SPECIFIC ISSUES RELATED TO AGE

Hepatocellular Carcinoma**Liver Resection, Liver Transplantation, and Locoregional Therapy**

- Published data (primarily retrospective) demonstrate age-related differences in patterns of care; however, there was no major difference in outcomes between well-selected older adults and younger patients with hepatocellular carcinoma (HCC).¹⁻⁵
- A few centers have successfully transplanted highly selected patients older than 70 years, but the data are inadequate to make a recommendation regarding liver transplantation in older adults with HCC.¹
- Based on retrospective analyses, older patients may benefit from liver resection or transplantation for HCC, but they need to be carefully selected, as OS is lower than for younger patients.^{6,7,8}
- Stereotactic body radiation therapy (SBRT)/stereotactic ablative radiotherapy (SABR) should be considered for older patients, particularly those with comorbidities or compromised performance status, who may not be suitable for liver resection or transplantation. Because it is noninvasive, the successful completion rate of SBRT/SABR is high.⁹ Toxicity to treatment can be minimized by careful patient selection, appropriate radiation dosing, and optimized dosimetry to meet normal tissue constraints. Ideal patients are those with good liver function (Child Pugh Class A) and limited volume of disease.

Systemic Therapy

In a retrospective analysis of patients with advanced HCC treated with single-agent sorafenib, grade 3 or 4 adverse events and survival outcomes were similar in patients ≥ 70 and < 70 years; however, treatment with sorafenib was associated with increased incidence of grade 3 or 4 neutropenia, malaise, and mucositis in patients ≥ 70 years.¹⁰

(References)

- ¹Kozyreva ON, Chi D, Clark JW, et al. A multicenter retrospective study on clinical characteristics, treatment patterns, and outcome in elderly patients with hepatocellular carcinoma. *Oncologist* 2011;16:310-318.
- ²Mirici-Cappa F, Gramenzi A, Santi V, et al. Treatments for hepatocellular carcinoma in elderly patients are as effective as in younger patients: a 20-year multicentre experience. *Gut* 2010;59:387-396.
- ³Ozanne V, Bouattour M, Goutte N, et al. Prospective evaluation of the management of hepatocellular carcinoma in the elderly. *Dig Liver Dis* 2011; 43:1001-5.
- ⁴Peng ZW, Liu FR, Ye S, et al. Radiofrequency ablation versus open hepatic resection for elderly patients (> 65 years) with very early or early hepatocellular carcinoma. *Cancer* 2013;119(38):12-20.
- ⁵Thornton RH, Covey A, Petre EN, et al. A comparison of outcomes from treating hepatocellular carcinoma by hepatic artery embolization in patients younger or older than 70 years. *Cancer* 2009;115:5000-5006.
- ⁶Kim J, Ko ME, Nelson RA, et al. Increasing age and survival after orthotopic liver transplantation for patients with hepatocellular cancer. *J Am Coll Surg* 2014;218:431-438.
- ⁷Faber W, Stockmann M, Schirmer C, et al. Significant impact of patient age on outcome after liver resection for HCC in cirrhosis. *Eur J Surg Oncol* 2014;40:208-213.
- ⁸Fan HL, Hsieh CB, Chang WC, et al. Advanced age is not a contraindication for liver resection in cases of large hepatocellular carcinoma. *Eur J Surg Oncol* 2014;40:214-219.
- ⁹Bujold A, Massey CA, Kim JJ, et al. Sequential phase I and II trials of stereotactic body radiotherapy for locally advanced hepatocellular carcinoma. *J Clin Oncol* 2013; 31:1631-1639.
- ¹⁰Wong H, Tang YF, Yao TJ, et al. The outcomes and safety of single-agent sorafenib in the treatment of elderly patients with advanced hepatocellular carcinoma (HCC). *Oncologist* 2011;16:1721-1728.

Version 2.2016 © National Comprehensive Cancer Network, Inc. 2016. All rights reserved. The NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN®.

OA0-B
17 OF 32

required a posttreatment increase in corticosteroid dosage (49% vs only 23% of those who received shorter-course RT). In a small randomized study that assessed supportive care alone or in combination with RT (50 Gy in 25 daily fractions) in patients aged 70 years or older ($n=85$), at a median follow-up of 21 weeks, the median survival was longer for those who received supportive care plus postoperative RT compared with supportive care alone (29 and 17 weeks, respectively).²⁵ RT was not associated with severe adverse events and the results of quality-of-life and cognitive evaluations over time also did not differ significantly between the treatment groups.

The NCCN Guidelines Panel recommends that postoperative hypofractionated accelerated-course RT (with the goal of completing treatment in 2–3 weeks) either alone or in combination with concurrent and adjuvant temozolomide is a reasonable treatment option for patients aged 70 years or older with newly diagnosed GBM. Hypofractionated accelerated-course RT with

concurrent and adjuvant temozolomide has been shown to be superior to hypofractionated accelerated-course RT alone in older patients (≥ 65 years) with newly diagnosed GBM.¹⁹ The panel does not recommend withholding temozolomide for older patients with newly diagnosed GBM in the absence of a specific contraindication. MGMT gene promoter methylation status has been identified as a predictive marker for survival benefit in patients treated with temozolomide, which could be useful for the selection of older patients suitable for treatment with temozolomide in combination with RT.^{26–28}

Hepatocellular Carcinoma

Older patients with hepatocellular carcinoma (HCC) may benefit from liver resection or transplantation.^{29–31} Available evidence (primarily from retrospective studies) has shown no major difference in outcomes between carefully selected older patients and younger patients with HCC.^{32–36}

Older Adult Oncology, Version 2.2016

DISEASE-SPECIFIC ISSUES RELATED TO AGE

Non-Small Cell Lung Cancer***Surgery¹⁻⁶**

- Few prospective studies exist.
- Retrospective analyses demonstrate that older patients who are selected for surgery tolerate it well.
- There is caution with pneumonectomy in older adults.

Stereotactic Body Radiation Therapy (SBRT)/Stereotactic Ablative Radiotherapy (SABR)⁷⁻⁹

- SABR (also known as SBRT) is recommended for patients who are medically inoperable or who refuse to have surgery after thoracic surgery evaluation. SABR has achieved primary tumor control rates and OS comparable to lobectomy and higher than 3D-CRT in prospective and population-based comparisons in medically inoperable or older patients.^{7,8} (See NCCN Guidelines for Non-Small Cell Lung Cancer)
- The outcomes in terms of high tumor control and low toxicity are similar in older patients to those reported in younger patients.⁹

Adjuvant Chemotherapy¹⁰⁻¹¹

- The benefits of adjuvant chemotherapy are similar with age.

Locally Advanced Disease¹²⁻¹⁶

- Combined modality therapy: While efficacy is maintained, older adults (especially those with a KPS <90) are more likely to have side effects (ie, esophagitis, pneumonitis, myelosuppression).

Advanced Disease¹⁷⁻²⁷

- As in younger patients, chemotherapy is associated with improved quality of life in comparison to best supportive care.
- Emerging data are confirming the survival benefit of doublet chemotherapy in comparison to single-agent treatment.
- A retrospective subset analysis of ECOG 4599 and a recent SEER-Medicare analysis both suggest that older patients may not benefit from the addition of bevacizumab to carboplatin-paclitaxel.

¹Cangemi V, Volpino P, D'Andrea N, et al. Lung cancer surgery in elderly patients. *Tumori* 1996;82:237-241.

²Naunheim KS, Kesler KA, D'Orazio SA, et al. Lung cancer surgery in the octogenarian. *Eur J Cardiothorac Surg* 1994;8:453-456.

³Jack CI, Lye M, Lesley F, et al. Surgery for lung cancer: age alone is not a contraindication. *Int J Clin Pract* 1997;51:423-426.

⁴Morandi U, Stefani A, Golinelli M, et al. Results of surgical resection in patients over the age of 70 years with non small-cell lung cancer. *Eur J Cardiothorac Surg* 1997;11:432-439.

⁵Ishida T, Yokoyama H, Kaneko S, et al. Long-term results of operation for non-small cell lung cancer in the elderly. *Ann Thorac Surg* 1990;50:919-922.

⁶Mizushima Y, Noto H, Sugiyama S, et al. Survival and prognosis after pneumonectomy for lung cancer in the elderly. *Ann Thorac Surg* 1997;64:193-198.

⁷Palma D, Visser O, Lagerwaard FJ, Belderbos J, Slotman B, Senan S. Treatment of stage I NSCLC in elderly patients: a population-based matched-pair comparison of stereotactic radiotherapy versus surgery. *Radiother Oncol* 2011;101:240-244. doi: 10.1016/j.radonc.2011.06.029. Epub 2011 Jul 19.

⁸Chang JY, Senan S, Paul MA, Mehran RJ, et al. Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials. *Lancet Oncol* 2015;16:630-637.

⁹Samuels Michael A, et al. Stereotactic Body Radiotherapy in Patients With Stage I Non-Small-Cell Lung Cancer Aged 75 Years and Older: Retrospective Results From a Multicenter Consortium. *Clinical Lung Cancer*;14(4):446-451.

Continue

 OAO-B
25 OF 32

Version 2.2016 © National Comprehensive Cancer Network, Inc. 2016. All rights reserved. The NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN®.

Available evidence (primarily from nonrandomized clinical trials and retrospective analyses) supports the use of SBRT in the management of patients with unresectable or locally advanced HCC. In a large prospective series of 102 patients with locally advanced HCC and Child-Pugh A liver function treated in sequential phase I and II trials, SBRT resulted in a 1-year local control rate of 87% and median survival of 17 months.³⁷ Most of these patients were at high risk with relatively advanced-stage tumors. Limited safety data are available in patients with Child-Pugh B or poorer liver function.³⁸⁻⁴¹ The safety of SBRT for patients with Child-Pugh C cirrhosis has not been established. In a retrospective analysis of 185 patients treated with SBRT at 2 different dose levels (40 Gy in 5 fractions for patients with Child-Pugh A liver function and 35 Gy in 5 fractions for those with Child-Pugh B liver function), the 3-year local control and OS rates were 91% and 70%, respectively, with no significant differences in outcomes between dose levels.⁴¹

The panel decided to include a section highlighting the benefit of SBRT for older patients with HCC who may not be able to tolerate liver resection or transplantation and locoregional therapies. The panel recommends that SBRT be considered for those who may not be suitable for liver resection or transplantation due to the presence of comorbidities or compromised performance status. Patients with good liver function (Child-Pugh A) and limited volume of disease are ideal candidates for SBRT, although those with Child-Pugh B cirrhosis can safely be treated with dose modifications and strict dose constraint adherence. Treatment toxicity can be minimized by careful patient selection, appropriate radiation dose, and optimized dosimetry to meet normal tissue constraints.

Lung Cancers

Non-Small Cell Lung Cancer

Surgical resection and mediastinal lymph node dissection is the standard treatment for patients with

DISEASE-SPECIFIC ISSUES RELATED TO AGE

Non-Small Cell Lung Cancer* (continued)

(References)

- ¹⁰Pepe C, Hasan B, Winton TL, et al. Adjuvant vinorelbine and cisplatin in elderly patients: National Cancer Institute of Canada and Intergroup Study JBR.10. *J Clin Oncol* 2007;25:1553-1561.
- ¹¹Ganti AK, Williams CD, Gajra A, Kelley MJ. Effect of age on the efficacy of adjuvant chemotherapy for resected non-small cell lung cancer. *Cancer*. 2015 Aug 1;121(15):2578-85.
- ¹²Movsas B, Scott C, Sause W, et al. The benefit of treatment intensification is age and histology-dependent in patients with locally advanced non-small cell lung cancer (NSCLC): a quality-adjusted survival analysis of radiation therapy oncology group (RTOG) chemoradiation studies. *Int J Radiat Oncol Biol Phys* 1999;45:1143-1149.
- ¹³Werner-Wasik M, Scott C, Cox JD, et al. Recursive partitioning analysis of 1999 Radiation Therapy Oncology Group (RTOG) patients with locally-advanced non-small-cell lung cancer (LA-NSCLC): identification of five groups with different survival. *Int J Radiat Oncol Biol Phys* 2000;48:1475-1482.
- ¹⁴Langer CJ, Hsu C, Curran WJ, et al. Elderly patients (pts) with locally advanced non-small cell lung cancer (LA-NSCLC) benefit from combined modality therapy: secondary analysis of Radiation Therapy Oncology Group (RTOG) 94-10. *Proc Am Soc Clin Oncol* 2002;21:Abstract 1193.
- ¹⁵Schild SE, Stella PJ, Geyer SM, et al. The outcome of combined-modality therapy for stage III non-small-cell lung cancer in the elderly. *J Clin Oncol* 2003;21:3201-3206.
- ¹⁶Atagi S, Kawahara M, Yokoyama A, et al. Thoracic radiotherapy with or without daily low-dose carboplatin in elderly patients with non-small-cell lung cancer: a randomised, controlled, phase 3 trial by the Japan Clinical Oncology Group (JCOG0301). *Lancet* 2012;13(7):671-678.
- ¹⁷Kelly K, Giarritta S, Akerley W, et al. Should older patients (pts) receive combination chemotherapy for advanced stage non-small cell lung cancer (NSCLC)? An analysis of Southwest Oncology Trials 9509 and 9308. *Proc Am Soc Clin Oncol* 2001;20:Abstract 1313.
- ¹⁸Langer CJ, Manola J, Bernardo P, et al. Cisplatin-based therapy for elderly patients with advanced non-small-cell lung cancer: implications of Eastern Cooperative Oncology Group 5592, a randomized trial. *J Natl Cancer Inst* 2002;94:173-181.
- ¹⁹Langer CJ, Vangel M, Schiller J, et al. Age-specific subanalysis of ECOG 1594: Fit elderly patients (70-80 YRS) with NSCLC do as well as younger pts (<70). *Proc Am Soc Clin Oncol* 2003;22:Abstract 2571.
- ²⁰Lilenbaum RC, Herndon JE, List MA, et al. Single-agent versus combination chemotherapy in advanced non-small-cell lung cancer: the cancer and leukemia group B (study 9730). *J Clin Oncol* 2005;23:190-196.
- ²¹Ramalingam SS, Dahlborg SE, Langer CJ, et al; Eastern Cooperative Oncology Group. Outcomes for elderly, advanced-stage non-small-cell lung cancer patients treated with bevacizumab in combination with carboplatin and paclitaxel: analysis of Eastern Cooperative Oncology Group Trial 4599. *J Clin Oncol* 2008;26:60-65.
- ²²Gridelli C. The ELVIS trial: a phase III study of single-agent vinorelbine as first-line treatment in elderly patients with advanced non-small cell lung cancer. Elderly Lung Cancer Vinorelbine Italian Study. *Oncologist* 2001;6 Suppl 1:4-7.
- ²³Frasci G, Lorusso V, Panza N, et al. Gemcitabine plus vinorelbine yields better survival outcome than vinorelbine alone in elderly patients with advanced non-small cell lung cancer. A Southern Italy Cooperative Oncology Group (SICOG) phase III trial. *Lung Cancer* 2001;34 Suppl 4:65-69.
- ²⁴Gridelli C, Perrone F, Gallo C, et al. Chemotherapy for elderly patients with advanced non-small-cell lung cancer: the Multicenter Italian Lung Cancer in the Elderly Study (MILES) phase III randomized trial. *J Natl Cancer Inst* 2003;95:362-372.
- ²⁵Kudo S, Takeda K, Nakagawa K, et al. Phase III study of docetaxel compared with vinorelbine in elderly patients with advanced non-small-cell lung cancer: results of the West Japan Thoracic Oncology Group Trial (WJTOG 9904). *J Clin Oncol* 2006;24:3657-3663.
- ²⁶Quoix E, Zalcman G, Oster JP, et al. Carboplatin and weekly paclitaxel doublet chemotherapy compared with monotherapy in elderly patients with advanced non-small-cell lung cancer: IFCT-0501 randomised, phase 3 trial. *Lancet* 2011;378:1079-1088.
- ²⁷Zhu J, Sharma DB, Gray SW, et al. Carboplatin and paclitaxel with vs. without bevacizumab in older patients with advanced non-small cell lung cancer. *JAMA* 2012;307(15):1593-1601.
- *For comparison of efficacy and toxicity of various targeted therapies between younger and older patients, see Gonsalves W, Ganti AK. Targeted anti-cancer therapy in the elderly. *Crit Rev Oncol Hematol* 2011;78:227-242.

Version 2.2016 © National Comprehensive Cancer Network, Inc. 2016. All rights reserved. The NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN®.

OAO-B
26 OF 32

early stage non-small cell lung cancer (NSCLC). SBRT has recently emerged as an effective treatment option for patients with medically inoperable, early-stage NSCLC, resulting in high rates of local control and OS. The panel reviewed data from retrospective studies and population-based analysis that evaluated the efficacy of SBRT compared with lobectomy in older patients with early-stage NSCLC.⁴²⁻⁴⁴ A SEER database analysis of 9,093 patients (median age, 75 years) compared the outcomes of lobectomy, sublobar resection, or SABR as a definitive treatment for early-stage, node-negative NSCLC.⁴² In the propensity score matching analysis, lobectomy and SABR were associated with similar OS and lung cancer-specific survival, suggesting that SBRT may be a good option among patients with very advanced age and multiple comorbidities. In a multi-institutional retrospective analysis of older patients (≥75 years) treated with SBRT for stage I NSCLC, the outcomes in terms of high tumor control and low toxicity were similar to those reported in younger patients.⁴³ The

results of a pooled analysis of 2 randomized trials (designed to assess the efficacy of SBRT compared with lobectomy for early-stage NSCLC in operable patients, but which closed due to poor accrual) suggest that SBRT could be an alternative option for early-stage NSCLC in patients who are not surgical candidates. In the intent-to-treat analysis of 58 patients randomly assigned to SBRT and surgery, the estimated 3-year OS rate was 95% in the SBRT group compared with 79% in the surgery group ($P=.037$). The 3-year recurrence-free survival rates were 86% and 80%, respectively ($P=.54$).⁴⁴ Based on these findings, the panel recommends SBRT for patients who are medically inoperable or who decline to have surgery after thoracic surgery evaluation.

In older patients with locally advanced NSCLC, combined modality therapy (concurrent chemotherapy with RT given once or twice daily) has resulted in disease control and survival rates similar to those observed in younger patients; however, toxicities (esophagitis, pneumonitis, and

Older Adult Oncology, Version 2.2016

DISEASE-SPECIFIC ISSUES RELATED TO AGE

Small Cell Lung Cancer

- Available data suggest that older adults derive benefit from standard doses of combination systemic chemotherapy (platinum and etoposide); however, toxicity related to bone marrow suppression is higher.^{1,2}
- Attenuated doses of chemotherapy are associated with inferior outcomes and should be avoided if possible.¹
- Cisplatin and carboplatin appear to have similar efficacy in the first-line treatment of small cell lung cancer. However, toxicity profiles are different, with carboplatin having a higher hematologic toxicity and cisplatin having a higher non-hematologic toxicity.³
- Age-related subset analyses of cisplatin + etoposide and concurrent external beam radiation therapy demonstrate similar response rates between older and younger patients, but older adults are at risk for increased toxicity (ie, myelosuppression, esophagitis, pneumonitis) and increased rate of treatment-related deaths (1% vs. 3% in NCCTG; 1% vs. 10% in INT 0096). Despite this, OS appears to be similar in both age groups.^{4,5}

Prophylactic Cranial Irradiation

- Patients 70 years and older with extensive stage and response to chemotherapy may benefit from prophylactic cranial irradiation (PCI), with improved OS.⁶ Other studies have also suggested a benefit from PCI in patients with limited stage and good response after chemotherapy, without differences in risk reduction by age. However, PCI is associated with more adverse events and increased neurotoxicity in older patients compared to younger patients.^{7,8} PCI is not recommended in patients with poor performance status or impaired neurocognitive functioning.

¹Ardizzone A, Favaretto A, Boni L, et al. Platinum-etoposide chemotherapy in elderly patients with small-cell lung cancer: results of a randomized multicenter phase II study assessing attenuated-dose or full-dose with lenograstim prophylaxis—a Forza Operativa Nazionale Italiana Carcinoma Polmonare and Gruppo Studio Tumori Polmonari Veneto (FONICAPGSTPV) study. *J Clin Oncol* 2005;23:569-575.

²Capraro LC, Kent DM, Trikalinos TA, Strauss GM. Determinants of chemotherapy administration and effects of chemotherapy on survival in elderly patients with small cell lung cancer (SCLC): A SEER-Medicare analysis. *J Clin Oncol* 2011;29:7083.

³Rossi A, Di Maio M, Chiodini P, et al. Carboplatin- or cisplatin-based chemotherapy in first-line treatment of small-cell lung cancer: the COCIS meta-analysis of individual patient data. *J Clin Oncol* 2012;30:1692-1698.

⁴Yuen AR, Zou G, Turrisi AT, et al. Similar outcome of elderly patients in intergroup trial 0096: Cisplatin, etoposide, and thoracic radiotherapy administered once or twice daily in limited stage small cell lung carcinoma. *Cancer* 2000;89:1953-1960.

⁵Schild SE, Stella PJ, Brooks BJ, et al. Results of combined-modality therapy for limited-stage small cell lung carcinoma in the elderly. *Cancer* 2005;103:2349-2354.

⁶Rule WG, Foster NR, Meyers JP, et al. Prophylactic cranial irradiation in elderly patients with small cell lung cancer: findings from a North Central Cancer Treatment Group pooled analysis. *J Geriatr Oncol* 2015;6(2):119-126.

⁷Wolfson AH, Bae K, Komaki R, et al. Primary analysis of a phase II randomized trial Radiation Therapy Oncology Group (RTOG) 0212: impact of different total doses and schedules of prophylactic cranial irradiation on chronic neurotoxicity and quality of life for patients with limited-disease small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2011;81(1):77-84.

⁸Le Pechoux C, Laplanche A, Faivre-Finn C, et al. Clinical neurological outcome and quality of life among patients with limited small-cell cancer treated with two different doses of prophylactic cranial irradiation in the intergroup phase III trial (PCI99-01, EORTC 22003-08004, RTOG 0212 and IFCT 99-01). *Ann Oncol* 2011;22(5):1154-1163.

myelosuppression) were more pronounced in older patients, especially in those with poor performance status.^{45,46} Combined modality therapy is therefore an effective treatment option for selected fit older patients with locally advanced disease; however, careful attention to the management of toxicities is needed.

Small Cell Lung Cancer

Combined modality therapy is the recommended treatment for patients with limited-stage disease, whereas chemotherapy alone is the standard treatment option for patients with extensive-stage disease. Prophylactic cranial irradiation (PCI) is effective in decreasing the incidence of cerebral metastases in patients with SCLC (limited and extensive stage) responding to initial chemotherapy. A recent report from a pooled analysis of 4 prospective trials showed that PCI was also associated with significant improvement in survival among older patients (aged ≥70 years) with SCLC,

and the survival advantage was more significant in patients with extensive-stage SCLC.⁴⁷ However, PCI is also associated with more adverse events and increased neurotoxicity in older patients compared with younger patients, with older age being the most significant predictor of chronic neurotoxicity.^{48,49}

The panel concluded that patients aged 70 years and older with extensive-stage SCLC that responds to chemotherapy may benefit from PCI. However, given the strong relationship between declining cognitive function and age, the panel emphasized that patients with poor performance status or impaired neurocognitive functioning should not be treated with PCI.

Prostate Cancer

The use of long-term androgen deprivation therapy (ADT) in combination with RT is an effective treatment option (associated with improved cancer-specific survival and OS) for all patients with high-

DISEASE-SPECIFIC ISSUES RELATED TO AGE

Prostate Cancer

- For treatment of clinically localized or locally advanced prostate cancer, see the NCCN Guidelines for Prostate Cancer.
- In men of advanced age with high-risk prostate cancer and moderate-to-severe comorbidity, shorter course (4–6 months) of androgen deprivation therapy (ADT) with RT can be considered over longer course (28–36 months).^{1,4}
- There are no significant age-related differences in docetaxel efficacy in patients with castration-recurrent prostate cancer. Every-3-week dosing remains the preferred method for fit older patients who should be monitored closely for toxicity. Growth factor support should be considered in patients 65 years or older to decrease the risk of neutropenic complications.^{5,6,7} See the NCCN Guidelines for Myeloid Growth Factors.
- There are no age-related differences in cabazitaxel efficacy in patients with castration-recurrent prostate cancer. Growth factor support is strongly recommended in patients 65 years or older to decrease the risk of neutropenic complications in older patients.^{8,9} See the NCCN Guidelines for Myeloid Growth Factors.
- ADT is associated with an increased risk of fracture. Attention to bone health is warranted.¹⁰ ADT significantly decreases muscle mass, and treatment-related sarcopenia appears to contribute to frailty and increased risk of falls in older men.^{11,12} See the NCCN Guidelines for Prostate Cancer.
- In older adults, newer hormonal therapies can potentially replace or delay the usage of cytotoxic chemotherapy and may be used in patients who would otherwise be ineligible for chemotherapy.

¹Piccirillo JF, Vlahiotis A, Barrett LB, Flood KL, Spitznagel EL, Steyerberg EW. The changing prevalence of comorbidity across the age spectrum. *Crit Rev Oncol Hematol* 2008;67(2):124–32.

²Thompson IM, Ankerst DP, Chi C, et al. Assessing prostate cancer risk: results from the Prostate Cancer Prevention Trial. *J Natl Cancer Inst* 2006;98(8):529–34.

³D'Amico AV, Chen MH, Renshaw AA, Loffredo M, Kantoff PW. Androgen suppression and radiation vs radiation alone for prostate cancer: a randomized trial. *JAMA* 2008;299(3):289–95.

⁴D'Amico AV, Renshaw AA, Loffredo B, Chen MH. Duration of testosterone suppression and the risk of death from prostate cancer in men treated using radiation and 6 months of hormone therapy. *Cancer* 2007;110(8):1723–1728.

⁵Tannock IF, de Wit R, Berry WR, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. *N Engl J Med* 2004;351:1502–1512.

⁶Sinibaldi VJ. Docetaxel treatment in the elderly patient with hormone refractory prostate cancer. *Clin Interv Aging* 2007;2:555–560.

⁷Horgan AM, Seruga B, Pond GR, et al. Tolerability and efficacy of docetaxel in older men with metastatic castrate-resistant prostate cancer (mCRPC) in the TAX 327 trial. *J Geriatr Oncol* 2014;5:119–126.

⁸Pal SK, Twardowski P, Sartor O. Critical appraisal of cabazitaxel in the management of advanced prostate cancer. *Clin Interv Aging* 2010;5:395–402.

⁹de Bono JS, Oudard S, Ozguroglu M, et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. *Lancet* 2010;376:1147–1154.

¹⁰Shahinian VB, Kuo YF, Freeman JL, Goodwin JS. Risk of fracture after androgen deprivation for prostate cancer. *N Engl J Med* 2005;352(2):154–164.

¹¹Smith MR, Finkelstein JS, McGovern FJ, et al. Changes in body composition during androgen deprivation therapy for prostate cancer. *J Clin Endocrinol Metab* 2002;87(2):599–603.

¹²Bylow K, Dale W, Mustian K, et al. Falls and physical performance deficits in older patients with prostate cancer undergoing androgen deprivation therapy. *Urology* 2008;72(2):422–427.

Version 2.2016 © National Comprehensive Cancer Network, Inc. 2016. All rights reserved. The NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN®.

OA0-B
32 OF 32

risk prostate cancer. However, the significant side effects of long-term ADT (increased risk of fracture due to osteoporosis, glucose intolerance, and thromboembolic events) are of particular concern in older men, who often present with multiple comorbidities.^{50–52} The efficacy of short-course ADT (4–6 months) in combination with RT for locally advanced prostate cancer has also been demonstrated in randomized clinical trials.^{53–56} In one randomized trial (that also assessed the interaction between the level of comorbidity and treatment), the survival benefit associated with the addition of 6 months of ADT to RT was restricted only to men without moderate or severe comorbidity.⁵³ A report from another study also suggests that a 6-month course of ADT produces long-term testosterone suppression, which may provide the cancer-specific survival benefit observed with long-term hormonal therapy in men of advanced age.⁵⁷

Based on these findings, the panel concluded that for men of advanced age with high-risk prostate

cancer and moderate-to-severe comorbidity, a shorter course (4–6 months) of ADT with RT can be considered over a longer course (28–36 months).

NCCN Recommendations

The decision to offer RT to older patients with cancer should be based on the following factors: (1) evaluation of the benefits and risks associated with RT; (2) careful consideration of the patient's underlying functional reserve; and (3) an understanding of the differences in the biology of cancers and their responsiveness to therapy in this patient population. Treatment should be individualized based on the nature of the disease and the performance status of the patient.

- Omission of RT (after lumpectomy with negative margins) can be considered for selected older women with stage I estrogen receptor-positive breast cancer who are likely to complete 5 years of endocrine therapy.

Older Adult Oncology, Version 2.2016

- Hypofractionated accelerated-course RT (either alone or in combination with concurrent and adjuvant temozolomide) is a reasonable treatment option for patients aged 70 years or older with newly diagnosed GBM. Hypofractionated accelerated-course RT with concurrent and adjuvant temozolomide is superior to hypofractionated accelerated-course RT alone in older patients (≥ 65 years) with newly diagnosed GBM.
- SBRT should be considered for older patients with HCC, particularly for those with comorbidities or a compromised performance status, who may not be suitable for liver resection or transplantation and locoregional therapies.
- SBRT is also recommended for early-stage NSCLC in older patients who are medically inoperable or who decline to have surgery after thoracic surgery evaluation.
- Older patients with extensive-stage SCLC and response to chemotherapy may benefit from PCI; however, it should not be used for patients with poor performance status or impaired neurocognitive functioning.
- Shorter-course ADT with RT can be considered over longer-course ADT in older men with high-risk prostate cancer and moderate-to-severe comorbidity.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA Cancer J Clin* 2016;66:7–30.
2. Altekruse SF, Krapcho M, Neyman N, et al, eds. SEER Cancer Statistics Review, 1975–2007: National Cancer Institute. Bethesda, MD, based on November 2009 SEER data submission, posted to the SEER web site, 2010. Available at: http://seer.cancer.gov/csr/1975_2007/. Accessed October 12, 2016.
3. Smith BD, Smith GL, Hurria A, et al. Future of cancer incidence in the United States: burdens upon an aging, changing nation. *J Clin Oncol* 2009;27:2758–2765.
4. Talarico L, Chen G, Pazdur R. Enrollment of elderly patients in clinical trials for cancer drug registration: a 7-year experience by the US Food and Drug Administration. *J Clin Oncol* 2004;22:4626–4631.
5. Balducci L. Management of cancer in the elderly. *Oncology (Williston Park)* 2006;20:135–143.
6. Saltzstein SL, Behling CA. 5- and 10-year survival in cancer patients aged 90 and older: a study of 37,318 patients from SEER. *J Surg Oncol* 2002;81:113–116; discussion 117.
7. Extermann M. Management issues for elderly patients with breast cancer. *Curr Treat Options Oncol* 2004;5:161–169.
8. Zachariah B, Balducci L. Radiation therapy of the older patient. *Hematol Oncol Clin North Am* 2000;14:131–167.
9. Smith GL, Smith BD. Radiation treatment in older patients: a framework for clinical decision making. *J Clin Oncol* 2014;32:2669–2678.
10. Zachariah B, Balducci L, Venkattaramanabalaaji GV, et al. Radiotherapy for cancer patients aged 80 and older: a study of effectiveness and side effects. *Int J Radiat Oncol Biol Phys* 1997;39:1125–1129.
11. Mitsuhashi N, Hayakawa K, Yamakawa M, et al. Cancer in patients aged 90 years or older: radiation therapy. *Radiology* 1999;211:829–833.
12. Wasil T, Lichtman SM, Gupta V, Rush S. Radiation therapy in cancer patients 80 years of age and older. *Am J Clin Oncol* 2000;23:526–530.
13. Kunkler IH, Audisio R, Belkacemi Y, et al. Review of current best practice and priorities for research in radiation oncology for elderly patients with cancer: the International Society of Geriatric Oncology (SIOG) task force. *Ann Oncol* 2014;25:2134–2146.
14. Donato V, Valeriani M, Zurlo A. Short course radiation therapy for elderly cancer patients. Evidences from the literature review. *Crit Rev Oncol Hematol* 2003;45:305–311.
15. Hughes KS, Schnaper LA, Berry D, et al. Lumpectomy plus tamoxifen with or without irradiation in women 70 years of age or older with early breast cancer. *N Engl J Med* 2004;351:971–977.
16. Hughes KS, Schnaper LA, Bellon JR, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343. *J Clin Oncol* 2013;31:2382–2387.
17. Kunkler IH, Williams LJ, Jack WJ, et al. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial. *Lancet Oncol* 2015;16:266–273.
18. Stupp R, Hegi M, Mason W, et al. Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomized phase III study: 5-year analysis of the EORTC-NCIC trial. *Lancet Oncol* 2009;10:459–466.
19. Perry JR, Laperriere N, O'Callaghan CJ, et al. A phase III randomized controlled trial of short-course radiotherapy with or without concomitant and adjuvant temozolomide in elderly patients with glioblastoma (CCTG CE.6, EORTC 26062-22061, TROG 08.02, NCT00482677) [abstract]. *J Clin Oncol* 2016;34(18 Suppl):Abstract LBA2.
20. Minniti G, Lanzetta G, Scaringi C, et al. Phase II study of short-course radiotherapy plus concomitant and adjuvant temozolomide in elderly patients with glioblastoma. *Int J Radiat Oncol Biol Phys* 2012;83:93–99.
21. Behm T, Horowski A, Schneider S, et al. Concomitant and adjuvant temozolomide of newly diagnosed glioblastoma in elderly patients. *Clin Neurol Neurosurg* 2013;115:2142–2146.
22. Minniti G, Scaringi C, Lanzetta G, et al. Standard (60 Gy) or short-course (40 Gy) irradiation plus concomitant and adjuvant temozolomide for elderly patients with glioblastoma: a propensity-matched analysis. *Int J Radiat Oncol Biol Phys* 2015;91:109–115.
23. Arvold ND, Tanguturi SK, Aizer AA, et al. Hypofractionated versus standard radiation therapy with or without temozolomide for older glioblastoma patients. *Int J Radiat Oncol Biol Phys* 2015;92:384–389.
24. Roa W, Brasher PM, Bauman G, et al. Abbreviated course of radiation therapy in older patients with glioblastoma multiforme: a prospective randomized trial. *J Clin Oncol* 2004;22:1583–1588.
25. Keime-Guibert F, Chinot O, Taillandier L, et al. Radiotherapy for glioblastoma in the elderly. *N Engl J Med* 2007;356:1527–1535.
26. Minniti G, Salvati M, Arcella A, et al. Correlation between O6-methylguanine-DNA methyltransferase and survival in elderly patients with glioblastoma treated with radiotherapy plus concomitant and adjuvant temozolomide. *J Neurooncol* 2011;102:311–316.
27. Wick W, Platten M, Meisner C, et al. Temozolomide chemotherapy alone versus radiotherapy alone for malignant astrocytoma in the elderly: the NOA-08 randomised, phase 3 trial. *Lancet Oncol* 2012;13:707–715.
28. Malmstrom A, Gronberg BH, Marosi C, et al. Temozolomide versus standard 6-week radiotherapy versus hypofractionated radiotherapy in patients older than 60 years with glioblastoma: the Nordic randomised, phase 3 trial. *Lancet Oncol* 2012;13:916–926.
29. Kim J, Ko ME, Nelson RA, et al. Increasing age and survival after orthotopic liver transplantation for patients with hepatocellular cancer. *J Am Coll Surg* 2014;218:431–438.
30. Faber W, Stockmann M, Schirmer C, et al. Significant impact of patient age on outcome after liver resection for HCC in cirrhosis. *Eur J Surg Oncol* 2014;40:208–213.
31. Fan HL, Hsieh CB, Chang WC, et al. Advanced age is not a contraindication for liver resection in cases of large hepatocellular carcinoma. *Eur J Surg Oncol* 2014;40:214–219.
32. Thornton RH, Covey A, Petre EN, et al. A comparison of outcomes from treating hepatocellular carcinoma by hepatic artery embolization in patients younger or older than 70 years. *Cancer* 2009;115:5000–5006.
33. Mirici-Cappa F, Gramenzi A, Santi V, et al. Treatments for hepatocellular carcinoma in elderly patients are as effective as in younger patients: a 20-year multicentre experience. *Gut* 2010;59:387–396.

Older Adult Oncology, Version 2.2016

34. Kozyreva ON, Chi D, Clark JW, et al. A multicenter retrospective study on clinical characteristics, treatment patterns, and outcome in elderly patients with hepatocellular carcinoma. *Oncologist* 2011;16:310–318.
35. Ozenne V, Bouattour M, Goutte N, et al. Prospective evaluation of the management of hepatocellular carcinoma in the elderly. *Dig Liver Dis* 2011;43:1001–1005.
36. Peng ZW, Liu FR, Ye S, et al. Radiofrequency ablation versus open hepatic resection for elderly patients (> 65 years) with very early or early hepatocellular carcinoma. *Cancer* 2013;119:3812–3820.
37. Bujold A, Massey CA, Kim JJ, et al. Sequential phase I and II trials of stereotactic body radiotherapy for locally advanced hepatocellular carcinoma. *J Clin Oncol* 2013;31:1631–1639.
38. Tse RV, Hawkins M, Lockwood G, et al. Phase I study of individualized stereotactic body radiotherapy for hepatocellular carcinoma and intrahepatic cholangiocarcinoma. *J Clin Oncol* 2008;26:657–664.
39. Cardenes HR, Price TR, Perkins SM, et al. Phase I feasibility trial of stereotactic body radiation therapy for primary hepatocellular carcinoma. *Clin Transl Oncol* 2010;12:218–225.
40. Andolino DL, Johnson CS, Maluccio M, et al. Stereotactic body radiotherapy for primary hepatocellular carcinoma. *Int J Radiat Oncol Biol Phys* 2011;81:e447–453.
41. Sanuki N, Takeda A, Oku Y, et al. Stereotactic body radiotherapy for small hepatocellular carcinoma: a retrospective outcome analysis in 185 patients. *Acta Oncol* 2014;53:399–404.
42. Palma D, Visser O, Lagerwaard FJ, et al. Treatment of stage I NSCLC in elderly patients: a population-based matched-pair comparison of stereotactic radiotherapy versus surgery. *Radiother Oncol* 2011;101:240–244.
43. Samuels MA, Kandula S, Koru-Sengul T, et al. Stereotactic body radiotherapy in patients with stage I non-small-cell lung cancer aged 75 years and older: retrospective results from a multicenter consortium. *Clin Lung Cancer* 2013;14:446–451.
44. Chang JY, Senan S, Paul MA, et al. Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials. *Lancet Oncol* 2015;16:630–637.
45. Schild SE, Stella PJ, Geyer SM, et al. The outcome of combined-modality therapy for stage III non-small-cell lung cancer in the elderly. *J Clin Oncol* 2003;21:3201–3206.
46. Atagi S, Kawahara M, Yokoyama A, et al. Thoracic radiotherapy with or without daily low-dose carboplatin in elderly patients with non-small-cell lung cancer: a randomised, controlled, phase 3 trial by the Japan Clinical Oncology Group (JCOG0301). *Lancet Oncol* 2012;13:671–678.
47. Rule WG, Foster NR, Meyers JP, et al. Prophylactic cranial irradiation in elderly patients with small cell lung cancer: findings from a North Central Cancer Treatment Group pooled analysis. *J Geriatr Oncol* 2015;6:119–126.
48. Wolfson AH, Bae K, Komaki R, et al. Primary analysis of a phase II randomized trial Radiation Therapy Oncology Group (RTOG) 0212: impact of different total doses and schedules of prophylactic cranial irradiation on chronic neurotoxicity and quality of life for patients with limited-disease small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2011;81:77–84.
49. Le Pechoux C, Laplanche A, Faivre-Finn C, et al. Clinical neurological outcome and quality of life among patients with limited small-cell cancer treated with two different doses of prophylactic cranial irradiation in the intergroup phase III trial (PCI99-01, EORTC 22003-08004, RTOG 0212 and IFCT 99-01). *Ann Oncol* 2011;22:1154–1163.
50. Shahinian VB, Kuo YF, Freeman JL, Goodwin JS. Risk of fracture after androgen deprivation for prostate cancer. *N Engl J Med* 2005;352:154–164.
51. Keating NL, O'Malley AJ, Smith MR. Diabetes and cardiovascular disease during androgen deprivation therapy for prostate cancer. *J Clin Oncol* 2006;24:4448–4456.
52. Ehdai B, Atoria CL, Gupta A, et al. Androgen deprivation and thromboembolic events in men with prostate cancer. *Cancer* 2012;118:3397–3406.
53. D'Amico AV, Chen MH, Renshaw AA, et al. Androgen suppression and radiation vs radiation alone for prostate cancer: a randomized trial. *JAMA* 2008;299:289–295.
54. Roach M, Bae K, Speight J, et al. Short-term neoadjuvant androgen deprivation therapy and external-beam radiotherapy for locally advanced prostate cancer: long-term results of RTOG 8610. *J Clin Oncol* 2008;26:585–591.
55. Denham JW, Steigler A, Lamb DS, et al. Short-term neoadjuvant androgen deprivation and radiotherapy for locally advanced prostate cancer: 10-year data from the TROG 96.01 randomised trial. *Lancet Oncol* 2011;12:451–459.
56. Jones CU, Hunt D, McGowan DG, et al. Radiotherapy and short-term androgen deprivation for localized prostate cancer. *N Engl J Med* 2011;365:107–118.
57. D'Amico AV, Renshaw AA, Loffredo B, Chen MH. Duration of testosterone suppression and the risk of death from prostate cancer in men treated using radiation and 6 months of hormone therapy. *Cancer* 2007;110:1723–1728.

Instructions for Completion

To participate in this journal CE activity: 1) review the learning objectives and author disclosures; 2) study the education content; 3) take the posttest with a 66% minimum passing score and complete the evaluation at <http://education.nccn.org/node/79757>; and 4) view/print certificate. After reading the article, you should be able to answer the following multiple-

choice questions. Credit cannot be obtained for tests completed on paper. You must be a registered user on NCCN.org. If you are not registered on NCCN.org, click on “New Member? Sign up here” link on the left hand side of the Web site to register. Only one answer is correct for each question. Once you successfully answer all posttest questions you will be able to view and/or print your certificate. Software requirements: Internet

Posttest Questions

1. Which of the following options are recommended by the NCCN Guidelines for older men with high-risk prostate cancer and moderate-to-severe comorbidity?
 - a. Long-term ADT and RT
 - b. Shorter course ADT with RT
 - c. Long-term ADT
 - d. Shorter course ADT
2. True or False: Hypofractionated accelerated-course RT (alone or in combination with concurrent and adjuvant temozolomide) is a reasonable treatment option for older patients with newly diagnosed GBM.

3. Which of the following older patients are considered suitable candidates for SBRT?

- a. Older patients with HCC who may not be suitable for liver resection or transplantation and locoregional therapies (due to the presence of comorbidities or compromised performance status)
- b. Older patients with early-stage NSCLC who are medically inoperable or who decline to have surgery
- c. A and B
- d. Older patients with extensive-stage SCLC