A round-up of ASCO's 2013-2014 guideline releases, updates, and endorsements

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During the past year, the American Society of Clinical Oncology (ASCO) has published 7 special articles that create, update, or endorse clinical practice guidelines. All 7 articles are the subject of this month's review.

Follow-up care, surveillance, and secondary prevention measures for survivors of colorectal cancer[1, 2]

Since 2006, ASCO has adopted a policy of endorsing clinical practice guidelines developed by others in order to increase the number of such guidelines available for ASCO membership. Recently, the society endorsed the guidelines for colon cancer follow-up created by the Cancer Care Ontario (CCO). These guidelines include surveillance recommendations that are very similar to the 2005 ASCO guidelines and the current NCCN guidelines, with a few minor differences. However, unlike NCCN and previous ASCO guidelines, the current guidelines include statements about secondary prevention, written survivorship plans for the patient's other providers, and the futility of surveillance tests in patients who are not candidates for surgery or systemic therapy due to comorbid disease.

Which of the following was specifically recommended in the endorsed CCO guidelines for the follow-up care of patients with colon cancer:

a) PET/CT chest, abdomen, and pelvis annually
b) Complete blood count (CBC) and liver function tests
c) Chest X-ray
d) Maintaining healthy body weight, physical activity, and eating a healthy diet

Key points

The current ASCO-endorsed guidelines (as well as those of the NCCN) specifically recommend against the use of PET scans for surveillance after colon cancer treatment outside of a clinical trial because of lack of evidence and the danger of false positives. Likewise, the routine chest X-ray has little use when CT scans of the chest are being done periodically.

Routine laboratory studies other than the carcinoembryonic antigen (CEA) blood test, such as CBC and liver function tests have not been recommended since before 2005. Finally, the current guidelines recommend secondary prevention efforts such as maintaining body weight, physical activity, and a healthy diet, although there is little high-quality evidence for these behaviors.

Answer: d

Sentinel lymph node biopsy for women with early-stage breast cancer[3,4]

Since the 2005 ASCO guidelines for sentinel node biopsy were published, there have been 9 randomized clinical trials and 13 cohort studies pertinent to the issue of sentinel node biopsy (SLB) and axillary node dissection (ALND) available for expert panel review. The current version includes some changes in the standard of care. A direct comparison of the 2005 and 2014 recommendations is online.

Sentinel node biopsy should be offered to women with breast cancer in the following circumstances:

a) Operable breast cancer and multicentric disease
b) Large or locally advanced breast cancer
c) Pregnant women with breast cancer
d) DCIS in women undergoing breast conservation and radiation therapy

Axillary lymph node dissection should be performed in:

a) Women with 1-2 sentinel lymph nodes who are being treated with breast conservation and whole breast radiation therapy.
b) Women without sentinel node metastases.

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c) Women with sentinel node metastases who are being treated with mastectomy.
d) Women with DCIS

Key points
According to the guidelines, women may be not be candidates for SLB if they have DCIS and are undergoing breast conservation and radiation therapy, because of a lack of evidence about its efficacy and concerns about lymphedema. Likewise, there is insufficient evidence to justify SLB in women with large and locally advanced invasive tumors, inflammatory breast cancer, and in pregnancy. However, there is moderately strong evidence to support SLB in women with multicentric tumors.

Review of the literature and analysis has led to strong recommendations for not performing ALND in women with negative SLB, in those with DCIS, and even in those with 1 or 2 SLN metastases, based on recent trials. However, ALND is recommended in women being treated with mastectomy who had positive SLB.

Answers: a and c, respectively

Margins for breast-conserving surgery with whole-breast irradiation in stage I and II invasive breast cancer[5-7]

A multidisciplinary consensus panel review reviewed data from 33 studies comprising 28,162 patients and analyzed the surgical margin and its relationship to the development of ipsilateral breast cancer recurrence. The consensus guideline developed by the Society of Surgical Oncology and the American Society for Radiation Oncology was endorsed by ASCO. The results are practice changing, and this new standard for the adequate margin for invasive cancer should reduce re-excision rates and health care costs, as well as improve overall cosmetic results.

Surgical margins for the lumpectomy specimen for women undergoing breast-conserving surgery with whole-breast radiation should be (include all that are correct):
a) No ink on tumor
b) 2 mm
c) Wider in younger women, especially under age 30
d) Wider margins for extensive intraductal component to the cancer

Key points
For women choosing breast conserving surgery with whole breast irradiation instead of modified radical mastectomy, the surgical margin may be a determining factor in the risk of ipsilateral breast cancer recurrence. A positive margin, defined as ink on tumor, is associated with a twofold increase in breast cancer recurrence which is not improved by a boost of radiation therapy, systemic adjuvant therapy, or clinical factors such as favorable biology. Moreover, results are not improved by re-excising for wider margins compared to negative margins as defined by no ink on tumor. This applies to patients who are younger than 40, those with increased intraductal component to the tumor, and those with higher grade tumors biologically. Implementation of these new guidelines will result in a decrease in re-excision rates, which will improve cosmetic results, and a reduction in overall health care costs.

Answer: a only

Adjuvant endocrine therapy for women with hormone receptor–positive breast cancer[8-11]

In late May 2014, the Journal of Clinical Oncology published a focused update of the previous guidelines and updates that had been published in 2002, 2003, 2004, and 2010. However, even this, the most recent guideline for adjuvant endocrine therapy of early breast cancer, is already somewhat out of date because of recent data. The early results of the SOFT/TEXT trials presented at ASCO 2014 and recently published, provided a new option for premenopausal women – exemestane plus ovarian ablation.

According to the guidelines, which of the following is not currently a recommended adjuvant hormonal therapy for a menopausal woman:
a) Tamoxifen for 10 years
b) Aromatase inhibitor for 5 years
c) Tamoxifen for 5 years, followed by an aromatase inhibitor for 5 years
d) Tamoxifen for 2-3 years, followed by an aromatase inhibitor for up to 5 years for up to a total of 8 years
e) Aromatase inhibitor for 10 years

Key points
For postmenopausal women, the guideline recommendations have changed since the publication of the ATLAS trial earlier this year. For women who received tamoxifen for an initial 5-year course, a decision must be made as to whether to administer another 5 years of tamoxifen or switch the patient to an aromatase inhibitor for 5 years. Either course of action is acceptable according to the new guidelines. For those women who had already received tamoxifen for 2-3 years, aromatase inhibitor may be given for up to 5 years, for a total of up to 8 years of endocrine therapy.

There are insufficient data to recommend an aromatase inhibitor for longer than 5 years, either as initial therapy or following tamoxifen. For patients who begin their therapy with an aromatase inhibitor, but are intolerant and cannot

complete 5 years, tamoxifen may be given to complete a total of 5 years.

Answer, e

Screening, assessment, and management of fatigue in adult survivors of cancer[12]

Most cancer patients will experience fatigue during their treatment, and almost one-third will continue to complain for years after treatment. For the current ASCO fatigue guideline, adaptation methodology was used to adapt already existing guidelines from the pan-Canadian and NCCN guidelines for screening, assessment and care of cancer-related fatigue plus the NCCN guidelines for survivorship.

Which of the following does not reduce fatigue in cancer survivors?
a) Modafinil
b) Mindfulness-based intervention
c) Cognitive behavior therapy
d) Maintaining physical activity

Key points
There are conflicting reports of the usefulness of psychostimulants in cancer patients, with recent randomized trials being more negative than positive. However, there is scant evidence that such drugs are useful to treat fatigue in cancer survivors. Other psychosocial interventions, including mindfulness-based intervention and cognitive behavioral therapy as well as initiating and maintaining physical activity have been proven to be useful.

Answer, a

Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers[13]

For guideline development, 48 randomized clinical trials published over a period of 23 years were drawn from 1,252 potential citations. Each trial was assessed for study quality, and usefulness of pharmacologic agents in prevention or treatment of chemotherapy-induced neuropathy.

With of the following ameliorates the symptoms of chemotherapy-induced neuropathy?
a) Duloxitine
b) Acetyl-L-carnitine
c) Lamotrigine
d) Calcium and magnesium infusions

Key points
After careful evaluations of the current evidence, the ASCO panel found no evidence for the efficacy of any neuroprotective agents, although there was intriguing evidence for a benefit for venlafaxine from a small study, but not enough to recommend yet. Larger trials of this agent were recommended. For treatment of existing neuropathy only duloxetine could be recommended, particularly for oxaliplatin neuropathy. Calcium and magnesium infusions were thought to protect from neuropathy in early studies, but subsequent confirmatory trials were negative. Acetyl-L carnitine and lamotrigine have been found to have no benefit in phase 3 studies.

Answer: a

Systemic therapy for patients with advanced human epidermal growth factor receptor 2-positive breast cancer[14]

ASCO has created a new guideline for the treatment of metastatic disease in the HER2-positive patient, and includes recommendations based on data for newer agents that have been recently approved including pertuzumab and emtansine (T-DM1). New first-, second-, and third-line recommendations are offered, as well as guidance about the use of hormone therapy in such patients.

Appropriate choices for the third-line treatment metastatic breast cancer in a woman with HER2-positive and ER-positive disease includes all *except:*
a) Emtansine (T-DM1)
b) Pertuzumab
c) Lapatinib + capecitabine
d) Hormonal therapy
e) Chemotherapy

Key points
According to the guidelines, third-line therapy for patients with HER-2 positive breast cancer includes T-DM1 or pertuzumab for those who haven't yet received these agents, lapatinib plus capecitabine, lapatinib and trastuzumab, hormonal therapy with or without an HER2-targeted therapy if the tumor was ER positive. Chemotherapy alone without HER2-targeted therapy was not recommended.

Answer: e

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