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ASCO SPECIAL ARTICLE

Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update

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Editor's note: This American Society of Clinical Oncology (ASCO) Clinical Practice Guideline provides recommendations, with comprehensive review and analyses of the relevant literature for each recommendation. Additional information, including an abbreviated Data Supplement with new studies, a Methodology Supplement, slide sets, clinical tools and resources, and links to patient information at www.cancer.net, is available at www.asco.org/survivorship-guidelines.

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ABSTRACT

Purpose
To provide current recommendations about fertility preservation for adults and children with cancer.

Methods
A systematic review of the literature published from January 2013 to March 2017 was completed using PubMed and the Cochrane Library. An Update Panel reviewed the identified publications.

Results
There were 61 publications identified and reviewed. None of these publications prompted a significant change in the 2013 recommendations.

Recommendations
Health care providers should initiate the discussion on the possibility of infertility with patients with cancer treated during their reproductive years or with parents/guardians of children as early as possible. Providers should be prepared to discuss fertility preservation options and/or to refer all potential patients to appropriate reproductive specialists. Although patients may be focused initially on their cancer diagnosis, providers should advise patients regarding potential threats to fertility as early as possible in the treatment process so as to allow for the widest array of options for fertility preservation. The discussion should be documented. Sperm, oocyte, and embryo cryopreservation are considered standard practice and are widely available. There is conflicting evidence to recommend gonadotrophin-releasing hormone agonists (GnRHa) and other means of ovarian suppression for fertility preservation. The Panel recognizes that, when proven fertility preservation methods are not feasible, and in the setting of young women with breast cancer, GnRHa may be offered to patients in the hope of reducing the likelihood of chemotherapy-induced ovarian insufficiency. GnRHa should not be used in place of proven fertility preservation methods. The panel notes that the field of ovarian tissue cryopreservation is advancing quickly and may evolve to become standard therapy in the future. Additional information is available at www.asco.org/survivorship-guidelines.

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INTRODUCTION

The goal of this update is to provide oncologists, other health care providers, and caregivers with recommendations regarding fertility preservation for adults, adolescents, and children with cancer.

The American Society of Clinical Oncology (ASCO) first published evidence-based clinical practice guidelines on fertility preservation in 2006, and an updated guideline was published in 2013.[1] The goal of this 2018 guideline update is to provide current guidance regarding fertility preservation options for people with cancer anticipating treatment. The current 2018 update assesses whether the 2013 recommendations remain valid. A complete list of 2013 and 2018 recommendations is available at www.asco.org/survivorship-guidelines and in Data Supplement 1.

METHODS

Guideline Update Process

ASCO uses a signals[2] approach to facilitate guideline updating. This approach is intended to identify new, potentially practice-changing data—signals—that might translate into revised practice recommendations. The approach relies on routine literature searching and the expertise of ASCO guideline panel members to identify signals. The Methodology Supplement

ASSOCIATED CONTENT

Appendix
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Data Supplement
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THE BOTTOM LINE

Fertility Preservation in Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update

Guideline Question

What are fertility preservation options for patients with cancer who will receive anticancer treatment?

Target Population

Patients with cancer at risk for infertility due to anticancer treatment.

Target Audience

Medical oncologists, radiation oncologists, gynecologic oncologists, urologists, hematologists, pediatric oncologists, surgeons, nurses, social workers, psychologists, and other nonphysician providers.

Methods

A systematic review of the literature published from January 2013 to March 2017 was completed using PubMed and the Cochrane Library. An Update Panel reviewed the identified publications, and relevant evidence was evaluated for inclusion into this updated clinical practice guideline.

Recommendations

Recommendation 1.1. People with cancer are interested in discussing fertility preservation. Health care providers caring for adult and pediatric patients with cancer (including medical oncologists, radiation oncologists, gynecologic oncologists, urologists, hematologists, pediatric oncologists, surgeons, and others) should address the possibility of infertility as early as possible before treatment starts.

Recommendation 1.2. Health care providers should refer patients who express an interest in fertility preservation (and those who are ambivalent) to reproductive specialists.

Recommendation 1.3. To preserve the full range of options, fertility preservation approaches should be discussed as early as possible, before treatment starts. The discussion can ultimately reduce distress and improve quality of life. Another discussion and/or referral may be necessary when the patient returns for follow up after completion of therapy and/or if pregnancy is being considered. The discussions should be documented in the medical record.

Adult Men

Recommendation 2.1. Sperm cryopreservation: Sperm cryopreservation is effective, and health care providers should discuss sperm banking with postpubertal males receiving cancer treatment.

Recommendation 2.2. Hormonal gonadoprotection: Hormonal therapy in men is not successful in preserving fertility. It is not recommended.

Recommendation 2.3. Other methods to preserve male fertility: Other methods, such as testicular tissue cryopreservation and reimplantation or grafting of human testicular tissue, should be performed only as part of clinical trials or approved experimental protocols.

Recommendation 2.4. Postchemotherapy: Men should be advised of a potentially higher risk of genetic damage in sperm collected after initiation of therapy. It is strongly recommended that sperm be collected before initiation of treatment because the quality of the sample and sperm DNA integrity may be compromised after a single treatment. Although sperm counts and quality of sperm may be diminished even before initiation of therapy, and even if there may be a need to initiate chemotherapy quickly such that there may be limited time to obtain optimal numbers of ejaculate specimens, these concerns should not dissuade patients from banking sperm. Intracytoplasmic sperm injection allows the future use of a very limited amount of sperm; thus, even in these compromised scenarios, fertility may still be preserved.

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THE BOTTOM LINE (CONTINUED)

Adult Women

Recommendation 3.1. Embryo cryopreservation: Embryo cryopreservation is an established fertility preservation method, and it has routinely been used for storing surplus embryos after in vitro fertilization.

Recommendation 3.2. Cryopreservation of unfertilized oocytes: Cryopreservation of unfertilized oocytes is an option, and may be especially well suited to women who do not have a male partner, do not wish to use donor sperm, or have religious or ethical objections to embryo freezing. Oocyte cryopreservation should be performed in centers with the necessary expertise. As of October 2012, the American Society for Reproductive Medicine no longer deems this procedure experimental.

Qualifying statement. More flexible ovarian stimulation protocols for oocyte collection are now available. Timing of this procedure no longer depends on the menstrual cycle in most cases, and stimulation can be initiated with less delay compared with old protocols. Thus, oocyte harvesting for the purpose of oocyte or embryo cryopreservation is now possible on a cycle day–independent schedule. Of special concern in estrogen-sensitive breast and gynecologic malignancies is the possibility that these fertility preservation interventions (eg, ovarian stimulation regimens that increase estrogen levels) and/or subsequent pregnancy may increase the risk of cancer recurrence. Aromatase inhibitor–based stimulation protocols are now well established and may ameliorate this concern. Studies do not indicate increased cancer recurrence risk as a result of aromatase inhibitor–supplemented ovarian stimulation and subsequent pregnancy.

Recommendation 3.3. Ovarian transposition: Ovarian transposition (oophoropexy) can be offered when pelvic irradiation is performed as cancer treatment. However, because of radiation scatter, ovaries are not always protected, and patients should be aware that this technique is not always successful. Because of the risk of remigration of the ovaries, this procedure should be performed as close to the time of radiation treatment as possible.

Recommendation 3.4. Conservative gynecologic surgery: It has been suggested that radical trachelectomy (surgical removal of the uterine cervix) should be restricted to stage IA2 to IB cervical cancer with diameter < 2 cm and invasion < 10 mm. In the treatment of other gynecologic malignancies, interventions to spare fertility have generally centered on doing less radical surgery, with the intent of sparing the reproductive organs as much as possible. Ovarian cystectomy can be performed for early-stage ovarian cancer.

Recommendation 3.5 (updated). Ovarian suppression: There is conflicting evidence to recommend GnRHa and other means of ovarian suppression for fertility preservation. The Panel recognizes that, when proven fertility preservation methods such as oocyte, embryo, or ovarian tissue cryopreservation are not feasible, and in the setting of young women with breast cancer, GnRHa may be offered to patients in the hope of reducing the likelihood of chemotherapy-induced ovarian insufficiency. However, GnRHa should not be used in place of proven fertility preservation methods.

Recommendation 3.6 (updated). Ovarian tissue cryopreservation and transplantation: Ovarian tissue cryopreservation for the purpose of future transplantation does not require ovarian stimulation and can be performed immediately. In addition, it does not require sexual maturity and hence may be the only method available in children. Finally, this method may also restore global ovarian function. However, it should be noted further investigation is needed to confirm whether it is safe in patients with leukemias.

Qualifying statement. As of the time of this publication, ovarian tissue cryopreservation remains experimental. However, emerging data may prompt reconsideration of this designation in the future (this technique is already considered nonexperimental in some countries, and its experimental status is undergoing evaluation in the United States).

Role of Health Care Providers

Recommendation 4.1. All oncologic health care providers should be prepared to discuss infertility as a potential risk of therapy. This discussion should take place as soon as possible once a cancer diagnosis is made and can occur simultaneously with staging and the formulation of a treatment plan. There are benefits for patients in discussing fertility information with providers at every step of the cancer journey.

Recommendation 4.2. Encourage patients to participate in registries and clinical studies, as available, to define further the safety and efficacy of these interventions and strategies.

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THE BOTTOM LINE (CONTINUED)

Recommendation 4.3. Refer patients who express an interest in fertility, as well as those who are ambivalent or uncertain, to reproductive specialists as soon as possible.

Recommendation 4.4. Refer patients to psychosocial providers when they are distressed about potential infertility.

Special Considerations: Children

Recommendation 5.1. Suggest established methods of fertility preservation (eg, semen or oocyte cryopreservation) for postpubertal children, with patient assent and parent or guardian consent. For prepubertal children, the only fertility preservation options are ovarian and testicular cryopreservation, which are investigational.

Additional Resources

More information, including a Data Supplement with new studies, a Methodology Supplement, slide sets, clinical tools and resources, is available at www.asco.org/survivorship-guidelines. Patient information is available at www.cancer.net

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate.

available at www.asco.org/survivorship-guidelines provides additional information about the signals approach.

This systematic review-based guideline product was developed by a multidisciplinary Expert Panel, which included a patient representative and an ASCO guidelines staff with health research methodology expertise. PubMed and the Cochrane Library were searched for randomized controlled trials, systematic reviews, meta-analyses, and clinical practice guidelines for the period from January 1, 2013 through March 29, 2017. The disease and intervention search terms were those used for the 2013 guideline. An Expert Panel (members listed in Appendix Table A1, online only), formed in accordance with the ASCO Conflict of Interest Management Procedures for Clinical Practice Guidelines, reviewed the abstracts identified for predefined signals that would suggest the need to change a previous recommendation. Additional information about the results of the updated literature search (Data Supplement 2) and updated search strategy string and results (Data Supplement 3), as well as a discussion of the ASCO signals approach to guideline updating, are available at www.asco.org/survivorship-guidelines and in the 2018 Data Supplement and 2018 Methodology Supplement, respectively. A QUOROM diagram of the updated search and the clinical questions are provided in Data Supplements 4 and 5, respectively.

The Expert Panel considered the evidence for each of the 2018 recommendations. The guideline was circulated in draft form to the Expert Panel. ASCO's Clinical Practice Guidelines Committee leadership reviewed and approved the final document. All funding for the administration of the project was provided by ASCO.

Guideline Disclaimer

The Clinical Practice Guidelines and other guidance published herein are provided by the American Society of Clinical Oncology, Inc. (ASCO) to assist providers in clinical decision making. The information herein should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time information is developed and when it is published or read. The information is not continually updated and may not reflect the most recent evidence. The information addresses only the topics specifically identified therein and is not applicable to other interventions, diseases, or stages of diseases. This information does not mandate any particular course of medical care. Further, the information is not intended to substitute for the independent professional judgment of the treating provider, as the information does not account for individual variation among patients. Recommendations reflect high, moderate, or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like "must," "must not," "should," and "should not" indicates that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in individual cases. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. ASCO provides this information on an "as is" basis and makes no warranty, express or implied, regarding the information. ASCO specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. ASCO assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information, or for any errors or omissions.

This is the most recent information as of the publication date. For the most recent information, please visit www.asco.org/survivorship-guidelines.

Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with ASCO's Conflict of Interest Policy Implementation for Clinical Practice Guidelines ("Policy," found at http://www.asco.org/rwc). All members of the Expert Panel completed ASCO's disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria, consulting or advisory role; speaker's bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the Expert Panel did not disclose any relationships constituting a conflict under the Policy.

RESULTS

The search yielded 61 publications. After careful review of the identified publications, the Expert Panel concluded the results warranted a clarification to Recommendations 3.5 and 3.6 from the 2013 guideline update.[1] A bibliography of the results of the updated literature search is provided in Data Supplement 2.

Gonadotrophin-Releasing Hormone Agonists in Fertility Preservation

Seven randomized controlled trials, four systematic reviews, and seven guidelines provide the evidence base for gonadotrophin-releasing hormone agonists (GnRHa) in fertility preservation.

Seven randomized controlled trials[3-9] reported pregnancy outcomes (Table 1). One major limitation of the trials evaluating GnRHa has been reliance on surrogate markers, such as menstrual status or untimed estradiol or follicle-stimulating hormone evaluation, to determine the potential for fertility. The criteria used for defining ovarian insufficiency also varies widely between reports, which makes a uniform comparison challenging. Use of long-term live birth rates is the most appropriate marker of fertility, but few studies have evaluated this outcome or have sufficient length of follow-up or numbers of patients to make definitive conclusions. The only trial that reported number of pregnancies as a preplanned end point was the POEMS (Prevention of Early Menopause Study) trial.[7] The POEMS trial[7] reported significantly higher rates of pregnancy in women with hormone receptor–negative breast cancer receiving chemotherapy plus goserelin versus chemotherapy alone (21% *v* 11%; $P = .03$), although these findings are weakened by missing data and lack of adjustment for pregnancy intent. In contrast, the remaining six randomized trials did not report significant differences in pregnancies between treatment groups, although it was not a prespecified outcome for most.[3-6,8,9] A definitive trial with proper end points, including live birth rates, adjustment for pregnancy intent, and sufficient power, is needed to answer the controversy on the effectiveness of GnRHa in preserving ovarian function.

Of the four systematic reviews[10-13] that analyzed pregnancy (Table 2), two found significantly higher rates of pregnancy in patients receiving chemotherapy plus GnRHa versus chemotherapy alone.[12,13] The systematic review by Munhoz et al[13] noted the analysis on rates of pregnancy was not considered a valid end point for a main analysis but was performed as an exploratory analysis. One systematic review reporting six versus five births with GnRHa when compared with control did not report further analyses,[10] and one systematic review did not report a significant difference between treatment groups.[11] Three of the systematic reviews analyzed patients with breast cancer,[10,12,13] and one systematic review included both patients with breast cancer and patients with lymphoma.[11] Additionally, Lambertini et al[14] presented a pooled analysis of individual patient data of five randomized trials, analyzing three of the identified trials' rates of pregnancy at the 2017 San Antonio Breast Cancer Symposium. This analysis revealed a statistically greater number of pregnancies in the GnRHa group, with all pregnancies occurring in women ≤ 40 years. However, these data were not corrected for pregnancy intent. The panel will await full publication but does not anticipate any changes to the recommendations based on the data presented.

Of the seven guidelines[15-21] identified (Table 3), two recommend the use of GnRHa for fertility preservation in premenopausal patients with breast cancer,[15,17] three recommend GnRHa for fertility preservation for premenopausal patients with estrogen receptor–negative breast cancer,[16,18,21] and two do not recommend GnRHa as a method of fertility preservation.[19,20]

Therefore, given the current state of the evidence, GnRHa should not be considered a proven fertility preservation method, and patients should always be counseled to rely on methods with proven effectiveness in fertility preservation. Providers may have a discussion about GnRHa that includes careful counseling on the controversy and uncertainty regarding its role as an ovarian preservation strategy. The Panel recognizes that, when proven fertility preservation methods are not feasible, GnRHa is offered by many providers in the hope of reducing the likelihood of chemotherapy-induced ovarian insufficiency, especially in breast cancer. However, the panel wishes to stress that studies have shown conflicting results regarding the risk reduction for premature ovarian insufficiency, especially when all cancer types are considered. Therefore, GnRHa should not be used in place of proven fertility preservation methods.

Table 1. Randomized Controlled Trials

First Author, Year, Trial	No. of Patients		Agents	Disease Sites	Follow-Up (years)	Primary Outcome	No. of Pregnancies (%)	*P*
	Enrolled	Evaluable						
Leonard, 2017, OPTION[9]	106	95	GnRHa	Breast	5.0*	POV	9 (9)	NR
	121	107	Control				6 (6)	
Demeestere, 2016[8]	65	32	GnRHa	Lymphoma	5.33	POF	17 (53.1)	NS
	64	35	Control				15 (42.8)	
Moore, 2015, POEMS[7]	126	105	GnRHa	Breast	4.1	POV	22 (21)	.03
	131	113	Control				12 (11)	
Lambertini, 2015, PROMISE-GIM6[6]	148	148	GnRHa	Breast	7.3	POV	8 (5)	NS
	133	133	Control				3 (2)	
Elgindy, 2013[5]	25	17	GnRHa	Breast	1.0	Resumption of menses	1 (4)	NS
	25	17	Control				1 (4)	
	25	17	GnRHa				1 (4)	NS
	25	17	Control				0 (0)	
Munster, 2012[4]	27	26	GnRHa	Breast	1.6	POV	0 (0)	NS
	22	21	Control				2 (10)	
Gerber, 2011[3]	30	30	GnRHa	Breast	4.0	Resumption of menses	1 (3)	NS
	31	30	Control				1 (3)	

Abbreviations: GnRHa, gonadotrophin-releasing hormone agonist; NR, not reported; NS, not significant; OPTION, Ovarian Protection Trial In Premenopausal Breast Cancer Patients; POEMS, Prevention of Early Menopause Study; POF, premature ovarian failure; POV, preservation of ovarian function; PROMISE-GIM6, Prevention of Menopause Induced by Chemotherapy: A Study in Early Breast Cancer Patients—Gruppo Italiano Mammella 6.
*Median not reported.

Table 2. Systematic Reviews

First Author, Year	Total Studies Included	RCTs Addressing Pregnancy	No. of Patients	Agents	No. of Pregnancies (%)	OR	95% CI	*P*
Munhoz, 2016[13]	7	NR	NR	GnRHa	NR	1.85	1.02 to 3.36	.04
			NR	Control	NR			
Elgindy, 2015[11]	10	8	427	GnRHa	30	1.63	0.94 to 2.82	NS
			412	Control	20			
Lambertini, 2015[12]	12	5	359	GnRHa	33 (9.2)	1.83	1.02 to 3.28	.041
			347	Control	19 (5.5)			
Turner, 2013[10]	12	4		GnRHa	6	NR	NR	NR
				Control	5			

Abbreviations: GnRHa, gonadotrophin-releasing hormone agonist; NR, not reported; NS, not significant; OR, odds ratio; RCT, randomized controlled trial.

The Expert Panel acknowledges that GnRHa may have other medical benefits, such as reduction of vaginal bleeding when patients have low platelet counts as a result of chemotherapy or prevention of menometrorrhagia in patients with pancytopenia.[22] The adverse events associated with GnRHa are generally reversible and limited and include hot flashes, headaches, sweating, and vaginal dryness.[7] The panel agrees that there is conflicting evidence to recommend GnRHa as a method of fertility preservation but that it may be considered in young women with breast cancer, recognizing the limitations, controversy, and potential risks. While the use of GnRHa may have other medical benefits, those benefits and recommendations for use in that setting are beyond the scope of this document.

Ovarian Tissue Cryopreservation and Transplantation

Since the publication of the guideline, success rates of ovarian tissue transplantation have been published in a recent meta-analysis, reporting live birth and ongoing pregnancy rates of 37.7%.[23,24] Additionally, the prospective cohort study by Jadoul et al[25] reported from a cohort of 545 patients; 21 underwent ovarian cortex autotransplantation, and seven of these 21 patients (33%) conceived post-transplantation. In addition, successful recovery and cryopreservation of oocytes following in vitro maturation in tandem with ovarian tissue freezing have raised the possibility to expand the scope of this technique.

The panel has updated Recommendation 3.6 on ovarian tissue cryopreservation and transplantation to reflect these emerging data.

RECOMMENDATIONS

The 2018 recommendations are listed in the Bottom Line Box. The panel updated Recommendations 3.5 and 3.6 and combined the statement from previous Recommendation 3.7 into Recommendation 3.2. Additional edits were made for clarity to the 2013 recommendations.

ASCO believes cancer clinical trials are vital to inform medical decisions and improve cancer care and that all patients should have the opportunity to participate.

HEALTH DISPARITIES

Although ASCO clinical practice guidelines represent expert recommendations on the best practices in disease management to provide the highest level of cancer care, it is important to note that many patients have limited access to medical care. Racial and ethnic disparities in health care contribute significantly to this problem in the United States. Patients with cancer who are members of racial/ethnic minorities suffer disproportionately from comorbidities, experience more substantial obstacles to receiving care, are more likely to be uninsured, and are at greater risk of receiving care of poor quality than other Americans.[26-29] Many other patients lack access to care because of their geographic location and distance from appropriate treatment facilities. Awareness of these disparities in access to care should be considered in the context of this clinical practice guideline, and health care providers should strive to deliver the highest level of cancer care to these vulnerable populations.

Reproductive care is part of the standard care of all oncology patients. Cost, access, and time for proven fertility preservation methods may prevent patients from receiving optimal reproductive care.

PATIENT AND CLINICIAN COMMUNICATION

Recommendations 1.1, 1.2, and 1.3 from the last guideline update highlight the importance of patient and clinician communication in the discussion of fertility preservation. Though the panel did not update these recommendations in this update, it is key to reiterate these recommendations, and providers should initiate the discussion on fertility as early as possible in all patients for whom it is appropriate.

Recommendation 1.1 People with cancer are interested in discussing fertility preservation. Health care providers caring for adult and pediatric patients with cancer (including medical oncologists, radiation oncologists, gynecologic oncologists, urologists, hematologists, pediatric oncologists, surgeons, and others) should address the possibility of infertility as early as possible before treatment starts.

Recommendation 1.2 Health care providers should refer patients who express an interest in fertility preservation (and those who are ambivalent) to reproductive specialists

Recommendation 1.3 To preserve the full range of options, fertility preservation approaches should be discussed as early as possible, before treatment starts. The discussion can ultimately reduce distress and improve quality of life. Another discussion and/or referral may be necessary when the patient returns for follow up after completion of therapy and/or if pregnancy is being considered. The discussions should be documented in the medical record.

Table 3. Guidelines

Guideline	Recommendation
NCCN Breast Cancer 2017[21]	Randomized trials have shown that ovarian suppression with GnRH agonist therapy administered during adjuvant chemotherapy in premenopausal women with ER-negative tumors may preserve ovarian function and diminish the likelihood of chemotherapy-induced amenorrhea. Smaller historical experiences in patients with ER-positive disease have reported conflicting results with regard to the protective effect of GnRH agonist therapy on fertility.
NCCN AYA Oncology 2017[20]	Some data suggest that menstrual suppression with GnRH agonists may protect ovarian function. However, evidence that menstrual suppression with GnRH agonists protects ovarian function is insufficient, so this procedure is not currently recommended as an option for fertility preservation.
AIOM 2016[15]	Temporary ovarian suppression with LHRHa during chemotherapy should be recommended to all premenopausal patients with breast cancer undergoing chemotherapy who are interested in ovarian function and/or fertility preservation.
SEOM 2016[16]	The use of GnRHa could be an option to discuss with patients with early-stage receptor-negative breast cancer if embryo or oocyte cryopreservation not feasible. The use of GnRHa to preserve fertility in women with other cancer should not be recommended.
BCY2 2016[17]	The most recent data suggested a protective ovarian effect of LHRHa in both patients with hormone receptor–positive and –negative disease with no signal for harm from a breast cancer recurrence standpoint. The BCY2 Panel therefore agreed this strategy can be discussed with patients interested in potentially preserving fertility and/or ovarian function.
St Gallen 2015[18]	LHRH agonist therapy during chemotherapy proved effective to protect against premature ovarian failure and preserve fertility in young women with ER-negative breast cancer undergoing chemotherapy.
ESMO 2013[19]	The use of GnRH analogs concomitantly with chemotherapy should not be regarded as a reliable means of preserving fertility. Data on long-term ovarian function and pregnancy rates in these cohorts are warranted.

Abbreviations: AIOM, Italian Association of Medicine; AYA, Adolescent and Young Adult; BCY2, International Consensus Conference for Breast Cancer in Young Women; ER, estrogen receptor; ESMO, European Society for Medical Oncology; GnRHa, gonadotrophin-releasing hormone agonist; LHRH, luteinizing hormone-releasing hormone; LHRHa, luteinizing hormone-releasing hormone agonists; NCCN, National Comprehensive Cancer Network; SEOM, Sociedad Española de Oncología Médica.

For recommendations and strategies to optimize patient-clinician communication, see Patient-Clinician Communication: American Society of Clinical Oncology Consensus Guideline.[30]

COST IMPLICATIONS

Increasingly, individuals with cancer are required to pay a larger proportion of costs through deductibles and coinsurance.[31,32] Higher patient out-of-pocket costs have been shown to be a barrier to initiating and adhering to recommended treatments.[33,34]

Discussion of cost can be an important part of shared decision making.[35] Providers should discuss with patients the use of less expensive alternatives when it is practical and feasible for treatment of the patient's disease and there are two or more treatment options that are comparable in terms of benefits and harms.[35]

Patient out-of-pocket costs may vary depending on insurance coverage. Coverage may originate in the medical or pharmacy benefit, which may have different cost-sharing arrangements. Patients should be aware that different products may be preferred or covered by their particular insurance plan. Even with the same insurance plan, the price may vary between different pharmacies. When discussing financial issues and concerns, patients should be made aware of any financial counseling services available to address this complex and heterogeneous landscape.[35]

ADDITIONAL RESOURCES

More information, including Data and Methodology Supplements, slide sets, and clinical tools and resources, is available at www.asco.org/survivorship-guidelines. Patient information is available at www.cancer.net.

Related ASCO Guidelines

Patient-Clinician Communication[30] (http://ascopubs.org/doi/10.1200/JCO.2017.75.2311)

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at jco.org.

AUTHOR CONTRIBUTIONS

Manuscript writing: All authors
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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Appendix

Table A1. Fertility Preservation Guideline Update Panel Membership

Member	Affiliation	Role/Area of Expertise
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Abbreviation: PGIN, Practice Guideline Implementation Network.