

# Management and Care of Women With Invasive Cervical Cancer: American Society of Clinical Oncology Resource-Stratified Clinical Practice Guideline Summary

*Linus T. Chuang, MD, Sarah Temin, MSPH, and Jonathan S. Berek, MD*

Icahn School of Medicine at Mt Sinai, New York, NY; American Society of Clinical Oncology, Alexandria, VA; and Stanford Comprehensive Cancer Institute, Stanford, CA

The purpose of the recently published ASCO guideline<sup>1</sup> is to provide expert guidance to clinicians and policymakers in all resource settings on the work-up, treatment, and palliative care for women diagnosed with invasive cervical cancer. There are large disparities in incidence and mortality regionally and globally regarding cervical cancer, resulting in part from disparities in the provision of mass screening (separate ASCO resource-stratified guidelines will provide guidance on vaccination and screening). Treatment of cervical cancer is dependent on stage of disease. Treatment may include surgical treatments such as conization, extrafascial or radical hysterectomy, radiation therapy, and/or chemotherapy. Different regions of the world, both among and within countries, differ with respect to access to these treatments. In particular, regions with lower resources tend to have poorer screening programs, and patients present with more advanced disease that requires either radical surgery or chemoradiotherapy, neither of which is readily available in these areas. For this reason, standard guidelines that assume ideal availability of surgery and radiotherapy may not be applicable. The goal of this guideline is to recommend options in settings in which ideal treatment regimens may not be available.

Approximately 85% of incident cervical cancers occur in less developed regions (also known as low- and middle-income countries) around the world, representing 12% of women's cancers in those regions. Eighty-seven percent of deaths resulting from cervical cancer occur in these less developed regions.<sup>2</sup> Some of the regions in the world with the highest mortality rates include the WHO South-East Asia and Western Pacific regions, followed by India and Africa.<sup>2</sup> As a result of these disparities, the ASCO Resource-Stratified Guidelines Advisory Group chose cervical cancer as a priority topic for guideline development.

Disparities exist not only among countries and global regions but also within countries. For example, within the United States, some regions have higher incidences of cervical cancer (eg, Texas, 9.2; Arkansas, 9.8; and Mississippi, 9.7 per 100,000 women)<sup>3</sup> as well as rates of poverty greater than 17%.<sup>4</sup> In the United States, black women experience higher incidence of and mortality from cervical cancer than women of other races or ethnicities.<sup>3</sup> 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 all women.

ASCO has established a process for resource-stratified guidelines, which includes

 DOI: [10.1200/JOP.2016.014290](https://doi.org/10.1200/JOP.2016.014290); published online ahead of print at [jop.ascopubs.org](http://jop.ascopubs.org) on June 21, 2016.

## THE BOTTOM LINE

### **Recommendations for the Management and Care of Women With Invasive Cervical Cancer: American Society of Clinical Oncology Resource-Stratified Clinical Practice Guideline**

#### ***Guideline Question***

In basic-, limited-, enhanced-, and maximal-resource settings, what are the appropriate care options for women diagnosed with invasive cervical cancer?

#### ***Target Population***

Women at all levels of resource settings diagnosed with invasive cervical cancer.

#### ***Target Audience***

This clinical practice guideline globally targets health care providers (including gynecologic oncologists, medical oncologists, radiation oncologists, obstetricians and gynecologists, surgeons, nurses, and palliative care clinicians), policymakers, patients, and caregivers.

#### ***Methods***

A multinational, multidisciplinary expert panel was convened to develop clinical practice guideline recommendations based on a systematic review of the medical literature and/or an expert consensus process.

#### ***Author's Note.***

It is the view of the American Society of Clinical Oncology (ASCO) that health care providers and health care system decision makers should be guided by the recommendations for the highest stratum of resources available. ASCO guidelines are intended to complement but not replace local guidelines.

#### ***Key Points\****

- If follow-up is available, the expert panel recommends cone biopsy for women with stage IA2 disease in basic settings and cone biopsy plus pelvic lymphadenectomy in limited settings. In enhanced and maximal settings, radical trachelectomy is recommended for patients with stage IB1 cervical cancer with tumor size up to 2 cm who desire fertility-sparing surgery.
- In basic settings where patients cannot be treated with radiation therapy, extrafascial hysterectomy either alone or after chemotherapy may be an option for women with stage IA1 to IVA cervical cancer.
- In basic settings, for women with larger tumors or advanced-stage cervical cancer, neoadjuvant chemotherapy is recommended whenever chemotherapy is available, for the purpose of shrinking the tumor before performing hysterectomy.
- Concurrent radiotherapy and chemotherapy is standard in enhanced and maximal settings for women with stage IB to IVA disease.
- The panel stresses the addition of low-dose chemotherapy during radiotherapy, but not at the cost of delaying radiation therapy if chemotherapy is not available.

**THE BOTTOM LINE**

- In limited-resource settings where there is no brachytherapy, the ASCO expert panel recommends extrafascial hysterectomy or its modification for women who have residual tumor 2 to 3 months after concurrent chemoradiotherapy and additional boost.
- For patients with stage IV or recurrent cervical cancer, single-agent chemotherapy (carboplatin or cisplatin) is recommended in basic settings.
- If the resources are available and the patient cannot receive treatment with curative intent, palliative radiotherapy should be used to relieve symptoms of pain and bleeding.
- Where resources are constrained, single- or short-course radiotherapy schemes can be used with retreatments if feasible for persistent or recurrent symptoms.

**Qualifying Statements**

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.

Palliative care and pain management are part of the treatment of cancers, including cervical cancer, to avoid unnecessary suffering during the final stages of disease. Pain control is a vital component of palliative care, a basic human right often neglected in cancer control programs.

**Additional Resources**

More information, including a Data Supplement with additional evidence tables, a Methodology Supplement with information about evidence quality and strength of recommendations, slide sets, and clinical tools and resources, is available at [www.asco.org/rs-cervical-cancer-treatment-guideline](http://www.asco.org/rs-cervical-cancer-treatment-guideline). Patient information is available at [www.cancer.net](http://www.cancer.net).

(\*) Not all recommendations for all settings are listed. Please see Tables 3 to 7 in full guideline.<sup>1</sup>

mixed methods of guideline development, adaptation of the clinical practice guidelines developed by experts on behalf of organizations, and formal expert consensus. This guideline summarizes the results of that process and presents resource-stratified recommendations for areas in low- and middle-income countries based on existing guidelines and formal consensus for the work-up, care, and palliation of women with invasive cervical cancer.

This ASCO guideline<sup>1</sup> reinforces selected recommendations offered in the Canadian Cancer Care Ontario (CCO),<sup>5,6</sup> European Society of Medical Oncology,<sup>7</sup> Japan Society of Gynecologic Oncology,<sup>8</sup> US National Comprehensive Cancer Network,<sup>9</sup> and multinational WHO<sup>10</sup> guidelines and acknowledges the effort put forth by the authors and aforementioned societies to produce evidence-based and/or consensus-based guidelines for women with invasive cervical cancer. In developing resource-stratified guidelines, ASCO has adopted its framework from the four-tier approach (basic, limited, enhanced, and maximal) developed by the Breast Health Global Initiative

and modifications to that framework based on the Disease Control Priorities 3 and used an evidence-based approach to inform guideline recommendations.<sup>11-13</sup>

**WORK-UP**

The purpose of work-up is to assess a patient's overall health status and gather data to inform treatment. Modalities include history and physical examination, biopsies, blood tests, and imaging. Tests available in maximal settings, such as magnetic resonance imaging or positron emission tomography-computed tomography, are optional.

**TREATMENT**

The treatment of invasive cervical cancer consists of surgery, chemotherapy, and radiation therapy, sometimes in combination. Selected treatment recommendations for women with stage IA1 to IV disease are discussed in the guideline summary bottom line box.

## FOLLOW-UP

The ASCO expert panel concluded that there is insufficient evidence to guide follow-up in all resource settings, especially those that are resource constrained. ASCO informally endorsed a Canadian CCO guideline on follow-up for cervical cancer<sup>6</sup> and provides similar intervals as a guide.

## PALLIATIVE CARE

Women with advanced cervical cancer with or without access to tumor-directed therapy may have specific late-stage symptoms that require clinicians to perform urogenital-specific interventions. This guideline adapts guidance on palliative care provided in a WHO guideline<sup>10</sup> on women with cervical cancer. The management of primary symptoms, which is discussed in the WHO guideline, includes but is not limited to addressing pain, fistula, loss of appetite, wasting, bleeding, and gastrointestinal and genitourinary symptoms. The ASCO guideline<sup>1</sup> also discusses specific measures to address these symptoms.

In addition, the ASCO guideline<sup>1</sup> explores cost implications, radiation therapy shortages, and the importance of ongoing and future research. Additional information on the guideline and the methods of its development is available at [www.asco.org/rs-cervical-cancer-treatment-guideline](http://www.asco.org/rs-cervical-cancer-treatment-guideline). **JOP**

### Acknowledgment

*Management and Care of Women With Invasive Cervical Cancer: American Society of Clinical Oncology Resource-Stratified Clinical Practice Guideline<sup>1</sup> was developed and written by: Linus T. Chuang, Sarah Temin, Rolando Camacho, Alfonso Dueñas-Gonzalez, Sarah Feldman, Murat Gultekin, Vandana Gupta, Susan Horton, Graciela Jacob, Elizabeth A. Kidd, Kennedy Lishimpi, Carolyn Nakisige, Joo-Hyun Nam, Hextan Yuen Sheung Ngan, William Small, Gillian Thomas, and Jonathan S. Berek.*

*This guideline has been endorsed by the Society of Gynecologic Oncology and the Gynecologic Cancer InterGroup.*

### Authors' Disclosures of Potential Conflicts of Interest

Disclosures provided by the authors are available with this article at [jop.ascopubs.org](http://jop.ascopubs.org).

### Author Contributions

**Conception and design:** All authors

**Administrative support:** Sarah Temin

**Data analysis and interpretation:** Linus T. Chuang, Jonathan S. Berek

**Manuscript writing:** All authors

**Final approval of manuscript:** All authors

*Corresponding author: American Society of Clinical Oncology, 2318 Mill Road, Suite 800, Alexandria, VA 22314; e-mail: [guidelines@asco.org](mailto:guidelines@asco.org).*

## References

1. Chuang LT, Temin S, Camacho R, et al: Management and care of women with invasive cervical cancer: American Society of Clinical Oncology resource-stratified clinical practice guideline. *J Glob Oncol* doi:10.1200/JGO.2016.003954, 2016
2. International Agency for Research on Cancer: GLOBOCAN 2012 cervical cancer: Estimated incidence, mortality and prevalence worldwide in 2012. <http://globocan.iarc.fr/old/FactSheets/cancers/cervix-new.asp>
3. Howlader N, Noone AM, Krapcho M, et al: SEER cancer statistics review, 1975-2012, National Cancer Institute. [http://seer.cancer.gov/csr/1975\\_2012/](http://seer.cancer.gov/csr/1975_2012/)
4. Catholic Campaign for Human Development: Interrelationships of three year average state poverty rates: 2011-2013. <http://www.povertyusa.org/the-state-of-poverty/poverty-map-state/#>
5. Hirte H, Kennedy EB, Elit L, et al: Systemic therapy for recurrent, persistent, or metastatic cervical cancer: A clinical practice guideline. *Curr Oncol* 22:211-219, 2015
6. Elit L, Kennedy EB, Fyles A, et al: Follow-up for cervical cancer. <https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=340742>
7. Colombo N, Carinelli S, Colombo A, et al: Cervical cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 23:vii27-vii32, 2012 (suppl 7)
8. Ebina Y, Yaegashi N, Katabuchi H, et al: Japan Society of Gynecologic Oncology guidelines 2011 for the treatment of uterine cervical cancer. *Int J Clin Oncol* 20: 240-248, 2015
9. Koh WJ, Greer BE, Abu-Rustum NR, et al: Cervical cancer, version 2.2015. *J Natl Compr Canc Netw* 13:395-404, 2015 quiz 404
10. World Health Organization: Comprehensive Cervical Cancer Control: A Guide to Essential Practice. (ed 2). [http://apps.who.int/iris/bitstream/10665/144785/1/9789241548953\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/144785/1/9789241548953_eng.pdf)
11. Reference deleted
12. Anderson BO, Shyyan R, Eniu A, et al: Breast cancer in limited-resource countries: An overview of the Breast Health Global Initiative 2005 guidelines. *Breast J* 12:S3-S15, 2006 (suppl 1)
13. Horton S, Gauvreau CL: Cancer in low- and middle-income countries: An economic overview, in Gelband H, Jha P, Sankaranarayanan R, et al (eds): *Cancer Disease Control Priorities* (ed 3). Washington, DC, International Bank for Reconstruction and Development/World Bank, 2015

**AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**

**Management and Care of Women With Invasive Cervical Cancer: American Society of Clinical Oncology Resource-Stratified Clinical Practice Guideline Summary**

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to [www.asco.org/rwc](http://www.asco.org/rwc) or [jop.ascopubs.org/site/misc/ifc.xhtml](http://jop.ascopubs.org/site/misc/ifc.xhtml).

**Linus T. Chuang**

No relationship to disclose

**Sarah Temin**

No relationship to disclose

**Jonathan S. Berek**

**Consulting or Advisory Role:** Atara Biotherapeutics

**Research Funding:** Tesaro (Inst)