

# Key issues in the management of cervical cancer: consensus recommendations by a Brazilian expert panel

## Questões-chave no manejo do câncer de colo do útero: recomendações por consenso de um painel de especialistas brasileiros

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### ABSTRACT

**Objective:** We report the results of a panel of Brazilian experts and provide recommendations for the management of these patients. **Material and Methods:** The panel convened composed by 28 local opinion leaders, addressed 59 multiple-choice questions taking into account the published scientific literature and their own clinical experience. The level of agreement among panel members was qualified as (1) consensus, when at least 75% of the voting panel members; (2) majority vote (50%-74.9%); or (3) less than majority vote. **Results:** There was at least majority vote for eight of 10 questions on

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staging and follow-up; for 14 of 23 questions on the treatment of early-stage disease; for 12 of 14 questions related to the treatment of locally-advanced disease; and for seven of the 12 questions related to the treatment of recurrent/metastatic disease. Conclusion: The current recommendations may help practitioners from Brazil and other countries to improve the care they provide to patients.

**Keywords:** Chemoradiotherapy; Gynecologic surgical procedures; Immune checkpoint inhibitors; Platinum compounds; Uterine cervical neoplasms.

## RESUMO

**Objetivo:** Relatamos os resultados de um painel de especialistas brasileiros e fornecemos recomendações para o manejo desses pacientes. **Material e Métodos:** O painel constituído por 28 formadores de opinião locais, abordou 59 questões de escolha múltipla tendo em conta a literatura científica publicada e a sua própria experiência clínica. O nível de concordância entre os membros do painel foi qualificado como: (1) consenso, quando pelo menos 75% dos membros do painel votaram; (2) voto majoritário (50%-74,9%); ou (3) menos do que a maioria dos votos. **Resultados:** Houve pelo menos maioria de votos para oito das 10 questões sobre estadiamento e acompanhamento; para 14 de 23 perguntas sobre o tratamento da doença em estágio inicial; para 12 das 14 questões relacionadas ao tratamento da doença localmente avançada; e para sete das 12 questões relacionadas ao tratamento da doença recorrente/metastática. **Conclusão:** As recomendações atuais podem ajudar profissionais do Brasil e de outros países a melhorar o atendimento que prestam aos pacientes.

**Descritores:** Quimiorradioterapia; Procedimentos cirúrgicos ginecológicos; Inibidores do checkpoint imunológico; Compostos de platina; Neoplasias do colo uterino.

## INTRODUCTION

Worldwide, 604,000 new cases of, and 342,000 deaths from, cervical cancer were estimated in 2020, making it the fourth most frequent malignancy and fourth cause of cancer death among females.<sup>(1)</sup> The burden of cervical cancer has been unequally distributed between low-/middle-income (LMIC) and high-income countries (HIC) for several decades.<sup>(1,2)</sup> Although the incidence of, and mortality from, cervical cancer have decreased by nearly 75% over the past 50 years in HIC, around 85% of new cases of this disease are diagnosed in LMIC.<sup>(1,3,4)</sup> In HIC, the reduced burden of cervical cancer has been ascribed mostly to the use of effective screening programs and the ability to diagnose and treat patients with non-invasive lesions; conversely, low population coverage, poor-quality cytology, incomplete follow-up of screen-positive women, and barriers to effective treatment are thought to underlie the relatively unsuccessful control of cervical-cancer in LMIC.<sup>(2,3,5)</sup>

In Brazil, cervical cancer is the third most frequent malignancy among women,<sup>(6)</sup> and recent studies suggests that most patients are diagnosed with locally advanced or metastatic disease.<sup>(7-9)</sup> These findings likely reflect inadequate screening strategies, where below-target rates of Pap smears

have been reported recently.<sup>(9,10)</sup> Moreover, regional disparities have been reported to impact survival rates after adjustment for relevant covariates, suggesting that inequalities in access to adequate treatment plays an important role in outcomes.<sup>(11)</sup> Although such inequalities might be linked to various socioeconomic factors<sup>(12-14)</sup> as well as to treatment delays,<sup>(8,15,16)</sup> disparities in survival rates and other treatment outcomes may be linked to heterogeneity in access to and implementation of evidence-based medical care. Our aim was to report the results of a panel of experts and provide countrywide recommendations for the management of patients with cervical cancer.

## MATERIAL AND METHODS

The expert panel was composed by 28 physicians from Brazil; these physicians are opinion leaders on cervical cancer in their respective fields of gynecologic oncology, medical oncology, and radiation oncology. The panel was coordinated by a committee composed by three of the current authors (GB, FCM and EP), who prepared 59 multiple-choice questions addressing issues related to staging, follow-up and treatment of early-stage, locally advanced, and recurrent or metastatic cervical cancer. The panel convened by teleconference in December 2021 and was made possible by an educational grant from

Merck, Sharp & Dohme, who had no influence on the creation of the questions, the panel conduct, or the writing of the manuscript, all of which resting under the entire responsibility of the coordinating committee and authors.

In order to provide recommendations, panel members were expected to take into account the published scientific literature and their own clinical experience. For each question, voters had the option to abstain when they felt impeded to provide a qualified response for any reason, including the fact that the topic fell outside their area of expertise (mostly surgical versus medical oncology). Of note, the staging system used by the panel was the 2018 International Federation of Obstetrics and Gynecology classification.<sup>(17)</sup> Recommendations were provided in an anonymous manner using an online system that also tabulated the results after the end of the voting period for each question. The results for each of the 59 questions addressed by the panel were analyzed descriptively, having in the denominator only the members who voted for a specific question. The computed percentages of responses to each question included the option "abstain" in their denominator. The level of agreement among voters was ascertained by classifying responses to each question as (1) consensus, (2) majority vote, or (3) less than majority vote. Consensus was considered to be present when at least 75% of the voting panel members chose a particular answer to a given question. When between 50% and 74.9% of the voting members chose a particular answer, this was considered as majority vote. The 59 questions posed to the panel are displayed in the Supplementary Materials, alongside the detailed results of the voting process. In the following, however, only consensus recommendations and majority vote are shown; for the latter, more than two options are shown when panel members had chosen only two predominant answers.

## RESULTS

### 1. Surveillance and staging of cervical cancer

#### 1.1. Consensus recommendations

1.1.1. Vaginal cytology should be performed in patients with early-stage cervical cancer who have undergone radical hysterectomy.

1.1.2. Patients treated curatively for early-stage disease ( $\leq$ IB2) should be followed every 3 months for the first 2 years and every 6 months until completion of 5 years from treatment.

1.1.3. Patients treated curatively for locally-advanced disease should be followed every 3-6 months for the first 2 years and every 6-12 months until completion of 5 years from treatment.

#### 1.2. Majority vote

1.2.1. The additional imaging methods for stage IB1 or IB2 disease are magnetic resonance imaging (MRI) of the abdomen and pelvis, and chest X-ray.

1.2.2. The additional imaging methods for stage  $\leq$ IB1 disease in which radical trachelectomy is being considered are MRI of the abdomen and pelvis, and chest X-ray.

1.2.3. The additional imaging methods for stage IB3-IVA disease are MRI of the abdomen and pelvis, and positron emission tomography (PET)-computed tomography (CT).

1.2.4. Patients with an indication for chemoradiotherapy and suspected para-aortic lymph nodes (by PET-CT, MRI or CT) can start treatment with extended-field radiotherapy; however, surgical staging is also an option, albeit with less than majority vote.

1.2.5. The follow-up of patients treated curatively for locally-advanced disease consists of physical examination, vaginal cytology, CT or MRI of the abdomen and pelvis, and chest X-ray.

## 2. Treatment of early-stage disease

### 2.1. Consensus recommendations

2.1.1. Patients with stage IB1/IB2 disease who are not concerned with fertility preservation should be treated with radical hysterectomy and lymph node assessment.

2.1.2. Patients with stage IB1 disease who are concerned with fertility preservation should be treated with radical trachelectomy and lymph node assessment.

2.1.3. Patients with stage IB3 to IIB disease should be treated with chemoradiation followed by brachytherapy.

2.1.4. Patients with early-stage disease meeting Sedlis criteria (lymphovascular space invasion, cervical stromal invasion, or tumor size  $\geq$ 2-4cm) after surgical treatment should receive adjuvant radiotherapy.

2.1.5. Patients with early-stage disease with at least one high-risk feature (positive surgical margins, positive lymph node, or parametrial involvement) after surgery should receive adjuvant chemoradiation.

2.1.6. Patients with micrometastasis (0.2-2mm) in the sentinel lymph node (SLN) should receive adjuvant chemoradiation.

### 2.2. Majority vote

2.2.1. Patients with stage IA1 disease with lymphovascular space or IA2 diagnosed by conization and with free margins who are not concerned with fertility preservation can be treated with radical hysterectomy and lymph node assessment; however, simple hysterectomy and lymph node assessment is also an option, albeit with less than majority vote.

2.2.2. Patients with stage IIA1 who are not concerned with fertility preservation can be

treated with radical hysterectomy and lymph node assessment; however, chemoradiation is also an option, albeit with less than majority vote.

2.2.3. Patients with stage IA1 disease, without lymphovascular space invasion, diagnosed by conization and with free margins who are concerned with fertility preservation can be treated with simple trachelectomy; however, no additional intervention is also an option, albeit with less than majority vote.

2.2.4. Patients with stage IA1 disease with lymphovascular space invasion or IA2, diagnosed by conization and with free margins who are concerned with fertility preservation can be treated with radical trachelectomy and lymph node assessment.

2.2.5. As a general rule, laparotomy is indicated for the surgical treatment of tumors  $\leq 4$ cm.

2.2.6. As a general rule, SLN evaluation is sufficient in patients with stage IA1 tumors with lymphovascular space invasion or IA2.

2.2.7. As a general rule, SLN evaluation followed by lymphadenectomy is the proper procedure for patients with stage IB2 tumors.

2.2.8. As a general rule, observation is sufficient for patients with isolated tumor cells ( $<0.2$ mm) in the SLN who does not fulfill Sedlis criteria and is not at high risk factors.

### 3. Treatment of locally-advanced disease

#### 3.1. Consensus recommendations

3.1.1. Patients with stages IIIA to IVA disease should be treated with chemoradiation followed by brachytherapy.

3.1.2. Adjuvant chemotherapy should not be recommended after definitive treatment with chemoradiotherapy followed by brachytherapy.

3.1.3. Neoadjuvant chemotherapy followed by surgery should be recommended for patients with stages IB3, IIA2, and IIB disease if radiotherapy is not available.

3.1.4. Adjuvant hysterectomy should not be recommended in stages IB3 to IVA and complete clinical response to chemoradiation followed by brachytherapy and no evidence of disease on physical examination or imaging.

3.1.5. If free margins are deemed feasible, hysterectomy should be recommended to patients with locally-advanced disease who undergo chemoradiation followed by brachytherapy and persist with biopsy-confirmed residual disease in the cervix.

3.1.6. Extended-field chemoradiation followed by brachytherapy should be recommended to patients suspected or pathology-confirmed para-aortic lymph node involvement.

3.1.7. Patients with HIV/AIDS or other types of immunosuppression should be treated, like immunocompetent patients, with chemoradiation followed by brachytherapy.

3.1.8. Weekly cisplatin should be the preferred radiosensitizing agent.

3.1.9. Carboplatin should be used as radiosensitizing agent in patients who are not eligible to receive cisplatin.

#### 3.2. Majority vote

3.2.1. If brachytherapy is not available or not feasible due to anatomical changes, patients with stages IB3 to IVA disease can be treated with chemoradiation followed by boost external-beam radiation.

### 4. Treatment of recurrent or metastatic disease

#### 4.1. Consensus recommendation

4.1.1. The first-line treatment for HIV/AIDS and other immunosuppressed patients who are stable from the standpoint of the underlying disease should be the same as for immunocompetent patients.

#### 4.2. Majority vote

4.2.1. When locoregional salvage treatment is not feasible and there are no contraindications for platinum or antiangiogenic therapy, if sufficient resources are available, first-line treatment can be done with a platinum agent, paclitaxel and pembrolizumab, with or without bevacizumab; however, a platinum agent and paclitaxel, with or without bevacizumab, is also an option, albeit with less than majority vote.

4.2.2. Patients with potentially resectable local recurrence without suspected lymph node involvement and without comorbidities who have undergone previous surgery without adjuvant treatment can be treated with chemoradiation; however, salvage surgery can be done before chemoradiation, albeit with less than majority vote.

4.2.3. Patients with potentially resectable locoregional recurrence in a previously irradiated area without suspected lymph node involvement can be treated with salvage surgery; however, salvage surgery followed by chemotherapy is also an option, albeit with less than majority vote.

4.2.4. Patients with potentially resectable locoregional lymph node recurrence in a previously irradiated area and without comorbidities can be treated with salvage surgery followed by chemotherapy; however, salvage surgery alone is also an option, albeit with less than majority vote.

4.2.5. Patients treated with a first-line platinum-based therapy within  $<6$  months who need second-line treatment can be treated with immunotherapy.

4.2.6. Patients with previously treated metastatic disease for whom no clinical trial is available can be treated with best supportive care alone if they have a performance status >2 (not due to the latest treatment).

## DISCUSSION

This consensus panel aimed to provide recommendations for management of patients with cervical cancer in Brazil, and the results may be applicable to countries and settings with similar healthcare environments. It should be noted that the questions posed to the panel include both those about issues that have supporting literature with high-level evidence and those for which there is considerable uncertainty and controversy in the scientific community. For the first type of question, consensus elicitation is aimed mostly at confirming that international and evidence-based recommendations are feasible and have high enough uptake in our country. For the second type of question, consensus elicitation – not always successful – aimed mostly at providing guidance to practitioners based on the opinion of experts in their corresponding fields.

Regarding staging and follow-up of patients with cervical cancer, there was at least majority vote for eight of 10 questions posed to the panel. The role of vaginal vault cytology in the follow-up of patients treated for early-stage disease, although limited (or absent, according to some authors<sup>(18,19)</sup> appears sufficient to warrant its recommendation in some guidelines.<sup>(20,21)</sup> Similarly, the panel recommended by majority vote the inclusion of vaginal cytology as part follow-up for patients with locally-advanced disease (alongside physical examination and imaging studies). With regard to the frequency of follow-up, despite no study provides high-level evidence in cervical cancer, the current panel recommendations are in line with those from the European Society of Gynecological Oncology (ESGO).<sup>(18)</sup> Regarding imaging methods for staging, the panel provided majority recommendation for MRI of the abdomen and pelvis and chest X-ray for stage <IB3 disease, and MRI of the abdomen and pelvis plus PET-CT for stage IB3-IVA disease. These recommendations are in line with those provided by ESGO and the National Comprehensive Cancer Network (NCCN),<sup>(18,20)</sup> as well as with increasing evidence for the utility of PET-CT in locally advanced disease.<sup>(22)</sup> Finally, the majority recommendation of extended-field radiotherapy for patients with suspected involvement of para-aortic lymph nodes scheduled to receive chemoradiation is also supported by current guidelines.<sup>(18,20)</sup> The two questions for which there was more considerable uncertainty related to additional imaging methods required in patients with microscopic disease in a cone specimen (stage IA1 with lymphovascular space invasion or IA2), and the follow-up of patients with stage IA-IB2 disease treated with curative intent (see Supplementary Materials).

There was at least a majority vote for 14 of 23 questions on the treatment of early-stage disease posed to the panel. Consensus recommendations for radical hysterectomy and lymph node assessment for patients with stage IB1/IB2 disease who are not concerned with fertility preservation, and radical trachelectomy and lymph node assessment for patients with stage IB1 disease concerned with fertility preservation are in line with international guidelines.<sup>(18-20)</sup> Likewise, the recommendations of chemoradiation followed by brachytherapy for patients with stage IB3 to IIB disease and of adjuvant radiotherapy for patients with early-stage disease meeting Sedlis criteria<sup>(23)</sup> are in line with those same guidelines. Moreover, the recommendation of adjuvant chemoradiation in patients with early-stage disease with at least one high-risk feature is supported by randomized evidence and guideline recommendations.<sup>(18-20,24)</sup> Finally, there was consensus recommendation for adjuvant chemoradiation for patients with micrometastasis in the SLN; this recommendation, supported by ESGO guidelines,<sup>(18)</sup> is based on the adverse prognostic role of micrometastasis,<sup>(25)</sup> regardless of the lack of evidence from therapeutic randomized trials.

In addition to the above issues, for which there was consensus, the literature about the treatment of patients with early-stage disease is characterized by general agreement on several important issues.<sup>(19,20)</sup> For example, patients with stage IA1 disease without lymphovascular space invasion can be managed with conization or simple trachelectomy if they wish to preserve fertility, whereas simple hysterectomy can be offered otherwise. In stage IA1 with lymphovascular space invasion, surgical assessment of pelvic lymph nodes assumes greater importance. In patients with stage IA2, IB and IIA disease, radical hysterectomy with bilateral lymph node dissection is standard treatment for patients not concerned with fertility. Radical hysterectomy and lymph node assessment was recommended by majority vote for patients with stage IA1 disease with LVI, IA2 diagnosed by conization and with free margins, and for patients with IIA1 disease, all of whom not concerned with fertility preservation. However, alternatives suggested by the panel were simple hysterectomy and lymph node assessment for stage IA1 disease with lymphovascular space invasion or stage IA2 diagnosed by conization and with free margins, as well as chemoradiation for stage IIA1 disease. The lack of clear consensus for treatment of these patients reflects current doubts in the literature. For patients concerned with fertility diagnosed by conization and with free margins, the panel recommended by majority vote simple trachelectomy for patients with stage IA1 disease, without lymphovascular space invasion, and radical trachelectomy and lymph node assessment for those with stage IA1 disease with lymphovascular space invasion or IA2.

The assessment of the SLN, whose definitive role is the subject of ongoing studies,<sup>(26,27)</sup> can be considered from stage IA1 with lymphovascular space invasion to stage IIA disease.<sup>(18-20)</sup> The panel recommended SLN evaluation alone in patients with stage IA1 tumors with lymphovascular space invasion or IA2, and SLN evaluation followed by lymphadenectomy for stage IB2 tumors. For patients with isolated tumor cells (<0.2mm) in the SLN not fulfilling Sedlis criteria and not at high risk, the panel recommended by majority vote no further intervention. Of note, the management of patients with isolated tumor cells remains controversial.<sup>(28,29)</sup> Surgical approach, whether by laparotomy or laparoscopy (which can be robotically assisted), is still subject to debate or local preference,<sup>(30)</sup> but the panel recommended by majority vote laparotomy for the surgical treatment of tumors  $\leq 4$ cm, in line with recent evidence favoring open surgery.<sup>(20,31,32)</sup>

There was at least a majority vote for 12 of 14 questions related to the treatment of locally-advanced disease. This level of agreement likely reflects the fact that the management of patients with locally-advanced cervical cancer is based on widely accepted strategies. For example, cisplatin-based chemoradiation plays a key role in the management of these patients.<sup>(24,33)</sup> Moreover, as indicated by the panel, weekly cisplatin is the preferred radiosensitizing agent, but carboplatin should be used as radiosensitizing agent in patients who are not eligible to receive cisplatin.<sup>(34)</sup> Chemoradiation followed by brachytherapy should also be administered to suitable HIV/AIDS patients, notwithstanding their inferior survival, when compared with their HIV-negative counterparts.<sup>(35,36)</sup> On the other hand, constraints may exist in many institutions when it comes to applying state-of-the-art treatment strategies. This is particularly relevant in areas where surgeons do not have full training in gynecologic oncology. Even though cisplatin-based concomitant chemoradiation leads to superior results when compared with neoadjuvant chemotherapy followed by radical surgery,<sup>(37)</sup> radiotherapy may not be available in some centers, the likely reason why the panel recommended neoadjuvant chemotherapy followed by surgery for patients with stages IB3, IIA2 and IIB disease if radiotherapy is not available. Other positive consensus recommendations were for hysterectomy in patients with locally-advanced disease who undergo chemoradiation followed by brachytherapy and persist with biopsy-confirmed residual disease in the cervix, as long as free margins are deemed feasible,<sup>(38)</sup> and for extended-field chemoradiation followed by brachytherapy for patients suspected or pathology-confirmed para-aortic lymph node involvement.<sup>(18,20)</sup> On the other hand, there were consensus recommendations against adjuvant hysterectomy in stages IB3 to IVA and complete clinical response to chemoradiation followed by brachytherapy,<sup>(39)</sup> and against adjuvant chemotherapy after definitive treatment with chemoradiotherapy followed by brachytherapy.

<sup>(20,40,41)</sup> Finally, if brachytherapy is not feasible, there was majority vote in favor of treating patients with stages IB3 to IVA disease with chemoradiation followed by boost external-beam radiation.<sup>(24)</sup>

Regarding locally-advanced disease, it should be noted that recommendation 3.1.2 above accounts for the results of two questions related to adjuvant chemotherapy after chemoradiation and brachytherapy – see Supplementary Material, questions 35 and 36). Moreover, majority vote was also obtained for a question on what neoadjuvant chemotherapy regimen should be used; since 70.8% of members expressed that they do not recommend neoadjuvant therapy, this question is only shown in the Supplementary Material (question 46). Therefore, only 10 recommendations are shown in the “Results” section above - 3.1.1.

Notably, consensus was reached for only one question related to the treatment of recurrent or metastatic disease, whereas a majority vote was present for an additional six of the total of 12 questions. This level of agreement among panel members likely reflects, at least in part, the controversies and insufficient evidence base for the management of recurrent or metastatic cervical cancer. The only consensus recommendation in this setting was for the use of conventional first-line treatment of patients with HIV/AIDS or other immune deficiencies who are stable from their underlying condition. Even though the evidence base for such a recommendation is still scarce, the recommendation is supported by expert opinion and limited studies.<sup>(20,42)</sup> By majority vote, first-line treatment can be done with a platinum agent, paclitaxel and pembrolizumab, with or without bevacizumab if locoregional salvage treatment is not feasible and there are no contraindications;<sup>(43)</sup> alternatively, treatment can be done with a platinum agent and paclitaxel, with or without bevacizumab.<sup>(44-46)</sup> Of note, there was less than majority vote for the need to have programmed cell death ligand 1 (PD-L1) positivity for the use of immunotherapy in the first or second line, likely as a consequence of recent results demonstrating benefit in all subgroups of PD-L1 expression when using pembrolizumab in the first line,<sup>(43)</sup> and notwithstanding the requirement for such positivity in second line.<sup>(47)</sup> For patients treated with a first-line platinum-based therapy within <6 months who need second-line treatment, immunotherapy was suggested by majority vote, and by 44% of voters for patients progressing >6 months after first-line platinum-based therapy (see Supplementary Materials, question 55).<sup>(48-50)</sup> Even though the panel emphasized poor performance status as the major indication for best supportive care.<sup>(51,52)</sup>

With regard to salvage locoregional therapy, panel recommendations clearly reflected current controversies in the literature. Chemoradiation was preferred to salvage surgery followed by chemoradiation (the latter with less than majority vote) for patients with previous surgery without

adjuvant treatment and with potentially resectable local recurrence without suspected lymph node involvement. Despite the absence of randomized trials, cisplatin-based chemoradiation is the treatment of choice when feasible for patients not previously exposed to radiation therapy.<sup>(20,53-55)</sup> For patients with potentially resectable recurrence in a previously irradiated area without suspected lymph node involvement, salvage surgery was preferred to salvage surgery followed by chemotherapy (the latter with less than majority vote). In this setting, salvage surgery is arguably the only modality with potential for cure.<sup>(56,57)</sup> Finally, salvage surgery followed by chemotherapy was preferred to salvage surgery alone (the latter with less than majority vote) for patients with potentially resectable locoregional lymph node recurrence in a previously irradiated area and without comorbidities.

Although the current recommendations are generally in line with those from international guidelines, such as from ESGO,<sup>(18)</sup> the European Society of Medical Oncology,<sup>(19,58)</sup> and NCCN,<sup>(20)</sup> the implementation of international guidelines is often challenging in countries facing resource limitations or unique health-care landscapes.<sup>(59,60)</sup> One option for these countries is to follow adapted guidelines from prominent organizations, such as the American Society of Clinical Oncology<sup>(61)</sup> and NCCN.<sup>(62,63)</sup> Another option is to develop country-specific guidelines and consensus panels, as we did in the current work. We hope that the current recommendations may help practitioners from Brazil and other countries to improve the care they provide to women with cervical cancer.

## AUTHORS' CONTRIBUTIONS

**EP:** Collection and assembly of data, Conception and design, Data analysis and interpretation, Final approval of manuscript, Manuscript writing, Provision of study materials or patient.

**GB:** Collection and assembly of data, Conception and design, Data analysis and interpretation, Final approval of manuscript, Manuscript writing, Provision of study materials or patient.

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**MAV:** Collection and assembly of data, Conception and design, Data analysis and interpretation, Final approval of manuscript, Provision of study materials or patient.

**MS:** Collection and assembly of data, Conception and design, Data analysis and interpretation, Final approval of manuscript, Provision of study materials or patient.

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**TPB:** Collection and assembly of data, Conception and design, Data analysis and interpretation, Final approval of manuscript, Provision of study materials or patient.

**FCM:** Collection and assembly of data, Conception and design, Data analysis and interpretation, Final approval of manuscript, Manuscript writing, Provision of study materials or patient.

## REFERENCES

- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021 May;71(3):209-49.
- Denny L, Sanjose S, Mutebi M, Anderson BO, Kim J, Jeronimo J, et al. Interventions to close the divide for women with breast and cervical cancer between low-income and middle-income countries and high-income countries. *Lancet.* 2017 Feb;389(10071):861-70.
- Maza M, Schocken CM, Bergman KL, Randall TC, Cremer ML. Cervical precancer treatment in low- and middle- income countries: a technology overview. *J Glob Oncol.* 2017;3(4):400-8.
- Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer.* 2015 Mar;136(5):E359-E86.
- Olson B, Gribble B, Dias J, Curryer C, Vo K, Kowal P, et al. Cervical cancer screening programs and guidelines in low- and middle-income countries. *Int J Gynaecol Obstet.* 2016 Sep;134(3):239-46.
- Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). Estimativa 2020: incidência de cancer no Brasil [Internet]. Rio de Janeiro: INCA; 2019; [access in 2022 Jan 11]. Available from: <https://www.inca.gov.br/sites/ufu.sti.inca.local/files/media/document/estimativa-2020-incidencia-de-cancer-no-brasil.pdf>
- Rodrigues AN, Melo AC, Calabrich AFC, Cronenberger E, Torres KL, Damian F, et al. Characteristics of patients diagnosed with cervical cancer in Brazil: preliminary results of the prospective cohort EVITA study (EVA001/LACOG 0215). *Int J Gynecol Cancer.* 2022;32(2):141-6.
- Paulino E, Melo AC, Silva-Filho AL, Maciel LF, Thuler LCS, Goss P, et al. Panorama of gynecologic cancer in Brazil. *JCO Glob Oncol.* 2020 Oct;6:1617-30.
- Peroni FMA, Lindelow M, Souza DO, Sjoblom M. Realizing the right to health in Brazil's Unified Health System through the lens of breast and cervical cancer. *Int J Equity Health.* 2019 Jun;18:39.
- Oliveira MM, Andrade S, Oliveira PPV, Azevedo e Silva G, Silva MMA, Matal DC. Pap-test coverage in women aged 25 to 64 years old, according to the National Health Survey and the Surveillance System for Risk and Protective Factors for Chronic Diseases by Telephone Survey, 2013. *Rev Bras Epidemiol.* 2018;21:e180014.
- Carvalho NP, Pilecco FB, Cherchiglia ML. Regional inequalities in cervical cancer survival in Minas Gerais State, Brazil. *Cancer Epidemiol.* 2021 Apr;71(Pt A):101899.
- Dantas DB, Costa TL, Silva ASA, Gomes FC, Melo-Neto JS. Mortality from cervical cancer in Brazil: an ecological epidemiologic study of a 22-year analysis. *Ecanermedicalscience.* 2020;14:1064.
- Oliveira NPD, Siqueira CADS, Lima KYN, Cancela MC, Souza DLB. Association of cervical and breast cancer mortality with socioeconomic indicators and availability of health services. *Cancer Epidemiol.* 2020 Feb;64:101660.
- Theme Filha MM, Leal MD, Oliveira EF, Esteves-Pereira AP, Gama SGN. Regional and social inequalities in the performance of Pap test and screening mammography and their correlation with lifestyle: Brazilian national health survey, 2013. *Int J Equity Health.* 2016;15:136.
- Silva IF, Ferreira da Silva I, Koifman RJ. Cervical cancer treatment delays and associated factors in a cohort of women from a developing country. *J Glob Oncol.* 2019;5:1-11.
- Ribeiro CM, Silva IS, Eluf Neto J, Cury LCPB, Azevedo e Silva G. Follow-up of women screened for cervical cancer in Sao Paulo, Brazil: An analysis of the times to diagnostic investigation and treatment. *Cancer Epidemiol.* 2021;72:101940.
- Bhatla N, Berek JS, Fredes MC, Denny LA, Grenman S, Karunaratne K, et al. Revised FIGO staging for carcinoma of the cervix uteri. *Int J Gynaecol Obstet.* 2019;145:129-35.
- Cibula D, Potter R, Planchamp F, Avall-Lundqvist E, Fischerova D, Haie-Meder C, et al. The European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology guidelines for the management of patients with cervical cancer. *Int J Gynecol Cancer.* 2018 Jun;28:641-55.

19. Marth C, Landoni F, Mahner S, McCormack M, Gonzalez-Martin A, Colombo N, et al. Cervical cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2017 Jul;28(Suppl 4):iv72-iv83.
20. National Comprehensive Cancer Network (NCCN). NCCN Practice Guidelines in Oncology. Cervical Cancer - v.1.2022 [Internet]. Plymouth Meeting: NCCN; 2022; [access in 2022 Jan 07]. Available from: <http://www.nccn.org>
21. Elit L, Fyles AW, Devries MC, Oliver TK, Fung-Kee-Fung M; Gynecology Cancer Disease Site Group. Follow-up for women after treatment for cervical cancer: a systematic review. *Gynecol Oncol*. 2009 Sep;114(3):528-35.
22. Elit LM, Fyles AW, Gu CS, Pond GR, D'Souza D, Samant R, et al. Effect of positron emission tomography imaging in women with locally advanced cervical cancer: a randomized clinical trial. *JAMA Netw Open*. 2018 Sep;1(5):e182081.
23. Sedlis A, Bundy BN, Rotman MZ, Lentz SS, Muderspach LI, Zaino RJ. A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: a Gynecologic Oncology Group Study. *Gynecol Oncol*. 1999 May;73(2):177-83.
24. Peters WA, Liu PY, Barrett RJ, Stock RJ, Monk BJ, Berek JS, et al. Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. *J Clin Oncol*. 2000 Apr;18(8):1606-13.
25. Cibula D, Abu-Rustum NR, Dusek L, Zikán M, Zaal A, Sevcik L, et al. Prognostic significance of low volume sentinel lymph node disease in early-stage cervical cancer. *Gynecol Oncol*. 2012 Mar;124(3):496-501.
26. Cibula D, Kocian R, Plaikner A, Jarkovsky J, Klat J, Zapardiel I, et al. Sentinel lymph node mapping and intraoperative assessment in a prospective, international, multicentre, observational trial of patients with cervical cancer: the SENTIX trial. *Eur J Cancer*. 2020 Sep;137:69-80.
27. Lecuru FR, McCormack M, Hillemanns P, Anota A, Leitao M, Mathevet P, et al. SENTICOL III: an international validation study of sentinel node biopsy in early cervical cancer. A GINECO, ENGOT, GCIG and multicenter study. *Int J Gynecol Cancer*. 2019 May;29(4):829-34.
28. Guani B, Mahiou K, Crestani A, Cibula D, Buda A, Gaillard T, et al. Clinical impact of low-volume lymph node metastases in early-stage cervical cancer: a comprehensive meta-analysis. *Gynecol Oncol*. 2022 Feb;164(2):446-54.
29. Guani B, Dorez M, Magaud L, Buenerd A, Lecuru F, Mathevet P. Impact of micrometastasis or isolated tumor cells on recurrence and survival in patients with early cervical cancer: SENTICOL Trial. *Int J Gynecol Cancer*. 2019 Mar;29(3):447-52.
30. Wenzel HHB, Smolders RGV, Beltman JJ, Lambrechts S, Trum HW, Yigit R, et al. Survival of patients with early-stage cervical cancer after abdominal or laparoscopic radical hysterectomy: a nationwide cohort study and literature review. *Eur J Cancer*. 2020 Jul;133:14-21.
31. Melamed A, Margul DJ, Chen L, Keating NL, Del Carmen MG, Yang J, et al. Survival after minimally invasive radical hysterectomy for early-stage cervical cancer. *N Engl J Med*. 2018 Nov;379:1905-14.
32. Ramirez PT, Frumovitz M, Pareja R, Lopez A, Vieira M, Ribeiro R, et al. Minimally invasive versus abdominal radical hysterectomy for cervical cancer. *N Engl J Med*. 2018 Nov;379(20):1895-904.
33. Green JA, Kirwan JM, Tierney JF, Symonds P, Fresco K, Collingwood M, et al. Survival and recurrence after concomitant chemotherapy and radiotherapy for cancer of the uterine cervix: a systematic review and meta-analysis. *Lancet*. 2001 Sep;358(9284):781-6.
34. Xue R, Cai X, Xu H, Wu S, Haung H. The efficacy of concurrent weekly carboplatin with radiotherapy in the treatment of cervical cancer: a meta-analysis. *Gynecol Oncol*. 2018 Sep;150(3):412-9.
35. Dryden-Peterson S, Bvochora-Nsingo M, Suneja G, Efstathiou JA, Grover S, Chiyapo S, et al. HIV infection and survival among women with cervical cancer. *J Clin Oncol*. 2016 Nov;34(31):3749-57.
36. Ghebrey RG, Grover S, Xu MJ, Chuang LT, Simonds H. Cervical cancer control in HIV-infected women: past, present and future. *Gynecol Oncol Rep*. 2017 Jul;21:101-8.
37. Gupta S, Maheshwari A, Parab P, Mahantshetty U, Hawaldar R, Chopra SS, et al. Neoadjuvant chemotherapy followed by radical surgery versus concomitant chemotherapy and radiotherapy in patients with stage IB2, IIA, or IIB squamous cervical cancer: a randomized controlled trial. *J Clin Oncol*. 2018 Jun;36(16):1548-55.
38. Sardain H, Lavoue V, Redpath M, Bertheuil N, Foucher F, Levêque J. Curative pelvic exenteration for recurrent cervical carcinoma in the era of concurrent chemotherapy and radiation therapy. A systematic review. *Eur J Surg Oncol*. 2015 Aug;41(8):975-85.
39. Pergialiotis V, Bellos I, Douligeris A, Thomakos N, Rodolakis A, Haidopoulos D. The impact of adjuvant hysterectomy on survival outcomes of patients with locally advanced cervical cancer: a network meta-analysis. *Eur J Surg Oncol*. 2022 Jan;48(1):261-7.
40. Horeweg N, Mittal P, Gradowska PL, Boere I, Chopra S, Nout RA. Adjuvant systemic therapy after chemoradiation and brachytherapy for locally advanced cervical cancer: a systematic review and meta-analysis. *Cancers (Basel)*. 2021 Apr;13(8):1880.
41. Kokka F, Bryant A, Brockbank E, Powell M, Oram D. Hysterectomy with radiotherapy or chemotherapy or both for women with locally advanced cervical cancer. *Cochrane Database Syst Rev*. 2015 Apr;2015:CD010260.

42. Simonds HM, Botha MH, Neugut AI, Van Der Merwe FH, Jacobson JS. Five-year overall survival following chemoradiation among HIV-positive and HIV-negative patients with locally advanced cervical carcinoma in a South African cohort. *Gynecol Oncol*. 2018 Nov;151(2):215-20.
43. Colombo N, Dubot C, Lorusso D, Caceres MV, Hasegawa K, Shapira-Frommer R, et al. Pembrolizumab for persistent, recurrent, or metastatic cervical cancer. *N Engl J Med*. 2021 Nov;385(20):1856-67.
44. Tewari KS, Sill MW, Long HJ, Penson RT, Huang H, Ramondetta LM, et al. Improved survival with bevacizumab in advanced cervical cancer. *N Engl J Med*. 2014 Feb;370:734-43.
45. Tewari KS, Sill MW, Penson RT, Huang H, Ramondetta LM, Landrum LM, et al. Bevacizumab for advanced cervical cancer: final overall survival and adverse event analysis of a randomised, controlled, open-label, phase 3 trial (Gynecologic Oncology Group 240). *Lancet*. 2017 Oct;390(10103):1654-63.
46. Suzuki K, Nagao S, Shibutani T, Yamamoto K, Jimi T, Yano H, et al. Phase II trial of paclitaxel, carboplatin, and bevacizumab for advanced or recurrent cervical cancer. *Gynecol Oncol*. 2019 Sep;154(3):554-7.
47. KEYTRUDA® (pembrolizumab). Highlights of prescribing information [Internet]. New Jersey: Food and Drug Administration (FDA); 2021; [access in 2022 Jan 23]. Available from: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2021/125514s096lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125514s096lbl.pdf)
48. Chung HC, Ros W, Delord JP, Perets R, Italiano A, Shapira-Frommer R, et al. Efficacy and safety of pembrolizumab in previously treated advanced cervical cancer: results from the phase II KEYNOTE-158 study. *J Clin Oncol*. 2019 Jun;37(17):1470-8.
49. Frenel JS, Le Tourneau C, O'Neil B, Ott PA, Pihapaul SA, Gomez-Roca C, et al. Safety and efficacy of pembrolizumab in advanced, programmed death ligand 1-positive cervical cancer: results from the phase Ib KEYNOTE-028 Trial. *J Clin Oncol*. 2017 Dec;35(36):4035-41.
50. Rischin D, Gil-Martin M, Gonzalez-Martin A, Braña I, Hou JY, Cho D, et al. PD-1 blockade in recurrent or metastatic cervical cancer: Data from cemiplimab phase I expansion cohorts and characterization of PD-L1 expression in cervical cancer. *Gynecol Oncol*. 2020 Nov;159(2):322-8.
51. Allen D, Narayan K. Managing advanced-stage cervical cancer. *Best Pract Res Clin Obstet Gynaecol*. 2005 Aug;19(4):591-609.
52. Ramondetta L. What is the appropriate approach to treating women with incurable cervical cancer? *J Natl Compr Canc Netw*. 2013 Mar;11(3):348-55.
53. Maneo A, Landoni F, Cormio G, Colombo A, Placa F, Pellegrino A, et al. Concurrent carboplatin/5-fluorouracil and radiotherapy for recurrent cervical carcinoma. *Ann Oncol*. 1999 Jul;10(7):803-7.
54. Cerrotta A, Gardan G, Cavina R, Raspagliese F, Stefanon B, Garassino I, et al. Concurrent radiotherapy and weekly paclitaxel for locally advanced or recurrent squamous cell carcinoma of the uterine cervix. A pilot study with intensification of dose. *Eur J Gynaecol Oncol*. 2002;23(2):115-9.
55. Windschall A, Ott OJ, Sauer R, Strnad V. Radiation therapy and simultaneous chemotherapy for recurrent cervical carcinoma. *Strahlenther Onkol*. 2005 Aug;181(8):545-50.
56. Mabuchi S, Matsumoto Y, Komura N, Sawada M, Tanaka M, Yokoi E, et al. The efficacy of surgical treatment of recurrent or persistent cervical cancer that develops in a previously irradiated field: a monoinstitutional experience. *Int J Clin Oncol*. 2017 Oct;22(5):927-36.
57. Rema P, Mathew AP, Suchetha S, Ahmed I. Salvage surgery for cervical cancer recurrences. *Indian J Surg Oncol*. 2017 Jun;8(2):146-9.
58. Marth C, Landoni F, Mahner S, McCormack M, Gonzalez-Martin A, Colombo N, et al. Cervical cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2018;29:iv262.
59. Carlson RW, Larsen JK, McClure J, Fitzgerald CL, Venook AP, Benson AB, et al. International adaptations of NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2014 May;12(5):643-8.
60. Chopra SJ, Mathew A, Maheshwari A, Bhatla N, Singh S, Rai B, et al. National Cancer Grid of India Consensus Guidelines on the Management of Cervical Cancer. *J Glob Oncol*. 2018 Jul;4:1-15.
61. Chuang LT, Temin S, Camacho R, Dueñas-Gonzales A, Feldman S, Gultekin M, et al. Management and care of women with invasive cervical cancer: American Society of Clinical Oncology resource-stratified clinical practice guideline. *J Glob Oncol*. 2016 Oct;2(5):311-40.
62. Jazieh AR, Azim HA, McClure J, Jahanzeb M. The process of NCCN guidelines adaptation to the Middle East and North Africa region. *J Natl Compr Canc Netw*. 2010 Jul;8(Suppl 3):S5-7.
63. Akaza H. What is the Asian Consensus Statement on NCCN clinical practice guidelines in oncology (NCCN-ACS)? *Jpn J Clin Oncol*. 2016 Apr;46(4):299-302.

## Supplementary Materials

Consensus panel questions and answers.

Q#	Question	Answers
1	After the diagnosis of microscopic cervical cancer in a cone specimen (stage IA1 with positive lymphovascular involvement or IA2), is it necessary to perform any additional imaging staging tests?	A. Abdominal/pelvic/transvaginal ultrasound and chest X-ray; <b>0.0% (0/21)</b> B. CT of the abdomen and pelvis and chest X-ray; <b>23.8% (5/21)</b> C. Abdominal, pelvic, and chest CT; <b>4.8% (1/21)</b> D. MRI of the abdomen and pelvis and chest X-ray; <b>47.6% (10/21)</b> E. MRI of abdomen and pelvis and PET-CT; <b>0.0% (0/21)</b> F. None; <b>23.5% (5/21)</b> G. Abstention <b>0.0% (0/21)</b>
2	Which additional imaging method is indicated for cervical cancer, clinical stage IB1 or IB2 (FIGO 2018)?	A. Abdominal/pelvic/transvaginal ultrasound and chest X-ray; <b>0.0% (0/21)</b> B. CT of the abdomen and pelvis and chest X-ray; <b>9.5% (2/21)</b> C. Abdominal, pelvic, and chest CT; <b>4.8% (1/21)</b> D. MRI of the abdomen and pelvis and chest X-ray; <b>61.9% (13/21)</b> E. MRI of abdomen and pelvis and PET-CT; <b>23.8% (5/21)</b> F. None; <b>0.0% (0/21)</b> G. Abstention <b>0.0% (0/21)</b>
3	Which additional imaging method is indicated for cervical cancer, clinical stage IB1 or lower if radical trachelectomy is being considered?	A. Abdominal/pelvic ultrasound and chest X-ray; <b>4.8% (1/21)</b> B. Abdominal and pelvic CT and chest X-ray; <b>4.8% (1/21)</b> C. Abdominal, pelvic, and chest CT; <b>0.0% (0/21)</b> D. Abdominal and pelvic MRI and chest X-ray; <b>66.7% (14/21)</b> E. MRI of abdomen and pelvis and PET-CT; <b>23.8% (5/21)</b> F. None; <b>0.0% (0/21)</b> G. Abstention <b>0.0% (0/21)</b>
4	Which additional imaging method is indicated for clinical stages IB3-IVA?	A. Abdominal/pelvic/transvaginal ultrasound and chest X-ray; <b>0.0% (0/22)</b> B. CT of the abdomen and pelvis and chest X-ray; <b>9.1% (2/22)</b> C. Abdominal, pelvic, and chest CT; <b>4.5% (1/22)</b> D. MRI of the abdomen and pelvis and chest X-ray; <b>13.6% (3/22)</b> E. MRI of abdomen and pelvis and PET-CT; <b>72.7% (16/22)</b> F. None; <b>0.0% (0/22)</b> G. Abstention <b>0.0% (0/22)</b>
5	What is the next step in patients with an indication for chemoradiotherapy and suspected para-aortic lymph nodes (by PET-CT, MRI or CT)?	A. Surgical staging; <b>45.5% (10/22)</b> B. Image-guided percutaneous biopsy; <b>4.5% (1/22)</b> C. Start treatment without further investigation with extended field radiotherapy; <b>50.0% (11/22)</b> D. Abstention <b>0.0% (0/22)</b>
6	For patients with early-stage cervical cancer who have undergone radical hysterectomy, should vaginal cytology be performed?	A. Yes; <b>81.8% (18/22)</b> B. No; <b>18.2% (4/22)</b> C. Abstention <b>0.0% (0/22)</b>
7	How often do you follow patients treated with early-stage disease ( $\leq$ IB2) after curative treatment?	A. Every 3 months for the first 2 years; thereafter, every 6 months up to 5 years from treatment; <b>76.2% (16/21)</b> B. Every 6 months up to 5 years from treatment; <b>4.8% (1/21)</b> C. Annually up to 5 years after treatment; <b>0.0% (0/21)</b> D. Every 6 months for the first 2 years, thereafter, annually until 5 years from treatment; <b>19.0% (0/21)</b> E. None; <b>0.0% (0/21)</b> F. Abstention <b>0.0% (0/21)</b>

8	What is the best follow-up for patients with early-stage cervical cancer (FIGO 2018 IA-IB2) who have had curative treatment?	<p>A. Physical examination and imaging tests only in case of suspected recurrence; <b>10.0% (2/20)</b></p> <p>B. Physical examination, laboratory tests and imaging tests only in case of suspected recurrence; <b>15.0% (3/20)</b></p> <p>C. Physical examination, laboratory tests, vaginal cytology and imaging tests only in case of suspected recurrence; <b>45.0% (9/20)</b></p> <p>D. Physical examination, vaginal cytology, pelvic abdominal computed tomography and chest X-ray; <b>20.0% (4/20)</b></p> <p>E. Physical examination, vaginal cytology, HPV-DNA, pelvic abdominal US and chest X-ray; <b>10.0% (2/20)</b></p> <p>F. None; <b>0.0% (0/20)</b></p> <p>G. Abstention <b>0.0% (0/20)</b></p>
9	How often do you follow up patients treated with locally advanced disease after curative treatment?	<p>A. Every 3-6 months for the first 2 years; thereafter, every 6-12 months for up to 5 years from treatment; <b>100.0% (22/22)</b></p> <p>B. Every 6 months up to 5 years from treatment; <b>0.0% (0/22)</b></p> <p>C. Annually up to 5 years after treatment; <b>0.0% (0/22)</b></p> <p>D. None; <b>0.0% (0/22)</b></p> <p>E. Abstention <b>0.0% (0/22)</b></p>
10	What is the recommended follow-up assessment for patients with locally advanced cervical cancer (FIGO IB3-IVA) who have had curative treatment?	<p>A. Physical examination only; <b>4.5% (1/22)</b></p> <p>B. Physical examination, HPV DNA and laboratory work; <b>0.0% (0/22)</b></p> <p>C. Physical examination, laboratory evaluation, PET-CT 3-6 months later, MRI of the pelvis 3-6 months and vaginal cytology; <b>22.7% (5/22)</b></p> <p>D. Physical examination, vaginal cytology, CT or MRI of the abdomen/pelvis 3-6 months later and chest X-ray; <b>59.1% (13/22)</b></p> <p>E. Physical examination, pelvic abdominal tomography and chest X-ray; <b>9.1% (2/22)</b></p> <p>F. None; <b>4.5% (1/22)</b></p> <p>G. Abstention <b>0.0% (0/22)</b></p>
11	What is your treatment recommendation for women with stage IA1 cervical cancer, no LVI, diagnosed by conization and free margins (no desired fertility)?	<p>A. Observation after conization <b>31.8% (7/22)</b></p> <p>B. Adjuvant radiotherapy; <b>0.0% (0/22)</b></p> <p>C. Radical hysterectomy; <b>13.6% (3/22)</b></p> <p>D. Simple hysterectomy; <b>40.9% (9/22)</b></p> <p>E. Radical trachelectomy; <b>13.6% (3/22)</b></p> <p>F. Abstention <b>0.0% (0/22)</b></p>
12	What is your treatment recommendation for women with stage IA1 cervical cancer with ILV or IA2 diagnosed by conization and free margins (no desired fertility)?	<p>A. Observation after conization; <b>0.0% (0/22)</b></p> <p>B. Adjuvant chemoradiotherapy; <b>0.0% (0/22)</b></p> <p>C. Radical hysterectomy + Lymph node evaluation; <b>54.5% (12/22)</b></p> <p>D. Simple hysterectomy + lymph node evaluation; <b>45.5% (10/22)</b></p> <p>E. Simple hysterectomy; <b>0.0% (0/22)</b></p> <p>F. Abstention <b>0.0% (0/22)</b></p>
13	What is your treatment recommendation for women with cervical cancer stage FIGO 2018 IB1, IB2 (no desired fertility)?	<p>A. Curative chemoradiotherapy; <b>13.6% (3/22)</b></p> <p>B. Curative radiotherapy; <b>0.0% (0/22)</b></p> <p>C. Radical hysterectomy + Lymph node evaluation; <b>81.8% (18/22)</b></p> <p>D. Simple hysterectomy + lymph node evaluation; <b>4.5% (1/22)</b></p> <p>E. Radical hysterectomy only; <b>0.0% (0/22)</b></p> <p>F. Abstention <b>0.0% (0/22)</b></p>

14	What is your treatment recommendation for women with cervical cancer stage FIGO 2018 IIA1 (no desired fertility)?	<p>A. Curative chemoradiotherapy; <b>40.9% (9/22)</b></p> <p>B. Curative radiotherapy; <b>0.0% (0/22)</b></p> <p>C. Radical hysterectomy + lymph node evaluation; <b>54.5% (12/22)</b></p> <p>D. Simple hysterectomy + lymph node evaluation; <b>0.0% (0/22)</b></p> <p>E. Radical hysterectomy only; <b>4.5% (1/22)</b></p> <p>F. Abstention <b>0.0% (0/22)</b></p>
15	What is your treatment recommendation for women with stage IA1 cervical cancer, without LVI, diagnosed by conization and free margins, and who wish to maintain fertility?	<p>A. Would indicate ovarian transposition and curative chemoradiotherapy; <b>0.0% (0/21)</b></p> <p>B. Indicate ovarian ovarian transposition and curative radiotherapy; <b>0.0% (0/21)</b></p> <p>C. Would indicate simple hysterectomy with ovarian preservation; <b>0.0% (0/21)</b></p> <p>D. Would indicate simple trachelectomy; <b>52.4% (11/21)</b></p> <p>E. Conization only after free margins; <b>47.6% (10/21)</b></p> <p>F. Abstention <b>0.0% (0/21)</b></p>
16	What is your treatment recommendation for women with stage IA1 cervical cancer with LVI or IA2 diagnosed by conization and clear margins and a desire to maintain fertility?	<p>A. Would indicate ovarian transposition and curative chemoradiotherapy; <b>0.0% (0/21)</b></p> <p>B. Would indicate simple hysterectomy + lymph node evaluation with ovarian preservation; <b>0.0% (0/21)</b></p> <p>C. Would indicate simple trachelectomy + lymph node evaluation; <b>28.6% (6/21)</b></p> <p>D. Would indicate radical trachelectomy + lymph node evaluation; <b>52.4% (11/21)</b></p> <p>E. Only conization after free margins + Lymph node evaluation; <b>9.5% (2/21)</b></p> <p>F. Abstention <b>9.5% (2/21)</b></p>
17	What is your treatment recommendation for women with stage IB1 cervical cancer who want to maintain fertility?	<p>A. Would indicate ovarian transposition and curative chemoradiotherapy; <b>0.0% (0/23)</b></p> <p>B. Would indicate simple hysterectomy + lymph node evaluation with ovarian preservation; <b>0.0% (0/23)</b></p> <p>C. Would indicate simple trachelectomy + lymph node evaluation; <b>4.3% (1/23)</b></p> <p>D. Would indicate radical trachelectomy + lymph node evaluation; <b>82.6% (19/23)</b></p> <p>E. Only conization after free margins + Lymph node evaluation; <b>8.7% (2/23)</b></p> <p>F. Abstention <b>4.3% (1/23)</b></p>
18	What is your treatment recommendation for women with stage IB2 cervical cancer who want to maintain fertility?	<p>A. Would indicate ovarian transposition and curative chemoradiotherapy; <b>4.2% (1/24)</b></p> <p>B. Would indicate radical hysterectomy + lymph node evaluation; <b>8.3% (2/24)</b></p> <p>C. Would indicate simple trachelectomy + lymph node evaluation; <b>4.2% (1/24)</b></p> <p>D. Would indicate radical trachelectomy + lymph node evaluation; <b>29.2% (7/24)</b></p> <p>E. Would indicate neoadjuvant chemotherapy followed by radical trachelectomy + lymph node evaluation; <b>41.7% (10/24)</b></p> <p>F. Abstention <b>12.5% (3/24)</b></p>
19	What is the surgical access for the surgical treatment of cervical cancer ( $\leq 4$ cm)?	<p>A. Open (laparotomy); <b>69.6% (16/23)</b></p> <p>B. Minimally Invasive (laparoscopic or robotic); <b>8.7% (2/23)</b></p> <p>C. Minimally invasive (laparoscopic or robotic) but without the use of a uterine manipulator and with a protective vaginal closure maneuver <b>8.7% (2/23)</b></p> <p>D. Abstention <b>13.0% (3/23)</b></p>
20	Which surgical access is indicated for patients with cervical cancer $\leq 2$ cm?	<p>A. Open (laparotomy); <b>45.5% (10/22)</b></p> <p>B. Minimally Invasive (laparoscopic or robotic); <b>18.2% (4/22)</b></p> <p>C. Minimally invasive (laparoscopic or robotic) but without the use of a uterine manipulator and with a protective vaginal closure maneuver; <b>31.8% (7/22)</b></p> <p>D. Abstention <b>4.5% (1/22)</b></p>

21	In case of absence of clinical and imaging residual tumor after conization/trachelectomy and free margins, which surgical access is indicated for the surgical treatment of cervical cancer?	A. Open (laparotomy); <b>33.3% (8/24)</b> B. Minimally Invasive (laparoscopic or robotic), <b>16.7% (4/24)</b> C. Minimally invasive (laparoscopic or robotic) but without the use of a uterine manipulator and with a protective vaginal closure maneuver; <b>33.3% (8/24)</b> D. Abstention <b>16.7% (4/24)</b>
22	When would simple hysterectomy be indicated in the surgical treatment of cervical cancer?	A. Tumors <2 cm, <10 mm stromal invasion, no ILV and no lymph node metastasis; <b>47.8% (11/23)</b> B. All tumors <2 cm; <b>0.0% (0/23)</b> C. I do not think simple hysterectomy is appropriate in this setting; <b>43.5% (10/23)</b> D. abstention <b>8.7% (2/23)</b>
23	What is the proper procedure for lymph node evaluation in patients with stage IA1 tumors with LVI or IA2?	A. Pelvic ± paraaortic lymphadenectomy; <b>0.0% (0/23)</b> B. Sentinel lymph node investigation followed by lymphadenectomy; <b>30.4% (7/23)</b> C. Sentinel lymph node survey only; <b>60.9% (14/23)</b> D. There is no need for lymph node evaluation in this setting; <b>4.3% (1/23)</b> E. Abstention <b>4.3% (1/23)</b>
24	What is the proper procedure for lymph node evaluation in patients with stage IB1 tumors?	A. Pelvic ± paraaortic lymphadenectomy; <b>8.7% (2/23)</b> B. Sentinel lymph node investigation followed by lymphadenectomy; <b>47.8% (11/23)</b> C. Sentinel lymph node survey only; <b>39.1% (9/23)</b> D. There is no need for lymph node evaluation in this setting; <b>0.0% (0/23)</b> E. Abstention <b>4.3% (1/23)</b>
25	What is the proper procedure for lymph node evaluation in patients with stage IB2 tumors?	A. Pelvic ± paraaortic lymphadenectomy; <b>31.8% (7/22)</b> B. Sentinel lymph node investigation followed by lymphadenectomy; <b>59.1% (13/22)</b> C. Sentinel lymph node survey only; <b>9.1% (2/22)</b> D. There is no need for lymph node evaluation in this setting; <b>0.0% (0/22)</b> E. Abstention <b>0.0% (0/22)</b>
26	What is your treatment recommendation for women with stage IB3 to IIB cervical cancer?	A. Curative treatment with chemoradiotherapy followed by brachytherapy; <b>100.0% (22/22)</b> B. Neoadjuvant chemoradiotherapy followed by surgery; <b>0.0% (0/22)</b> C. Surgery followed by chemoradiotherapy; <b>0.0% (0/22)</b> D. Neoadjuvant chemotherapy followed by surgery; <b>0.0% (0/22)</b> E. Neoadjuvant chemotherapy followed by radiotherapy; <b>0.0% (0/22)</b> F. Neoadjuvant chemotherapy followed by surgery and radiotherapy; <b>0.0% (0/22)</b> G. Abstention <b>0.0% (0/22)</b>
27	After an incidental diagnosis of IA2 without lymphovascular invasion in a simple hysterectomy specimen and absence of enlarged pelvic lymph nodes assessed by computed tomography, what is the best approach?	A. Strict follow-up; <b>47.4% (9/19)</b> B. External radiotherapy; <b>0.0% (0/19)</b> C. Simultaneous chemoradiation; <b>5.3% (1/19)</b> D. Colpectomy + parametrectomy + Pelvic lymphadenectomy; <b>15.8% (3/19)</b> E. Pelvic lymphadenectomy; <b>31.6% (6/19)</b> F. Abstention <b>0.0% (0/19)</b>

28	What is your treatment recommendation for early-stage women who meet Sedlis criteria after surgical treatment (lymphovascular invasion, cervical stromal invasion, or tumor size $\geq 2-4$ cm)?	<p>A. Observation; <b>0.0% (0/23)</b>          B. Adjuvant radiotherapy; <b>82.6% (19/23)</b>          C. Concomitant adjuvant chemoradiotherapy; <b>17.4% (4/23)</b>          D. Adjuvant chemotherapy; <b>0.0% (0/23)</b>          E. Abstention <b>0.0% (0/23)</b></p>
29	What is your treatment recommendation for women with early-stage cervical cancer after surgery with at least one high-risk feature (positive surgical margins, positive lymph node, or compromised parametrium)?	<p>A. Observation; <b>0.0% (0/22)</b>          B. Adjuvant radiotherapy; <b>0.0% (0/22)</b>          C. Concomitant adjuvant chemoradiotherapy; <b>95.5% (21/22)</b>          D. Adjuvant chemotherapy; <b>0.0% (0/22)</b>          E. Concomitant adjuvant chemoradiotherapy followed by chemotherapy; <b>4.5% (1/22)</b>          F. Abstention <b>0.0% (0/22)</b></p>
30	What is your recommendation for adjuvant treatment in the case of isolated tumor cells ( $< 0.2$ mm) in the sentinel lymph node in a patient without Sedlis criteria or at high risk?	<p>A. Observation; <b>68.2% (15/22)</b>          B. Adjuvant radiotherapy; <b>13.6% (3/22)</b>          C. Concomitant adjuvant chemoradiotherapy; <b>18.2% (4/22)</b>          D. Adjuvant chemotherapy; <b>0.0% (0/22)</b>          E. Concomitant adjuvant chemoradiotherapy followed by chemotherapy; <b>0.0% (0/22)</b>          F. Abstention <b>0.0% (0/22)</b></p>
31	What is your recommendation for adjuvant treatment in case of micrometastasis (0.2-2 mm) in the sentinel node?	<p>A. Observation; <b>8.7% (2/23)</b>          B. Adjuvant radiotherapy; <b>8.7% (2/23)</b>          C. Concomitant adjuvant chemoradiotherapy; <b>82.6% (19/23)</b>          D. Adjuvant chemotherapy; <b>0.0% (0/23)</b>          E. Concomitant adjuvant chemoradiotherapy followed by chemotherapy; <b>0.0% (0/23)</b>          F. Abstention <b>0.0% (0/23)</b></p>
32	Do you recommend vaginal vault brachytherapy after external radiotherapy, as a booster, for patients with early-stage cervical cancer in the presence of intermediate or high-risk features (Sedlis or Peters)?	<p>A. Yes (for both scenarios), <b>35.0% (7/20)</b>          B. Yes (for Peters criteria only); <b>15.0% (3/20)</b>          C. Yes (for Sedlis criteria only); <b>5.0% (1/20)</b>          D. Recommend only for positive vaginal margin; <b>40.0% (8/20)</b>          E. I don't recommend it ;<b>5.0% (1/20)</b>          F. Abstention <b>0.0% (0/20)</b></p>

33	In cervical cancer patients scheduled for radical hysterectomy and pelvic lymphadenectomy, if you find suspicious lymph nodes early in surgery, what is your recommendation?	<p>A. Proceed with surgery as planned (radical hysterectomy with pelvic ± para-aortic lymphadenectomy); <b>0.0% (0/22)</b></p> <p>B. Resect the suspected lymph node and send it for freezing. In case of confirmed metastasis, abort the surgery without any further dissection; <b>27.3% (6/22)</b></p> <p>C. Resect the suspected lymph node and send it for freezing. In case of confirmed metastasis, perform pelvic lymphadenectomy and maintain the uterus; <b>9.1% (2/22)</b></p> <p>D. Resect the suspected lymph node and send it for freezing. In case of confirmed metastasis, perform para-aortic lymphadenectomy to staging and maintain the uterus; <b>40.9% (9/22)</b></p> <p>E. Resect the suspected lymph node and send it for freezing. In case of confirmed metastasis, perform pelvic + para-aortic lymphadenectomy and maintain the uterus; <b>18.2% (4/22)</b></p> <p>F. Abstention <b>4.5% (1/22)</b></p>
34	What is your treatment recommendation for women with stage IIIB through IVA cervical cancer?	<p>A. Surgery followed by radiotherapy; <b>0.0% (0/23)</b></p> <p>B. Surgery followed by chemoradiotherapy; <b>0.0% (0/23)</b></p> <p>C. Neoadjuvant chemotherapy followed by surgery; <b>0.0% (0/23)</b></p> <p>D. Curative treatment with chemoradiotherapy followed by brachytherapy; <b>100.0% (23/23)</b></p> <p>E. Neoadjuvant chemotherapy followed by surgery and radiotherapy; <b>0.0% (0/23)</b></p> <p>F. Neoadjuvant chemotherapy followed by radiotherapy; <b>0.0% (0/23)</b></p> <p>G. Abstention <b>0.0% (0/23)</b></p>
35	Do you recommend adjuvant chemotherapy after definitive treatment with chemoradiotherapy followed by brachytherapy?	<p>A. Yes, for all cases of locally advanced disease; <b>4.5% (1/22)</b></p> <p>B. Yes, only for positive lymph nodes (pelvic or para-aortic); <b>0.0% (0/22)</b></p> <p>C. Yes, only for positive para-aortic lymph nodes; <b>4.5% (1/22)</b></p> <p>D. No; <b>86.4% (19/22)</b></p> <p>E. Abstention <b>4.5% (1/22)</b></p>
36	If adjuvant chemotherapy is indicated, which regimen?	<p>A. Carboplatin and paclitaxel; <b>4.5% (1/22)</b></p> <p>B. Cisplatin and paclitaxel; <b>4.5% (1/22)</b></p> <p>C. Cisplatin and gemcitabine; <b>9.1% (2/22)</b></p> <p>D. Another regimen; <b>0.0% (0/22)</b></p> <p>E. I do not recommend adjuvant chemotherapy; <b>77.3% (17/22)</b></p> <p>F. Abstention <b>4.5% (1/22)</b></p>
37	In patients with locally advanced stage IB3, IIA2 and IIB cervical cancer, what is the best treatment when radiotherapy is not available?	<p>A. Isolated chemotherapy; <b>0.0% (0/22)</b></p> <p>B. Neoadjuvant chemotherapy followed by surgery; <b>77.3% (17/22)</b></p> <p>C. Isolated surgery; <b>0.0% (0/22)</b></p> <p>D. Surgery followed by chemotherapy; <b>18.2% (4/22)</b></p> <p>E. None; <b>0.0% (0/22)</b></p> <p>F. Abstention <b>4.5% (1/22)</b></p>
38	In situations where brachytherapy is not feasible (due to anatomical changes or unavailability of brachytherapy) how do you treat patients with cervical cancer in stages IB3 to IVA?	<p>A. Chemoradiotherapy followed by surgery; <b>17.4% (4/23)</b></p> <p>B. Chemoradiotherapy followed by external radiotherapy boost; <b>69.6% (16/23)</b></p> <p>C. Chemoradiotherapy only and reserve surgery in case of residual disease; <b>13.0% (3/23)</b></p> <p>D. Neoadjuvant chemotherapy followed by surgery; <b>0.0% (0/23)</b></p> <p>E. Neoadjuvant chemotherapy followed by surgery and radiotherapy; <b>0.0% (0/23)</b></p> <p>F. Abstention; <b>0.0% (0/23)</b></p>

39	<p>Patients with cervical cancer in stages IB3 to IVA and complete clinical response with combined treatment followed by brachytherapy. Is there a role for adjuvant hysterectomy (no disease on physical examination or imaging)?</p>	<p>A. Yes, for bulky tumors; <b>0.0% (0/23)</b>          B. Yes, for adenocarcinoma histology; <b>4.3% (1/23)</b>          C. Yes, for answer A and B; <b>4.3% (1/23)</b>          D. There is no role for adjuvant hysterectomy; <b>91.3% (21/23)</b>          E. Abstention <b>0.0% (0/23)</b></p>
40	<p>In patients with locally advanced cervical cancer who undergo combined treatment followed by brachytherapy and only persist with residual disease in the cervix (with biopsy confirming), what would be your approach?</p>	<p>A. Hysterectomy if surgically feasible disease with free margins; <b>90.5% (19/21)</b>          B. Pelvic exenteration; <b>9.5% (2/21)</b>          C. Start palliative chemotherapy; <b>0.0% (0/21)</b>          D. Initiate palliative chemotherapy only after clinical or imaging progression; <b>0.0% (0/21)</b>          E. Booster radiotherapy (Boost) if feasible; <b>0.0% (0/21)</b>          F. Abstention <b>0.0% (0/21)</b></p>
41	<p>For women with stages IB3 to IVA treated only with primary chemoradiation or radiation therapy, what is the maximum acceptable duration of radiation therapy (total pelvic radiation + brachytherapy or external beam reinforcement)?</p>	<p>A. 8 weeks; <b>42.9% (9/21)</b>          B. 12 weeks; <b>47.6% (10/21)</b>          C. 15 weeks; <b>4.8% (1/21)</b>          D. 20 weeks; <b>4.8% (1/21)</b>          E. Abstention <b>0.0% (0/21)</b></p>
42	<p>For women with cervical cancer and suspected or pathology-confirmed para-aortic lymph node involvement, what is your treatment recommendation?</p>	<p>A. Extended-field chemoradiotherapy followed by brachytherapy; <b>87.0% (20/23)</b>          B. Palliative chemotherapy; <b>0.0% (0/23)</b>          C. Neoadjuvant chemotherapy followed by chemoradiotherapy and brachytherapy; <b>0.0% (0/23)</b>          D. Chemotherapy followed by surgery; <b>0.0% (0/23)</b>          E. Retroperitoneal lymphadenectomy followed by extended field chemoradiotherapy; <b>13.0% (3/23)</b>          F. Abstention <b>0.0% (0/23)</b></p>
43	<p>What is the best treatment for HIV/AIDS and other immunosuppressed patients with locally advanced cervical cancer?</p>	<p>A. Standard combination treatment followed by equal brachytherapy for immunocompetent; <b>91.7% (22/24)</b>          B. Standard combination treatment followed by brachytherapy but with reduced chemotherapy dose; <b>8.3% (2/24)</b>          C. Radiotherapy followed by brachytherapy; <b>0.0% (0/24)</b>          D. Abstention <b>0.0% (0/24)</b></p>

44	In patients with locally advanced cervical cancer, what is the preferred radiosensitizing agent?	<p>A. Weekly cisplatin; <b>100.0% (23/23)</b></p> <p>B. Cisplatin every 3 weeks; <b>0.0% (0/23)</b></p> <p>C. Cisplatin and fluorouracil; <b>0.0% (0/23)</b></p> <p>D. Cisplatin and gemcitabine; <b>0.0% (0/23)</b></p> <p>E. Other regimen; <b>0.0% (0/23)</b></p> <p>F. Abstention <b>0.0% (0/23)</b></p>
45	In patients with locally advanced cervical cancer who are not eligible to receive cisplatin, what would be your approach?	<p>A. Use carboplatin as a radiosensitizer; <b>87.5% (21/24)</b></p> <p>B. Use carboplatin and fluorouracil; <b>4.2% (1/24)</b></p> <p>C. Use fluorouracil; <b>0.0% (0/24)</b></p> <p>D. Use a taxane; <b>4.2% (1/24)</b></p> <p>E. Use gemcitabine; <b>0.0% (0/24)</b></p> <p>F. Treat with radiotherapy alone; <b>0.0% (0/24)</b></p> <p>G. Abstention <b>4.2% (1/24)</b></p>
46	If you recommend neoadjuvant chemotherapy for locally advanced cervical cancer, what is the best chemotherapy regimen?	<p>A. Carboplatin and paclitaxel; <b>16.7% (4/24)</b></p> <p>B. Cisplatin and paclitaxel; <b>12.5% (3/24)</b></p> <p>C. Carboplatin and gemcitabine; <b>0.0% (0/24)</b></p> <p>D. Cisplatin and gemcitabine; <b>0.0% (0/24)</b></p> <p>E. Cisplatin and fluorouracil; <b>0.0% (0/24)</b></p> <p>F. Paclitaxel, ifosfamide and cisplatin; <b>0.0% (0/24)</b></p> <p>G. Isolated cisplatin; <b>0.0% (0/24)</b></p> <p>H. I do not recommend neoadjuvant chemotherapy; <b>70.8% (17/24)</b></p> <p>I. Abstention <b>0.0% (0/24)</b></p>
47	Should ovarian transposition in the setting of locally advanced cervical cancer always be offered at childbearing age?	<p>A. Yes, if there is no ovarian involvement; <b>20.8% (5/24)</b></p> <p>B. Yes, if squamous-cell histology; <b>4.2% (1/24)</b></p> <p>C. Alternatives 2 and 3; <b>41.7% (10/24)</b></p> <p>D. The benefits do not justify the routine indication; <b>33.3% (8/24)</b></p> <p>E. Abstention <b>0.0% (0/24)</b></p>
48	What is the recommended first-line treatment in the metastatic or relapse setting, not amenable to locoregional salvage treatment, without contraindications for platinum or antiangiogenic, when all resources are available?	<p>A. Cisplatin-paclitaxel-bevacizumab. In case of contraindication or use of cisplatin, I would previously change cisplatin to carboplatin; <b>45.8% (11/24)</b></p> <p>B. Carboplatin-paclitaxel with or without bevacizumab; <b>0.0% (0/24)</b></p> <p>C. Topotecan-paclitaxel with or without bevacizumab; <b>0.0% (0/24)</b></p> <p>D. Platinum (carboplatin or cisplatin as indicated)-paclitaxel-pembrolizumab +/- bevacizumab; <b>50.0% (12/24)</b></p> <p>E. Abstention <b>4.2% (1/24)</b></p>
49	In what situation would you add pembrolizumab to the initial first-line schema?	<p>A. For all patients regardless of CPS <b>32.0% (8/25)</b></p> <p>B. For patients with CPS <math>\geq</math> to 1 <b>24.0% (6/25)</b></p> <p>C. For patients with CPS <math>\geq</math> to 10 <b>4.0% (1/25)</b></p> <p>D. Would not recommend pembrolizumab even though it is available <b>4.0% (1/25)</b></p> <p>E. Abstention <b>36.0% (9/25)</b></p>

50	<p>What is the recommended first-line treatment for AIDS and other immunosuppressed patients who are stable from the standpoint of the underlying disease, with metastatic or recurrent cervical cancer not amenable to locoregional salvage treatment?</p>	<p>A. Same as immunocompetent patients; <b>84.0% (21/25)</b>          B. Same regimen for immunocompetent patients but with reduced dose; <b>4.0% (1/25)</b>          C. Platinum agent monotherapy; <b>0.0% (0/25)</b>          D. Non-platinum agent monotherapy; <b>0.0% (0/25)</b>          E. Best supportive care; <b>0.0% (0/25)</b>          F. Abstention <b>12.0% (3/25)</b></p>
51	<p>What is the recommended treatment option for patients with potentially resectable local recurrence without suspected lymph node involvement and without comorbidities who have undergone previous surgery without adjuvant treatment?</p>	<p>A. Combined chemotherapy and radiation therapy; <b>64.0% (16/25)</b>          B. Radiotherapy alone; <b>0.0% (0/25)</b>          C. Isolated salvage surgery; <b>0.0% (0/25)</b>          D. Rescue surgery followed by combined chemotherapy and radiation therapy; <b>36.0% (9/25)</b>          E. Palliative chemotherapy; <b>0.0% (0/25)</b>          F. Best supportive care; <b>0.0% (0/25)</b>          G. Abstention <b>0.0% (0/25)</b></p>
52	<p>What is the recommended treatment option for a resectable locoregional recurrence without suspected lymph node involvement in patients without comorbidities in a previously irradiated area?</p>	<p>A. Reirradiation with or without cisplatin; <b>4.0% (1/25)</b>          B. Isolated salvage surgery; <b>64.0% (16/25)</b>          C. Rescue surgery followed by reradiation; <b>4.0% (1/25)</b>          D. Rescue surgery followed by chemotherapy; <b>28.0% (7/25)</b>          E. Palliative chemotherapy; <b>0.0% (0/25)</b>          F. Best supportive care; <b>0.0% (0/25)</b>          G. Abstention <b>0.0% (0/25)</b></p>
53	<p>What is the recommended treatment option for a locoregional resectable lymph node recurrence in a patient without comorbidities initially treated with surgery alone?</p>	<p>A. Combined chemotherapy and radiation therapy; <b>48.0% (12/25)</b>          B. Radiotherapy alone; <b>0.0% (0/25)</b>          C. Isolated salvage surgery; <b>0.0% (0/25)</b>          D. Rescue surgery followed by radiotherapy; <b>8.0% (2/25)</b>          E. Rescue surgery followed by combined chemotherapy and radiation therapy; <b>40.0% (10/25)</b>          F. Palliative chemotherapy; <b>4.0% (1/25)</b>          G. Best supportive care; <b>0.0% (0/25)</b>          H. Abstention <b>0.0% (0/25)</b></p>

54	What is the recommended treatment option for a resectable locoregional lymph node recurrence in a patient without comorbidities in a previously irradiated area?	<p>A. Reirradiation with or without cisplatin; <b>0.0% (0/24)</b></p> <p>B. Isolated salvage surgery; <b>25.0% (6/24)</b></p> <p>C. Rescue surgery followed by reradiation; <b>0.0% (0/24)</b></p> <p>D. Rescue surgery followed by chemotherapy; <b>66.7% (16/24)</b></p> <p>E. Palliative chemotherapy; <b>8.3% (2/24)</b></p> <p>F. Best supportive care; <b>0.0% (0/24)</b></p> <p>G. Abstention <b>0.0% (0/24)</b></p>
55	What is the recommended second-line treatment for patients who have failed first-line platinum-based treatment > 6 months ago?	<p>A. Non-platinum monotherapy (paclitaxel, pemetrexed, gemcitabine, topotecan, irinotecan, etc); <b>8.0% (2/25)</b></p> <p>B. Immunotherapy (eg, pembrolizumab or cemiplimab); <b>44.0% (11/25)</b></p> <p>C. Re-exposure to initial platinum regimen; <b>20.0% (5/25)</b></p> <p>D. Better supportive care; <b>0.0% (0/25)</b></p> <p>E. Abstention <b>28.0% (7/25)</b></p>
56	What is the recommended second-line treatment for patients who have failed first-line platinum-based treatment < 6 months ago?	<p>A. Non-platinum monotherapy (paclitaxel, pemetrexed, gemcitabine, topotecan, irinotecan, etc); <b>12.5% (3/24)</b></p> <p>B. Immunotherapy (eg, pembrolizumab or cemiplimab); <b>54.2% (13/24)</b></p> <p>C. Re-exposure to initial platinum regimen; <b>0.0% (0/24)</b></p> <p>D. Better supportive care; <b>0.0% (0/24)</b></p> <p>E. Abstention <b>33.3% (8/24)</b></p>
57	For women with previously treated metastatic cervical cancer and no clinical trial available, when do you recommend the best supportive care in an area with limited resources?	<p>A. After first-line treatment; <b>16.7% (4/24)</b></p> <p>B. After second-line treatment; <b>12.5% (3/24)</b></p> <p>C. After third-line treatment or more; <b>8.3% (2/24)</b></p> <p>D. Performance status &gt; 2, not related to treatment line; <b>54.2% (13/24)</b></p> <p>E. Abstention <b>8.3% (2/24)</b></p>
58	In the case of using second-line immunotherapy, which situation would you indicate?	<p>A. For all patients regardless of CPS; <b>25.0% (6/24)</b></p> <p>B. For patients with CPS <math>\geq</math> 1; <b>33.3% (8/24)</b></p> <p>C. For patients with CPS <math>\geq</math> 10; <b>0.0% (0/24)</b></p> <p>D. Would not indicate immunotherapy even if available; <b>0.0% (0/24)</b></p> <p>E. Abstention <b>41.7% (10/24)</b></p>
59	Would you consider metastasectomy or radiotherapy for oligometastatic cervical cancer (<4 lesions and restricted to one organ) (excluding bone metastasis)?	<p>A. In most patients, and I prefer surgery; <b>12.0% (3/25)</b></p> <p>B. In most patients, and I prefer radiation; <b>24.0% (6/25)</b></p> <p>C. In a minority of patients, and I prefer surgery; <b>12.0% (3/25)</b></p> <p>D. In a minority of patients, and I prefer radiation; <b>28.0% (7/25)</b></p> <p>E. I consider both as equivalent; <b>16.0% (4/25)</b></p> <p>F. I do not recommend; <b>8.0% (2/25)</b></p> <p>G. Abstention <b>0.0% (0/25)</b></p>