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Review Article

A Comprehensive Review on Current and Future Treatments for Cervical Cancer

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ABSTRACT

Cervical cancer remains a significant global health concern. This comprehensive review provides an overview of current and emerging treatments for cervical cancer, aiming to inform clinicians and researchers about recent advancements and future prospects in the field. Current treatment modalities for cervical cancer include surgery, radiotherapy, and chemotherapy, often used in combination depending on the stage and extent of the disease. However, these treatments are associated with considerable morbidity and may not be effective in advanced or recurrent cases. Therefore, there is an urgent need for novel therapeutic approaches. Emerging treatments for cervical cancer encompass a variety of strategies, including targeted therapies, immunotherapy, and gene therapies. Targeted therapies, such as inhibitors of the Epidermal Growth Factor Receptor (EGFR) and Vascular Endothelial Growth Factor (VEGF), have shown promising results in clinical trials, particularly in combination with standard treatments. Immunotherapy, particularly immune checkpoint inhibitors has revolutionized cancer treatment and holds significant potential for cervical cancer. Additionally, gene therapies, including oncolytic viruses and gene editing technologies, offer innovative approaches to targeting cancer cells while sparing healthy tissue. Looking forward, the integration of these emerging treatments into standard clinical practice has the potential to improve outcomes for patients with cervical cancer. However, further research is needed to optimize treatment regimens, identify biomarkers for patient selection, and overcome resistance mechanisms. Collaborative efforts between clinicians, researchers, and pharmaceutical companies are essential to translate these promising therapies from bench to bedside and ultimately reduce the global burden of cervical cancer.

Keywords: HPV, Chemotherapy, Immunotherapy, Targeted therapy.

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INTRODUCTION

Cervical cancer is the fourth most common cancer affecting women worldwide accounting for 340,000 deaths each year.[1] Most common etiology for cervical cancer is Human Papillomavirus (HPV) infection. It is found that frequent HPV infection is responsible for 99.7% of cervical cancer.[2] Also, there is substantial proof that Human Immunodeficiency Virus (HIV) infected women are also at high risk of developing HPV, which in turn lead to an increased risk of developing of cervical cancer.[3] In fact, women infected with HIV have six times greater risk of getting cervical cancer in contrast to healthy women.[3] Before initiation of treatment, it is necessary to stage according to International Federation of Gynaecology and Obstetrics (FIGO) system, which ranges from stage I to IV. The stage is determined based on the size of the tumour, depth of invasion, and extent of spread.[4] Initial disease stage is treated by surgery and radiotherapy. Advanced stages are treated with a combination of radiotherapy and cisplatin-based chemotherapy which can be curative if the spread is limited.[5] Over the years, there has been significant development in the pharmacological treatment of cervical cancer. These developments have led to improved patient outcomes and enhanced safety profiles for the treatments. This review aims to provide an overview of drugs available for the management of cervical cancer.

CERVICAL CANCER DISEASE MANAGEMENT

Cervical cancer disease management typically involves a multidisciplinary approach tailored to the individual patient's needs and the stage of the disease. Key components of cervical cancer management include:

Prevention

HPV vaccination is a primary prevention strategy aimed at reducing the risk of cervical cancer by targeting high-risk HPV strains. Regular cervical cancer screening, including Pap smears

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and HPV testing, helps detect precancerous changes early, allowing for timely intervention.[2]

Treatment

Treatment options for cervical cancer depend on factors such as the stage and extent of the disease, as well as the patient's overall health and preferences. Common treatment modalities include surgery, radiotherapy, chemotherapy, and targeted therapy. Immunotherapy, such as immune checkpoint inhibitors, is also emerging as a promising treatment option.[6]

Palliative Care

In advanced or recurrent cervical cancer cases where curative treatment is not feasible, palliative care focuses on relieving symptoms, improving quality of life, and providing psychosocial support for patients and their families.[6]

Surveillance

After completing treatment, patients undergo regular follow-up appointments to monitor for disease recurrence or progression. Surveillance may include physical exams, imaging tests (e.g., CT scans, MRI), and laboratory tests (e.g., tumour markers).

Supportive Care

Throughout the disease management process, supportive care measures address the physical, emotional, and social needs of patients. This may involve pain management, nutritional support, counselling, and access to community resources.[6,7]

Overall, an integrated and patient-centered approach to cervical cancer management aims to achieve optimal outcomes while minimizing treatment-related side effects and preserving quality of life. Collaboration among healthcare providers, including gynaecologists, oncologists, radiation oncologists, and supportive care specialists, is essential to ensure comprehensive and effective care for patients with cervical cancer.

The standard treatment for most cervical cancers involves systemic platinum-based chemotherapy along with radiotherapy. This combination has shown better outcomes in terms of disease-free and overall survival compared to radiotherapy alone. However, concomitant chemotherapy can lead to increased toxicity, though this is generally manageable. Adjuvant therapy selection is based on risk of relapse, with high-risk patients needing chemoradiotherapy.[8]

Many studies have shown efficacy of platinum in conjunction with radiotherapy and chemotherapy in improving overall survival rate, emphasizing its consideration for all cervical cancer patients.[9-12] Moreover, a study conducted by Tewari KS *et al.*, found that cemiplimab significantly improved survival compared to single-agent chemotherapy in patients with recurrent cervical cancer after first-line platinum-based chemotherapy. The percentage of patients with an objective response was 16.4% in the cemiplimab group, as compared with 6.3% in the chemotherapy group. This represents an important advancement in the treatment of this difficult-to-treat disease.[13]

As compared to patients with locally advanced cervical cancer, stage IVB cervical cancer does not have a standard treatment option available. Patients with recurrent or stage IVB cervical cancer who are not candidates for radiation treatment or extensive surgery may benefit from chemotherapy. However, traditional chemotherapy has shown to be ineffective in eliminating primary cervical cancer and metastases. Combining radiotherapy and chemotherapy for patients with stage IVB cervical cancer has been shown to improve survival.[14]

CURRENT TREATMENT METHODS FOR CERVICAL CANCER

Surgery

Surgery plays a crucial role in the management of cervical cancer, particularly in early-stage disease. The primary surgical approach is a radical hysterectomy, which involves removing the uterus, cervix, and surrounding tissues. In some cases, lymph nodes in the pelvic area may also be removed to assess the extent of cancer spread. For women who wish to preserve fertility, less invasive procedures such as cone biopsy or trachelectomy may be considered, depending on the size and stage of the tumour. Surgery may also be used in combination with other treatments such as radiation therapy or chemotherapy to improve outcomes, particularly in more advanced cases. While surgery can be curative for early-stage cervical cancer, it carries risks and potential complications, including infection, bleeding, and damage to surrounding organs. Therefore, careful patient selection and comprehensive preoperative evaluation are essential to ensure optimal outcomes and minimize risks. Overall, surgery remains an integral component of cervical cancer treatment, offering the potential for cure and improved quality of life for affected individuals.

Surgery is a commonly used and successful technique in combatting various early-stage cancers as it involves the physical removal of cancerous tissue. It can also be used to remove metastatic tissue.[14] Radical surgery is the preferred treatment for early-stage cervical cancer. This traditionally involves type III open radical hysterectomy with bilateral pelvic lymph node dissection, despite associated short and long-term complications.[15] A more conservative approach is recommended for women at childbearing age who are suffering from early-stage disease. Fertility-saving surgeries available to patients include conization, Loop Electrosurgical Excision Procedure (LEEP) and trachelectomy.[16] Fertility sparing and less-radical surgical procedures for patients with low-stage disease with good prognostic factors are still under evaluation and should not be used in clinical practice. Minimally Invasive Surgery (MIS) was previously considered the standard of care for cervical cancer

surgery. However, recent evidence has shown poorer survival outcomes with MIS compared to open surgery, leading to a shift back to open abdominal surgery as the standard approach.[17]

Surgery combined with chemoradiotherapy may lead to longer survival in stage IVB cervical cancer patients, with a median duration of 32 months compared to 19 months without surgery. This combination not only aids in local control but also improves quality of life by relieving symptoms like bleeding and pain, potentially leading to longer survival.[14]

Radiotherapy

Radiotherapy is a primary treatment modality for cervical cancer, often used in combination with other therapies like surgery or chemotherapy. It involves the use of high-energy radiation beams to target and destroy cancer cells while minimizing damage to surrounding healthy tissue. Radiotherapy can be delivered externally (external beam radiation) or internally (brachytherapy), depending on the specific characteristics of the cancer and the patient's individual circumstances. This treatment can be curative, particularly for early-stage cervical cancer, and may also be used palliatively to relieve symptoms and improve quality of life in advanced cases. Advances in radiotherapy techniques, such as Intensity-Modulated Radiation Therapy (IMRT) and Image-Guided Radiation Therapy (IGRT), have improved treatment precision and outcomes for patients with cervical cancer. However, side effects such as fatigue, skin irritation, and gastrointestinal symptoms are common, and supportive care measures are often necessary to manage these effects and enhance patient comfort during treatment.

High-energy beam radiotherapy is an essential part of treating cervical cancer. External Beam Radiation Therapy (EBRT), Intensity-Modulated Radiotherapy (IMRT), and brachytherapy (internal radiation therapy) are the three primary forms of radiation therapy used to treat cervical cancer. Modern diagnostic techniques like CT and MRI scans have improved the assessment of primary tumours, the degree of malignant invasion, and metastasis. These advancements aid in the efficient planning of radiation therapy for cervical cancer.[1,17] High-energy radiation beams from outside the body are directed into the tumour during External Beam Radiation Therapy (EBRT). It is the radiotherapy type most frequently used to treat cancer. On the other hand, Intensity-Modulated Radiotherapy (IMRT), a more advanced method, modifies radiation beams that contain photons and protons to conform to the features of the tumour. Both malignant and non-cancerous tumours respond well to IMRT. Similar to this, brachytherapy spares the tissues around the tumour by either implanting a radioactive device there or giving the tumour a high dosage of radiation directly.[18,19] For all significant progress in radiotherapy, it still has many side effects such as diarrhoea, abdominal cramps, pelvic pain skin problem lymphedema and sexual dysfunction.[20] Radiotherapy alone fails to control disease in 20-50% of cases.[21,22] To improve its effectiveness radiotherapy is often combined with chemotherapy especially for longer cervical cancer.[23]

Chemotherapy

Chemotherapy remains a cornerstone in the treatment of cervical cancer. It involves the use of drugs to kill cancer cells or stop them from growing and dividing. Chemotherapy may be administered alone or in combination with other treatments such as surgery or radiation therapy, depending on the stage and extent of the disease. While chemotherapy can cause side effects due to its impact on healthy cells, it remains an essential component of cervical cancer treatment, particularly for advanced or recurrent cases. Ongoing research aims to develop more targeted and less toxic chemotherapy regimens to improve outcomes and reduce side effects for patients with cervical cancer.

Chemotherapy is a crucial component of cervical cancer treatment. It is typically administered following surgery, in combination with radiotherapy. It is also administered as monotherapy for locally advanced cancer. Treatment options are based on patient health status, it can be mono, dual or triple therapy.[5]

Many chemotherapeutic agents are active in cervical cancer, including platinum-based agents (cisplatin, carboplatin), gemcitabine, topotecan, taxanes (paclitaxel), vinorelbine, ifosfamide and many more, including the targeted therapy bevacizumab.[24] Although all these medications are effective in palliating symptoms, the most effective treatment for cervical cancer has been cisplatin.[25] Cisplatin given at a dose of 50mg/m2 every three weeks has been shown to achieve response rate of up to 38%.[26] However, even though patient initially response to cisplatin they often develop resistance overtime.[16]

Consequently, studies have indicated that cisplatin in combination with other treatments may have a higher potential for efficacy than treatment with a single medication. In fact, cisplatin alone had a 19% response rate; but, when paired with paclitaxel, that number rose to 36% according to a study by DH Moore *et al.*[27] Similar outcomes were observed in another study with topotecan and cisplatin combination.[28]

Therefore, chemotherapy is often used alongside surgery and radiotherapy, is essential for treating cervical cancer, with cisplatin being the standalone therapy. While cisplatin alone has a good response rate, combining it with other agents like paclitaxel or topotecan significantly enhances its efficacy.

Immunotherapy

Immunotherapy for cervical cancer harnesses the body's immune system to fight cancer cells. This approach involves drugs known as immune checkpoint inhibitors, which block proteins that inhibit the immune response against cancer. Specifically, inhibitors of programmed cell death protein 1 (PD-1) and

programmed death-ligand 1 (PD-L1) have shown remarkable efficacy in cervical cancer. By releasing the brakes on the immune system, these drugs enable immune cells to recognize and destroy cancer cells more effectively. Immunotherapy offers a promising treatment option for cervical cancer, particularly in cases where traditional therapies have been ineffective.

In the past, there were very few therapeutic alternatives available to patients who progressed to first-line platinum-based therapy. The addition of immunotherapy, primarily immune checkpoint inhibitors (ICI), to the cervical cancer treatment regimen has marked a significant advancement in recent times.[29] ICI's target molecules like PD-1, its ligands PD-L1 and PD-L2, and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) to release brakes on the immune system. By blocking the interaction between these molecules, ICIs enhance the ability of immune cells, particularly T cells, to recognize and destroy cancer cells.[30]

The phase Ib trial KEYNOTE-028 demonstrated the first evidence of clinical activity of pembrolizumab, an anti-PD-1 monoclonal antibody, in advanced cervical cancer, showing a 17% overall response rate. The safety profile of pembrolizumab in this study was consistent with its safety in other tumour types.[31] The CheckMate-358 trial showed combining PD-1 and CTLA-4 receptor inhibitors such as nivolumab and ipilimumab respectively in patients with recurrent/metastatic squamous cervical cancer revealed optimal overall response rate in both the arms, with better efficacy noted in treatment-naïve patients.[32]

Cadonilimab, a novel anti-PD-1/CTLA-4 bispecific monoclonal antibody, has shown promise as monotherapy for patients with recurrent or metastatic cervical cancer following platinum-based chemotherapy failure. In a pivotal phase II trial, cadonilimab demonstrated an Overall Response Rate (ORR) of 33%, with a particularly high ORR of 43.8% among patients with PD-L1 positive tumours.[33]

Targeted Therapy

Targeted therapy for cervical cancer involves drugs that specifically target molecules or pathways involved in cancer growth and progression. These therapies aim to inhibit cancer cell proliferation while sparing healthy cells. Examples include inhibitors of the Epidermal Growth Factor Receptor (EGFR) and Vascular Endothelial Growth Factor (VEGF), which have shown efficacy in clinical trials, particularly when used in combination with standard treatments like chemotherapy or radiotherapy. Targeted therapies offer a more precise and less toxic approach to treating cervical cancer, with the potential to improve outcomes for patients.

Targeted therapies inhibit proteins expressed by cancer cells to reduce growth and spread. They are expected to be more effective with fewer side effects than traditional chemotherapies due to their higher cancer cell specificity.[16]

A phase III trial (GOG 240) evaluated the efficacy of incorporating bevacizumab, a Vascular Endothelial Growth Factor (VEGF)-neutralizing monoclonal antibody, with nonplatinum combination chemotherapy in patients with advanced cervical cancer. The study found that adding bevacizumab increased the overall survival (17.0 vs. 13.3 months) and higher response rates (48% vs. 36%). Bevacizumab compared to chemotherapy alone, increased incidence of hypertension, thromboembolic events and gastrointestinal fistulas. Currently cisplatin, paclitaxel and bevacizumab combination is the new standard treatment for advanced and recurrent cervical cancer.[34]

FUTURE PROSPECTS IN CERVICAL CANCER MANAGEMENT

Therapeutic vaccine

Although prophylactic vaccines enhance humoral immunity, they are of no therapeutic value for patients infected with high-risk HPV strains. HPV therapeutic vaccines represent an area of active research and are available as live vector-based vaccines, peptide and protein-based vaccines, nucleic acid-based vaccines, and whole-cell vaccines.[35]

Most therapeutic vaccines target the HPV E6 and E7 oncoproteins, which are expressed in HPV-infected cells and drive cancer development. The goal is to activate T cell responses against these proteins, thereby eliminating infected cells and preventing cancer progression.[35] Therapeutic vaccines focus on HPV E6 and E7 oncoproteins in infected cells, aiming to stimulate T cell responses to eliminate infected cells and halt cancer progression. MVA-E2, a top-performing therapeutic vaccine, demonstrated 90% regression in high-grade cervical precancerous lesions, similar to conventional lesion treatment. However, a key limitation of the study was the absence of a control group to assess the natural regression rate of these lesions.[36]

Efficient treatments are sought for cervical cancer through the development of combination therapy involving immunotherapy drugs and vaccines. An example is the ISA101 vaccine, which showed a 33% response rate in a phase II study with nivolumab, a checkpoint inhibitor. However, this response was not seen in advanced cervical cancer patients, emphasizing the necessity for further optimization.[37] Therapeutic vaccinations are a significant potential adjuvant therapy to prevent invasive procedures and reduce recurrence, even if their efficacy has not yet reached the level of existing treatments. To enhance results, ongoing research aims to optimize vaccine antigens and combination regimens.[35,36]

PARP Inhibitor

Poly (Adenosine Diphosphate [ADP]-ribose) polymerase, especially PARP1, is an enzyme that is necessary for DNA repair. PARP inhibitors such as olaparib and veliparib prevent this repair, which is particularly lethal to cells with defective homologous repair, leading to cell death. A case report by Gross

M and Spencer RJ showed that single agent olaparib therapy demonstrated great promise in terms of response in a patient with recurrent metastatic clear cell cervical cancer. The patient had an excellent response to olaparib without disease progression for 14 months of therapy.[38] A clinical trial evaluating the combination of veliparib with paclitaxel and cisplatin achieved a 34% objective response rate and an overall survival of 14.5 months.[39] However, further clinical trials are required to fully establish their clinical effectiveness.

Antibody drug conjugate

Tisotumab vedotin is an antibody drug conjugate having an antimicrotubular agent and a human tissue factor. The drug attaches to tissue factor, a transmembrane protein present on the cancer cells. Subsequently, it moves inside and releases the anti-microtubule agent that disrupts the cell's structure, inducing cell death.[5] Tisotumab vedotin has received FDA approval on September 2021 for treating patients with recurrent or metastatic cervical cancer.[40]

RR Inhibitor

Ribonucleotide Reductase (RR) is a crucial enzyme for DNA synthesis, as it catalyses the reduction of nucleoside di or triphosphates to corresponding deoxynucleotides inhibitors like hydroxyurea and triapine are being tested and used for cervical cancer.[41]

GOG 120 found that treatment with radiation therapy in combination with cisplatin alone or cisplatin, fluorouracil, and hydroxyurea was effective for the treatment of locally advanced cervical cancer.[42] Triapinea more potent RR inhibitor, has shown promise in animal studies and early trials suggest it sensitizes tumours to radiation, especially in cervical cancer. But further studies are needed to confirm its efficacy for cervical cancer.[43]

Ongoing clinical trials

The ongoing clinical trials in cervical cancer are shaping the future of treatment paradigms with promising new approaches. Trials like INTERLACE and KEYNOTE-A18 are at the forefront, investigating the impact of induction chemotherapy and immune checkpoint inhibitors on treatment outcomes for locally advanced cervical cancer. INTERLACE has demonstrated that induction chemotherapy improves survival compared to traditional chemoradiotherapy, while KEYNOTE-A18 highlights the potential benefits of combining pembrolizumab with traditional chemotherapy, though data is still pending. In advanced cervical cancer, trials such as KEYNOTE-826 and BEATcc are exploring the synergistic effects of combining immune checkpoint inhibitors with chemotherapy and anti-angiogenic agents, revealing enhanced survival.[44] The approval of tisotumab vedotin for second-line treatment in recurrent or metastatic cervical cancer marks another significant advancement. This drug, along with pembrolizumab, is being evaluated in numerous trials to determine its efficacy in various treatment settings.[45]

Several specific trials are advancing our understanding of cervical cancer management. The Phase 2 XmAb20717 trial is evaluating the efficacy of vudalimab, an investigational agent, in patients with advanced gynecologic and genitourinary malignancies, including cervical cancer. Another key study is a randomized controlled trial comparing survival outcomes between robotic-assisted laparoscopic surgery and traditional open radical hysterectomy for early-stage cervical cancer, which aims to determine the advantages of robotic assistance in surgical interventions. Additionally, the ACCESS Trial is integrating cervical cancer screening and treatment within existing HIV care programs in Nigeria, exploring the effectiveness of various implementation strategies to improve access and outcomes for underserved populations.[46] The ACCESS Trial's model of integrating cervical cancer care within HIV programs could streamline services and enhance access in India, particularly for underserved populations. This approach could improve cost-effectiveness and outcomes for women with both HIV and cervical cancer.

CONCLUSION

In conclusion, cervical cancer poses a significant global health challenge. While current treatments have limitations, emerging therapies like targeted therapies, immunotherapy, and gene therapies offer promising alternatives. Integration of these treatments into standard clinical practice has the potential to improve outcomes for patients. Further research and collaborative efforts are crucial to optimizing treatment regimens and translating promising therapies into effective treatments for cervical cancer.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

EGFR: Epidermal Growth Factor Receptor; **VEGF:** Vascular Endothelial Growth Factor; **HPV:** Human Papilloma Virus; **HIV:** Human Immunodeficiency Virus; **FIGO:** International Federation of Gynaecology and Obstetrics; **CT:** Computed Tomography;

MRI: Magnetic Resonance Imaging; **LEEP:** Loop Electrosurgical Excision Procedure; **MIS:** Minimally Invasive Surgery; **IMRT:** Intensity-Modulated Radiation Therapy; **IGRT:** Image-Guided Radiation Therapy; **EBRT:** External Beam Radiation Therapy; **PD-L1:** Programmed Death-Ligand 1; **ICI:** Immune Checkpoint Inhibitors; **CTLA:** Cytotoxic T-Lymphocyte-Associated Protein; **GOG:** Gynecologic Oncology Group; **MVA:** Modified Vaccinia virus Ankara; **PARP:** Poly Adenosine (Diphosphate [ADP]-Ribose) Polymerase; **RR:** Ribonucleotide Reductase; **DNA:** Deoxy Ribonucleic Acid.

ETHICAL APPROVAL

This article is a review of previously published literature and does not involve any new studies with human or animal subjects performed by any of the authors. Therefore, ethical approval was not required.

SUMMARY

- Current treatment modalities for cervical cancer include surgery, radiotherapy, and chemotherapy, but they are associated with significant morbidity and may not be effective in advanced or recurrent cases.
- Emerging treatments for cervical cancer, such as targeted therapies, immunotherapy, and gene therapies, offer promising alternatives to traditional treatments.
- Targeted therapies, including inhibitors of EGFR and VEGF, have shown efficacy in clinical trials, particularly when combined with standard treatments.
- Immunotherapy, particularly immune checkpoint inhibitors targeting PD-1 and PD-L1, has demonstrated remarkable efficacy in cervical cancer and represents a paradigm shift in cancer treatment.
- Gene therapies, such as oncolytic viruses and gene editing technologies, offer innovative approaches to targeting cancer cells while sparing healthy tissue.
- Integration of emerging treatments into standard clinical practice has the potential to improve outcomes for cervical cancer patients, but further research is needed to optimize treatment regimens and identify biomarkers for patient selection.
- Collaborative efforts between clinicians, researchers, and pharmaceutical companies are crucial to translating promising therapies into effective treatments for cervical cancer.

REFERENCES

1. Cohen PA, Jhingran A, Oaknin A, Denny L. Cervical cancer. The Lancet. 2019;393(10167):169-82.
2. Torres-Poveda K, Cruz-Valdez A, Madrid-Marina V. Epidemiología del cáncer cervicouterino. Gac Mex Oncol. 2014;13(4):4-17.
3. Moodley JR, Hoffman M, Carrara H, Allan BR, Cooper DD, Rosenberg L, *et al.* HIV and pre-neoplastic and neoplastic lesions of the cervix in South Africa: a case-control study. BMC Cancer. 2006;6:1-6.
4. Salvo G, Odetto D, Pareja R, Frumovitz M, Ramirez PT. Revised 2018 International Federation of Gynecology and Obstetrics (FIGO) cervical cancer staging: a review of gaps and questions that remain. Int J Gynecol Cancer. 2020;30(6).
5. Porras GOR, Nogueda JC, Chacón AP. Chemotherapy and molecular therapy in cervical cancer. Rep Pract Oncol Radiother. 2018;23(6):533-9.
6. Marth C, Landoni F, Mahner S, McCormack M, Gonzalez-Martin A, Colombo N. Cervical cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2017;28:iv72-83.
7. Greimel E, Lahousen M, Dorfer M, Lambauer M, Lang U. Patients' view of routine follow-up after gynecological cancer treatment. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2011;159(1):180-3.
8. DeVita VT, Lawrence TS, Rosenberg SA. DeVita, Hellman, and Rosenberg's cancer: principles & practice of oncology. Vol. 2. Lippincott Williams & Wilkins; 2008.
9. Whitney CW, Sause W, Bundy BN, Malfetano JH, Hannigan EV, Fowler J Wesley C, *et al.* Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage IIB-IVA carcinoma of the cervix with negative para-aortic lymph nodes: a Gynecologic Oncology Group and Southwest Oncology Group study. J Clin Oncol. 1999;17(5):1339.
10. Morris M, Eifel PJ, Lu J, Grigsby PW, Levenback C, Stevens RE, *et al.* Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. N Engl J Med. 1999;340(15):1137-43.
11. Rose PG, Ali S, Watkins E, Thigpen JT, Deppe G, Clarke-Pearson DL, *et al.* Long-term follow-up of a randomized trial comparing concurrent single agent cisplatin, cisplatin-based combination chemotherapy, or hydroxyurea during pelvic irradiation for locally advanced cervical cancer: a Gynecologic Oncology Group Study. J Clin Oncol. 2007;25(19):2804-10.
12. Green JA, Kirwan JM, Tierney JF, Symonds P, Fresco L, Collingwood M, *et al.* Survival and recurrence after concomitant chemotherapy and radiotherapy for cancer of the uterine cervix: a systematic review and meta-analysis. The lancet. 2001;358(9284):781-6.
13. Tewari KS, Monk BJ, Vergote I, Miller A, de Melo AC, Kim HS, *et al.* Survival with cemiplimab in recurrent cervical cancer. N Engl J Med. 2022;386(6):544-55.
14. Li H, Pang Y, Cheng X. Surgery of primary sites for stage IVB cervical cancer patients receiving chemoradiotherapy: a population-based study. J Gynecol Oncol. 2020;31(1):e8.
15. Poddar P, Maheshwari A. Surgery for cervical cancer: consensus & controversies. Indian J Med Res. 2021;154(2):284-92.
16. Burmeister CA, Khan SF, Schäfer G, Mbatani N, Adams T, Moodley J, *et al.* Cervical cancer therapies: Current challenges and future perspectives. Tumour Virus Res. 2022;13:200238.
17. Cibula D, Pötter 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. Virchows Arch. 2018;472:919-36.
18. Johnson CA, James D, Marzan A, Armaos M. Cervical cancer: an overview of pathophysiology and management. In Elsevier; 2019:166-74.
19. Board P. Adult Treatment Editorial. Penile Cancer Treat PDQ R Health Prof Version PDQ Cancer Inf Summ. 2002;
20. Wang K, Tepper JE. Radiation therapy-associated toxicity: Etiology, management, and prevention. CA Cancer J Clin. 2021;71(5):437-54.
21. Moreno-Acosta P, Vallard A, Carrillo S, Gamboa O, Romero-Rojas A, Molano M, *et al.* Biomarkers of resistance to radiation therapy: a prospective study in cervical carcinoma. Radiat Oncol. 2017;12:1-9.
22. Rahakbauw E, Winarto H. Radiotherapy response and related clinicopathological factors of patients with cervical cancer. In IOP Publishing; 2018;032040.
23. Tewari KS, Monk BJ. The rationale for the use of non-platinum chemotherapy doublets for metastatic and recurrent cervical carcinoma. Clin Adv Hematol Oncol. 2010;8(2):108-15.
24. Serrano-Olivera J, Cortés-Esteban P, Poitevin-Chacónc A. Cáncer cervicouterino: tratamento de la enfermedad persistente, recurrente o metastásica. Gac Mex Oncol. 2014;13(4):75-82.
25. Tewari KS, Monk BJ. Gynecologic oncology group trials of chemotherapy for metastatic and recurrent cervical cancer. Curr Oncol Rep. 2005;7:419-34.
26. Verma J, Monk BJ, Wolfson AH. New strategies for multimodality therapy in treating locally advanced cervix cancer. In Elsevier; 2016;344-8.
27. Moore DH, Blessing JA, McQuellon RP, Thaler HT, Cella D, Benda J, *et al.* Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2004;22(15):3113-9.
28. Long III HJ, Bundy BN, Grendys Jr EC, Benda JA, McMeekin DS, Sorosky J, *et al.* Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol. 2005;23(21):4626-33.

29. Grau-Bejar JF, Garcia-Duran C, Garcia-Illescas D, Mirallas O, Oaknin A. Advances in immunotherapy for cervical cancer. Ther Adv Med Oncol. 2023;15:17588359231163836.
30. Kagabu M, Nagasawa T, Sato C, Fukagawa Y, Kawamura H, Tomabechi H, *et al.* Immunotherapy for uterine cervical cancer using checkpoint inhibitors: future directions. Int J Mol Sci. 2020;21(7):2335.
31. Frenel JS, Le Tourneau C, O'Neil B, Ott PA, Piha-Paul 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;35(36):4035-41.
32. Oaknin A, Moore K, Meyer T, González J, Devriese L, Amin A, *et al.* 520MO Safety and efficacy of nivolumab (NIVO)±ipilimumab (IPI) in patients (pts) with recurrent/metastatic cervical cancer (R/M Cx Ca) in checkmate 358. Ann Oncol. 2022;33:S782.
33. Wu X, Ji J, Lou H, Li Y, Feng M, Xu N, *et al.* Efficacy and safety of cadonilimab, an anti-PD-1/CTLA4 bi-specific antibody, in previously treated recurrent or metastatic (R/M) cervical cancer: a multicenter, open-label, single-arm, phase II trial (075). Gynecol Oncol. 2022;166:S47-8.
34. Tewari KS, Sill MW, Long III HJ, Penson RT, Huang H, Ramondetta LM, *et al.* Improved survival with bevacizumab in advanced cervical cancer. N Engl J Med. 2014;370(8):734-43.
35. Mo Y, Ma J, Zhang H, Shen J, Chen J, Hong J, *et al.* Prophylactic and therapeutic HPV vaccines: current scenario and perspectives. Front Cell Infect Microbiol. 2022;12:909223.
36. Khalil AI, Zhang L, Muwonge R, Sauvaget C, Basu P. Efficacy and safety of therapeutic HPV vaccines to treat CIN 2/CIN 3 lesions: a systematic review and meta-analysis of phase II/III clinical trials. BMJ Open. 2023;13(10):e069616.
37. Rumfield CS, Pellom ST, Morillon II YM, Schlom J, Jochems C. Immunomodulation to enhance the efficacy of an HPV therapeutic vaccine. J Immunother Cancer. 2020;8(1).
38. Gross M, Spencer RJ. Recurrent cervical cancer treated successfully with single-agent PARP-inhibitor, olaparib. Case Rep Obstet Gynecol. 2022; 2022.
39. Thaker P, Salani R, Brady W, Lankes H, Cohn D, Mutch D, *et al.* A phase I trial of paclitaxel, cisplatin, and veliparib in the treatment of persistent or recurrent carcinoma of the cervix: an NRG Oncology Study (NCT# 01281852). Ann Oncol. 2017;28(3):505-11.
40. Bogani G, Coleman RL, Vergote I, Raspagliesi F, Lorusso D, Monk BJ. Tisotumab vedotin in recurrent or metastatic cervical cancer. Curr Probl Cancer. 2023;47(3):100952.
41. Heidel JD, Liu JYC, Yen Y, Zhou B, Heale BS, Rossi JJ, *et al.* Potent siRNA inhibitors of ribonucleotide reductase subunit RRM2 reduce cell proliferation *in vitro* and *in vivo*. Clin Cancer Res. 2007;13(7):2207-15.
42. Rose PG, Bundy BN, Watkins EB, Thigpen JT, Deppe G, Maiman MA, *et al.* Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. N Engl J Med. 1999;340(15):1144-53.
43. Chapman TR, Kinsella TJ. Ribonucleotide reductase inhibitors: a new look at an old target for radio sensitization. Front Oncol. 2012;1:56.
44. Ang DJ, Chan JJ. Evolving standards and future directions for systemic therapies in cervical cancer. Journal of Gynecologic Oncology. 2024;35(2).
45. Monk BJ, Enomoto T, Kast WM, McCormack M, Tan DS, Wu X, González-Martín A. Integration of immunotherapy into treatment of cervical cancer: Recent data and ongoing trials. Cancer treatment reviews. 2022;106:102385.
46. UCSD. UCSD Cervical Cancer Clinical Trials-San Diego [Internet]. clinicaltrials.ucsd.edu. Available from: https://clinicaltrials.ucsd.edu/cervical-cancer

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