touch™ ONCOLOGY

Guideline-based treatment of recurrent/metastatic cervical cancer

Practice aid for treatment of cervical cancer

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NCCN guidelines for R/M cervical cancer[1]

First-line systemic therapy

PREFERRED REGIMENS

- PD-L1–positive tumours:
  - Pembrolizumab + cisplatin/paclitaxel ± bevacizumab*
  - Pembrolizumab + carboplatin/paclitaxel ± bevacizumab*
- Cisplatin/paclitaxel/bevacizumab*
- Carboplatin/paclitaxel/bevacizumab*

Also recommended by ASCO in enhanced/maximal settings[2]

OTHER RECOMMENDED REGIMENS

- Cisplatin/paclitaxel
- Carboplatin/paclitaxel
- Topotecan/paclitaxel/bevacizumab
- Topotecan/paclitaxel
- Cisplatin/topotecan
- Cisplatin
- Carboplatin

Second-line systemic therapy

PREFERRED REGIMENS

- Pembrolizumab for TMB-H, MSI-H/dMMR or PD-L1–positive tumours
- Cemiplimab†
- Tisotumab vedotin

OTHER RECOMMENDED REGIMENS

- Bevacizumab*
- Paclitaxel
- Docetaxel
- Fluorouracil
- Gemcitabine
- Pemetrexed
- Albumin-bound paclitaxel
- Topotecan
- Vinorelbine
- Irinotecan

USEFUL IN CERTAIN CIRCUMSTANCES

- PD-L1–positive tumours: Nivolumab
- HER2-positive tumours (IHC 3+ or 2+): Trastuzumab deruxtecan
- *RET* gene fusion-positive tumours: Selpercatinib
- *NTRK* gene fusion-positive tumours: Larotrectinib, entrectinib

*An FDA-approved biosimilar is an appropriate substitute for bevacizumab.
†Cemiplimab is not currently approved by the FDA for cervical cancer.

ESGO/ESTRO/ESP guidelines for R/M cervical cancer[3]

First-line systemic therapy

- Platinum-based chemotherapy ± bevacizumab is recommended for chemotherapy-naive, medically fit patients with R/M disease
  - Carboplatin/paclitaxel and cisplatin/paclitaxel are the preferred regimens
  - Addition of bevacizumab to platinum-based chemotherapy is recommended when the risk of significant GI/GU toxicities has been carefully assessed and discussed with the patient
- PD-L1–positive tumours (CPS ≥1): Addition of pembrolizumab to platinum-based chemotherapy ± bevacizumab is recommended

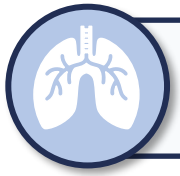
Second-line systemic therapy

- If patients have not previously received immunotherapy and regardless of PD-L1 tumour status, patients should be offered cemiplimab, an anti-PD-1 agent
- If patients have previously received immunotherapy, chemotherapy is recommended if ECOG PS ≤2 and best supportive care is recommended if ECOG PS >2

Inclusion of patients with R/M disease in clinical trials is strongly recommended

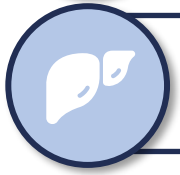
Immune checkpoint inhibitors

Cemiplimab[4]* and pembrolizumab:[5,6] Monitoring for AEs of special interest[7]



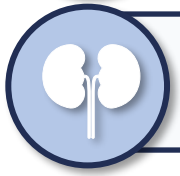
PNEUMONITIS

- Symptoms include dyspnoea, persistent cough, chest pain, fever and hypoxia
- If pneumonitis is suspected, high-resolution chest CT should be performed; consider PFTs if CT scan is negative



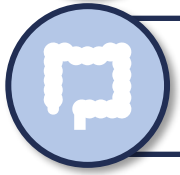
HEPATITIS

- Often asymptomatic; typically manifests as an elevation in ALT and/or AST serum levels
- LFTs should be checked prior to each ICI infusion and rechecked weekly for patients experiencing grade 1 or grade 2 liver toxicities and every 1–2 days for patients with liver toxicities of grade ≥3



NEPHRITIS

- Manifests as reduced renal function including rising serum creatinine, low-grade proteinuria and sterile pyuria
- Urinalysis should be considered to evaluate for baseline kidney disease



COLITIS

- Diarrhoea is a common symptom; alarm symptoms are pain and haematochezia
- For grade 1 diarrhoea/colitis symptoms, perform CBC, CMP and faecal lactoferrin
- For grade ≥2 symptoms, perform faecal calprotectin and stool infectious analysis

CUTANEOUS REACTIONS

- Symptoms include rash often accompanied by pruritus
- Monitor for pruritus, development of a rash; be aware of rash with blisters, mucosal involvement or bullous formation

ENDOCRINOPATHIES

- Symptoms are often non-specific and difficult to diagnose without additional testing
- TSH and fT4 should be monitored prior to beginning ICI therapy and intermittently throughout the course of treatment

CBC with differential, CMP, TSH and fT4 should be performed prior to initiating ICI therapy and intermittently throughout the course of treatment[6]

*Cemiplimab is not currently approved by the FDA for cervical cancer.

Management of AEs[8]

There should be a high level of suspicion that new symptoms are treatment related

GRADE 1

- ICI therapy should be continued with close monitoring except for some neurologic, haematologic and cardiac toxicities

GRADE 2

- Consider holding immune checkpoint inhibitor and resume when symptoms and/or laboratory values revert to grade ≤1
- Corticosteroids (initial dose of 0.5–1 mg/kg/d of prednisone or equivalent) may be administered

GRADE 3

- Hold ICIs and initiate high-dose corticosteroids (prednisone 1–2 mg/kg/d or equivalent)
  - Corticosteroids should be tapered, and infliximab may be an option for some toxicities if steroids do not improve symptoms
  - When AEs revert to grade ≤1, rechallenging with ICIs may be offered; however, caution is advised, especially in those patients with early-onset irAEs. Dose adjustments are not recommended

GRADE 4

- Warrants permanent discontinuation of ICI

Antibody–drug conjugate

Ocular toxicity with tisotumab vedotin: Monitoring, prevention and management[9]

MONITORING

- Refer patients to an eye care provider for an ophthalmic exam including visual acuity and slit lamp exam at baseline, prior to each dose and as clinically indicated

PREVENTION

Adhere to the following recommendations to reduce the risk of ocular adverse reactions:

Ophthalmic exam at baseline, prior to each dose and as clinically indicated

Use cooling eye pads during the infusion

Advise patients to avoid wearing contact lenses for the entire duration of therapy

- Topical ocular vasoconstrictor drops prior to each infusion
- Topical corticosteroid eye drops prior to each infusion and for 72 hours after infusion
- Topical lubricating eye drops for the duration of therapy and for 30 days after the last dose

MANAGEMENT

- Promptly refer patients to an eye care provider for any new or worsening ocular signs and symptoms
- Withhold, reduce the dose or permanently discontinue based on the severity of the adverse reaction*

*Refer to product information for details of recommended dose reductions.

Antibody–drug conjugate

Tisotumab vedotin: Monitoring and management of AEs of special interest[9]

PNEUMONITIS

- Monitor patients for pulmonary symptoms indicative of pneumonitis
- Symptoms may include hypoxia, cough, dyspnoea or interstitial infiltrates on radiologic exams
- Infectious, neoplastic and other causes for such symptoms should be excluded through appropriate investigations
- Withhold therapy for patients who develop persistent or recurrent grade 2 pneumonitis and consider dose reduction*
- Permanently discontinue in all patients with grade 3 or 4 pneumonitis

HAEMORRHAGE

- Monitor patients for signs and symptoms of haemorrhage
- Treatment should be permanently discontinued for patients experiencing any grade pulmonary or CNS haemorrhage, a second occurrence of grade 3 haemorrhage in any other location, or a a grade 4 haemorrhage in any other location
- For grade 2 or first occurrence of grade 3 haemorrhage in any other location, withhold until resolved and then resume treatment at same dose

PERIPHERAL NEUROPATHY

- Monitor patients for signs and symptoms of neuropathy, such as paraesthesia, tingling or a burning sensation, neuropathic pain, muscle weakness or dysesthesia
- For patients experiencing new or worsening peripheral neuropathy, depending on the severity, either withhold dose, then resume at lower dose*, or permanently discontinue

*Refer to product information for details of recommended dose reductions.

Abbreviations and references

Abbreviations

AE, adverse event; ALT, alanine transaminase; ASCO, American Society of Clinical Oncology; AST, aspartate aminotransferase; CBC, complete blood count; CMP, comprehensive metabolic panel; CNS, central nervous system; CPS, combined positive score; CT, computerized tomography; dMMR, mismatch repair deficient; ECOG PS, Eastern Cooperative Oncology Group performance status; ESGO, European Society of Gynaecological Oncology; ESP, European Society of Pathology; ESTRO, European Society for Radiotherapy and Oncology; FDA, US Food and Drug Administration; fT4, free thyroxine; GI, gastrointestinal; GU, genitourinary; HER2, human epidermal growth factor receptor 2; ICI, immune checkpoint inhibitor; IHC, immunohistochemistry; irAE, immune-related AE; LFT, liver function test; MSI-H, microsatellite instability-high; NCCN, National Comprehensive Cancer Network; NTRK, neurotrophic tyrosine receptor kinase; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PFT, pulmonary function test; R/M, recurrent/metastatic; TMB-H, tumour mutational burden-high; TSH, thyroid-stimulating hormone.

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