Anal Carcinoma Treatment Regimens

Clinical Trials: The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The National Comprehensive Cancer Network Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Note: All recommendations are category 2A unless otherwise indicated.

▶Localized Cancer[1]

REGIMEN	DOSING
Preferred Regimens	
Capecitabine + Mitomycin + Radiotherapy[2-4,a]	**Days 1-5, 8-12, 15-19, 22-26, 29-33, 36-38:** Capecitabine 825mg/m^2 orally twice daily **Days 1,29:** Mitomycin 10mg/m^2 IV (max 20 mg) push. Administer for one 6-week cycle with radiation. **OR** **Days 1-5, 8-12, 15-19, 22-26, 29-33, 36-40:** Capecitabine 825mg/m^2 orally twice daily **Day 1:** Mitomycin 12mg/m^2 (max 20mg) IV push. Administer for one 6-week cycle with radiation.
Fluorouracil + Mitomycin + Radiotherapy[5,6,b]	**Days 1-4, 29-32:** Fluorouracil 1,000mg/m^2 IV continuous infusion over 24 hours **Days 1,29:** Mitomycin 10mg/m^2 (max 20mg) IV push. Administer for one 5-week cycle with radiation. **OR** **Days 1-4, 29-32:** Fluorouracil 1,000mg/m^2 IV continuous infusion over 24 hours **Day 1:** Mitomycin 12mg/m^2 (max 20mg) IV push, with radiation. Administer for one 5-week cycle with radiation.
Other Recommended Regimens	
Fluorouracil + Cisplatin + Radiotherapy[5,7,b,c]	**Days 1-4, 29-32:** Fluorouracil 1,000mg/m^2 IV continuous infusion over 24 hours **Days 1,29:** Cisplatin 75mg/m^2 IV over 2 hours. Administer for one 8-week cycle without radiation, **followed by:** one cycle with radiation.

▶Metastatic Cancer[1]

Preferred Regimens	
Carboplatin + Paclitaxel[8-10,d] ***Premedication is required.***	**Day 1:** Paclitaxel 175mg/m^2 IV over 3 hours, **followed by:** **Day 1:** Carboplatin AUC 5 IV over 30 minutes. Repeat cycle every 3 weeks. **OR** **Day 1,8,15:** Paclitaxel 80mg/m^2 IV over 1 hour, **followed by:** **Day 1:** Carboplatin AUC 5 IV over 30 minutes. Repeat cycle every 4 weeks.
Other Recommended Regimens	
Fluorouracil + Cisplatin[8,11,b,c]	**Day 1:** Cisplatin 60mg/m^2 IV over 1 hour **Days 1-4:** Fluorouracil 1,000mg/m^2 IV continuous infusion over 24 hours daily. Repeat cycle every 3 weeks. **OR** **Day 1:** Cisplatin 75mg/m^2 IV over 2 hours **Days 1-5:** Fluorouracil 750mg/m^2 IV continuous infusion over 24 hours daily. Repeat cycle every 4 weeks.
FOLFCIS (Fluorouracil continuous infusion/Leucovorin/ Cisplatin)[12,b,c]	**Day 1:** Cisplatin 40mg/m^2 IV over 30 minutes, **with:** **Day 1:** Leucovorin 400mg/m^2 IV over 30 minutes, **followed by:** **Day 1:** Fluorouracil 400mg/m^2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1000mg/m^2 IV continuous infusion daily (2,000mg/m^2 IV over 46-48 hours). Repeat cycle every 2 weeks.

continued

Anal Carcinoma Treatment Regimens

▶Metastatic Cancer[1] (continued)

REGIMEN	DOSING
Other Recommended Regimens (continued)	
mFOLFOX (Fluorouracil continuous infusion/Leucovorin/ Oxaliplatin) [13,b,e-g]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Day 1:** Fluorouracil 400mg/m^2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion daily (2,400 mg/m^2 IV over 46-48 hours). Repeat cycle every 2 weeks.
Modified DCF (Docetaxel/ Fluorouracil/Cisplatin)[14,b,c,h,i] ***Premedication is required.***	**Day 1:** Cisplatin 40mg/m^2 IV over 1 hour **Day 1:** Docetaxel 40mg/m^2 IV over 1 hour **Days 1-2:** Fuorouracil 1,200mg/m^2 IV continuous infusion daily (2,400 mg over 46-48 hours). Repeat cycle every 2 weeks for maximum of 8 cycles.

▶Subsequent Therapy[1]

Preferred Therapy	
Nivolumab[15,16,j]	**Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks. **OR** **Day 1:** Nivolumab 3mg/kg IV over 30 minutes. Repeat cycle every 2 weeks. **OR** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks.
Pembrolizumab[17-19,j]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks up to 2 years. **OR** **Day 1:** Pembrolizumab 2mg/kg IV over 30 minutes. Repeat cycle every 3 weeks. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks up to 2 years.

[a] Patients with dihydropyrimidine dehydrogenase (DPD) deficiency are unable to metabolize capecitabine normally and may have severe unexpected toxicity.

[b] Patients with dihydropyrimidine dehydrogenase (DPD) deficiency are unable to metabolize fluorouracil normally and may have severe unexpected toxicity.

[c] Hydration is required with supplemental electrolyte pre- and post-administration of Cisplatin.

[d] For Paclitaxel: premedication for hypersensitivity is required. H2 antagonist – famotidine 20mg IV or orally (or equivalent H2 blockers) 30-60 minutes pre-paclitaxel AND H1 antagonist – diphenhydramine 12.5-50mg IV or orally 30-60 minutes pre-paclitaxel AND dexamethasone (21-day regimen) – 20mg orally approximately 12 and 6 hours pre-paclitaxel OR dexamethasone 20mg orally 30 minutes pre-paclitaxel OR dexamethasone (for weekly regimens) – 10mg IV 30 minutes pre-paclitaxel. In the absence of infusion reactions for Doses 1-3, may consider dexamethasone 4mg IV 30 minutes pre-paclitaxel starting with Dose 4.

[e] CSFs (Colony stimulating factor) may be considered for primary prophylaxis based on febrile neutropenia risk of the chemotherapy regimen.

[f] Discontinuation of Oxaliplatin should be strongly considered after 3 – 4 months of therapy (or sooner if neurotoxicity grade 2 or greater develops) while maintaining other agents until time of tumor progression. Oxaliplatin may be reintroduced if it was discontinued for neurotoxicity rather than for disease progression.

[g] Leucovorin infusion time should match the infusion time of Oxaliplatin when these agents are given concurrently.

[h] For Docetaxel: premedication with dexamethasone for fluid retention is required. One recommended dosing strategy is: dexamethasone 8mg orally twice daily for three consecutive days starting day 1 prior to docetaxel administration.

[i] Filgrastim, Pegfilgrastim, or clinically appropriate biosimilar are recommended to start the day following or up to 3-4 days after completion of chemotherapy.

[j] Early and late-onset immune-related adverse events affecting multiple organ systems can occur in patients receiving immune checkpoint inhibitors. Patients with neurologic or life-threatening autoimmune disorders as well as those receiving high levels of immunosuppression for their underlying disease should be approached with caution when considering immunotherapy. All patients will require extensive resources including ongoing intensive monitoring and supportive care.

References

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