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**Evidence-based Series 2-8 Version 2 IN REVIEW**

# A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

# Management of Squamous Cell Cancer of the Anal Canal

*Members of the Gastrointestinal Cancer Disease Site Group*

**An assessment conducted in December 2025 placed Evidence-based Series (EBS) 2-8 Version 2 IN REVIEW. This means that it is undergoing a review for currency and relevance. It is still appropriate for this document to be available while this updating process unfolds. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol)**

**EBS 2-8 Version 2 consists of 4 sections. You can access the summary and full report here: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/386**

**Section 1: Clinical Practice Guideline (ENDORSED)**
**Section 2: Evidentiary Base**
**Section 3: EBS Development Methods and External Review Process**
**Section 4: Guideline Review Summary & Tool**

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# Guideline Report History

| GUIDELINE VERSION | SYSTEMATIC REVIEW | | PUBLICATIONS | NOTES AND KEY CHANGES |
|---|---|---|---|---|
| | Search Dates | Data | | |
| Original version March 2009 | 1980-2008 | Full Report | Web publication | NA |
| Current Version 2 November 2013 | 2008- 2013 | New data found in Section 4: Document Summary and Review Tool | Updated Web publication | 2009 recommendations is **ENDORSED** |

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**Evidence-Based Series 2-8 Version 2: Section 1**

# Management of Squamous Cell Cancer of the Anal Canal: Guideline Recommendations

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A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

**Report Date: March 31, 2009**

**These guideline recommendations have been ENDORSED, which means that the recommendations are still current and relevant for decision making. Please see Section 4: Document Review Summary and Tool for a summary of updated evidence published between 2008 and 2013, and for details on how this Clinical Practice Guideline was ENDORSED.**



## INTENDED USERS

This guideline is intended for use by clinicians and health care providers involved in the management or referral of adult patients with squamous cell cancer of the anal canal.

## QUESTIONS

1. Does the addition of chemotherapy (CT) to radiotherapy (RT) improve outcome for patients with squamous cell cancer of the anal canal?
2. What are the optimal CT drugs for the treatment of patients with squamous cell cancer of the anal canal?
3. Does the use of induction CT before concurrent CT and RT improve outcome for patients with squamous cell cancer of the anal canal?
4. What is the best management for patients with squamous cell cancer of the anal canal who are human immunodeficiency virus (HIV) positive?

Outcomes of interest are colostomy rate, local failure, survival, disease-free survival, acute and late adverse effects, and quality of life.

**TARGET POPULATION**

These recommendations apply to adult patients (age ≥18 years) with a primary diagnosis of biopsy-proven squamous cell cancer of the anal canal, including basaloid, cloacogenic, and transitional cell tumours. These recommendations do not apply to patients who have previously undergone resection of their tumour. The management of patients who later develop extra-pelvic metastases is not considered in this guideline.

**RECOMMENDATIONS**

- For all stages of localized squamous cell cancer of the anal canal, concurrent CT and RT is recommended over RT alone to improve local control and decrease colostomy rates.
- The optimal CT drug combination for squamous cell cancer of the anal canal is 5-fluorouracil (5FU) plus mitomycin C (MMC), given concurrently with radiation treatment.
- At this time, induction CT before concurrent CT and RT should be considered an investigational approach.
- It is the expert opinion of the Gastrointestinal Cancer Disease Site Group (GI DSG) that HIV-positive patients with squamous cell cancer of the anal canal should be managed in the same way as patients without known HIV. Treating physicians should be aware that a greater than average risk of toxicity is possible.

**QUALIFYING STATEMENTS**

- No randomized controlled trials (RCTs) were identified that addressed the management of squamous cell cancer of the anal canal in HIV-positive patients. See the Discussion in Section 2 for a description of non-randomized data available on this topic.
- Only two RCTs included patients with T1 lesions of the anal canal, and results were not reported by disease stage. See the Discussion in Section 2 for further discussion on management of patients with T1N0 disease.
- Two RCTs included patients with squamous cell cancer of the perianal skin. A limited discussion of perianal cancer is included in the Discussion in Section 2.
- James et al. 2013 (ACT II), studied maintenance chemotherapy versus none following chemoradiation and found that maintenance chemotherapy does not improve overall survival or colostomy-free survival. Therefore, maintenance chemotherapy following chemoradiation is not recommended in the management of squamous cell carcinoma of the anal canal. See Section 4 for more details.
- In the trials using MMC in the 5FU-MMC combination regimens, MMC schedules include dose of 12 or 15mg/me day 1 only, and a 10mg/m2 Day 1, 29 dosing. There is no comparative data to allow a recommendation of a preferred schedule.

**KEY EVIDENCE**

- The United Kingdom Coordinating Committee for Cancer Research (UKCCCR) trial (1) and the European Organisation for Research and Treatment of Cancer (EORTC) trial (2) demonstrated lower rates of colostomy and local failure in patients who received concurrent RT and CT (5FU plus MMC) compared with patients who received RT alone (Section 2, Table 3). Neither trial demonstrated a significant difference in overall survival between treatment arms.
- The Radiation Therapy Oncology Group (RTOG) 87-04 trial (3) demonstrated that the omission of MMC from the standard combination of 5FU plus MMC resulted in a higher colostomy rate (22% versus [vs.] 9%; p=0.002) and local failure rate (34% vs. 16%; p=0.0008) and lower disease-free survival (51% vs. 73%; p=0.0003) at four years, although overall

survival rates were not significantly different. Acute hematologic toxicity rates were significantly lower in the RT plus 5FU alone arm (3% vs. 18%; p<0.001).

- The RTOG 98-11 trial (4) compared the standard RT plus 5FU and MMC approach with concurrent RT plus 5FU and cisplatin, following two courses of induction CT with 5FU and cisplatin. The 5FU and cisplatin combination was associated with a higher colostomy rate at five years (19% vs. 10%; hazard ratio [HR] 1.68; log-rank p=0.02) compared with the standard 5FU and MMC combination. Local failure, overall survival, and disease-free survival were not significantly different between treatment arms. Severe hematologic toxicity rates were lower in the cisplatin arm compared with the MMC arm (42% vs. 61%; p<0.001), but overall acute adverse effects and severe late adverse effects were similar between arms.
- Updated data on RTOG 98-11 shows OS/PFS advantage for 5FU/MMC (Gunderson et al., 2012). See Section 4 for more details.

**CLINICAL CONSIDERATIONS**

*The following issues are beyond the scope of this guideline but warrant consideration in the management of squamous cell cancer of the anal canal. See the Discussion in Section 2 for further discussion of these issues.*

- Optimal doses and schedules of RT and CT have not been studied systematically. Readers should refer to Section 2 (Table 1) for details regarding treatment used in the available randomized trials.
- Once patients have completed definitive treatment, regularly scheduled clinical follow-up over a five-year period by an experienced specialist is essential since incomplete response or local recurrence may be amenable to salvage surgery.

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