

Treatment of Stage I-III Squamous Cell Carcinoma (SCC) of the Anal Canal

Draft Key Questions (KQs)

KQ1: What is the comparative effectiveness of different modalities of initial treatment for stages I-III squamous cell anal cancer?

KQ2: What is the comparative effectiveness of different radiation therapy doses and fractionation schemes for initial treatment of stage I-III squamous cell anal cancer?

KQ3: What is the comparative effectiveness of different radiation therapy types for initial treatment of stages I-III squamous cell anal cancer?

KQ4: What is the comparative effectiveness of different chemotherapy types or combinations of chemotherapy types and dose de-escalation for initial treatment of stages I-III squamous cell anal cancer?

KQ5: What is the effectiveness of immunotherapy for initial treatment of stages I-III squamous cell anal cancer?

- a. How do outcomes vary based on the conditions surrounding immunotherapy (e.g., other treatments given, patient characteristics, tumor characteristics)? What is the effectiveness and what are the harms of radiation therapy in the palliative treatment of bone metastases?

Background

Anal cancer is a disease in which malignant cells form in the tissues of the anus and at the end of the large intestine, below the rectum. Based on data from 2017 to 2019, roughly 0.2 percent of people will be diagnosed with anal cancer at some point in their lifetime, and the five-year survival rate is approximately 70 percent. While the condition is relatively uncommon, age-adjusted death rates have been rising an average of 3.5 percent each year over the last decade.¹ An analysis conducted in 2019 found that the average lifetime cost of anal cancer was estimated to be approximately \$50,000 for patients, and the disease-related lifetime economic burden for Medicare patients in the United States was approximately \$112 million.²

Major risk factors for anal carcinoma include human papillomavirus (HPV)-16 and HPV-18, two strains of HPV with genes that can cause healthy cell to act abnormally. Conditions with lowered immunity also increase the risk of anal carcinoma. This would include things like acquired immune deficiency syndrome (AIDS), which is advanced HIV infection without current suppressive treatments); taking medications that cause immunosuppression for organ

transplants; and smoking.³ The treatment of anal cancer is dependent upon the stage of an individual’s carcinoma, their overall health, and their personal preferences.⁴ Treatment may include chemotherapy, radiation, and/or surgery.

The [Patient-Centered Outcomes Research Institute \(PCORI\)](#) is partnering with the Agency for Healthcare Research and Quality (AHRQ) to develop a systematic evidence review on Treatment of Stage I-III Squamous Cell Carcinoma (SCC) of the Anal Canal. The American Society for Clinical Oncology (ASCO) and the American Society for Radiation Oncology (ASTRO) plan to use this systematic evidence review to develop related clinical guidelines.

Draft Analytic Framework

Figure 1. Draft analytic framework

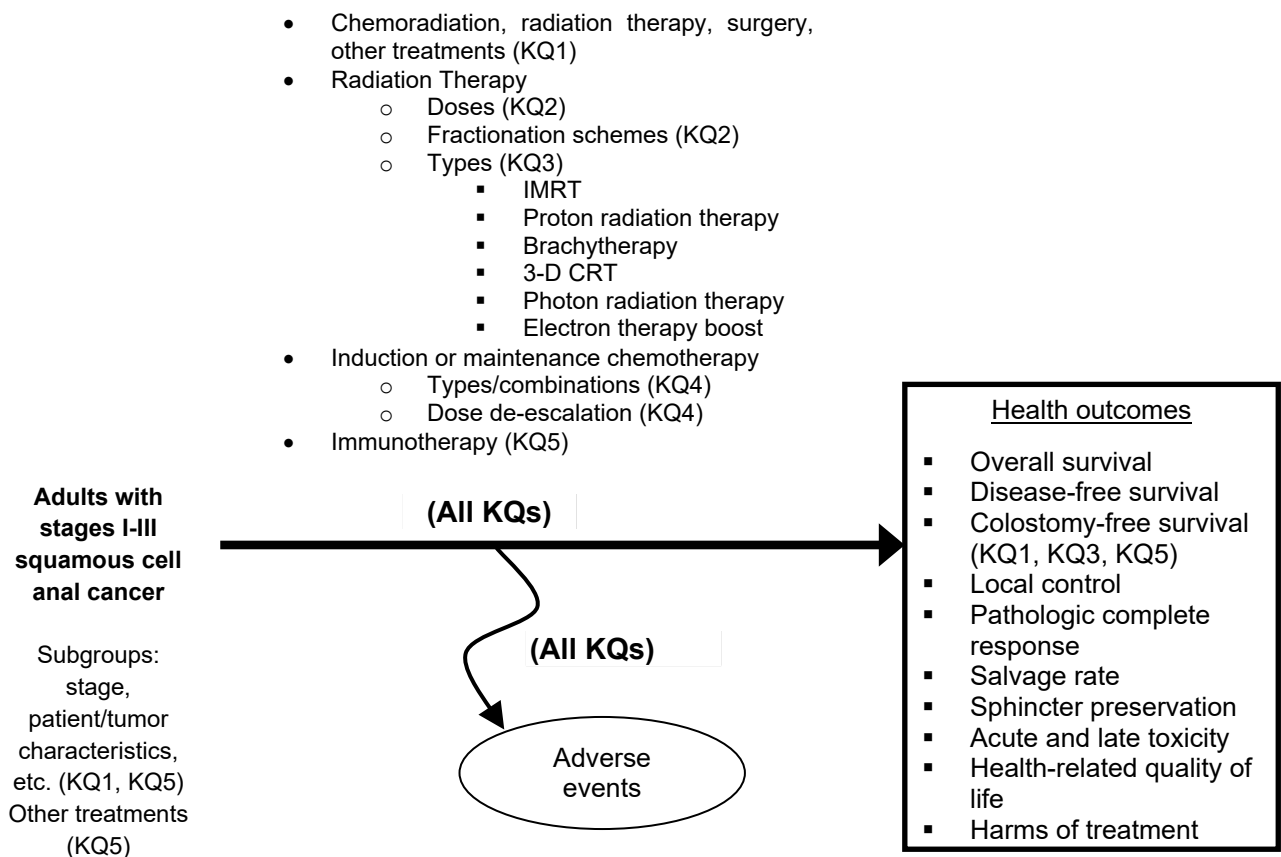


Table 1. Questions and PICOs (population, intervention, comparator, outcome) for KQ1 & KQ2

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|----------------------|--|---|
| Questions | 1. Comparative effectiveness of initial treatment modalities | 2. Comparative effectiveness of radiation therapy doses and fractionation schemes of initial treatment |
| Population | Adults with stages I-III squamous cell anal cancer Subgroup: stage, age, tumor characteristics, etc. | Adults with stages I-III squamous cell anal cancer |
| Interventions | a. Chemoradiation b. Induction or maintenance chemotherapy c. Surgery | Radiation therapy: a. Doses b. Fractionation schemes |
| Comparators | a. Radiation Therapy b. Chemoradiation c. Other treatment | Other: a. Doses b. Fractionation schemes |
| Outcomes | Overall survival Disease-free survival Colostomy-free survival Local control Pathologic complete response Salvage rate Sphincter preservation Acute and late toxicity Health-related quality of life Harms of treatment | Overall survival Disease-free survival Local control Pathologic complete response Salvage rate Sphincter preservation Acute and late toxicity Health-related quality of life Harms of treatment |

Table 2. Questions and PICOs (population, intervention, comparator, outcome) for KQ3 & KQ4

| | | |
|----------------------|--|---|
| Questions | 3. Comparative effectiveness of radiation therapy types for initial treatment | 4. Comparative effectiveness of different chemotherapy types or combinations of chemotherapy types and dose de-escalation for initial treatment |
| Population | Adults with stages I-III squamous cell anal cancer | Adults with stages I-III squamous cell anal cancer |
| Interventions | a. IMRT b. Proton radiation therapy c. Brachytherapy | a. Chemotherapy types/combinations (e.g., fluorouracil, mitomycin, cisplatin) b. Dose de-escalation |
| Comparators | a. 3-D CRT b. Photon radiation therapy c. Electron therapy boost | a. Chemotherapy types/combinations (e.g., fluorouracil, mitomycin, cisplatin) b. Other dose de-escalation |
| Outcomes | Overall survival Disease-free survival Colostomy-free survival Local control Pathologic complete response Salvage rate Sphincter preservation Acute and late toxicity | Overall survival Disease-free survival Local control Pathologic complete response Salvage rate Sphincter preservation Acute and late toxicity Health-related quality of life |

| | | |
|--|--|--------------------|
| | Health-related quality of life Harms of treatment | Harms of treatment |
|--|--|--------------------|

Abbreviations: IMRT=intensity-modulated radiation therapy; 3-D CRT= three-dimensional conformal radiation therapy.

Table 3. Questions and PICO (population, intervention, comparator, outcome) for KQ5

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|----------------------|--|
| Questions | 5. Effectiveness of immunotherapy for initial treatment of stages I-III anal carcinoma a. How do outcomes vary based on the conditions surrounding immunotherapy |
| Population | Adults with stages I-III squamous cell anal cancer Subgroup: other treatments, patient characteristics, tumor characteristics, stage |
| Interventions | Immunotherapy (e.g., pembrolizumab, nivolumab) |
| Comparators | Other treatment (e.g., chemotherapy, radiation, chemotherapy + radiation) |
| Outcomes | Overall survival Disease-free survival Colostomy-free survival Local control Pathologic complete response Salvage rate Sphincter preservation Acute and late toxicity Health-related quality of life Harms of treatment |

References

1. Cancer Stat Facts: Anal Cancer. NIH National Cancer Institute. doi: <https://seer.cancer.gov/statfacts/html/anus.html#:~:text=Rate%20of%20New%20Cases%20and%20Deaths%20per%20100%2C000%3A,age-adjusted%20and%20based%20on%202015%E2%80%932019%20cases%20and%20deaths.>
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