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Anal cancer

Background

There are approximately 1,000–1,200 registrations of squamous carcinoma of the anus per year in the UK. Despite its rarity, a succession of phase III trials have been conducted which have established the standard treatment of this disease; radical treatment with chemoradiotherapy allowing sphincter preservation.

Radical treatment

Both the United Kingdom Co-ordinating Committee on Cancer Research (UKCCCR) anal cancer trial (45 Gray [Gy] in 20 or 25 fractions with a boost) and an European Organisation for Research and Treatment of Cancer (EORTC) trial demonstrated improved outcome for concomitant chemoradiotherapy using mitomycin C and 5-fluorouracil (5-FU) when compared with radiotherapy alone.^{1,2} A statistically significant reduction in locoregional failure was demonstrated in both trials. A further phase III trial performed by the Radiotherapy Oncology Group (RTOG) demonstrated improved colostomy-free survival when mitomycin C was added to 5-FU chemoradiation.³ Chemoradiotherapy improves outcome in anal cancer compared to radiotherapy alone (Level 1b).⁴

The UKCCCR ACT2 trial compared concomitant mitomycin C and 5-FU with cisplatin and 5-FU when combined with a two-phase radiotherapy technique delivering a total dose of 50.4 Gy in 28 fractions.⁵ A second randomisation tested the role of two subsequent cycles of cisplatin 5-FU chemotherapy against no further treatment. There was no significant difference between concurrent chemotherapy regimens, and no progression-free survival benefit to the addition of adjuvant chemotherapy (Level 1b).⁴

The EXTRA trial was a phase II study substituting capecitabine for 5-FU chemotherapy that reported minimal toxicity and acceptable compliance.⁶ Substitution of 5-FU with capecitabine has been thoroughly investigated in other tumour sites and the two drugs have been proven to be equally effective (Level 2b).⁴

Treatment technique

The phase 2 RTOG 0529 trial treated patients with inverse planned intensity-modulated radiotherapy (IMRT) and reported reduced toxicity to that seen in the RTOG 9811 trial where standard conformal radiotherapy techniques were used (Level 2b).^{4,7,8}

It is recommended that a standard atlas for delineating volumes is used for IMRT or arc radiotherapy. Expert opinion was sought from a number of UK clinicians to create a consensus guideline which is based on ACT II volumes but adapted for inverse planning.^{9,10}

Recommendations

For standard planned two-phase radical chemoradiation for anal cancers:

50.4 Gy in 28 daily fractions (Grade A)

Phase 1: 30.6 Gy in 17 fractions over 3.5 weeks

Phase 2: 19.8 Gy in 11 fractions over 2.2 weeks

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based medicine.⁴

Node positive patients

Analyses of both the UKCCR ACT II and RTOG 9811 trial have highlighted that locally advanced and node-positive tumours have a significantly reduced disease-free survival and overall survival.^{5,8} As a result, current guidance and recent trials have used a higher dose for these patients when using IMRT or arc radiotherapy.

However, due to the excellent outcomes in ACT II in node-negative cancers, the recommended prophylactic nodal dose remains the same and has been calculated to deliver the same biologically effective dose over 28 fractions with IMRT or arc radiotherapy which was previously delivered over 17 fractions during standard 2-phase radiotherapy (Level 5).^{4,11}

Recommendations

For radical inverse planned IMRT or arc radiotherapy (chemoradiotherapy) of anal cancers

Dose to primary (early stage):

50.4 Gy in 28 fractions over 5.5 weeks (Grade D)

Dose to primary and involved nodes (advanced stage):

53.2 Gy in 28 fractions over 5.5 weeks (Grade D)

Dose to uninvolved nodes (prophylactic):

40 Gy in 28 fractions over 5.5 weeks (Grade D)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based medicine.⁴

The Personalising Anal Cancer Radiotherapy Dose (PLATO) trial looking at dose escalation in locally advanced anal cancers and dose de-escalation in early small-node negative tumours is currently in set up in the UK and will inform dose fractionation for anal cancers in the future.¹²

Palliative treatment

There are no good-quality trials evaluating different dose fractionation schedules for palliative treatment. An appropriate regime should be chosen after considering the patient's likely prognosis, disease burden, symptoms and performance status.

Recommendations

For palliative treatment of anal cancer (Grade D):

30 Gy in 10 fractions over 2 weeks

20 Gy in 5 fractions over 2 weeks

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based medicine.⁴

References

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