Metastatic Anal Carcinoma: The Role of Radiotherapy

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Over the past 30 years, the incidence of invasive anal carcinoma in the United States has increased at a rate of roughly 2% per year.¹ Most patients present with locoregionally confined disease; distant metastases often involving liver, lung, or extrapelvic lymph nodes are found in only 5% to 8% of patients at initial presentation and in 10% to 20% of patients after curative locoregional treatment. Current standard treatment for locoregionally confined disease, developed based on many clinical trials, includes combined chemoradiation using 5-fluorouracil (5-FU)/mitomycin, capecitabine/mitomycin, or 5-FU/cisplatin. These approaches have resulted in a 5-year survival rate of 60% to 80%, and 60% to 75% local control with anal preservation.²

In contrast, only a few studies have addressed treatment approaches for patients with metastatic anal carcinoma (MAC). Based on several small-scale retrospective studies, including one case report, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Anal Carcinoma recommend using 5-FU/cisplatin, carboplatin/paclitaxel, or FOLFOX (5-FU/leucovorin/oxaliplatin) as first-line treatment for MAC.² The recently reported randomized, international, multicenter, phase II InterAACT study found that, compared with 5-FU/cisplatin, treatment with carboplatin/paclitaxel yielded more durable treatment response, superior overall survival (OS), and fewer serious adverse events.³ In this study, treatment response rates were 59.0% for carboplatin/paclitaxel compared with 57.1% for 5-FU/cisplatin. Median OS was 20 months for carboplatin/paclitaxel versus 12.3 months for 5-FU/cisplatin (hazard ratio, 2.0; P=.014). Thus, this international study provides support for establishing carboplatin/paclitaxel as standard first-line treatment for MAC. For patients with metastatic disease that has progressed after first-line treatment, immune checkpoint inhibitors such as pembrolizumab and nivolumab are now recommended, and response rates of 17% to 24% have been reported.⁴,⁵

Clearly, room for improvement in treatment remains, raising the question for the role of radiotherapy (RT) in patients with newly diagnosed MAC. RT is generally thought to be palliative, and doses up to 30 to 37.5 Gy given over 10 to 15 fractions are often used to control disease locally for patients with a symptomatic bulky primary tumor.² The response rate to initial chemotherapy can be high and durable. Therefore, to control the primary disease in a more reliable way, radiation oncologists can reasonably treat primary tumors to a definitive dose (eg, ≥45 Gy). This is especially true for patients for whom chemotherapy has provided good control of systemic disease and/or who have potential for surgical resection of the metastases.

In this issue of the journal, Yuefeng Wang, MD, PhD, et al examine the role of definitive pelvic RT for patients with newly diagnosed stage IV MAC. The authors identified 437 patients who received chemotherapy alone and 1,020 patients who received pelvic chemoradiation (CRT) between 2004 and 2015 from the National Cancer Database (NCDB) and compared outcomes. At a median follow-up of 17.3 months, univariate and multivariate analyses revealed that pelvic CRT may be associated with better OS in patients with distant lymph node metastases and those with distant organ disease (propensity score–

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and the study of local consolidative therapy

References


3. Rao S, Scalfani F, Eng C, et al. InterAACT: a multicenter open label randomized phase II advanced anal cancer trial of cisplatin (CDDP) plus 5-fluorouracil (5-FU) vs carboplatin (C) plus weekly paclitaxel (P) in patients (pts) with inoperable locally recurrent (LR) or metastatic treatment naïve disease—an International Rare Cancers Initiative (IRCI) trial. Presented at the 2018 ESMO Congress; October 19-23, 2018; Munich, Germany.


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