S alivary gland cancer is an uncommon cancer that accounts for 0.5% of all malignancies and 7% of head and neck cancers. The incidence of salivary gland cancer is increasing and the mortality rate has not decreased. This group of tumours is heterogeneous in terms of location, histology and prognosis. Increasing age is the most important risk factor for salivary gland cancer. Most patients with salivary gland cancer are given a diagnosis of metastatic disease on presentation. The most common site of distant metastasis is the lung.1

Because of the rarity of this disease, there are no adequate randomized controlled data that outline the best approach for management. The mainstay of treatment in localized disease is surgical resection. A Canadian study found that older adults represented 40% of patients with salivary gland cancers.2 However, these patients were less likely to undergo surgical resection owing to their comorbidities.2 Patients who are not candidates for surgical resection receive radiation therapy, and the 10-year overall survival is between 15% and 25%.3 It has been postulated that salivary duct carcinoma is histologically similar to prostate cancer, given androgen receptor overexpression in 40%–93% of cases.4 Several case reports1,3–5 and one case series6 have shown that androgen deprivation therapy can be used safely and effectively in patients with metastatic salivary gland cancer.

Box 1 describes a case in which we used androgen deprivation therapy with apparent success. The response was dramatic, albeit not complete. The patient went from having symptomatic pleural effusions and having an Eastern Cooperative Oncology Group (ECOG) performance status of 3 to no longer needing his pleural drains and an ECOG of 0. We were able to control his disease and maintain a good quality of life; therefore the term “success.” There were still brain lesions, but these had stopped growing and the patient was no longer symptomatic.

What is androgen deprivation therapy?

Androgen deprivation therapy is widely used in the standard treatment of advanced prostate cancer. Luteinizing hormone–releasing hormone analogues are used to suppress the production of androgens in the testes. In addition to a luteinizing hormone–releasing hormone analogue, a direct androgen antagonist is added to the regimen to suppress the effects of androgens in the adrenal glands. These direct androgen antagonists inhibit the binding of dihydrotestosterone to the androgen receptor. Bicalutamide is the most well-studied direct androgen antagonist5 and has the most favourable adverse effect profile. Bicalutamide is usually prescribed orally as 150 mg/d and continued until disease progression.5

Several case reports have reported bicalutamide’s safety and efficacy in patients with metastatic salivary gland tumours (Box 2). The patients described in these reports were not clearly symptomatic from their disease, and only one patient had brain metastases. Our patient had marked impairment in his quality of life secondary to metastatic pleural effusions and brain metastases. After androgen deprivation therapy, he no longer required the insertion of a tunneled pleural catheter for pleural effusions and he was able to resume functioning.

Who is eligible?

In patients who have recurrent or metastatic or unresectable, locally advanced androgen receptor–positive salivary gland cancers despite standard of care therapy, androgen deprivation therapy may be considered. There are no absolute contraindications to this treatment.6

What are the harms?

Although there are no absolute contraindications, androgen deprivation therapy may cause adverse effects that can affect the
A 72-year-old man presented to the oncology clinic for management of his metastatic salivary gland cancer. The patient was initially treated with total parotidectomy, followed by adjuvant chemotherapy with weekly carboplatin and paclitaxel, as well as radiation therapy. On routine follow-up computed tomography scan three weeks after completion of treatment, the patient was found to have mediastinal lymphadenopathy. He underwent active surveillance for two years and was stable until he developed progressive general deterioration with a decline in performance status to Eastern Cooperative Oncology Group (ECOG) 3. Computed tomography scan of his chest revealed progression of mediastinal lymphadenopathy, new multiple bilateral spiculated lung nodules and a moderately sized pericardial effusion. The patient had also developed interval new bilateral pleural effusions that required tunneled pleural catheter placement and intermittent drainage. A magnetic resonance imaging scan of the brain revealed a focal-enhancing 18 mm lesion in the inferior aspect of the right cerebellar hemisphere compatible with a leptomeningeal metastasis, as well as a second 6 mm lesion in the upper right cerebellar hemisphere. The patient underwent endobronchial ultrasound-guided biopsy of a mediastinal lymph node, and the pathology revealed metastatic adenocarcinoma with morphology and immunophenotype compatible with salivary duct carcinoma. Androgen receptor was tested and was positive.

Given the lack of available standard therapeutic options, androgen deprivation therapy was recommended and the patient was treated with goserelin (a luteinizing hormone–releasing hormone agonist) and bicalutamide. Within two weeks of therapy, the patient no longer required intermittent drainage of his pleural effusion and the catheters were therefore removed. His performance status improved to ECOG 0. Computed tomography scan after two months of androgen deprivation therapy showed resolution of the pleural effusions and pericardial effusions, as well as a decrease in size of the pulmonary nodules (7 × 4 mm nodule that had previously measured 8 × 5 mm, as well as a 3 mm nodule that had previously measured 7 mm in the right upper lobe), and near complete resolution of left upper lobe pulmonary nodules. Magnetic resonance imaging of the brain showed stability of the two brain lesions.

### Box 1: Case description

A 72-year-old man presented to the oncology clinic for management of his metastatic salivary gland cancer. The patient was initially treated with total parotidectomy, followed by adjuvant chemotherapy with weekly carboplatin and paclitaxel, as well as radiation therapy. On routine follow-up computed tomography scan three weeks after completion of treatment, the patient was found to have mediastinal lymphadenopathy. He underwent active surveillance for two years and was stable until he developed progressive general deterioration with a decline in performance status to Eastern Cooperative Oncology Group (ECOG) 3. Computed tomography scan of his chest revealed progression of mediastinal lymphadenopathy, new multiple bilateral spiculated lung nodules and a moderately sized pericardial effusion. The patient had also developed interval new bilateral pleural effusions that required tunneled pleural catheter placement and intermittent drainage. A magnetic resonance imaging scan of the brain revealed a focal-enhancing 18 mm lesion in the inferior aspect of the right cerebellar hemisphere compatible with a leptomeningeal metastasis, as well as a second 6 mm lesion in the upper right cerebellar hemisphere. The patient underwent endobronchial ultrasound-guided biopsy of a mediastinal lymph node, and the pathology revealed metastatic adenocarcinoma with morphology and immunophenotype compatible with salivary duct carcinoma. Androgen receptor was tested and was positive.

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### Box 2: Characteristics of cases of salivary duct adenocarcinoma treated with androgen deprivation therapy

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of cases</th>
<th>Age, yr (median)</th>
<th>Androgen deprivation therapy</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Locati et al.5</td>
<td>7</td>
<td>68</td>
<td>Bicalutamide + LHRH analogue</td>
<td>1 CR</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 PR</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 SD</td>
</tr>
<tr>
<td>Jaspers et al.5</td>
<td>10</td>
<td>66</td>
<td>9 bicalutamide, 1 bicalutamide + LHRH analogue</td>
<td>2 PR</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3 SD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5 PD</td>
</tr>
<tr>
<td>Soper et al.3</td>
<td>1</td>
<td>87</td>
<td>Bicalutamide + LHRH analogue + RT</td>
<td>CR</td>
</tr>
<tr>
<td>Yamamoto et al.11</td>
<td>1</td>
<td>66</td>
<td>Bicalutamide</td>
<td>CR</td>
</tr>
<tr>
<td>Agbarya et al.1</td>
<td>1</td>
<td>57</td>
<td>Bicalutamide</td>
<td>CR</td>
</tr>
<tr>
<td>Urban et al.4</td>
<td>1</td>
<td>45</td>
<td>Abiraterone, prednisone and LHRH analogue</td>
<td>CR</td>
</tr>
<tr>
<td>Our patient (Box 1)</td>
<td>1</td>
<td>72</td>
<td>Bicalutamide + LHRH analogue</td>
<td>PR</td>
</tr>
</tbody>
</table>

Note: CR = complete response, LHRH = luteinizing hormone–releasing hormone, PD = progressive disease, PR = partial response, RT = radiation therapy, SD = stable disease.
Furthermore, the types of androgen deprivation therapy used in the case reports and case series were heterogeneous, and more studies are required to determine the optimal choice of androgen deprivation therapy.

References


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