Table 1. Frequency of symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Granisetron, n (%) (n = 29)</th>
<th>Ondansetron, n (%) (n = 28)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headaches</td>
<td>7 (24.1)</td>
<td>8 (28.6)</td>
<td>0.770</td>
</tr>
<tr>
<td>Abnormal vision</td>
<td>1 (3.4)</td>
<td>2 (7.1)</td>
<td>0.611</td>
</tr>
<tr>
<td>Dizziness</td>
<td>2 (6.9)</td>
<td>4 (14.3)</td>
<td>0.423</td>
</tr>
<tr>
<td>At least one</td>
<td>10 (34.5)</td>
<td>12 (42.9)</td>
<td>0.592</td>
</tr>
</tbody>
</table>

P values from Fisher’s exact test.

References


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Intratumoral injection of herpes simplex virus HF10 in recurrent breast cancer

Breast cancer is one of the most common and feared cancers. Although there have been many advances in clinical studies, breast cancer remains a major contributor to the number of cancer deaths [1]. Advances in genetic engineering techniques have enabled investigators to develop more effective viruses for oncolytic viral therapy. We previously reported that a replication-competent, spontaneous herpes simplex virus-I (HSV-1) variant, HF10 [2], was effective in treating disseminated peritoneal colon carcinoma and breast cancer in an immunocompetent mouse model [3–5]. To assess the therapeutic potential of HF10 in human disease, we did a preliminary study of toxicity and possible efficacy in six patients with recurrent metastatic breast cancer. All patients gave written informed consent, and the study was approved by the local ethics committee and institutional review board of our hospital. All six patients had pathologically proven recurrent breast cancer with cutaneous or subcutaneous metastatic nodules accessible to direct intratumoral injection. For each patient, a test nodule was injected with an HF10 diluent of various content [patient 1, 10^6 plaque-forming units (p.f.u.)/0.5 ml; patient 2, 10^5 p.f.u./0.5 ml; patient 3, 10^5 p.f.u./0.5 ml × 3 days; patient 4, 5 × 10^5 p.f.u./0.5 ml; patient 5, 5 × 10^5 p.f.u./0.5 ml × 3 days; patient 6, 5 × 10^5 p.f.u./0.5 ml × 3 days]. A second nodule was injected with 0.5 ml sterile saline. All patients were monitored for systemic adverse effects, and the injected nodules were examined for sign and size of inflammation. The injected nodules were excised in all patients 14 days after injection for examination by conventional haematoxylin and eosin staining and immunofluorescence examination using anti-herpes simplex virus type 1 (DAKO, Glostrup, Denmark) antibody. All patients tolerated HF10 well, were seropositive for HSV before virus injection, and their IgG and IgM titres did not substantially alter during the trial. There was no virus shedding or reactivation of endogenous latent HSV in any patient. No clinical change was seen in the HF10-injected nodules in any patient.

No patient showed evidence of regression of tumour mass at any other adjacent or distant tumour site. Pathological examination of excised nodules showed no cell death in the saline-injected nodules (Figure 1A). However, tumour cell death and nuclear viral inclusion bodies in breast cancer cells were observed in HF10-injected nodules (Figure 1B). Death was observed among 30–100% of cancer cells overall.

Immunofluorescence examination of excised HF10-injected nodules showed evidence of viral infection confined to breast cancer cells in all patients (Figure 1C). HF10 was seen in the breast cancer cells from the virus-treated nodules, with no antigen staining in the adjacent normal connective tissue. The fact that each of the patients was seropositive for HSV before HF10 injection indicates that the ability of the virus to replicate within tumour cells is not blocked by previous exposure to HSV.

This preliminary study shows that HF10 replicates in breast cancer cells to cause tumour cell death, and is not toxic. The results are sufficiently encouraging to continue HF10 in patients with metastatic breast cancer, as well as in other types of cancer.

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References

3. Takakura H, Goshima F, Nozawa N et al. Oncolytic viral therapy using a spontaneously generated herpes simplex virus type 1 variant for dissemi-
Serum and plasma vascular endothelial growth factor levels in testicular cancer patients

I read with interest Aigner and colleagues’ article [1] published recently in *Annals of Oncology*. Although the authors should be congratulated for their results on the study of pleiotrophin and fibroblast growth factor, I would like to report some methodological issues concerning the measurement of vascular endothelial growth factor (VEGF) levels.

Despite the fact that the authors reported the use of ‘serum’ for the measurement of various growth and angiogenesis factors in patients with testicular cancer, the blood samples were collected in EDTA-coated tubes. Adding anticoagulants to the blood samples...