Intratumoral Coxsackievirus A21 increases immune-cell infiltrates and up-regulates immune-checkpoint molecules in the tumor microenvironment of advanced melanoma patients: Phase II CALM Extension study

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#CT053

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Coxsackievirus A21 induces immune cell infiltration in the micro-environment of melanoma lesions

Coxsackievirus A21 injection up-regulates interferon-induced genes and immune checkpoint molecules within the tumor microenvironment of melanoma lesions (Image/Slide analysis Patient Cancer Immunomodulating Panel)

Introduction

UNIQUE: an oncolytic immunotherapy, is a live-attenuated oncolytic strain of Coxsackievirus A21 (CVA21). Future clinical evaluation of CVA21 will be informed by evaluation of 2 clinical experiments: (1) CVA21 preferentially infects CD8+ expressing tumor cells, resulting in viral replication, cell killing, and a systemic, antitumor, immune response. The Phase II CALM study investigated efficacy and safety of CVA21 in patients with advanced melanoma. Clinical evaluation of CVA21 will inform future clinical evaluation of CVA21, aligning with current international guidelines for evaluating oncolytic virus clinical trials. CVA21 induces a Th1-gene shift, with increases in interferon-induced genes.

Future Directions

- Clinical evaluation of the safety of intratumoral injection of CVA21 in combination with systemic administration of pembrolizumab in patients with unresectable melanoma currently underway (Phase1b CAPRA study: ClinicalTrials.gov Identifier:NCT2565992)
- Clinical evaluation of the safety of intratumoral injection of CVA21 in combination with systemic administration of ipilimumab/pembrolizumab in patients with unresectable melanoma currently underway (Phase1b CALM study: ClinicalTrials.gov Identifier:NCT2565992)
- CVA21 treatment may be used to reanimate the immune cells within the tumor microenvironment of cancer that currently resides partly in immune checkpoint blockade (e.g. melanoma, glioblastoma, colorectal and prostate lesions).

Study Design

Preliminary Data

Patient Characteristics and Overall Response

<table>
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<th>Code</th>
<th>Case #</th>
<th>Sex</th>
<th>Age</th>
<th>Race</th>
<th>Stage</th>
<th>Prior Treatment</th>
<th>Prior Combination</th>
<th>Lesion Infiltration</th>
<th>Lesion Response</th>
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<td>Pt#03&amp;043</td>
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<td>Surgery (3), Radiotherapy, Immunotherapy (ipilimumab, pembrolizumab)</td>
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<td>CD3</td>
<td>Progressive</td>
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<td>CD3</td>
<td>Progressive</td>
</tr>
</tbody>
</table>

Levels of lesion T-cell infiltrates: Multiplexed Images Obtained and Enumerated with PARKIN/EMER Vectra Imaging system and InForm Software

Conclusions

- CVA21 treated nonmetastatic lesions in the tumor microenvironment by inducing increases in immune cell infiltrates (CD8+ and IFIT1) and up-regulated interferon-induced antitumor genes, including CD40L, CD122, CXCL10, IL12, IFN-γ and PD-L1.
- Up-regulation of immune cell infiltrates and interferon-induced antitumor immunity (IL12, IFN-γ, IFIT1, etc.) in injected lesions may contribute to improved immune checkpoint blockade (e.g. anti-PD1 antibodies, costsensitive melanoma).

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