656LB - Interim Safety Analysis of CITN–12: Pembrolizumab in Patients with HIV and Cancer

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Background

Checkpoint inhibitors and Cancer
- Anti-PD-1 and anti-PD-L1 antibodies are becoming mainstays of cancer therapy.
- The safety of pembrolizumab, an anti-PD-1 humanized monoclonal antibody, is being evaluated in patients with HIV and cancer.
- The effect of anti-PD-1 therapy on HIV reservoirs is unknown.

Safety concerns in people with HIV in part due to:
- Immune dysregulation of unknown clinical significance
- PD-1 upregulation
- Perturbed TCR repertoire
- Potential concern related to concurrent infections

Methods

- Cancer Immunotherapy Trials Network (CITN)-12 is a multicenter study of pembrolizumab in patients with HIV and advanced cancers.
- Three CD4 defined cohorts (C) are accruing: C1: 100-199, C2: 200-350, and C3: >350 cells/μL.
- Eligibility: >4 weeks antiretroviral therapy (ART), HIV viral load <200 copies/mL, no HBV or HCV detectable in blood by PCR (seropositive not excluded).
- Treatment: pembrolizumab 200mg intravenously every 3 weeks for up to 2 years.
- Primary objective: assess safety and tolerability by summarizing CTCAE4 graded adverse events (AEs) and evaluating HIV viral load (VL) and CD4 counts.
- Immune mediated AEs are managed using standard guidelines.
- We performed an interim analysis of treatment emergent adverse events at least possibly related to pembrolizumab (tTEAEs), serious AEs, and CD4 counts on therapy.
- Plasma HIV VL was measured by an HIV gag single copy assay (SCA).
- One Serious Unexpected Adverse Event occurring after locking of the data for the interim analysis.

Results

- 17 patients were accrued starting April 2016 and followed through May 2017.
- Safety was observed over 100 total cycles, median 4 (range 1-20).

Adverse Events
- 82 tTEAEs were observed and comparable between cohorts.
- 93% were grade 1-2.
- Subsequent Unanticipated problem: Death from KSHV-associated lymphoproliferation in patient with likely undiagnosed multicentric Castleman disease.

Treatment emergent adverse events at least possibly related to pembrolizumab

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3-4</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>4</td>
<td>3</td>
<td>1 (3.1)</td>
<td>8 (22.2)</td>
</tr>
<tr>
<td>Nausea</td>
<td>6</td>
<td>3</td>
<td>1 (3.1)</td>
<td>10 (28.6)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>4 (11.4)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2 (5.7)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>3 (8.3)</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2 (5.7)</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>4 (11.4)</td>
</tr>
</tbody>
</table>

HIV Correlates

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Cycle</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6 or End</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV VL (copies/mL)</td>
<td>8 (47%)</td>
<td>5 (25%)</td>
<td>7 (35%)</td>
<td>9 (25%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4+ (cell/μL)</td>
<td>8 (47%)</td>
<td>7 (35%)</td>
<td>10 (52%)</td>
<td>10 (52%)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Conclusions

- Pembrolizumab has an acceptable safety profile to date in patients with HIV and cancer.
- CD4+ T-cells counts may increase on pembrolizumab and HIV control is maintained on ART.
- Anti-PD1 therapy is appropriate in patients with HIV for FDA-approved indications.
- Evaluation of pembrolizumab as first systemic therapy in patients with Kaposis sarcoma to start Spring 2018.
- Studies evaluating strategies to treat HIV that incorporate anti-PD-1/PD-L1 are warranted.
- Physicians should be aware of the possibility of emergent KSHV-associated multicentric Castleman disease with anti-PD-1 therapy and early treatment is advised.
- Accrual and correlative studies are ongoing.