Phase 1 Trial of CV301 in Combination With Anti-PD-1 Therapy in Non-Squamous NSCLC

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\textbf{Abstract}

Background: Pegylated interferon-α2b consisting of cancer vaccines and immune checkpoint inhibitors. Treatment results in generation of multifunctional tumor-associated antigen (TAA) responses.

Design & Treatment Schedule

<table>
<thead>
<tr>
<th>MVA-BN-CV301</th>
<th>FPV-CV301</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD1a+ CD8+ T cells for Cohort 1 (C1)</td>
<td>CD1a+ CD8+ T cells for Cohort 2 (C2)</td>
</tr>
<tr>
<td>2 Priming Doses</td>
<td>2 Boosting Doses</td>
</tr>
<tr>
<td>+ Anti-PD-1</td>
<td>+ Anti-PD-1</td>
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</tbody>
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\textbf{Subject Status per Cohort}

\begin{itemize}
  \item MVA \begin{itemize}
    \item MUC-1 CEACAM-1 LFA-3 B7.1
  \end{itemize}
  \item FPV \begin{itemize}
    \item TAA Response to at least 1 of the antigens tested
  \end{itemize}
\end{itemize}

\textbf{Demographics}

- Age (median): 64 years
- Gender: 9 Female, 3 Male
- Smoking: 1 Current smoker, 9 Former smokers, 2 Never smoked

\textbf{Change in Tumor Burden}

\textbf{Best Overall Response per RECIST x1, x (\%)}

- Complete Response
  - 1 (8.3)
- Partial Response
  - 0 (0)
- Stable Disease
  - 10 (83.3)
- Progressive Disease
  - 0 (0)
- Unassessable
  - 0 (0)

\textbf{Antigen Specific Responses}

- Antigen specific responses to MUC-1 and CEA could be analyzed in 4 patients.
- 4/6 patients developed T cell responses to at least 1 of the antigens tested.

\textbf{Multifunctional TAA responses, defined as CD4 or CD8 T cells that express 2 or more of the following markers: IFNγ, TNF, IL-2, or CV301 were also measured.}

- Multifunctional TAA specific T cells were generated after therapy in 50% of the patients to at least one of the antigens tested (using the criteria of a >10 fold increase post vaccination vs pre, or the presence of >1,000 multifunctional cells at post per 1x10\textsuperscript{6} PBMCs (if negative at pre)).

\textbf{Results - Multifunctional TAA Response}

\begin{itemize}
  \item Frequency of Patients with Multifunctional TAA Response
    \begin{itemize}
      \item MUC1 + (75%)
      \item CEA + (75%)
      \item TNF + (75%)
      \item IFNg + (75%)
      \item CD8 + (83.3)
      \item CD4 + (83.3)
      \item CEA + (83.3)
      \item TNF + (83.3)
      \item IFNg + (83.3)
      \item CD8 + (83.3)
      \item CD4 + (83.3)
    \end{itemize}
\end{itemize}

\textbf{Conclusions}

- Combination of CV301 with PD-1 Inhibitors is safe and clinically active in advanced non-squamous NSCLC.
- Treatment results in generation of multifunctional tumor-associated antigen T cell responses.
- These data support further evaluation of combination immunotherapy consisting of cancer vaccines and immune checkpoint inhibitors.

\textbf{TEAEs by max. CTCAE Grade}

\begin{itemize}
  \item MedDRA Preferred Term
    \begin{itemize}
      \item Injection site reaction 10 (83.3)
      \item Headache 4 (33.3)
      \item Diarrhea 3 (25.0)
      \item Nasal congestion 2 (16.7)
      \item Rash maculo-papular 2 (16.7)
      \item Pruritus 2 (16.7)
      \item Sinusitis 2 (16.7)
      \item Fatigue 2 (16.7)
      \item Infusion related reaction 1 (8.3)
      \item Pneumonitis 1 (8.3)
      \item Rash maculopapular 1 (8.3)
      \item Urinary tract infection 1 (8.3)
      \item Arthralgia 1 (8.3)
      \item Hypersensitivity 1 (8.3)
      \item Cerebrovascular accident 1 (8.3)
      \item Neutropenia 1 (8.3)
      \item Pneumonia 1 (8.3)
      \item Weight increased 1 (8.3)
      \item Proctitis 1 (8.3)
    \end{itemize}
\end{itemize}