Will Innovations in Oncolytic Viruses and Therapeutic Cancer Vaccines Disrupt the Oncology Landscape?

**Oncolytic viruses (OVs) and therapeutic cancer vaccines (TCVs) continue to be the modalities of interest, given their potential to reverse immunosuppressive tumor immune-microenvironments and expand the potential of PD-1/L1 inhibitors and other therapies (as combinations). They also lack the usual systemic toxicity seen with drug treatment.**

OVs, aside from T-Vec in melanoma, have not met with much success in the clinic due to virus neutralization and traditional payloads being insufficient to drive significant clinical benefit. Recently, there has been renewed interest and many OVs are entering early phase clinical trials with unique innovations.

**These innovations are driven by:**
- New payloads (increased efficacy compared to the conventional payloads such as GM-CSF)
- Engineered viral capsids (to overcome neutralization, increase selectivity)
- Alternate RoA-i.v. (to reach tumors not easily accessible for an intratumoral route)

Along with OVs, there is also an increased interest in TCVs, which are used to train a patient’s immune system before killing the cancer cells. They have the benefit of eliciting immune responses specific to tumor antigens (shared or neoantigens). Innovations around TCVs are centered around
- New vaccine platforms (mRNA/DNA)
- Novel tumor-associated antigens/tumor-specific antigens (TAAs/TSAs)
- Novel combinations with other OVs, vaccines, and targeted therapies

**ASCO 2021 provided insights on the stimulating array of advancements and SmartAnalyst has summarized select ASCO 2021 highlights on innovations in OVs and vaccines.**

<table>
<thead>
<tr>
<th>Oncolytic Virus</th>
<th>Therapeutic Cancer Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alternate RoA (i.v.)</strong></td>
<td><strong>Repertoire of self-antigens (TAAs/TSAs)</strong></td>
</tr>
<tr>
<td>2nd OV (after approved T-Vec) with promising Phase III efficacy (interim)</td>
<td>Superior efficacy in patient segments with unique molecular profile</td>
</tr>
<tr>
<td>- Ofiranergene obadenovec (VB-111, VBL Therapeutics) ongoing registrational trial has shown a promising efficacy in platinum-refractory/recurrent OvCa with elevated CA-125</td>
<td>- ‘Vigil’ (Gradalis) showed clinical benefit in ovarian cancer in BRCA-WT and homologous recombination proficient patients</td>
</tr>
<tr>
<td>- N=60, CA-125 ORR: 58%</td>
<td>- Vigil: N=47, mOS: NR @ 48 months, mRFS: 11.5 months</td>
</tr>
<tr>
<td><strong>OVs with encouraging early phase results in SCCHN and glioma</strong></td>
<td>Efficacy in “cold tumors”</td>
</tr>
<tr>
<td>- HB-201 +/- HB-202 (Hoopika Biotech.; SCCHN, HPV16+); Ph I/II, N=11, mPFS: 3.45 months, ORR: 18.2%</td>
<td>- DCVAC (Sotio) demonstrated improved PFS and OS outcomes in epithelial ovarian carcinoma</td>
</tr>
<tr>
<td>- CAN-3110 (Candel Therapeutics; Glioma): Ph I, N=30, mOS: 11.7 months</td>
<td>- DCVAC + Plt. based chemo: N=31, mOS: NR @ 84 months, mPFS: 20.3 months</td>
</tr>
</tbody>
</table>
**Oncolytic Virus Therapeutic Cancer Vaccine**

### New payloads

**Multiple payloads may have an incremental effect in boosting an immune response**

- **CARG-2020** (CaroGen Corporation; an artificial virus-carrying payloads IL-12, dn-IL-17RA and PD-L1 shRNA) exerts a broader spectrum of immuno response as compared to IL-12 alone (in syngeneic mouse model)

### Novel combination therapies

- **PDS0101** (PDS Biotech.; lipid nanoparticles carrying HPV antigens) along with **M7824** (a bifunctional fusion protein targeting PD-L1 and TGF-β) and **NHS-IL-12** (tumor-targeted immunocytokine) has greater anti-tumor activity in HPV+ cancers than any single/dual combination of these agents
- **PDS0101+ M9241+ Bintrafusp alfa**: HPV16+: N=18, OS @ 8 months: 88.9%, ORR: 55.6%

Overall, can these two modalities (OV/TCV) become transformative? Data presented at ASCO 2021 suggests that these modalities may represent an alternative treatment option for both advanced and early stage cancers. However, it is too early to conclude if these will change the future treatment paradigms without additional data in hand.

### Sources: