DepoVax™: A novel delivery formulation for cancer immunotherapy and infectious disease vaccines

May 10, 2017
The DepoVax™ Platform

- A patented oil-based formulation – NOT an adjuvant
- Creates powerful vaccines to treat cancer and protect against infectious diseases
- A novel mechanism of action: no release formulation
- Lead cancer immunotherapy (DPX-Survivac) in combination immunotherapy trials
- Phase 1 study for Respiratory Syncytial Virus (RSV) completed
Proprietary Platform & Products

- Protection and prolonged exposure of antigens to the immune system
- Broad applications
- Established GMP manufacturing process
- Years of shelf life stability

DepoVax™
Encapsulate in a Liposome + Lyophilize + Suspend in Oil

- Survivin cancer target
  - Recognized as one the most promising target
  - 20+ indications
- RSV candidate vaccine
  - No vaccine on market
  - Next blockbuster vaccine
Clearance Antigen from DepoVax vs. Emulsion Formulations using Iron Labelling and MRI Imaging

Brewer et al, 2014 Vaccine 32:6956
**DPX-Survivac: Phase 1 Trial in Ovarian Cancer**

Non-randomized, Dose Finding:

- **Cohort A**: 0.5 mL DPX-Survivac (N=7)
- **Cohort B**: 0.1 mL DPX-Survivac + low dose Cyclophosphamide (N=6)
- **Cohort C**: 0.5 mL DPX-Survivac + low dose Cyclophosphamide (N=6)

**Immune Monitoring:**
- Antigen specific IFN\(\gamma\) ELISpot
- CD8\(^+\) Tetramer
- Polyfunctionality by ICS
- Gene up-regulation by exploratory mRNA analysis
- Markers (CA-125, MDSC, Treg, B cells)

*Berrinstein et al. OncoImmunology, 2015*
High Levels of Sustained Immune Response are Induced by DPX-Survivac in Ovarian Cancer Subjects

- Immunogenicity enhanced with low dose oral cyclophosphamide, dose response observed

Berinstein et al. OncoImmunology, 2015
Clinical Results in Ovarian Cancer

- Ongoing Phase 1b study testing multiple dosing regimens
- Secondary objective is to determine if there any evidence of clinical regression based upon standard of care investigations and CA-125

CA-125 Response

Immune Response

ASC0 2014, 2015
Summary of DPX-Survivac Results in OvC

• DPX-Survivac safety/ immunogenicity in cancer patients
  - Sustained polyfunctional antigen-specific CD8⁺ T central memory and differentiated CD8⁺ T cells induced
  - High immune responder rate, statistically significant T cell immunity dose response demonstrated by multiple assays
  - Injection site reactions observed in the majority of patients, criteria established to manage these local on target side effects and limit their occurrence/ severity

• DPX-Survivac clinical signal in cancer patients
  - A trend of delayed progression observed in patients treated with combination therapy
  - Clinical activity in combination with cyclophosphamide documented in a patient with measurable disease and rising CA-125
  - Indications from clinical samples that increases in checkpoint inhibitor targets are seen, supporting use of combination immunotherapy.
Combination immunotherapy is key to more effective treatment

Combination immunotherapy is the way forward to maximize the number of patients who will see durable responses.

The majority of clinical trials in immuno-oncology are focused on the combination of a checkpoint inhibitor with another type of immunotherapy.

Ai et al. CII 2015;64:885-892
Blockade of PD-1:PD-L1 Increases Control of Established Tumors with DepoVax + mCPA

Animal results support testing combinations in the clinic

**Immunotherapy with anti-PD1**

**Immunotherapy with anti-PDL1**

Weir, JITC, 2016

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Anti-PD-1 Did Not Further Increase Immune Infiltration to Tumor

Weir, JITC, 2016
Anti-PD-1 Increases Clonality of T cells Infiltrating the Tumor

Weir, JITC, 2016
Ongoing Combination Clinical Trials

**Phase 1b: DPX-Survivac + IDO1 inhibitor**

- DPX-Survivac + epacadostat in recurrent ovarian cancer
- Platinum resistant and sensitive subjects who have completed first-line treatment with any number of subsequent lines of therapy
- Must have evidence of progressive disease, measurable by RECIST v 1.1
- 16 evaluable patients, single arm, open-label, safety and effectiveness study
- Company sponsored - Immunovaccine leading the trial
- Up to 10 sites in US and Canada
- Interim results: Q1 2017

**Phase 2: DPX-Survivac + anti-PD-1**

- DPX-Survivac + pembrolizumab (anti-PD-1) in recurrent ovarian cancer
- Platinum resistant and sensitive subjects who have completed first-line treatment with no more than 4 lines of previous therapy
- Must have radiologic evidence of progressive disease, measurable by RECIST v 1.1
- Up to 42 subjects, non-randomized, open-label efficacy study
- Investigator sponsored - Princess Margaret Hospital leading the study, funded by Merck
- Sites in Canada
- Anticipated start: March 2017
RSV SHe Vaccine Development

• Collaboration between Immunovaccine, VIB (Belgium) and the Canadian Center for Vaccinology

• Immunovaccine has exclusive worldwide license from VIB on SHe protein patent family (WO 2012/065997 A1)

• Scientific advisors
  - Dr Joanne Langley (Principal Investigator) Department of Pediatrics, Department of Community Health and Epidemiology at Dalhousie University
  - Dr Scott Halperin, Director of the Canadian Center for Vaccinology
  - Dr Xavier Saelens, VIB Medical Biotechnology Center
  - Dr Barney Graham, Senior Investigator. Viral Pathogenesis Laboratory. NIAID/VRC
Small Hydrophobic Protein (SH)

That third very small RSV surface protein:

MENSTITIEFSKFWPYFTLHMMTTISSILISIMIAINKLCEYNVFHNKTFELPRARVNT

SHe: 23 AA vs (vs Fe: 513 AA; Ge: 235)

- Poorly immunogenic
- Pentameric viroporin
- Inflamasome
- Anti-apoptotic
- Non-essential
  - In vitro: ΔSH enhanced
  - In vivo: attenuated
DPX-RSV: First-in-man SHe based RSV vaccine

- Advantages to formulation in DepoVax™
  - Only oil formulation that facilitates microdosing (50 µl)
  - Ability to remove requirement for KLH coupling
  - Ability to customize adjuvant to desired immune response

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<thead>
<tr>
<th></th>
<th>Infectious Disease</th>
<th>Cancer</th>
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</thead>
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<tr>
<td><strong>Antigen quantity</strong></td>
<td>ug quantities</td>
<td>mg quantities</td>
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<td><strong>Adjuvant</strong></td>
<td>Lipopeptide (humoral and cellular responses)</td>
<td>Polynucleotide (cellular response)</td>
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<tr>
<td><strong>Number of Immunizations</strong></td>
<td>1-2</td>
<td>Repeated boosting</td>
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Investigator Driven Phase 1 Clinical Trial

Objectives

• To demonstrate that a single dose plus booster of a novel RSV antigen (SHe) combined with DepoVax™ is well tolerated by healthy participants 50-64 years of age
  - Demonstrate good tolerability of first dose
  - If a single dose of DPX-RSV(A) is well tolerated, demonstrate that a booster (second) dose is well tolerated
• To determine if antibody to the novel antigen can be produced following one or two doses of DPX-RSV(A) vaccine

Design

• randomized, observer-blind, controlled, multi-arm parallel group trial
• 2:2:1 randomized to DPX: Alum:Placebo (N=8:8:4 for 10 µg and 25µg dose level)
• Safety features: staggered enrolment and dose escalation
• N = 40
Safety summary

• Most common solicited local AE was pain at injection site
  - 14/15 had grade 1 pain
  - no increase in pain with second dose

• Common solicited general AE were drowsiness and muscle aches
  - 7 rated grade 1 and 1 rated Grade 3
  - Unsolicited AE occurred in all groups
  - No pIMD
  - No SAE

Langley et al, ID Week 2016
Circulating immune response to SH persists for greater than one year post booster vaccination with DPX-RSV

Step 2 D28
Step 2 D56
Step 2 D63
Step 2 D84
Step 2 D236
Step 2 D421

Langley et al, ID Week 2016

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Antigen specific ELISA correlates with functional immune assays

**SHe ELISA (IgG)**

**SH binding assay**

**Phagocytosis Assay**

Langley et al, ID Week 2016

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Summary

• Vaccination with a DepoVax\textsuperscript{TM}-based RSV vaccine targeting SH protein had an acceptable safety profile with no serious AEs reported.

• Vaccination with DPX-RSV(A) generated antigen-specific immune responses in the majority of vaccinated subjects, including 75\% of patients vaccinated at the 10 µg dose and 100\% of patients at the 25 µg dose. Greater than 60\% of subjects demonstrated antigen specific immune responses prior to the second vaccination, in both dose levels.

• Preliminary data with exploratory assays confirm the binding of antigen-specific antibodies to the RSV SH protein, and their ability to stimulate macrophage phagocytosis.

\textit{Langley et al, ID Week 2016}