Cancer Vaccines

A novel approach to treat ovarian cancer

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Ovarian Cancer

- ✓ Unmet medical need in ovarian cancer
- ✓2000 diagnosed in Australia, 800 die per annum
- ✓318,000 women diagnosed globally
- ✓Generally diagnosed at late stage
- ✓Only 20-30% of patients with late stage disease survive 5 years
- ✓Median progression-free survival after optimal surgery & chemotherapy is only 22 months

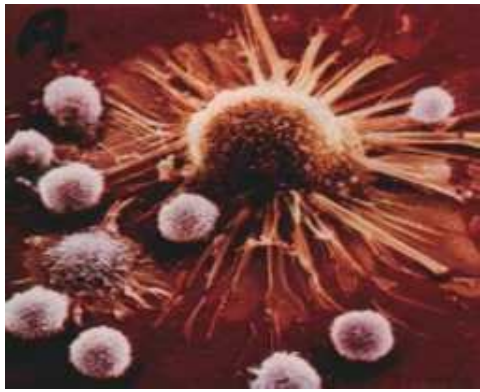
Immunotherapy: New class of cancer treatment

- Considered the fourth modality of cancer treatment after chemotherapy, radiation, and surgery
- Based on re-educating the patient's immune system to retarget the tumour
- Restore antigen visibility
- Cancer vaccines fall under this category of treatment

Cancer Vaccines

- Majority are used for treatment not prevention
- Restore functional ability to destroy abnormal cells
- Traditional prophylactic vaccines: As with the HPV vaccine, provide immunity to a particular disease.
- At this time, with the exception of Provenge ® for refractory prostate cancer in the US, cancer treatment vaccines are only available in clinical trials

Cancer Vaccine Players



- Dendritic Cell:

  Remarkable ability to capture and process antigen

  Antigen presenting cell-presents antigen to T-cell to mount an immune response

- T-Cell: When activated, mediates immune response as a killer T Cell

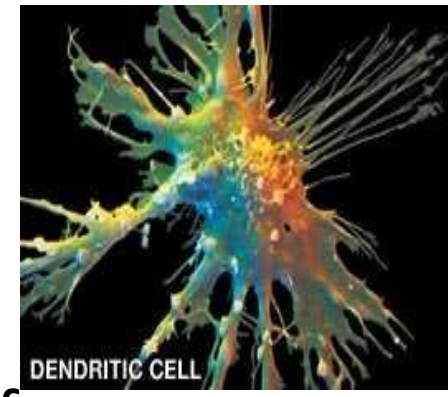
Four Main Types of Ovarian Cancer Vaccines in Development

- Tumor cell lysate vaccines
- Dendritic cell vaccines
- Antigen vaccines
- DNA vaccines

Tumor Lysate Vaccines

- Utilizes whole tumour cells rendered safe by irradiation
- Specific immune response initiated when injected into body
- Either: Autologous-removed tumour cells
- Or: Allogenic tumour cells
- Many different epitopes are recognized.
- Studies ongoing in melanoma, colorectal cancer, renal, ovarian, breast, lung, and leukemia
- May be combined with dendritic cells

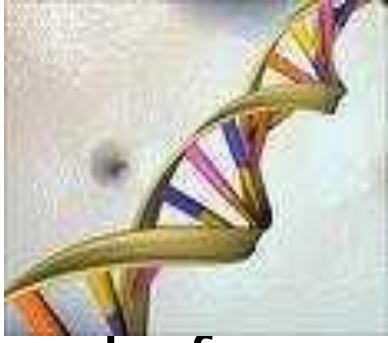
Dendritic Cell Vaccines



- Dendritic cells are matured ex-vivo from autologous peripheral blood monocytes
- Dendritic cells are made capable of recognizing antigen by IL-4 and GM CSF maturation with exposure to antigen
- Dendritic cells injected into the individual stimulate an immune response
- Multiple potential antigens being studied

Antigen Vaccines

- This includes peptide vaccines: only one specific epitope is injected
- Copious amounts of antigen can be manufactured
- Some antigens are specific for a specific tumour type; others may induce an immune response in several cancers.



DNA vaccines

- Introduction of tumor genes instead of tumor antigen itself
- Cells in the body take up the injected DNA. Specific antigens are then produced on a continuous basis
- A constant supply of antigen(s) allows a continuous immune response to occur
- Studies ongoing in prostate cancer, leukemia, melanoma, and head and neck cancer

Immune therapeutics in development for ovarian cancer

RXi Pharmaceuticals	Folate Biding Protein E39
Immunovaccine	DPX Survivac
Avax Technologies	OVax
Prima BioMed Ltd	CVac ™
Accentia	BioVax ID
NCI	Poxvirus MUC-1 CEA
BioCancell	BC 819 plasmid H19
Northwest	DC-Vax
Immunovaccine	DPX-0907 peptide liposome
Loyola	ONTAK DC
NCI	PANVAC
U. Pennsylvania	DC-Vac L
Fox Chase CC	DC-Ova

Most advanced ovarian cancer vaccine in development for maintenance: Cvac ™

- CVac is an autologous, dendritic-cell based therapy or cancer vaccine targeting abnormal mucin-1
- Proven technology with FDA approval of Provenge ®
- Well tolerated in all studies to date
- Granted orphan product status by the U.S. FDA & EMA
  - Additional several years of exclusivity and priority regulatory treatment
- Phase I & Phase IIa trials are complete with promising results
- Phase IIb is fully recruited and ongoing

Safety Profile of CVac

- Over 80 patients have received Cvac to date in clinical trials or SAS treatment
- Generally very well tolerated
- No AE's that were definitely or probably related to Cvac
- Possibly related: gastrointestinal(2), CNS(2) and flu like symptoms(1) in Phase I and IIa
- Mild local injection site reactions observed in some patients

Safety Profile of CAN-003

- DSMB reviews to date support progression of the study
- Five SAE (two standard of care (SOC), three Cvac)
- Abdominal pain (resolved) requiring hospitalization (1 Cvac, 1 SOC)
- One death (cerebral haemorrhage) in SOC
- Disease progression and hospitalization prior to receiving Cvac (Cvac)
- Disease progression requiring taxotere with febrile neutropenia hospitalization (Cvac)
- No Cvac related adverse events

CANcer VAccine Study (CANVAS)

- 1000 patients, 800 evaluable
- Epithelial Ovarian Cancer: first remission
- Double Blind, Placebo Controlled
- Powered to demonstrate clinically significant effect on PFS and OS (HR 0.77, p=0.049, 90% power
- 22 countries, 120 investigative sites
- Australia is a key country for recruitment
- First patients already enrolled in the US

Summary

- Malignant tumours evolve to fool the immune system
- Re-education of the immune system may be an effective modality
- Vaccines are in clinical development for ovarian cancer
- Vaccine therapy will complement existing approaches
- **Vaccines could mean better quality of life and longer survival for our patients**