Conference report: 3rd Int'l Symposium on Immunotherapy

LONDON, UK----16th May 2017----ExpertREACT. iOnco Analytics was pleased to attend the Third International Symposium on Immunotherapy hosted by the Institute for Cancer Vaccines and Immunotherapy, 12-13th May 2017, The Royal Society, London (ICVI). Here is our report.

Key themes of the ICVI symposium were:

- How chemotherapy alters the immunogenicity of tumour cells
- The effects of chemotherapy on immune regulation
- How chemotherapy can be combined to best effect with vaccines or other immunotherapies
- Clinical studies exploring the combinations of chemotherapy and immunotherapy
- Clinical studies exploring the combinations of different immunotherapy drugs

An opening presentation was given by **Ignacio Melero (Clinica Universidad de Navarra)** on '**Intricate combinatorial cancer immunotherapy strategies under translation**.' The synergy of therapies including vaccines, chemotherapy, radiotherapy and immunotherapy were discussed, noting that there are currently >900 trials listed in clinicaltrials.gov involving combination therapies. The use of anti-CD137 mAbs were discussed as partners for combination therapies with checkpoint inhibitor anti-PD-1 strategies. The use of anti-CD137 in adoptive T cell transfer was also highlighted as a potential therapy. It was noted that toxicity increases with checkpoint inhibitor combinations due to their systemic administration and that local administration should be tested although this is not usually popular with pharmaceutical companies due to their usual requirements to adhere to strict dosing protocols. The selection of dosing levels of investigative therapies was also highlighted to be somewhat random during trials as the optimal doses to test were not always known. Sequential treatment was also suggested as a possibility for future investigation since many studies are currently performed without the knowledge of whether it was best to add therapies under investigation to the existing treatments or whether current treatments should be stopped to test the new therapy. The theme of optimal dosing and sequence of treatments was revisited by further speakers during the conference.

A presentation from **Richard Viles (Mayo Clinic)** on **'Oncolytic Viroimmunotherapy for Cancer'** began with the history of T-VEC, a HSV-1 derived oncolytic immunotherapy with added GM-CSF and now approved in Europe and the US. Current trials with T-VEC are investigating combinations with checkpoint inhibitors (Ipilimumab, Pembrolizumab) and are the most likely future path for these agents. The presentation covered development of oncolytic therapy using Reovirus (REO13), a dsDNA virus of the ras pathway. REO13 has been shown to access liver tumours in a previous trial in PBMC cells rather than in plasma and thereby evading antibodies already present in most people due to common childhood exposure. REO13 was tested in patients with brain metastases or high grade glioma and delivered to patient brains and correlated with upregulation of PDL-1, leading to the hypothesis that REO13 primes the patients for checkpoint blockade. Further studies are ongoing looking at the combination of REO13 with anti-PDL-1 checkpoint testing in murine models which may form the basis for combination trials for brain tumour patients in the future.

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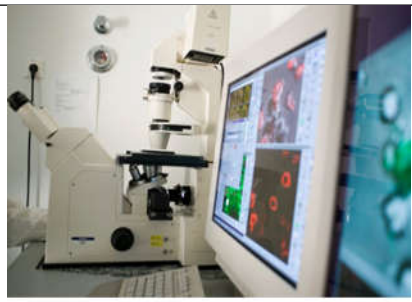

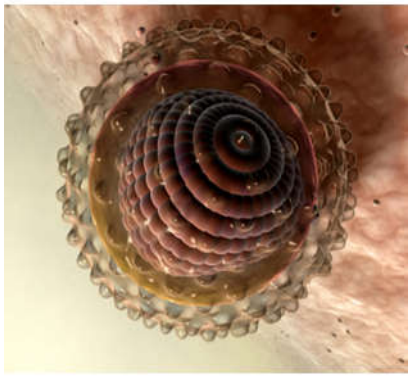

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Michael R. Shurin (University of Pittsburgh) presented on **'Targeted delivery chemotherapy to the tumour microenvironment.'** The issues of delivering chemotherapy with regard to maximum tolerated dose (MTD) leading to immunosuppression and chemo-resistance were discussed. The mechanism by which this occurs was discussed in the context of Myeloid Derived Suppressor cells (MDSC) since it has been shown that the enzymatic activity of MDSC (myeloperoxidase) degrades doxorubicin. Hence levels of MDSC may correlate with patient responses. The prospect of using nano-delivery was described with the use of Single Walled Carbon Nanotubes (SWCNT), shown to improve the stability of doxorubicin. When tested in melanoma cells, MDSC abolished the cytotoxic effect of free doxorubicin but not CNT-doxorubicin. Further development was described as nano-cups corked with gold which could effectively be opened by myeloperoxidase in the tumour microenvironment.

Thomas Joseph Sayers (NCI, Frederick) presented on **'Can enhancement of cancer cell death also improve immunotherapy?'……**

For the remainder of this article (free of charge) including summaries of the following talks:

- ***Antigen engineered DC vaccine +/- IFN-alpha for melanoma***
- ***Metronomic chemo immunotherapy in Glioma Models***
- ***PRIMMO study: combining PD-1 blockade, radiation and immunomodulation to tackle cervical and uterine cancer***
- ***Overcoming tolerance to tumour antigens through combination therapies targeting myeloid derived suppressor cells***
- ***Correlation between strength of T cell response against HPV16 and survival after vaccination with HPV16 long peptides in combination with chemotherapy for late stage cervical cancer***
- ***A new frontier in T-cell activation and targeting***
- ***Roadblocks to cancer immunotherapy***

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Keywords: anti-CD137, adoptive T cell transfer, Reovirus (REO13), anti-PDL-1 checkpoint, Single Walled Carbon Nanotubes (SWCNT), TRAIL apoptosis sensitiser, adoptive T cell transfer, Sipuleucel-T, CD8a, GzMB, Prf1, fas, TNFR family agonists, gamma-C cytokines, TGF-beta antagonists. SLP®, SCIB1, Moditope®, MODI-1, macrophage inhibitory cytokine GDF-15, Scancell Ltd