AACR 2021

Transformation in Cancer Treatment – Destroy vs. Inhibit?

The field of protein degraders is booming with innovation and intense drug development, largely in preclinical development. Unlike inhibition approaches where the protein function is restored after disassociation of the 'inhibitior', protein degraders destroy the target itself, and thus nullify the activity. Small molecules can induce selective degradation of the target protein of interest (POI) by adding a tag recognized by the degradation machinery.

This space is attractive especially for:

- its potential to target 'undruggable proteins'
- the broad spectrum activity, including resistant variants
- rapid action that should prevent emergence of resistant clones
- its potential to be more efficacious

However, the question is how differentiated the protein degraders will be from the inhibitors in the clinic, since nearly one-fourth of all the protein degraders in drug development are likely to be in clinical development in the next one year.

Therapeutic Cancer Vaccines/Oncolytic Viruses with Conventional and Checkpoint Blockade Agents – A Wave of the Future?

Oncolytic viruses (OVs) and therapeutic cancer vaccines (TCVs) are a continued modality of interest given their potential to reverse immunosuppressive tumor immune microenvironments and expand the potential of PD-1/L1i (as combinations).

They also alleviate the usual systemic toxicity seen with the drug treatment. Besides T-VEC in melanoma, these modalities, however, have not met with much success in the clinic due to virus neutralization and traditional payloads being insufficient to drive significant clinical benefit.

Recently, to address these issues there has been a surge in innovation with these modalities around new payloads, engineered viral capsids, and personalized approaches using cell/molecular/vector-based vaccines.

Teaching an Old Dog New Tricks – New Ways to Use Immune-Cytokines in Tumor Immunity

Scientific rationale to transform tumor microenvironment into an immune-stimulatory state presents cytokines as potential complementary strategy to diversity of immunotherapies. However, cytokines are a double-edged sword and may cause context dependent inhibition or induction of tumorigenesis. While development of suppressive cytokines as immune-oncology therapeutics recently experienced another setback with Merck KGaA/GSK fusion protein which combines PD-L1 blockade with TGF beta inhibition, failing in NSCLC and cholangiocarcinoma, current excitement around class of engineered immune stimulatory cytokines stems from:

- their increased half-life
- directed cytokine activity to the tumor microenvironment
- specific stimulation of effector immune cells

Promising early data further provided impetus to the development so much that pipeline is brimming with several next generation stimulatory cytokines with novel mechanisms of action, new targets, and fusion proteins.

~20 studies presented at AACR showcase new constructs, modalities, targets, and early scientific evidence that highlights cytokines as potential immune-oncology partners.

We will focus on some key highlights from presentations made by pharma/biotech companies on protein degraders, oncolytic viruses and therapeutic cancer vaccines, and novel OV/TCV approaches, including PD-1/L1i combinations, at AACR 2021.

SmartAnalyst is helping the clients interpret the data presented at AACR 2021 (April 9-14) focusing on key developments in cancer research.

Please contact:
John.L'Ecuyer@smartanalyst.com

GLOBAL HEADQUARTERS
(New York, USA)
285 Madison Ave
22nd Floor, New York
NY 10017
Tel.: (212)-331-0010

EUROPE
(London, UK)
1.04 Power Road Studios 114
Power Road, Chiswick, London
W4 5PY
Mobile: +44-(0)-752-163-8242
Mobile: +44-(0)-772-574-4296

ASIA PACIFIC
(Gurgaon, INDIA)
First Floor, DLF Plaza Tower
DLF Qutub Enclave, DLF City
Phase-I, Gurgaon 122002,
Haryana, India
Tel.: 91-124-4313800