Human Vaccines & Immunotherapeutics: News May 2022

**Covid-19 vaccine offers limited protection from long-term symptoms**

Vaccination with one of the Covid-19 mRNA vaccines decreases the risk of ‘long Covid’ by only 15%, according to a study of 34,000 breakthrough cases from 2021 in US.\(^1\) This adds to an earlier study from UK, in which vaccine effectiveness was estimated at 50%.\(^2\) ‘long Covid’ is a little-explored set of symptoms, including respiratory, cardiovascular and neurological conditions, that persist for months after infection.

The BNT162b2 vaccine (Pfizer & BioNTech) demonstrated safety and immunogenicity in children aged 6 months to 5 years. The preliminary efficacy after three doses was estimated at 80%, based on 10 symptomatic cases. The Phase 2/3 trial enrolled 1,700 children.

In contrast, the effectiveness of the CoronaVac vaccine (Sinovac) is only 40% against symptomatic disease in children, according to two studies from Latin America.\(^3,4\) At the same time, the Chinese-produced vaccine prevented 65–70% of hospitalizations.

In the randomized, double-blind, placebo-controlled Phase 3 TOGETHER trial involving 2,000 high-risk subjects, single injection of Peginterferon Lambda (Eiger BioPharmaceuticals) administered early in the course of Covid-19 infection reduced hospitalization by half. The drug is a type III interferon, which is critical for early antiviral immune response, suppressing the viral replication cycle.

The US Food and Drug Administration has restricted the use of the Ad26.COV2.S vaccine (J&J) to adults without access to other vaccines, due to blood clots that on rare occasions appear within two weeks of vaccination.

A single booster dose of the VLP vaccine ABNCoV2 (Bavarian Nordic) following a primary course with mRNA or adenovirus vaccine induced high levels of neutralizing antibodies specific for the Omicron variant.

Influenza vaccination has been implicated in protection from Covid-19 as well. In a study of 31,000 healthcare workers in Qatar, the seasonal vaccine prevented 90% of severe Covid-19 cases.\(^5\) The duration of the effect, which is considered nonspecific, is unknown.

**Oncolytic virotherapy promising for lung cancer patients**

Eighty-seven percent disease control rate following treatment with a combination of the oncolytic immunotherapeutic CAN-2409 (Candel Therapeutics) with immune checkpoint inhibitors was reported from a Phase 2 trial with advanced non-small cell lung cancer (NSCLC) patients, who had progressed after previous anti-PD-1 therapy. The regimen was safe and induced 15% partial responses.

CAN-2409 consists of orally administered valacyclovir and tumor-targeted, replication-deficient adenovirus encoding the herpes simplex virus thymidine kinase, which converts the drug into a toxic compound that kills neighboring cells and releases neoantigens into the tumor microenvironment.

**Immunotherapy combination is beneficial in HPV-positive cervical cancer**

The cancer vaccine VB10.16 (Nykode) together with the PD-L1 inhibitor atezolizumab (Tecentriq, Genentech) achieved an objective response rate at the 6-month mark of 21% including two complete responses in 39 heavily pretreated patients with advanced cervical cancer. According to interim results of the Phase 2 VB C-02 trial, clinical benefit was observed regardless of PD-L1 status.

VB10.16 is an off-the-shelf therapeutic DNA vaccine targeting the HPV16 strain, which accounts for the majority of cervical cancer cases.

**Norovirus vaccine candidates progresses in clinical development**

A randomized, double-blind, placebo-controlled Phase 2b trial has started to test safety and efficacy of the norovirus vaccine HIL-214 (HilleVax) in infants aged 5 months.

HIL-214 is an alum-adjuvanted bivalent VLP vaccine, which targets the two most common strains of norovirus, which is the most common cause of acute gastroenteritis in infants globally.

**Trispecific antibody shows activity against solid tumors in an early trial**

Safety and 40% partial response rate were reported from a dose-escalation phase 1/2a trial testing the trispecific antibody immunotherapeutic HPN328 (Harpoon Therapeutics) in solid cancers. No dose-limiting toxicities were observed in 18 patients with small-cell lung cancer and neuroendocrine cancers.

HPN328 is a T cell-activating trispecific antibody that binds the T-cell coreceptor CD3, albumin, and the Notch ligand Dll3. The latter is overexpressed in several cancer type.
**Listeria-Based immunotherapy is tested in lung cancer**

The *Lm* immunotherapy ADXS-503 (Advaxis) together with the PD-1 inhibitor pembrolizumab (Merck) induced disease control in two of three treatment-naïve patients with metastatic NSCLC in a Phase 1/2 trial. Subjects, who had progressed after initial therapy with pembrolizumab alone, achieved a disease control rate of 36%.

ADXS-503 consists of live attenuated *Listeria monocytogenes* bacteria engineered to secrete tumor-specific antigens into the tumor microenvironment.

**CTLA-4 inhibitor safe in patients with solid tumors**

A novel checkpoint inhibitory MAb ADG126 (Adagene) was safe with no serious adverse events in subjects with advanced metastatic solid cancers enrolled to a dose-escalation Phase 1/2 trial. Two patients with immunologically idle tumors reported increased CD8+ levels and durable responses.

ADG126 is a ‘SAFEbody’ with a masked antigen-binding site for enhanced safety. It is un-masked in the tumor microenvironment, which leads to depletion of immune-inhibiting Tregs.

**CAR T-cell therapy induces complete responses in early trial with non-Hodgkin lymphoma**

The chimeric antigen receptor (CAR) T-cell therapy CB-010 (Caribou Biosciences) induced four complete and one partial responses in five patients with relapsed or refractory B-cell non-Hodgkin lymphoma involved in the Phase 1 ANTLER trial. An acceptable safety profile allowed for continued recruitment for a higher dosage level.

CB-010 contains allogeneic anti-CD19 T cells with a CRISPR-engineered PD-1 knockout to avoid inhibition in the tumor microenvironment.

**CAR T-cell regimen approved for treatment of follicular lymphoma**

The FDA has granted accelerated approval to tisagenlecleucel (Kymriah, Novartis) for adults with follicular lymphoma, who had relapsed after at least two lines of previous therapy. The approval, which is contingent on further confirmatory clinical trials, is based on results showing that the treatment induced 68% complete responses in 90 patients.

Tisagenlecleucel, which is already used in two other indications, consists of autologous T cells engineered to target the CD19 antigen, which is overexpressed in B-cell malignancies.

**Disclosure statement**

No potential conflict of interest was reported by the author(s).

**Funding**

The author(s) reported there is no funding associated with the work featured in this article.

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