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Human vaccines and immunotherapeutics: News February 2024

Food-allergy immunotherapeutic approved for children and adults, prevents anaphylaxis

The US Food and Drug Administration (FDA) has approved the anti-IgE MAb omalizumab (Xolair, Roche) for reduction of allergic reactions and prevention of anaphylaxis following accidental exposure to peanut, milk, egg, wheat, cashew, hazelnut or walnut, in subjects aged 1–55 y.

The Phase 3 OUtMATCH trial showed that 67% of children with moderate-to-severe allergy to peanut and at least two other foods could consume an equivalent of 2.5 peanuts following treatment with omalizumab, compared to 7% in the placebo cohort.[1]

Omalizumab, which is not approved for post-exposure emergency treatment, is administered subcutaneously every two or four weeks for 16–20 weeks.

Fast-track designation for two HSV-based cancer immunotherapies

The FDA has granted its Fast-Track designation to two immunotherapy regimens involving recombinant herpes simplex virus (HSV).

CAN-3110 (Candel Therapeutics), fast-tracked for use in recurrent high-grade glioma, is a replication-competent HSV administered by a single intratumoral injection. Its virulence genes are controlled by the nestin promoter, which is active specifically in cells of a brain tumor. CAN-3110 was safe and increased survival in a Phase 1 trial.

KB707 (Krystal Biotech) consists of HSV engineered to express the cytokines IL-2 and IL-12, which induce an intratumoral immune reaction. It has been fast-tracked as a treatment of solid tumors with relapsed or refractory pulmonary metastases, although a clinical trial in this patient population is yet to start.

Autologous T-cell immunotherapy approved for melanoma

The tumor-infiltrating lymphocyte immunotherapy lifileucel (Amtagvi, Iovance Biotherapeutics) received FDA's accelerated approval as second-line treatment of unresectable or metastatic melanoma. The decision is based on results from the Phase 2 C-144-01 trial demonstrating >30% objective response rate and durable responses.

The lifileucel regimen consists of isolating autologous T cells from a piece of resected tumor tissue, expanding them *in vitro*, and infusing them back into the patient in a single dose.

T-cell receptor immunotherapy induces durable responses in blood-cancer patients

The engineered T-cell receptor (TCR) immunotherapies TSC-100 and TSC-101 (TScan Therapeutics) following allogeneic hematopoietic stem-cell transplantation (HSCT) led to complete engraftment of donor cells in all eight subjects with acute myeloid leukemia, acute lymphocytic leukemia or myelodysplastic syndromes enrolled in a dose-escalation Phase 1 trial.

TSC-100 and TSC-101, which consist of T cells targeting the minor histocompatibility antigens HA-1 and HA-2, respectively, are designed to treat residual disease following HSCT.

Cholesterol vaccine shows promise in a preclinical trial

The anti-cholesterol vaccine VXX-401 (Vaxxinity) induced sustained reduction of low-density lipoprotein (LDL) cholesterol in macaques.[2] A Phase 1 clinical trial investigating the potential of VXX-401 for treatment of hypercholesterolemia and prevention of atherosclerotic cardiovascular disease is underway.

The vaccine targets the proprotein convertase subtilisin/kexin type 9 (PCSK9), thereby inhibiting the clearance of LDL receptor and lowering circulating LDL cholesterol, which is a major risk factor for stroke and other cardiovascular diseases.

Innate immunity-activating small-molecule therapeutic fast-tracked by FDA

The inhibitor of dipeptidyl peptidases BXCL701 (BioXcel Therapeutics) in combination with the PD-1 inhibitor pembrolizumab (Keytruda, Merck) received the FDA's Fast-Track designation for treatment of metastatic small cell neuroendocrine prostate cancer. The regimen had improved survival in a different prostate cancer indication in a previous clinical trial.

BXCL701 is an oral immunotherapy designed to induce inflammation in the tumor microenvironment.

New Covid-19 booster vaccine was safe and immunogenic in a phase 2 trial

The COVID-19 vaccine GEO-CM04S1 (GeoVax) was safe and induced both antibody and T-cell responses after one month as a booster dose. The Phase 2 trial investigated two dosage levels

in 63 healthy adults who had received one of the mRNA vaccines.

GEO-CM04S1 is based on a modified vaccinia Ankara vector expressing both spike and nucleocapsid antigens from SARS-CoV-2.

References

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