HUMAN VACCINES & IMMUNOTHERAPEUTICS
2023, VOL. 19, NO. 1, 2168389
https://doi.org/10.1080/21645515.2023.2168389

Taylor & Francis
Taylor & Francis Group

NEWS, POLICY, & PROFILES

OPEN ACCESS Check for updates

Human vaccines & immunotherapeutics: News December 2022

Clinical development of bispecific antibodies for cancer therapy

The CD3/CD20-targeting bispecific antibody mosunetuzumab (Roche) was approved by the Food and Drug Administration (FDA) as the third-line treatment of adults with relapsed or refractory follicular lymphoma. Continued approval is contingent on confirmatory trials. CD3 and CD20 are present on T- and B-cells, respectively, and mosunetuzumab is designed to induce anti-tumor T-cells by bringing them in proximity with malignant B-cells.

Another therapeutic antibody targeting the same two antigens, epcoritamab (Genmab), is being tested in multiple clinical trials involving diffuse large B-cell lymphoma, follicular lymphoma and Richter's syndrome (a type of lymphocytic leukemia). Notably, the Phase 1b/2 EPCORE NHL-2 trial reported 85% and 67% objective and complete response rates, respectively, in 27 subjects with refractory or relapsed diffuse large B-cell lymphoma, who received epcoritamab in combination with anti-CD20 rituximab and chemotherapy.

A third T-cell-engaging antibody, teclistamab (Tecvayli, Janssen), targeting CD3 and the B-cell maturation antigen, induced a 94% overall response rate after a median of 8 months in subjects with refractory or relapsed multiple myeloma enrolled in the Phase 1/2 MajesTEC-1 trial. The regimen also included the anti-CD38 daratumumab (Darzalex, Janssen) and chemotherapy.

Additionally, the CD3/MAGE-A4 bispecific antibody IMC-C103C (Immunocore) induced partial responses and stable disease in two and five patients with heavily pretreated ovarian cancer, respectively. The MAGE-A4 antigen is overexpressed in many tumor types.

Finally, a Phase 1/2a trial investigates the safety and optimal dose for the immunotherapeutic LAVA-051 (LAVA Therapeutics) in treating chronic lymphocytic leukemia and multiple myeloma. The antibody stimulates antitumor Vγ9 Vδ2 T- and NK-cells by targeting both the Vδ2 chain and the CD1d glycoprotein, which marks cells in several types of hematologic cancers.

Covid-19/influenza combination vaccine on the horizon

The bivalent, Omicron-adapted Covid-19 vaccine BNT162b2 (BioNTech and Pfizer) was approved by the US FDA for use in children 6 months of age and older. Clinical trials have demonstrated safety and immunogenicity of a low-dose formulation in this age group.

The FDA has also granted the fast-track designation to an mRNA vaccine targeting both Covid-19 and influenza (BioNTech and Pfizer). The single-dose vaccine is being tested for safety and immunogenicity in a Phase 1 trial. The development of a combined vaccine, which could lead to increased patient uptake, has been identified as a public health priority.

Microneedle patch demonstrates immunogenicity in an early trial

H1N1 influenza vaccine delivered via the slow-release microneedle patch VX-103 (Vaxess) induced 85% seroconversion rate at the higher dose in 45 healthy subjects enrolled into a dose-escalation Phase 1 trial. Previous preclinical study showed that the vaccine patch induces enhanced, long-lasting humoral and cell responses.[1]

VX-103 is based on the MIMIX technology delivering vaccines intradermally for a prolonged period of time. The patch does not require refrigeration and is therefore suitable for long-distance shipping and administration in low-resource settings.

Combination immunotherapy beneficial in lymphoma

Safety and hints of clinical benefit were observed in an open-label, dose-escalation Phase 1 trial testing the combination of checkpoint inhibitors tifcemalimab (anti-BTLA) and toripalimab (anti-PD-1, both Junshi Biosciences) in patients with both Hodgkin's and non-Hodgkin's lymphomas. Of 28 evaluable subjects, one complete response, 10 partial responses, and 13 stable disease cases were reported. Tifcemalimab monotherapy led to just one partial response and seven stable disease cases in 25 subjects.

BTLA receptor, which is expressed on T-, B-, and dendritic cells, plays a role in inhibiting intratumoral CD8+ T-cells.

Genital herpes vaccine enters clinical trials

Safety and immunogenicity of the HSV-2 vaccine candidate BNT163 (BioNTech) is being investigated in a placebo-controlled, dose-escalation Phase 1 trial, which aims to enroll 100 healthy adults up to 55 years old. The mRNA vaccine encodes for three HSV-2 glycoproteins designed to induce broad immune responses directed at different parts of the virus.

500 million people are estimated to suffer from genital infection by HSV-2, for which there is no approved vaccine. The virus causes persisting infections that can lead to genital lesions and or meningitis.

Dupilumab approved for treatment of prurigo nodularis in EU

The European Commission extended the authorization of the IL4 receptor inhibitor dupilumab (Dupixent, Regeneron and

Sanofi) to include treatment of prurigo nodularis. The decision is based on Phase 3 data showing that 60% of dupilumab recipients had reduced symptoms compared to 18% for placebo.

Prurigo nodularis is an inflammatory skin disease of unknown etiology, which causes painful itches and thick skin lesions. It affects ~70,000 adults in Europe.

Phase 1 trial initiated for malaria vaccine

Safety and immunogenicity of the mRNA malaria vaccine BNT165b1 (BioNTech) will be tested in 60 healthy volunteers enrolled in a placebo-controlled, dose-escalation Phase 1 trial. The vaccine, which encodes for parts of the *Plasmodium* circumsporozoite protein, is designed to prevent blood-stage malaria.

No highly effective malaria vaccines are in use. The RTS,S/AS01 vaccine, which is being deployed in a pilot program in sub-Saharan Africa, is <50% effective. Recently, however, the R21/Matrix-M vaccine demonstrated ~80% efficacy in a Phase 2 clinical trial.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

The authors reported there is no funding associated with the work featured in this article.

Reference

1. Stinson JA, Boopathy AV, Cieslewicz BM, Zhang Y, Hartman NW, Miller DP, Dirckx M, Hurst BL, Tarbet EB, Kluge JA, et al. Enhancing influenza vaccine immunogenicity and efficacy through infection mimicry using silk microneedles. Vaccine. 2021;39(38):5410–21. doi:10.1016/j.vaccine.2021.07.064.

Ronald Ellis
Editor-in-Chief, Jerusalem, Israel
rellis.hvi@gmail.com

Adam Weiss
Acquisitions Editor, Prague, Czech Republic