HUMAN VACCINES & IMMUNOTHERAPEUTICS
2022, VOL. 18, NO. 5, e2051346 (2 pages)
https://doi.org/10.1080/21645515.2022.2051346

Taylor & Francis
Taylor & Francis Group

NEWS, POLICY, & PROFILES

Human vaccines & immunotherapeutics: news February 2022

Covid-19 in infants can be prevented by maternal immunization

The rate of hospitalization due to Covid-19 in infants aged <6 months decreased by 60% when their mothers had been vaccinated with the full two-dose regimen during pregnancy.[1] Receiving the vaccine in later stages of pregnancy was more effective than in earlier stages.

Vaccinating parents may also prevent infection in older children. A study of 150,000 households in Israel, conducted at times of school closures, found that full vaccination status of parents prevented 72% and 58% of cases in their children during the Alpha and Delta waves, respectively.[2]

First strain-adapted mRNA vaccines are being tested for efficacy against the Omicron variant of SARS-CoV-2. However, two preclinical trials testing booster doses of mRNA-1273 (Moderna) showed no significant benefit of Omicron-specific boost, compared to the conventional Wuhan strain boost, in mice[3] and macaques.[4]

A report from Israel, where the fourth vaccine dose is being offered to the elderly population, suggests that the fourth dose increases the rate of protection from infection and severe illness 2- and 4-fold, respectively, compared to the three-dose course.[5] However, the effect might be one of restoring the level of immunity, rather than boosting it further, as antibody titers were comparable following the third and fourth doses in another study.[6]

In other clinical developments,

- a thermostable, adjuvanted, protein-based vaccine (Sanofi & GSK) demonstrated 100% and 58% efficacy against severe and symptomatic disease, respectively, in the Phase 3 VAT08 trial.
- the multiepitope peptide vaccine UB-612 (Vaxxinity) elicited three times higher antibody titers against Omicron than the approved mRNA vaccines in a Phase 2 trial involving 90 subjects.

Dupilumab receives Priority Review for add-on treatment of pediatric atopic dermatitis

The US Food and Drug Administration (FDA) has granted Priority Review to dupilumab (Dupixent, Sanofi & Regeneron) for moderate-to-severe atopic dermatitis in children aged 6 months to 5 years, whose disease cannot be controlled by topical steroids. The decision is based on a Phase 3 trial, which showed that dupilumab added to standard-of-care therapy reduced disease severity.

Dupilumab, which is approved for people aged ≥6 years, inhibits IL-4 and IL-13 pathways that play a key role in type 2 inflammation typical of atopic dermatitis, asthma and other immune diseases.

Clinical development of RSV vaccines for older adults

The respiratory syncytial virus (RSV) vaccine candidate mRNA-1345 (Moderna) has advanced into a Phase 3 clinical trial, which will enroll 34,000 adults 60 years of age or older. The mRNA vaccine, which is based on the same technology as the company's Covid-19 vaccine, had been fast-tracked by FDA.

Another RSV vaccine, MVA-BN RSV (Bavarian Nordic), received the FDA's Breakthrough designation in the same age group. MVA-BN RSV is a Modified Vaccinia Ankara-vectored pentavalent vaccine designed to elicit both antibody and T-cell responses.

There is no approved vaccine against RSV, which usually causes mild cold-like symptoms, but which leads to >50,000 hospitalizations and >14,000 deaths annually in the US alone.

Engineered WT-1-targeting T-cell therapy has promising results in AML

T-cell receptor (TCR) therapy targeting the Wilms' tumor antigen 1 (WT1) protein effectively killed acute myeloid leukemia (AML) cells *in vitro* and in a mouse model. The treatment also overcame resistance in one patient, who had relapsed following earlier TCR therapy targeted against a different region of the WT1 protein.[7,8]

WT1 expression is associated with hematological malignancies. Its targeting might also be beneficial in solid tumors, as the TCR treatment reduced tumor burden in a mouse model of pancreatic cancer.

Lyme disease vaccine candidate advances to a late-stage trial

The Lyme disease vaccine VLA15 (Valneva) was safe and immunogenic in adults up to 65 years old. The dose-finding Phase 2 trial, which also investigates the vaccine in children, confirmed robust antibody responses, and guided the selection of a three-dose primary regimen for the next step in clinical development.

VLA15 targets the OspA antigen from six strains of *Borrelia burgdorferi*. Its clinical program received FDA's Fast Track designation.

Ebola vaccine induces immunity for >6 months in the field

Antibodies against Ebola persisted for at least six months in 96% of 600 individuals vaccinated with rVSVΔG-ZEBOV-GP (Merck) in the Democratic Republic of the Congo.[9] The vaccine was administered to >300,000 people in the country in the 2018–20 outbreak.

References

1. Halasa NB, Olson SM, Staat MA, Newhams MM, Price AM, Boom JA, Sahni LC, Cameron MA, Pannaraj PS, Bline KE, et al. Overcoming COVID-19 investigators. Effectiveness of maternal vaccination with mRNA COVID-19 vaccine during pregnancy against COVID-19–associated hospitalization in infants aged <6 Months — 17 States, July 2021–January 2022. MMWR Morb Mortal Wkly Rep. 2022;71(7):264–70. doi:10.15585/mmwr.mm7107e3.
2. Hayek S, Shaham G, Ben-Shlomo Y, Kepten E, Dagan N, Nevo D, Lipsitch M, Reis BY, Balicer RD, Barda N. Indirect protection of children from SARS-CoV-2 infection through parental vaccination. Science. 2022:eabm3087.
3. Ying B, Scheaffer SM, Whitener B, Liang CY, Dmytrenko O, Mackin S, Wu K, Lee D, Avena LE, Chong Z, et al. Boosting with Omicron-matched or historical mRNA vaccines increases neutralizing antibody responses and protection against B.1.1.529 infection in mice. BioRxiv. [preprint]. 2022. doi:10.1101/2022.02.07.479419.
4. Gagne M, Moliva JI, Foulds KE, Andrew SF, Flynn BJ, Werner AP, Wagner DA, Teng IT, Lin BC, Moore C, et al. mRNA-1273 or mRNA-Omicron boost in vaccinated macaques elicits comparable B cell expansion, neutralizing antibodies and protection against Omicron. BioRxiv. [preprint]. 2022. doi:10.1101/2022.02.03.479037.
5. Bar-On YM, Goldberg Y, Mandel M, Bodenheimer O, Amir O, Freedman L, Alroy-Preis S, Ash N, Huppert A, Milo R. Protection by 4th dose of BNT162b2 against Omicron in Israel. MedRxiv. [preprint]. 2022. doi:10.1101/2022.02.01.22270232.
6. Regev-Yochay G, Gonen T, Gilboa M, Mandelboim M, Indenbaum V, Amit S, Meltzer L, Asraf K, Cohen C, Fluss R, et al. 4th Dose COVID mRNA vaccines' immunogenicity & efficacy against Omicron VOC. MedRxiv. [preprint]. 2022. doi:10.1101/2022.02.15.22270948.
7. Lahman MC, Schmitt TM, Paulson KG, Vigneron N, Buenrostro D, Wagener FD, Voillet V, Martin L, Gottardo R, Bielas J, et al. Targeting an alternate Wilms' tumor antigen 1 peptide bypasses immunoproteasome dependency. Sci Transl Med. 2022;14(631):eabg8070. doi:10.1126/scitranslmed.abg8070.
8. Ruggiero E, Carnevale E, Prodeus A, Magnani ZI, Camisa B, Merelli I, Politano C, Stasi L, Potenza A, Cianciotti BC, et al. CRISPR-based gene disruption and integration of high-avidity, WT1-specific T cell receptors improve antitumor T cell function. Sci Transl Med. 2022 Feb 9;14(631):eabg8027. doi:10.1126/scitranslmed.abg8027.
9. Hoff NA, Bratcher A, Kelly JD, Musene K, Kompany JP, Kabamba M, Mbala-Kingebeni P, Dighero-Kemp B, Kocher G, Elliott E, et al. Immunogenicity of rVSVΔG-ZEBOV-GP Ebola vaccination in exposed and potentially exposed persons in the Democratic Republic of The Congo. Proc Natl Acad Sci U S A. 2022;119(6):e2118895119. doi:10.1073/pnas.2118895119.