Human vaccines & immunotherapeutics: News October 2022

Ronald Ellis\textsuperscript{a} and Adam Weiss\textsuperscript{b}

\textsuperscript{a}Biotech & Biopharma, Jerusalem, Israel; \textsuperscript{b}Taylor & Francis Group

mRNA-based COVID-19 vaccines receive extended approvals

The European Medicines Agency’s advisory committee has recommended the authorization of the COVID-19 mRNA vaccines BNT162b2 (Pfizer & BioNTech) and mRNA-1273 (Moderna) for use in children aged ≥6 months. Clinical trials have demonstrated the safety and immunogenicity of low-dose formulations in this age group.

The US Food and Drug Administration (FDA) has extended the emergency-use authorization of the bivalent Omicron BA.4/BA.5-adapted version of the BNT162b2 vaccine to include children 5–11 y old. The BA.4/BA.5 strains of SARS-CoV-2 currently dominate in circulation worldwide.

The FDA has also approved a booster dose of the adjuvanted protein subunit vaccine NVX-CoV2373 (Novavax) for adults ≥6 months after the primary course, based on Phase 3 Prevent-19 trial data showing robust immunogenicity.

Other COVID-19 vaccines in development include PTX-COV19-B (Providence Therapeutics), which demonstrated safety and neutralizing antibody immunogenicity non-inferior to BNT162b2 in >500 healthy adults enrolled in the Phase 2 PRO-CL-002 trial, and the VLP vaccine ABNCoV2 (Bavarian Nordic), which restored strong protective immunity lasting at least 6 months as a booster dose following primary vaccination with an mRNA vaccine.

Interleukin inhibitor improves eosinophilic esophagitis in children

The IL-4Ra inhibitor dupilumab (Dupixent, Sanofi & Regeneron) induced histological disease remission in 68% of children with eosinophilic esophagitis. The remission rate was 58% in the low-dose cohort. The randomized, placebo-controlled Phase 3 trial, which reported disease symptoms 16 weeks after treatment, enrolled 68 subjects aged 1–11 y.

Dupilumab had been previously approved for older children and adults with eosinophilic esophagitis, a chronic inflammatory condition of the esophagus with symptoms such as reflux, vomiting, and abdominal pain.

RSV vaccine prevents disease in the elderly

The RSV vaccine RSVPreF3 (GSK) was 83% and 94% efficacious against RSV lower respiratory tract infection and severe disease, respectively, in adults aged ≥60 y. The randomized, placebo-controlled Phase 3 AReSVi-006 trial involved 25,000 subjects in 17 countries.

The subunit vaccine consists of the recombinant prefusion form of the F glycoprotein antigen administered with AS01 adjuvant. There is no licensed RSV vaccine.

Personalized immunotherapy elicits responses against neoantigens in early trial

The personalized cancer vaccine VB10.NEO (Nykode) was safe and immunogenic in patients with locally advanced or metastatic solid tumors involved in a Phase 1/2a trial. Twenty-one of 22 subjects reported both CD4+ and CD8+ T-cell responses that lasted at least 1 y. Multiple vaccine doses increased the magnitude of the response.

VB10.NEO, a DNA vaccine encoding neoantigens identified individually in each patient, is being tested in skin, lung, bladder, kidney, and head-and-neck cancers.

PCV-24 was safe and immunogenic in adults

The 24-valent pneumococcal conjugate vaccine VAX-24 (Vaxcyte) showed satisfactory safety and immunogenicity in 800 healthy adults aged 18–64 enrolled in a Phase 1/2 dose-escalation trial. Immune responses were non-inferior or higher than those induced by 20-valent Prevnar 20 administered to a control group. The safety profiles were comparable.

Immunotherapy improves outcomes in septic shock

The TREM-1 inhibitor peptide nangibotide (Inotrem) improved patient scores on an organ failure assessment scale in 360 subjects with septic shock and high TREM-1 levels in the double-blind Phase 2b Aston trial. The current standard of care for septic shock involves antibiotics and symptom treatment.

TREM-1 is expressed on the surface of some myeloid cells and is associated with severe immune deregulation in sepsis.

Checkpoint inhibitors in development to fight solid cancers

The FDA has approved a combination of checkpoint inhibitors for the treatment of hepatocellular carcinoma. The anti-PD-L1 tremelimunab (Imjudo) and the anti-CTLA-4 durvalumab
Imfinzi, both from AstraZeneca) improved survival rate after 3 y by 20% compared to chemotherapy in a Phase 3 trial.

The PD-1 inhibitor toripalimab (Coherus & Junshi) plus chemotherapy doubled the progression-free survival rate at the 1-y mark to 37% compared to chemotherapy alone as a first-line treatment for non-small-cell lung cancer (NSCLC). According to the results of the Phase 3 CHOICE-01 trial, which enrolled almost 500 patients, median overall survival was not yet reached in the experimental group (17 months in the control group).

The immunotherapy combination eftilagimod-alpha (Immutep) and pembrolizumab (Keytruda, Merck) has received the FDA’s fast-track designation as a first-line treatment for NSCLC. Both checkpoint inhibitors are designed to activate tumor-infiltrating T cells: eftilagimod-alpha by targeting the LAG-3 surface protein and enhancing antigen presentation and pembrolizumab by inhibiting PD-1 and preventing T-cell exhaustion.

Reference

1. Wang Z, Wu L, Li B, Cheng Y, Li X, Wang X, Han L, Wu X, Fan Y, Yu Y, et al. Toripalimab plus chemotherapy for patients with treatment-naive advanced non-small-cell lung cancer: a multicenter randomized phase III trial (CHOICE-01). J Clin Oncol. 2022;JCO2200727. doi:10.1200/JCO.22.00727.