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Covid-19 vaccines protect from the dominant Omicron strain of SARS-CoV-2

The US Food and Drug Administration (FDA) has expanded the emergency-use authorization of the two mRNA Covid-19 vaccines to include a booster dose of bivalent formulations ≥2 months after the primary course. The updated boosters target both Alpha and Omicron strains of SARS-CoV-2.

Vaccination reduces the risk of Omicron transmission by >20%, according to a study of breakthrough infections in US prisons.1 A similar reduction was observed for prior infection, while the rate of transmission to close contacts was cut by >40% in subjects with both vaccination and past infection.

The BNT162b2 vaccine (Pfizer & BioNTech) demonstrated 73% efficacy in >1,000 children aged six months to four years enrolled into a Phase 3 trial. The vaccine is conditionally approved for this age group in US and under regulatory scrutiny in EU.

A third booster dose of the CpG/Alum-adjuvanted protein subunit vaccine SCB-2019 (Clover) induced high levels of antibodies that neutralized the dominant Omicron variant BA.5. Moreover, a parallel Phase 2/3 trial showed that SCB-2019 elicited two-fold higher antibody levels in adolescents 12–17 years old than in young adults, a group in which the vaccine had demonstrated high protection levels.

Another CpG/Alum-adjuvanted vaccine, the inactivated vaccine VLA2001 (Valneva), showed safety and non-inferior neutralizing immunogenicity, compared to the licensed ChAdOx1 vaccine (AstraZeneca), as heterologous booster 2 months following primary vaccination. In addition, VLA2001 induced broad T-cell responses.

Finally, the Omicron-specific, second-generation mRNA vaccine CV0501 (CureVac) is being tested as a heterologous booster dose in a Phase 1 trial involving 180 healthy adults.

RSV vaccine candidate >80% efficacious in older adults

The bivalent RSV vaccine RSVpreF (Pfizer) demonstrated 67% and 86% efficacy against lower-tract respiratory illness and severe disease, respectively, in the randomized, double-blind, placebo-controlled Phase 3 RENOIR trial involving 37,000 adults aged ≥60 years. RSVpreF consists of stabilized, recombinant prefusion forms of the surface F antigens from RSV strains A and B. The vaccine is also being tested in pregnant women for protection of newborns.

RSV is particularly dangerous in the elderly, accounting for almost 200,000 annual hospitalizations and 14,000 deaths in the US alone.

Clinical development of checkpoint inhibitors in solid tumors

The anti-PD-L1 sugemalimab (EQRx) extended progression-free survival by 70%, compared to placebo, to >10 months in patients with locally advanced, unresectable non-small cell lung cancer (NSCLC) who remained without disease progression after concurrent or sequential chemoradiotherapy. The Phase 3 GEMSTONE-301 trial also reported no new safety concerns.

Subcutaneous formulation of another PD-L1-specific MAb atezolizumab (Tecentriq, Roche) showed non-inferior blood levels in recipients, compared to the standard intravenous administration in the Phase 3 IMvsin001 trial in subjects with immunotherapy-naïve subjects with locally advanced or metastatic NSCLC. Subcutaneous administration reduces treatment time by up to 10-fold.

Finally, the Fc-enhanced, tumor-selective CTLA-4 inhibitor XTX101 (xilio) was established in circulation without reaching the maximum tolerated dose in patients with solid tumors enrolled in a dose-escalation Phase 1 trial.

Neoantigen mRNA vaccine had promising results in early trial with solid cancers

Personalized cancer vaccine regimen GRANITE (Gritstone) had an acceptable safety profile and showed signs of clinical activity in 29 patients with advanced metastatic solid tumors enrolled in a dose-finding Phase 1/2 trial.2 The vaccine induced durable, tumor-specific CD8+ T-cell responses and improved overall survival in several subjects with microsatellite-stable colorectal cancer.

The regimen consists of a chimpanzee adenovirus (ChAd68)-vected prime and a self-amplifying mRNA boost carrying neoepitopes identified by individual tumor sequencing, combined with the checkpoint inhibitors nivolumab (anti-PD1) and ipilimumab (anti-CTLA-4; both BMS).

20-valent pneumococcal vaccine is immunogenic in infants

Four doses of the 20-valent pneumococcal conjugate vaccine 20vPnC (Prevnar 20, Pfizer) demonstrated safety and immunogenicity which was non-inferior to the licensed Prevnar 13 in the shared strains and comparable in the additional seven strains. The vaccine was safe, with most common reported adverse events bronchitis, gastroenteritis and pneumonia.

20vPnC, which was previously approved for adults, has been tested in >5,000 infants and toddlers.

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CAR-T immunotherapy of colorectal cancer starts clinical testing in US

An open-label, single-arm, dose-escalation Phase 1 trial has been started to test safety and efficacy of the chimeric-antigen receptor (CAR) T-cell therapy GCC19CART (Innovative Cellular Therapeutics) in 30 patients with relapsed or refractory metastatic colorectal cancer. GCC19CART, which consists of a single infusion of autologous T cells engineered to target the colorectal cancer antigen guanylate cyclase-C, showed safety in a smaller trial in China and has been granted the FDA’s fast-track designation.

CAR-T technologies have so far been successful only in hematological cancers.

Dengue vaccine approved in Indonesia

Indonesia has become the first country to approve the dengue vaccine Qdenga (Takeda) for use in people 4–45 years old irrespective of prior dengue exposure. The decision is based on the ongoing Phase 3 TIDES trial, which showed efficacy of 62% and 84% in preventing disease and hospitalization, respectively, in 20,000 children aged 4–16.

The mosquito-borne dengue fever is a major public-health concern in Southeast Asia. The temporary approval of another vaccine, Dengvaxia (Sanofi), has had a negative impact on vaccine acceptance in the Philippines after it was shown to enhance disease in people without prior infection.

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