First Covid-19 vaccine fully approved

The US Food and Drug Administration (FDA) has approved the BNT162b2 vaccine (Pfizer & BioNTech) for use in people 16 years of age and older. All Covid-19 vaccines have so far been administered under emergency-use authorization.

The regulator is also evaluating the third, booster dose of BNT162b2, which was shown in a clinical trial with 300 people to increase antibody levels by >3-fold compared to the standard two-dose regimen. Three doses are currently recommended for immunocompromised subjects only.

However, rich countries should stop administering booster doses until at least 10% of people in poorer countries are vaccinated, according to the World Health Organization. Despite international initiatives to provide vaccines to developing regions, there is still a significant disparity in coverage.

A homologous booster to the single-dose Ad26.COV2.S vaccine (J&J) also improves responses, a small follow-up study showed. Antibody levels were 6- to 9-fold higher 4 weeks after the booster dose, compared to 4 weeks after the primary dose. Responses were investigated for two booster dosage levels administered 6 months after the first vaccination: higher dose in young adults and lower in older adults.

BNT162b2 and the adenovirus-based vaccine ChAdOx1 nCoV-19 (AstraZeneca) were shown to protect against the severe Delta strain of SARS-CoV-2 in a large study comparing >350,000 people each tested during the time when the Delta and Alpha strains predominated. However, protection from high viral load waned from 92% after 2 weeks to 78% after 3 months.

It is still unclear whether antibody levels following vaccination are a useful correlate of protection. A study matching 50 Covid-19 cases with controls without infection, all vaccinated with the mRNA-1273 vaccine (Moderna), showed that subjects with low antibody counts were more likely to develop the disease, indicating that antibody profiling might be a useful predictor of protection.

Text-message reminders might increase compliance, a study from California suggests. More than 90,000 people were drawn from the healthcare system and randomized to receive a text message one day after becoming eligible for vaccination. One message increased appointment and acceptance rates by 6% and 3.6%, respectively, a second message led to further increases by >1% in both measures.

In other clinical developments, the adenovirus vectored Sputnik V vaccine demonstrated 81% efficacy in preventing hospitalizations in a sample of 14,000 people. The CpG-adjuvanted subunit vaccine MVC-COV1901 (Medigen & Dynavax) received emergency-use authorization in Taiwan and is being administered to hundreds of thousands of people in the country. Finally, the two-dose VLP vaccine ABNCoV2 (Bavarian Nordic) was safe and immunogenic in a Phase 1/2 trial with 45 healthy volunteers. Neutralizing titers were demonstrated against all virus variants of concern. This vaccine is also being investigated as a booster to natural or vaccine-induced immunity.

Progress in NSCLC immunotherapy

A Phase 3 trial testing the PD-1 inhibitor cemiplimab (Libtayo, Regeneron & Sanofi) together with chemotherapy in locally advanced and metastatic non-small cell lung cancer (NSCLC) was stopped early due to significant benefits. The treatment led to a 30% reduction of the risk of death compared to chemotherapy alone with median overall survival of 22 and 13 months, respectively.

The PD-L1 inhibitor atezolizumab (Tecentriq, Roche) was granted Priority Review designation by the FDA as adjuvant treatment of NSCLC following surgery and chemotherapy in patients with high PD-L1 levels. The decision was based on Phase 3 data showing that the immunotherapeutic reduced risk of relapse by a third compared to the best supportive care.

PCV-15 safe in infants

The 15-valent pneumococcal conjugate vaccine (Vaxneuvance, Merck) was non-inferior in terms of safety and immunogenicity to the marketed 13-valent PCV Prevnar 13 (Pfizer) in infants. The Phase 3 PNEU-PED trial enrolled >1,700 children 42–90 days old and tested a 4-dose regimen of PCV-15. The vaccine is currently approved for adults.

Off-the-shelf neoepitope immunotherapy is tested in ovarian cancer

A Phase 2 trial has started for the neoepitope vaccine Tedopi (OSE Immunotherapeutics) in patients with ovarian cancer. Tedopi, which contains a set of typical tumor-associated antigens, is being tested alone or in combination with the PD-1 inhibitor pembrolizumab (Keytruda, Merck) as a maintenance treatment following chemotherapy.

Since ovarian cancer rarely responds to checkpoint inhibitors due to immunologically cold tumor microenvironment, Tedopi is designed to elicit immune responses rendering the tumor immune hot.
Chikungunya vaccine was immunogenic in a late-stage trial

The chikungunya vaccine candidate VLA1553 (Valneva) was safe and induced neutralizing antibodies in 98% of >4,000 adults enrolled into the Phase 3 VLA1553-301 trial. The vaccine, which had previously received the FDA’s Breakthrough Designation, also demonstrated immunogenicity in elderly subjects.

VLA1553 is a single-dose, live attenuated vaccine against the mosquito-borne viral infection, which is a significant public health burden in tropical regions of the world.

Sjögren’s syndrome immunotherapy advances through clinical testing

The IL-7 R-targeting immunotherapeutic OSE-127/S95011 (OSE Immunotherapeutics) is tested in a Phase 2 trial for treatment of Sjögren’s syndrome. One of the most common systemic autoimmune diseases, Sjögren’s syndrome is characterized by lymphatic infiltration of moisture-producing glands leading to dry mouth and eyes and sometimes seriously affecting other organs.

OSE-127/S95011, which is a humanized MAb specific for the alpha subunit of the IL-7 receptor, is designed to inhibit the migration of pathogenic T cells.

Passive immunization protects against malaria in an early trial

The monoclonal antibody CIS43LS was safe and effective in preventing malaria in a Phase 1 trial. None of the nine malaria-naïve participants who received the antibody developed parasitemia following challenge with mosquitoes carrying *Plasmodium falciparum* sporozoites, compared to five of six subjects in the control group.

CIS43LS, which targets a conserved epitope in the *Plasmodium* circumsporozoite protein, is a modified antibody with extended half-life, produced in hamster ovary cells.

Immunotherapeutic combination benefits melanoma patients

The telomerase vaccine UV1 (Ultimovacs) combined with pembrolizumab shrank tumors in six out of 10 patients with metastatic melanoma with three complete responses and 90% overall survival after 1 year. Median progression-free survival was not reached at that timepoint.

UV1 targets human telomerase, which is overexpressed in >80% of all cancers. It could therefore be used as a ‘universal’ vaccine in treatment of multiple cancer types.

Natural killer cell immunotherapy shows activity against B-cell lymphoma

Two variants of an off-the-shelf natural killer (NK) cell-based therapy (Fate Therapeutics) were safe and met objective response rates in a dose-escalation Phase 1 trial in refractory B-cell lymphoma. FT516 induced responses in eight of 11 patients with six complete responses. FT596 elicited responses in 10 of 14 patients with seven complete responses.

FT516 consists of NK cells engineered with a non-cleavable CD16 Fc receptor designed to enhance antibody-dependent cellular toxicity. FT596 contains additional CD19-specific chimeric antigen receptor and IL-15 receptor fusion for increased NK cell activity and longevity. Both treatments are combined with chemotherapy and the anti-CD20 MAb rituximab.

Combination of immunotherapy with epigenetic inhibitor was safe in solid cancers

The anti-PD-1 MAb nivolumab (Opdivo, BMS) with the histone deacetylase inhibitor entinostat were safe with few adverse events in 33 patients with advanced solid cancers. The combination, which was tested with or without the CTLA-4 inhibitor ipilimumab (Yervoy, BMS), led to median overall survival of 10.6 months and progression-free survival of 6 months. 60% of subjects achieved disease stabilization with one complete response.

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