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Omicron-specific mRNA Covid-19 vaccines are being deployed

The European Medicines Agency’s advisory body recommended full approval of Omicron-adapted mRNA vaccines BNT162b2 (Pfizer & BioNTech) and mRNA-1273 (Moderna) as well as booster doses for children aged 5–11 years. The dominant Omicron variants are expected to be predominant in the Northern Hemisphere.

Other Covid-19 vaccines are in clinical development, mostly as booster doses due to much of the world having received one of the approved vaccines. These include:

- the peptide vaccine EuCorVac-19 (EuBiologics), which enters a Phase 3 trial with 4,000 healthy participants in the Philippines. EuCorVac-19 displays the antigen on the spontaneous-nanoliposome antigen particle (POP Bio).
- oral pill vaccine VXa-CoV2-1.1-S (Vaxart), which demonstrated safety and Omicron-neutralizing mucosal immunogenicity in a Phase 2 trial.
- T cell-targeting peptide vaccine VB10.2210 (Nykode), which was safe and immunogenic in a dose-escalation Phase 1/2 trial. The vaccine encodes 96 antigens from eight SARS-CoV-2 proteins.

CAR-T cell therapy was successful against lupus in a pilot study

A 100% remission rate was reported from a small trial of CD19 CAR-T immunotherapy of systemic lupus erythematosus. Five subjects, who had been refractory to several immunosuppressive drug treatments, responded within 3 months of treatment.

In the procedure, autologous T cells were collected, engineered to target the CD19 B-cell antigen, and re-infused following lymphodepletion. The regimen was relatively well tolerated, inducing only a mild form of cytokine-release syndrome.

Malaria vaccine 80% efficacious after one year

The malaria vaccine R21 demonstrated 80% efficacy after 1 year of the initial course in a randomized, double-blind Phase 2 trial involving 400 children in Burkina Faso. R21, which is administered with the saponin-based Matrix-M adjuvant (Novavax), was administered in three doses plus two dosage levels of a booster. The efficacy was 70% in the low-dose group.

Malaria is one of the most significant public-health concerns, with around a quarter billion cases and 600 K deaths annually. No effective vaccine with lasting effect has been developed thus far.

Interleukin antagonist immunotherapy improves symptoms of prurigo nodularis

Sixty percent of patients with prurigo nodularis reported reduced itch and skin lesions 24 weeks after receiving the IL-4 receptor inhibitor dupilumab (Dupixent; Regeneron & Sanofi), compared to 18% in the placebo group. Half of the dupilumab-treated subjects achieved clear skin.

The randomized, double-blind Phase 3 PRIME trial enrolled 151 adults with prurigo nodularis, which could not be controlled with topical treatments. Prurigo nodularis is an inflammatory skin disease of unknown etiology, which causes painful itches and thick skin lesions.

PD-1 pathway inhibitors mark clinical progress in solid cancers

The US Food and Drug Administration (FDA) has approved the anti-PD-L1 MAb durvalumab (Imfinzi, AstraZeneca) in combination with chemotherapy for adults with locally advanced or metastatic biliary tract cancer. The decision is based on data from the Phase 3 TOPAZ-1 trial showing a survival benefit of 20% compared to chemotherapy alone.

Another PD-L1 inhibitor, atezolizumab (Tecentriq, Roche), doubled the survival rate at the two-year mark in patients with advanced platinum-ineligible non–small cell lung cancer (NSCLC) involved in the Phase 3 IPASS trial. Overall survival was 24% and 12% for subjects in atezolizumab and chemotherapy cohorts, respectively.

The PD-1-targeting MAb camrelizumab (Elvar Therapeutics) combined with rivoceranib extended survival in unresectable hepatocellular carcinoma by 7 months to 22 months, compared to the standard-of-care sorafenib. Response rate was 25% and 6%, respectively, in a randomized, open-label Phase 3 trial, which included 543 patients.

Finally, a combination of the BTK3A inhibitor ICT01 (ImCheck) and anti-PD-1 pembrolizumab (Keytruda, Merck) demonstrated acceptable safety and clinical benefit in patients with solid tumors, who had failed prior treatment with checkpoint inhibitors. The dose-escalation Phase 1 EVICTION trial reported disease control in 42% of melanoma and 22% of both NSCLC and bladder cancer patients.

Two virotherapies promising in multiple cancer types

The engineered herpes simplex virus RP2 (Replimune) was safe with no serious adverse events and induced responses in 10 out of 40 patients with solid tumors. The Phase 1 trial, which tested RP2 with and without the PD1 inhibitor nivolumab (Opdivo, BMS), also reported one complete response for ≥15 months in
mucoepidermoid carcinoma. All subjects had exhausted their treatment options, including checkpoint-inhibition immunotherapy. RP2 is based on HSV-1 expressing CTLA-4 inhibitor, fusogenic protein GALV-GP R.

The adenovirus-based virotherapy CAN-2409 (Candel Therapeutics) in combination with valacyclovir received the FDA’s orphan-drug designation for treatment of high-grade glioma. The regimen consists of intratumorally administered adenovirus expressing HSV thymidine kinase, which converts valacyclovir into a cytotoxic compound.

35% tumor control rate following interleukin-2 superagonist therapy

The IL-2 superagonist MDNA11 (Medicenna) induced one partial response in a patient with metastatic pancreatic ductal adenocarcinoma, who had failed three lines of prior treatment, including chemotherapy and checkpoint inhibition.

The dose-escalation Phase 1/2 ABILITY trial, which tests MDNA11 monotherapy in solid tumors, reported that five of 14 subjects achieved tumor control.

Lassa virus vaccine starts clinical testing

First patients have been enrolled into a randomized, placebo-controlled, dose-escalation Phase 1 trial evaluating the safety and immunogenicity of the Lassa virus vaccine EBS-LASV (Emergent BioSolutions). The rVSV-vectorized vaccine will be tested in 36 healthy adults in Ghana.

Reference

1. Mackensen A, Müller F, Mougiakakos D, Böltz S, Wilhelm A, Aigner M, Völkl S, Simon D, Kleyer A, Munoz L, et al. Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus. Nat Med. 2022;28:2124–32. doi:10.1038/s41591-022-02017-5.

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