



## Human Vaccines & Immunotherapeutics: news

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### COVID-19 outbreak stimulates vaccine development on multiple fronts

The newly emerged coronavirus SARS-CoV-2 that causes COVID-19 disease has spread around the world, infecting >300,000 people and killing >82,000 in virtually every country. Only 2% of the affected population are people <20 years of age, while the severe form of the disease is experienced by the elderly and subjects with comorbidities.

Several vaccine candidates are likely to emerge soon. Sanofi plans to utilize a platform, which provided partial protection against the related ‘SARS’ virus in a preclinical challenge study. It could enter clinical trials in 2021, the company said.

Another candidate comes from the Trimer-Tag technology (Clover Biopharmaceuticals), in which covalently trimerized fusion proteins are recombinantly expressed in mammalian cell culture. It has been employed for the development of vaccines against other enveloped RNA viruses, such as HIV and influenza. The vaccine will be formulated with the AS03 adjuvant (GSK).

A fourth candidate, a ‘molecular clamp’ vaccine developed at the University of Queensland, utilizes purified viral fusion proteins stabilized in a pre-fusion conformation, thus exposing neutralizing epitopes, and also is formulated with AS03 adjuvant.

Efforts to develop vaccine against COVID-19 might be accelerated by the fact that the viral genome has been fully sequenced<sup>1</sup> and the structure has been determined for its spike protein, which the virus uses for cell entry.<sup>2</sup>

### CRISPR-engineered T-cells used to treat cancer in an early study

Three cancer patients underwent therapy with CAR-T cells engineered with the high-efficiency genome editing tool CRISPR-Cas9. The subjects had NY-ESO-1-positive, advanced sarcoma or multiple myeloma with few treatment options left. As a proof of principle, the method showed safety and feasibility, even though the disease worsened in all patients, with one of them having died.<sup>3</sup>

In the procedure, patients’ own T-cells are harvested, and the endogenous T-cell receptors (TCR) are knocked out along with the PD-1 protein to prevent the cancer from down-regulating the immune response. Next, a recombinant, NY-ESO-1-specific TCR is introduced and the cells are expanded and infused back into the patients.

The CAR-T cells persisted for at least 9 months, compared to ~2 months typical for conventional CAR-T cells with intact endogenous TCR and PD-1.

### Around 50% influenza vaccine effectiveness is reported in North America at mid-point of season

The 2019/20 influenza vaccine is 45% effective overall in the U.S., according to mid-term analysis by the Centers for Disease Control and Prevention.<sup>4</sup> In a season dominated by influenza B, the highest benefit was reported for children and adolescents. Conversely, only 5% protection was seen in adults against the H1N1 strain. The study collected data on >4,000 acute respiratory illnesses from five sites across the country.

In Canada, the vaccine was 58% effective in preventing medically-attended disease.<sup>5</sup> As in the U.S. the younger cohort saw the highest level of benefit with 74% effectiveness in individuals up to 19 years of age and 18% in older people over the age of 65.

### Two influenza vaccines approved in U.S.

The U.S. Food and Drug Administration (FDA) has approved the quadrivalent influenza vaccine Fluvad (Seqirus) for use in adults 65 years and older. The accelerated decision is conditional on further trials confirming Fluvad’s benefits.

Another influenza vaccine approved by FDA is the pandemic H1N1 monovalent vaccine Audenz (Seqirus), produced in cell culture. This vaccine can be stockpiled and rapidly deployed in case of a pandemic.

Both vaccines are administered with the squalene-based MF59 adjuvant to stimulate helper T cell response.

### Adjuvant immunotherapy effective in oral cancer patients

Two doses of the PD-1 inhibitor nivolumab with or without the CTLA-4-targeting ipilimumab, given pre-operatively, induced tumor regression in half of 30 patients with newly diagnosed tongue, gum or mouth cancer. In the randomized Phase 2 trial, four subjects showed >90% response. The immunotherapy allowed all patients to enter the standard course of treatment starting with surgery.

“Oral cavity cancer is a notoriously difficult cancer with high rates of disease recurrence and death,” lead author Jonathan Schoenfeld of Dana-Farber Cancer Institute said. “Our hope is that even a couple doses of immunotherapy can stimulate an immune response that continues to prevent the cancer from coming back after patients have surgery and other therapy.”

### Full vaccination in childhood provides lifelong protection from diphtheria and tetanus

Adults do not need booster doses to be protected from the bacterial infections diphtheria and tetanus, a study suggests.<sup>6</sup> Comparing disease rates from 2001-16 in countries that require booster vaccination (typically every 10 years) and in

countries without such requirements, the authors found no difference. The data on millions of subjects were pooled from 31 European and North American countries.

Discontinuing booster vaccinations against these two diseases might save the healthcare system \$1 billion annually in the U.S. alone.

### First Ebola vaccine was licensed in Africa

The Ebola vaccine rVSV-ZEBOV (Merck) has been approved in The Democratic Republic of the Congo (DRC), Burundi, Ghana and Zambia. Other countries in the region are expected to follow suit following prequalification by the World Health Organization and licensure by U.S. and European authorities.

The single-dose rVSV-ZEBOV, which targets the Zaire strain of Ebola, has been administered to almost 300,000 people in DRC, where an ongoing outbreak has claimed >2,000 lives. Preliminary results indicate >97% efficacy in preventing the disease.

### Another study suggests that a single dose of HPV vaccine might be sufficient

A single dose of HPV vaccine was comparable with two- and three-dose regimens in preventing preinvasive cervical disease in a retrospective study that looked at medical records of 133,000 U.S. women between 2006 and 2015.<sup>7</sup> The three regimens reduced the risk of disease by 36, 28 and 34 percent, respectively, compared to unvaccinated subjects. It remains to be determined whether long-term immunogenicity is comparable for all regimens as well.

HPV vaccine coverage is <10% worldwide, and a single-dose schedule might facilitate the logistics in inaccessible regions, thereby increasing vaccine uptake.

### Gavi launches measles vaccination campaign in developing countries

Gavi plans measles vaccination for 45 million children in Bangladesh, Central African Republic, Ethiopia, Kenya, Nepal, Somalia and South Sudan. In addition, the vaccine alliance will help Madagascar and Mauritania implement a second dose. Measles cases decreased by ~90% between 2000 and 2016, but the incidence has increased again, largely due to vaccine skepticism.

“While the headlines might focus on rising cases in Europe and the US, it is sadly still the case that the vast majority of measles deaths are happening in the world’s poorest countries, where poor health systems mean children are often left to fight the disease without treatment or support,” Gavi CEO Seth Berkley said. “The measles

vaccine is safe, effective and low-cost – there is no reason children should still be dying of this disease.”

### Another HIV vaccine candidate fails

Clinical testing of HIV vaccine combination was stopped after a committee had determined it was not working. The placebo-controlled HVTN 702 trial enrolled 5,400 young adults in South Africa and reported 129 and 123 infections in the vaccine and placebo cohorts, respectively.

The regimen consisted of canarypox-vectored ALVAC-HIV (Sanofi) vaccine and a two-component gp120 subunit vaccine (GSK) adjuvanted with MF59. The combination was administered in a regimen of 0-12-18 months.

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