**Human Vaccines & Immunotherapeutics: News**

**Measles has been eliminated from the Americas**

The Americas has become the first region in the world to get rid of measles, the Pan American Health Organization/World Health Organization (PAHO/WHO) council declared. Measles has thus become the fifth vaccine-preventable disease eliminated from the two continents, after smallpox (1971), poliomyelitis (1994), and rubella and congenital rubella syndrome (2015).

“I would like to emphasize that our work on this front is not yet done,” director of PAHO/WHO Carissa Etienne told the media. “Measles still circulates widely in other parts of the world, and so we must be prepared to respond to imported cases. It is critical that we continue to maintain high vaccination coverage rates, and it is crucial that any suspected measles cases be immediately reported to the authorities for rapid follow-up.”

Measles is a highly contagious infection and one of the leading causes of death in young children. Before mass vaccination was introduced in 1980s, measles was responsible for nearly 2.6 million annual deaths worldwide. This number was down to 115,000 in 2014.

According to WHO, >17 million deaths from measles were prevented by immunization during 2000–14 making the measles vaccine one of the most cost-effective measures in public health history. The vaccine—either alone or in combination with mumps and rubella vaccines—has been a part of national immunization programs throughout the world. As a result, around 85% of the world’s children receive at least one dose of measles vaccine.

**IMM-101 immunotherapy promising for pancreatic cancer treatment**

An investigational immunotherapy IMM-101 (Immodulon) showed benefit in metastatic pancreatic cancer patients. In a randomized Phase 2 trial reported in the British Journal of Cancer,1 median overall survival increased by 59% (+2.6 months) in subjects who received chemotherapy in combination with IMM-101 compared to a chemotherapy-only cohort.

Metastatic pancreatic cancer is one of the deadliest tumor types with median survival of less than one year. Its treatment has seen very little progress over the past decades.

IMM-101 consists of heat-killed *Mycobacterium obuense*, which boosts the immune response to limit cancer progression. The immunotherapeutic is also tested for treatment of melanoma and colorectal cancer.

1. Dalgleish AG, Stebbing J, Adamson DJ, Arif SS, Bidoli P, Chang D, Cheeseman S, Diaz-Beveridge R, Fernandez-Martos C, Glynne-Jones R, Granetto C, Massuti B, McAdam K, McDermott R, Martin AJ, Papamichael D, Pazo-Cid R, Vietez JM, Zaniboni A, Carroll KJ, Wagle S, Gaya A, Mudan SS. Randomised, open-label, phase II study of gemcitabine with and without IMM-101 for advanced pancreatic cancer. Br J Cancer. 2016; 115(7):789-96.

**Immunization campaign reduced meningitis B cases by half in the U.K.**

Ten months after the U.K.’s government launched a campaign to vaccinate infants and children against meningitis serogroup B, the incidence of the disease plummeted by 50% compared to a 4-year average. The meningitis B vaccine Bexsero (GSK) has been offered for free to British infants in two doses at 2 and 4 months with a booster dose at 12–13 months of age. >90% of them received both doses, according to the manufacturer’s data.

The U.K. is the first country in the world with a national meningitis B vaccination program. Prior to its launch, estimated 1,000 children were infected every year, 1% of whom died and ~30% were left with a permanent disability including deafness, mental retardation, or loss of one or more limbs.

**CAR-T immunotherapy promising for non-Hodgkin lymphoma**

Two recent studies have highlighted the potential of chimeric antigen receptor T-cell (CAR-T) therapy of B-cell non-Hodgkin lymphoma (NHL). In an interim analysis of Phase 2 ZUMA-1 trial of KTE-C19 immunotherapy (Kite Pharma) assessing 62 patients with three types of chemo-refractory aggressive NHL after three months of therapy, nearly half of the subjects went into complete remission. In KTE-C19 therapy, the CAR-T cells recognize antigen CD19, which is expressed on the cell surface of B-cell lymphomas and leukemias. KTE-C19 has received Breakthrough Therapy Designation in the U.S.

In another study,1 CD19-targeting CAR-T cells were administered to 20 patients with refractory NHL together with fludarabine, which resulted in 50% complete remission compared to 8% in the control group without fludarabine. This drug induces lympho-depletion, which makes it easier for the recombinant T cells to proliferate in the patient.

1. Turtle CJ, Hanafi LA, Berger C, Hudecek M, Pender B, Robinson E, Hawkins R, Chaney C, Cherian S, Chen X, Soma L, Wood B, Li D, Heimfeld S, Riddell SR, Maloney DG. Immunotherapy of non-Hodgkin’s lymphoma with a defined ratio of CD8+ and CD4+ CD19-specific chimeric antigen receptor-modified T cells. Sci Transl Med. 2016; 8(355):355ra116.

**Shingles vaccine candidate efficacious in the elderly**

The experimental shingles vaccine Shingrix (GSK) demonstrated a 90% efficacy in a randomized, placebo-controlled
Phase 3 ZOE-70 study conducted in ~15,000 adults ≥70 years of age. These results complement data from the ZOE-50 trial, in which the vaccine reduced the risk of shingles by 97% in people aged 50 and older. The high rate of efficacy was maintained for at least four years. The vaccine also reduced by almost 90% postherpetic neuralgia, a painful complication of shingles. Shingrix is an adjuvanted subunit vaccine containing varicella zoster virus surface glycoprotein E.

1. Cunningham AL, Lai H, Kovac M, Chilbek R, Hwang S, Díez-Domingo J, Godenius O, Levin MJ, McElhaney JE, Puig-Barberá J, Vanden Abeele C, Vesikari T, Watanabe D, Zábal T, Ahonen A, Athan E, Barba-Gomez JF, Campora L, de Looze F, Downey HJ, Ghesquiere W, Gorbik I, Korhonen T, Leung E, McNeil SA, Oostvogels L, Rombo L, Smetana J, Weckx L, Yeo W, Heineman TC; ZOE-70 Study Group. Efficacy of the herpes zoster subunit vaccine in adults 70 years of age or older. N Engl J Med. 2016; 375(11):1019-32.

HPV vaccination dramatically reduced virus prevalence

Vaccine strains of the human papillomavirus (HPV) have decreased by >90% in incidence in vaccinated women in a U.S. community, according to a study published in Clinical Infectious Diseases. Due to herd immunity, a decrease by >30% was also noted among unvaccinated women. The researchers therefore expect that vaccination will have substantial effect on the rates of HPV-related cancers.

“The tremendous decrease in vaccine-type HPV prevalence – from 35 percent to 3 percent in vaccinated women – is even more notable given that the decrease was among sexually active women who may have been infected prior to vaccination and may have received fewer than the recommended three doses, both of which could reduce vaccine effectiveness,” lead author Jessica Kahn of Cincinnati Children’s Hospital stated in a press release.

Almost 1,200 sexually experienced women in total were studied prior to vaccine introduction (2006–7) and seven years after that (2014). “The substantial decrease in vaccine-type HPV was likely due to excellent HPV vaccine efficacy and high vaccination rates in this population,” Kahn noted.

1. Kahn JA, Widdice LE, Ding L, Huang B, Brown DR, Franco EL, Bernstein DI. Substantial Decline in Vaccine-Type Human Papillomavirus (HPV) Among Vaccinated Young Women During the First 8 Years After HPV Vaccine Introduction in a Community. Clin Infect Dis. 2016; doi: 10.1093/cid/ciw533.

A dengue vaccine candidate in a late-stage trial

The dengue vaccine TAK-003 (Takeda) has entered a double-blind placebo-controlled Phase 3 clinical trial. It will recruit >20,000 subjects 4–16 years of age in dengue-endemic countries of Latin America and Asia. TAK-003 is a live attenuated tetravalent vaccine administered in two doses 90 days apart.

A report published in Science has warned that another dengue vaccine, the only licensed vaccine Dengvaxia (Sanofi), might cause an increase in the rate of severe dengue if applied in a low-prevalence setting. Only in areas where dengue is more common will the vaccine benefit the population. The authors analyzed clinical data from 30,000 people in 10 countries and concluded that, under optimal circumstances, Dengvaxia can decrease hospitalizations by 20–30%.

According to WHO, dengue is a threat for 40% of the world’s population. So far Dengvaxia has been approved in Brazil, El Salvador, Mexico and the Philippines.

1. Ferguson NM, Rodríguez-Barraquer I, Dorigatti I, Mier-Y-Terán-Romero L, Laydon DJ, Cummings DA. Benefits and risks of the Sanofi-Pasteur dengue vaccine: Modeling optimal deployment. Science. 2016; 353(6303):1033-1036.

Chikungunya vaccine candidate advances to a Phase 2 clinical trial

A vaccine against the Chikungunya virus (Themis Bioscience) is being tested for optimal dose in a Phase 2 study. 320 volunteers from Austria and Germany will receive the middle or high dose level in one or two injections. The vaccine is a recombinant measles virus expressing selected Chikungunya proteins, which is delivered directly into antigen-presenting cells.

Chikungunya is a tropical infection borne by mosquitoes. It is endemic in Asia and parts of Africa, but it has spread to other parts of the world with the increase in traveling and global temperatures.

RSV vaccine candidate fails late-stage trial

An F-protein recombinant nanoparticle respiratory syncytial virus (RSV) vaccine (Novavax) failed to meet primary and secondary endpoints of a Phase 3 trial involving 12,000 adults aged ≥60 years. The lack of efficacy was demonstrated shortly after the candidate had been fast-tracked by the U.S. Food and Drug Administration earlier in 2016. The vaccine is being tested in children and pregnant mothers.

RSV infection leads to >200,000 annual hospitalizations and 16,000 deaths in the elderly population. No licensed vaccine against the virus infection is available.

Malaria vaccine candidate fast-tracked by FDA

The malaria vaccine PfSPZ (Sanaria) received a Fast-Track Designation by the U.S. FDA. This push follows a Phase 1 study, in which the vaccine protected 100% of subjects after three weeks and 55% after 14 months. PfSPZ contains non-replicating irradiated whole sporozoites of Plasmodium falciparum. It is being tested for the optimal dose level in trials in the U.S., EU and Africa, and a large-scale trial is planned for 2017.

Preclinical testing gives hope for a vaccine against common cold

A polyvalent rhinovirus vaccine induced neutralizing antibodies in animal models. In a study published in Nature Communications, scientists mixed 25 and 50 strains of rhinovirus and injected them into mice and rhesus macaques, respectively. The
antibodies generated in response to the vaccine were able to prevent infection in human cell culture.

Rhinoviruses are the most frequent cause of common cold. Efforts to develop a vaccine have been hindered by the high degree of variability in subtypes. Senior author Martin Moore of Emory University suggests this can be overcome by simple mixing of strains. “We think that creating a vaccine for the common cold can be reduced to technical challenges related to manufacturing,” he said.

1. Lee S, Nguyen MT, Currier MG, Jenkins JB, Strobert EA, Kajon AE, Madan-Lala R, Bochkov YA, Gern JE, Roy K, Lu X, Erdman DD, Spearman P, Moore ML. A polyvalent inactivated rhinovirus vaccine is broadly immunogenic in rhesus macaques. Nat Commun. 2016; 7:12838.