


Overview: Influenza Vaccines in Development

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Agenda

- **New seasonal / pandemic vaccines**
- **Universal influenza vaccines**
- **Influenza monoclonal antibodies (mAbs)**



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Overarching considerations

- Focus primarily on vaccines in clinical trials in humans (Phase I-III) and less so pre-clinical development (animal data)
- Data sources:
 - Bio MedTracker subscription data base www.biomedtracker.com
 - Press releases, websites and publications by vaccine developers
 - Published articles on general vaccine development
 - www.Clinicaltrials.gov



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New seasonal flu vaccines



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New vaccines leverage faster technologies that could also boost the vaccine immune response

- **New technologies being utilized:**
 - Cell
 - Recombinant
 - ❖ VLP
 - ❖ Plant-based
 - ❖ Oral tablet
 - ❖ Nasal
 - Novel adjuvants
 - mRNA
- **Many candidates have data on both seasonal and pandemic strains**
- **Many companies plan to combine Influenza and COVID-19**



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Novel Vaccines in Later Stage Development

	Company	Technology	Population(s)	Compared to	Key results
Phase III					
	Medicago	Recombinant, plant-based quadrivalent VLP (injection)	Adults 18-64; Adults 65+	Placebo; QIV vaccine	18-64: did not meet primary endpoint 65+: demonstrated non-inferiority Generally well tolerated
	Novavax	Recombinant quadrivalent nanoparticle with Matrix-M adjuvant (injection)	Older adults	Fluzone QIV	Achieved primary endpoints for efficacy; demonstrated antigen-specific CD4+ T cell immunity Generally well tolerated
Phase II					
	Seqirus	Cell-based quadrivalent with MF-59 adjuvant (injection)	Adults 50 and over	None: 8-arm dose ranging	Results not yet published: Phase II ongoing with Phase III planned for 2H2022
	Vaxart	Recombinant oral tablet	Older adults	Double blind; Fluzone QIV	Human challenge model study; Single tablet provided efficacy (reduction in disease and infection rates);
	Sanofi	Fluzone HD pediatric	Children 6-35 months old	Standard QIV	Enrollment underway



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Numerous companies are pursuing mRNA for influenza vaccines

- **Several mRNA and self-amplifying mRNA vaccines are in Phase I / II trials**
 - Moderna - multiple Phase I and II trials of both seasonal and potentially pandemic strains; studies designed to demonstrate safety, tolerability and immunogenicity (some compared to current vaccines).
 - Pfizer – announced a randomized Phase 1 study of safety, efficacy and tolerability of vaccine made with dominant seasonal strains
 - Sanofi – Initial data show potential benefit of mRNA vaccine at various doses; plan to initiate Phase I modified mRNA monovalent trial 1H2022 and quadrivalent in second half of 2022
 - Seqirus – plan to initiate Phase I trials for self-amplifying mRNA seasonal and pandemic vaccines in 2H2022



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Universal flu vaccines



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Universal influenza vaccines are progressing through clinical trials

FluGen

- **A New Approach: M2SR = M2 Deleted Single Replication Live Virus Vaccine**
- Supra-seasonal and intranasal one dose vaccine
- Published, randomized, placebo-controlled, human challenge, Phase II trial in adults 18-64 years against highly drifted H3N2 virus
- Subjects produced vaccine-induced neutralizing antibodies that were protective against infection and illness after being challenged with a highly drifted strain of H3N2
- Vaccine was generally well tolerated



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Universal influenza vaccines are progressing through clinical trials

IMUTEX

- **Broad spectrum “Universal” Flu vaccine that targets conserved internal proteins common to all influenza viruses**
- Adjuvanted one dose or two dose vaccine
- Study 1 - Published randomized, placebo-controlled Phase II trial in adults 18-60 years
 - Subjects produced vaccine-induced neutralizing antibodies that were statistically higher than placebo
- Study 2 - Published randomized, placebo-controlled, human challenge Phase II study in adults 18-55 years; intranasal challenge of H1N1 with a primary endpoint of mild / moderate influenza disease
 - Both vaccine groups experienced significantly lower disease symptoms compared to the placebo group
- Vaccine was generally well tolerated in both studies



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Universal influenza vaccines are progressing through clinical trials

Vivaldi Biosciences

- Self-adjuvanting vaccine
- Immunized volunteers generated antibodies with broad cross-neutralizing activities in the nasal passages and blood serum against unmatched influenza strains.
- A comparison of Phase 1 results showed a superior immune response achieved versus other vaccine approaches for protection against influenza H5N1. After a single dose, 75% of volunteers achieved seroconversion (a key measure of antibody response) while other vaccine approaches, including adjuvanted vaccines, achieved just 5% to 58% seroconversion.
- Vaccine was generally well tolerated in both studies



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Influenza mAbs



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Long-acting monoclonal antibodies offer a potential option to preventive vaccines

Vir

- VIR-2482 is a fully human immunoglobulin G1 mAb directed against a highly conserved epitope in the influenza A hemagglutinin stem region for prevention of influenza A illness.
- Phase I conclusions show that, following a single IM dose in health subjects, VIR-2482 has been well tolerated at doses up to 1800 mg and maintained systemic exposure for greater than/equal to 20 weeks.
- The preliminary pharmacokinetic data demonstrates potential for once-per-season dosing.
- Overall, first-in-human data support initiation of Phase II study to evaluate efficacy
- Preclinical data show that VIR-2482 has broad binding and neutralizing potential against all major strains of influenza A, including pandemic strains, from the last 100 years.
- VIR-2482 administered prophylactically 24 hours prior to lethal doses of influenza significantly reduced morbidity and prevented mortality in mouse models.

NIAID

- Researching other mAbs against various influenza types



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Questions?



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