Human metapneumovirus (hMPV) and parainfluenza virus type 3 (PIV3) are important causes of upper and lower respiratory tract infections, particularly in young children. Despite their public health impact, no effective therapeutic or preventive options are available. mRNA-1653 is a mRNA-based investigational combination vaccine against hMPV and PIV3, and consists of two distinct mRNA sequences encoding the fusing proteins of hMPV and PIV3, co-formulated in lipid nanoparticles.

mRNA-1653 vaccine: Combines Antigens from hMPV and PIV3

Results: Safety

- An interim analysis of safety was performed through study Day 56.
- mRNA-1653 vaccine was generally well-tolerated at all dose levels.
- The most common solicited local adverse event was injection site pain. More severe (Grade 3) injection site pain events occurred after the first vaccination overall, and at the 300 µg dose level in particular.
- The most common solicited systemic adverse events were headache, fatigue, and myalgia, and appeared to increase with dose level.
- No SAEs, AEs of special interest (AEI), or AEs leading to withdrawal were reported.

Methods: mRNA-1653 Phase 1 study

This phase 1, first-in-human, randomized, placebo-controlled, dose-ranging study assesses the safety and immunogenicity of mRNA-1653 in healthy adults aged 18-49. The 124-subject study is conducted across 3 US sites, and evaluates four vaccine dose levels (25, 75, 150, and 300 µg) administered intranasally in either single-dose or two-dose (Days 1 and 28) vaccination schedules, with follow up through 1 year after the last vaccination. Objectives include safety and immunogenicity measured by hMPV- and PIV3-specific neutralizing antibody titters.

Dose-escalation (N=20)
Sequential enrollment
- mRNA-1653 50 µg (4) or placebo (1)
- mRNA-1653 75 µg (4) or placebo (1)
- mRNA-1653 100 µg (4) or placebo (1)
- mRNA-1653 150 µg (4) or placebo (1)

Dose-selection (N=104)
Parallel enrollment
- mRNA-1653 25 µg (26)
- mRNA-1653 75 µg (26)
- mRNA-1653 100 µg (26)
- mRNA-1653 150 µg (26)
- mRNA-1653 300 µg (26)

All subjects received 2 doses (Days 1 & 28).

Results: Immunogenicity

- An interim analysis of immunogenicity was performed through study Day 196 on the Per Protocol Immunogenicity Set.
- Neutralizing antibodies against hMPV and PIV3 were present at baseline in all subjects, consistent with prior exposure to both viruses.
- A single dose of mRNA-1653 boosted serum neutralization titers against both hMPV and PIV3, and the magnitude of boosting was similar at all dose levels.
- The geometric mean ratio of Day 28 to baseline titers was approximately 6 for hMPV and 3 for PIV3.
- A second dose of mRNA-1653 at Day 28 was not associated with further increase of hMPV or PIV3 neutralization titers.
- Neutralizing antibody titers remained above baseline through Day 196.

Results: Demographics

Baseline Demographics by Treatment Group, Exposed Set

- mRNA-1653 is well-tolerated and induces a functional immune response, and is therefore a promising vaccine candidate for the prevention of pediatric respiratory tract diseases caused by hMPV and PIV3. Moderna is next planning to initiate a Phase 1b study of mRNA-1653 in seropositive toddler subjects.

Acknowledgements

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William Seger MD, Benchmark Research, Fort Worth, TX
Laurence Chu MD, Benchmark Research, Austin, TX

Conclusions