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First-in-human study to assess the safety and immunogenicity of an investigational respiratory syncytial virus (RSV) vaccine based on ChAd155 viral vector expressing RSV viral proteins F, N, and M2-1 in healthy adults

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Background: There is currently no licensed vaccine against RSV, a major cause of morbidity in infants. This randomised observer-blind, placebo controlled first-in-human study (NCT02491463) evaluated safety and immunogenicity of an investigational vaccine (ChAd155-RSV) using chimpanzee adenovirus 155 (ChAd155) as a viral vector encoding 3 RSV proteins (fusion [F], nucleocapsid [N], transcription antitermination [M2-1]).

Material/methods: Healthy 18-45 year olds received 2 doses of ChAd155-RSV, placebo or control (licensed group B meningococcal vaccine) at day (D)0 and D30. Dose escalation from low dose (ChAd155-RSV-LD: $5x10^9$ viral particles) to high dose (ChAd155-RSV-HD:$5x10^{10}$ viral particles) occurred after the enrolment of the first 16/72 participants. Endpoints were solicited adverse events (AEs) (D0-6 post-vaccination), unsolicited AEs (D0-29 post-vaccination), serious AEs (SAEs) (D0-60) cell-mediated immunogenicity (D0,7,30,37,60), humoral immunogenicity [functional neutralising antibody (NAb)] titres at D0,30,60. Frequency of IFN-gamma secreting T cells (to peptide pools covering F, N and M2-1 proteins) and anti-F IgG and IgA antibody-secreting B cells were determined by ELISpot on fresh peripheral blood mononuclear cells (PBMC); serum RSV-A NAb titres were measured by NAb assay (cut-off: 5 ED50).

Results: Seventy-two participants were recruited (median age 28 years, 57% female, 89% Caucasian). Seven received ChAd155-RSV-LD, 31 ChAd155-RSV-HD, 15 control vaccine, 19 placebo. The most common solicited grade 2/3 AEs were injection-site pain (27% [ChAd155-RSV]; 0% [placebo]; 80% [control]) and headache (22% [ChAd155-RSV]; 21% [placebo]; 33% [control]).No SAEs, persistent grade-3 solicited AEs, or clinically-significant changes in haemoglobin and in coagulation parameters were reported up to D60. The geometric mean titres ratio (post- /pre- immunisation) of RSV-A NAb following ChAd155-RSV administration were 2.4 (95%CI: 0.9-6.7) at D30 and 1.4 (95%CI: 0.5-3.6) at D60. Following ChAd155-RSV-HD administration, these ratios were 2.6 (95%CI: 1.8-3.6) at D30 and 2.3 (95%CI: 1.8-2.9) at D60; following placebo and control they were 1.4 (95%CI: 1.1-1.9) and 1.2 (95%CI: 1.0-1.5) at D30, and 1.0 (95%CI: 0.8-1.3) and 0.9 (95%CI: 0.8-1.1) at D60, respectively. Circulating anti-F IgG and IgA antibody-secreting B cells were observed at D7 after ChAd155-RSV-HD administration (IgG-secreting B cells: median 133.3 [IQR: 56.7-240]/ 10^6 PBMCs; IgA-secreting B cells: median 16.7 [IQR: 5-30]/ 10^6 PBMCs) but not following placebo or control. Median frequency of RSV-F specific IFN-γ-secreting T-cells per 10^6 of PBMCs at D30 after ChAd155-RSV-HD administration was 108.3 (IQR: 51.7-175) compared with 41.7 (IQR: 13.3-80) in placebo and 41.7 (IQR: 6.7-56.7) in control recipients, with no further increase after booster.

Conclusions: Up to D60, immunisation of healthy adults with ChAd155-RSV raised no safety concerns and was well tolerated. An increase in RSV NAb-neutralising titers was observed after the administration of the first dose of ChAd155-RSV with no booster effect. Further studies in RSV-naïve infants are needed to better asses the immune response of this candidate vaccine in the clinically relevant population.