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Microarray patch delivery of un-adjuvanted influenza vaccine induces potent and broad-spectrum immune responses in a phase I clinical trial

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MICROARRAY PATCH DELIVERY OF UN-ADJUVANTED INFLUENZA VACCINE INDUCES POTENT AND BROAD-SPECTRUM IMMUNE RESPONSES IN A PHASE I CLINICAL TRIAL

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Microarray patches (MAPs) offer the possibility of improved vaccine thermostability and dose-sparing potential as well as the potential to be safer, more acceptable, easier to use and more cost-effective for the administration of vaccines than injection by needle and syringe. Here, we report a phase I trial (ACTRN12618000112268/U1111-1207-3550) using the Vaxxas high-density MAP (HD-MAP) to deliver a monovalent influenza vaccine to evaluate the safety, tolerability, and immunogenicity of lower doses of influenza vaccine delivered by MAPs. To the best of our knowledge, this is the first study determining dose reduction potential using MAPs in humans. Monovalent, split inactivated influenza virus vaccine containing A/Singapore/GP1908/2015 [H1N1] haemagglutinin (HA) was delivered by MAP into the volar forearm or upper arm, or given intramuscularly (IM) once. Participants (20 per group) received HD-MAPs delivering doses of 15, 10, 5, 2.5 or 0 µg of HA or an IM injection of quadrivalent influenza vaccine (QIV). In two subgroups, skin biopsies were taken on days 1 (pre-vaccination) and 4 for analysis of the cellular composition from the HD-MAP application sites. All laboratory investigators were blind to treatment and participant allocation. The primary objectives of the study were safety and tolerability. Secondary objectives included immunogenicity and dose de-escalation assessments of the influenza vaccine delivered by HD-MAP. Both objectives were assessed for up to 60 days post-vaccination. The vaccine coated onto HD-MAPs was antigenically stable when stored at 40°C for 12 months. HD-MAP vaccination was safe and well-tolerated, with mild to moderate responses. Local AEs were application-site reactions such as erythema. HD-MAP administration of 2.5 µg HA induced haemagglutination inhibition (HAI) and microneutralisation (MN) titres that were not significantly different to those induced by 15 µg HA injected IM. Additional exploratory immunoassays encompassing antibody-dependent cellular cytotoxicity, CD4+ T cell cytokine production, memory B cell activation, and recognition of non-vaccine strains indicated that overall, Vaxxas MAP delivery induced immune responses that were similar to, or higher than, those induced by IM injection of QIV. Study limitations included small group sizes and the use of monovalent influenza vaccine in HD-MAP groups. In conclusion, vaccination using the HD-MAP was safe and well-tolerated and resulted in immune responses that were similar to or significantly enhanced compared with IM injection. Using the HD-MAP, 1/6 of the standard dose induced HAI and MN titres like those induced by 15 µg HA injected IM.