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67 Bridging the gap: Linking early post-vaccine events to reactogenicity and later immune responses after viral-vectored and mRNA-based SARS-CoV-2 vaccines

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Adenoviral vector (AdV) and mRNA vaccines were carefully developed to optimise distinct early immune encounters. However, differential mechanisms driving unique early and late immune responses are unclear. We therefore compared the potential drivers and consequences of early human vaccine responses, focusing on "innate-like" lymphocytes known to influence early reactivity and immunogenicity.

Using longitudinal samples from healthcare workers, we profiled the earliest immune responses after homologous prime-boost with mRNA (BNT162b2, n = 36) and AdV (ChAdOx1-nCoV-19, n = 20) vaccines using a systems immunology approach (FACS, bulk and sc-RNAseq, ELISA) coupled with in vitro functional assays, focussing on mechanisms of innate-like lymphocyte activation.

AdV and mRNA vaccines have opposite patterns of early immune responses to prime-boost. Both modalities induce significant IFNγ via innate-like lymphocyte activation, but the mode of activation dictates the divergent patterns observed. Unique AdV-prime specific early signals (type I IFN, inflammasome) drive innate-like lymphocyte IFNγ, which correlates with spike-specific adaptive responses generated. However, at boost, innate-like lymphocyte-derived IFNγ is dampened with AdV but augmented after mRNA vaccination. Adaptive spike-specific IFNγ transactivates and is amplified by IFNγ-responsive innate-like lymphocyte networks. Reduced adaptive immunity at boost - observed with extended dosing intervals - corresponds to muted innate-like lymphocyte IFNγ, and may underpin robust differences in immunogenicity and reactogenicity.

The integration of innate and adaptive immunity in response to novel vaccines can be bidirectional, acting through bridging innate-like cells at critical early timepoints. These data link manipulable distinct early responses to vaccine-specific patterns of reactogenicity and immunogenicity, with implications for optimising antiviral responses in patients

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77 Malaria cases at a Northern tertiary hospital over a five-year period and potential impact of implementing an ambulatory care pathway

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Background

Malaria is one of the most common imported tropical diseases in the UK (1) with well-established national guidelines on diagnosis and management (1). With increased bed pressures over the last 10 years (2) there is a need to consider safe ambulatory care where clinically appropriate. This service evaluation aimed to review current practice within our Trust and conduct a preliminary assessment for the implementation of an ambulatory malaria pathway.

Methods

All positive malaria tests over a five-year period from September 2016 to September 2021 were identified by searching the laboratory database (Telepath). Domains for data collection included demographics, travel history, malaria species, parasitaemia, severity, and timing to presentation, diagnosis, and management.

Results

129 care episodes were included in analysis. Average age was 35.6 years with a higher proportion of males (59.7 %) to females (40.3 %). The most common area for recent travel was West Africa (52.7 %). All cases were imported except for one case of congenital malaria. 72.1 % cases were Plasmodium falciparum, including three cases of mixed species infection. 90.7 % (117/129) were treated as inpatients of which 0.05 % (6/117) required ICU or PICU admission. There were no recorded deaths. 84 of the 129 patients had uncomplicated malaria appropriate for oral treatment, 72 of these were treated as inpatients

Conclusion

Over this 5-year period, had an ambulatory pathway been in place, applying national guidance, 195.5 overnight stays could have been avoided. Further work up to assess the suitability and practicalities of implementing a safe ambulatory malaria pathway locally is needed.

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79 Results from TRUNCATE-TB-time for a change in strategy for TB-treatment shortening?

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Background

The standard management strategy for drug-sensitive pulmonary TB is to treat with multiple drugs for six months, although the majority of patients can be cured with much shorter treatment. TRUNCATE-TB (NCT03474198) evaluates an alternative strategy of treating patients with DS-TB for 2 months with combinations including new drugs or optimised doses of currently available drugs, chosen for their sterilising efficacy.

Methods

Participants with rifampicin-susceptible pulmonary TB at 18 Asian/African sites were randomised (adaptive design) to receive the standard regimen for 24 weeks or one of four novel 5-drug regimens for 8-weeks (up to 12 weeks).

Results

674 participants 18 to 65 years of age were randomly assigned to undergo either standard treatment with a 24-week rifampin-based regimen or a strategy involving initial treatment with an 8-week regimen, extended treatment for persistent clinical disease, monitoring after treatment, and retreatment for relapse. Non-inferiority was assessed in the two strategy groups (initial regimens of high- dose rifampin–linezolid and bedaquiline–linezolid (each with isoniazid, pyrazinamide, and ethambutol). The primary outcome was a composite of death, ongoing treatment, or active disease at week 96.