SEROLOGICAL SURVEILLANCE FOR IMMUNITY TO COVID-19 DURING BOOSTER EFFORTS IN THE UK

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Background:
As COVID-19 boosters are rolling out to individuals that are >6 months from their final dose, it becomes increasingly important to monitor antibody titers when considering diagnosis and surveillance. Not much serological data has been made available since distribution of booster doses began, however this group in the UK obtained geometric mean titers (GMTs) to monitor antibody kinetics and immunologic response prior to and after receiving booster doses. All participants of the study were monitored up to 38 weeks following their second doses of Pfizer-BioNTech (PB) or AstraZeneca (AZ) vaccines. For some individuals in the UK, recommended administration second doses were extended to 12 weeks to conserve supply, as opposed to the standard 3-4 weeks in the US.

Results:
From 626 participants over the study period, individuals received extended AZ doses, standard or extended PB for their first two doses. Standard PB (n=87) GMTs declined by 68% from baseline at 36-38 weeks post-second dose while the PB extended (n=299) and AZ extended (n=240) groups showed 85% and 78% decline in GMT respectively by weeks 24-29. GMTs were higher at 24-29 weeks in PB extended groups (GMT=942) than AZ extended (GMT=183) and PB standard (GMT=208). Interestingly, in the AZ and PB extended groups who became infected by SARS-CoV-2, GMT declines were shown to be less severe than their un-infected, vaccinated counterparts. After dose 2, GMTs in all groups at all timepoints were higher in previously infected individuals than un-infected groups. For booster analysis, AZ (n=50), PB extended (n=131) and PB standard (n=52) participants were analyzed. PB extended group had a lower response (GMT=13,980) 2-4 weeks following dose 3 than PB standard (GMT=18,104) and AZ extended (GMT=10,799). Finally, the group seeing the highest increase in titer post-booster was PB standard (76.3-fold), AZ extended (57.2-fold) and PB extended (4.9-fold).

What does this mean?
In terms of second dosages, this data set shows conflicting support for extending immunization with the second dose beyond what was seen in the US and other countries. However, it does show a first look at booster titers in groups of varying vaccine/infection status. Data requires careful consideration as there is considerable variation in times between doses within groups. However, this data set and similar analyses will be important in determining complicated COVID vaccine algorithms and informing protocols of other mRNA-based, multi-dose and booster-requiring immunizations.

Further Considerations:
Moving forward in determining vaccine efficacy, it will be important to understand titer levels. Assays characterizing successful passive immunity with or without booster versus a boost in titer attributed to exposure or infection will be helpful in determining this. Further, a need for more clinical data is clear. While this study did not see age impact significance, however many individuals receiving early doses were high-risk, and this skew should be taken into consideration in predicting waning titers in other populations. Alternative
dosing schedule could reserve doses an improve immune response in those countries and regions lagging in immunization success.

**Salivary High-Risk Human Papillomavirus (HPV) DNA as a Biomarker for HPV-Driven Head and Neck Cancers**

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*Journal*: Journal of Molecular Diagnostics (JMD)

**Background:**
About 70% of Head and Neck cancers (HNC) is contributed by human papillomavirus (HPV) and oropharyngeal cancer (OPC) is responsible for majority of HNC cases. Diagnosis of HNC/OPC is particularly challenging due to the anatomical location of the cancer and a higher chance to metastasize even at an early stage. Currently, there are no definitive guidelines or tests available for early detection of HNC. This study described a potential application of high risk salivary HPV as a biomarker for early detection of HNC/OPC.

**Results:**
Samples from 491 patients with primary HNC and 10 with recurrent HNC were collected from two hospitals in Brisbane, Australia. 43.2% of primary HNC patients were tested positive for salivary high risk HR-HPV DNA, among which 92% was positive with HPV16, one of the high risk HPV strains for HPV-derived cancers. Majority of HNC patients were men, and 91.5% of positive HR-HPV was diagnosed with oropharyngeal cancer (OPC). There is a direct correlation between salivary HR-HPV and tumor p16 immunohistochemistry (IHC) results, and detection of both can be useful in the diagnosis or a prognostic indicator of OPC. Six out of 10 (60%) were positive for salivary HR-HPV DNA in recurrent HNC cohorts, with 5 of them positive for p16. The salivary HPV16 viral load was heterogeneous in OPC patients, and HPV16 physical status (episomal versus integrated form) did not correlate with the survival rate.

**What does this mean?**
Although there was a direct association of salivary HR-HPV and p16 expression in the majority of OPC patients in this study, 18.6% of p16 positive OPC cases was negative for salivary HR-HPV. Other studies pointed out that p16 overexpression in OPC cases were not necessarily positive for HPV. Nevertheless, supported by other studies, this article underscored the utility of salivary HR-HPV not only in early detection of HNC, but also for continuous monitoring of the disease. Combined testing of salivary HR-HPV and tumor p16 could be a powerful tool in determining the prognosis of OPC.

**Further Considerations:**
While the clinical utility of salivary HR-HPV for detection and monitoring of HNC was well described in this paper, future studies will be necessary to examine the direct correlation of tumor HPV levels, tumor growth, and salivary HPV status. HPV testing is performed in women for cervical cancer screening. However, non-invasive tests are not currently available nor standardized for diagnosis or screening of HPV-associated oropharyngeal cancer. Additionally, more than 80% of HPV-derived oropharyngeal cancer occurs in men, and currently there is no approved test for men. Salivary HR-HPV testing would be a game changer for an early diagnosis of HNC in any genders; larger longitudinal studies and clinical trials are unquestionably in need for future clinical applications.

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