Timing and sequence of vaccination against COVID-19 and influenza (TACTIC): a single-blind, placebo-controlled randomized clinical trial

Summary

Background
Novel mRNA-based vaccines have been used to protect against SARS-CoV-2, especially in vulnerable populations who also receive an annual influenza vaccination. The TACTIC study investigated potential immune interference between the mRNA COVID-19 booster vaccine and the quadrivalent influenza vaccine, and determined if concurrent administration would have effects on safety or immunogenicity.

Methods
TACTIC was a single-blind, placebo-controlled randomized clinical trial at the Radboud University Medical Centre, the Netherlands. Individuals ≥60 years, fully vaccinated against COVID-19 were eligible for participation and randomized into one of four study groups: 1) 0·5ml influenza vaccination Vaxigrip Tetra followed by 0·3ml BNT162b2 COVID-19 booster vaccination 21 days later, (2) COVID-19 booster vaccination followed by influenza vaccination, (3) influenza vaccination concurrent with the COVID-19 booster vaccination, and (4) COVID-19 booster vaccination only (reference group). Primary outcome was geometric mean concentration (GMC) of IgG against the spike (S)-protein of the SARS-CoV-2 virus, 21 days after booster vaccination. We performed a non inferiority analysis of concurrent administration compared to booster vaccines alone with a predefined non-inferiority margin of -0·3 on the log10-scale.
Trial registration number EudraCT: 2021-002186-17.

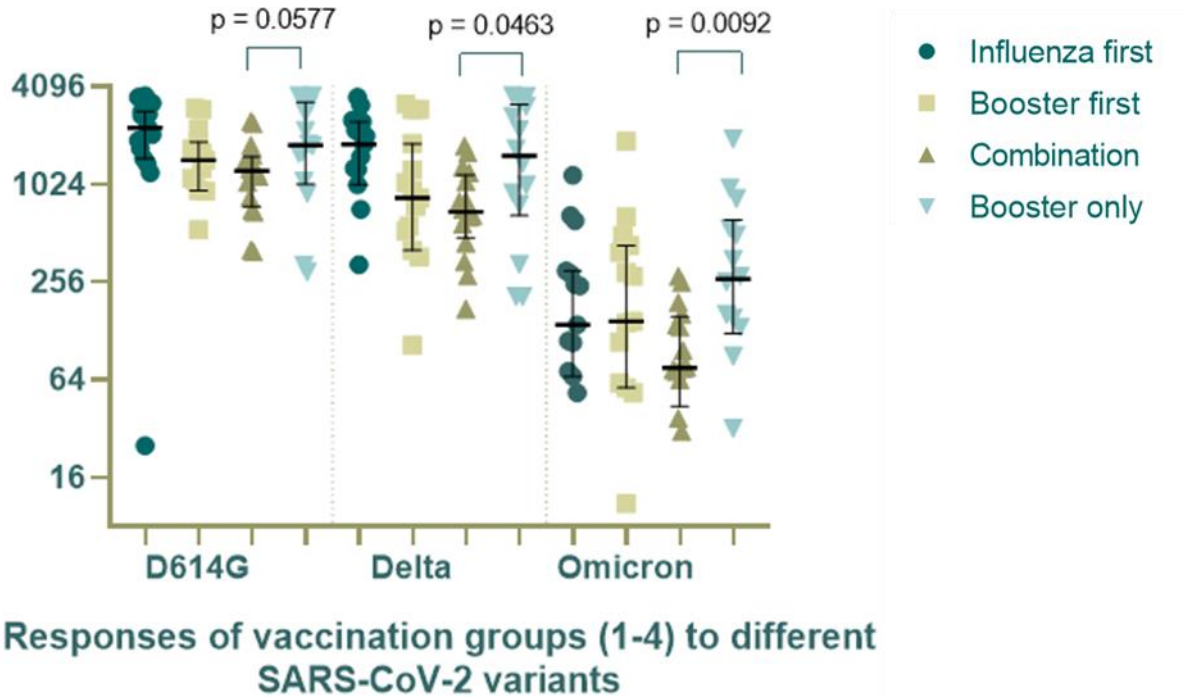
Findings
154 individuals participated from October, 4, 2021, until November, 5, 2021. Anti-S IgG GMCs for the co-administration and reference group were 1684 BAU/ml and 2435 BAU/ml, respectively. Concurrent vaccination did not meet the criteria for non-inferiority (estimate -0·1791, 95% CI -0·3364 to -0·02170) and antibodies showed significantly lower neutralization capacity compared to the reference group. Reported side-effects were mild and did not differ between study groups.

Interpretation
Although concurrent administration of both vaccines is safe, the quantitative and functional immunological responses were lower compared to booster vaccination alone. Lower protection against COVID-19 may be expected with concurrent administration of COVID-19 and influenza vaccination, which should be taken into consideration for public health decisions.

Funding
The study was supported by the ZonMw COVID-19 Programme.

Results secondary endpoints (for EudraCT results reporting):

50% plaque-reducing neutralization titers (PRNT-50) for the D614G, delta and omicron variant of the SARS-CoV-2 virus, compared between all groups at 42 days after first study vaccinations (Visit 3). Error bars display median with interquartile range.



Responses of vaccination groups (1-4) to different SARS-CoV-2 variants

Proteomics: volcano plot with fold changes of proteins in all four groups, 42 days after first study vaccine compared to baseline. Significantly changed proteins indicated by a red color. Results adjusted for multiple testing.