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Carlo LA VECCHIA, Stefano CENTANNI, Alberto G GERLI

Panminerva Medica 2021 Jan 22

DOI: 10.23736/S0031-0808.21.04286-5

Article type: Letter to the Editor

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Article first published online: January 22, 2021

Manuscript accepted: January 21, 2021

Manuscript received: January 7, 2021

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Why two doses of the BNT162b2 mRNA Covid-19 vaccine?

A different strategy to speed up the vaccination process: single-dose of the BNT162b2 mRNA Covid-19 –and other - vaccines.

Carlo LA VECCHIA ¹ , Stefano CENTANNI ² , Alberto Giovanni GERLI ^{3*}

¹Department of Clinical Sciences and Community Health (DISCCO), University of Milan, Milan, Italy; ² Respiratory Unit, Department of Health Sciences, ASST Santi Paolo e Carlo, Università degli Studi di Milano, Milan, Italy; ³ Management Engineering Tourbillon Tech srl, Padova, Italy.

*Corresponding author: Alberto Giovanni Gerli, Section, Management Engineering, Tourbillon Tech, Passaggio Corner Piscopia, 10, 35137, Padova, Italy,
alberto@albertogerli.it

Worldwide vaccination process for Covid-19 has started with a 2-dose approach for all vaccines available and approved now, facing an obvious shortage of doses available for the population.

With reference to the Pfizer vaccine (BNT162b2), Polack et al (1) gave an estimate of vaccine efficacy (VE) for BNT162b2 of 52.4% after dose 1 to before dose 2, as compared to a VE of 94.8% 7 days or more after dose 2.

However, most cases of Covid-19 occurrence were registered in days 1-11, when – as expected – there is no VE.

After day 11, the curve of BNT162b2 diverge from that of placebo, and only 4/41 Covid-19 cases in the BNT162b2 group were observed from day 11 to 21. VE should be therefore $37/41=90\%$. This estimate is similar to the table from 2 to 7 days after second dose (2 out of 21=95,2%), therefore we can estimate a VE close to 90% already from 11 to 28 days.

Assuming the little effect of the second dose between day 21 and day 33, there is no evidence that the curve in the BNT162b2 group is different from day 12 to 33 compared to day 34-112, or from day 11 to 28 as compared to day 29-112, assuming a 6-day lag for dose 2.

Even if Pollack et al (2) state that their study was not designed to assess the efficacy of a single dose regimen and Walsh et al² showed higher concentration of recombinant S1-binding-IgG and 50% neutralization titers after dose 2; still, it is important to have a separate estimate of VE after dose 1 excluding the first 12 days.

Considering the Moderna vaccine, Baden et al (3) in the study on the efficacy of the mRNA-1273 SARS-CoV-2 Vaccine found out fewer occurrences of symptomatic SARS-CoV-2 infection after a single dose of mRNA-1273, VE after one dose was estimated estimated at 80.2% (95% CI 55.2, 92.5%) at 28 days (4).

With reference to the Astra Zeneca viral vector vaccine, VE was assessed at 73% (95% CI 49-86%) 22 days after one dose until two weeks after second dose (4).

Based on the analysis oof the published data, given the immediate importance of vaccination and the limited availability of BNT162b2 (Pfizer), the possibility of prioritizing a single dose strategy – with a possible second dose when adequate availability will be reached – could be considered. This line of reasoning can be applied to other vaccines as well and it is the background for the UK Joint Committee for Vaccination and Immunization (JCIV) to delay the second dose of the Astra Zeneca vaccine to 120 days (4).

REFERENCES

- 1 Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, Pérez Marc G, Moreira ED, Zerbini C, Bailey R, Swanson KA, Roychoudhury S, Koury K, Li P, Kalina WV, Cooper D, Frenck RW Jr, Hammitt LL, Türeci Ö, Nell H, Schaefer A, Ünal S, Tresnan DB, Mather S, Dormitzer PR, Şahin U, Jansen KU, Gruber WC; C4591001 Clinical Trial Group. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N Engl J Med.* 2020 Dec 10. doi: 10.1056/NEJMoa2034577. Epub ahead of print. PMID: 33301246.
- 2 Walsh EE, Frenck RW Jr, Falsey AR, Kitchin N, Absalon J, Gurtman A, Lockhart S, Neuzil K, Mulligan MJ, Bailey R, Swanson KA, Li P, Koury K, Kalina W, Cooper D, Fontes-Garfias C, Shi PY, Türeci Ö, Tompkins KR, Lyke KE, Raabe V, Dormitzer PR, Jansen KU, Şahin U, Gruber WC. Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates. *N Engl J Med.* 2020 Oct 14;NEJMoa2027906. doi: 10.1056/NEJMoa2027906. Epub ahead of print. PMID: 33053279; PMCID: PMC7583697.
- 3 Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, Diemert D, Spector SA, Rouphael N, Creech CB, McGettigan J, Kehtan S, Segall N, Solis J, Brosz A, Fierro C, Schwartz H, Neuzil K, Corey L, Gilbert P, Janes H, Follmann D, Marovich M, Mascola J, Polakowski L, Ledgerwood J, Graham BS, Bennett H, Pajon R, Knightly C, Leav B, Deng W, Zhou H, Han S, Ivarsson M, Miller J, Zaks T; COVE Study Group. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med.* 2020 Dec 30. doi: 10.1056/NEJMoa2035389. Epub ahead of print. PMID: 33378609.
- 4 <https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-astrazeneca/information-for-healthcare-professionals-on-covid-19-vaccine-astrazeneca>

Conflicts of interest.—

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Funding.—not reported

Authors' contributions.— CLV designed the model, performed the computational framework and data mining, supervised the findings of the study and contributed to the interpretation of the results; AGG wrote the manuscript with input from all authors and supported the data analysis; SC supervised and encourage the study. All authors discussed the results and approved the final version of the manuscript.