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SHORT COMMUNICATION

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NVX-Cov2373 Novavax Covid-19 vaccine: A further analysis of its efficacy using multiple modes of expression

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Abstract

A fifth vaccine against Covid-19, NVX-CoV2373 Nuvavoxid® (Novavax), a protein-based adjuvanted vaccine, was recently marketed in Europe. The main clinical trial before marketing concluded to a 'vaccine efficacy' of 89.7% without talking about other validated efficacy parameters. We further analysed the data of this clinical trial using the different validated methods of risk expression: absolute risks (AR), AR reduction (ARR) and number needed to treat (NNT). ARR and NNT values were 1.22% and 82, respectively, for an RR value of 0.10. Description of these parameters allowed defining some interesting characteristics of NVX-CoV2373 efficacy according to age, race, variant and coexisting illness. Finally, we ask that the results of clinical trials be systematically presented, using not only RR but also including AR, ARR and NNT.

KEYWORDS

absolute risk reduction, Covid-19 vaccines, number needed to treat, NVX-Cov2373 Covid-19 vaccine, relative risk

1 | INTRODUCTION

In a previous work [1], we detailed the results of large premarketing clinical trials concerning the four main Covid-19 vaccines: the two mRNA vaccines, tozinameran Comirnaty® (Pfizer) and elasomeran Spikevax® (Moderna), and the two adenovirus vaccines, Vaxzevria® (Astra Zeneca) and Ad26.COV2.S (Janssen) [2]. We have emphasized that the results of large international clinical trials should include several efficacy variables, and not only the sole relative risk (RR), which gives an incomplete idea of the efficacy of drugs in general, and vaccines in particular [1].

The marketing in Europe of a fifth vaccine, NVX-CoV2373 Nuvavoxid® (Novavax), a protein-based adjuvanted vaccine with a special mechanism of action [3], gives us the opportunity to complete this presentation. Thus, as clinical pharmacologists, we calculated the different methods of efficacy expression of this NVX-CoV2373 vaccine, in order to better specify the clinical efficacy of this new Covid-19 vaccine.

2 | METHODS

As in the previous work [1], we extracted data from the main phase III trial [3], a randomized, observer-blinded, placebo-controlled trial comparing two intramuscular 5-μg doses of NVX-CoV2373 or placebo administered 21 days apart with, as primary efficacy end point, virologically confirmed mild, moderate or severe SARS-CoV-2 infection with an onset at least 7 days after the second injection in participants who were serologically negative at baseline. Thus, we calculated the different following validated expressions of risk:

Absolute risks (AR), that is. the risks in the exposed group (patients receiving vaccine) and in the unexposed group (control);

1. Absolute risk reduction (ARR), that is, the arithmetic difference between the risk in the treatment group and the risk in the control group;
2. Number needed to treat (NNT) calculated as the reciprocal of the ARR;

3. Relative risk (RR) with its 95% confidence interval (CI) defined as the ratio of the cumulative incidence of the outcome in the exposed group to the cumulative incidence in the control group [1, 4, 5].

Results were calculated in five specific subgroups: total population with per protocol or intention-to-treat evaluations, age groups (18–64 years, 65–84 years), race (white, other), variant (non-B.1.1.7, B.1.1.7) and presence or not of coexisting illness.

3 | RESULTS

Table 1 shows the different evaluation parameters for the vaccine. According to the five specific subgroups, AR values in exposed population varied from 0.01% to 0.66%, ARR from 0.40% to 203% and RR from 0.04 to 0.30. NNT was 82 in total per protocol population with extreme values between 42 and 256 according to the different subgroups.

4 | DISCUSSION

The present study was performed to clearly present the different modes of expression of the efficacy of the NVX-Cov2373 Covid-19 vaccine. In the Heath's paper, the authors indicated a vaccine efficacy of 89.7% (95% CI 80.2–94.6) [3] without talking about other parameters. In fact, it is well known that the sole presentation of results in terms of 'vaccine efficacy' (a value derived from RR value) does not clearly show the clinical reality of drugs' efficacy. Thus, we further calculated in the present work RR but also other validated parameters, like AR, ARR and NNT [4, 5].

Results of this paper allow making three kinds of comments about (1) the disease, (2) NVX-Cov2373 Covid-19 vaccine, and (3) vaccines marketed to date in Europe against Covid-19.

The first comments concern the disease, Covid-19. AR in placebo patients, that is in non-vaccinated patients, was relatively low (1.86% in total population). This value is in line with the previous paper [1], which gave values between 0.74% and 1.70%. Even if it is not possible to compare the different populations in these trials, since they do not necessarily have the same characteristics, particularly chronological, these low values could explain, at least in part, the difficulties of perception of Covid-19 risks by some parts of the population. This observation is a new example of a classic topic in social pharmacology [6]: assess the balance between the basic risks of the disease itself and the risks of social, therapeutic and/or drug interventions.

Second, analysis of the five calculated values for NVX-Cov2373 Covid-19 vaccine allows to better specifying its clinical efficacy depending on the parameters studied. Although no age difference appeared when the sole RR values were considered, taking into account ARR and NNT showed that the NVX-Cov2373 Covid-19 vaccine seems to be more active in 18–64 year olds than in 65–84 year olds. RR values also indicate that NVX-Cov2373 Covid-19 vaccine failed to show any clinical efficacy of NVX-Cov2373 Covid-19 vaccine in non-white patients, in contrast to Caucasians. This

TABLE 1 Risk of Covid-19 infections in specific subgroups expressed as absolute risk (AR), absolute risk reduction (ARR), number needed to treat (NNT), and relative risk (RR) with its 95% confidence interval (CI) with the NVX-CoV2373 Covid-19 vaccine

	Results in exposed patients	Results in placebo patients	AR in exposed patients	AR in placebo patients	ARR	NNT	RR (95% CI)
Populations							
Per-protocol	10/7020	96/7019	0.14%	1.36%	1.22%	82	0.10 (0.05–0.19)
Intention-to-treat	42/7569	141/7570	0.55%	1.86%	1.31%	76	0.30 (0.21–0.42)
Age							
18–64 years	9/5067	87/5062	0.18%	1.72%	1.54%	65	0.10 (0.05–0.20)
v65–84 years	1/1953	9/1957	0.05%	0.45%	0.40%	250	0.11 (0.01–0.87)
Race							
White	8/6625	85/6635	0.12%	1.28%	1.08%	93	0.09 (0.04–0.19)
Other	2/302	8/297	0.66%	2.69%	2.03%	49	0.25 (0.05–1.19)
Variant							
Non-B.1.1.7	1/7020	28/7020	0.01%	0.40%	0.39%	256	0.04 (0.01–0.29)
B.1.1.7	8/7020	58/7020	0.11%	0.83%	0.72%	139	0.14 (0.07–0.29)
Coexisting illness							
Yes	3/3117	33/3143	0.35%	1.04%	0.69%	144	0.09 (0.03–0.23)
No	7/3903	63/3876	0.18%	1.62%	1.44%	69	0.11 (0.05–0.24)

Note: Data were extracted from Heath et al. [3].

conclusion, which did not appear clearly in the Heath's paper [3], once again demonstrates the value of our type of presentation using multiple efficiency indexes. Analysis of ARR and NNT values also suggests differences in NVX-Cov2373 efficacy according to the studied variant (B.1.1.7) and coexisting illness: NNT was higher in comorbid patients. These conclusions were not evident in Heath's paper [2]. Finally, in the whole intention-to-treat population, ARR and NNT were 1.31% and 76: these values were much higher than those observed in the previous paper with Ebola vaccine (ARR = 9.4%, NNT = 11), indicating a lower clinical efficacy for NVX-Cov2373 Covid-19 vaccine compared to Ebola one.

Third, it is possible to make some comments about the different vaccines. Of course, the aim of this work was not to statistically compare the different vaccines. Such a comparison is not possible since exposed and control populations were not strictly comparable. However, this type of analysis can provide practical, quick and clear clinical informations to the prescriber. Following these kind of analysis and reasoning and using data from our previous study [1], it appears that efficacy of NVX-CoV2373 vaccine could be of the same order than that of elasomeran Spikevax® (Moderna) and Vaxzevria® (Astra Zeneca) and higher than that of tozinameran Comirnaty® (Pfizer) and Ad26.COV2.S (Janssen). Once again, in the absence of a feasible statistical comparison, these conclusions should only be considered as trends, to be confirmed later, using for example indirect comparisons.

The paper has several limitations, as the previous one [1]: use of data from scientific international publications and not regulatory data packages, impossibility of making strict comparisons between the different vaccines as already mentioned above, no account taken of adverse events or different clinical forms of the disease and lack of reliable CIs NNT. Of course, as in Heath's original publication [2], patients infected with the omicron variant were not included in the study, which was performed from 28 September to November 2020 in the United Kingdom. Moreover, interpretation of subgroup analyses according to age class and ethnic group is limited by (i) the fact that the original study [2] was not powered to detect differences of treatment effects between subgroups (even if they truly exist) and (ii) the absence of interaction tests. Finally, comparisons between different groups are also difficult to interpret because of variations in baseline risk.

In conclusion, the present analysis is a further example of the great interest to include not only RR (which does not take into account baseline risks and tends to exaggerate benefits of treatments especially when basis risk is low) but also other parameters of clinical effectiveness like AR, ARR and NNT. We believe that this request should be relayed to the authors and editors of medical journals because of its medical and economic importance to patients and their doctors, to health and government authorities and to payers.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

JLM and AS designed the study. JLM extracted the data and performed the statistical analysis. JLM, PB and AS analysed the data. JLM wrote the paper. The three authors reviewed the successive versions of the manuscript and approved the final version.

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