Philippine COVID-19 Living Clinical Practice Guidelines
Institute of Clinical Epidemiology, National Institutes of Health, UP Manila
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EVIDENCE SUMMARY

Is rAd26 (Sputnik Light) effective and safe in the prevention of COVID-19 infections?: A Rapid Review

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RECOMMENDATIONS

1. **We suggest the use of the rAd26 (Sputnik Light), given as 10^{11}vp per 0.5ml, single dose, intramuscularly to prevent symptomatic SARS-CoV-2 infection in:**
   a. Healthy adults *(Low certainty, Weak recommendation)*
   b. Older adults (60 years and older) *(Low certainty, Weak recommendation)*
   c. Adults with comorbidities *(Low certainty, Weak recommendation)*

2. **We suggest against the use of rAd26 (Sputnik Light) to prevent symptomatic SARS-CoV-2 infection in:**
   a. Children (3-17 years) *(No evidence, Weak recommendation)*
   b. Pregnant and lactating women *(No evidence, Weak recommendation)*
   c. Immunocompromised *(No evidence, Weak recommendation)*

3. **In areas where Alpha, Beta or Delta is the predominant variant of concern, we suggest the use of rAd26 (Sputnik Light) to prevent COVID-19 infection.** *(Very Low certainty, Weak recommendation)*

Consensus Issues

The Panel was unanimous in all their recommendations. No issues were raised during the meeting.

Key Findings

Five observational studies provided low to very low certainty evidence on the effectiveness and safety of rAd26 (Sputnik Light) against COVID-19 infection. Immunogenicity studies showed that rAd26 induced significant humoral and cellular response against SARS-COV-2 and its variants. Observational studies found rAd26 to provide sufficient protection against COVID-19 infection, hospitalization and death, particularly for the older person and those with comorbidities. Associated adverse events were mostly due to reactogenicity and were mild and transient. No evidence was found on the effect of rAd26 on children, pregnant women and the immunocompromised.

Introduction

A COVID-19 vaccine that is easy to manufacture and administer is needed to address the global supply shortage and hasten wide vaccine coverage. The development of the rAd26 (Sputnik Light), an Ad26-vectored vaccine similar to the first dose of the Gam-COVID-Vac heterologous prime-boost vaccination (rAd26-S + rAd5) was a response to this need. One dose of rAd26 contains 10^{11}vp per 0.5ml and is given intramuscularly. The vaccine is produced as a 5-dose 3 ml vial or a 0.5ml ampule, stored at -18 to -22'C with a shelf life of 10 months.[1]

Review Methods

The search followed the strategy used for all the vaccine reviews in this series. Briefly, this covered Pubmed, living COVID-19 evidence registries including the Living Overview Evidence platform, the COVID-NMA and the Metaevidence.org, the reference list of the WHO Situational reports, the WHO COVID-19 literature on coronavirus disease database and the VIEW-Hub Resource Library.

Results

Search Results

The search performed on October 31, 2021 yielded five studies on the effect of rAd26 (Sputnik Light) for the prevention of COVID-19 disease. All were nonrandomized studies. One is a Phase1/2 open label comparative immunologic study(1), one is a matched cohort population-based study(2), one is a retrospective cohort (3) and two were single cohort self-controlled immunologic studies.(4)(5)

Clinical Efficacy

No randomized controlled trial has been identified providing clinical efficacy data for rAd26 (Sputnik Light).

Real World Evidence: Effectiveness

Two studies provided clinical effectiveness information on rAd26, one of which was in the background of Delta variant predominance.

A matched cohort study demonstrated the protective effect of rAd26 among the older population (aged 60 to 79 years old) in Buenos Aires, Argentina. Matching was based on age and the presence of comorbidities. After an observation period of 21 to 40 days post-vaccination, the vaccine effectiveness of rAd26 for laboratory-confirmed infection was 78.6% (95% CI 74.8-81.7), for hospitalization was 87.6% (95% CI 80.3-92.2), and for mortality was 84.8% (95% CI 75.0-90.7). A subgroup analysis among those with comorbidities showed VE rates for laboratory–confirmed infection was 78.6% (95% CI 73.2-82.8), for hospitalization was 87.1% (95% CI 76.9-92.7), and for death was 87.5 (95% CI 75.9-93.5).[2]

The study providing rAd26 effectiveness against variants is presented below.

Immunogenicity

One open label, prospective non-randomized Phase 1/2 study was identified that provided immunogenicity evidence supporting the use of rAd26 vaccination.[1] The study population included 110 participants with a mean age of 35.4 years, mostly infection naïve (87% seronegative at baseline), without concomitant disease and with "general" (or low) risk of infection. The outcomes of the study included self-reported adverse events (see safety section below), and immunologic parameters at baseline, day 1, day 10 and day 28 post vaccination

including CD3, CD4, CD8, CD16, CD19, CD4/8 cells, total IgM, IgG, IgA, IgE titers, compared with convalescent plasma.

Vaccination increased RBD-specific IgGs as early as day 10 (GMR 69.39), reaching maximal levels on day 28 (GMT 2395) and day 42 (GMT 2285). Seropositivity was 99.07% by day 28 post vaccination. The study noted a difference in the rate of rise in titers between those who were seronegative at baseline (i.e. infection naïve) and those who were seropositive. The seronegative subpopulation's titer started to increase at day 10 and was maximal at day 28. On the other hand, the seropositives demonstrated a significant increase in titers at day 10 and a non-significant decrease at day 28 and day 42 compared with day 10. Compared with the convalescent plasma titers, post-vaccination titers were lower in the seronegative group but higher in the seropositives at all time points. Neutralizing antibody seropositivity rates were 62.7% at day 28 post vaccination and 83.2% at day 42. Titers were 16.25 by day 28 and 24.45 by day 42. Cellular response was studied in 25 seronegative-baseline samples. Results showed that antigen-specific IFN-γ secretion were found in 96% of seronegatives at day 10 after immunization.

Table 2 details the Phase 1/2 study providing immunologic effectiveness and safety data for rAd26.

Similar findings were reported in a single cohort study involving 84 Moscow residents vaccinated with rAd26 and their blood was collected prior to and on days 7 and 21 after vaccination. Immunologic (humoral and cellular) response was robust and immediate on the 7th day in previously infected participants whereas titers peaked at 21 days in the infection naïve. A reduced response to the Delta variant was also shown in this study.[3]

Another single cohort study from Pakistan involving 100 patients showed that there was seroconversion of 85% of participants 21 days after rAd26 administration. High titers (>250AU/ml) were seen in 34.9% of the participants.[4]

Safety

Only one study (the above-mentioned Phase 1/2 open label study) provided the safety data for rAd26 (Sputnik Light). It reported an overall adverse event rate of 67.2% within 28 days after injection, mostly from local and systemic reactogenicity. All reported events were mild to moderate (Grade 1-2). Local adverse events were less common, with pain at injection site being the most common at 5.5%. Systemic adverse event rate was 65.5% with flu-like symptoms being the most common (49.1%). No serious adverse event was reported.[1]

Special Populations

The search failed to identify any study on the effect of rAd26 on children, pregnant women and the immunocompromised.

Effectiveness Against Variants

The effect of rAd26 on the Alpha and Beta variants was reported by one study. It was shown to have minimal decline in effectiveness (in terms of immunogenicity at day 28) against the Alpha (1.11-fold decline) and Beta (1.99-fold decline) variants when compared against the B.1.1.1 strain.[1] No clinical outcomes were available.

A retrospective study done in Russia at the peak of the Delta surge showed high efficacy of rAd26 against the variant in the first three months after vaccination. VE against COVID infection

was established at 69.85% (95% CI 64.08-74.70).[5] In the Russian study mentioned earlier, a 2-fold reduction in neutralizing antibody response was demonstrated against the Delta variant by serum from rAd26 vaccine recipients.[3]

No study was identified on the effect of rAd26 on the Gamma variant.

Table 3 details all the observational studies included in the review. Table 4 presents the risk of bias assessment. Table 5 and 6 presents the summary of findings table.

Booster Vaccination

No study was identified using rAd26 as part of a booster vaccination regimen.

Authorizations

On August 20, 2021, the Philippine FDA granted emergency use authorization to rAd26 (Sputnik Light) for the prevention of COVID-19 infection for persons 18 years and older.[6] As of November 1, 2021, rAd26 (Sputnik Light) received authorization for use in 17 other countries, apart from the Philippines.[7]

Ongoing Trials

As of November 1, 2021, two studies on Sputnik Light are registered in Clinicaltrials.gov. Table 7 presents the details of these studies.

References

[1] Tukhvatulin A, Dolzhikova I, Shcheblakov D, Zubkhova O, Dzharullaeva A. An open, non-randomised, 1/2 phase study on the safety, tolerability, and immunogenicity of single dose “Sputnik Light” Vaccine for Prevention of Coronavirus Infection in healthy adults [Internet]. SSRN. 2021 [cited 2021 Sep 3]. Available from: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3886430

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[4] Saeed U, Uppal S, Pichara Z, Khan A, Rasheed A, Waheed A. Evaluation of SARS-CoV-2 spike antibody levels among Sputnik V first dose vaccinated people in Pakistan: formulation of national anti-COVID-19 mass vaccination strategy [Internet]. Research Square. 2021 [cited 2021 Oct 30]. Available from: https://doi.org/10.21203/rs.3.rs-480406/v1

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[6] Food and Drug Administration Philipines. Emergency Use Authorization (EUA) for Gamaleya National Center of Epidemiology and Microbiology Sputnik Light COVID-19 Vaccine [Internet]. [cited 2021 Sep 5]. Available from: https://www.fda.gov.ph/wp-content/uploads/2021/08/Sputnik-Light-COVID-19-Vaccine.pdf

[7] COVID19 Vaccine Tracker. Gamaleya: Sputnik Light [Internet]. [cited 2021 Nov 1]. Available from: https://covid19.trackvaccines.org/vaccines/126/

Appendix 1. Evidence to Decision

Table 1. Summary of Initial Judgements Prior to Panel Discussion (N = 8)

FACTORS	JUDGEMENT						RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS
Problem	No	Yes (8)					
Benefits	Large (2)	Moderate (5)	Small	Uncertain (1)			• Significant increase in antibody titers from day 28 to day 42, with seropositivity day 28 values reaching 99.7% (RBD-binding antibodies) day 42 values reaching 83.2% (neutralizing antibodies). Minimal decline in immunogenicity at day 28 for Alpha (1.11-fold) and Beta (1.99-fold).
Harm	Large (2)	Small (5)	Uncertain (1)				• Overall adverse event rate of 67.2%, mostly mild to moderate in severity, with local (e.g., pain at injection site) and systemic reactogenicity (e.g., flu-like symptoms). • No serious adverse events reported.
Certainty of evidence	High	Moderate	Low (1)	Very Low (7)			• Very low
Balance of effects	Favors vaccine (7)	Does not favor vaccine (1)	Uncertain				

Values	Important uncertainty or variability	Possibly important uncertainty or variability (4)	Possibly no important uncertainty or variability (3)	No important uncertainty or variability (1)			
Resources required	Uncertain	Large cost	Moderate cost (6)	Negligible cost or savings	Moderate savings (1)	Large savings (1)	• Storage of Sputnik Light is at -18°C to -22°C, requiring the use of freezers. • Sputnik Light (India Rs 700), approximately PHP 470.12.
Certainty of evidence of resources required	No included studies (8)	Very low	Low	Moderate	High		
Cost effectiveness	No included studies (8)	Favors the comparison	Does not favor either the intervention or the comparison	Favors the intervention			
Equity	Uncertain (8)	Reduced	Probably no impact	Increased			• Addresses wide disparity in vaccine coverage: 85.1% fully-vaccinated senior citizens in NCR; only 28.3% in BARMM
Acceptability	Uncertain (1)	No	Yes (7)				• Sputnik Light was given EUA by the Philippine FDA on August 20, 2021.
Feasibility	Uncertain	No	Yes (8)				

Appendix 2. Characteristics and results of the Phase 1/2 study on rAd26 (Sputnik Light)

Parameter	Description
Data Source	Preprint article: Tukhvatulin 2021 (SSRN) Clinical trial protocol registration: NCT04713488
Population	- N=110 (30 included in IFN-γ and 30 in T cell proliferation analysis) - Females 50% - Mean (SD) age: 35.4 (14.84) - Age >= 60 = 16% - All white ethnicity - Risk of infection: 93% general, 7% medium - Concomitant disease: 92.5% none - Dropouts: 2 withdrew consent, 1 missed day 42 assessment Exclusions: - history of COVID-19 or prior contact with patients with COVID-19 within 14 days of participation - receipt of any other vaccines within 30 days - therapy with steroids, immunoglobulins, other blood-derived products within 30 days - intake of immunosuppressive drugs for more than 3 months - allergy to immunobiological preparations including any vaccine component
Intervention	rAd26 at 10^{11}vp per 0.5ml, single dose, intramuscular (storage: -18 to -22'C, shelf life 10 months, 5-dose 3ml vial or 0.5ml amp)
Control	none
Outcomes	Blood chemistries/Lab results at 0 and 28 days Immune parameters (at 0,1 day, 10 days, 28 days post vaccination): - absolute and relative numbers of CD3, CD4, CD8, CD16, CD19, CD4/8 cells, total IgM, IgG, IgA, IgE - Change from baseline of IgG at 10 days, 28 days, 42 days, 90 days, and 180 days) - Neutralizing antibody response (day 1, day 28, day 42, microneutralization assay) - Cell-mediated immune response at day 1, day 10: CD4+ and CD8+ T cells, quantity of interferon-gamma producing cells (day 10) Self-reported adverse events (at day 10, day 28 and day 42 post vaccination)
Methods	Open label, prospective Comparative study for immunologic response versus plasma taken from convalescent donors Immune tests used: - ELISA for IgG and IgG - Microneutralization assay for neutralizing antibody - Flow cytometry by IFN-gamma release of PBMCs using ELIS and ELISpot methods

	Timing of blood extractions: 0, 28 and 42 days Safety and reactogenicity up to day 28
Risk of Bias Assessment	Observational study Unclear sampling, with missing data, no control of confounders Overall certainty: LOW
Results: Safety	reported up to 28 days post vaccination: - any AE: 74 (67.2%), all Grade 1and 2 - pain in injection site: 6 (5.5%) - redness: 1 (0.9%) - systemic AE: 72 (65.5%) - flu-like symptoms: 54 (49.1%) - fatigue: 6 (5.5%) - headache: 5 (4.5%) - no serious adverse events reported
Results: Immunologic	RBD specific IgG (mean titers): - seronegative: start of increase at day 10 and maximal at day 28 - seropositive: significant increase at day 10 and non-significant decrease at day 28 and day 42 compared with day 10 titers In comparison with convalescent plasma, post-vaccination titers were lower in the seronegatives but higher in the seropositives at all timepoints RBD specific IgG (seropositivity): 99.07% by day 28 for all (seronegative and seropositive) Neutralizing antibody seroconversion: day 28=62.7%, day 42=83.2% Versus Alpha and Beta (N=96), vs B.1.1.1 strain - versus Alpha: 1.11-fold reduction in Nab titers - versus Beta: 1.99-fold reduction Cellular immune response: - IFN-g positivity 96% at day 10 with median 554.3 spots per 1 million - Antigen-specific IFN-γ secretion 96% positive rAd26 neutralizing GMT: increased from 18.2 to 782.9 at day 28

Appendix 3. Characteristics and Results of Real World Evidence on rAd26 (Sputnik Light)

Study ID	Design	Population	Intervention / Comparator	Outcomes/Results
Gonzales (Argentina)	Matched cohort Matched by age, gender, comorbidities	older adults (60 to 79 years old)	rAd26 vaccinated: 60-69: 12195 70-79: 28192 Unvaccinated: 60-69: 12345 (matched) 70-79: 26633	VE (95% CI) After 40 days of monitoring VE for lab-confirmed infection - Overall: 78.6 (74.8-81.7) - 60-69y/o: 82.9 (77.9-86.8) - 70-79y/o: 74.7 (69.0-79.4) - with comorbidity: 78.6 (73.2-82.8) VE for hospitalization - overall: 87.6 (80.3-92.2) - 60-69y/o: 86.3 (65.2-94.6) - 70-79y/o: 88.3 (80.0-93.1) - with comorbidity: 87.1 (76.9-92.7) VE for death: - overall: 84.8 (75.0-90.7) - 60-69y/o: 87.3 (58.0-96.2) - 70-79y/o: 85.1 (75.5 – 95.5) - with comorbidity: 87.5 (75.9-93.5)
Dolzhikova (Russia)	Retrospective cohort (linked databases) / Case-control Study performed at the time of Delta variant predominance No adjustments mentioned, VEs presented by age bands	General population, at least 18 years old	rAd26 vaccinated Unvaccinated, with no prior infection	VE (95% CI) Overall: 69.85 (64.08-74.70) Vaccinated: 126: 28322 (Dis/No Dis) Unvaccinated: 82196: 5569885 (Dis/No Dis) 18-59 y/o: 75.28 (69.24-80.13) 60+ y/o: 51.98 (35.61-64.19)

Saeed (Pakistan)	Single cohort	100 adults	rAd26 vaccination	21 days post vaccination anti-spike IgG seroconversion (>1.5 AU/ml): 85% >250AU/ml: 34.9% > 100AU/ml: 12.7% >25 AU/ml: 9.5% >1.5 – 2.5: 27%
Komissarov (Russia)	Single cohort	84 Moscow residents	Pre-vaccination antibody and T-cell response levels	Pre vaccination / day 7 / day 21 Anti-RBD IgG (seropositive rate) 52.4% / 57.1%, 100% * described 3 types of response: (1) no increase on day 7 but elevated at day 21 (2) immediate rise on day 7 with further increase at day 21 (3) minimal change throughout Virus neutralizing activity vs B.1.1.1 and B.1.617.2 strains 2-fold reduction in VNA vs delta compared with B.1.1.1 strain IFN-gamma ELISpot (T-cell response specific to S-protein) 36.1% / 86.6% / 96.4%

Appendix 4. Risk of Bias Assessment of Included Studies

Study ID	Design	Randomization	Allocation Concealment	Blinding Particip	Blinding Carer/ Assessor	Followup	Selective Reporting	Others	Age	Comorbidities	Exposure	Confounding	OVERALL
Tukhvatulin (Russia)	Prospective single cohort	HIGH	HIGH	HIGH	HIGH	HIGH	UNCLEAR	NA	HIGH	HIGH	HIGH	HIGH	SERIOUS
Gonzales (Argentina)	Matched cohort	HIGH	HIGH	HIGH	HIGH	HIGH	UNCLEAR	NA	LOW	LOW	UNCLEAR	LOW	SERIOUS
Dolzhikova (Russia)	Retro cohort	HIGH	HIGH	HIGH	HIGH	HIGH	UNCLEAR	NA	LOW	HIGH	HIGH	HIGH	SERIOUS
Saeed (Pakistan)	Single cohort	HIGH	HIGH	HIGH	HIGH	LOW	UNCLEAR	NA	HIGH	HIGH	HIGH	HIGH	SERIOUS
Komissarov (Russia)	Single cohort	HIGH	HIGH	HIGH	HIGH	LOW	UNCLEAR	NA	HIGH	HIGH	HIGH	HIGH	SERIOUS

Appendix 5. Summary of Findings Table on the Efficacy of rAd26 (Sputnik Light)

Efficacy Outcome		Quality Assessment					Summary of Findings			Certainty
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Overall Assessment	Vaccine n/N (%)	Control n/N (%)	Vaccine Efficacy (CI)	
1: Symptomatic COVID-19 infection	1 OBS	Serious (observational)	Not assessed	Not assessed	Not assessed	Serious	na	na	69.8% (64.1-74.7)	++ Low
2: Severe COVID-19 infection	1 OBS	Serious (observational)	Not assessed	Not serious	Not serious	Serious	na	na	87.6% (80.3-92.2)	++ Low
3. Asymptomatic COVID-19 infection	na	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	na	na	na	na
4. Any COVID-19 infection	1 OBS	Serious (observational)	Not assessed	Not serious	Not serious	Serious	na	na	78.6 % (74.8-81.9)	++ Low
5. Symptomatic COVID-19 infection after first dose, before the second dose	na	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	na	na	na	na
6. Death from COVID-19 infection	1 OBS	Serious (observational)	Not assessed	Not serious	Not serious	Serious	na	na	84.8% (75.0-90.7)	na
7. Symptomatic COVID-19 infection, older adults (>=60yo)	2 OBS	Serious (observational)	Not serious	Not serious	Not serious	Serious	na	na	78.6 % (74.8-81.9) 52% *(Delta)* (35.6-64.2)	++ Low
8. Symptomatic COVID-19 infection, with pre-existing	1 OBS	Serious (observation	Not assessed	Not serious	Not serious	Serious	na	na	78.6% (73.2-82.8)	++ Low

medical condition		al)								
9. Symptomatic COVID-91 infection, children (<18yo)	na	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	na	na	na	na
10. Any COVID-19 infection, B.1.1.7/Alpha variant	1 OBS	Serious (observational)	Not assessed	Serious (Immuno)	Not assessed	Very Serious	1.11-fold reduction in neutralizing antibody titers			+ Very Low
Efficacy Outcome		**Quality Assessment**					**Summary of Findings**			**Certainty**
		Risk of Bias	**Inconsistency**	**Indirectness**	**Imprecision**	**Overall Assessment**	**Vaccine n/N (%)**	**Control n/N (%)**	**Vaccine Efficacy (CI)**	
11. Any COVID-19 infection, B.1.151/Beta variant	1 OBS	Serious (observational)	Not assessed	Serious (Immuno)	Not assessed	Very serious	1.99-fold reduction in neutralizing antibody titers			++ Very Low
12. Any COVID-19 infection, B.167.2/Delta lineage	1 OBS	Serious (observational)	Not assessed	Not serious	Not assessed	Serious	126: 28322 (Dis/No Dis)	82196: 5569885 (Dis/No Dis)	69.85 (64.08-74.70)	++ Low

Appendix 6. Summary of Findings Table on the Safety of rAd26 (Sputnik Light)

Safety Outcome		Quality Assessment					Summary of Findings			Certainty
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Overall Assessment	Vaccine	Control	Relative Risk (95%CI)	
1: Solicited adverse reaction	1 OBS	Serious (observational)	Not reported	Not reported	Not reported	Serious	67.2%	na	na	++ Low
2: Local adverse reaction	1 OBS	Serious (observational)	Not serious	Not serious	Not serious	Serious	5.5%	na	na	++ Low
3: Systemic adverse reaction	1 OBS	Serious (observational)	Not serious	Not serious	Not serious	Serious	65.5%	Na	Na	++ Low
4. Unsolicited adverse event (28d)	na	Not reported	Not serious	Not serious	Not serious	Not reported	na	na	na	na
5: Serious adverse event	1 OBS	Serious (short ffup)	Not serious	Not serious	Serious (no event)	Very serious	0%			+ Very Low
6: Related serious adverse event (All medically attended adverse events (MAAEs)	na	Not reported	Not reported	Not reported	Not reported	Not reported	na	na	na	na
7: Withdrawals due to adverse event	na	Not reported	Not reported	Not reported	Not reported	Not reported	na	na	na	na
8: Death	na	Not reported	Not reported	Not reported	Not reported	Not reported	na	na	na	na

Appendix 7. Trials on Sputnik Light registered in Clinicaltrials.gov as of November 1, 2021

NCT Number	Title	Status	Outcome Measures	Sponsor/Collaborators	Phases	Completion Date
NCT04741061	Study to Evaluate Efficacy, Immunogenicity and Safety of the Sputnik-Light	Recruiting	Incidence and severity of adverse events in study subjects | Percentage of study subjects with COVID-19 cases developed after vaccination | Humoral immunogenicity (Quantitative IgG antibodies to SARS-CoV-2 S Protein) | Humoral immunogenicity (IgG SARS-CoV-2 N-antibodies)	Gamaleya Research Institute of Epidemiology and Microbiology, Health Ministry of the Russian Federation | Russian Direct Investment Fund | CRO: iPharma | Government of the city of Moscow	Phase 3	31-Jan-22
NCT04713488	An Open Study on the Safety, Tolerability, and Immunogenicity of "Sputnik Light" Vaccine	Active, not recruiting	Changing of antibody levels against the SARS-CoV-2 glycoprotein S | Number of Participants With Adverse Events | Changing of virus neutralizing antibody titer | Changing of antigen-specific cellular immunity level	Gamaleya Research Institute of Epidemiology and Microbiology, Health Ministry of the Russian Federation | Russian Direct Investment Fund	Phase 1 Phase 2	31-Jul-21