Journal Club at the Laboratory of Clinical Psychopharmacology of Addictions (LCPA) is a monthly gathering to discuss research papers with a focus on addiction.

Mission: to promote a better understanding of the research process and an improve ability to critically appraise research in addiction and related diseases (e.g. infectious, mental health, etc.).

Discussion topics and learning objectives include (but not limited by) the concepts of addiction, terminology used in the field, socio-cultural and biological risk factors, contemporary public health issues and policies, prevention, treatment and treatment systems.

Values:

- Learning
- Respect
- Collaboration
- Multidisciplinary
- Excellence

Please be open, flexible, realistic, and understanding!

Housekeeping notes

Video-recording

The meeting will be entirely video-recording and published on the Pavlov University website and YouTube, so if you wish not be in the recorded video, please make sure that your webcam off during the meeting.

Q&A

The seminar is interactive and we strongly encourage you to actively ask questions during the presentation but keep in mind that we have dedicated time at the end of the webinar (10 minutes) to group discussion and Q&A. Please raise your hand if you have any questions or comment. You also may use chat option to post your questions or comments.

Mic and Video

Please keep your mic mute during entire meeting unless you want to make a question or comment. We recommend keeping your camera on during the meeting.

Post-meeting survey

After the meeting we would like to send you the survey. Please make sure that we have your email.

Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia

Ekaterina Protsenko, 5-year medical student

1й Мед

ФГБОУ ВО ПСПбГМУ им. Павлова Минздрава России

PROBLEM

- Despite the large global effort to develop vaccine for protection against COVID-19, there is still no available approved COVID-19 vaccine.

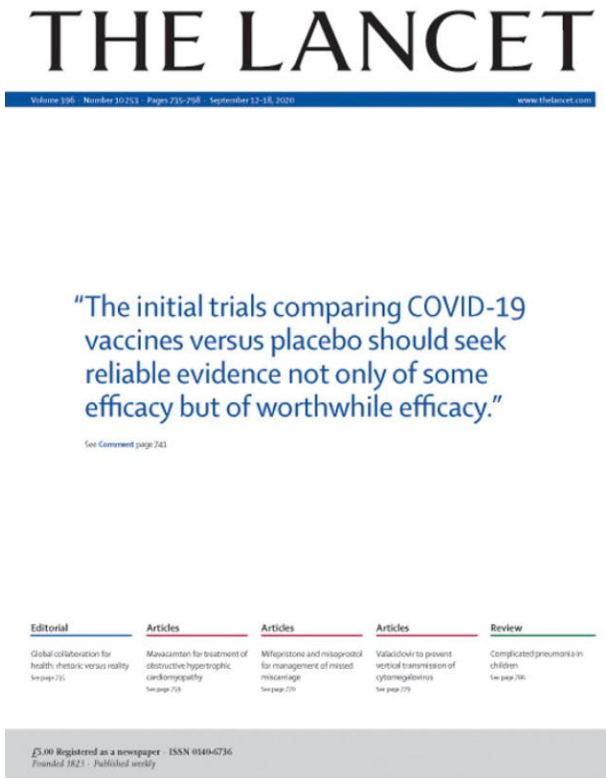
- Why it is important?

As of Aug 15, 2020 > 21 million laboratory-confirmed COVID-19 cases
>750 000 related deaths

Vaccination could restrict the spread of COVID-19, reduce mortality and decrease economical and social adverse consequences

Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia

Denis Y Logunov*, Inna V Dolzhikova*, Olga V Zubkova, Amir I Tukhvatullin, Dmitry V Shcheblyakov, Alina S Dzharullaeva, Daria M Grousova, Alina S Erokhova, Anna V Kovyrshina, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Nadezhda L Lubenets, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Lola F Morozova, Elena A Smolyarchuk, Evgeny V Kryukov, Vladimir F Babira, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg



Published: September 04, 2020

Impact Factor:* 60.4
*2019

STUDY OBJECTIVE

- To assess safety and immunogenicity of the new heterologous adenoviral vector-based vaccine (in two formulations)
- to compare the formed humoral immune response with that recorded in people who have recovered from COVID-19

STUDIES DESIGN

- Open, phase 1/2, non-randomised

- Studies sites: 1 - Burdenko Hospital, Moscow
  2 - Sechenov University, Moscow

PARTICIPANTS

Inclusion criteria

- 18-60 years old
- BMI of 18,5-30 kg/m^2
- negative PCR and negative IgG and IgM to SARS-CoV-2
- with no history of COVID-19 or contact with patients with COVID-19
- no infectious diseases at the time of vaccination and for 14 days before vaccination
- did not receive any other vaccinations within 30 days of participation in the study

PARTICIPANTS

Non-inclusion criteria

- volunteer involvement in another study over the last 90 days
- respiratory symptoms in the last 14 days;
- the administration of immunoglobulins or other blood products in the last 3 months;
- regular current or past use of narcotic drugs;
- subject has received immunosuppressive and/or immunomodulating agents within 6 months before the start of the study;
- pregnancy or breast feeding;
- exacerbation of allergic diseases at the time of vaccination;
- subject has systolic blood pressure less than 100 mm Hg or greater than 139 mm Hg; diastolic blood pressure less than 60 mm Hg or greater than 90 mm Hg; heart rate lower than 60 beats per minute or above 100 beats per minute;
- a burdened allergic history;
- a history of autoimmune diseases in the volunteer's medical history and in relatives' medical history of the 1-2 degree of kinship;
- subject smokes more than 10 cigarettes per day;
- alcohol intake exceeding the low-risk level: no more than 20 grams of pure alcohol per day, no more than 5 days a week, alcohol intake within 48 hours before the administration of the drug;
- planned hospitalization and/or surgery during the period of participation in the study, as well as 4 weeks before the expected date of the administration of the drug;
- the presence of an associated disease that may affect the assessment of the results of the study;
- any conditions that, according to the researcher's doctor, may be a contraindication to the participation in the study.

STUDIED VACCINES

1 Heterologous vaccine:

viral vectors	**antigen**
Recombinant adenovirus type 26 +	gene for SARS-Cov-2 full-length glycoprotein S
Recombinant adenovirus type 5 +	gene for SARS-Cov-2 full-length glycoprotein S

2 formulations

- frozen ***Gam-COVID-Vac***
- lyophilized ***Gam-COVID-Vac-Lyo***

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ADENOVIRAL VECTORS

- Recombinant adenovirus vectors have been used for a long time with safety confirmed in clinical studies of various preventive and therapeutic drugs.[1-3]

1. Wold WS, Toth K. Adenovirus vectors for gene therapy, vaccination and cancer gene therapy. *Curr Gene Ther* 2013; **13:** 421–33
2. Zhang WW, Li L, Li D, et al. The first approved gene therapy product for cancer Ad-p53 (Gendicine): 12 years in the clinic. *Hum Gene Ther* 2018; **29:** 160–79.
3. Zhang C, Zhou D. Adenoviral vector-based strategies against infectious disease and cancer. Hum Vaccin Immunother 2016;**12:** 2064–74.

PRIME-BOOSTING VACCINATION -

one of the standard approaches to vaccination regimen (i.e. HBV-vaccine schedule 0-1-6)

Heterologous prime-boost immunization – boosting via two different vectors, in order to overcome cross-immunity reaction

STUDIED VACCINES

Developed, produced and manufactured according to *Good Manufacture Practice*

- A full dose of the vaccine was 10^{11} viral particles per dose for both recombinant adenoviruses, all participants received full doses; the dose was set based on findings of preclinical studies (data unpublished)

- Both vaccine formulations were administered intramuscularly into the deltoid muscle

COMPARISON GROUP

- ***4817 people*** who had recovered from COVID-19 in Moscow (March 29 - Aug 11, 2020) - convalescent plasma samples were collected

- **The average time from recovery to plasma collection was about 1 month**
- People with mild (fever ≤39 without pneumonia) or moderate (fever >39 with pneumonia) disease severity were included

PRIMARY OUTCOMES

for safety:

number of participants with adverse events

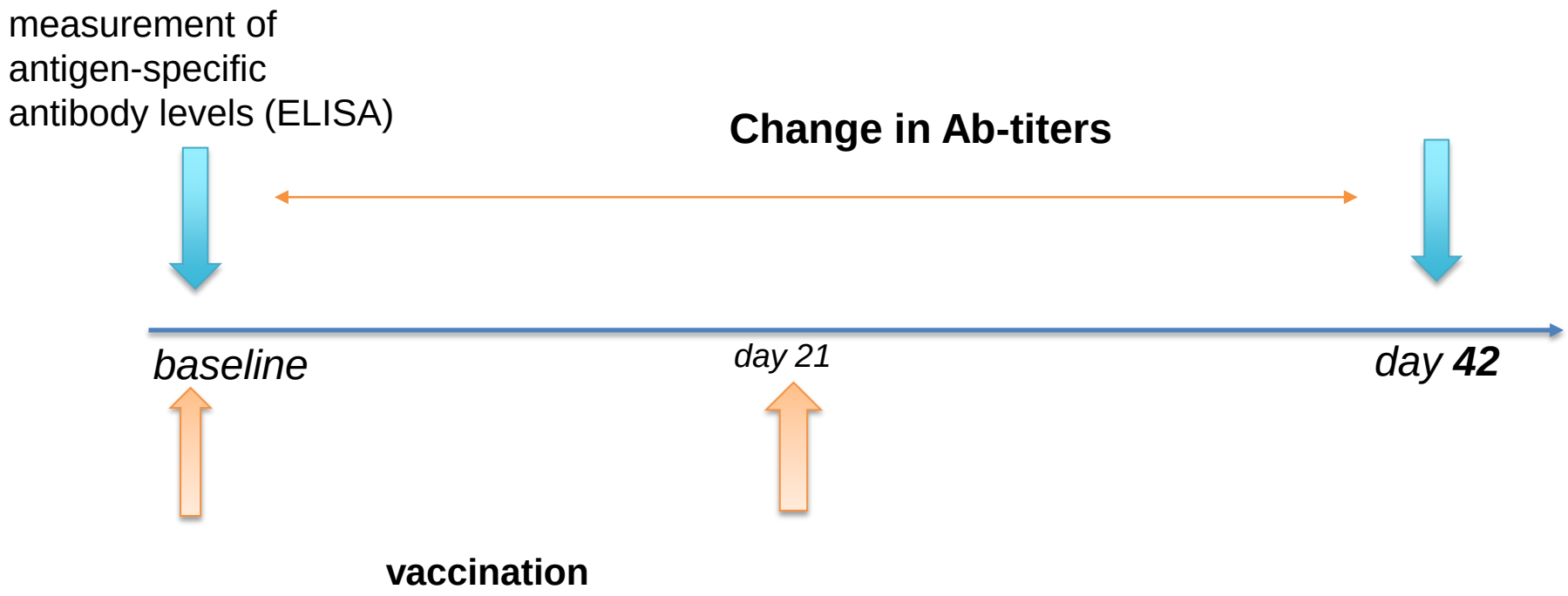
phase 1 *(n=9)*
from day 0 to 28

phase 2 *(n=20)*
from day 0 to 42

- Adverse events were registered daily

PRIMARY OUTCOMES

for immunogenicity:

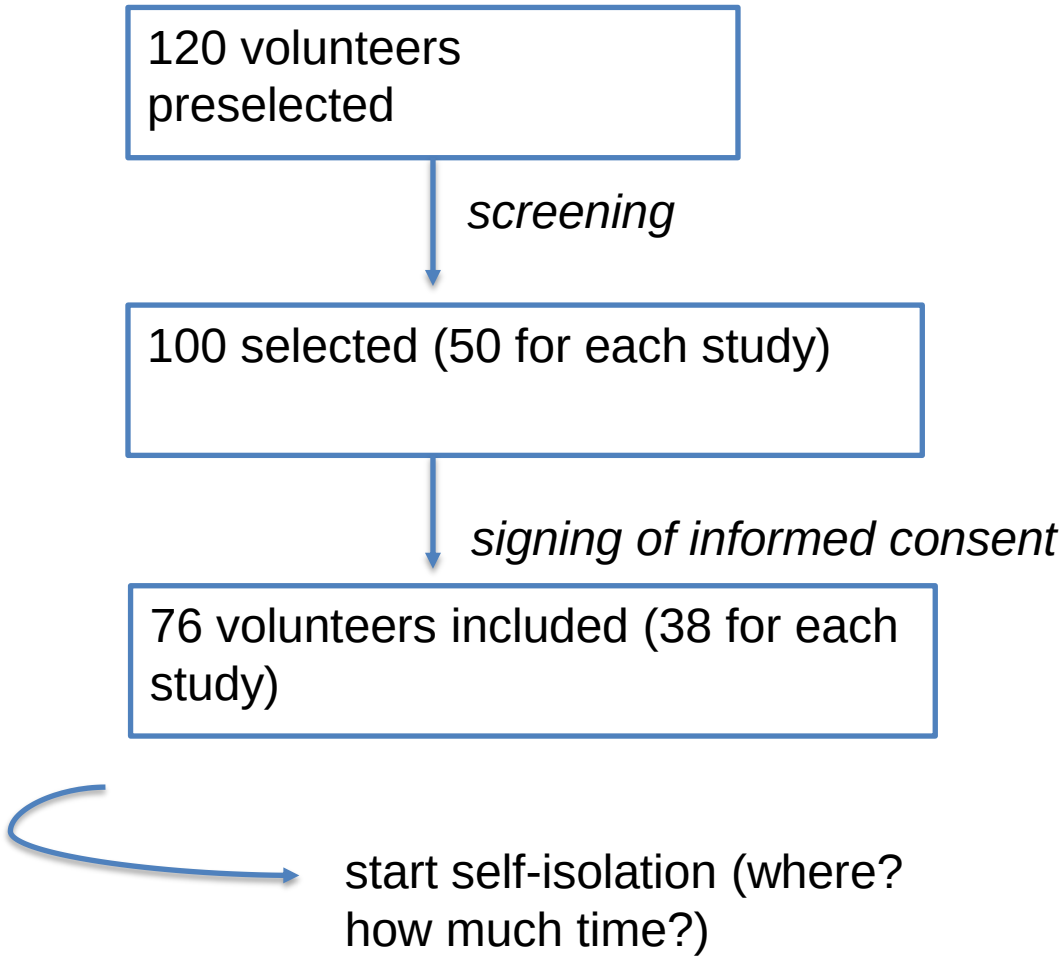


SECONDARY OUTCOMES

1. **virus neutralizing antibody titers** (on days 0, 14, and 28 after vaccination in phase 1 and on days 0, 14, 28, and 42 after vaccination in phase 2)

2. determination of **antigen-specific cellular immunity** (specific T-cell immunity and interferon-γ production or lymphoproliferation) on days 0, 14, and 28 after vaccination

STUDY FLOW



STUDY PROFILE

*28 days after vaccination were in-patient

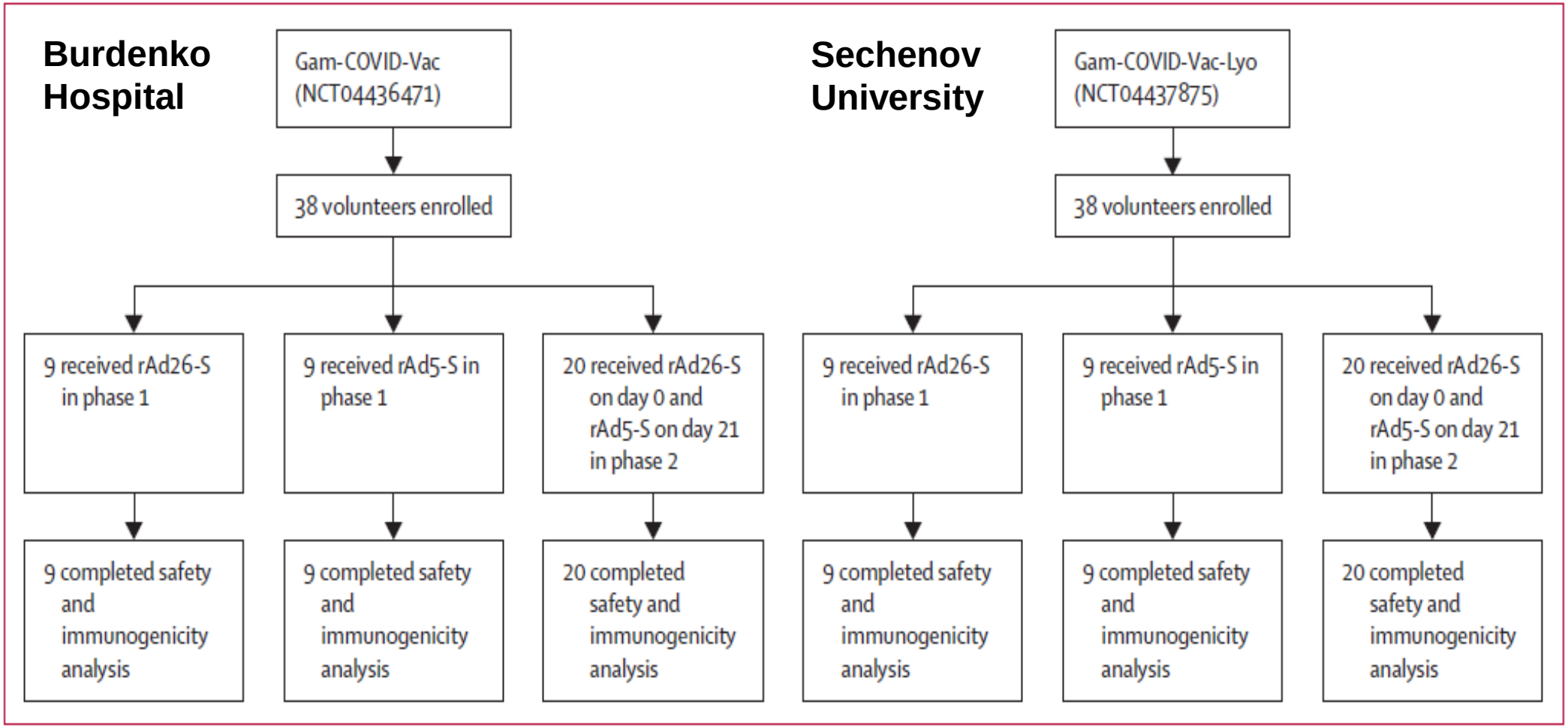
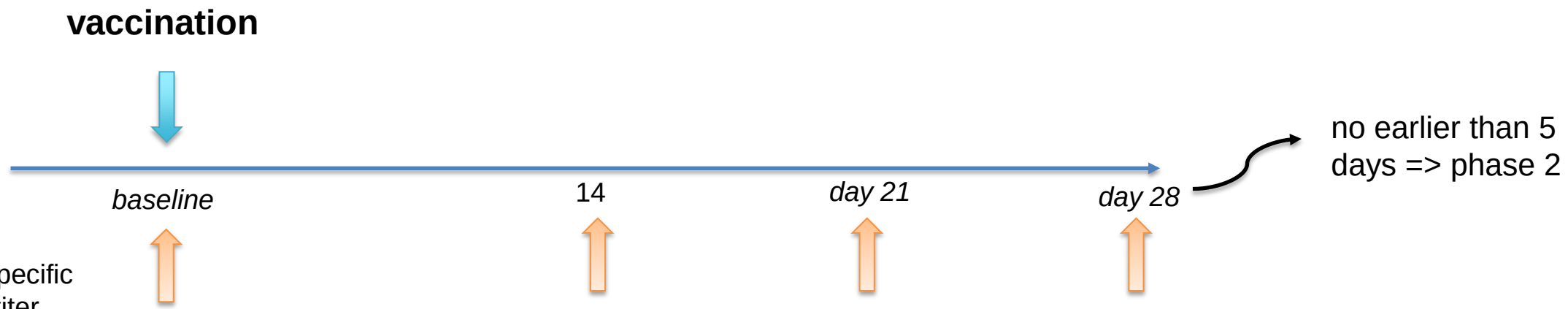


Figure 1: Trial profile

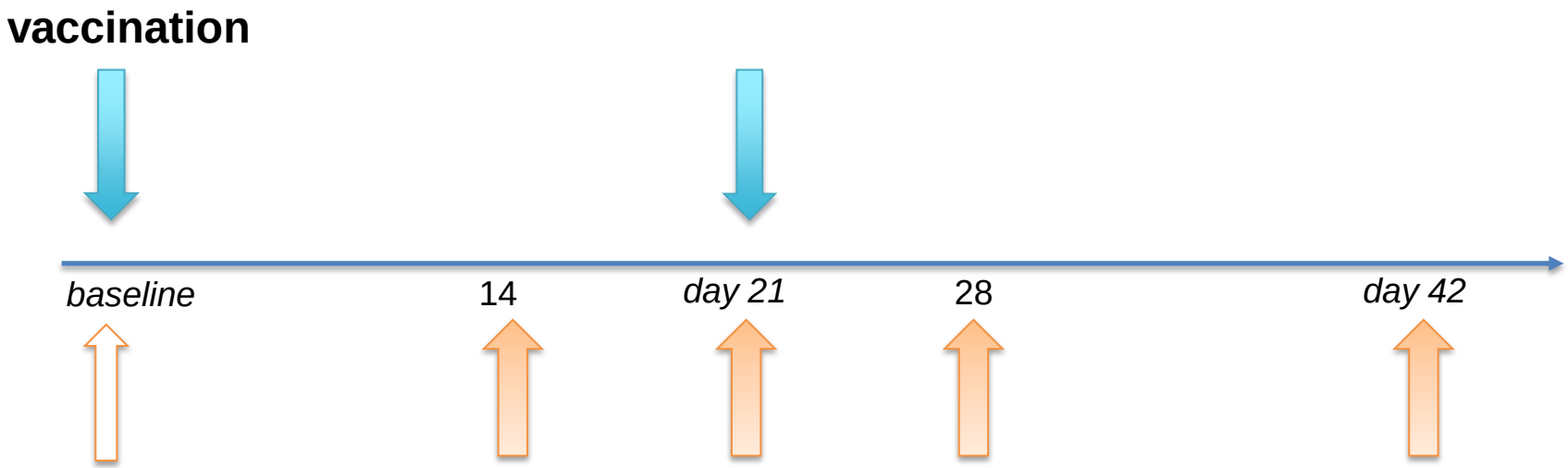
STUDY FLOW. PHASE 1



- antigen-specific antibody titer
- neutralizing antibody titer
- cell-mediated immunity

adverse events daily

STUDY FLOW. PHASE 2



- **antigen-specific antibody titer**
- **neutralizing antibody titer**
- **cell-mediated immunity**

+ adverse events daily

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RESULTS. participants characteristics

	Gam-COVID-Vac			Gam-COVID-Vac-Lyo		
	rAd26-S (n=9)	rAd5-S (n=9)	rAd26-S plus rAd5-S (n=20)	rAd26-S (n=9)	rAd5-S (n=9)	rAd26-S plus rAd5-S (n=20)
Sex						
Male	9 (100%)	9 (100%)	14 (70%)	5 (56%)	2 (22%)	14 (70%)
Female	0	0	6 (30%)	4 (44%)	7 (78%)	6 (30%)
Height, m	1·8 (0·1)	1·8 (0·1)	1·7 (0·1)	1·7 (0·1)	1·7 (0·1)	1·8 (0·1)
Bodyweight, kg	80·6 (6·0)	83·4 (13·8)	74·6 (12·5)	72·1 (13·1)	65·8 (9·4)	72·0 (12·6)
Age, years	27·8 (5·1)	25·3 (6·1)	26·4 (4·4)	31·4 (8·2)	27·0 (7·7)	26·7 (5·8)
Ethnicity						
White	9 (100%)	9 (100%)	20 (100%)	8 (89%)	9 (100%)	19 (95%)
Asian	0	0	0	1 (11%)	0	1 (5%)
SARS-CoV-2 IgM and IgG negative	9 (100%)	9 (100%)	20 (100%)	9 (100%)	9 (100%)	20 (100%)

Data are n (%) or mean (SD). Gam-COVID-Vac=frozen vaccine formulation. Gam-COVID-Vac-Lyo=lyophilised vaccine formulation. rAd26-S=recombinant adenovirus type 26 carrying the gene for SARS-CoV-2 full-length glycoprotein S. rAd5-S=recombinant adenovirus type 5 carrying the gene for SARS-CoV-2 full-length glycoprotein S. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

Table 1: **Baseline characteristics**

ARE THE RESULTS OF THE STUDY VALID?

- Is the study sample homogeneous?
- What are characteristics of the comparison group?
- Is the choice of the primary outcome justified?
- Is the time interval between administration of prime and boost components optimal?

RESULTS: SAFETY

- Most common systemic and local reactions were:

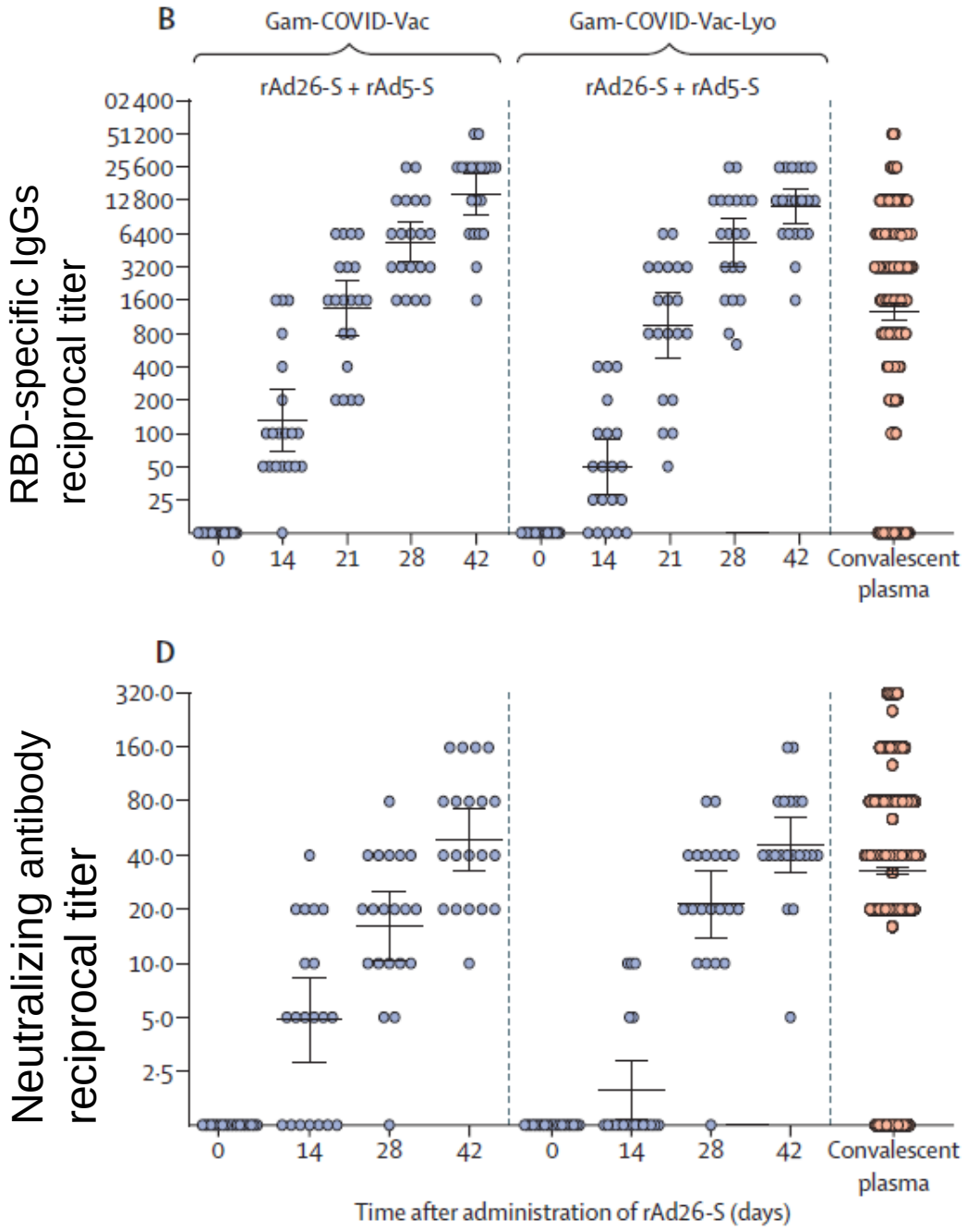
  pain at injection site (44 [58%])
  hyperthermia (38 [50%])
  headache (32 [42%])
  asthenia (21 [28%])
  muscle and joint pain (18 [24%])

- In volunteers who received both vaccine components (rAd26-S and rAd5-S), most adverse events occurred after the second vaccination.
- No serious adverse events were reported and all participants were clinically well throughout the study.

- In general, adverse events identified during phase 1 and phase 2 of both studies are typical for most vaccines (particularly those based on recombinant viral vectors).

RESULTS: IMMUNOGENICITY

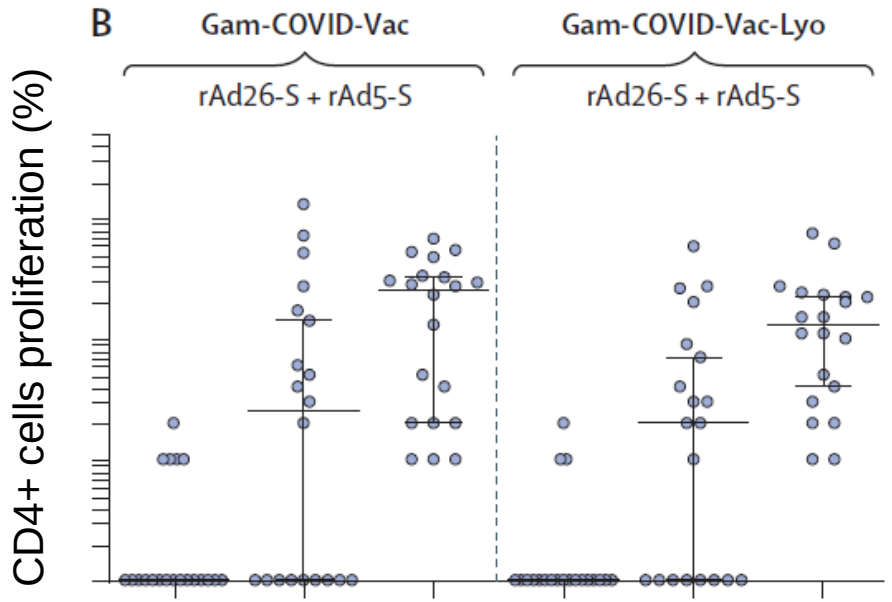
Humoral immunity

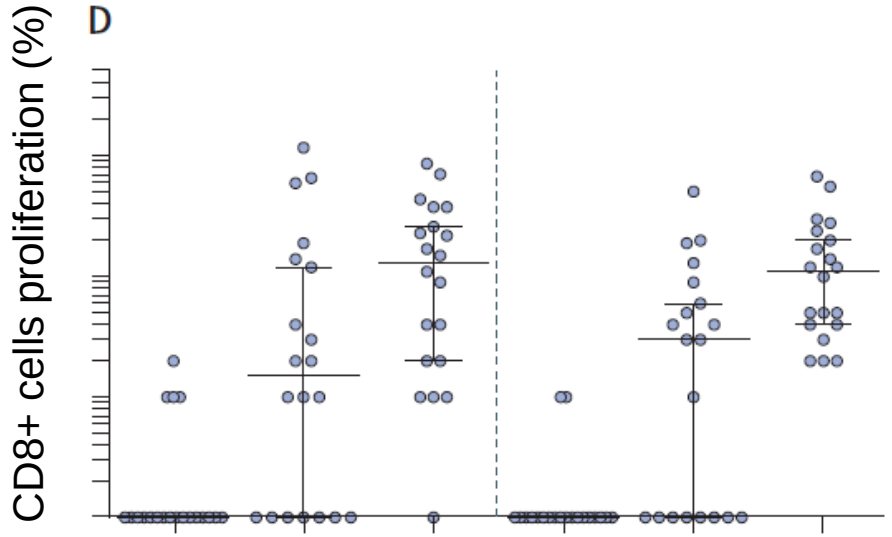


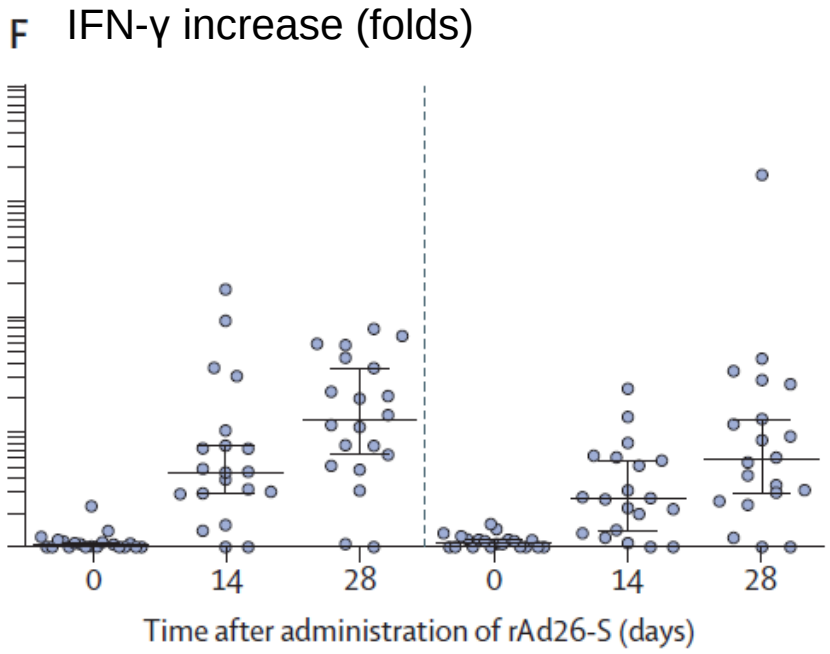
significant difference (p<0.001) on days 28,42

no significant difference

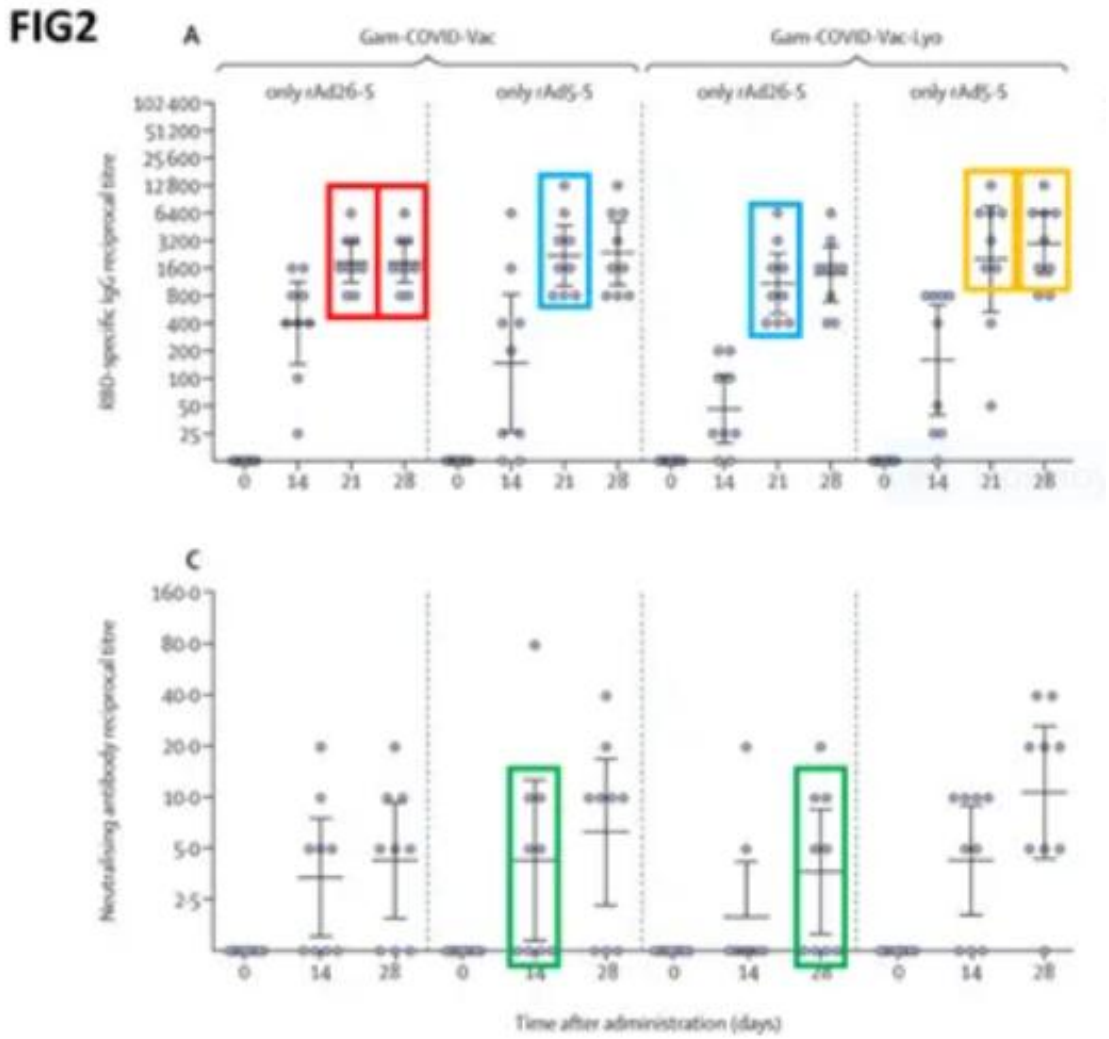
Cellular immunity







ARE THE RESULTS OF THE STUDY VALID?



*From **"Open letter to DY Logunov et al.":** https://cattiviscienziati.com/2020/09/07/note-of-concern/*

Published September, 7

Authors pay attention to many cases of data duplication, which they marked in color boxes

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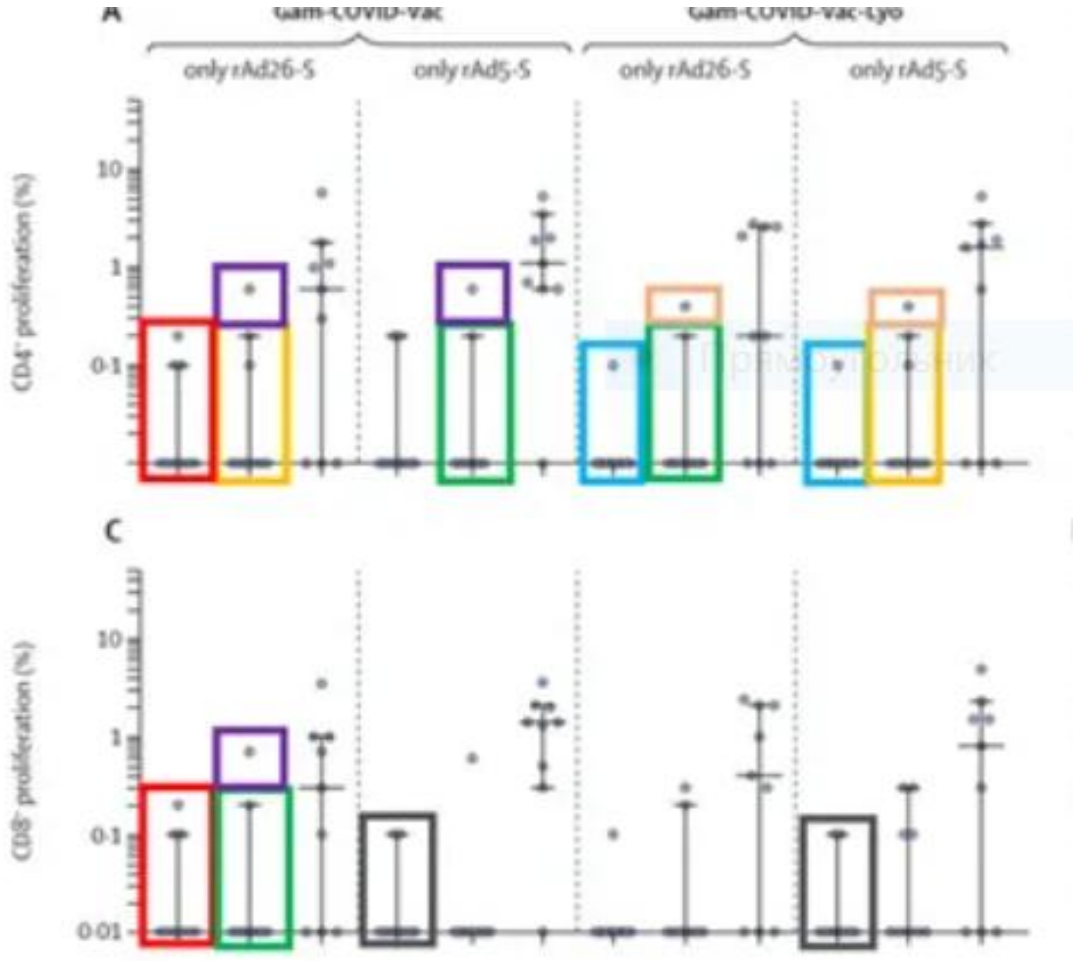
ARE THE RESULTS OF THE STUDY VALID?

FIG3



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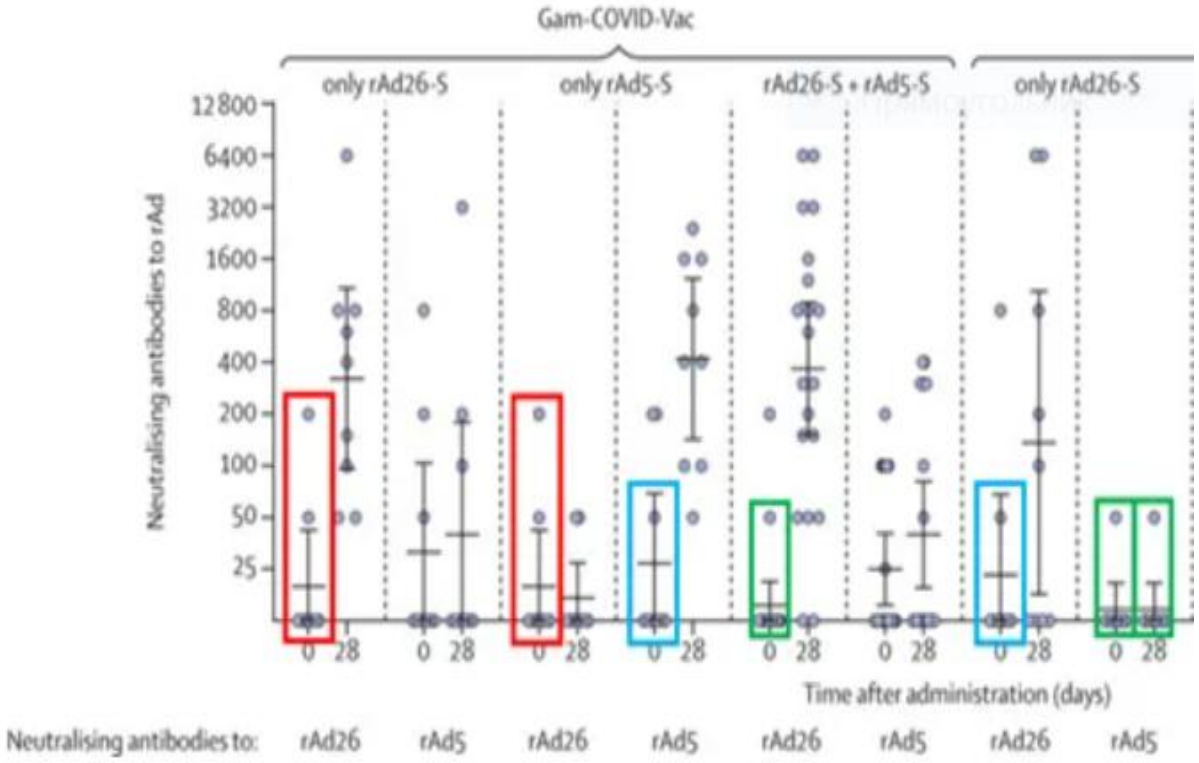
ARE THE RESULTS OF STUDY VALID?



also:

- Why authors didn’t compare cell immunity characteristics with convalescents?
- Why results of ELISA looks like categorical variable?

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LIMITATIONS

- Short follow-up period
- Little sample
- Only man in Gam-COVID-Vac phase 1
- Fairly young sample
- No control/compare vaccine

SUMMARY

- What do you think about results of these study?