Tocilizumab, Sarilumab, Bamlanivimab, Etesenimab Sputnik V

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¡Al fin, fase 3 de la Vacuna Rusa!

Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia

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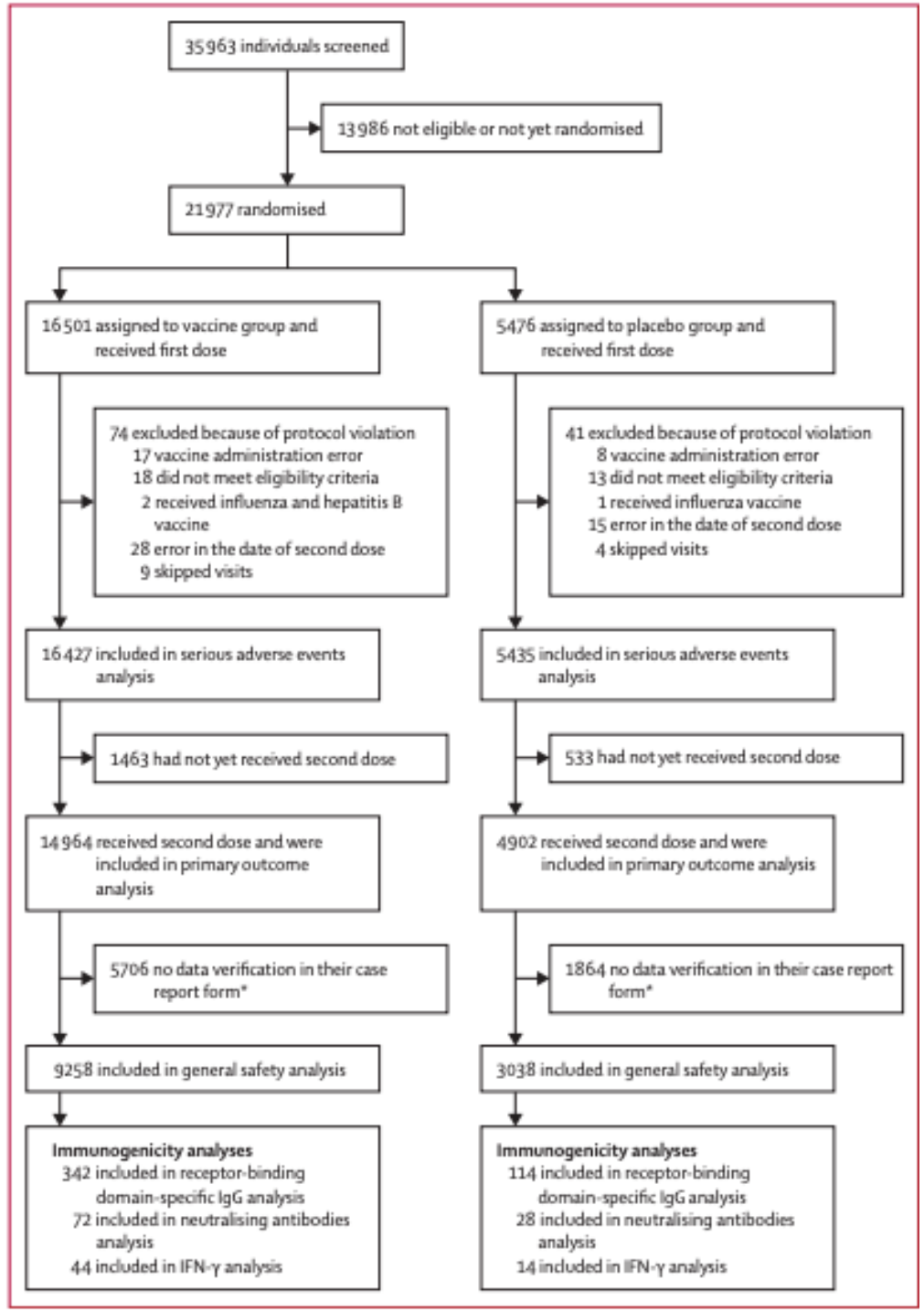

35 963 individuals screened
13 986 not eligible or not yet randomised
21 977 randomised
16 501 assigned to vaccine group and received first dose
5476 assigned to placebo group and received first dose
74 excluded because of protocol violation
17 vaccine administration error
18 did not meet eligibility criteria
2 received influenza and hepatitis B vaccine
28 error in the date of second dose
9 skipped visits
41 excluded because of protocol violation
8 vaccine administration error
13 did not meet eligibility criteria
1 received influenza vaccine
15 error in the date of second dose
4 skipped visits
16 427 included in serious adverse events analysis
5435 included in serious adverse events analysis
1463 had not yet received second dose
533 had not yet received second dose
14 964 received second dose and were included in primary outcome analysis
4902 received second dose and were included in primary outcome analysis
5706 no data verification in their case report form*
1864 no data verification in their case report form*
9258 included in general safety analysis
3038 included in general safety analysis
Immunogenicity analyses
342 included in receptor-binding domain-specific IgG analysis
72 included in neutralising antibodies analysis
44 included in IFN-γ analysis
Immunogenicity analyses
114 included in receptor-binding domain-specific IgG analysis
28 included in neutralising antibodies analysis
14 included in IFN-γ analysis

	Vaccine (n=14 964)	Placebo (n=4902)
Sex		
Female	5821 (38·9%)	1887 (38·5%)
Male	9143 (61·1%)	3015 (61·5%)
Race		
White	14741 (98·5%)	4830 (98·5%)
Asian	217 (1·5%)	69 (1·4%)
Other*	6 (<0·1%)	3 (<0·1%)
Age group, years		
18–30	1596 (10·7%)	521 (10·6%)
31–40	3848 (25·7%)	1259 (25·7%)
41–50	4399 (29·4%)	1443 (29·4%)
51–60	3510 (23·5%)	1146 (23·4%)
>60	1611 (10·8%)	533 (10·9%)
Age, years	45·3 (12·0)	45·3 (11·9)
Bodyweight, kg	81·3 (17·5)	81·6 (17·7)
Height, cm	173·1 (9·1)	173·3 (9·0)
Body-mass index, kg/m^2	26·75 (4·56)	26·75 (4·55)
Concomitant diseases (diabetes, hypertension, ischaemic heart disease, obesity)†	3687/14 944 (24·7%)	1235/4892 (25·2%)
Risk of infection in volunteers†‡		
High	65/14 567 (0·4%)	23/4778 (0·5%)
Medium	3853/14 567 (26·5%)	1280/4778 (26·8%)
General	10649/14 567 (73·1%)	3475/4778 (72·7%)

	Total cases	Vaccine group	Placebo group	Vaccine efficacy (95% CI)	p value
First COVID-19 occurrence from 21 days after dose 1 (day of dose 2)*					
Overall	78	16/14 964 (0·1%)	62/4902 (1·3%)	91·6% (85·6–95·2)	<0·0001
Age group (years)					
18–30	5	1/1596 (0·1%)	4/521 (0·8%)	91·9% (51·2–99·3)	0·0146
31–40	17	4/3848 (0·1%)	13/1259 (1·0%)	90·0% (71·1–96·5)	<0·0001
41–50	19	4/4399 (0·1%)	15/1443 (1·0%)	91·3% (73·7–96·9)	<0·0001
51–60	27	5/3510 (0·1%)	22/1146 (1·9%)	92·7% (81·1–97·0)	<0·0001
>60	10	2/1611 (0·1%)	8/533 (1·5%)	91·8% (67·1–98·3)	0·0004
Sex					
Female	32	9/5821 (0·2%)	23/1887 (1·2%)	87·5% (73·4–94·2)	<0·0001
Male	46	7/9143 (0·1%)	39/3015 (1·3%)	94·2% (87·2–97·4)	<0·0001
Moderate or severe cases	20	0/14 964	20/4902 (0·4%)	100% (94·4–100·0)	<0·0001
First COVID-19 occurrence after dose 1†					
Any time after dose 1	175	79/16 427 (0·5%)	96/5435 (1·8%)	73·1% (63·7–80·1)	<0·0001
From 14 days after dose 1	109	30/14 999 (0·2%)	79/4950 (1·6%)	87·6% (81·1–91·8)	<0·0001
First COVID-19 occurrence after dose 2 (28 days after dose 1)*					
All	60	13/14 094 (0·1%)	47/4601 (1·0%)	91·1% (83·8–95·1)	<0·0001

Data are n/N (%), unless otherwise stated. *Includes those who received both doses. †Includes participants who received at least one dose.

Table 2: **Interim results on vaccine efficacy**

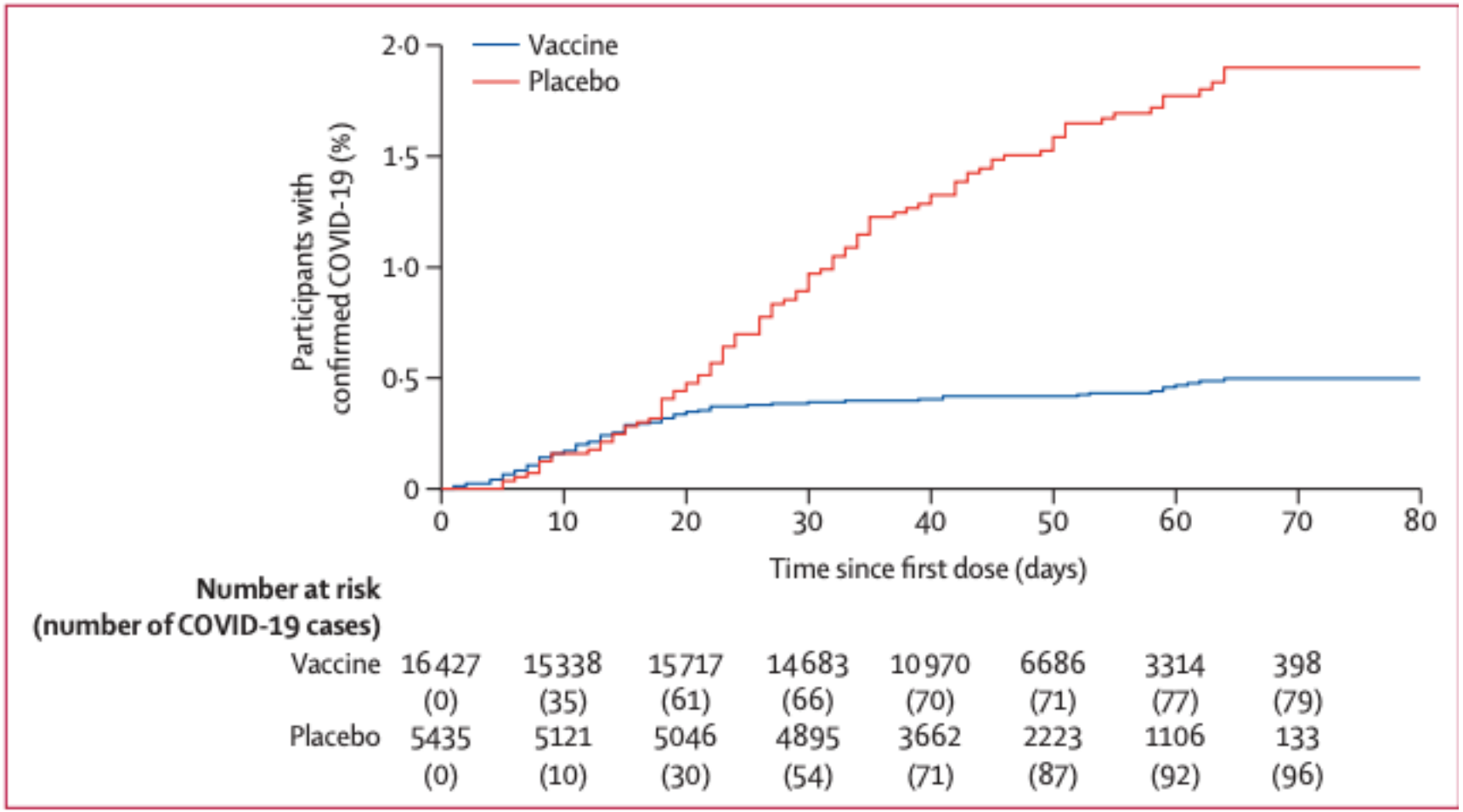


***Figure 2*: Kaplan-Meier cumulative incidence curves for the first symptomatic, PCR-positive COVID-19 after dose 1, in participants who received at least one dose of vaccine or placebo**

Safety

-Most reported adverse events were grade 1 (7485 [94·0%] of 7966 total events).

Serious Adverse Events:

45 (0·3%) of 16427 in the vaccine group

23 (0·4%) of 5435 in the placebo group

none were considered associated with vaccination,

-Four deaths were reported during the study:

3 of 16 427 participants (<0.1%) in the vaccine group (2 deaths due to early COVID19

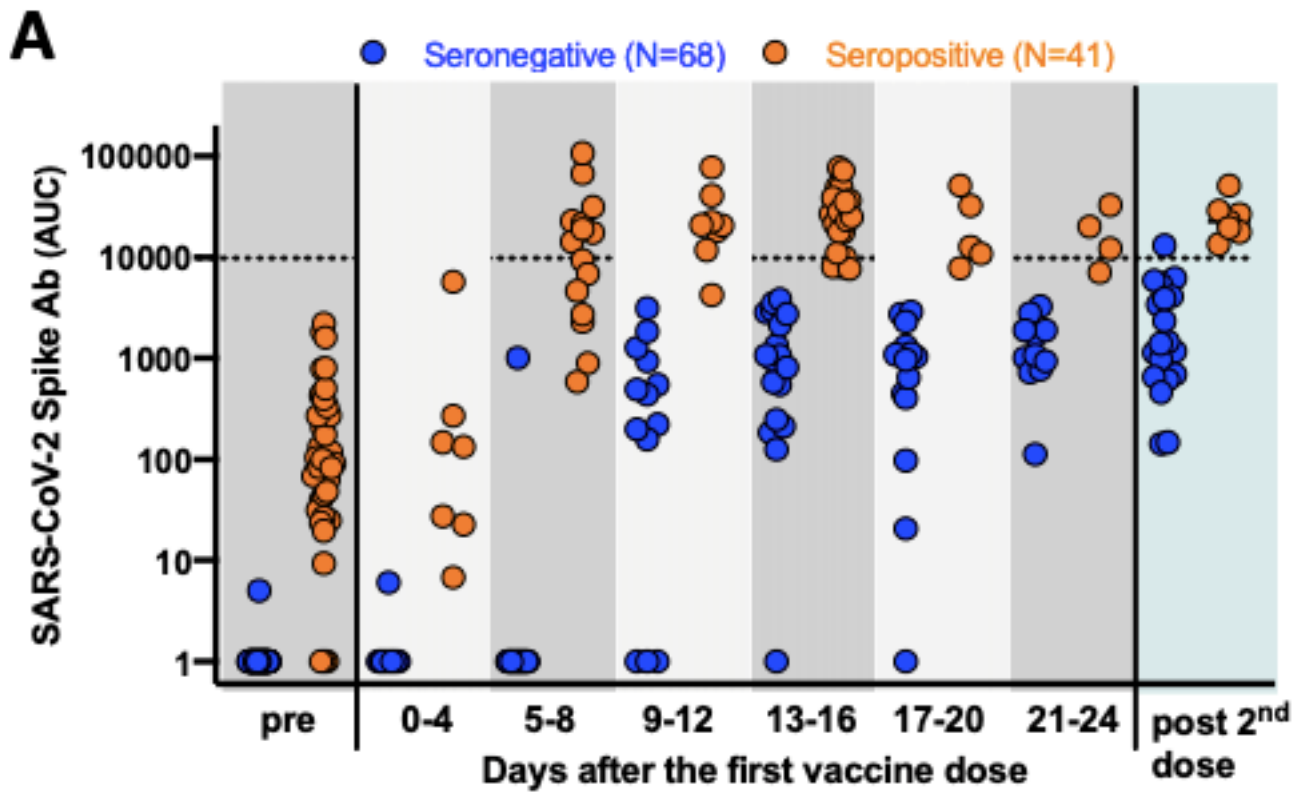
1 of 5435 participants (<0.1%) in the placebo group),

none of which were considered related to the vaccine

¿Una sóla dosis de vacuna post-COVID19?

Robust spike antibody responses and increased reactogenicity in seropositive individuals after a single dose of SARS-CoV-2 mRNA vaccine

Florian Krammer[1$], Komal Srivastava[1], the PARIS team[1*], and Viviana Simon[1,2,3$]



medRxiv preprint doi:
https://doi.org/10.1101/2021.01.29.21250653;

Otro estudio en favor de Tocilizumab

REMAP-CAP (IL-6 Receptor Inhibitor Arm)

- Design: International, multifactorial, adaptive platform trial
- Analysis of IL-6 receptor inhibitor (Tocilizumab 8mg/kg vs Sarilumab 400mg vs SOC) (open label)

  (93.3% received Steroids, 29.9% 2nd dose of Toci)

  Inclusion: 24h of commencing organ support in ICU COVID+ patients
  (28.8% HFNC, 41.5% NIV, 29,5% MechVent)
- Primary Model: ordinal scale combining in-hosp. Mortality and days free of organ support at 21d
- Enrollment: 353 Toci, 48 Sari, 402 SOC

Preprint doi: https://doi.org/10.1101/2021.01.07.21249390

REMAP-CAP

Intervention	Support Free Days (Hospital Mortality)	Odds ratio for support free days	Odds Ratio for Hospital Survival
Tocilizumab	10 days (28%)	1.64 (1.25-2.14)	1.64 (1.14-2.35)
Sarilumab	11 days (22.2%)	1.76 (1.17.2.91)	2.01 (1.18-4.71)
Standard of Care	0 days (35.8%)		

¡Combinación de monoclonals Evita las hospitalizaciones!

Blaze 1: Bamlanivimab vs. Bam+Etesenimab vs. Placebo in **Mild to Moderate** COVID-19

- 5 arm Double Blind, Study n=613, PCR+ plus 1 mild-mod symptoms <3d of their PCR test
- Primary End Point: Viral load at day 11
- Secondary End Points: VL at other time points, Symptom and Cliical Outcome (hospitalization)

Study Arm	Viral Load day 11	Hospitalization (%)
Bam 700mg	-3.72	1.0%
Bam 2800mg	-4.08	1.9%
Bam 7000mg	-3.49	2.0%
Bam 2800mg+Etesenimab 2800mg	-4.37	0.9%
Placebo	-3.80	5.8%

JAMA Published online Jan 21 2021

Monoclonal antibodies can prevent COVID-19—but successful vaccines complicate their future

By Jon Cohen | Jan. 22, 2021 , 4:20 PM

965 Nursing Home residents (n=299) and staff (n=666)
Single dose of Bamlanivimab 4,200mg versus Placebo
Decrease of 57% the risk of developing symptomatic COVID19
(OR 0.43 p=0-00021)
Among NH Residents an **80% decrease** was reported (OR 0.2 p=0.00026)

https://investor.lilly.com/news-releases/news-release-details/lillys-neutralizing-antibody-bamlanivimab-ly-cov555-prevented

¿Inmunización pasiva mientras llega la vacuna?

Regeneron Passive Immunity

- Phase 3, n=400 exploratory analysis
- House-hold exposure
- Intervention: RegenCOV 1200mg SQ
- Results:

1. 100% prevention of symptomatic infection (0/186 vs. 8/223)
2. 50% lower rate of overall infection (10/186 vs. 23/223)
3. Decreased peak viral levels (100fold less) (0 over 104 vs 62% in Pbo)
   Decreased duration of viral shedding and diseases duration:
   <1 week with RegenCOV vs. 40% 3-4 weeks in Placebo arm
4. Safety: AEs 12% RegenCOV vs 18% Placebo

https://investor.regeneron.com/news-releases/news-release-details/regeneron-reports-positive-interim-data-regen-covtm-antibody

Gracias