FINAL REPORT

Phase I study, open, adaptive and monocentric, to evaluate the safety, reactogenicity and explore the immunogenicity of the prophylactic vaccine candidate FINLAY-FR-1A against SARS-CoV-2, in convalescent of COVID-19.

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IFV/COR/07

Appendix 1. Outcomes.

Primary outcome(s):

Serious Adverse Events-SAE (It was measured as: -Occurrence of the SAE (Yes, No), - Duration (Time from start date until end date of event), -Description of the event, Result (Recovered, Recovered with squeals, Persists, Death, Unknown), - Causality (Causal association consistent with vaccination, Undetermined, Inconsistent causal association with vaccination, not classifiable). Measurement time: daily for 28 days after dose.

Key secondary outcomes:

1) Solicited Local and systemic Adverse Events (AE). They was measured as: -Occurrence of the AE (Yes, No), Duration (Time from start date until end date of event), -Intensity of the AE (mild, moderate, severe), -Severe (Serious, not serious), -Result (Recovered, Recovered with sequelae, Persists, Death, Unknown), -Causation (causal association consistent with vaccination, indeterminate, causal association inconsistent with vaccination, not classifiable). Measurement time: daily for 7 days after dose.

2) Unsolicited Adverse Events (AE). They was measured as: Description of the AE (name of the event), Duration (Time from start date until end date of event), -Intensity of the AE (mild, moderate, severe), -Severe (Serious, not serious), -Result (Recovered, Recovered with sequelae, Persists, Death, Unknown), -Causality (causal association consistent with vaccination, Undetermined, causal association inconsistent with vaccination, not classifiable). Measurement time: daily for 28 days after dose.

3) Concentration of specific anti-RBD IgG antibodies, and percentage of subjects with seroconversion (≥4 fold). Measurement time: Prevaccination, Day 7, 14 and 28 after vaccination.

4) Conventional neutralizing antibody titer. Measurement time: Prevaccination and day 14 after vaccination.

5) % RBD:ACE2 inhibition. Measurement time: Prevaccination, 7, 14 and 28 days post-vaccination.

6) Half-maximal molecular virus neutralization titer ($mVNT_{50}$). It is the serum dilution inhibiting 50% of RBD:hACE2 interaction. Measurement time: Prevaccination, 7, 14 and 28 days post-vaccination.

7) Evaluation of RBD-specific T cells producing IFN-γ and TNF-α. Measurement time: Prevaccination and 28 days after vaccination.

Appendix 2. Study Selection Criteria.

Inclusion Criteria.

1. Understands and agrees to comply with the study procedures and provides written informed consent.
2. Adults, COVID-19 convalescents, 19 to 59 years of age, at time of consent.
3. Subjects with BMI of 18.5 to 29,9 kg/m^2
4. Women of childbearing potential must agree to use at least one acceptable primary form of contraception.

Exclusion Criteria.

1. Subjects with a history of SARS-CoV-2 infection:
   a) Known history of SARS-CoV-2 infection at time of recruitment or hospitalization for COVID-19 during the two months before recruitment.
   b) Known history of severe COVID-19 illness severe by clinical form or during medical interview.
2. Acute illness, febrile 7 days prior to administration of investigational product or at screening.
3. Current use of any prescription of non-steroidal anti-inflammatory drugs (NSAIDs) or antimicrobial medications within 7 days prior to vaccination.
4. Any medical disease or condition that, in the opinion of the clinical investigator, precludes study participation (chronic medical disease or condition. Subjects with respiratory disease (e.g., chronic obstructive pulmonary disease [COPD], asthma), Mellitus diabetes, thyroid disease, cardiovascular disease (e.g., congestive heart failure, hypertension, ischemic heart disease), psychiatric condition, Neurological conditions or bleeding disorder).
5. Subjects with an immunodeficiency of any cause.
6. Ongoing malignancy or recent diagnosis of malignancy.
7. Subjects with a history of alcohol abuse or other recreational drug use within 30 days before the first vaccine administration, except abstinence and smoking.
8. Subjects with demonstrated inability to comply with the study procedures (Mental problems or disorders).
9. History of hypersensitivity or severe allergic reaction (e.g., anaphylaxis, generalized urticarial, angioedema,).
10. History of hypersensitivity to thiomersal
11. Subjects that participated in another investigational study involving any investigational product within 3 month prior to the day of enrollment.
12. Subjects that has received a non-study vaccine within 30 days prior to the day of enrollment.
13. Has received systemic immunosuppressant or immune-modifying drugs, immunoglobulin or blood products, cytostatic, steroids, interferon, and others.
14. Transfusion of blood or blood products in the last 3 months. .

15. Subjects with difficult to comply with the schedule of clinical visit or to continue follow up clinical visits.
16. Splenectomy or splenic dysfunction
17. Pregnancy, puerperium, or breastfeeding.
18. Has any abnormality or permanent body art (e.g., tattoo) that would interfere with the ability to observe local reactions at the injection site (both deltoid region).
19. Has a positive test result for hepatitis B surface antigen, hepatitis C virus antibody, HIV types 1 or 2 antibodies or VDRL at screening.

Appendix 3. General Information.

Table 3-1: Demographic characteristics of the sample.

		Mild COVID-19 (n=11)		PCR+ Asymptomatic (n=10)		IgG+ PCR- (n=9)		Total (n=30)	
		N	%	N	%	N	%	N	%
Gender	Female	7	63.6	3	30.0	5	55.6	15	50.0
	Male	4	36.4	7	70.0	4	44.4	15	50.0
Skin color	White	8	72.7	5	50.0	3	33.3	16	53.3
	Black	1	9.1	2	20.0	2	22.2	5	16.7
	Mixed race	2	18.2	3	30.0	4	44.4	9	30.0
Age (years)	Mean (SD)	46.9 (8.8)		36.6 (10.4)		39.7 (14.0)		41.3 (11.6)	
	Median (IQR)	48.0 (13.0)		33.0 (14.0)		40.0 (30.0)		41.5 (21.0)	
	(Min; Max)	(30; 57)		(24; 55)		(22; 57)		(22; 57)	
Weight (kg)	Mean (SD)	76.8 (14.6)		70.0 (12.0)		70.1 (13.2)		72.5 (13.3)	
	Median (IQR)	75.0 (29.0)		71.0 (17.0)		71.0 (14.5)		71.0 (12.1)	
	(Min; Max)	(55; 100)		(47; 90)		(46; 92)		(46; 100)	
Height (cm)	Mean (SD)	169.3 (12.5)		167.9 (8.2)		167.2 (10.7)		168.2 (10.4)	
	Median (IQR)	163.0 (23.0)		169.0 (13.0)		164.0 (19.0)		166.0 (16.0)	
	(Min; Max)	(153; 188)		(152; 177)		(154; 186)		(152; 188)	
BMI	Mean (SD)	26.5 (1.9)		24.6 (2.8)		24.8 (3.4)		25.4 (2.8)	
	Median (IQR)	26.0 (3.7)		24.4 (4.4)		26.4 (4.9)		25.6 (4.2)	
	(Min; Max)	(23.5; 23.7)		(20.3; 29.7)		(18.7; 29.4)		(18.7; 29.7)	
HD (months)	Mean (SD)	8.4 (0.6)		7.8 (1.7)		7.9 (0.9)		8.0 (1.2)	
	Median (IQR)	8.5 (1.0)		8.2 (1.7)		8.2 (0.1)		8.2 (0.8)	
	(Min; Max)	(7.4; 9.4)		(4.7; 10.1)		(5.5; 8.3)		(4.7; 10.1)	

SD=Standard Deviation; IQR=Interquartile range; Min=Minimum; Max=Maximum; BMD=Body mass index; HD=Months from hospital discharge or serological diagnosis to vaccination.

Table 3-2. Medical treatment pre-vaccination

		Mild		Asymptomatic		IgG+PCR-		Total	
		N	%	N	%	N	%	N	%
		11	100.0	10	100.0	9	100.0	30	100.0
With some treatment	Yes	3	27.3	2	20.0	3	33.3	8	26.7
	No	8	72.7	8	80.0	6	66.7	22	73.3
Reasons	HBP	3	27.3	2	20.0	2	22.2	7	23.3
	Diabetes mellitus	1	9.1	1	10.0	--	--	2	6.7
	Allergy	--	--	--	--	1	11.1	1	3.3
	Glaucoma	1	9.1	--	--	--	--	1	3.3
	Hyperuricemia	1	9.1	--	--	--	--	1	3.3
	Bronchial Hyperreactivity	1	9.1	--	--	--	--	1	3.3
HBP		Enalapril, Amlodipina, Furosemida, Hidroclorotiazida		Enalapril, Losartan		Enalapril, Hidroclorotiazida			
Diabetes Mellitus		Metformina		Metformina					
Allergy						Loratadina			
Glaucoma		Dorzolamida							
Hyperuricemia		Alopurinol							
Bronchial Hyperreactivity		Dexclorferinamina							

Table 3-3. Months from hospital discharge or serological diagnosis to vaccination.

		Mild	Asymptomatic	IgG+PCR-	Total
		11	10	9	30
Months	Average (SD)	8.4 (0.6)	7.8 (1.7)	7.9 (0.9)	8.0 (1.2)
	Median (IQR)	8.5 (1.0)	8.2 (1.7)	8.2 (0.1)	8.2 (0.8)
	(Min; Max)	(7.4; 9.4)	(4.7; 10.1)	(5.5; 8.3)	(4.7; 10.1)

Appendix 4. Adverse Events.

Table 4-1. Concomitant treatments.

		Mild		Asymptomatic		IgG +		Total	
		N	%	N	%	N	%	N	%
		11	100.0	10	100.0	9	100.0	30	100.0
Some treatment	Yes	3	27.3	1	10.0	3	33.3	7	23.3
	No	8	72.7	9	90.0	6	66.7	23	76.7
To treat Adverse Events	Yes	2	18.2	1	10.0	2	22.2	5	16.7
	No	9	81.8	9	90.0	7	77.9	25	83.3
		HTA, Fever		Headache		HTA, sinus tachycardia, pain, migraine			
HBP	Captoril	1	9.1	--	--	--	--	1	3.3
	Enalapril	1	9.1	--	--	--	--	1	3.3
	PPG	--	--	--	--	1	11.1	1	3.3
	Vit C	--	--	--	--	1	11.1	1	3.3
	Aspirin	--	--	--	--	1	11.1	1	3.3
	Atenolol	--	--	--	--	1	11.1	1	3.3
	Oxygen	--	--	--	--	1	11.1	1	3.3
Migraine	Diclofenaco	--	--	--	--	1	11.1	1	3.3
	Gravinol	--	--	--	--	1	11.1	1	3.3
Sinus tachycardia	Digoxin	--	--	--	--	1	11.1	1	3.3
	Verapamil	--	--	--	--	1	11.1	1	3.3
Fever, Pain	Dipirona	1	9.1	--	--	1	11.1	2	6.7
Headache	Ibuprofen	--	--	1	10.0	--	--	1	3.3

Table 4-2. Summary of adverse events.

	Mild	Asymptomatic	IgG+PCR-	Total
	11	10	9	30
Subjects with at least one AE	3 (27.3)	4 (40.0)	5 (55.6)	12 (40.0)
Subjects with some vaccine-associated AE	0	3 (30.0)	3 (33.3)	6 (20.0)
Serious AE	0	0	0	0
Vaccine-associated serious AE	0	0	0	0
P (serious toxicity)	0.0833	0.0909	0.1000	0.0322
P (serious toxicity)>0.05	0.5403	0.5688	0.5987	0.2039
Subjects with at least one severe AE	0	0	1 (11.1)	1 (3.3)
Subjects with at least one severe vaccine-associated AE	0	0	1 (11.1)	1 (3.3)
AE Total	3	7	10	20
Vaccine-associated EA	0	4 (57.1)	3 (30.0)	7 (35.0)
Serious AE	0	0	0	0
Serious vaccine-associated AE	0	0	0	0
Severe AE	0	0	1 (10.0)	1 (5.0)
Severe vaccine-associated AE	0	0	1 (10.0)	1 (5.0)

Table 4-3. Global characterization of adverse events.

		Mild		Asymptomatic		IgG+PCR-		Total	
		N	%	N	%	N	%	N	%
		3	100.0	7	100.0	10	100.0	20	100.0
Intensity	Mild	3	100.0	6	85.7	5	50.0	14	70.0
	Moderate	0	0.0	1	14.3	4	40.0	5	25.0
	Severe	0	0.0	0	0.0	1	10.0	1	5.0
Gravity	No-Serious	3	100.0	7	100.0	10	100.0	20	100.0
Causality	Consistent with vaccination	0	0.0	4	57.1	3	30.0	7	35.0
	Indeterminate	1	33.3	1	14.3	2	20.0	4	20.0
	Inconsistent with vaccination	2	66.7	2	28.6	5	50.0	9	45.0
Results	Recovered	3	100.0	7	100.0	10	100.0	20	100.0
Type	Local	0	0.0	3	42.9	2	20.0	5	25.0
	Systemic	3	100.0	4	57.1	8	80.0	15	75.0
Solicited	Solicited	1	33.3	4	57.1	2	20.0	7	35.0
	Unsolicited	2	66.7	3	42.9	8	80.0	13	65.0
Beginning (hours)	≤ 60 min	0	0.0	2	28.6	4	40.0	6	30.0
	60 min-24 h	2	66.7	5	71.4	3	30.0	10	50.0
	24-48 h	0	0.0	0	0.0	1	10.0	1	5.0
	> 72 h	1	33.3	0	0.0	2	20.0	3	15.0
Duration (hours)	≤ 24 h	0	0.0	3	42.9	9	90.0	12	60.0
	24-48 h	1	33.3	3	42.9	0	0.0	4	20.0
	48-72 h	1	33.3	1	14.3	0	0.0	2	10.0
	> 72 h	1	33.3	0	0.0	1	10.0	2	10.0

Table 4-4. Characterization of each adverse event.

	Beginning				Duration				Intensity			Causality		
	≤ 60 m	60m-24h	24-48h	> 72h	≤ 24h	24-48h	48-72h	> 72h	L	M	S	C	Inc.	Ind.
Solicited-Local														
Pain	1 (33)	2 (67)	--	--	1 (33)	--	1 (33)	1 (33)	1 (33)	2 (67)		3 (100)		
Redness	--	2 (100)	--	--	2 (100)	--	--	--	2 (100)			2 (100)		
Solicited-Systemic														
General Malaise	--	1 (100)	--	--	1 (100)	--	--	--	1 (100)			1 (100)		
Fever	--	--	--	1 (100)		1 (100)	--	--	1 (100)				1 (100)	
Unsolicited-Systemic														
HBP	4 (57)	3 (43)	--	--	3 (43)	2 (29)	1 (14)		5 (71)	1 (14)	1 (14)	1 (14)	4 (57)	
Headache	--	2 (100)	--	--	1 (50)	1 (50)	--	--	2 (100)				1 (50)	1 (50)
Chill	--	--	1 (100)	--	1 (100)	--	--	--	1 (100)				1 (100)	2 (29)
Dry mouth	1 (100)	--	--	--	1 (100)	--	--	--	1 (100)					1 (100)
Migraine	--	--	--	1 (100)	1 (100)	--	--	--		1 (100)			1 (100)	
Sinus tachycardia	--	--	--	1 (100)	1 (100)	--	--	--		1 (100)			1 (100)	

L: Mild; M: Moderate; S: Severe

C: Consistent; Inc.: Inconsistent; Ind.: Indeterminate

Table 4-5. Frequency of Adverse Events.

			Mild COVID-19 (n=11)		PCR+ Asymptomatic (n=10)		IgG+ PCR- (n=9)		Total (n=30)	
			N	%	N	%	N	%	N	%
Subjects with some AE			3	27.3	4	40.0	5	55.6	12	40.0
Expected	Local	Site pain	0	0.0	2	20.0	1	11.1	3	10.0
		Redness	0	0.0	1	10.0	1	11.1	2	6.7
	Systemic	General malaise	0	0.0	1	10.0	0	0.0	1	3.3
		Fever	1	9.1	0	0.0	0	0.0	1	3.3
Unsolicited	Systemic	HBP	2	18.2	2	20.0	3	33.3	7	23.3
		Headache	0	0.0	1	10.0	1	11.1	2	6.7
		Chills	0	0.0	0	0.0	1	11.1	1	3.3
		Dry Mouth	0	0.0	0	0.0	1	11.1	1	3.3
		Migraine	0	0.0	0	0.0	1	11.1	1	3.3
		Sinus tachycardia	0	0.0	0	0.0	1	11.1	1	3.3
AE by subjects		Average (SD)	0.3 ± 0.5		0.7 ± 1.0		1.1 ± 1.9		0.7 ± 1.2	
		Median (IQR)	0 ± 1		0 ± 1		1 ± 1		0 ± 1	
		Min; Max	(0; 1)		(0; 3)		(0; 6)		(0; 6)	

AE=Adverse Event; SD=Standard Deviation; IQR=Interquartile Range; Min=Minimum; Max=Maximum; HBP=High Blood Pressure.

Table 4-6. Frequency of Vaccine-Associated Adverse Events.

			Mild COVID-19 (n=11)		PCR+ Asymptomatic (n=10)		IgG+ PCR- (n=9)		Total (n=30)	
			N	%	N	%	N	%	N	%
Subjects with some VAAE			0	0.0	3	30	3	33.3	6	20.0
Expected	Local	Site pain	0	0.0	2	20.0	1	11.1	3	10.0
		Redness	0	0.0	1	10.0	1	11.1	2	6.7
	Systemic	General malaise	0	0.0	1	10.0	0	0.0	1	3.3
Unsolicited Systemic		HBP	0	0.0	0	0.0	1	11.1	1	3.3
Total VAAE			0	0.0	4	40.0	3	33.3	7	23.3
VAAE by subjects		Average (SD)	0.0 ± 0.0		0.4 ± 0.7		0.3 ± 0.5		0.2 ± 0.5	
		Median (IQR)	0 ± 0		0 ± 1		0 ± 1		0 ± 0	
		Min; Max	(0; 0)		(0; 2)		(0; 1)		(0; 2)	

VAAE=Vaccine-Associated Adverse Event; SD=Standard Deviation; IQR=Interquartile range; Min=Minimum; Max=Maximum; HBP=High Blood Pressure.

Appendix 5. Laboratory Results.

Table 5-1. Laboratory Tests (Bonferrony alpha correction=0.0125).

			Mild	Asymptomatic	IgG+PCR-	Total
			11	10	9	30
Blood Group	A		1 (9.1%)	4 (40.0%)	2 (22.2%)	7 (23.3%)
	B		1 (9.1%)	1 (10.0%)	1 (11.1%)	3 (10.0%)
	AB		2 (18.2%)	0	1 (11.1%)	3 (10.0%)
	O		7 (63.6%)	5 (50.0%)	5 (55.6%)	17 (56.7%)
Rh	Neg		1 (9.1%)	0	2 (22.2%)	3 (10.0%)
	Pos		10 (90.9%)	10 (100.0%)	7 (77.8%)	27 (90.0%)
Hemoglobin	Pre	Average (SD)	140 (13)	141 (11)	139 (13)	131 (14)
		(Min.; Max)	(124; 160)	(120; 159)	(119; 165)	(113; 157)
	Post	Average (SD)	131 (12)	136 (12)	131 (14)	136 (12)
		(Min.; Max)	(114; 148)	(114; 153)	(113; 157)	(114; 153)
	p (t-Student)		0.000	0.002	0.001	0.000
Hematocrit	Pre	Average (SD)	43.6 (3.4)	43.9 (3.6)	43.1 (3.7)	43,5 (3,4)
		(Min,; Max)	(39.1; 49.1)	(38.5; 50.4)	(37.8; 51.2)	(37.8; 51.2)
	Post	Average (SD)	40.8 (3.3)	41.9 (3.2)	40.7 (4.0)	41.2 (3.4)
		(Min,; Max)	(36.5; 45.4)	(36.9; 48.2)	(35.3; 48.3)	(35.3; 48.3)
	p (t-Student)		0,000	0.000	0.000	0.000
Platelets	Pre	Median (IQR)	221 (41)	277 (61)	220 (46)	234 (58)
		(Min,; Max)	(147; 313)	(188; 335)	(163; 252)	(147; 335)
	Post	Median (IQR)	203 (37)	260 (62)	186 (60)	222 (66)
		(Min,; Max)	(184; 281)	(180; 357)	(158; 254)	(158; 357)
	p (Wilcoxon)		0,075	0.093	0.050	0.002
Leukocytes	Pre	Median (IQR)	6.8 (2.9)	7.6 (2.1)	5.9 (1.8)	7.0 (2,.2)
		(Min,; Max)	(3.5; 8.9)	(5.6; 10.0)	(4.1; 7.4)	(3.5; 10.0)
	Post	Median (IQR)	5.5 (1.8)	7.4 (2.5)	5.1 (2.0)	5.8 (2.4)
		(Min,; Max)	(3.8; 7.2)	(5.0; 9.7)	(4.2; 9.5)	(3.8; 9.7)
	p (Wilcoxon)		0,010	0.005	0.285	0.000

			Mild	Asymptomatic	IgG+PCR-	Total
			11	10	9	30
Neutrophils	Pre	Median (IQR)	3.7 (2.3)	4.3 (1.4)	3.6 (1.9)	3.9 (1.3)
		(Min,; Max)	(1.3; 6.6)	(3.1; 6.2)	(1.6; 4.4)	(1.3; 6.6)
	Post	Median (IQR)	3.4 (1.4)	3.7 (1.0)	2.9 (1.6)	3.3 (1.7)
		(Min,; Max)	(1.8; 4.3)	(2.2; 5.6)	(1.3; 7.3)	(1.3; 7.3)
	p (Wilcoxon)		0,013	0.005	0.214	0.000
Lymphocytes	Pre	Average (SD)	2.1 (0.4)	2.5 (0.6)	2.1 (0.5)	2.2 (0.5)
		(Min,; Max)	(1.4; 2.8)	(1.5; 3.5)	(1.4; 2.9)	(1.4; 3.5)
	Post	Average (SD)	1.9 (0.2)	2.7 (0.7)	2.0 (0.5)	2.2 (0.7)
		(Min,; Max)	(1.1; 2.9)	(1.6; 3.9)	(1.5; 2.9)	(1.1; 3.9)
	p (t-Student)		0,230	0.049	0.677	0.942
Monocytes	Pre	Average (SD)	0.4 (0.2)	0.6 (0.2)	0.4 (0.1)	2.2 (0.5)
		(Min,; Max)	(0.1; 0.7)	(0.4; 0.9)	(0.3; 0.5)	(1.4; 3.5)
	Post	Average (SD)	0.4 (0.2)	0.5 (0.2)	0.4 (0.1)	0.5 (0.2)
		(Min,; Max)	(0.1; 0.7)	(0.3; 0.9)	(0.2; 0.6)	(0.1; 0.9)
	p (t-Student)		0,209	0.226	0.699	0.069
Eosinophil	Pre	Median (IQR)	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)
		(Min,; Max)	(0.0; 0.4)	(0.1; 0.4)	(0.1; 0.2)	(0.0; 0.4)
	Post	Median (IQR)	0.2 (0.2)	0.2 (0.2)	0.1 (0.1)	0.1 (0.2)
		(Min,; Max)	(0.0; 0.3)	(0.1; 0.4)	(0.0; 0.5)	(0.0; 0.5)
	p (Wilcoxon)		0,075	0.445	0.859	0.136
Basophiles	Pre	Median (IQR)	0.01 (0.02)	0.01 (0.03)	0.02 (0.03)	0.01 (0.02)
		(Min,; Max)	(0.0; 0.04)	(0.01; 0.09)	(0.0; 0.05)	(0.0; 0.09)
	Post	Median (IQR)	0.01 (0.01)	0.01 (0.01)	0.01 (0.04)	0.01 (0.02)
		(Min,; Max)	(0.0; 0.07)	(0.0; 0.03)	(0.0; 0.06)	(0.0; 0.07)
	p (Wilcoxon)		0,646	0.203	0.398	0.349

			Mild	Asymptomatic	IgG+PCR-	Total
			11	10	9	30
Glucose	Pre	Median (IQR)	4.0 (1.2)	3.6 (1.4)	4.1 (1.0)	3.9 (1.0)
		(Min,; Max)	(2.9; 4.8)	(2.8; 4.8)	(2.9; 4.7)	(2.8; 4.8)
	Post	Median (IQR)	5.3 (0.2)	5.2 (0.8)	5.4 (0.6)	5.2 (0.5)
		(Min,; Max)	(4.6; 6.4)	(4.6; 7.1)	(4.7; 6.2)	(4.6; 7.1)
	p (Wilcoxon)		0,003	0.005	0.008	0.000
Creatinine	Pre	Median (IQR)	87 (23)	80 (12)	90 (22)	84 (20)
		(Min,; Max)	(73; 156)	(69; 116)	(59; 117)	(59; 156)
	Post	Median (IQR)	85 (20)	80 (18)	97 (25)	85 (25)
		(Min,; Max)	(52; 150)	(64; 110)	(67; 107)	(52; 150)
	p (Wilcoxon)		0,092	0.540	0.262	0.538
ASAT	Pre	Median (IQR)	19.1 (16.0)	19.9 (12.0)	20.3 (8.6)	19.9 (9.8)
		(Min,; Max)	(14.0; 48.0)	(15.0; 29.0)	(12.8; 25.7)	(12.8; 48.0)
	Post	Median (IQR)	19.3 (6.6)	20.1 (7.4)	20.3 (10.5)	20.1 (7.1)
		(Min,; Max)	(15.6; 34.3)	(16.8; 36.2)	(15.8; 30.5)	(15.6; 36.2)
	p (Wilcoxon)		0,722	0.678	0.515	0.713
ALAT	Pre	Median (IQR)	26.7 (29.4)	22.2 (22.3)	21.3 (13.1)	22.2 (22.4)
		(Min,; Max)	(10.4; 57.0)	(12.0; 49.0)	(13.0; 54.2)	(10.4; 57.0)
	Post	Median (IQR)	21.6 (12.4)	19.2 (15.8)	19.2 (17.4)	19.4 (13.0)
		(Min,; Max)	(9.7; 53.8)	(10.2; 44.8)	(10.4; 40.6)	(9.7; 53.8)
	p (Wilcoxon)		0.182	0.241	0.208	0.033

Appendix 6. Supplementary data of immune response induced by FINLAY-FR-1A vaccine.

Table 6-1. Anti-RBD IgG seroconversion rates (≥4).

		Mild		Asymptomatic		IgG+PCR-		Total	
		N	%	N	%	N	%	N	%
		11	100.0	10	100.0	9	100.0	30	100.0
T7	Yes	5	45.5	5	50.0	5	55.6	15	50.0
	No	6	54.5	5	50.0	4	44.4	15	50.0
	95% CI	(16.7; 76.6)		(18.7; 81.3)		(21.2; 86.3)		(31.3; 68.7)	
T14	Yes	9	71.8	6	60.0	5	55.6	20	66.7
	No	2	15.8	4	40.0	4	44.4	10	33.3
	95% CI	(48.2; 97.7)		(26.2; 87.8)		(21.2; 86.3)		(47.2; 82.7)	
T28	Yes	10	90.9	8	80.0	6	66.7	24	80.0
	No	1	9.1	2	20.0	3	33.3	6	20.0
	95% CI	(58.7; 99.8)		(44.4; 97.5)		(29.9; 92.5)		(61.4; 92.3)	

Table 6-2. Anti-RBD IgG concentration. Corrected alpha value =0.0033.

		Mild	Asymptomatic	IgG+PCR-	Total	P (K-W)
		11	10	9	30	
T0	Median (25th-75th)	34.2 (14.9; 70.0)	50.8 (13.8; 72.4)	28.2 (9.8; 59.8)	34.0 (14.0; 66.8)	0.588
T7	Median (25th-75th)	102.6 (38.4; 576.5)	172.2 (68.7; 4846.2)	103.7 (30.8; 5849.3)	146.6 (38.4; 709.2)	0.621
T14	Median (25th-75th)	371.6 (118.1; 651.7)	189.5 (118.9; 569.9)	307.0 (35.4; 656.4)	330.4 (117.2; 615.3)	0.961
T28	Median (25th-75th)	918.7 (252.0; 997.7)	593.9 (234.3; 937.0)	387.0 (84.7; 1493.9)	722.2 (230.6; 1058.1)	0.828
Wilcoxon (p)	7 vs, 0	0.021	0.013	0.028	0.000049	
	14 vs, 0	0.004	0.007	0.028	0.000005	
	28 vs, 0	0.003	0.005	0.008	0.000002	

Table 6-3. Seroconversion rates.

		Mild	Asymptomatic	IgG+PCR-	Total	P (K-W)
		11	10	9	30	
T7	Median (25th-75th)	2.8 (1.0; 12.8)	8.3 (1.4; 105.6)	5.3 (0.9; 172.3)	4.4 (1.1; 16.4)	0.723
T14	Median (25th-75th)	8.5 (5.5; 11.4)	7.5 (2.0; 18.7)	12.2 (0.9; 30.8)	8.8 (2.7; 17.9)	0.929
T28	Median (25th-75th)	12.7 (11.2; 29.5)	12.2 (0.9; 30.8)	8.5 (5.5; 11.4)	14.4 (6.0; 32.4)	0.731

K-W: Kruskall-Wallis Test

Table 6-4. Neutralizing antibodies. Corrected alpha value=0.008.

			Mild		Asymptomatic		IgG+PCR-		Total		p (t Student)
			Frec,	%	Frec,	%	Frec,	%	Frec,	%	
			11	100.0	10	100.0	9	100,0	30	100,0	
With neutralizing Abs	0	Yes	7	63.6	8	80.0	6	66,7	21	70,0	
		No	4	36.4	2	20.0	3	33,3	9	30,0	
	14	Yes	10	90.9	9	90.0	7	77,8	26	86,7	
		No	1	9.1	1	10.0	2	22,2	4	13,3	
	χ^2 McNemar (p)		0.250		1.000		1.000		0.063		
Neutralizing Abs titers	0	MGT	24.3		16.8		18.8		19.6		0.552
		95% CI	(13.6; 43.4)		(9.8; 28.7)		(9.0; 39.5)		(14.6; 26.3)		
	14	MGT	665.8		637.8		567.7		625.8		0.990
		95% CI	(388.9; 1140.1)		(262.0; 1552.4)		(221.8; 1452.8)		(427.3; 916.5)		
	p (t-Student)		0.000002		0.000097		0.000769		9.3555E-13		
Ratio 14/0	Median		31.9		38.3		27.4		32.0		0.807
	(25th-75th)		(22.3; 44.5)		(11.6; 107.4)		(1.4; 98.8)		(19.1; 45.1)		
Neutralizing Abs titers	0	MGT	9.8		11.0		8.9		9.9		0.936
		95% CI	(3.9; 24.3)		(5.1; 23.4)		(3.4; 23.4)		(6.3; 15.4)		
	14	MGT	292.2		291.2		140.6		234.3		0.701
		95% CI	(83.3; 1024.9)		(65.3; 1298.7)		(19.8; 995.5)		(106.4; 515.8)		
	p (t-Student)		0.000016		0.000128		0.001984		1.0406E-11		

Table 6-5. RBD:ACE2 inhibition %. Corrected alpha value=0.0033.

		Mild	Asymptomatic	IgG+PCR-	Total	P (K-W)
		11	10	9	30	
T0	Median (25th-75th	15.5 (9.9; 32.9)	18.6 (7.4; 23.3)	11.2 (3.6; 31.6)	15.4 (7.2; 23.3)	0.615
T7	Median (25th-75th	94.5 (38.2; 95.1)	94.2 (90.8; 95.2)	82.0 (37.6; 94.9)	94.2 (75.4; 94.9)	0.531
T14	Median (25th-75th	94.0 (93.8; 94.3)	94.0 (93.6; 94.6)	93.7 (49.6; 94.5)	94.0 (93.4; 94.4)	0.727
T28	Median (25th-75th	95.8 (95.0; 96.0)	95.9 (95.0; 96.2)	95.8 (52.8; 96.0)	95.8 (94.8; 96.0)	0.528
Wilcoxon (p)	7 vs, 0	0.004	0.005	0.008	0.000003	
	14 vs, 0	0.004	0.005	0.008	0.000003	
	28 vs, 0	0.004	0.005	0.008	0.000002	

Table 6-6. Humoral immune response induced by a single dose of FINLAY-FR-1A vaccine.

		Pre-vaccination	Days post-vaccination			CSSP
			7	14	28	
Anti-RBD IgG AU/mL	median	34.0	146.6	330.4	722.2	50.8
	25-75 perc.	14.0; 66.8	38.4;709.2	117.2; 615.3	2306; 1058.1	23.8; 94.0
RBD:hACE2 INH%	Median	15.4	94.2	94.0	95.8	32.0
	25-75 perc.	7.2; 23.3	75.4; 94.9	93.4; 94.4	94.8; 96.0	16.6; 62.2
$mVNT_{50}$	GMT	21.7	817.4	2509.3	2243.2	59.3
	95%CI	15.6; 30.2	366.8;1821.5	1234.9; 5098.7	1133.9; 4437.8	41.1; 85.5
cVNT*	GMT	19.6	..	625.8	..	70.7
	95%CI	14.6; 26.3	..	427.3; 916.5	..	52.1; 95.8
cVNT	GMT	9.9	..	234.3	..	46.4
	95%CI	6.3; 15.4	..	106.4; 515.8	..	31.5; 68.4

AU/mL=anti-RBD IgG concentration expressed in arbitrary units/mL; RBD:hACE2 INH%= RBD:hACE2 inhibition % at a dilution 1/100; $mVNT_{50}$=serum dilution inhibiting 50% of RBD:hACE2 interaction; cVNT*= conventional virus neutralization titer, not considering non-responders; cVNT=conventional virus neutralization titer, including non-responders; perc=percentile; CSSP=Cuban convalescent serum panel.

Table 6-7. Molecular virus neutralization titer (mVNT50), corrected alpha value=0.008.

			Mild	Asymptomatic	IgG+PCR-	Total	p (t Student)
			11	10	9	30	
mVNT50	0	MGT	29.6	19.2	17.5	21.7	0.391
		IC 95%	(13.0; 67.7)	(12.5; 29.5)	(6.9; 44.3)	(15.6; 30.2)	
	7	MGT	1152.3	1007.9	442.3	817.4	0.585
		IC 95%	(312.0; 4255.2)	(227.3; 4468.8)	(64.5; 3033.5)	(366.8; 1821.5)	
	14	MGT	2097.6	4139.0	1828.4	2509.3	0.618
		IC 95%	(583.0; 7547.4)	(1722.2; 9947.6)	(247.1; 12529.1)	(1234.9; 5098.7)	
	28	MGT	3105.9	3734.9	938.5	2243.2	0.196
		IC 95%	(1713.5; 5629.8)	(1715.4; 8131.9)	(116.5; 7559.9)	(1133.9; 4437.8)	
	p (t-Student) 7 vs, 0		0,000202	0.000003	0.002791	1.1966E-12	
	14 vs, 0		0,000008	1.3264E-7	0.000754	3.8363E-16	
	28 vs, 0		0,000006	7.9122E-8	0.000767	1.8566E-16	

Table 6-8. Cellular Immune Response.

			Mild	Asymptomatic	Total	P (M-W)
			10	10	20	
CD4+ TNFα+	T0	Median (25th-75th)	0.38 (0.20; 0.63)	0.38 (0.26; 0.72)	0.38 (0.22; 0.68)	0.734
	T28	Median (25th-75th)	3.84 (0.85; 5.12)	3.34 (2.10; 5.85)	3.60 (1.34; 5.45)	0.821
	Wilcoxon (p)	28 vs. 0	0.013	0.009	0.000254	
CD4+ IFNγ+	T0	Median (25th-75th)	0.64 (0.34; 1.14	0.34 (0.22; 1.00)	0.48 (0.28; 1.01)	0.257
	T28	Median (25th-75th)	0.32 (0.24; 0.67)	0.31 (0.24; 0.64)	0.32 (0.24; 0.60)	0.940
	Wilcoxon (p)	28 vs. 0	0.123	0.646	0.409	
CD3+ CD4- TNFα+	T0	Median (25th-75th)	0.38 (0.20; 0.63)	0.38 (0.26; 0.72)	0.38 (0.22; 0.68)	0.734
	T28	Median (25th-75th)	3.84 (0.85; 5.12)	3.34 (2.10; 5.85)	3.60 (1.34; 5.45)	0.821
	Wilcoxon (p)	28 vs. 0	0.013	0.009	0.000254	
CD3+ CD4- IFN-γ+	T0	Median (25th-75th)	0.43 (0.32; 1.39)	0.64 (0.21; 1.00)	0.50 (0.26; 1.20)	1.000
	T28	Median (25th-75th)	1.44 (1.18; 1.63)	1.42 (0.69; 2.98)	1.44 (1.02; 2.13)	0.880
	Wilcoxon (p)	28 vs. 0	0.139	0.093	0.030	

M-W: Test U de Mann-Whitney

Appendix 7. Correlation among immunological tests.

Table 7-1. Bivariate correlation at 14 days post-vaccination.

	IgG anti-RBD_14	Seroconversion rate_14	% RBD:ACE2 Inhibition_14	mVNT50_14
IgG anti-RBD_14	1.000			
	30			
Seroconversion rate_14	0.775**	1.000		
	0.000	.		
	30	30		
% RBD:ACE2 Inhibition_14	0.378*	0.342	1.000	
	0.039	0.064	.	
	30	30	30	
mVNT50_14	0.962**	0.799**	0.424*	1.000
	0.000	0.000	0.019	.
	30	30	30	30
cVNT_14	0.936**	0.730**	0.370*	0.946**
	0.000	0.000	0.044	0.000
	30	30	30	30

Table 7-2. Predictive value with respect to conventional virus neutralization test (cVNT; titer>1/100).

	Cut-off	Area	ES	Sig	95% CI	
IgG antiRBD_14	124.7	0.972	0.027	0.000	0.919	1.000
Seroconversion rate_14	3.23	0.931	0.051	0.001	0.830	1.000
% RBD:ACE2 Inhibition_14 (mVNT%1/100)	92.0	0.816	0.115	0.018	0.590	1.000
mVNT50_14	919	0.986	0.018	0.000	0.952	1.000

Figure 7-1. ROC Curve regarding cVNT

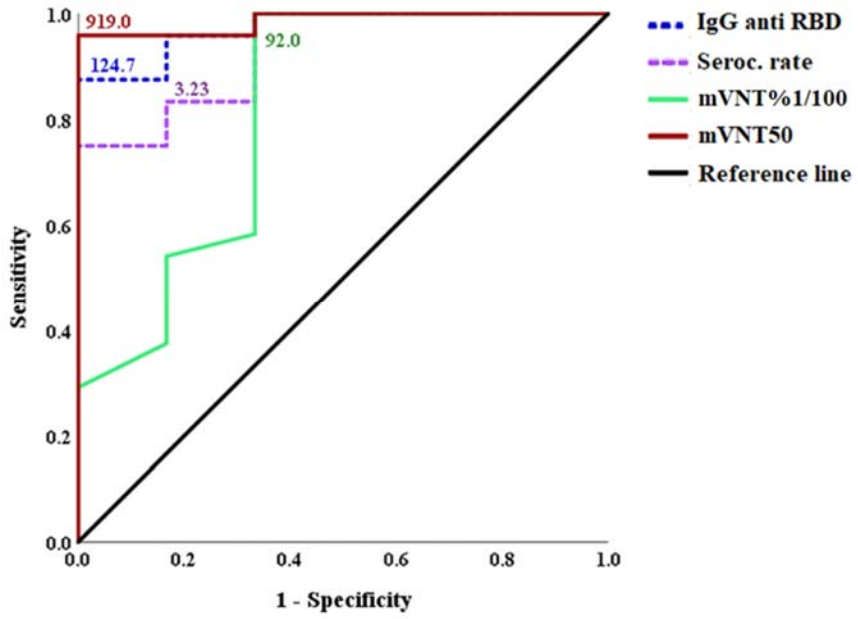
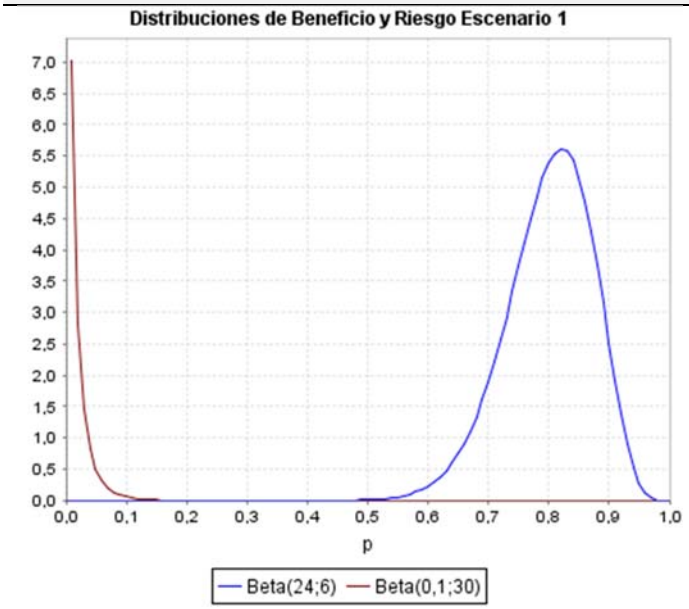


Table 7-3. Diagnostic measures with respect to cVNT.

		cVNT		Kappa	p	Efficiency (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PV+ (95% CI)	PV- (95% CI)
		> 100	≤ 100							
IgG anti-RBD AU/mL	> 124.7	21	0	0.737	0.000	90.0	87.5	100.0	100.0	54.6
		100.0%	0.0%			(77.6; 100.0)	(72.2; 100.0)	(91.7;100.0)	(97.6; 100.0)	(20.6; 88.5)
	≤ 124.7	3	6							
		33.3%	66.7%							
Ser. rate	> 3.23	20	1	0.561	0.001	83.3	83.3	83.3	95.2	55.6
		95.2%	4.8%			(68.3; 98.3)	(66.3; 100.0)	(45.2; 100.0)	(83.8; 100.0)	(17.5; 93.6)
	≤ 3.23	4	5							
		44.4%	55.6%							
mVNT50	> 919	23	0	0.902	0.000	96.7	95.8	100.0	100.0	85.7
		100.0%	0.0%			(88.6; 100.0)	(85.8; 100.0)	(91.7;100.0)	(97.8; 100.0)	(52.6; 100.0)
	≤ 919	1	6							
		14.3%	85.7%							

Appendix 8. Risk-Benefit Balance.

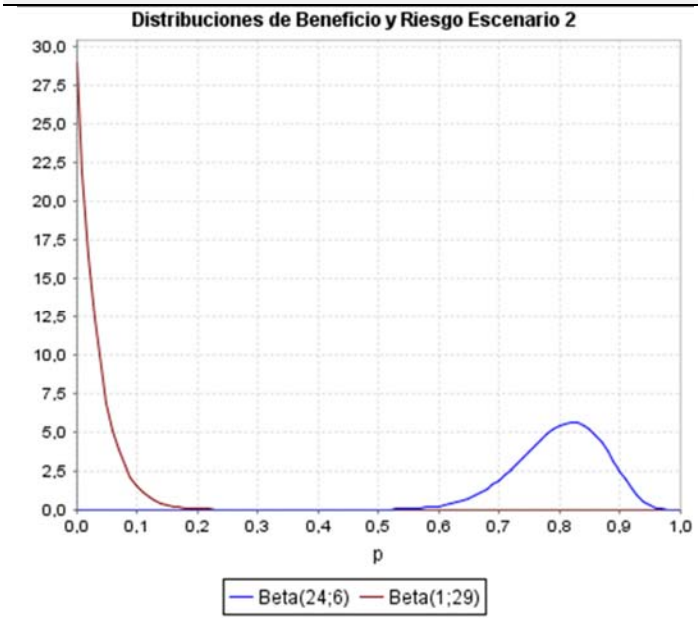
Figure 8-1. Risk-Benefit Balance.



$Benefit_1$ = Proportion of individuals with seroconversion (≥4-fold increase in antibody concentration over pre-immunization levels) at 28 days.

$Risk_1$ = Serious adverse events related to vaccination.

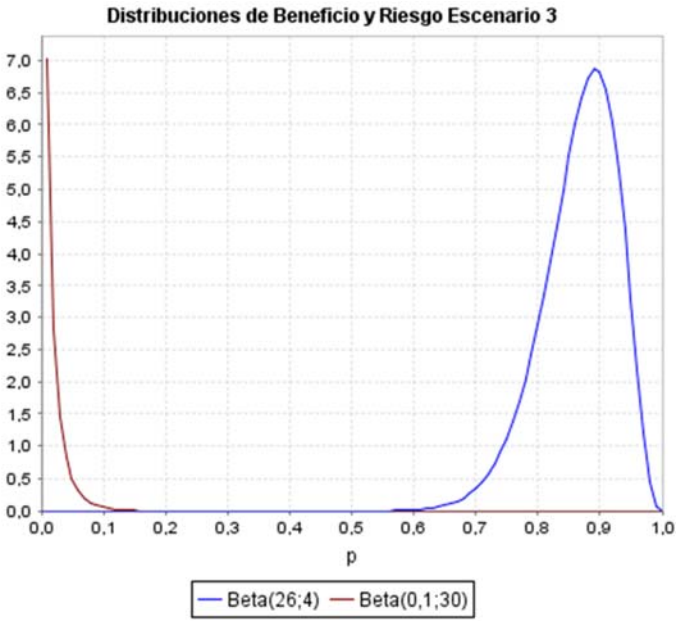
Bayes Factor: 266.7



$Benefit_1$ = Proportion of individuals with seroconversion (≥4-fold increase in antibody concentration over pre-immunization levels) at 28 days.

$Risk_2$ = Severe adverse events related to vaccination.

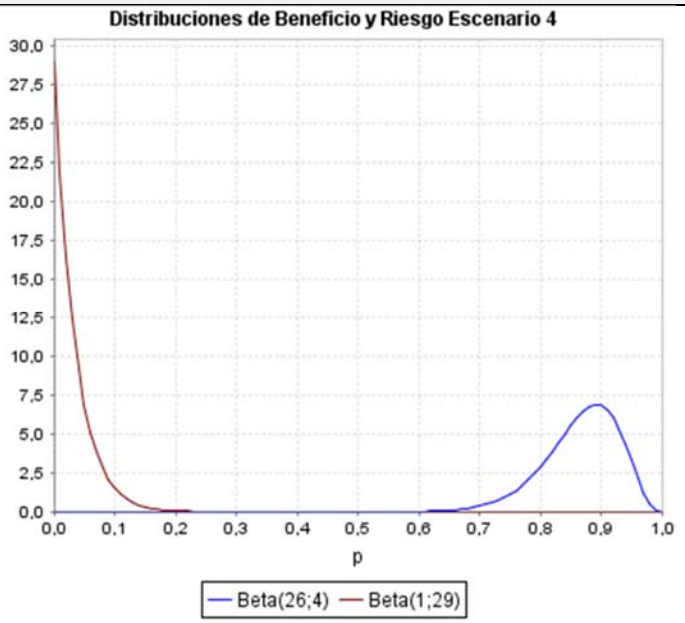
Bayes Factor: 24.2



$Benefit_2$ = Proportion of individuals with inhibitory antibodies greater than 70% of the RBD:ACE2 interaction at 28 days.

$Risk_1$ = Serious adverse events related to vaccination.

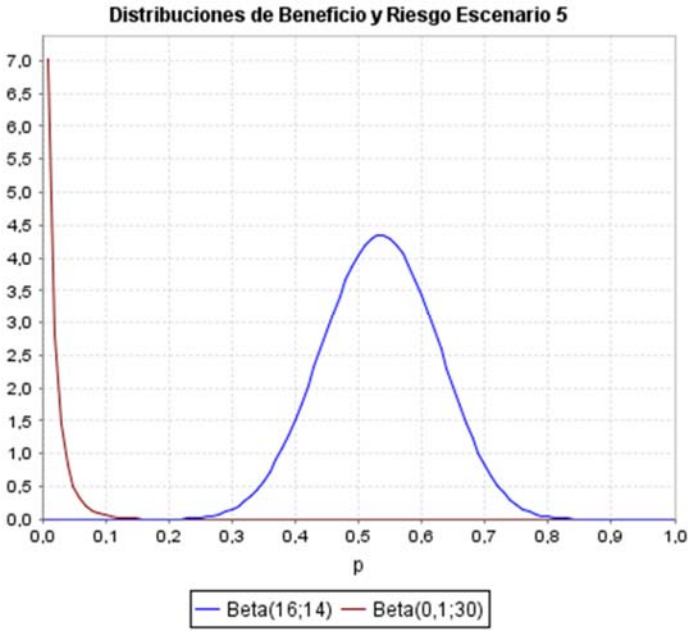
Bayes Factor: 289.0



$Benefit_2$ = Proportion of individuals with inhibitory antibodies greater than 70% of the RBD:ACE2 interaction at 28 days.

$Risk_2$ = Severe adverse events related to vaccination.

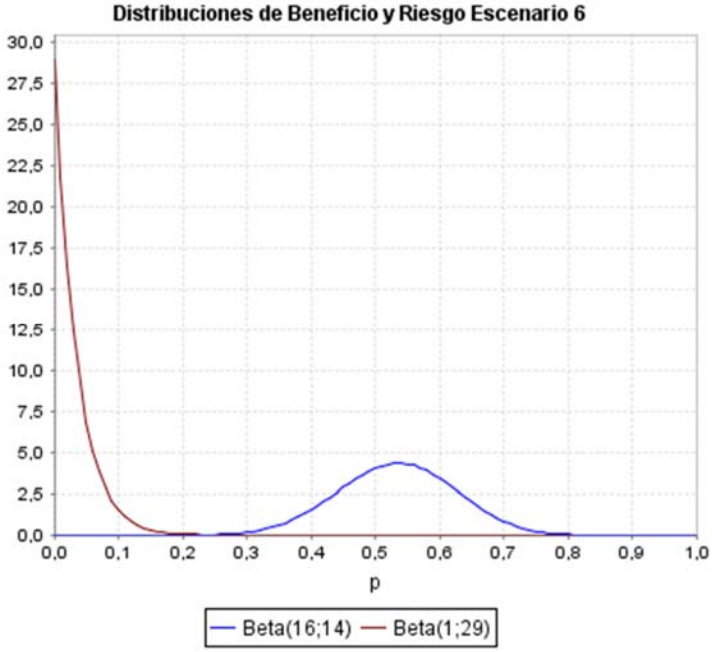
Bayes Factor: 26.3



$Benefit_3$ = Proportion of individuals with conventional neutralizing antibodies over selected value (final ratio/baseline=32) at 14 days.

$Risk_1$ = Serious adverse events related to vaccination.

Bayes Factor: 177.7



$Benefit_3$ = Proportion of individuals with conventional neutralizing antibodies over selected value (final ratio/baseline=32) at 14 days.

$Risk_2$ = Severe adverse events related to vaccination

Bayes Factor: 16.2