OS'16

European Commission for the Control of Foot-and.Mouth Disease

Effect of the Antigen Payload, Polyvalence and Revaccination in the Protection Conferred by FMD Vaccines Against Heterologous Challenge in Cattle

S. Di Giacomo, D. Bucafusco, F. Barrionuevo, J.M. Schammas, J. Pega, S. Cardillo, K. Guevara, A. Fernández-Acevedo, C. Pérez-Beascoechea, E. Maradei, A.V Capozzo, ***M. Pérez-Filgueira***

Instituto de Virología, CICVyA, INTA

Buenos Aires, Argentina

Open Session of the EuFMD - Cascais –Portugal 26-28 October 2016

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Vaccine 22 (2004) 4149–4162

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Reintroduction of foot-and-mouth disease in Argentina: characterisation of the isolates and development of tools for the control and eradication of the disease☆

Nora Mattion[a], Guido König[b], Cristina Seki[a], Eliana Smitsaart[c], Eduardo Maradei[d], Blanca Robiolo[a], Sergio Duffy[b], Emilio León[b], María Piccone[b], Ana Sadir[b], Rodolfo Bottini[d], Bernardo Cosentino[d], Abraham Falczuk[d], Ricardo Maresca[d], Osvaldo Periolo[d], Rodolfo Bellinzoni[c], Ana Espinoza[c], José La Torre[a], Eduardo L. Palma[b,*]

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Vaccine 27 (2009) 741–747

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Some guidelines for determining foot-and-mouth disease vaccine strain matching by serology

Nora Mattion[a,f,*,1], Nesya Goris[b,1], Tom Willems[b], Blanca Robiolo[a,f], Eduardo Maradei[c,f], Claudia Perez Beascoechea[c,f], Alejandro Perez[c,f], Eliana Smitsaart[e,f], Norberto Fondevila[d,f], Eduardo Palma[f], Kris De Clercq[b], José La Torre[a,f]

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, José La Torre[a,f]

Vaccine 28 (2010) 6235–6241

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Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Confidence in indirect assessment of foot-and-mouth disease vaccine potency and vaccine matching carried out by liquid phase ELISA and virus neutralization tests

Blanca Robiolo[a], José La Torre[a], Eduardo Maradei[b], Claudia Perez Beascoechea[b], Alejandro Perez[b], Cristina Seki[a], Eliana Smitsaart[c], Norberto Fondevila[d], Eduardo Palma[d], Nesya Goris[e,1], Kris De Clercq[e], Nora Mattion[a,*]

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Confidence in indire
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Vaccine 26 (2008) 3432–3437

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journal homepage: www.elsevier.com/locate/vaccine

Foot-and-mouth disease vaccine potency testing in cattle using homologous and heterologous challenge strains: Precision of the "Protection against Podal Generalisation" test

N. Goris[a,*,1], E. Maradei[b,g,1], R. D'Aloia[b,g], N. Fondevila[c,g], N. Mattion[d,g], A. Perez[b,g], E. Smitsaart[e,g], H.J. Nauwynck[f], J. La Torre[d,g], E. Palma[g], K. De Clercq[a]

background

- **A/Arg 2001 (A2001) was one of the FMDV strains responsible for the outbreaks occurring in Argentina during 2001**

- **Vaccines formulated with A24/Cruzeiro (A24) were not sufficiently effective in providing protective immunity against the A2001 strain (between 56% and 25% of protection in PPG tests)**

- **r_1 values for A24-A2001 were <0.2 (for VNT) and <0.3 (for LP-ELISA) → poorly antigenically related**

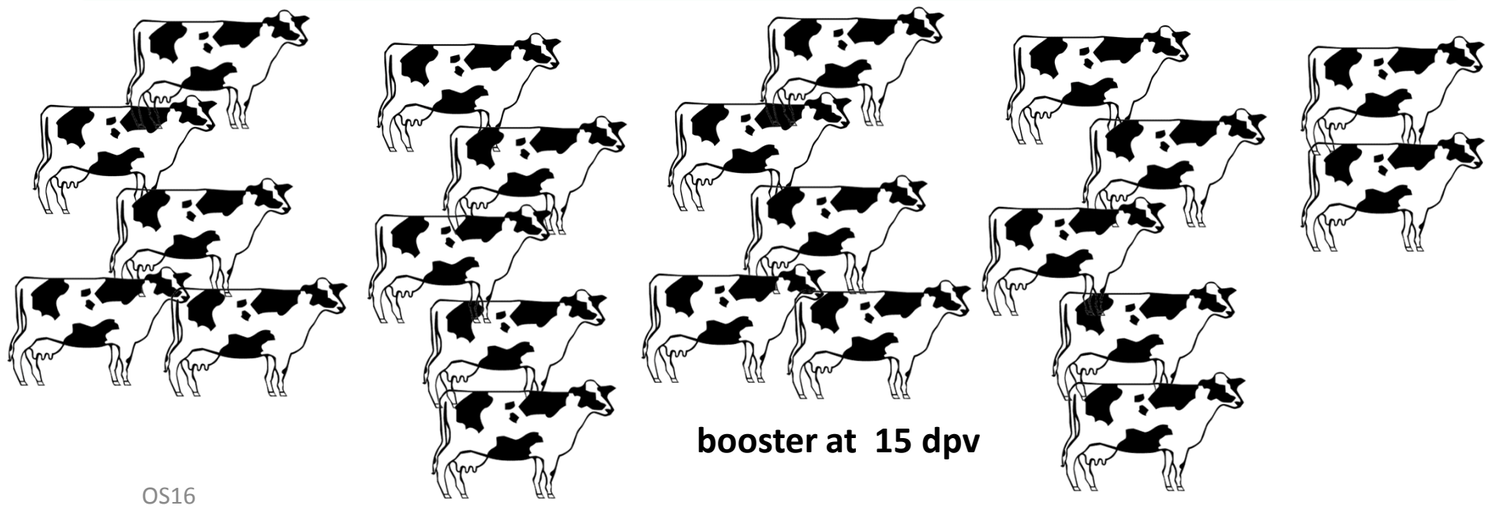
experimental design

- ***4 experimental groups immunized with oil emulsified FMD vaccines***
- ***weekly sampling until challenge at 30 dpv (A/Arg 2001 strain)***
- ***check for FMD symptoms during 1 week (daily sampling)***

vaccine and control groups

A24 **10** µg	A24 **40** µg	A24 **10** µg **x 2 doses**	A24 **10** µg/3CI 10 µg/ O1C 20 µg (**40** µg total)	Näive

n= 22 steers

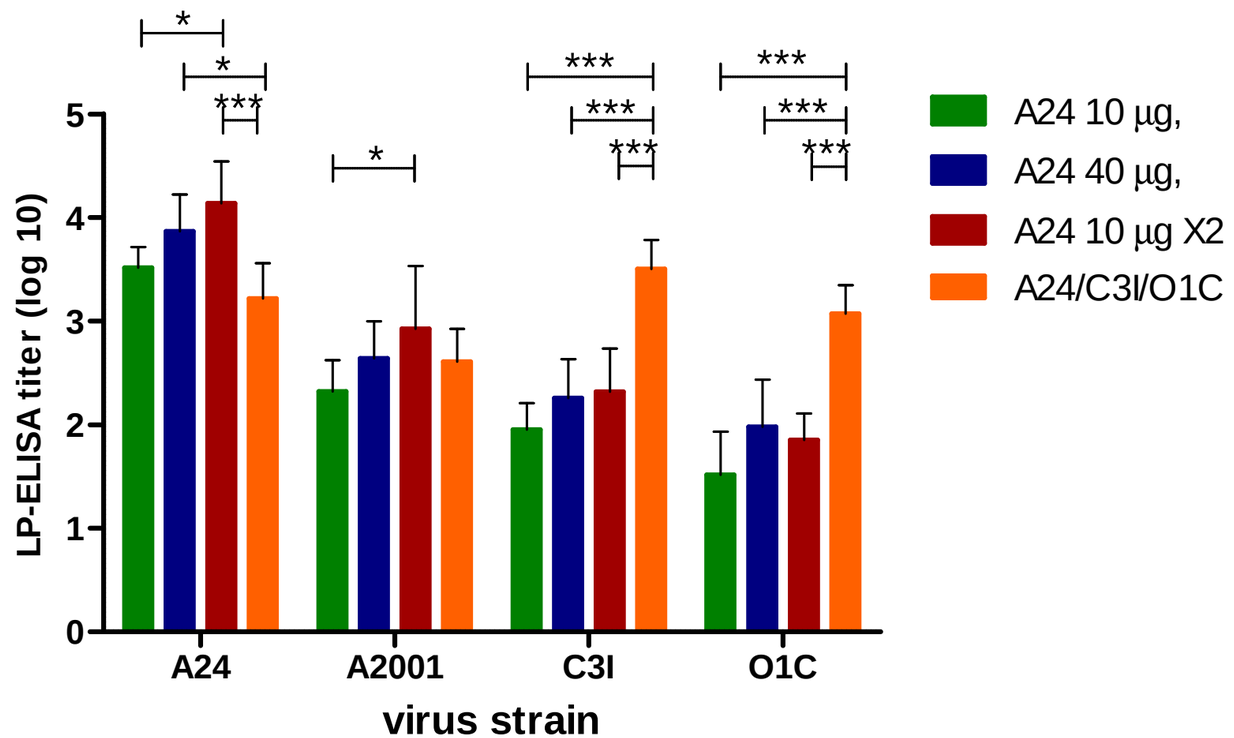


challenge at 30 dpv

A2001 10^4 $DITC_{50\%}$ by IDL route

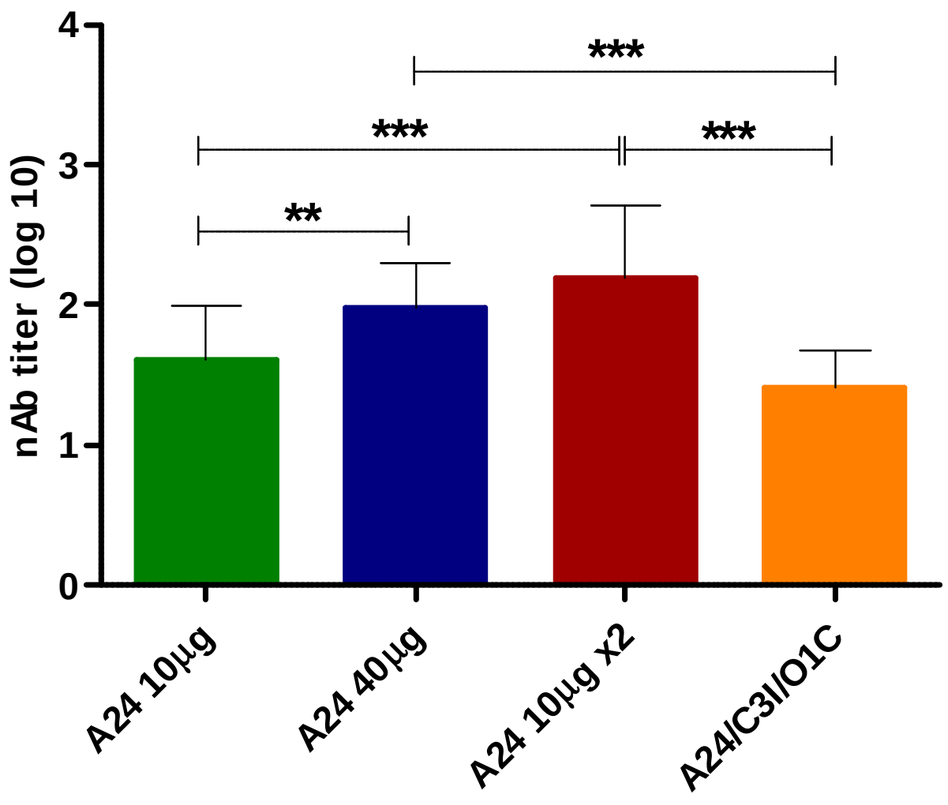
LP-ELISA at 30dpv

- mean Ab titers against A2001 were higher in the revaccinated group than in the low dose monovalent group ($p<0.05$).
- mean anti-A24 Ab in the revaccinated group were higher than in the low dose monovalent group ($p<0.05$) and the trivalent group ($p<0.001$); high dose monovalent group titers were also higher than those in the trivalent group ($p<0.05$)
- mean anti-C3I and –O1C Ab were higher in the trivalent group compared to all the other groups ($p<0.001$)

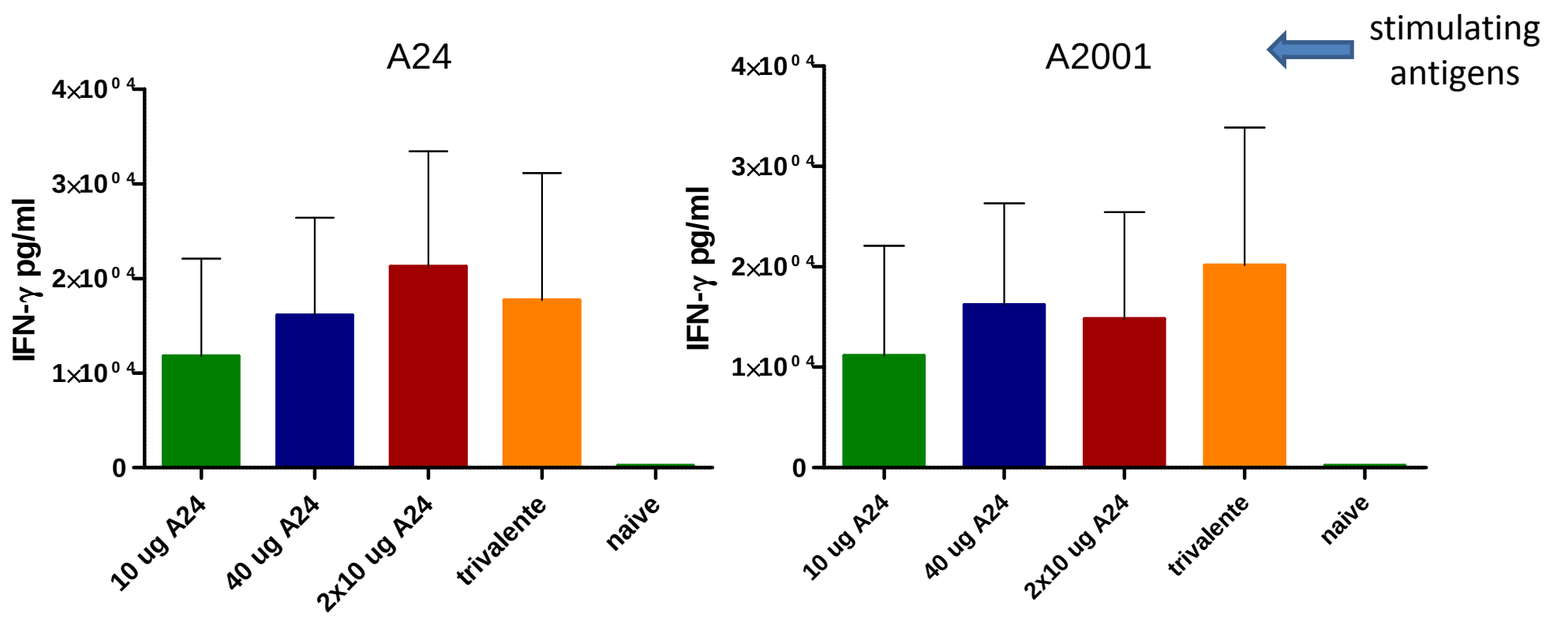


VNT for A2001 at 30dpv

- mean NAb titers against A2001 were higher in the revaccinated group than in the low dose monovalent and the trivalent vaccine groups($p<0.001$).
- mean anti-A2001 NAb in the high dose monovalent group were also higher than those in the low dose monovalent ($p<0.01$) and the trivalent vaccine groups ($p<0.001$)



FMDV-specific IFN-γ production

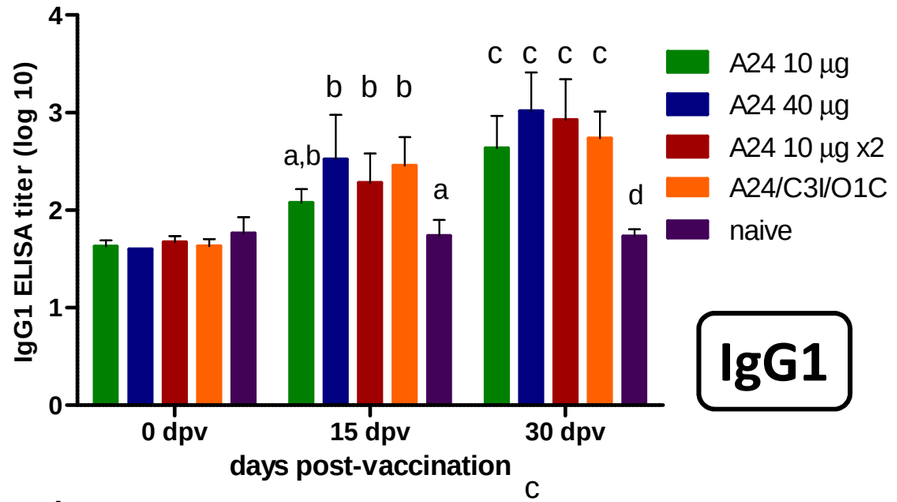


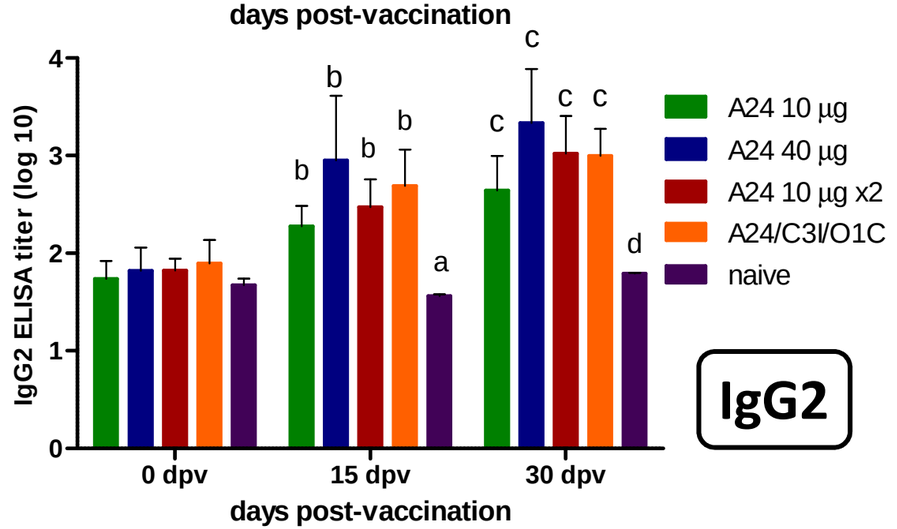
- no statiscally significant differences between experimental groups stimulated with the homologous (A24) or heterologous virus (A2001)
- highest mean IFN-γ production corresponded to the revaccinated (A24 Ag) and the trivalent vaccine groups (A2001 Ag)

IgG1 and IgG2 ELISA for A2001 at 0, 15 & 30dpv

- no significant differences among vaccine groups at 15 or 30 dpv for both isotypes.

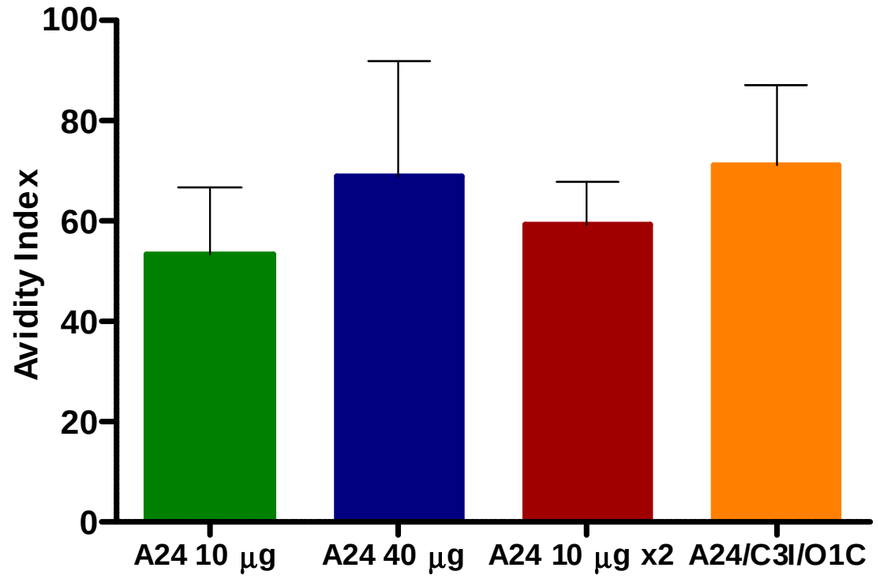
- Differences were only found significant with respect to the non vaccinated group at 15 and 30 dpv for both Ab subclasses





Avidity ELISA for A2001 (30 dpv)

- no significant differences in the mean avidity index among vaccine groups at 30 dpv

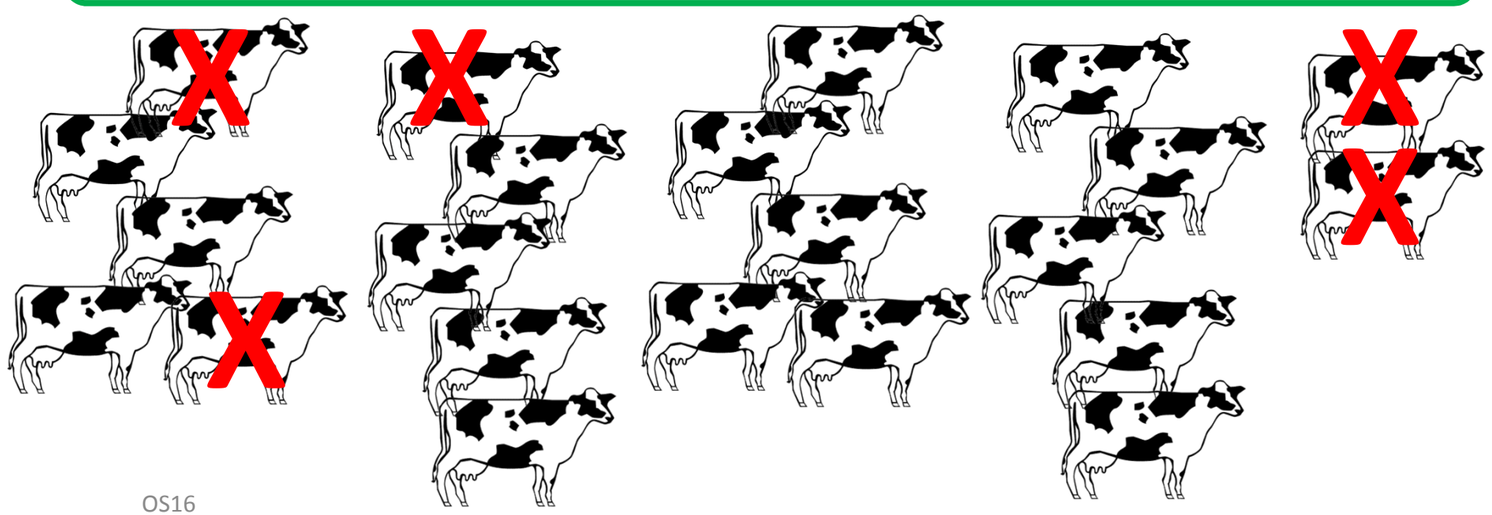


A2001 challenge results

- ***FMD symptoms were checked on daily bases for 7 days***
- ***cumulative clinical scores were assessed for each individual***

vaccine and control groups

A24 **10** µg	A24 **40** µg	A24 **10** µg **x 2 doses**	A24 **10** µg/3CI 10 µg/ O1C 20 µg	Näive



n= 22 steers

challenge at 30 dpv

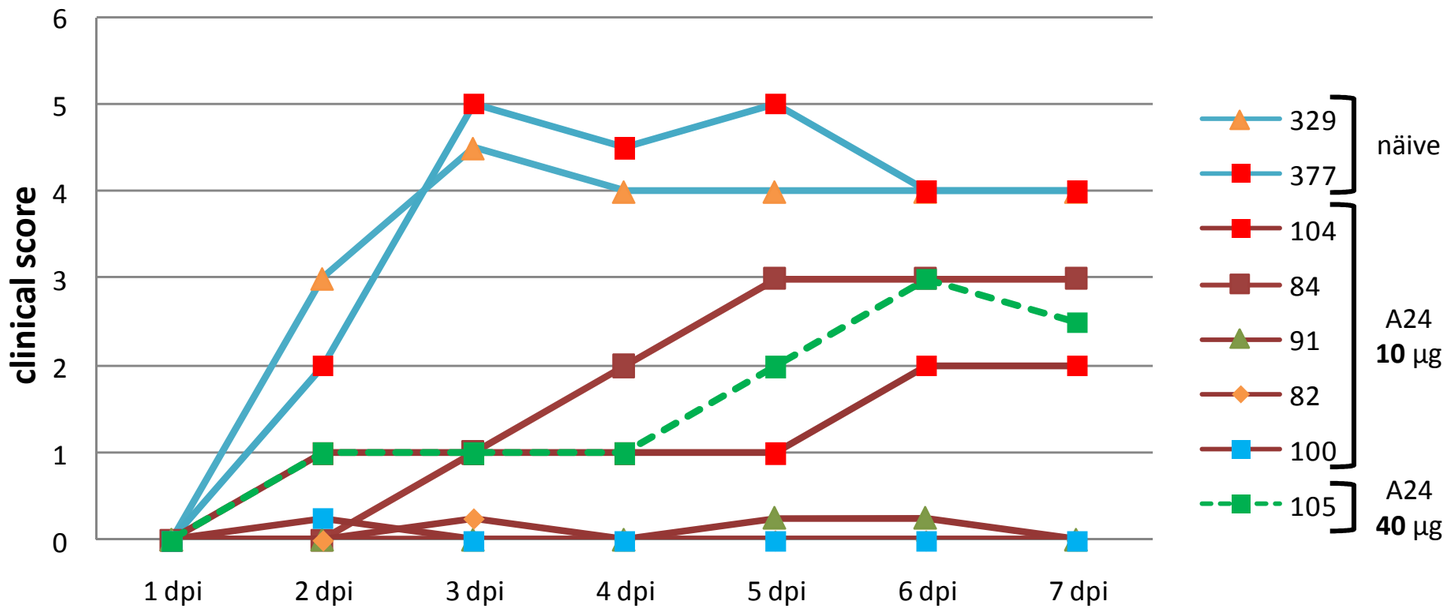
A2001 10^4 $DITC_{50\%}$ by IDL route

A2001 challenge results

- ***FMD symptoms were checked on daily bases for 7 days***
- ***cumulative clinical scores were assessed for each individual***

- non-protected vaccinated animals (2 from the A24 10 µg vaccine, 1 from the A24 40 µg vaccine) showed less severe and more delayed symptoms than naïve ones

- the rest of the animals from the A24 10 µg vaccination group showed at least 1 one day with a slight hyperthermia during the week following the challenge



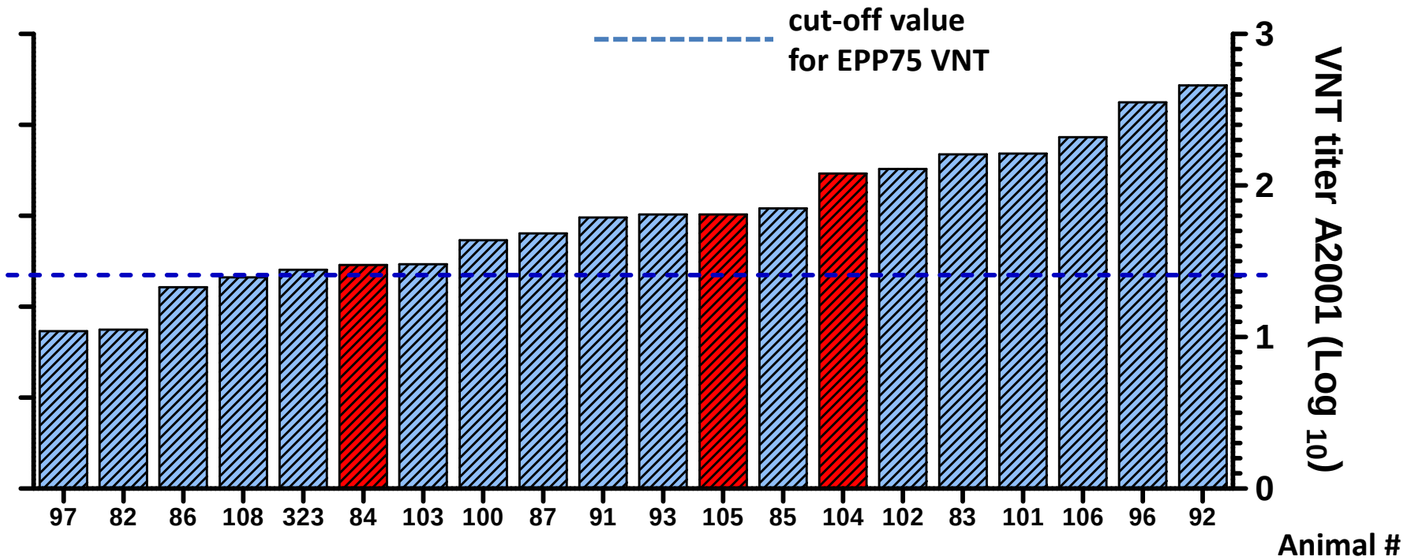
A2001 challenge results

Experimental group	# protected animal /total
A24 10 µg	3 / 5 (60%)
A24 40 µg	4 / 5 (80%)
A24 10 µg x2	5 / 5 (100%)
A24/C3I/O1C	5 / 5 (100%)
PBS	0 / 2 (0%)

- previous reports for vaccine matching assays with A24/A2001 strains (10µg A24 oil vaccine, single dose) showed between 56% and 25% of protection
- 6 out 17 protected animals showed Ab against FMDV NSP already at 7 dpv; 2 out 3 of the non-protected steers did not develop anti-NSP Ab (too early?), but were positive for virus isolation

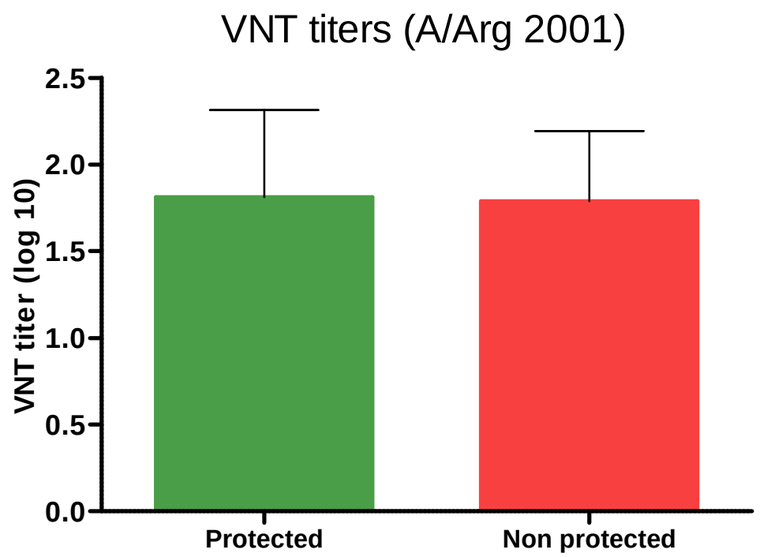
		anti-NSP Ab (ELISA)			VI
group	animal #	0 dpv	30 dpv	7 dpi	7 dpi
A24 10 µg	*82*	-	-	-	ND
	84	-	-	-	+
	91	-	-	+	ND
	100	-	-	+	ND
	104	-	-	+	+
A24 40 µg	*83*	-	-	-	ND
	85	-	-	+	ND
	93	-	-	-	ND
	101	-	-	-	ND
	105	-	-	-	+
A24 10 µg x2	*86*	-	-	-	ND
	92	-	-	-	ND
	96	-	-	-	ND
	102	-	-	-	ND
	106	-	-	-	ND
A24/C3I/O1C	*87*	-	-	+	ND
	97	-	-	-	ND
	103	-	-	-	ND
	108	-	-	+	ND
	323	-	-	+	ND
naive	*329*	-	-	+	+
	377	-	-	+	+

order according to VNT titers



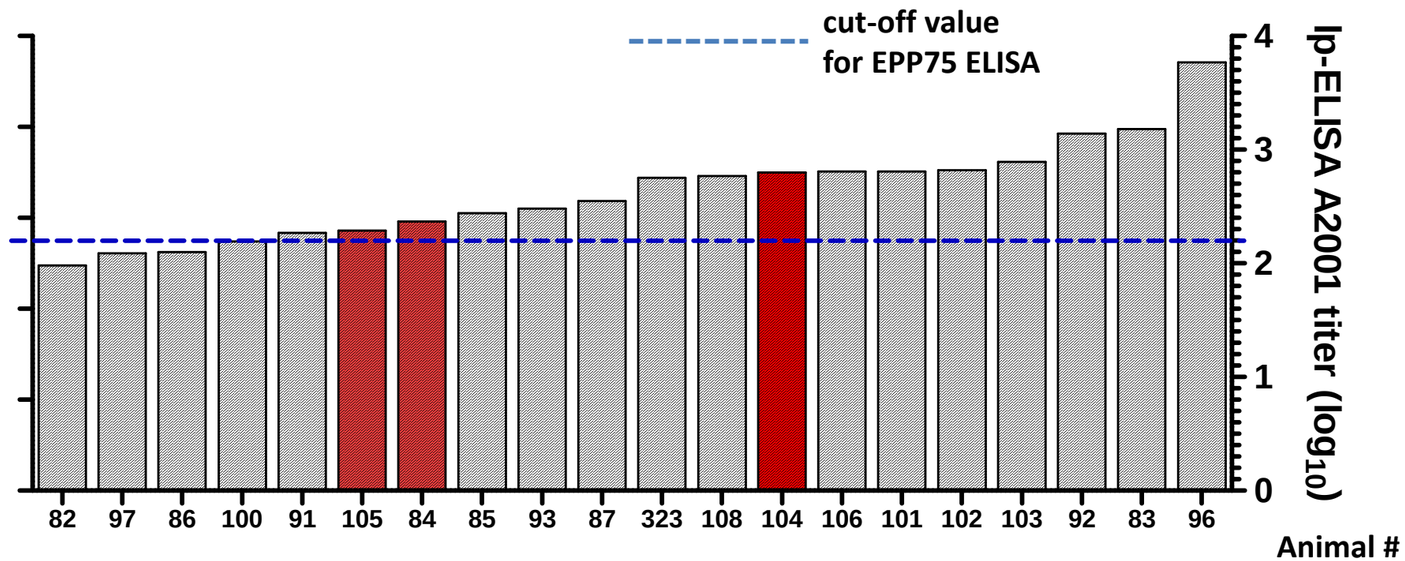
- all non-protected animals showed VNT titers above those established for 75% of expected protection (EPP75) for this assay
- 4 out 17 protected animals had mean VNT titers below those established for EPP75 for the A2001 strain

protected VS non-protected for VNT



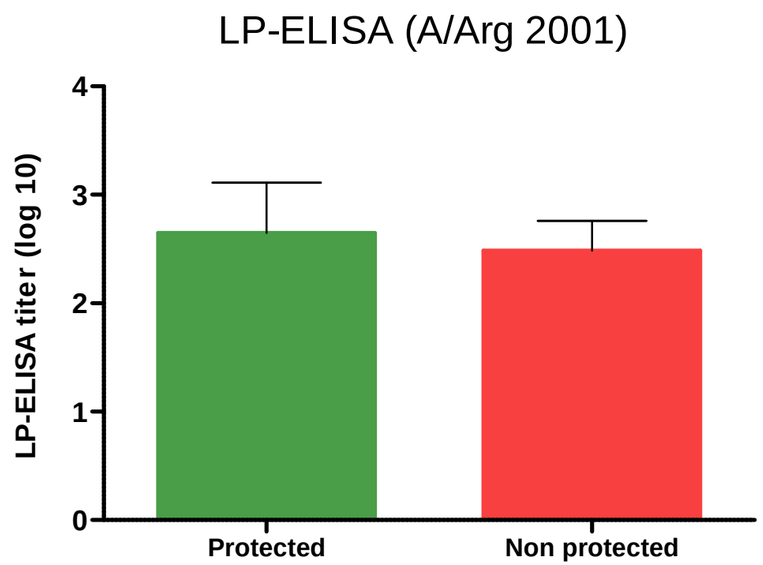
- no significant differences in VNT titers against A2001

order according to LP-ELISA titers



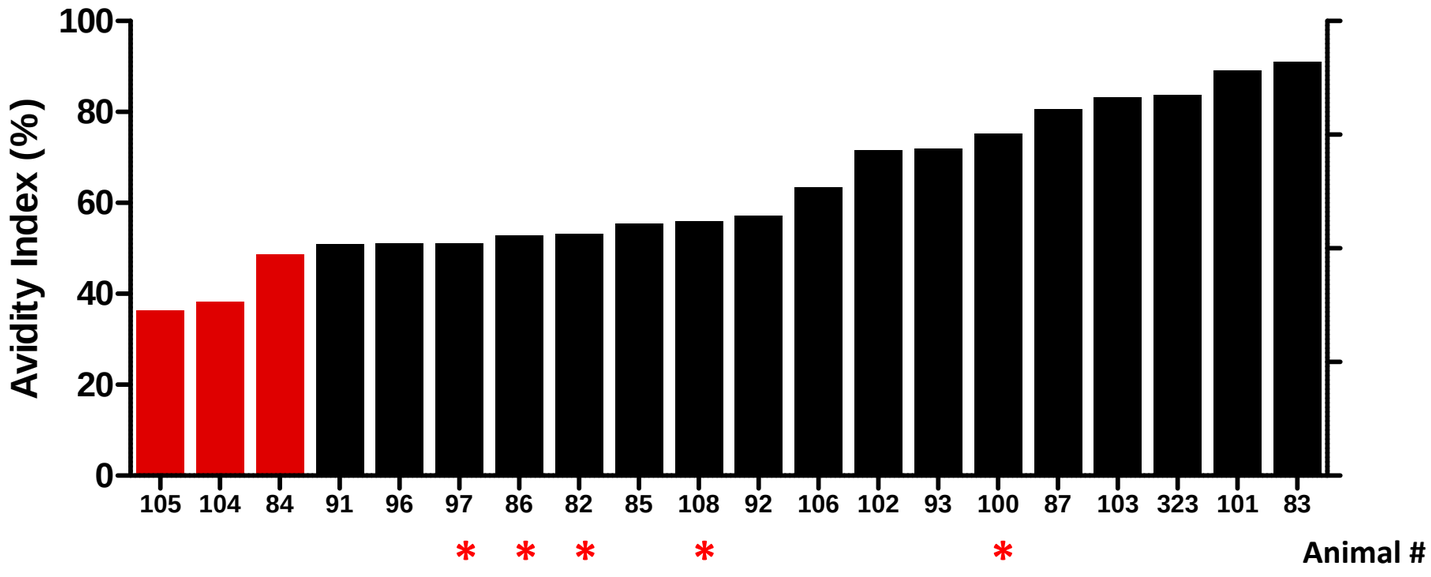
- all non-protected animals showed LP-ELISA titers above those established for 75% of expected protection (EPP75) for this assay
- 4 out 17 protected animals had mean LPELISA titers below those of the EPP75 for the A2001 strain

protected VS non-protected for LP-ELISA



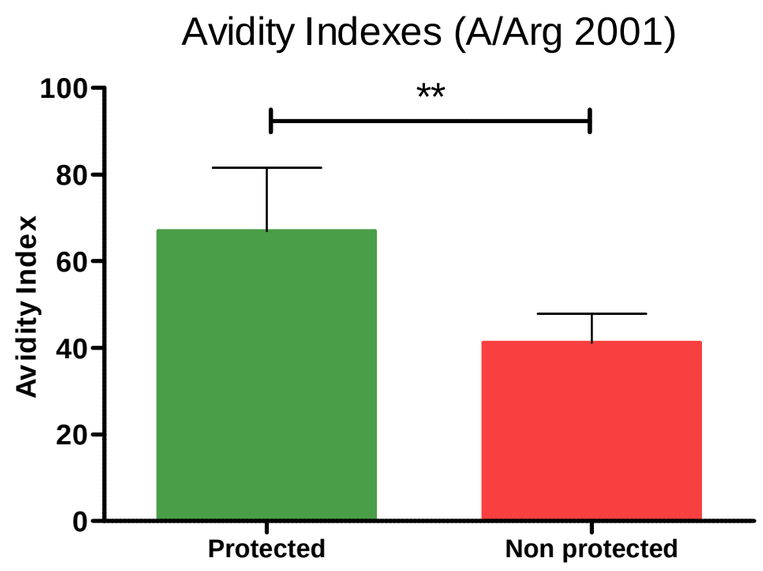
- no significant differences in LP-ELISA titers against A2001

order according to AI values



- Non-protected steers were those also showing the lowest avidity indexes against A2001 (between 36% and 46%)
- Protected animals with titers below the EPP75 cut off for LP-ELISA (82, 97, 86, 100) or EPP75 cut off for VNT (82, 97, 86, 108) showed AI between 53% and 75%

protected VS non-protected for avidity index



- mean avidity index in protected animals (n=17) was significantly higher ($p<0,01$) than that of the non-protected steers (n=3)

conclusions

- *only animals from the revaccinated group or those immunized with the polyvalent formulation did not present FMD-generalization symptoms*
- *protection % in the A24 10µg group was similar to that previously reported*
- *no statistical differences were found among groups for A2001-specific IFN-γproduction, IgG1/IgG2 titers, or avidity indexes.*

conclusions

- *significant differences among groups for A2001-specific Ab were more evident when analyzing VNT titers (A24 40µg & A24 10µg X2>A24 10µg & A24/C3I/O1C) than LP-ELISA (A24 10µg X2>A24 10µg)*
- *However, VNT and LP-ELISA titers did not show a clear correlation with the heterologous protection*
- ***Determination of the avidity of sera against the heterologous strain (A2001) was the only assay capable of differentiating protected from non-protected animals***

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Thank you for your attention!