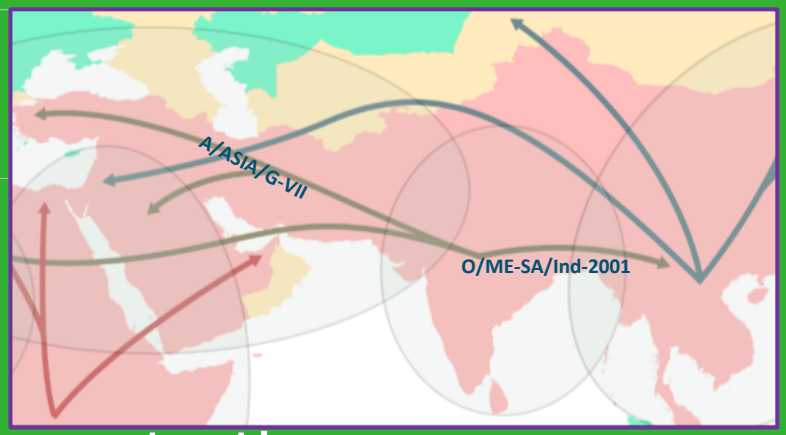
Efficacy of A/MAY/97 FMDV vaccine against heterologous challenge with a field virus from the emerging A/ASIA/G-VII lineage

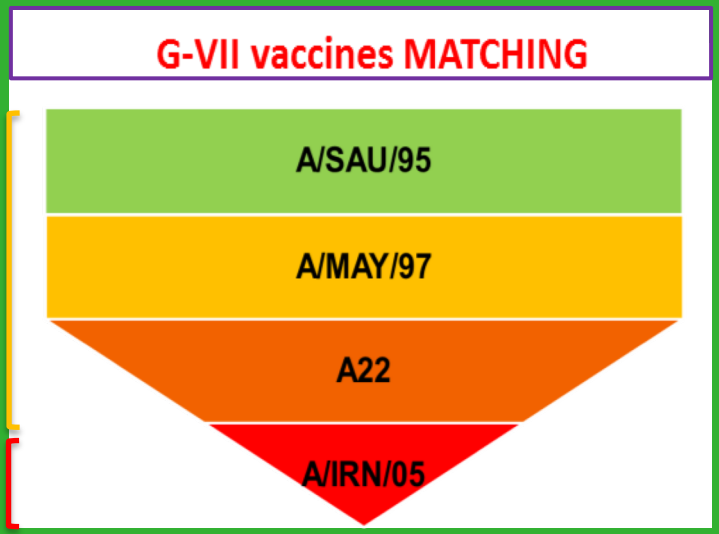
Phaedra Eblé, Anna Ludi, Beatriz Sanz-Bernardo, Don King, Nagendra Singanallur, Wilna Vosloo, Aldo Dekker

WAGENINGEN UNIVERSITY & RESEARCH
100years 1918 — 2018
THE Pirbright INSTITUTE
CSIRO
BOEHRINGER INGELHEIM

A/ASIA/G-VII



- Emerging strain A/ASIA/G-VII
- Vaccines used in the field → poor protection
- *In vitro* vaccine matching data:
  - Cross neutralisation, r1 value
  - A/ASIA/G-VII field viruses poorly matched with vaccines (A-SAU-95, A22 IRQ and A-IRN-05)
- New emerging strains problem for
  - Endemic countries
  - FMDV free countries



WAGENINGEN UNIVERSITY & RESEARCH

100years 1918 — 2018

A/ASIA/G-VII: heterologous protection?

Vaccine (2008) 26, 1681–1687

available at www.sciencedirect.com

ScienceDirect

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

High potency vaccines induce protection against heterologous challenge with foot-and-mouth disease virus

K.E. Brehm[a], N. Kumar[a], H.-H. Thulke[b], B. Haas[a,*]

[a] *Friedrich-Loeffler-Institute, Institute of Diagnostic Virology, Südufer 10, 17493 Greifswald-Insel Riems, Germany*
[b] *UFZ Helmholz Centre for Environmental Research, Department of Ecological Modelling, Permoserstrasse 15, 04318 Leipzig, Germany*

Received 4 September 2007; received in revised form 10 January 2008; accepted 11 January 2008
Available online 12 February 2008

KEYWORDS
Foot-and-mouth disease virus;
Protection by vaccines;
Serology

Summary In a series of three homologous and eight heterologous challenge experiments, it was shown that high potency vaccines against foot-and-mouth disease (FMD) serotype A can induce protection even against heterologous challenge infection with viruses that give low *r*-values with the vaccine strains.

The challenge virus specific neutralizing antibody response on the day of challenge (21 days post vaccination) generally correlated with protection.

A/ASIA/G-VII: heterologous protection?

- FMD free countries: vaccine banks
  - UK: European vaccine bank
  - Australia: national vaccine bank
  - The Netherlands: national vaccine bank
- Collaborative project: test type A vaccines of vaccine banks for efficacy against A/ASIA/G-VII
  - A/IRN/05
  - A/SAU/95
  - A/MAY/97
  - A22/IRQ

WAGENINGEN UNIVERSITY & RESEARCH

100years 1918 — 2018

A/ASIA/G-VII: vaccine in vivo protection?

Vaccine 36 (2018) 1901–1907

Contents lists available at ScienceDirect

Vaccine

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

Efficacy of a high-potency multivalent foot-and-mouth disease virus vaccine in cattle against heterologous challenge with a field virus from the emerging A/ASIA/G-VII lineage

Ryan Waters [a], Anna B. Ludi [a,*], Veronica L. Fowler [a], Ginette Wilsden [a], Clare Browning [a], Simon Gubbins [a], Bob Statham [a], Abdelghani Bin-Tarif [a], Valerie Mioulet [a], David J. King [a], Claire Colenutt [a], Emma Brown [a], Pascal Hudelet [b], Donald P. King [a]

[a] The Pirbright Institute, Ash Road, Pirbright, Woking, Surrey GU24 0NF, United Kingdom
[b] Boehringer Ingelheim, 29 Avenue Tony Garnier, 69007 Lyon, France

ARTICLE INFO

Article history:
Received 8 November 2017
Received in revised form 30 January 2018
Accepted 3 February 2018
Available online 2 March 2018

Keywords:
Foot-and-mouth disease virus
A/ASIA/G-VII
Podal generalisation test (PPG)
Challenge
Vaccine

ABSTRACT

In 2015, outbreaks of foot-and-mouth disease (FMD) in the Middle East were discovered to be caused by a viral lineage (A/ASIA/G-VII), which has recently emerged from the Indian sub-continent. *In vitro* vaccine matching data generated by the World Reference Laboratory (WRLFMD) indicated that A/ASIA/G-VII field viruses were poorly matched with vaccines (A-SAU-95, A22 IRQ and A-IRN-05) that are already used in the region. In order to assess the likely performance of one of these commercially available FMD vaccines, sixteen cattle were vaccinated with a polyvalent vaccine which contained two serotype A components (A-SAU-95 and A-IRN-05) with a homologous potency of at least $6PD_{50}$, and two cattle were left unvaccinated as controls. Twenty-one days later, all 18 cattle were challenged by tongue inoculation with an FMDV field isolate A/IRN/22/2015 from the A/ASIA/G-VII lineage, in line with the European Pharmacopeia PPG test conditions. The two control animals developed generalised FMD, and 7/16 vaccinated animals developed at least one foot lesion, thus only 56.3% were defined as protected. For the vaccine components, there was a significant increase in the probability of protection with increasing serological titres for A-SAU-95 ($p = 0.03$), but not for A-IRN-05 ($p = 0.42$). Analysis of FMDV in blood and nasal swabs suggested that vaccination reduced shedding and potential onward spread of FMD virus even if the animal developed foot lesions. In summary, the results from this study suggest that whilst this vaccine would not be appropriate for use in an emergency situation (in previously FMD-free countries), it may be partially effective in the field in endemic countries where repeat prophylactic vaccination is practiced. For emergency reactive vaccination, the findings from this study support the idea that a new vaccine strain should be developed that is tailored to the A/ASIA/G-VII lineage.

- Vaccine
  - A/SAU/95
  - A/IRN/05
- PPG test
  - 16 cattle
  - Full dose
- 9/16 protected
- <3 PD50

A/ASIA/G-VII: vaccine in vivo protection?

- Pilot study A22/IRQ and A/MAY/97
  - Full doses vaccine
  - 7 animals vaccinated with A/MAY/97, 7 animals with A22/IRQ
  - 3 unvaccinated control animals.

Vaccine	Podal generalization	Protected
A/MAY/97	2/7 (28.5%)	5/7 **(71.5%)**
A22	5/7 (71.5%)	2/7 (28.5%)

- A/MAY/97 best results
  - Vaccination with **A/MAY/97** reduced virus shedding in mouth swabs
  - Good correlation between VNT and protection (p=0.008)
  - A/MAY/97 72% protection ~ 3 PD_{50}/dose

A/ASIA/G-VII: A/MAY/97 PD_{50}

- A/MAY/97: PD_{50} study
  - Clinical protection
  - Virus excretion
  - Serological responses
    - Does it correlate with protection?
- Full, 1/3 and 1/9 doses of vaccine and 3 controls
- Challenge with A/ASIA/G-VII (A/IRN/22/15)
  - Tongue inoculation

A/MAY/97 PD_{50}: clinical, VI and PCR results

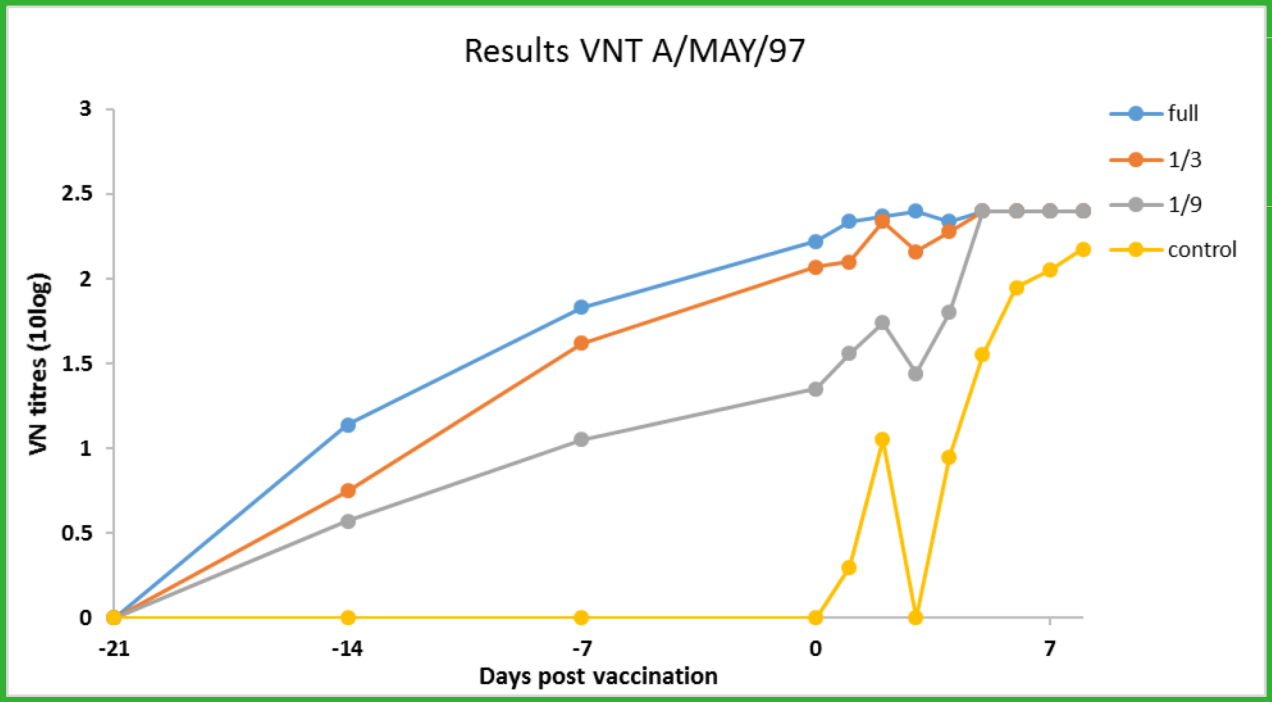
	Cow number	Feet lesions	Virus isolation (PFU/ml)			PCR		
			serum	nose	mouth	serum	nose	mouth
Full dose	1566	-	-	+	+	-	+	+
	1567	-	-	+	+	-	+	+
	1568	-	-	+	+	-	+	+
	1569	-	-	+	+	-	+	+
	1570	-	-	+	+	-	+	+
1/3 dose	1571	-	-	+	+	-	+	+
	1572	-	-	+	+	+	+	+
	1573	-	-	-	+	-	-	+
	1574	-	-	+	+	-	+	+
	1575	+	-	+	+	-	+	+
1/9 dose	1576	+	-	+	+	+	+	+
	1577	-	-	+	+	-	+	+
	1578	-	-	+	+	-	+	+
	1579	+	-	+	+	+	+	+
	1580	+	-	+	+	+	+	+
Control	1581	+	+	+	+	+	+	+
	1582	+	+	+	+	+	+	+
	1583	+	+	+	+	+	+	+

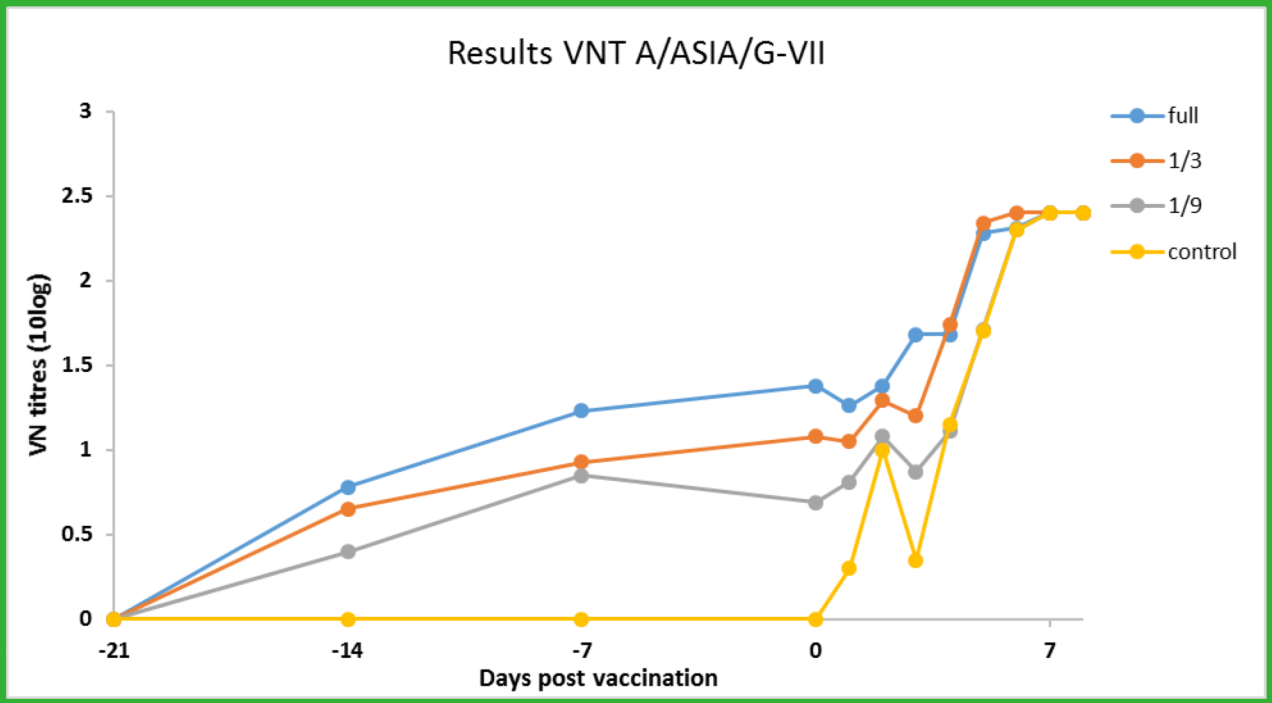
WAGENINGEN
UNIVERSITY & RESEARCH

100years
1918 — 2018

A/MAY/97 PD_{50}: clinical, VI and PCR results

- Heterologous 6.47 PD_{50}/dose (Spearman Karber)
- Full dose and 1/3 dose groups are significantly different from control groups for
  - virus shedding (PFU/ml)
  - duration of virus shedding





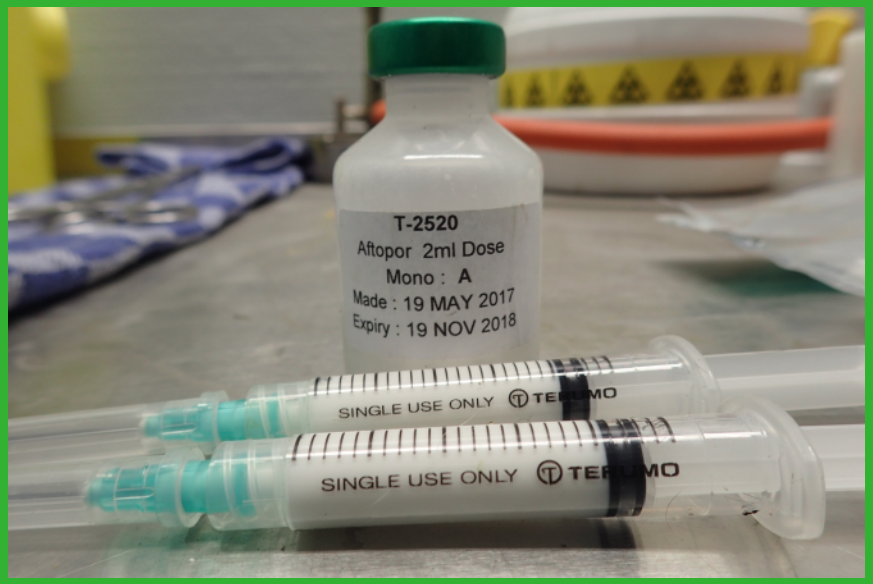
- Mean values at 0dpi:
- A/MAY/97
  - 2.22
  - 2.07
  - 1.35
- A/ASIA/G-VII
  - 1.38
  - 1.08
  - 0.69
- Correlation between VN-titre and protection (p=0.047)

A/MAY/97 PD_{50} conclusion & discussion

- A high potency A/MAY/97 vaccine can protect against heterologous challenge with A/ASIA/G-VII, even though *in vitro* results predict a poor antigenic match
- Probably highly dependent on quality / potency of the used vaccine

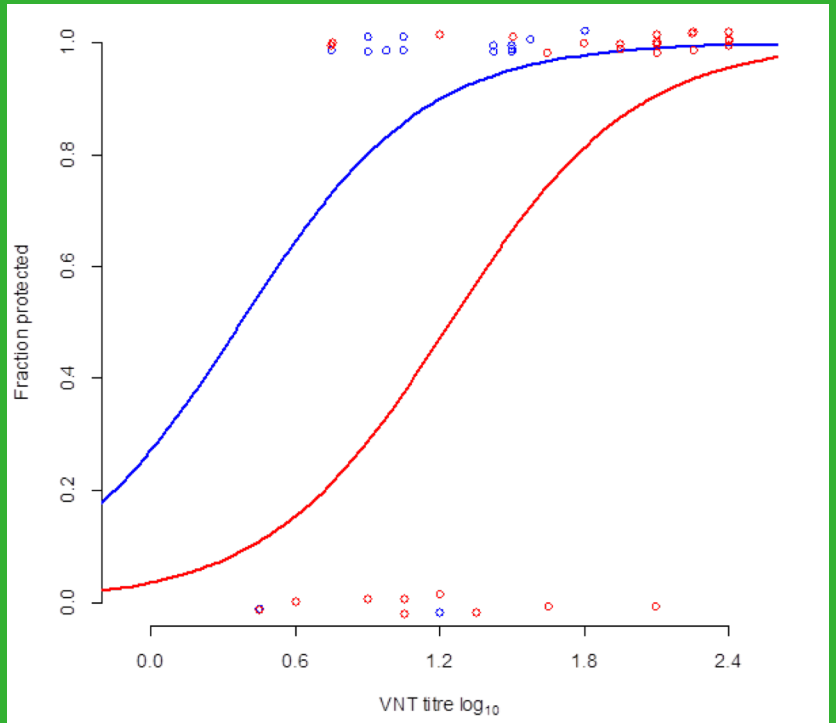
BUT: A/ASIA/G-VII vaccine is also available now

- New research Question:
  - Does A/ASIA/G-VII vaccine protect against other type A strains?



Future analysis:

- Is there a relation between the heterologous and homologous potency of a vaccine (~ r_1-value?)
- Can we predict the heterologous potency if we know the homologous potency of a vaccine?
- Or (vice versa) can we use 'super' potent vaccines to overcome difficulties related to strain differences?



Relation between VNT antibody titre against A MAY/97 and estimated protection in both homologous (blue) vaccinated and heterologous vaccinated cattle (red).

In the homologous potency A MAY/97 vaccine and A MAY/97 challenge virus was used. In the heterologous potency test A MAY/97 and A_{22}Iraq vaccine and A IRN/22/2015 challenge virus was used. The circles represent the observed protection (slightly displaced to avoid overlap).

Acknowledgements

Beatriz Sanz-Bernardo

Anna Ludi

Don King

Wilna Vosloo

Nagendra Singanallur

Aldo Dekker

Froukje van Hemert

Klaas Weerdmeester

Animal service department

Thank you for your attention

Questions?