CODA - CERVA

In vivo evaluation of Lumpy Skin Disease vaccine efficacy in controlled environment

Andy Haegeman, Laurent Mostin, Maria Vastag, Willem Van Campe, Nadav Galon, Estelle Venter, Annebel De Vleeschauwer, Eeva Tuppurainen, Kris De Clercq

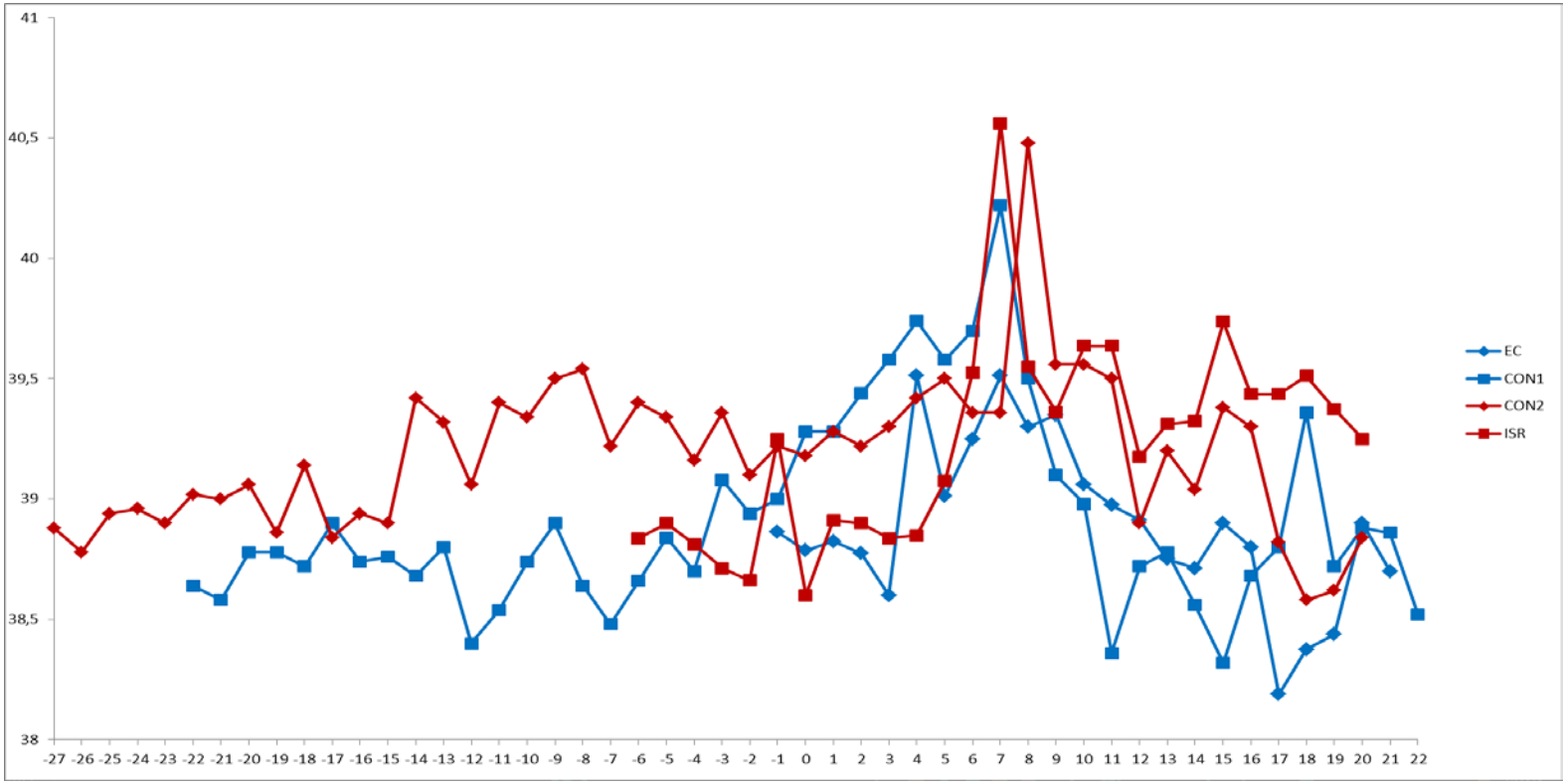
LSDV: Infection Model

- Infection route:
  - Intravenously
  - Intra-dermal: 4 sites, 2 on each side of the neck
- Infection dose:
  - $10^{5.4\text{-}6}$ $TCID_{50}$/100 µl
- Number of animals per group: N = 8
- Clinical scoring (21 days) includes:
  - Body temperature, Lnn swelling, nodule development (number and size), feed uptake, conjunctivitis, general behaviour, local reaction (vaccination and challenge sites)
- Sampling
  - EDTA blood, buccal swabs: PCR, Virus isolation
  - Bopsies, tissues and organs: PCR , Virus isolation
  - Serum: IPMA and virusneutralisation test
  - Heparinized blood: IFN release

LSDV: Infection Model

Neethling strain Vs a field isolate from Israel

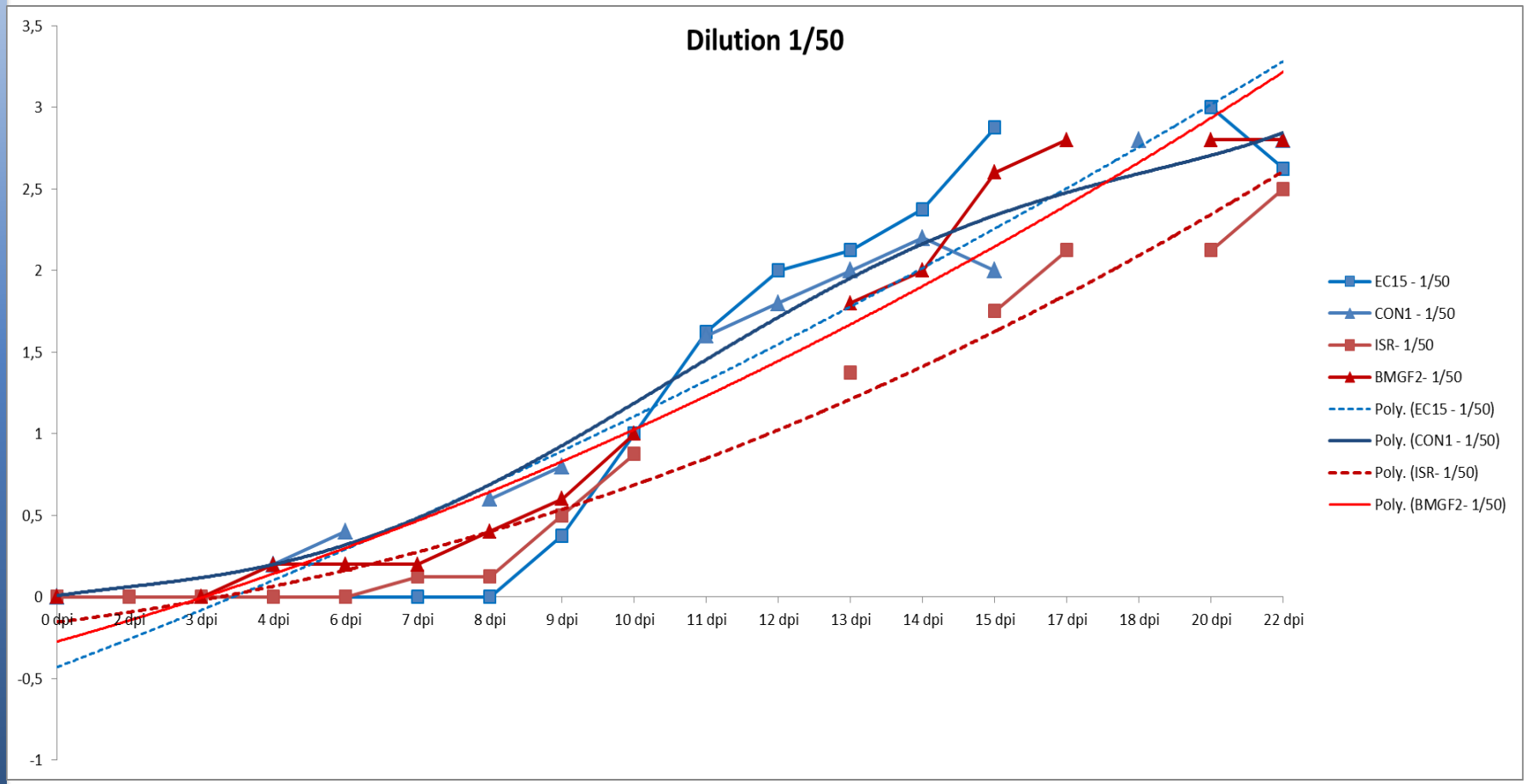
- Some data of the comparison: **Similarities**
  - Body temperatures:



→ **Both** show a fever spike around 7/8 dpi. Prolonged fever period can occur (app. 25% for both)

LSDV: Infection Model
Neethling strain Vs a field isolate from Israel

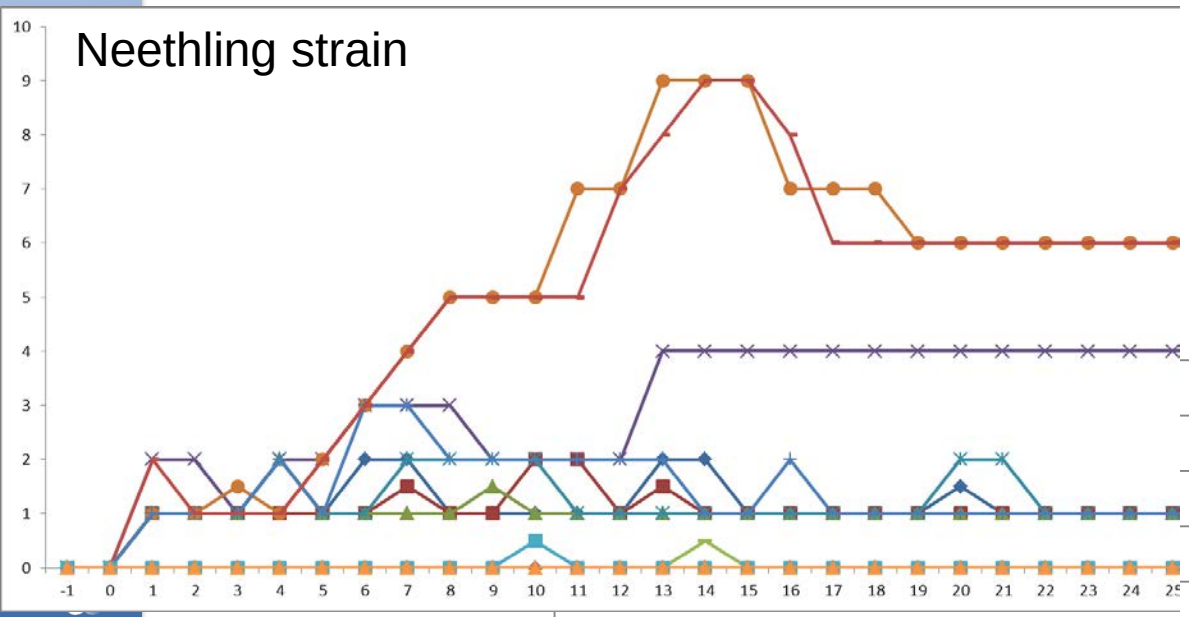
- Some data of the comparison: **Similarities**
  - Seroconversion

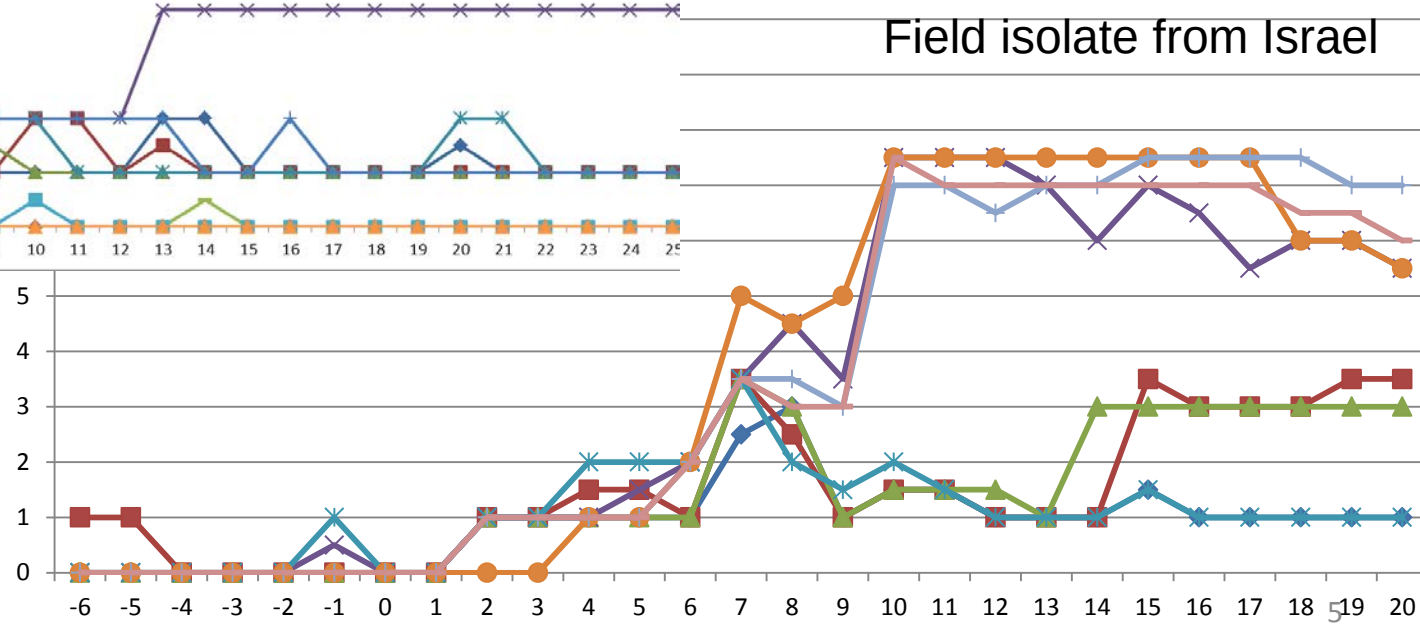


Onset : 4 to 13 dpi (**both**) → a tendency to have more Abs with Neethling

LSDV: Infection Model
Neethling strain Vs a field isolate from Israel

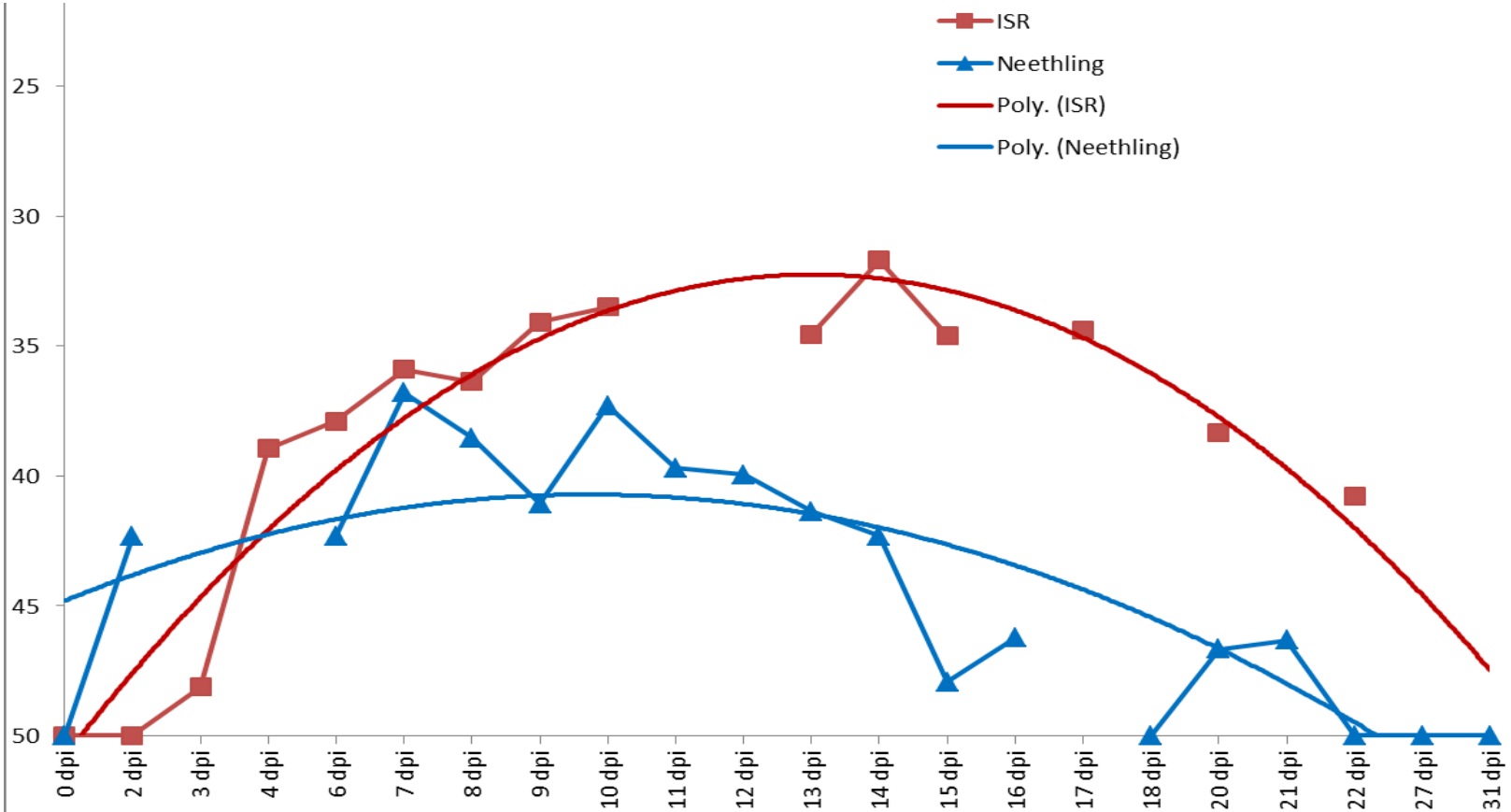
- Some data of the comparison: differences
  - Clinical signs after challenge Number of nodules / generalisation / clinical scores





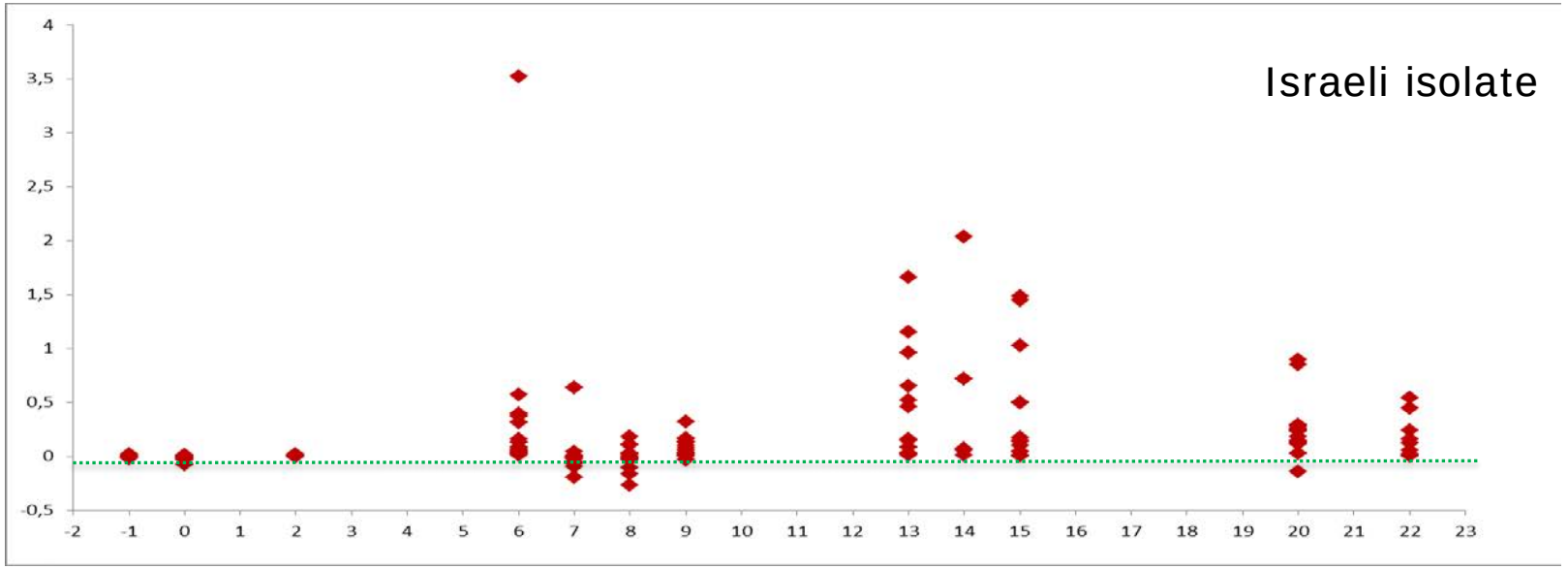
LSDV: Infection Model
Neethling strain Vs a field isolate from Israel

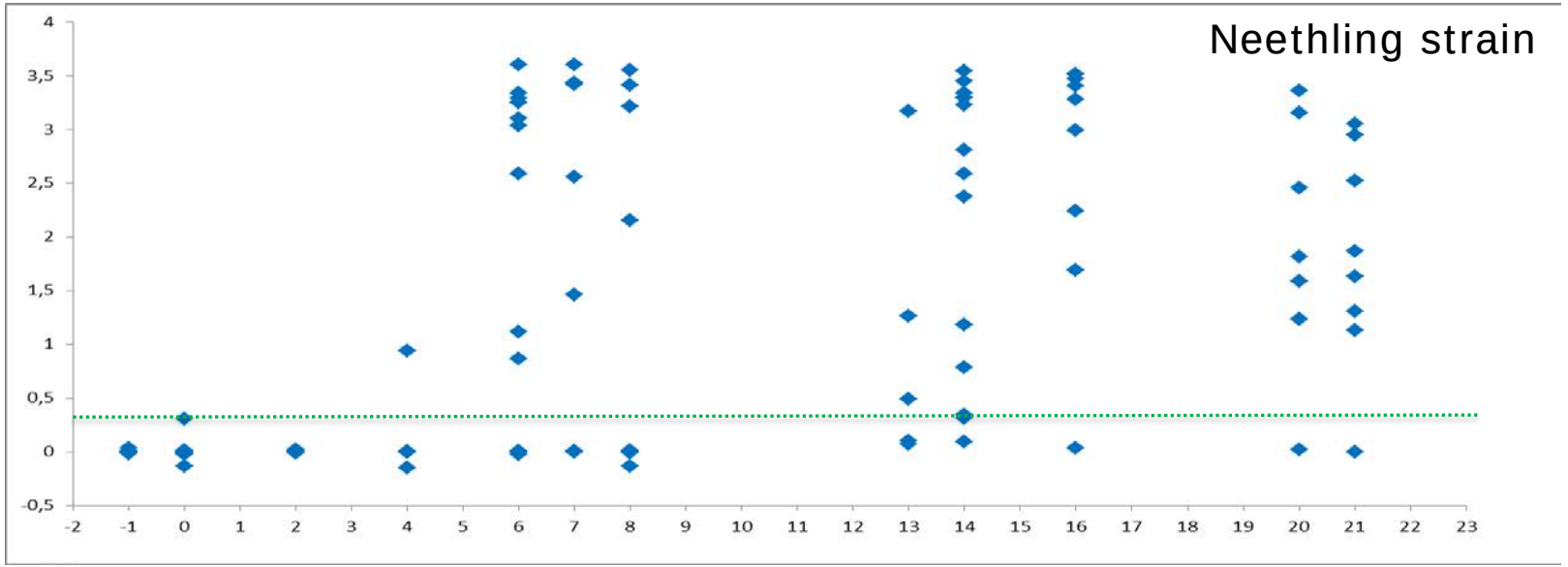
- Some data of the comparison: differences
  - Virus detection in blood: detection as early as 2/3 dpi for both. But vireamic period is **longer** and viral load in general **higher** with field isolate from Israel



° IFNg release upon stimulation in vitro:

Much **lower** IFNg release in animals infected with the Israeli field isolate.





LSDV: Infection Model
Neethling strain Vs a field isolate from Israel

- Some data of the comparison: Conclusion

When all data was analysed the Israeli field isolate is more interesting to be used for our vaccine trials.

LSDV: Vaccine trials

- **Commercial available → Live attenuated vaccines (LAV)**
  - Sheeppox based (RM-65)
    - ✓ JoviVac (Jordan Bio-Industries Center (JOVAC); Jordan)
    - ✓ Abic (Abic Biological Laboratories Ltd (Phibro); Israel)
    - ✓ Penpox (Pendink Institute; Turkey)
  - LSDV-based
    - ✓ OBP (Onderste Poort; South-Africa)
    - ✓ LumpyVax (MSD; South-Africa)
    - ✓ HerbiVac (Deltamune, South-Africa)
  - Goatpox based
    - ✓ CapriVac (Jordan Bio-Industries Center (JOVAC);Jordan)
  - Sheep and goatpox based or LSDV? (Cfr Tuppurainen et al., 2014)
    - ✓ KSGP 0240/0180 (Jordan Bio-Industries Center (JOVAC); Jordan)

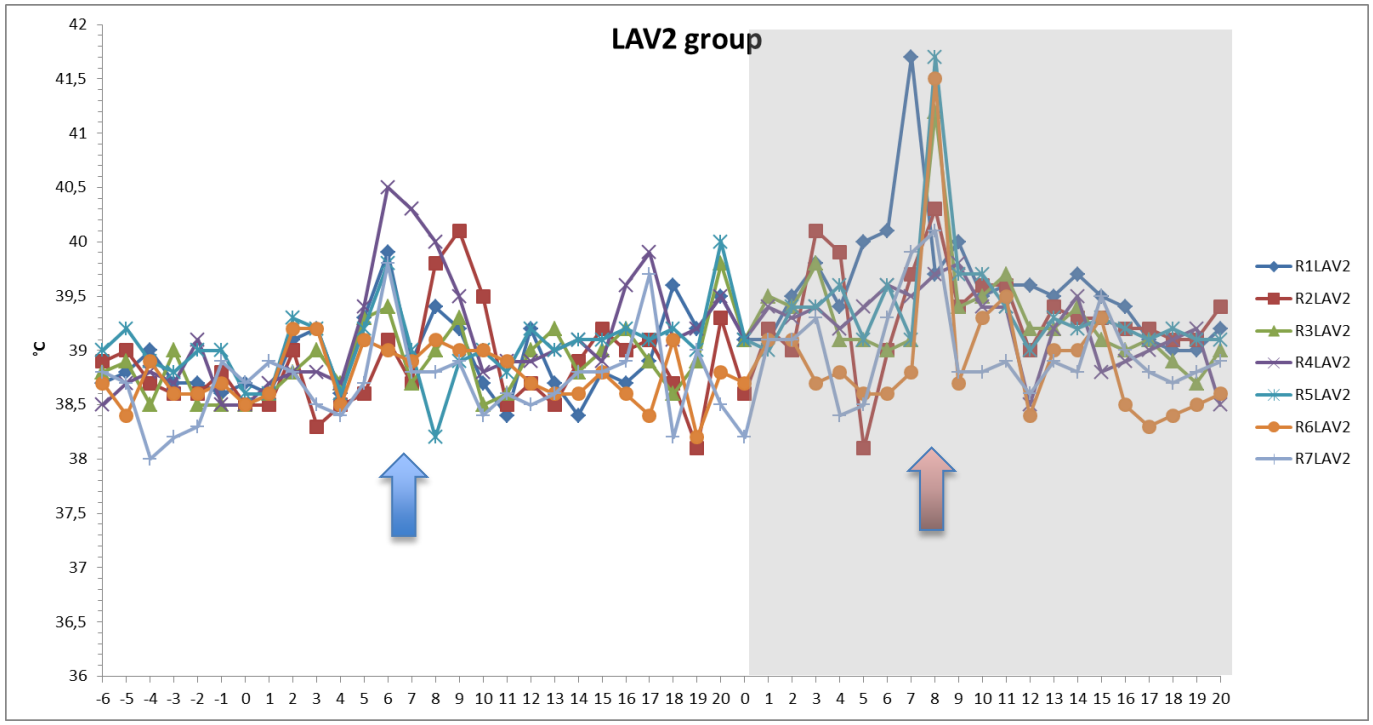
- **New Inactivated Vaccine (MCI, Morocco)**
  - Sheeppox-based
  - LSDV-based

LSDV: Vaccine trial set-up

- **Number of animals:**
  - 7 animals per vaccine group
  - 5 control animals (not vaccinated)
- **Vaccination: as described by company**
- **Single vaccination**
- **Challenge: 21 days after vaccination**
- **Sampling and follow-up: as described for model**

LSDV Vaccine trials: preliminary results

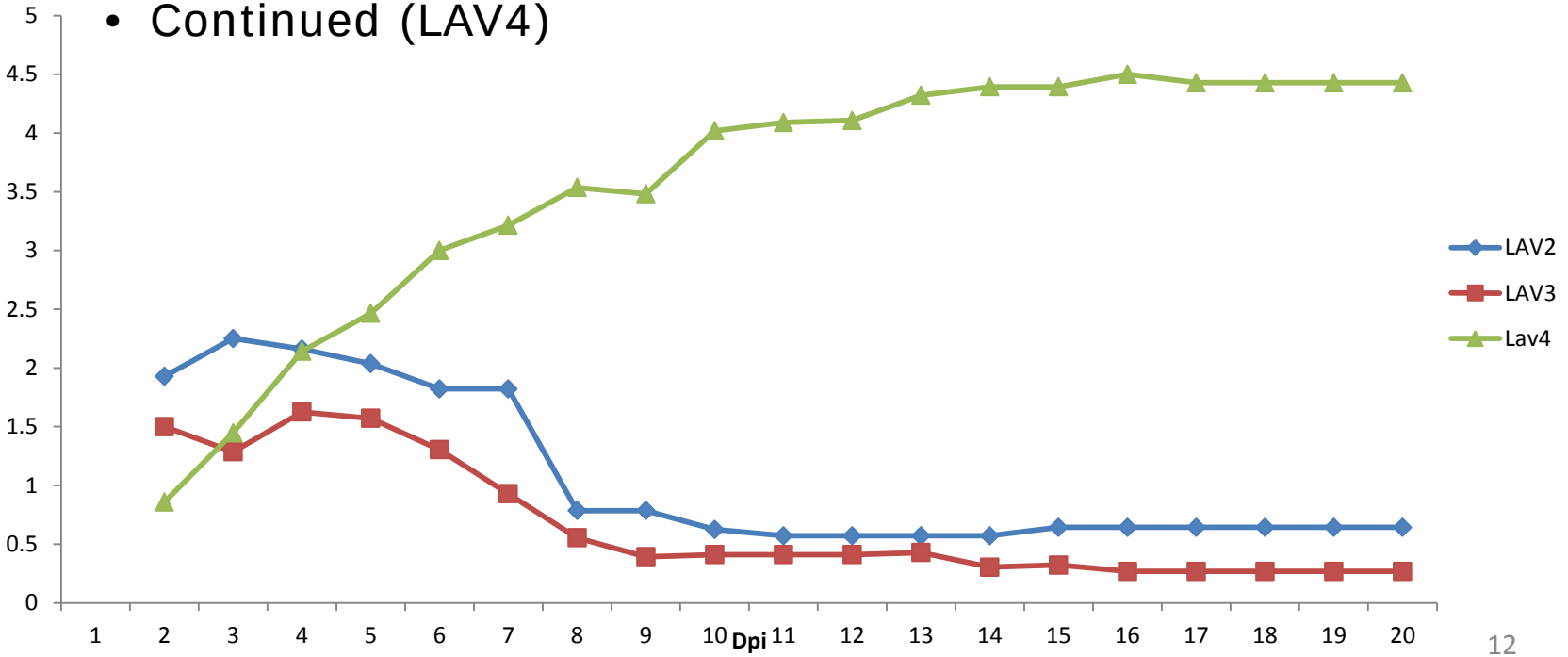
- Trials and analyzes are **still ongoing**, some **preliminary** results:
  - Limited side effects were seen for some vaccines:
    - → Elevated temperatures around 7/8 dpv (time point similar to the 7/8 dpi fever spike after infection)



LSDV Vaccine trials: preliminary results

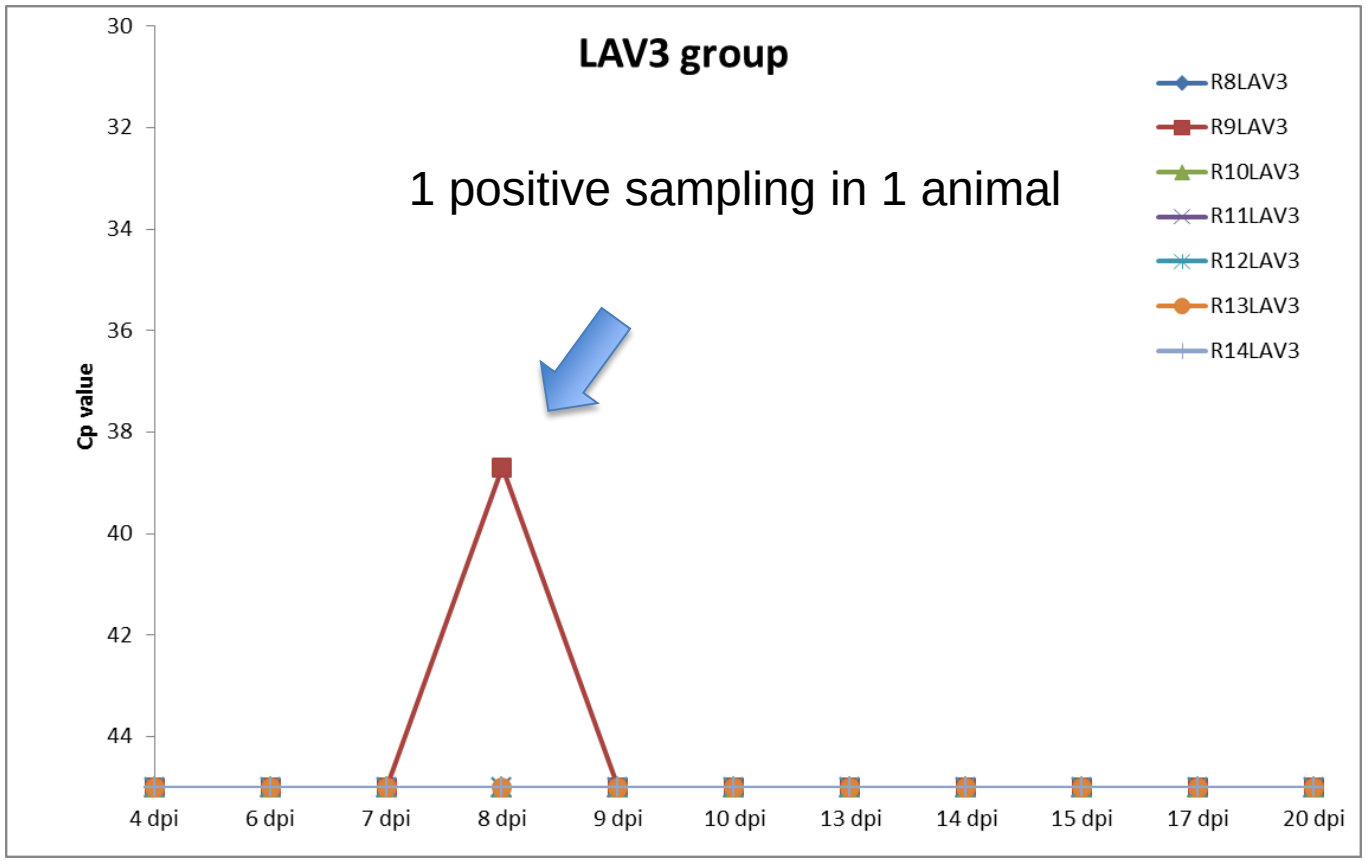
- Clinical signs
  - None (for example LAV2, LAV3)
  - Nodule formation (onset 7->9 dpi; similar to control group) (for example LAV4)

- Local reaction at inoculation site
  - Transiently (LAV2, LAV3)
  - Continued (LAV4)



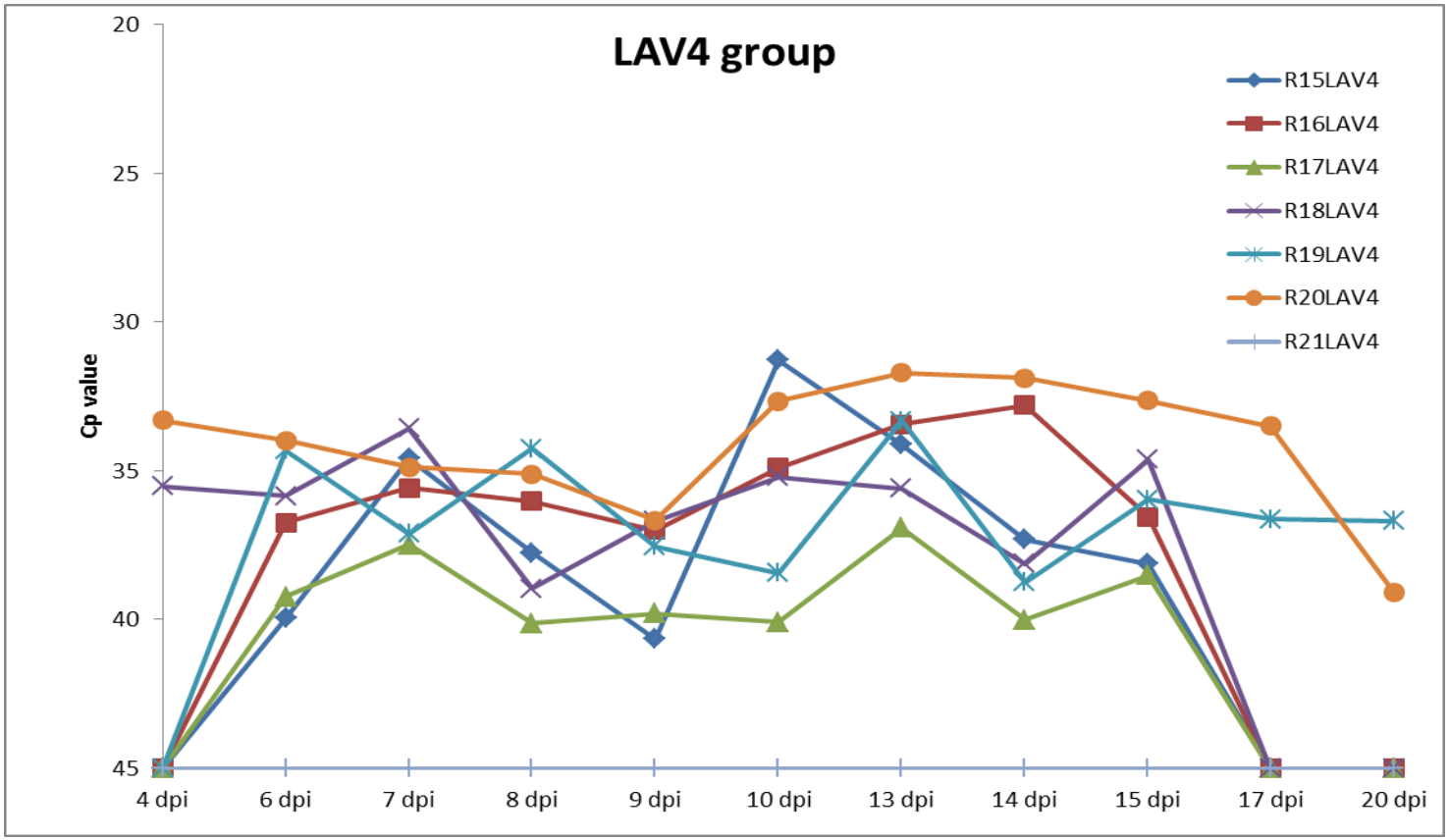
LSDV Vaccine trials: preliminary results

- Viremia following challenge:
  - Completely blocked → Strong Vaccine effect (LAV2)
  - Almost completely blocked→ Vaccine effect (LAV3)



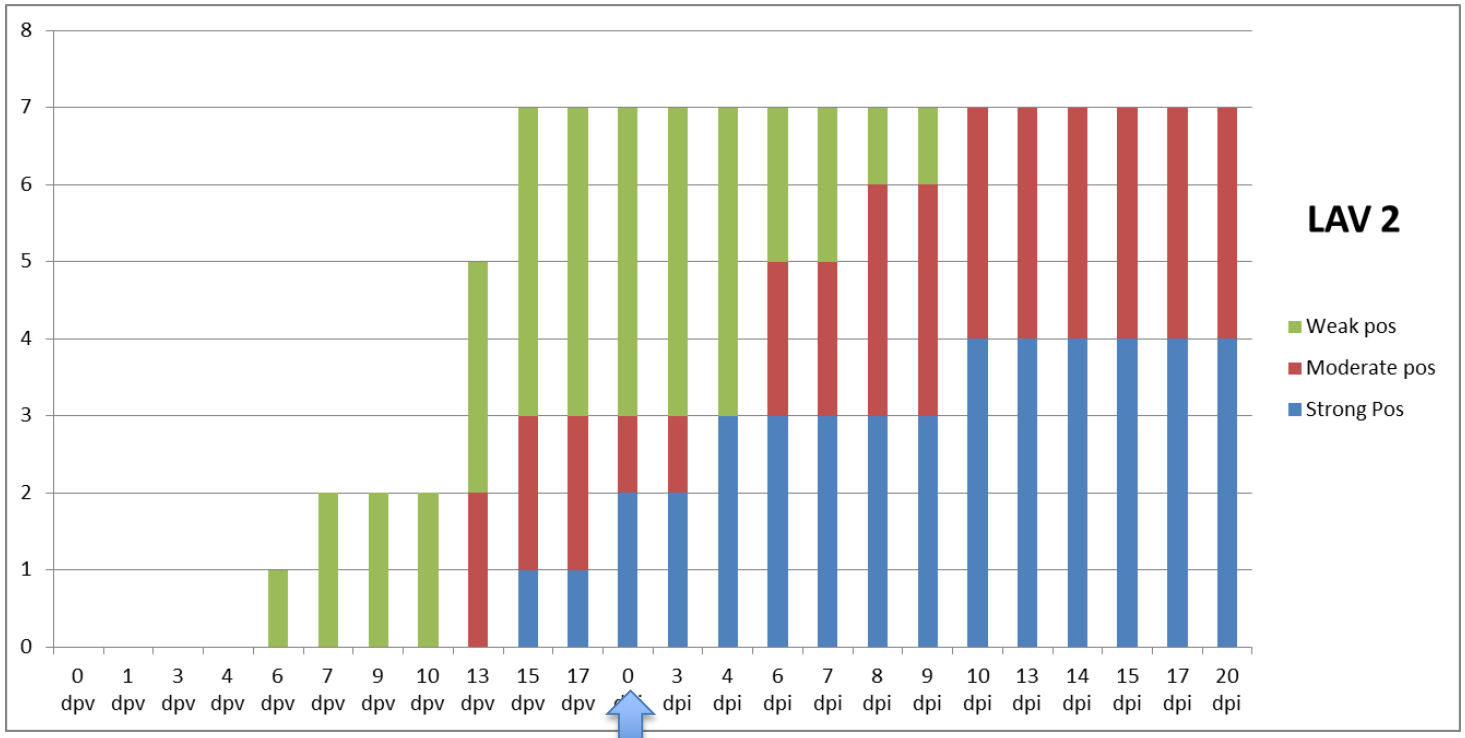
LSDV Vaccine trials: preliminary results

- Viremia following challenge:
  - Completely blocked → Strong Vaccine effect
  - All most completely blocked → Vaccine effect
  - No blocking → No Vaccine effect (LAV4)



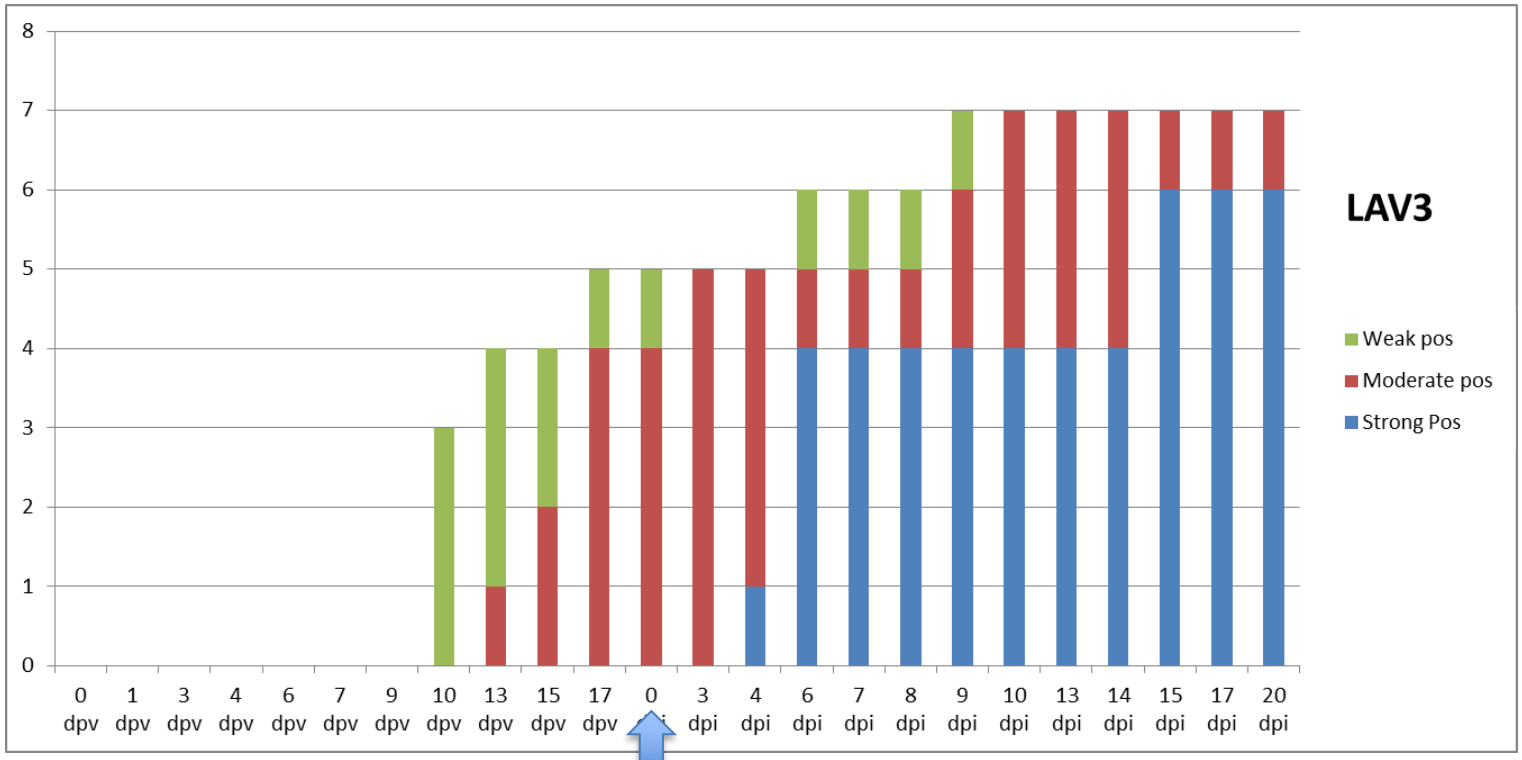
LSDV Vaccine trials: preliminary results

- Serological response:
  - **Strong**
    - ✓ Early detection
    - ✓ At moment of challenge:
      - 100% seroconverted
      - Some moderate to strong positive



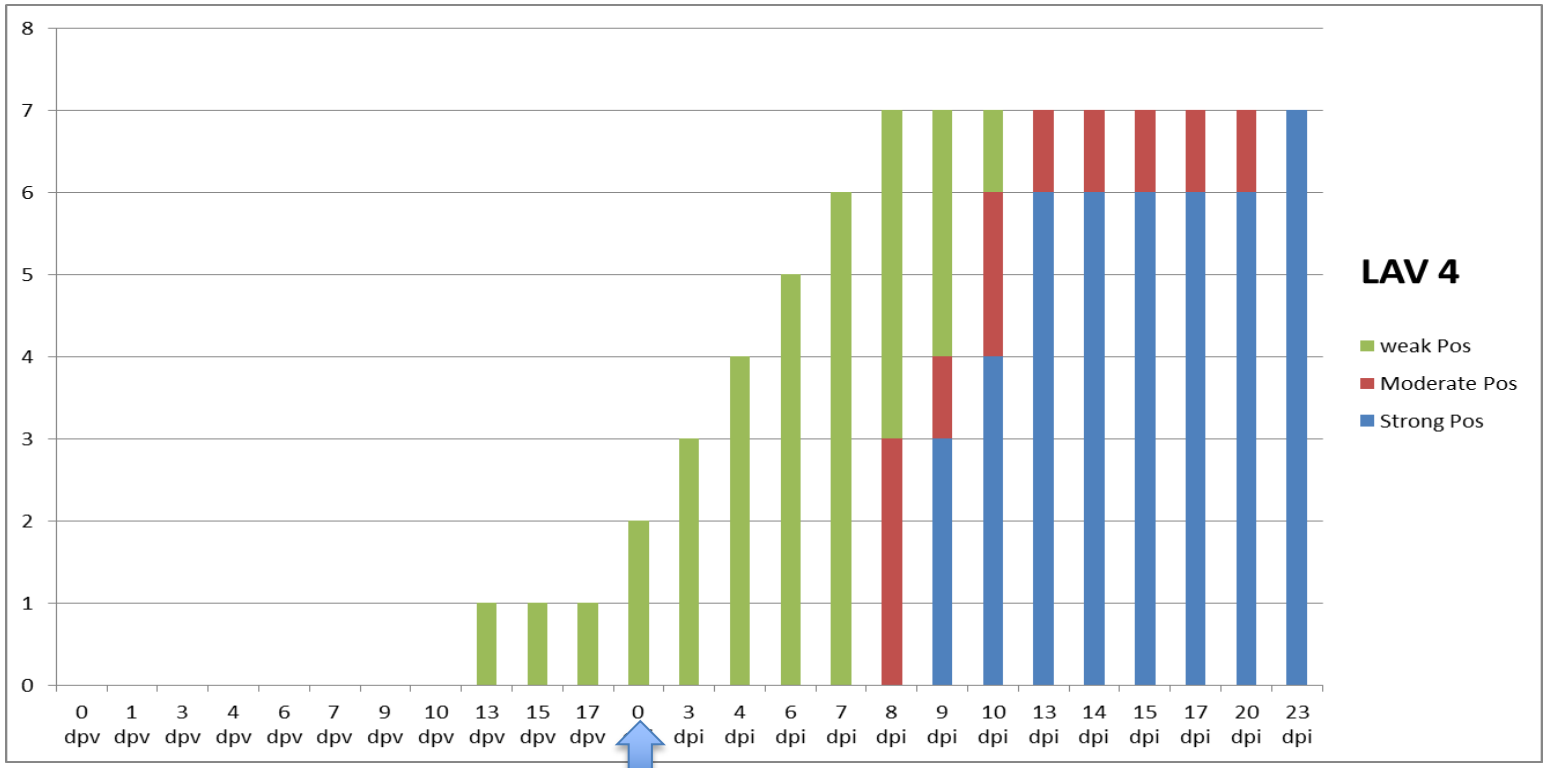
LSDV Vaccine trials: preliminary results

- Serological response:
  - **Moderate**
    - ✓ Starts later
    - ✓ At moment of challenge:
      - Not 100% seroconverted but the majority
      - Some moderate positive



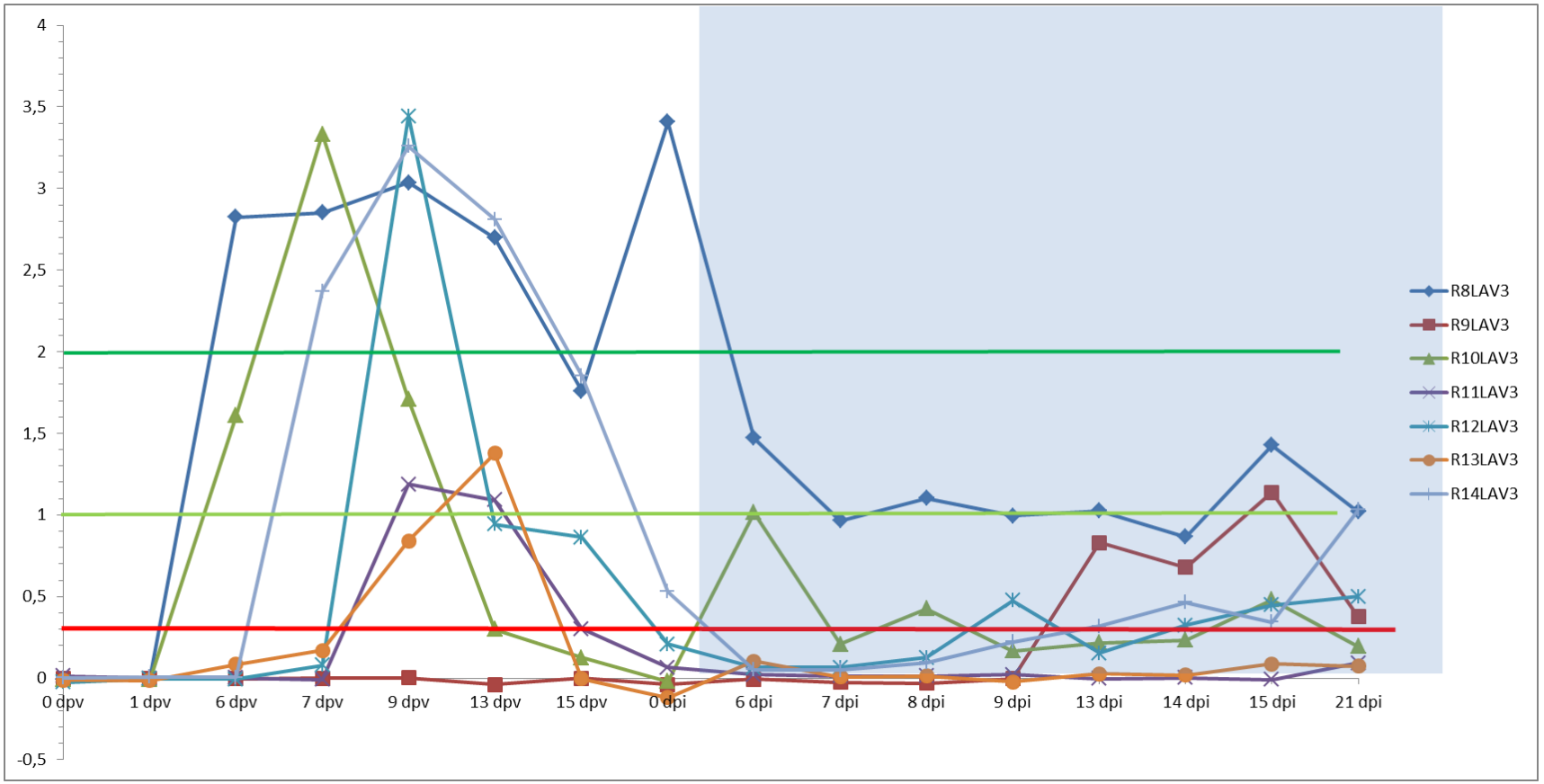
LSDV Vaccine trials: preliminary results

- Serological response:
  - **Weak**
    - ✓ Starts later
    - ✓ At moment of challenge:
      - Minority was seroconverted
      - Only weak positive



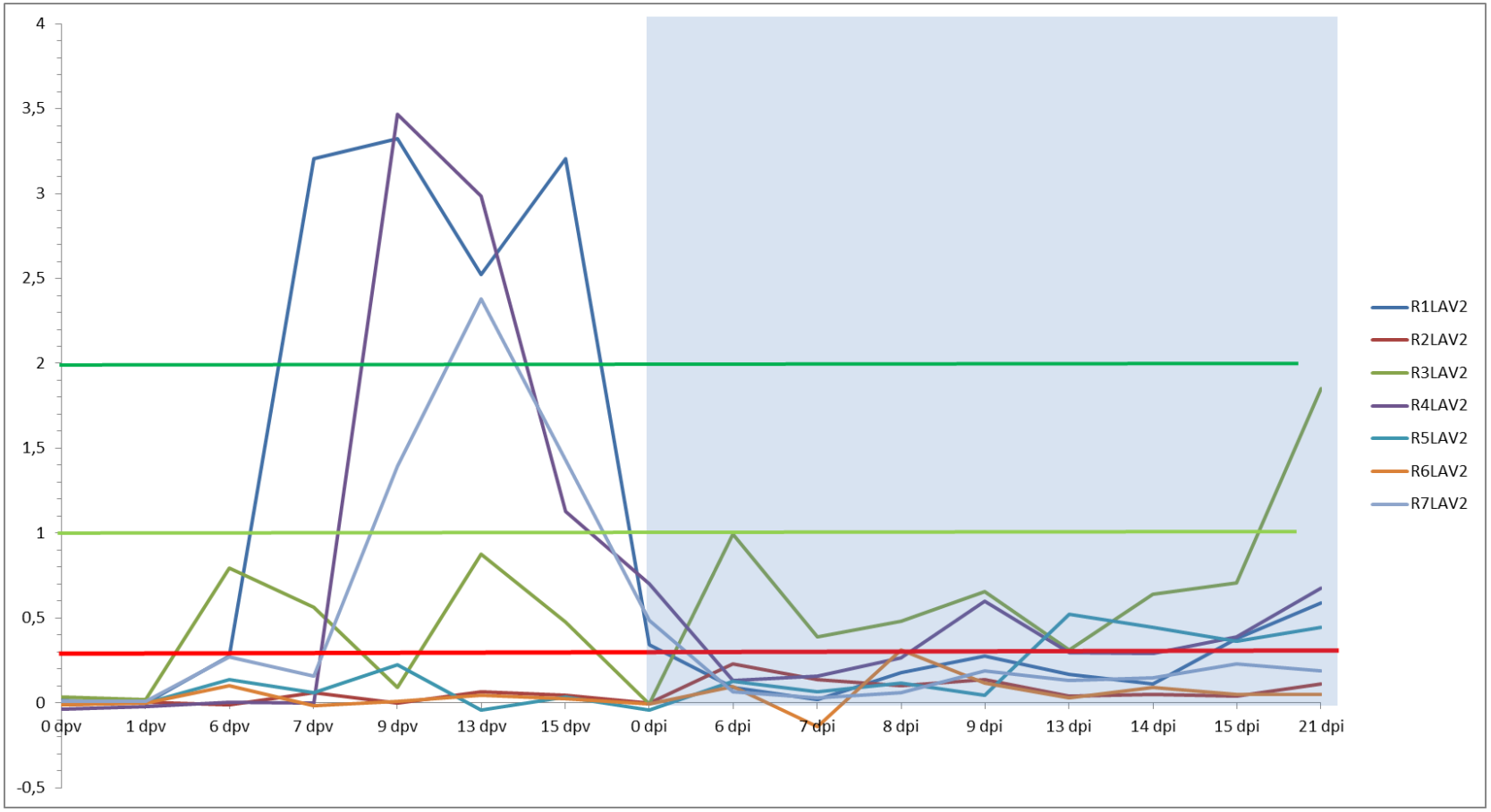
LSDV Vaccine trials:
preliminary results

- IFNgamma release upon stimulation:
  - **Strong**



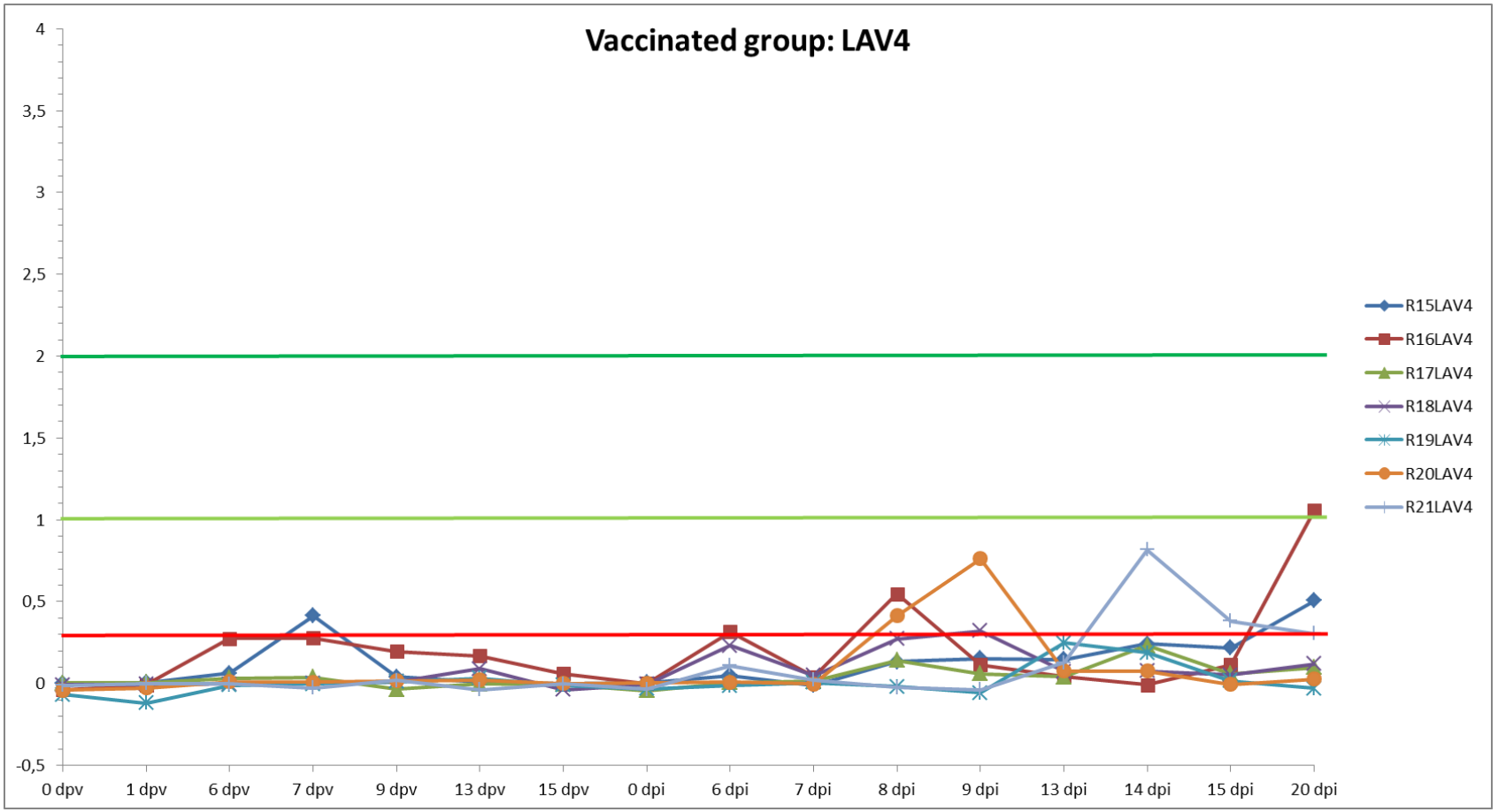
LSDV Vaccine trials: preliminary results

- IFNgamma release upon stimulation:
  - **Moderate**



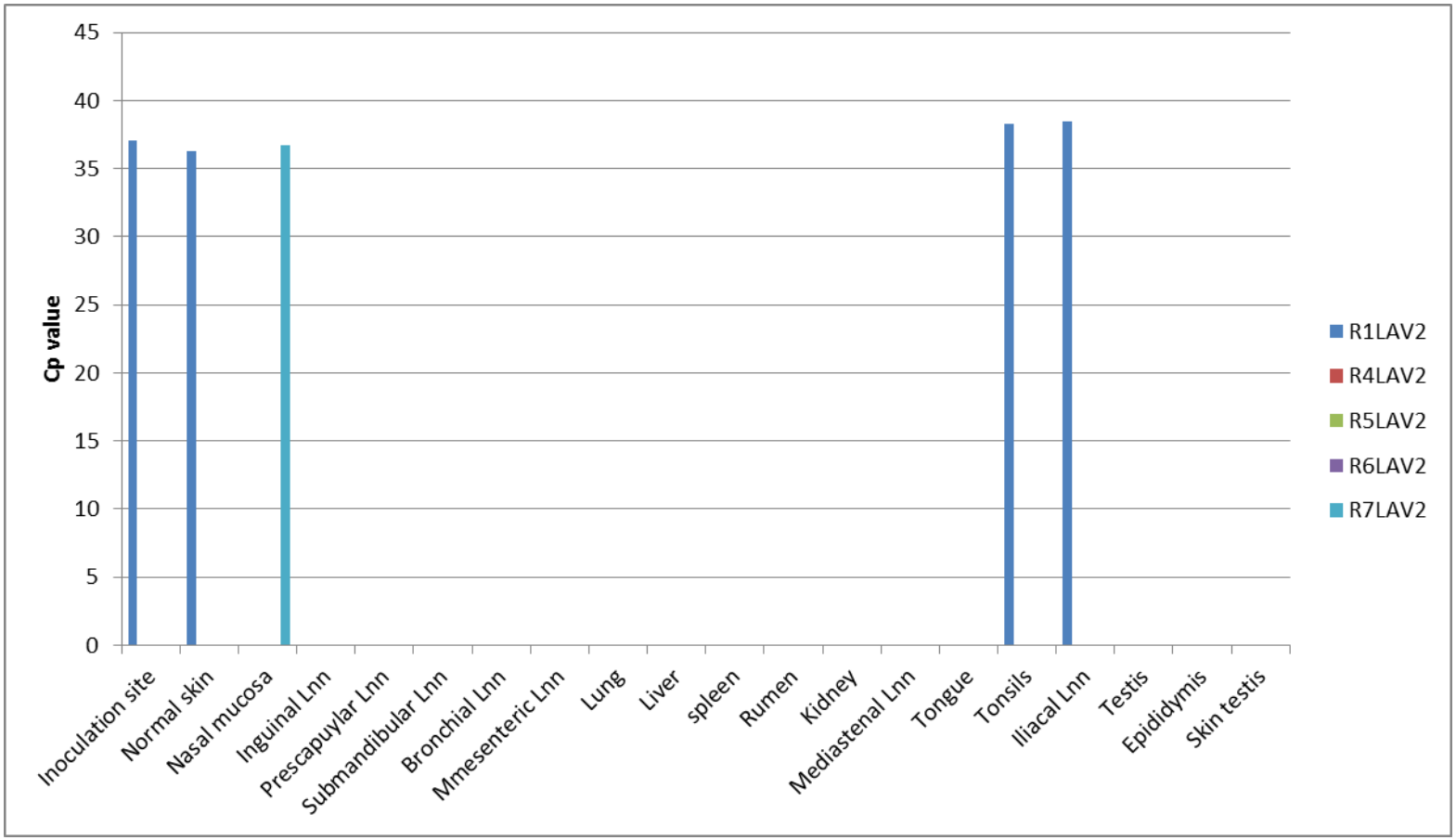
LSDV Vaccine trials: preliminary results

- IFNgamma release upon stimulation:
  - **Weak**



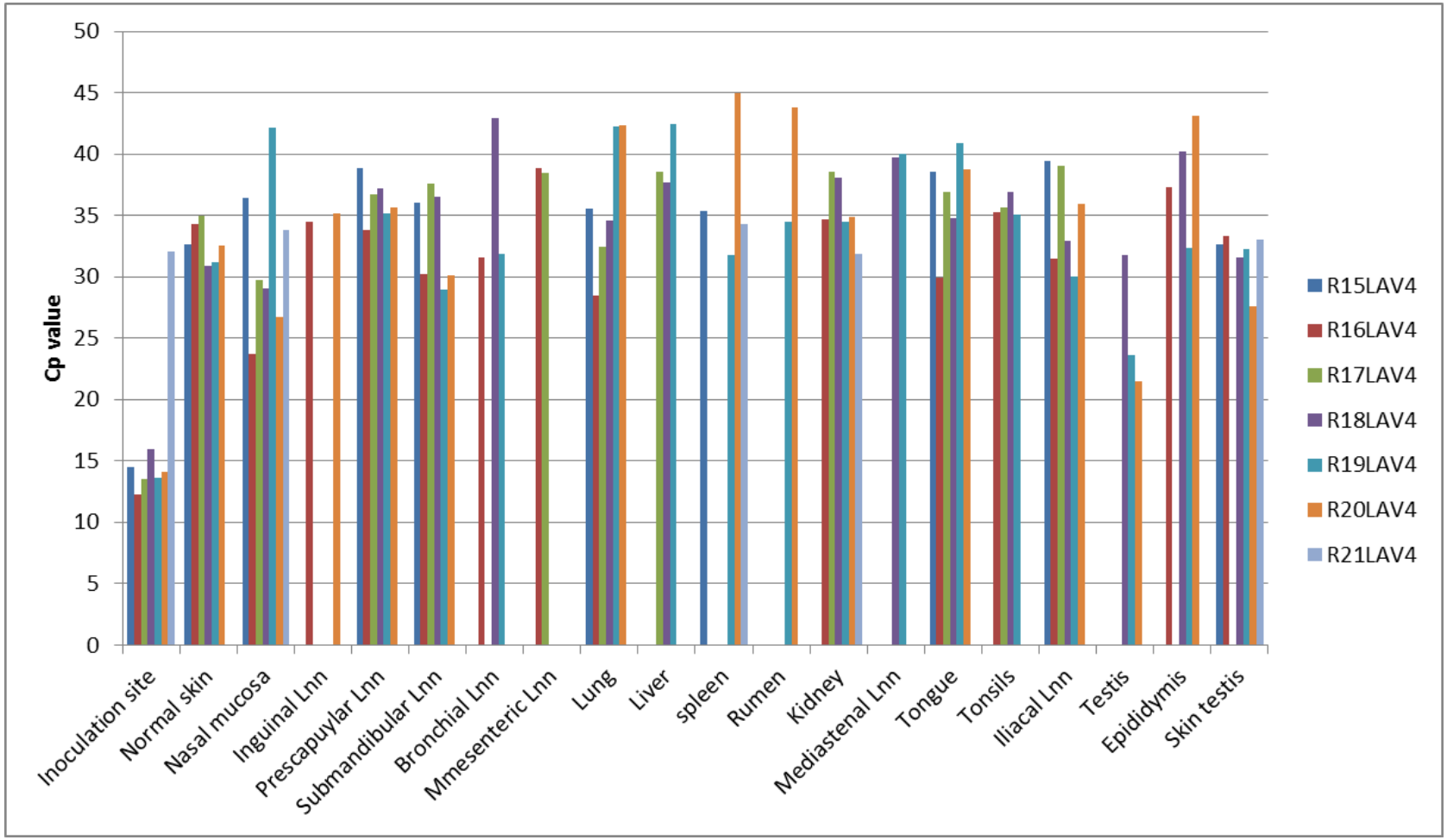
LSDV Vaccine trials: preliminary results

- Virus distribution in organs/tissues
  - **None or very limited** and with very low viral load (LAV2 and 3)



LSDV Vaccine trials: preliminary results

- Virus distribution in organs/tissues
  - **Broad** distribution pattern (LAV4)



LSDV Vaccine trials: First conclusions

The LSD challenge model allows the identification of:

- Vaccines with very good potential
  - **No** viremia, elicits **high** Abs response and **good** IFNg release, **almost no** traces of viral DNA found in organs
  - Although very slight side effects after vaccination (fever)
- Vaccines with good potential
  - **Almost no** viremia, elicts **good** Abs and IFNg response , **almost no** traces of viral DNA found in organs
- Vaccines (partially) failing to protect the animals
  - **Strong** viremia, **Low** Abs and IFNg response, virus **widely spread** in the organs. Animals in this groups also **secreted** the virus as detected by buccal swabs.
- None of the LAV vaccines protected against the initial fever spike !
- Inactivated vaccines: booster vaccination needed; promising results after one vaccination.

Acknowledgements

- Dr Eeva Tuppurainen
- Prof. E. Venter (S-Africa)
- Colleagues from Israel