### VVD-PP-48

## TITLE

IMMUNOPATHOGENESIS OF LUNG LESIONS DURING THE EARLY PHASE OF INFECTION WITH PRRSV1 STRAINS OF DIFFERENT VIRULENCE

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# CONTENT

Background and objectives

Outbreaks caused by very virulent PRRSV strains have been reported worldwide. The aim of the present study was to evaluate the immunopathogenesis of lung lesions caused by two PRRSV1 strains, one of low and the other of high- virulence.

### Material & Methods

Seventy-four-week old piglets were randomly distributed in 3 groups and inoculated intranasally with 105 TCID50 of either PRRSV1 strain 3249 (low virulence) or Lena strain (highly virulent), a group of pigs was mock inoculated (controls). Clinical signs were recorded daily, and animals were sequentially euthanized from day 1 to 8 post-inoculation. At necropsy, lung lesions were recorded, and lung samples were collected for histopathological and immunohistochemical studies against PRRSV N protein, CD163, FoxP3 and iNOS. Sera were collected to evaluate viremia (RT-qPCR). In addition, PRRSV-specific antibodies haptoglobin, lipopolysaccharide binding protein (LBP), soluble CD163, interferon ? (IFN-?), interleukin-10 (IL-10) and IL-6 were determined in sera by using commercial ELISAs.

#### Results

Lena-infected pigs showed the highest clinical scores, gross and microscopic lesions. Most of them had bronchopneumonia, with a maximum at 8 dpi. The number of PRRSV positive cells was always higher in Lena, peaking at 6 dpi. FoxP3 and iNOS immunolabelled cells progressively increased in both groups from 3 dpi onwards. However, CD163+ cell counts dropped intensely in Lena-infected piglets. In Lena-infected pigs viremia peaked at 6 dpi concurrently with the highest concentrations of IFN-? and IL-6 (6-8 dpi) compared to the 3249-group. For Hp, LBP, sCD163 or IL-10 in serum no differences between groups were observed.

#### Discussion and Conclusion

The virulent PRRSV-1 strain Lena caused severe clinical signs and lung lesions associated to earlier and higher PRRSV replication, lower frequency of CD163+ cells and an increased iNOS expression, reflecting a higher concentration of IFN-? and IL-6 in serum.