Porcilis® AR-T DF

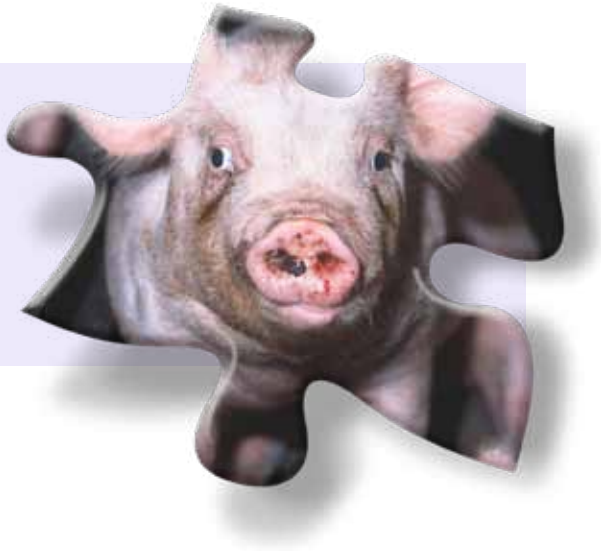
AR control requires the complete picture

High and **uniform** colostrum titers for the best protection.

Intervet
Schering-Plough Animal Health

Atrophic Rhinitis: an early infection causing long-lasting damage

Porcilis AR-T DF offers the highest possible level of protection against Atrophic Rhinitis in pigs and pig herds, without compromising safety or productivity. This brochure contains information about the disease itself, the composition of the vaccine, and its safety and efficacy in the field.



Atrophic Rhinitis is an infectious disease of swine which occurs enzootically or sporadically, depending on the herd immunity and various environmental conditions. The disease occurs in two forms: the mild and non-progressive form and the progressive form.

Non-Progressive disease

Bordetella bronchiseptica plays a major role in the non-progressive disease. The infection occurs over a short period, the inflammation does not progress and the damage is reversible. Although the non-progressive form causes little damage, the influence of *B. bronchiseptica* should not be underestimated, as these bacteria predispose to the development of Progressive Atrophic Rhinitis.

Progressive Atrophic Rhinitis (PAR)

In case of Progressive Atrophic Rhinitis toxin-producing strains of *Pasteurella multocida* are involved as well, and environmental and management factors also contribute to the severity and incidence of the disease.
Furthermore, the damage to the nasal mucosa caused by *B. bronchiseptica* during the suckling phase increases the severity of infection. *P. multocida* infections are usually acquired during the suckling period and disease may be evident from three weeks of age onward. The toxin produced by *Pasteurella multocid*a (PMT) causes a continual and progressive inflammation leading to atrophy of the tissues and nasal distortion. The delicate structures of the turbinate bones become damaged. They atrophy and may disappear altogether; and in PAR the damage is permanent.
The clinical signs are sneezing, twisted snouts and poor growth. Mortality is very low, but affected pigs grow slowly and may take many days longer to reach slaughter weight than unaffected pigs. The economic damage of PAR is directly correlated with the degree of turbinate atrophy.[1)]

Undamaged nose

Moderately damaged nose

Severely damaged nose

Different severity levels of atrophy of the turbinate bones

Diagnosis of Progressive Atrophic Rhinitis

PAR may be diagnosed on clinical signs but can be confused with other diseases. The disease is easily identified by post mortem examination of the nose, and the bacteria may be cultured from nasal swabs.

Treatment

Once infection has occurred, treatment is difficult. Antibiotic therapy can only limit the negative effect of secondary infections. Preventative treatment with antibiotics is only partially effective. As the majority of the infections take place during suckling, treatment needs to cover that period. But because compound feed is not a consistent constituent of the diet during this time, medication via feed and water is not possible, and parenteral antibiotics are expensive and their use is labour intensive.

Vaccination of gilts and sows

An effective way of controlling PAR is by vaccination of the breeding stock with a product containing an antigen that induces antibodies against the PMT [2)], preferably in combination with inactivated *B. bronchiseptica* cells. This vaccine should induce uniformly high levels of antibodies in the breeding stock, which are then transferred via the colostrum to their offspring.

Slaughterhouse equipment for collecting noses

Nasal swabbing for PCR analysis

100% immunogenicity, 0% toxicity

Porcilis AR-T DF is based on 3 componants:

- **Protein dO (non-toxic deletion derivate of *P. multocida* dermo-necrotic toxin)**
- **Inactivated *B. bronchiseptica* cells**
- **Diluvac Forte adjuvant**

Protein dO

The protein dO is derived from the *Pasteurella multocida* toxin (PMT). It is produced by deletion of the amino acids 28-148 from the binding factor of the native toxin [3]. Apart from these 121 amino acids, the primary structure of the derived protein is identical to that of PMT. **Thus the protein remains 100% immunogenic but has lost its ability to enter the target cells, and is therefore inactive.**

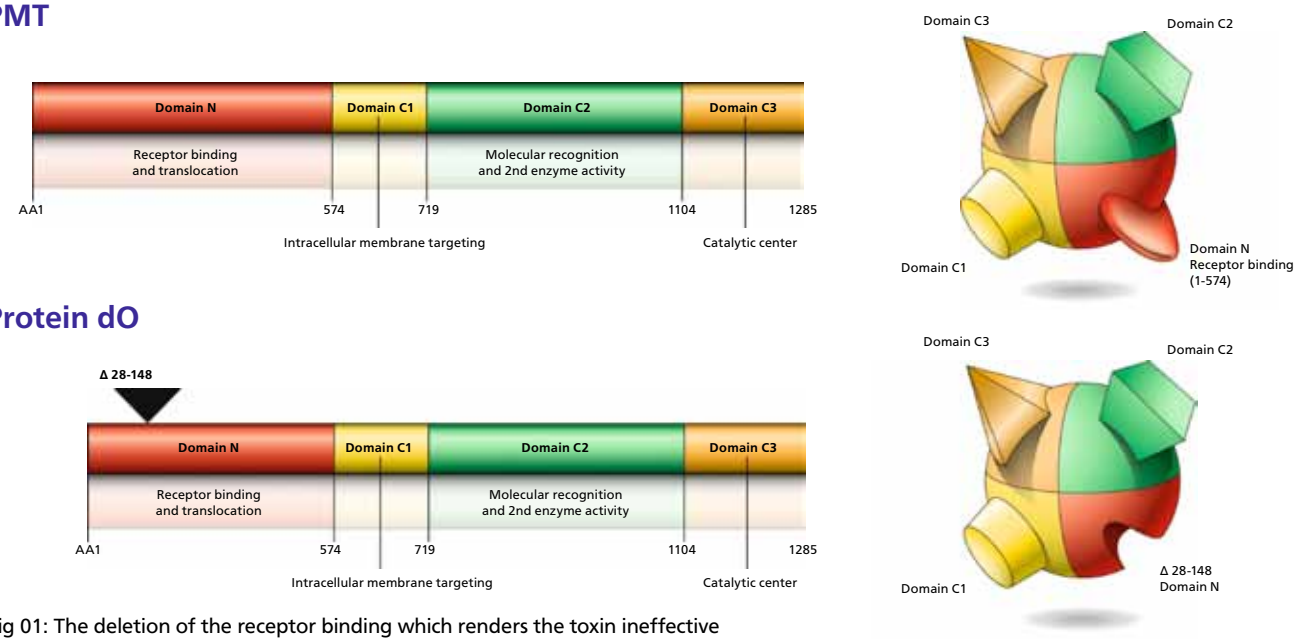


Fig 01: The deletion of the receptor binding which renders the toxin ineffective

Inactivated *B. bronchiseptica* cells

B. bronchiseptica used for vaccine production should be a Phase I virulent culture, and should be inactivated by formaldehyde [4]. Porcilis AR-T DF contains a (formaldehyde-) inactivated virulent *B. bronchiseptica* strain (strain 92932). This strain is also used in Porcilis AR-T. The vaccine induces high titers of antibodies against *B. bronchiseptica* in the sow which are transferred to the piglets via the colostrum. High maternal derived antibody titers are still present at 4 weeks of age in the progeny.

Efficacy of dO protein

The efficacy of the dO protein was tested in a challenge trial involving three groups of pigs: progeny from unvaccinated gilts, progeny from gilts vaccinated with a product containing PMT and progeny from gilts vaccinated with one containing the dO protein[1)]. These piglets were challenged between 2 and 5 days of age with *B. bronchiseptica* and a toxin-producing *P. multocida* strain.

There were significantly (P<0.01) fewer lesions in both the PMT and the dO groups compared to the controls. The dO group showed a slightly, but statistically significant, reduced degree of atrophy than the PMT group.

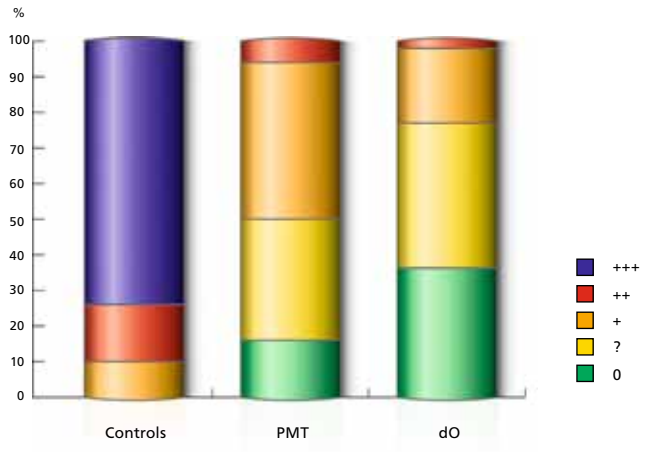


Fig. 02: Degree of turbinate atrophy

In the post weaning period there was a significant difference (P<0.01) in the average daily weight gain (ADWG) between the controls and the treated groups. The ADWG for the entire period is correlated with the mean turbinate perimeter ratio (TPR). The TPR is described as the length of the turbinate outline as a proportion of the length of the outline of the nasal cavity. Thus normal turbinates have a high TPR value and total turbinate atrophy would result in a value of zero. This means that there is a negative correlation between the severity of damage and the performance of the pig.

	Average daily weight gain (g)		
Vaccination group	Suckling	Post weaning	Entire period
Controls	270	725	599
PMT	253	834	657
dO	271	816	655

Table 01: Average daily weight gain from 0-149 days of age

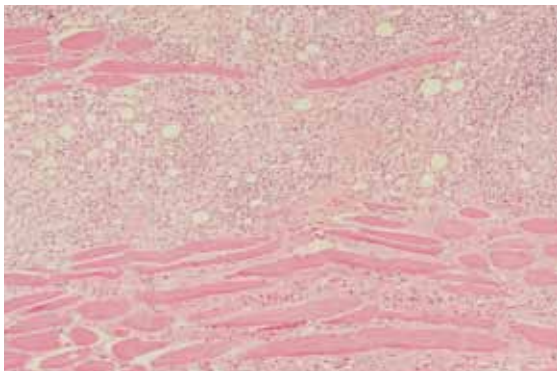
The dO protein provides safe, effective protection against the clinical, pathological and production-limiting effects of Progressive Atrophic Rhinitis.

Safety and convenience from the leader in AR protection

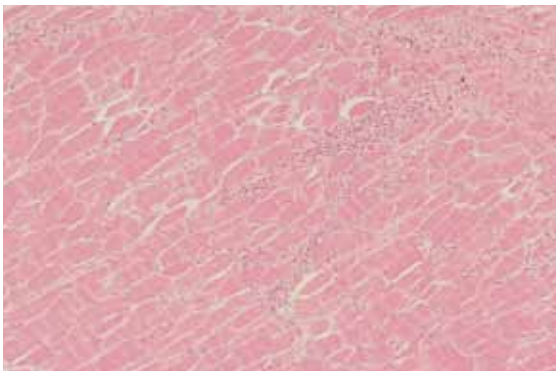
Porcilis AR-T DF combines the full efficacy of Porcilis AR-T with the safety profile and ease of use of all the other Porcilis vaccines. A safe, effective and convenient product for the veterinarian and pig farmer.

Diluvac Forte

Diluvac Forte is the first choice adjuvant for the Porcilis vaccines. Due to its specific composition (vitamin E is used as basis) the adjuvant combined excellent immune stimulation with tissue tolerance and good user friendly features.



Muscle tissue 14 days after Water-in-Oil injection



Muscle tissue 14 days after Diluvac Forte injection

The features of Diluvac Forte:

- **Unique patented Vitamin E-based formulation designed specifically for the swine industry.**
- **Stimulates T- and B- lymphocytes, increasing phagocytosis and protecting immune cells, thus boosting efficacy.**
- **Excellent tissue tolerance.**
- **Ease of use.**
- **Facilitates the mixing of vaccines.[5)]**

Safety of Porcilis AR-T DF

In a large field trial (25 commercial farms, approximately 50 sows per farm) pregnant sows were randomly assigned to one of two groups: one vaccinated with Porcilis AR-T, the other with Porcilis AR-T DF, to compare the safety profiles of both vaccines.[6)]

Shortly after vaccination with Porcilis AR-T DF some animals may show a slight reduction in activity and/or feed intake, returning to normal within a day after vaccination.

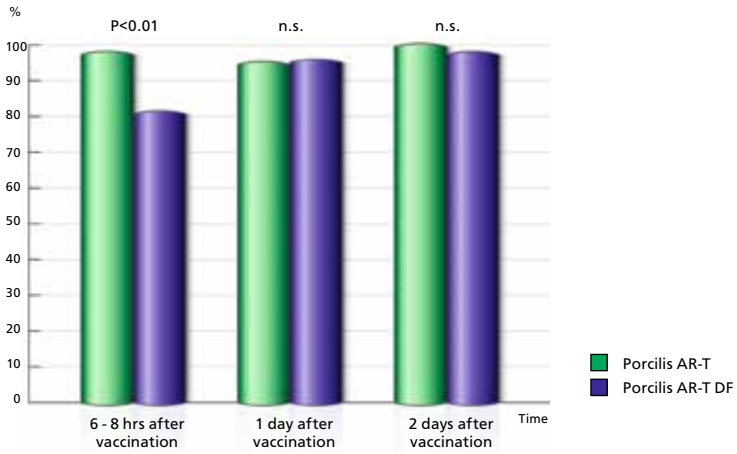


Fig.04: % of sows with normal feed intake at different intervals after vaccination

In the Porcilis AR-T DF group, the local reactions mostly disappeared within 5 days. This was significantly better than the sows vaccinated with Porcilis AR-T. Porcilis AR-T DF has a safety profile that is in line with that of other vaccines containing Diluvac Forte.

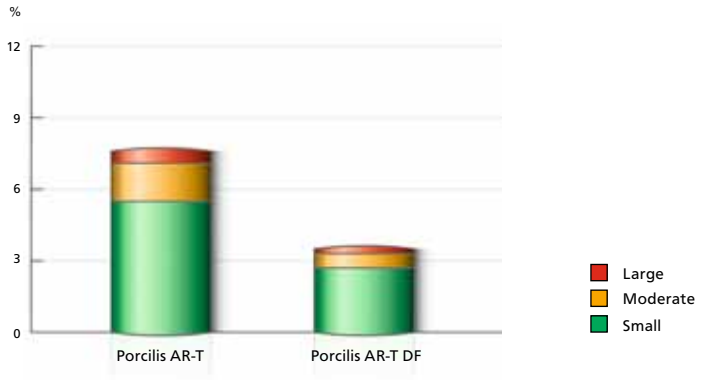


Fig.05: Local reactions on Day 5

There were no statistically significant differences between groups for any of the reproductive parameters observed.

	Porcilis AR-T	Porcilis AR-T DF
Born alive	11.32 ± 3.2	11.42 ± 2.8
Dead born	0.97 ± 1.4	0.95 ± 1.6

Table 02: Reproductive performance after AR vaccination

The safety of Porcilis AR-T DF was proven in a large field trial. There was no difference between this vaccine and Porcilis AR-T. Even the number of local reactions was reduced to a negligible level.

Protection of piglets against AR after vaccination with Porcilis AR-T DF

The efficacy of Porcilis AR-T DF was tested in two challenge experiments. In both trials piglets born from vaccinated and unvaccinated sows were challenged intranasally with *B. bronchiseptica* (at 3-7 days of age) and *P. multocida* (4 days later). [7)]

In the first trial, the pigs were kept until 174 days of age. They were weighed at birth, on day 28, day 70 and day 174, and the ADWG calculated. On days 40 and 70 the degree of brachygnathia superior (shortening of the upper jaw) was measured, and at slaughter (174 days of age), the atrophy of the turbinates was scored (0 to 4).

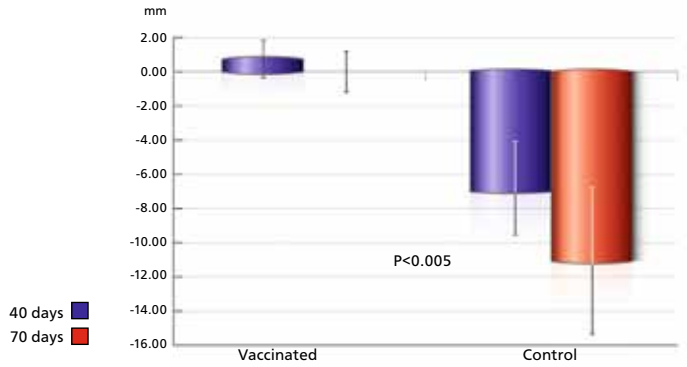


Fig. 06: Mean degree of brachygnathia superior (mm) at 40 and 70 days

In only a few pigs of the vaccinated group there was a minor degree of shortening (less than 2 mm), compared with more severe shortening (4-20 mm) in the unvaccinated controls.

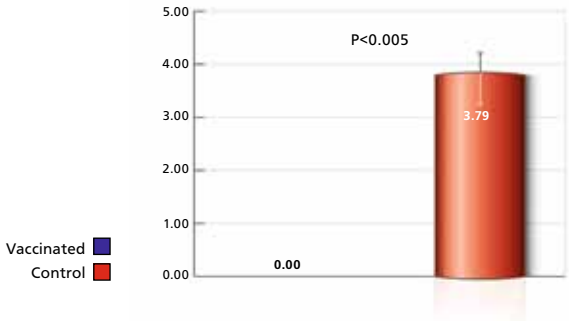


Fig 07: Atrophy of turbinates at slaughter (score 0-4)

In the pigs slaughtered on day 174, there were no lesions in the vaccinated group, but the individual atrophy scores in the control group were either 3 or 4 (the maximum) with an average of 3.8.

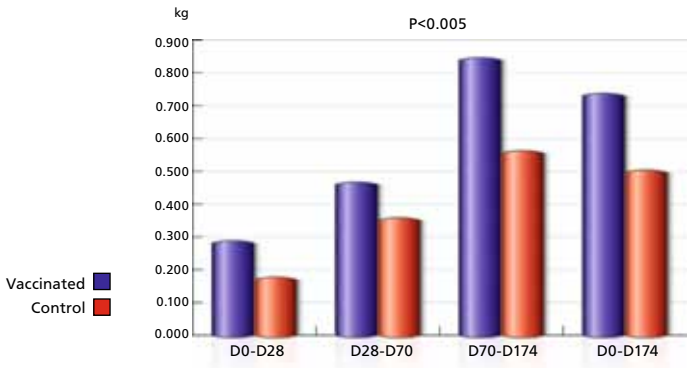


Fig. 08: Average Daily Weight Gain (kg) at various intervals

The differences in average daily weight gain confirm the damage AR can cause and the improvement that vaccination with Porcilis AR-T DF can bring in infected herds.

P. multocida and *B. bronchiseptica* were recovered much more frequently and consistently from the piglets from the unvaccinated sows than from the offspring of the vaccinated sows. This suggests that the regular vaccination of all the sows in a herd over a longer period could eradicate *P. multocida* infection and also reduce the level of *B. bronchiseptica* infection.

In the second trial, all the pigs were killed at six weeks of age and the extent of turbinate atrophy was measured according to the snout score index (scored 0 - 18). The serological response to PMT and *B. bronchiseptica* were also measured.

All vaccinated sows responded to both antigens of the vaccine and developed high titers.

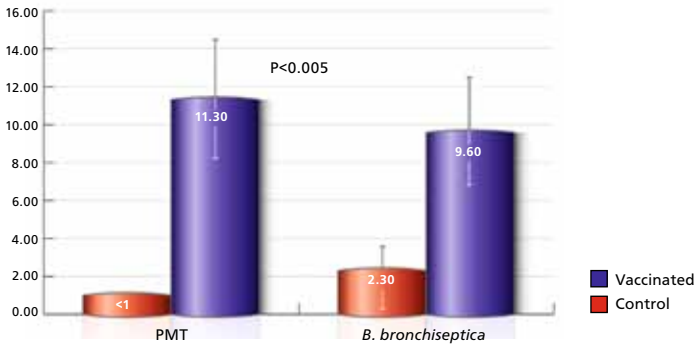


Fig. 09: Mean antibody titers against PMT and *B. bronchiseptica* in the colostrum of the sows

The pigs in the vaccinated group had an average score of 1.7 for all litters, with a mean score per litter ranging from 0.9 to 2.2. For the pigs in the control group, the average score was 13.8, with a mean score per litter ranging from 8.3 to 17.0. The differences between the groups were significant (P<0.005).

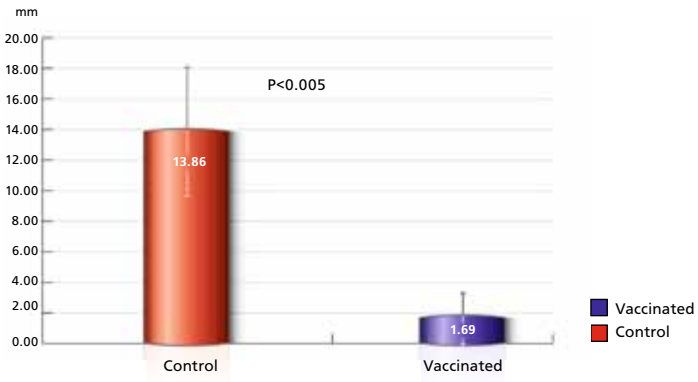


Fig. 10: Snout scores: mean turbinate atrophy (scored 0-18) at slaughter (42 days of age)

From these two trials it can be concluded that progeny born from sows vaccinated with Porcilis AR-T DF were very effectively protected against Atrophic Rhinitis, because:

- **There was a very good serological response to Porcilis AR-T DF in the sows.**
- **Antibodies were transferred via the colostrum to their piglets.**
- **The incidence of clinical signs was much lower in the pigs from the vaccinated sows.**
- **The levels of turbinate atrophy were much lower in the pigs from the vaccinated sows.**
- **The performance of the pigs from the vaccinated sows was significantly better.**
- **Vaccination reduced the frequency with which the bacteria involved in AR were isolated.**

PMT Antibody response after vaccination with Porcilis AR-T DF

Porcilis AR-T has been the "golden standard" vaccine in AR control over the last decades. With the help of this vaccine many farms were able to control AR or even eradicate the disease. Porcilis AR-T DF replaces this vaccine with at least as good efficacy.

A trial was conducted to compare antibody levels to PMT following the vaccination of pregnant sows with the two AR vaccines:

1) Porcilis AR-T
2) Porcilis AR-T DF

The antibodies levels were measured in the sows' colostrum, and the levels of maternal derived antibodies (MDA) in their offspring were also determined.

Relative PMT antibody titers of Porcilis AR-T and Porcilis AR-T DF in piglet serum

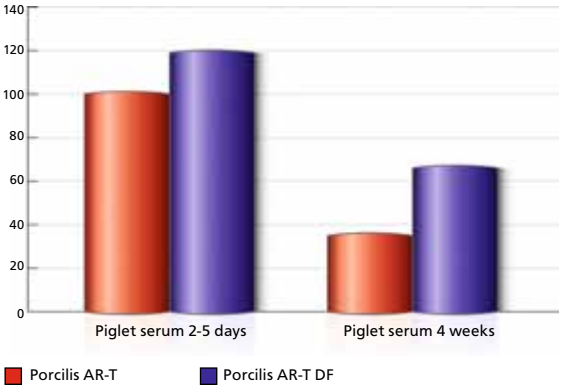


Fig. 11: MDA levels in the serum of the offspring of vaccinated sows

Relative PMT antibody titers of Porcilis AR-T and Porcilis AR-T DF in sows at farrowing

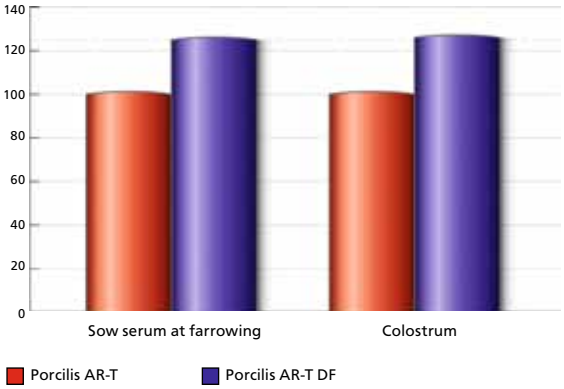


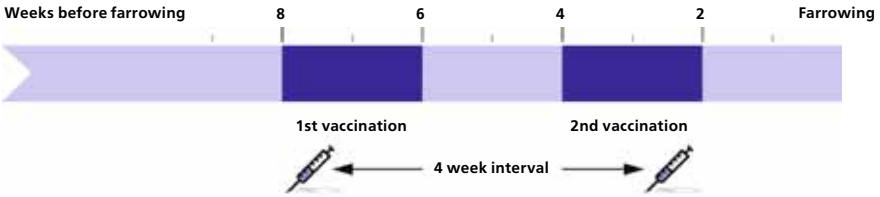
Fig. 12: Colostrum titers of the vaccinated sows

From this trail can be concluded:

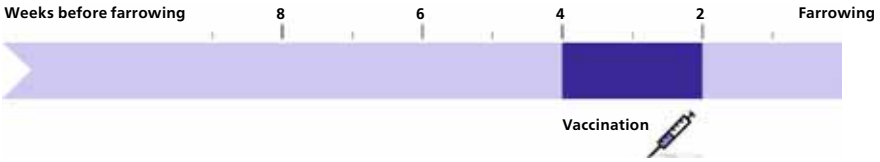
- **Antibody levels in the serum of the progeny of the sows reflected the antibody titers in colostrum.**
- **Anti-PMT antibodies could be measured in the piglets up to at least 4 weeks of age.**
- **The antibody titers in the progeny of the Porcilis AR-T DF vaccinated sows declined at a lesser rate than those of the piglets born from Porcilis AR-T vaccinated sows.**
- **Porcilis AR-T DF induces at least as high a level of PMT neutralizing antibodies as Porcilis AR-T.**
- **Several comparative vaccine trials have shown that both Porcilis AR-T and Porcilis AR-T DF consistently produce significantly higher and more uniform titers than competitor vaccines.[8,9)]**

Vaccination scheme:

- **Primary vaccination:**
  - A single i.m. vaccination of 1 dose (2ml) followed, after an interval of 4 weeks, by a second single vaccination of 1 dose (2ml)
  - The second vaccination should be given 2 to 4 weeks prior to farrowing



- **Booster vaccination:**
  - A single 2ml i.m. dose should be given 2 to 4 weeks prior to each subsequent farrowing.



Porcilis AR-T DF

ResPig
Breathe better. Grow better.

For high and uniform colostrum titers for the best protection.

- Uniformly high titers in sows and their colostrum (better protection for piglets) shown in comparative studies.
- 100% immunogenicity, 0% toxicity
- Diluvac Forte adjuvant :
  - The guarantee of a good safety profile.
  - Excellent tissue tolerance.
  - Ease of use.
  - The standard adjuvant for Porcilis® vaccines.

Active substances

- Protein dO (non-toxic deletion derivative of *P. multocida* dermo-necrotic toxin).
- Inactivated *B. bronchiseptica* cells.
- Diluvac Forte adjuvant.

Immunological properties

Stimulates active immunity in sows and gilts against *P. multocida* toxin and *B. bronchiseptica* in order to provide passive immunity to their progeny against progressive atrophic rhinitis (PAR).

Storage and handling

- Store at 2-8°C. Do not freeze.
- Protect from light.
- Shake vigorously before use.

Presentations

- PET vials of 10 doses (20ml), 25 doses (50ml) and 50 doses (100ml).

References
1) J.P Nielsen et. al., Vaccination against Progressive Atrophic Rhinitis with a recombinant *Pasteurella multocida* Toxin Derivate, Ca J Vet Res 1991; 55: 128-138
2) Foged et. al.,1989, Protection against progressive atrophic rhinitis by vaccination with *P. multocida* toxin purified by monoclonal antibodies. Vet. Rec. 125: 7-11
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9) Eggen et. al., Serological responses after administration of atrophic rhinitis vaccines, APVS 2011

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