Review

Universal protection against infectious bursal disease (IBD) induced by the vector vaccine VAXXITEK® HVT+IBD

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Abstract

Clinical protection against all pathotypes of the serotype 1 infectious bursal disease virus is induced, from the classical viruses to the very virulent and the variants, by the HVT-IBD vector vaccine VAXXITEK HVT+IBD. Clinical protection means protection against clinical signs of the disease, mainly with the very virulent form, mortality, hemorrhage, stringent bursa atrophy, as well as protection against immunosuppression in the variant forms of the disease. Such clinical protection and therefore protection against the negative consequences of immunosuppression, poor vaccine take, occurrence of intercurrent diseases, and huge negative impact on production performances is uniquely obtained with a vector vaccine HVT-IBD vaccination that allows early onset of immunity, either in ovo at transfer time around 18 days of embryonation, or at day old in the hatchery, in presence of IBD virus maternally-derived antibodies.

Introduction

The objective of this newsletter is to review the results of the protection induced by the HVT-IBD vector vaccine VAXXITEK HVT+IBD against different IBD virus challenges. All published material on VAXXITEK HVT+IBD and referring to protection against an IBD virus challenge was reviewed. First publication of such results occurred in 2003 [1].

The vector vaccine strain vHVT013-IBD [2] VAXXITEK HVT+IBD has been used since 2006 in the Americas, Asia, Africa, and Europe. Vaccination against Marek’s disease, as a HVT native virus can initiate, and against IBD represents the immune foundation vaccination program to be used at the hatchery. Clinical protection against IBD has been demonstrated with the HVT-IBD vector vaccine in all types of chicken species based type of production, broilers for meat production, layers for egg production, all over

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the world. The reasons of such a wide use of the HVT-IBD vector vaccine are analyzed in this bibliographical review.

**IBD virus variability in pathogenicity**

Infectious bursal disease (IBD), serotype 1, virus, was recognized in 1970 as a specific disease at the origin of lesions of the primary lymphoid organ, the bursa of Fabricius [3], and then regularly described on almost all places on earth. It was identified as one of the major threat to the poultry industry. Layer type genetics has been proven being more susceptible to IBD than the broiler type. IBD infections may be leading to either clear IBD disease with clear clinical signs and somehow mortality. There is also a more silent form of the disease, more related to immunosuppression. From classic to very virulent strains, an increased mortality rate was the main criterion for differentiation [4]. Variant strains trend to escape antigenically from the rest of the virus strains, and are mainly immunosuppressive [5].

*Classical IBD viruses*

Mainly bursitis associated with clinical signs of drowsiness, and decrease of performances in field conditions due to immunosuppression is described. Mortality may occur, and hemorrhage in muscles, as the most visible signs. The main target of the virus is the lymphoid organ structure [6].

*Very virulent (vv) IBD viruses*

First cases were described in Europe from the decade 1980 [7], and elsewhere, including recently in North America [8]. Clear clinical signs of hemorrhage in the bursa, the muscles, are noticed, with a higher mortality rate than with classic IBD infection.

*Variant IBD viruses*

Cases occurred in North America in the years 1980 at the same time, and were primarily described in the USA [5]. They spread later to South America, and more recently probably to Eurasia. Bursa atrophy is the main manifestation of the infection. Field conditions signs of immunosuppression with decreased performances of growth are mainly noted in broilers.

**Criteria to assess clinical protection against IBD virus infection**

Clinical signs, mainly for vvIBD challenge, may be monitored during a virus challenge study. Bursa size and weight may be recorded, as well as bursa to bodyweight ratio, a more precise measure of the bursa atrophy taking into account the organ size and weight inter individual variability, whatever the pathotype of IBD virus to use. Bursa lesions may also be recorded using histopathological lesion technique.
Protection against clinical signs

Mainly vvIBD virus challenges originate clinical signs, and especially in layer type birds. Main observations are:

. mortality, mainly in layer type birds,
. drowsiness, ruffled feather, poor external aspect,
. detection of IBD virus antigen (s) or viral genetic material in the bursa of Fabricius in dead birds.

Protection against bursa atrophy

All types of challenge studies may use monitoring of bursa size and/or weight. The measurement is the calculation of the bursa to bodyweight ratio on freshly collected organs at necropsy. One way to express the results may be based on bursa as defined for example:

. body weight ratio (B/BR) [9], bursa weight (g)/ total bodyweight (g),
. bursa index (BI) [10], bursa weight (g) x 1000/ body weight (g).

Protection against bursa lesions

All types of challenges studies may use monitoring of bursa lesions. The measurement is the bursa lesion rating performed on histopathological examination of bursa. One way to express the results id based on the mean severity index (MSI), severity of bursa lymphoid tissue lesions is scored from 0 to 4 on the basis of lymphoid necrosis and/ or lymphocytic depletion [9]:

. 0 = less than 5 % of the lymphoid follicles (per field) affected,
. 1 = 5 to less than 25 % of the lymphoid follicles (per field) affected,
. 2 = 25 to less than 50 % of the lymphoid follicles (per field) affected,
. 3 = 50 to less than 75 % of the lymphoid follicles (per field) affected,
. 4 = more than 75 % of the lymphoid follicles (per field) affected.

Clinical protection induced by VAXXITEK HVT+IBD

Review of results of all published protection studies in laboratory controlled conditions using the HVT-IBD vector vaccine worldwide provides a demonstration of the universal protection against IBD.

Classical IBD viruses

Protection against classic IBD virus challenges has been studied since the time of development of the vaccine [2] (Table 1). Either in ovo or day-old sub-cutaneous routes have been both tested providing clinical protection
against classic IBD challenge [2]. Most of the experiments were performed in specified-pathogen free chickens. Protection against IBD virus challenges were using homologous to the vHVT013-IBD vector vaccine VAXXITEK HVT+IBD virus, as the Faragher 52/70 first isolated in the United Kingdom [11]. Layer pullet type of birds was protected against Faragher 52/70 challenge [12]. Further published studies were mainly about hatchery vaccination program validation. VAXXITEK HVT+IBD was shown compatible with live Newcastle disease and infectious bronchitis Mass strain vaccines sprayed at day-old using a Faragher 52/70 challenge model [13]. Protection against STC United States originated challenge strain was also demonstrated [14]. That model, as well a Winterfield challenge model were selected to assess protection against challenge in the context of concomitant injection at day-old of VAXXITEK HVT+IBD and a Newcastle disease inactivated vaccine in oil emulsion [15] & [16].

**Very virulent (vv) IBD viruses**

Protection against very virulent (vv) IBD virus challenges has also been studied since the time of development of the vaccine [2] (Table 2). Either in ovo or day-old sub-cutaneous routes have been both tested providing clinical protection against vv IBD challenge [2]. Not only SPF chicken challenges have been performed so far, but also broiler [1] and layer pullet [16] challenges gave expected results of protection in VAXXITEK HVT+IBD vaccinates [17]. Two French isolates were used for studies, 89-163 and 91-168 isolates from the ANSES national reference laboratory. 77165 isolate from IZ Forli institute in Italy served as challenge strain for layer pullet protection studies [18], and broiler protection studies [19]. Interestingly VAXXITEK HVT+IBD injected either in ovo or at day-old showed protection against Brazilian molecular group 11 vvIBD virus isolate based challenge [11]. A study of protection against vvIBD challenge of progeny born to VAXXITEK HVT+IBD based vaccinated parents and vaccinated in ovo with VAXXITEK HVT+IBD confirmed the interest of the vector vaccine used as a primer in meat breeders, and of the early onset of immunity and induced protection against vvIBD before the waning of the protective maternally-derived antibodies [20] & [21].

**Variant IBD viruses**

Protection against variant IBD virus challenges has also been studied since the time of development of the vaccine [2] (Table 3). Either in ovo or day-old sub-cutaneous routes have been both tested providing clinical protection against variant IBD virus challenge [2]. Mainly variant E Delaware challenge model has been successfully used so far for protection studies [22] & [23]. Clinical protection induced by VAXXITEK HVT+IBD was fully demonstrated, emphasizing the correct choice of the Faragher 52/70 IBD protective VP2 gene to be inserted into the HVT vector virus. This strain was isolated at the first days of Gumboro disease and may be considered as a progenitor of all existing IBD viruses in the world. The variant E Delaware challenge test was also used for validation of induced protection of VAXXITEK HVT+IBD in the context of concomitant vaccination with an oil emulsion inactivated...
Newcastle disease vaccine at day-old at the hatchery [16] & [24]. A study of protection against three USA variant challenge strains, Delaware E, AVS-SU and AVS-DL, of progeny born to VAXXITEK HVT+IBD based vaccinated parents confirmed the interest of the vector vaccine used as a primer in meat breeders, and of the passive protection against these variant IBD strains before the waning of the protective maternally-derived antibodies [25] & [26].

**Protection against IBD**

IBD infections result in lesions of the bursa of Fabricius of different severity [3], [4] & [5], and therefore the immune system function is highly and negatively impacted. Most of live attenuated IBD vaccines may cause bursal atrophy and immunosuppression. Poor response to other vaccinations and occurrence of intercurrent infections may be a consequence of such vaccination [27]. Full protection against vvIBD and variant IBD may be incomplete with such vaccines [27]. The compromise between a possible early immunization and the overpassing of maternally-derived IBD antibodies is obtained with the HVT-IBD vector vaccine [1].

**References**


Program Using a Herpesvirus of Turkey-Infectious Bursal Disease (HVT-IBD) Vector Vaccine, World J. Vaccines, 3, 46-51.


Table 1: VAXXITEK HVT+IBD classic IBD virus protection against challenge studies.

<table>
<thead>
<tr>
<th>IBD virus challenge strain</th>
<th>Type of birds</th>
<th>Vaccination</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Faragher 52/70 UK</td>
<td>SPF chickens</td>
<td>In ovo &amp; day-old sub-cutaneous injection</td>
<td>Fernandez R al, 2006</td>
</tr>
<tr>
<td></td>
<td>SPF chickens</td>
<td>Day-old sub-cutaneous injection + live Newcastle disease &amp; infectious bronchitis vaccine spray</td>
<td>Loceha E al, 2007</td>
</tr>
<tr>
<td></td>
<td>Layer pullets</td>
<td>In ovo &amp; day-old sub-cutaneous injection</td>
<td>Cruz-Coy J al, 2006</td>
</tr>
<tr>
<td>STC USA</td>
<td>SPF chickens</td>
<td>In ovo &amp; day-old sub-cutaneous injection</td>
<td>Jay ML, 2009</td>
</tr>
<tr>
<td></td>
<td>SPF chickens</td>
<td>Day-old sub-cutaneous injection</td>
<td>Perozo F al, 2010</td>
</tr>
<tr>
<td>Winterfield USA</td>
<td>SPF chickens</td>
<td>Day-old sub-cutaneous injection + inactivated Newcastle disease oil emulsion vaccine</td>
<td>Fernandez R al, 2011</td>
</tr>
<tr>
<td></td>
<td>SPF chickens</td>
<td>Day-old sub-cutaneous injection + inactivated Newcastle disease oil emulsion vaccine</td>
<td>Lemiere S al, 2011</td>
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Table 2: VAXXITEK HVT+IBD very virulent (vv) IBD virus protection against challenge studies.

<table>
<thead>
<tr>
<th>IBD virus challenge strain</th>
<th>Type of birds</th>
<th>Vaccination</th>
<th>Reference</th>
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</thead>
<tbody>
<tr>
<td>91-168 ANSES France</td>
<td>Broilers</td>
<td>Day-old sub-cutaneous injection</td>
<td>Gouttebroze S al, 2003</td>
</tr>
<tr>
<td></td>
<td>SPF chickens</td>
<td>In ovo &amp; day-old sub-cutaneous injection</td>
<td>Bublot M al, 2007</td>
</tr>
<tr>
<td></td>
<td>SPF chickens</td>
<td>Day-old sub-cutaneous injection</td>
<td>Le-Gros FX al, 2009</td>
</tr>
<tr>
<td>89-163 ANSES France</td>
<td>SPF chickens</td>
<td>In ovo injection</td>
<td>Rautenschlein S al, 2009</td>
</tr>
<tr>
<td></td>
<td>Layer pullets</td>
<td>Day-old sub-cutaneous injection</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Meat breeder progeny*</td>
<td>In ovo injection</td>
<td>Lemiere S al, 2013</td>
</tr>
<tr>
<td>77165 Italy</td>
<td>Layer pullets</td>
<td>Day-old sub-cutaneous injection</td>
<td>Prandini F al, 2008</td>
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<tr>
<td></td>
<td>Layer pullets</td>
<td>Day-old sub-cutaneous injection</td>
<td>Massi P al, 2008</td>
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<td></td>
<td>Broilers</td>
<td>Day-old sub-cutaneous injection</td>
<td>Le-Gros FX al, 2009</td>
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<td>GM11 Brazil</td>
<td>SPF chickens</td>
<td>In ovo &amp; day-old sub-cutaneous injection</td>
<td>Fernandez R al, 2006</td>
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<tr>
<td></td>
<td>SPF chickens</td>
<td>Day-old sub-cutaneous injection</td>
<td>Cruz-Coy J al, 2006</td>
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*Progeny born to VAXXITEK HVT+IBD based vaccination program of parents.
Table 3: VAXXITEK HVT+IBD variant IBD virus protection against challenge studies.

<table>
<thead>
<tr>
<th>IBD virus challenge strain</th>
<th>Type of birds</th>
<th>Vaccination</th>
<th>Reference</th>
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<tbody>
<tr>
<td>Variant E Delaware USA</td>
<td>SPF chickens</td>
<td>In ovo &amp; day-old sub-cutaneous injection</td>
<td>Bublot M al, 2007</td>
</tr>
<tr>
<td></td>
<td>SPF chickens</td>
<td>Day-old sub-cutaneous injection</td>
<td>Perozo F al, 2009</td>
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<td></td>
<td>Broilers</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>SPF chickens</td>
<td>Day-old sub-cutaneous injection + inactivated Newcastle disease oil emulsion vaccine</td>
<td>Fernandez R al, 2011</td>
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<td></td>
<td>Lemiere S al, 2011</td>
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<tr>
<td>AVS-DL USA</td>
<td>Meat breeder progeny*</td>
<td>No IBD vaccination – USA approach</td>
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</table>

*Progeny born to VAXXITEK HVT+IBD based vaccination program of parents.