Quadrivalent meningococcal serogroups A, C, W, and Y tetanus toxoid conjugate vaccine (MenACWY-TT): a review

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Introduction: Meningococcal disease poses serious health risks globally. The six Neisseria meningitidis serogroups responsible for most of the disease burden are A, B, C, W, X and Y. The case fatality rate remains high worldwide and prevention by vaccination remains the best strategy. Because polysaccharide vaccines are poorly immunogenic in young children, conjugated vaccines were developed to overcome this drawback. The quadrivalent meningococcal conjugate vaccine (MenACWY-TT), comprising the serogroups A, C, W and Y conjugated to tetanus toxoid carrier protein (marketed under the trade name Nimenrix™), is the first quadrivalent vaccine to be approved in Europe as a single dose for ages 12 months and in Canada for ages 12 months to 55 years.

Areas covered: This review addresses the limitations posed by polysaccharide vaccines, compares them with the MenACWY-TT conjugated alternative, and focuses on the clinical studies that investigate the immunogenicity and reactogenicity of MenACWY-TT in various age groups and its co-administration with other vaccines compatible with each age group.

Expert opinion: Evidence suggests that MenACWY-TT has a good immunogenicity profile across a broad age range including toddlers, children, adolescents, and adults. It also has an acceptable safety profile and is well tolerated when administered with other vaccines.

Keywords: bactericidal activity, immunogenicity, MenACWY-TT, Neisseria meningitidis, Nimenrix™, quadrivalent meningococcal conjugate vaccine, reactogenicity safety

1. Introduction

Neisseria meningitidis infection causes potentially life-threatening diseases [1-3]. Two clinical forms exist: meningococcal meningitis and less commonly meningococcal septicemia [4,5]. The invasive form of the disease affects > 500,000 people worldwide with an approximate number of deaths reaching 50,000 and significant long-term disability in survivors [6,7]. The case fatality rate is around 10%, exceeding 50% with septicemia [7].

The incidence of invasive meningococcal disease (IMD) varies according to region [2]; North America and Europe have the least number of reported cases, around 0.5 and < 1 cases, respectively, per 100,000 people. This reaches 10 – 1000 per 100,000 in Africa during epidemics [6]. An area in Sub-Saharan Africa known as the 'meningitis belt' experiences the largest number of cases [8]. Infection is facilitated by overcrowding and large population movements due to pilgrimage, traditional markets, or wars [4,8]. This is evident during the Hajj season in the Kingdom of Saudi Arabia where millions of Muslims from all over the world converge on pilgrimage sites [9].
The burden of meningococcal disease was shown to be greatest in young adults [10]. Between 1998 and 2007 in the United States of America (USA), around 43% of cases were reported in ages > 24 years [11]. However, the highest attack rates remain in infants 3 – 12 months old [3,12,13].

Meningococcal meningitis is a major form of bacterial meningitis causing epidemics [5]. Twelve serogroups of N. meningitidis have been identified (A, B, C, H, I, K, L, W, X, Y, Z, and E) based on the characteristics of its polysaccharide capsule [7]. Serogroups W and E were previously known as serogroups W-135 and 29E, respectively [14]. Six of the identified serogroups have been known to cause epidemics (A, B, C, W, X, and Y) [15,16].

The predominant serogroups in the Middle East are A and W. In Central and South America and Europe, serogroups B and C are the most common, while in the USA and Canada serogroup Y predominates [17]. As for Asia and the meningitis belt, serogroup A is the most frequent, with the recent emergence of serogroup X in outbreaks [13,18,19].

N. meningitidis is strictly a human pathogen; no animal carrier exists [2,4]. It resides in the nasopharynx with a carriage rate around 4 – 5% of a population [12]. Transmission occurs from person to person through respiratory droplets [16]. The incubation period is 2 – 10 days and symptoms include high-grade fever, stiff neck, headache, light sensitivity, vomiting, and confusion [16,20].

Clinical observation, microscopic examination of the cerebrospinal fluid or blood as well as bacterial culture, or polymerase chain reaction techniques confirms the diagnosis [21].

The best strategy to prevent meningococcal disease is early vaccination [15,22]. Currently, three types of vaccine exist. Polysaccharide vaccines were the first to be developed in the 1960s and became available as monovalent (MenA or MenC), bivalent (groups A and C), trivalent (groups A, C, and W), or tetravalent (groups A, C, Y, and W) forms [7,20]. The second type of vaccine was developed targeting serogroup B. It uses outer membrane vesicles instead of polysaccharides due to the antigenic mimicry of group B capsular polysaccharide with human neurological tissue polysaccharides [7,23]. Recently, a multicomponent meningococcal serogroup B vaccine has been approved in Europe for the use in individuals ≥ 2 months of age [24]. The third type of vaccines is the polysaccharide-protein conjugate vaccines [4]. These are available as either monovalent (groups A or C) or quadrivalent (groups A, C, W, and Y) vaccines [12].

The Meningococcal C conjugate vaccine was introduced in 1999 after the rise in incidence of serogroup C disease in England and Wales [25]. The A conjugate vaccine became available in 2010 as a result of partnership between the World Health Organization (WHO) and the Program for Appropriate Technology in Health to eradicate the African meningitis epidemic [12].

The available quadrivalent polysaccharide vaccines are not immunogenic in toddlers, with the exception of serogroup A [20,26]. Polysaccharide vaccines do not confer immune memory against pathogen capsule [15]. Immunity lasts around 3 – 5 years post-vaccination [27] and repeated vaccine administration may lead to hyporesponsiveness to vaccine antigens, especially to group C [15,28]. Furthermore, they do not lessen mucosal carriage or confer herd immunity [15,29].

Conjugate vaccines can overcome these limitations; the chemical bonding of the polysaccharide to a protein moiety converts the immune response into a T-cell-dependent anti-polysaccharide antibody response. This makes it effective in toddlers < 2 years of age, in which the incidence of the disease is highest, and stimulates a strong immune memory response [28]. Conjugation of the polysaccharide has already been shown effective in other vaccines, and examples include the Haemophilus influenzae type b (Hib) [30] and Streptococcus pneumoniae vaccines [31-33].

Three types of carrier proteins have been used in conjugation of the meningococcal vaccine: the tetanus toxoid (TT), the diphtheria toxoid (DT), and the cross-reactive material 197 (CRM197) - a mutant type of DT protein [18,34].

The currently available quadrivalent vaccines for meningococcal disease include two non-conjugated polysaccharide vaccines, MPSV4 and Men-PS, and three conjugate vaccines, MenACWY-DT, MenACWY-CRM197, and MenACWY-TT conjugated to DT, CRM197, and TT, respectively [18,28,35].

The first quadrivalent vaccine to be licensed was MenACWY-DT in 2005 as a single dose for ages 11 – 55 years [36]. In 2010 it was approved by the Executive Board of the Health Ministers’ Council for Gulf Cooperation Council States. Currently, it is approved in Canada from 9 months of age but is still not licensed in Europe [18]. In 2010 the quadrivalent CRM197 conjugate vaccine became available for ages ≥ 2 years [12].

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**Box 1. Drug summary.**

<table>
<thead>
<tr>
<th>Drug name</th>
<th>MenACWY-TT (Nimenrix)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase</td>
<td>Licensed</td>
</tr>
<tr>
<td>Indication</td>
<td>Vaccine against N. meningitidis serogroups A, C, W, and Y in ages 12 months and above in Europe and 12 months – 55 years in Canada</td>
</tr>
<tr>
<td>Route of administration</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Pivotal trials</td>
<td>Refer to Table 1</td>
</tr>
</tbody>
</table>
The Advisory Committee on Immunization Practices recommends quadrivalent meningococcal conjugate vaccines for routine vaccination of adolescents ages 11 – 18 with a booster dose 3 – 5 years later, up to age 21 [37], and 9 months – 55 years at increased risk of meningococcal disease [38].

Neither MenACWY-DT nor MenACWY-CRM197 is approved in Europe for ages < 2 years. The first quadrivalent vaccine to be approved in Europe for subjects ≥ 12 months of age against serogroups A, C, W, and Y is MenACWY-TT [39]. This review describes the use of the MenACWY-TT in healthy toddlers, children, adolescents, and adults.

1.1 Introduction to the compound
MenACWY-TT (Nimenrix [8]) is a TT-conjugated quadrivalent meningococcal polysaccharide vaccine against Neisseria meningitidis serogroups A, C, W, and Y, developed by GlaxoSmithKline (GSK) Biologicals (Box 1). It was approved in April 2012 by the European Medicines Agency for active immunization against IMD in individuals ≥ 12 months [39,40]. It was also approved in Canada as a single dose for the immunization of individuals 12 months to 55 years of age [41].

2. Chemistry
TT was chosen as the carrier protein due to the positive experience with the Hib and the monovalent MenC-TT conjugate vaccines [34]. Three formulations of vaccines have been evaluated before the final formulation of MenACWY-TT was accepted. In the first formulation, the polysaccharide was directly conjugated to TT. In the second, the MenA polysaccharide was coupled to a spacer before conjugation to TT. In the third and final formulation, both MenA and MenC polysaccharides were first coupled to a spacer before conjugation to TT. In all formulations, MenY and MenW were always directly conjugated to the TT [34,42,43]. The active ingredients of the final approved MenACWY-TT in each 0.5 ml include 5 µg of each of the four polysaccharides conjugated to TT in sucrose and trometamol excipients; the TT used totals to 44 µg per dose. The vaccine is reconstituted with sterile saline before injection [28,34].

3. Mechanism of immunity
Conjugating the polysaccharide to a protein moiety with a T-cell epitope changes the human immune response to the polysaccharide antigen from T-cell-independent to T-cell-dependent response [37]. A study done by Muthukkumar and Stein on mice found that immunization with the meningococcal polysaccharide TT conjugate vaccine induces T-cell clones specific for the TT and T-cell clones that react with the polysaccharide in the conjugate [44]. Recognition of the polysaccharide by the T cells contributes to the efficacy of this conjugate vaccine in infants [37].

The MenACWY-TT induces bactericidal anti-capsular antibodies against serogroups A, C, Y, and W that confer protection through a complement-mediated bactericidal effect, measured as the serum bactericidal antibody (SBA) assay. The specific serogroup antibody binds to the target cell surface and activates the classical pathway of complement, ultimately resulting in death of the target cell [45].

The experience with the Hib, Streptococcus pneumoniae, MenA, and MenC conjugate vaccines was promising with regard to herd immunity, where indirect protection was extended to unvaccinated children and adults [46-49]. This has been hypothesized to occur through the reduction of carriage which in effect reduces transmission [50]. Further studies are needed to evaluate the effect of MenACWY-TT on herd immunity.

4. Pharmacokinetics
The WHO Guidelines on Nonclinical Evaluation of Vaccines as well as the Note for Guidance on Clinical Evaluation of New Vaccines CHMP 2005 determined that no pharmacokinetic testing is required for final vaccine formulation. So no pharmacokinetic studies were conducted during MenACWY-TT development [51,52].

5. Clinical efficacy
Several Phase II and III clinical studies were done showing that a single dose of MenACWY-TT is highly immunogenic one month following vaccination in toddlers, children, adolescents, and adults [22,42,43,53,54]. The measure of protection was an SBA done in the presence of either rabbit complement (rSBA) or human complement (hSBA) [54] against each polysaccharide (A, C, W, and Y) showing titers ≥ 1:8 and ≥ 1:4, respectively [18,22,45]. Titters were taken pre-vaccination and 1 month post-vaccination; seroconversion was considered as a ≥ 4-fold increase in SBA from pre- to post-vaccination in initially seropositive subjects and a titer ≥ 1:32 in initially seronegative subjects [18,28,39,40].

5.1 Phase II studies
Phase II trials (Table 1) were performed on healthy 12 – 14-month-olds, 3 – 5-year-olds [42], and 15 – 25-year-olds [43] showing immunogenicity of the different formulations of the MenACWY-TT vaccine [40]. In Finland, a Phase II study demonstrated that the MenACWY-TT vaccine induces a protective immune response against all four serogroups in children 2 – 10 years of age [22]. Klein et al. compared the immunogenicity of a single dose of MenACWY-TT at either 9 or 12 months to two doses at 9 and 12 months. A single dose was shown to be immunogenic at 9 months mostly for serogroups A and C, whereas response for all serogroups was seen when the single dose was administered at 12 months of age. However, the two-dose schedule...
starting at 9 months showed the highest hSBA response for all serogroups [55]. Further studies were done to compare the immunogenicity of MenACWY-TT: with MenACWY-DT in 10 - 25-year-olds [54] and with MenACWY polysaccharide vaccine in 2 – 10 [22] and 11 - 17-year-olds [56]. According to Baxter et al. the MenACWY-TT vaccine response was higher for serogroups A, W, and Y when compared to MenACWY-DT vaccine response [54]. When MenACWY-TT was compared to MenACWY polysaccharide vaccine in 2 – 10-year-olds (Table 1), the vaccine response rate and post-vaccination rSBA geometric mean titers (GMTs) were higher for all serogroups among MenACWY-TT recipients than among MenACWY polysaccharide recipients [22].

Concern about hyporesponsiveness following polysaccharide vaccination was studied in Lebanon, in 4.5 – 34-year-olds (Table 1) previously vaccinated with the MenACWY polysaccharide vaccine. Post-vaccination rSBA GMTs and vaccine response rates for all serogroups were significantly lower in subjects previously vaccinated with MenACWY polysaccharide vaccine [57].

5.2 Phase II persistency studies
Antibody persistence was also evaluated. Knuf et al. illustrated that a single dose of MenACWY-TT elicits both immune memory and persistence of the antibodies in toddlers 15 months post-priming [58]. Østergaard et al. and Borja-Tabora et al. demonstrated long-term immune protection, up to 42 months and 3 years, respectively, following one dose of MenACWY-TT in adolescents and adults [56,59]. Furthermore, Vesikari et al. showed that at 3 years post-vaccination of 12 - 23-month-olds, 90.8% of MenACWY-TT recipients retained rSBA titers ≥ 1:8 for all serogroups and 73.6% retained hSBA titers ≥ 1:4 for serogroups C, W, and Y. As for serogroup A, the percentage of toddlers with hSBA titers > 1:4 decreased to 28.1% at 3 years post-vaccination [60]. Further studies are needed to evaluate the clinical relevance of these findings, the persistence of antibodies beyond 42 months, and the possible need for booster dosing [59].

5.3 Phase III studies
MenACWY-TT vaccine immunogenicity is measured in terms of its noninferiority when compared to other licensed meningococcal vaccine [28]. Multiple Phase III studies were conducted comparing the MenACWY-TT to its polysaccharide counterpart (Table 2). In Lebanon and Philippines, MenACWY-TT vaccine was shown to be noninferior to the polysaccharide meningococcal vaccine, in both initially seronegative and seropositive 18 – 55-year-old subjects [27]. Similarly, a multicenter study conducted in India, Philippines, and Taiwan showed that the MenACWY-TT vaccine is immunogenic in Asian adolescents, 11 – 17 years of age, with a reactogenicity and safety profile similar to the licensed polysaccharide vaccine [53]. Memish et al. demonstrated similar results in 2 – 10-year-olds [61]. This acceptable safety profile and immunogenicity of MenACWY-TT in 2 – 10-year-olds was also illustrated by Knuf et al. in Germany and France [15]. In a recent study conducted in Lebanon in subjects ≥ 56 years of age, it was shown that one dose of MenACWY-TT induced a vaccine response rate of ≥ 76.0% [62].

6. Coadministration with other vaccines
Several trials were done on toddlers aged 12 – 23 months (Table 2) investigating the immunogenicity and safety of MenACWY-TT when coadministered with various other

### Table 1. Published Phase II clinical vaccination trials of MenACWY-TT conjugate vaccine.

<table>
<thead>
<tr>
<th>Phase</th>
<th>Country</th>
<th>Target Group</th>
<th>Age Schedule</th>
<th>N</th>
<th>Publication/Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>United States</td>
<td>Infants</td>
<td>9 - 12 months</td>
<td>349</td>
<td>Klein NP et al. 2013 [55]</td>
</tr>
<tr>
<td>II</td>
<td>Finland</td>
<td>Toddlers</td>
<td>12 - 23 months</td>
<td>304</td>
<td>Vesikari et al. 2012 [60]</td>
</tr>
<tr>
<td>II</td>
<td>Germany</td>
<td>Toddlers</td>
<td>12 - 14 months</td>
<td>508</td>
<td>Knuf et al. 2010 [42]</td>
</tr>
<tr>
<td>II</td>
<td>Austria</td>
<td>Children</td>
<td>3 - 5 years</td>
<td>203</td>
<td>Knuf et al. 2012 [58]</td>
</tr>
<tr>
<td>II</td>
<td>Germany</td>
<td>Toddlers</td>
<td>12 - 14 months</td>
<td>309</td>
<td>Vesikari et al. 2012 [22]</td>
</tr>
<tr>
<td>II</td>
<td>Finland</td>
<td>Toddlers</td>
<td>2 - 10 years</td>
<td>271</td>
<td>Dbaibo et al. 2012 [57]</td>
</tr>
<tr>
<td>II</td>
<td>Lebanon</td>
<td>Children</td>
<td>4.5 - 10 years</td>
<td>50</td>
<td>Østergaard et al. 2013 [59]</td>
</tr>
<tr>
<td>II</td>
<td>Denmark</td>
<td>Adolescents</td>
<td>15 - 19 years</td>
<td>175</td>
<td>Østergaard et al. 2009 [43]</td>
</tr>
<tr>
<td>II</td>
<td>USA</td>
<td>Adolescents</td>
<td>10 - 25 years</td>
<td>784</td>
<td>Baxter et al. 2011 [54]</td>
</tr>
<tr>
<td>II</td>
<td>Belgium, Denmark</td>
<td>Adolescents</td>
<td>15 - 25 years</td>
<td>203</td>
<td>2012 [58]</td>
</tr>
<tr>
<td>II</td>
<td>Philippines</td>
<td>Adolescents</td>
<td>11 - 55 years</td>
<td>500</td>
<td>Borja-Tabora et al. 2013 [56]</td>
</tr>
</tbody>
</table>

N: Number of subjects enrolled in the study.
Table 2. Published Phase III clinical vaccination trials of MenACWY-TT conjugate vaccine.

<table>
<thead>
<tr>
<th>Phase</th>
<th>Country</th>
<th>Target group</th>
<th>Age schedule</th>
<th>N</th>
<th>Publication/Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>III</td>
<td>Taiwan</td>
<td>Toddlers</td>
<td>12 – 23 months</td>
<td>363</td>
<td>M. Ruiz-Palacios et al. 2013 [65]</td>
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<tr>
<td></td>
<td>Mexico</td>
<td>Toddlers</td>
<td>12 – 23 months</td>
<td>1000</td>
<td>Vesikari et al. 2011 [63]</td>
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<td>III</td>
<td>Finland</td>
<td>Toddlers</td>
<td>12 – 23 months</td>
<td>793</td>
<td>Knuf et al. 2011 [64]</td>
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<tr>
<td>III</td>
<td>Austria</td>
<td>Toddlers</td>
<td>12 – 23 months</td>
<td>520</td>
<td>Åstergaard et al. 2012 [66]</td>
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<td></td>
<td>Germany</td>
<td>Adolescents</td>
<td>11 – 17 years</td>
<td>1025</td>
<td>Bermal et al. 2011 [53]</td>
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<td>III</td>
<td>Lebanon</td>
<td>Adults</td>
<td>18 – 55 years</td>
<td>1247</td>
<td>Dbaibo et al. 2012 [27]</td>
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<tr>
<td></td>
<td>Lebanon</td>
<td>Adolescents</td>
<td>11 – 17 years</td>
<td>520</td>
<td>Aplasca-De Los Reyes et al. 2012 [1]</td>
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<tr>
<td></td>
<td>Lebanon</td>
<td>Adults</td>
<td>56 – 103 years</td>
<td>400</td>
<td>Dbaibo et al. 2013 [62]</td>
</tr>
</tbody>
</table>

N: Number of subjects enrolled in the study.

age-appropriate vaccines [63-65]. The administration of Diphtheria-Tetanus-Acellular Pertussis-Hepatitis B-Inactivated Polio/Hemophilus influenzae type b vaccine (DTaP-HBV-IPV/Hib) with the MenACWY-TT during a single visit was shown to result in the same immune response and safety profile as their separate administration. Pain at injection site was reported more often as their administration at two different time points (p = 0.0218), and drowsiness and fever were more frequent (p ≤ 0.0037) when they were coadministered than when each was given alone [64].

In Finland (Table 2), a Phase III study demonstrated that coadministering MenACWY-TT with the Measles-Mumps-Rubella-Varicella vaccine at ages 12 – 23 months does not affect the immunogenicity or the safety of either of these vaccines [63]. Similarly, coadministration of Hepatitis B/A vaccine with the MenACWY-TT was found to be immunologically noninferior to administration of each vaccine alone and no safety changes were reported, in 11 – 17-year-olds [66].

Furthermore, coadministration with the seasonal influenza vaccine in 18 – 55-year-olds was investigated in Lebanon and Philippines. The MenACWY-TT seroconversion rate was 76.5 – 88.7% with 97.1% achieving SBA 1:128 antibody levels and the seroconversion rate to all three influenza strains was 61.9 – 75.7% with 96.2 – 99.0% achieving SBA 1:8 protective anti-hemagglutination inhibition antibodies. The safety profile of the MenACWY-TT was not altered [1].

A recent study published in 2013 reported comparable immunogenicity and safety profiles of administering the MenACWY-TT with the 10-valent pneumococcal-nontypeable Haemophilus influenzae-protein D conjugate vaccine as either vaccine alone. The immunogenicity of all the meningococcal serogroups and pneumococcal serotypes was noninferior, except for pneumococcal serotype 18C. The inferior response to serotype 18C, also conjugated to TT, is hypothesized to be due to the high TT dosage which might have interfered with the T-helper-cell response to serotype 18C [65]. The potential immune interference of MenACWY-TT with pneumococcal serotype 18C warrants further research of whether or not this vaccine can be used in conjunction with other conjugate vaccines.

7. Safety and tolerability

Diary cards were used to assess the reactogenicity and tolerability of MenACWY-TT vaccine in all these studies. The incidence of solicited local (pain, redness, and swelling) and systemic (drowsiness, fever, irritability, and loss of appetite in ages < 5 years; fatigue, fever, gastrointestinal symptoms, and headache in ages > 6 years) adverse events (AEs) was recorded for four or eight days post-vaccination. Unsolicited AEs and serious adverse events (SAEs) were recorded for 1 month and 6 months, respectively, post-vaccination [1,53,54,61].

In subjects receiving MenACWY-TT, redness in 2 – 5-year-olds and pain in 6 – 10-year-olds were the most common solicited local symptoms, reported in 35.2 and 43.9%, respectively, compared to 39.6 and 54.0%, respectively, in subjects receiving MenC-CRM197. The most common solicited general symptom in 2 – 5-year-olds was irritability in those receiving MenACWY-TT (15.4%) of
subjects) and irritability and drowsiness in the MenC-CRM197 group (each in 11.3% of subjects). As for the older age strata, 6–10-year-olds, fatigue was the most common solicited general symptom in both the MenACWY-TT and MenC-CRM197 groups (22.3 and 22.0%, respectively)[15]. Studies in 10–25-year-olds showed that pain and headaches were the most commonly reported solicited local and general symptoms occurring at a similar rate in MenACWY-TT (54.9 and 33.0%, respectively) and MenACWY-DT (54.1 and 37.1%, respectively) recipients[54]. When compared with MenACWY polysaccharide vaccine in 2–10-year-olds, the MenACWY-TT had an acceptable safety profile [61]. Pain at the injection site (approximately 70% of MenACWY-TT group vs. 40% of polysaccharide group), fatigue, and headache were the most common symptoms in 15–25-year-olds compared to controls receiving tetravalent polysaccharide vaccine [43]. This may be attributed to increased reactogenicity of conjugate vaccines as opposed to their polysaccharide counterparts [27,67].

8. Regulatory affairs

MenACWY-TT has been approved in Europe for active immunization against IMD in individuals ≥ 12 months of age and in Canada in individuals 12 months to 55 years [39].

9. Conclusion

Meningococcal meningitis remains a public health burden with vaccination being the most important prevention strategy [15,22]. The shortcomings of the quadrivalent polysaccharide vaccines were overcome with the advent of conjugate vaccines [18,34].

MenACWY-TT is a quadrivalent conjugated meningococcal vaccine for the active immunization of individuals ≥ 12 months [18,28]. It elicits an appropriate immune response, demonstrating an acceptable safety and reactogenicity profile when administered alone or when coadministered with other vaccines.

Ongoing Phase III trials are currently being conducted to address the safety and immunogenicity of MenACWY-TT in ages 6–12 weeks and in high-risk individuals ages 1–17 years, as well as coadministration with TT-reduced DT-acellular pertussis (Tdap) vaccine or with human papilloma virus vaccine or with DTaP-HBV-IPV/Hib and pneumococcal conjugate vaccines (Table 3) [68].

10. Expert opinion

MenACWY-TT is a promising addition to our armamentarium in controlling the devastating infections caused by Neisseria meningitidis around the globe. Its immunogenicity and safety in a wide range of age groups make it an excellent alternative for prevention in countries where it becomes available. While it does not offer major advantages over existing conjugate meningococcal vaccines, there is some evidence that it might be more immunogenic than the DT conjugate vaccine [54] although the clinical relevance of this remains to be determined. Another advantage, at least in Europe and Canada, is its approval for children as young as 12 months of age, a highly susceptible group. It is hoped that the price of this and other conjugate vaccines becomes affordable for countries that need it the most.

Declaration of interest

G Dhaibo has served on Advisory Boards, received grant support through his institution, and received honoraria for lectures from GlaxoSmithKline, Merck Sharpe and Dohme, Sanofi-Aventis, and Pfizer. All other authors have no interests to declare.

Table 3. Ongoing clinical trials on MenACWY-TT [68].

<table>
<thead>
<tr>
<th>Title</th>
<th>NCT</th>
<th>Age group</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunogenicity and safety study of GSK biologicals’ meningococcal conjugate vaccine when coadministered with routine vaccines in healthy infants and toddlers</td>
<td>NCT01340898</td>
<td>6 – 12 weeks</td>
<td>Lebanon; Mexico</td>
</tr>
<tr>
<td>Comparison of GSK134612 in subjects with increased risk for meningococcal disease versus healthy subjects</td>
<td>NCT01641042</td>
<td>1 – 17 years</td>
<td>Czech Republic; California (USA)</td>
</tr>
<tr>
<td>Immunogenicity and safety study of GSK Biologicals’ meningococcal vaccine with or without coadministration of Cervarix and Boostrix in female adolescents and young adults</td>
<td>NCT01755689</td>
<td>9 – 25 years</td>
<td>Dominican Republic; Estonia</td>
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<tr>
<td>Immunogenicity, reactogenicity and safety of GSK Biologicals’ MenACWY-TT vaccine administered 6 years Post-MenC primary vaccination in healthy subjects who were 12 – 18 months at primary vaccination</td>
<td>NCT01777308</td>
<td>12 – 18 months</td>
<td>Queensland (Australia)</td>
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<td>GSK 134612 coadministered with pneumococcal and DTPa-HBV-IPV/Hib vaccines</td>
<td>NCT01144663</td>
<td>6 – 12 weeks</td>
<td>Estonia; Germany; Spain</td>
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</tbody>
</table>
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