Poster 121

# Phase 1 Trial of a Tdap Booster Vaccine (Tdap-1018 CpG Adjuvanted) Compared With Boostrix in Healthy Adults and Adolescents

Robert Janssen,[1] Anthony McGirr,[2] Fiona Napier-Flood,[3] Amber Leah,[4] Terry Nolan,[5] Peter Richmond,[6] Tammy Boyce,[1] Fang Xie,[1] Olivier Godeaux,[1] Nicolas Wood[7]

[1]Dynavax Technologies Corporation, Emeryville, CA, USA; [2]Northern Beaches Clinical Research, Brookvale, NSW, Australia; [3]Paratus Clinical Research Western Sydney, Blacktown, NSW, Australia; [4]Paratus Clinical Research Canberra, Bruce, ACT, Australia; [5]The Peter Doherty Institute for Infection and Immunity, Murdoch Children's Research Institute, Melbourne, VIC, Australia; [6]University of Western Australia School of Medicine, Perth's Children Hospital, Nedlands, WA, Australia; [7]The Children's Hospital at Westmead, Westmead, NSW, Australia

## BACKGROUND

- Diphtheria (D), tetanus (T), and pertussis (P) are 3 vaccine-preventable infectious diseases in humans
- Pertussis (whooping cough) is a highly contagious respiratory infection that affects more than 151,000 individuals annually worldwide[1]
- In 2020, more than 17 million infants globally did not receive an initial DTP vaccine; an additional 5.6 million were partially vaccinated[2]
- In Australia, pertussis epidemics typically occur on a 3–4 year cycle[3]
- More than 63% of reported pertussis cases in the United States occurred in adolescents or adults, probably because of suboptimal or waning immunity induced by use of acellular compared with whole cell pertussis vaccines[4]
- A tetanus-diphtheria-pertussis (Tdap) booster vaccine combined with the CpG 1018 adjuvant (Tdap-1018, Dynavax Technologies Corporation) may induce higher antibody titers than aluminum-adjuvanted Tdap vaccines in adults and adolescents

## OBJECTIVE

- To compare the safety, tolerability, and immunogenicity of Tdap-1018 with those of Boostrix® (GlaxoSmithKline Biologicals) after administration of a booster dose to healthy adults and adolescents

## METHODS

- Boostrix is a tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (adsorbed) adjuvanted with alum for active booster immunization in individuals aged 10 years and older[5]
- In this randomized, participant-blind, active-controlled, multicenter phase 1 trial in Australia, healthy participants aged 10-22 years received a single booster injection of Tdap-1018 (same Tdap composition as in Boostrix and escalating CpG 1018 adjuvant doses of 1500 µg and 3000 µg) or Boostrix on day 1
  - Participants were required to have documentation of having received 2 or more prior acellular pertussis vaccinations and to be in good health
  - Participants were excluded from the study if they had received an acellular pertussis booster within the previous 3 years or if they had a history of diphtheria, tetanus, or pertussis disease
- Evaluation of pertussis immunogenicity assessed booster response for anti–pertussis toxin (anti-PT), anti–filamentous hemagglutinin (anti-FHA), anti-pertactin (anti-PRN) antibodies, and systems serology at week 4 after vaccination
- Booster response rates (BRRs) for antibodies were determined using the following criteria:
  - In initially seronegative participants, post-vaccination antibody concentrations ≥4 × 3.994 (LLoQ)
  - In initially seropositive participants with pre-vaccination antibody concentrations >4 × 3.994, an increase of ≥2 × the pre-vaccination antibody concentration
  - In initially seropositive participants with pre-vaccination antibody concentrations between ≥3.994 and 4 × 3.994, an increase of ≥4 × the pre-vaccination antibody concentration
- Safety and tolerability were assessed to determine solicited local and systemic postinjection reactions for 7 days and unsolicited adverse events for 12 weeks after vaccination

## RESULTS

### Study Population

- 87 adults and 30 adolescents were enrolled in the study (**Tables 1, 2**)
  - 80 adults (92.0%) and 30 adolescents (100.0%) completed the study
  - For adults, the median age was 19.0 years, 35% were male, 84% were White, and 98% were not Hispanic or Latino
  - For adolescents, the median age was 11.0 years, 47% were male, 87% were White, and 100% were not Hispanic or Latino

**Table 1. Participant Demographics and Baseline Characteristics for Adults (safety population)[a]**

| Characteristic | Tdap-1018 1500 µg n = 30 | Tdap-1018 3000 µg n = 29 | Boostrix n = 28 | Total N = 87 |
|---|---|---|---|---|
| Male, n (%) | 12 (40.0) | 8 (27.6) | 10 (35.7) | 30 (34.5) |
| Age, median (min, max), years | 19.5 (18.0, 22.0) | 19.0 (18.0, 22.0) | 19.0 (18.0, 22.0) | 19.0 (18.0, 22.0) |
| Race, White, n (%) | 25 (83.3) | 26 (89.7) | 22 (78.6) | 73 (83.9) |
| Ethnicity, not Hispanic or Latino, n (%) | 29 (96.7) | 29 (100.0) | 27 (96.4) | 85 (97.7) |

[a]Database not locked. Tdap-1018 indicates tetanus-diphtheria-pertussis booster vaccine combined with the CpG 1018 adjuvant.

**Table 2. Participant Demographics and Baseline Characteristics for Adolescents (safety population)[a]**

| Characteristic | Tdap-1018 1500 µg n = 12 | Tdap-1018 3000 µg n = 8 | Boostrix n = 10 | Total N = 30 |
|---|---|---|---|---|
| Male, n (%) | 5 (41.7) | 6 (75.0) | 3 (30.0) | 14 (46.7) |
| Age, median (min, max), years | 11.0 (10.0, 17.0) | 11.5 (11.0, 15.0) | 13.0 (10.0, 17.0) | 11.0 (10.0, 17.0) |
| Race, White, n (%) | 9 (75.0) | 8 (100.0) | 9 (90.0) | 26 (86.7) |
| Ethnicity, not Hispanic or Latino, n (%) | 12 (100.0) | 8 (100.0) | 10 (100.0) | 30 (100.0) |

[a]Database not locked. Tdap-1018 indicates tetanus-diphtheria-pertussis booster vaccine combined with the CpG 1018 adjuvant.

### Safety and Tolerability

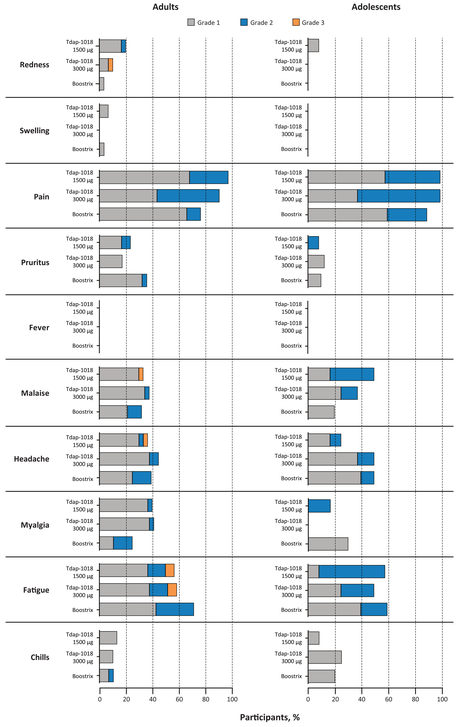
- Tdap-1018 1500 µg, Tdap-1018 3000 µg, and Boostrix were generally well tolerated in adults or adolescents, with no observed safety concerns (**Table 3, Figure 1**)

**Table 3. Summary of Adverse Events for Adults and Adolescents (safety population)[a]**

| | Adults | | | Adolescents | | |
|---|---|---|---|---|---|---|
| n (%) | Tdap-1018 1500 µg N = 30 | Tdap-1018 3000 µg N = 29 | Boostrix N = 28 | Tdap-1018 1500 µg N = 12 | Tdap-1018 3000 µg N = 8 | Boostrix N = 10 |
| Any AE | 7 (23.3) | 11 (37.9) | 7 (25.0) | 5 (41.7) | 5 (62.5) | 6 (60.0) |
| Any related AE | 3 (10.0) | 0 | 1 (3.6) | 2 (16.7) | 1 (12.5) | 2 (20.0) |
| Any SAE | 0 | 1 (3.4)[b] | 1 (3.6)[c] | 0 | 0 | 0 |
| Any related SAE | 0 | 0 | 0 | 0 | 0 | 0 |
| Any grade 3 or 4 AE | 0 | 1 (3.4)[b] | 1 (3.6)[c] | 0 | 0 | 0 |
| Any related grade 3 or 4 AE | 0 | 0 | 0 | 0 | 0 | 0 |
| Any AE leading to discontinuation | 0 | 0 | 0 | 0 | 0 | 0 |
| Any related AE leading to discontinuation | 0 | 0 | 0 | 0 | 0 | 0 |
| Death | 0 | 0 | 0 | 0 | 0 | 0 |

[a]Database not locked. [b]Participant experienced grade 3 depression that resolved by the end of the study. [c]Participant experienced grade 3 large intestine infection that resolved by the end of the study. AE indicates adverse event; SAE, serious adverse event; Tdap-1018, tetanus-diphtheria-pertussis booster vaccine combined with the CpG 1018 adjuvant.

**Figure 1. Solicited Local and Systemic Adverse Reactions Within 7 Days After Injection in Adults and Adolescents[a]**

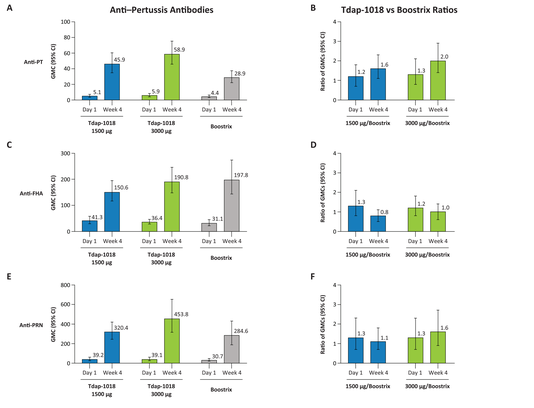



[a]Database not locked. Tdap-1018 indicates tetanus-diphtheria-pertussis booster vaccine combined with the CpG 1018 adjuvant. If a participant had the same type of reaction more than once, only the most severe reaction within the type was summarized. Local reactions included redness ≥25 mm, swelling ≥25 mm, and pain. Systemic reactions included fever (≥38°C), myalgia, fatigue, headache, malaise. Grade 3 redness and swelling: >100 mm; grade 3 fever: ≥39°C.

### Immunogenicity

- At week 4, similar or higher geometric mean concentrations of all investigated anti–pertussis antibodies were observed after administration of Tdap-1018 3000 µg compared with Boostrix in adults (**Figure 2**)

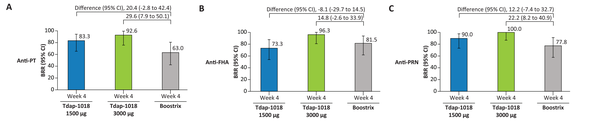
**Figure 2. Summary of Anti–Pertussis Antibodies by Vaccination Group Through Week 4 for Adults (mITT population)[a]**




[a]Database not locked. anti-FHA indicates anti–filamentous hemagglutinin antibodies; anti-PRN, anti–pertactin antibodies; anti-PT, anti–pertussis toxin antibodies; GMC, geometric mean concentration; mITT, modified intention-to-treat; Tdap-1018, tetanus-diphtheria-pertussis booster vaccine combined with the CpG 1018 adjuvant.

- BRRs were evaluated for antibodies to pertussis antigens (pertussis toxin, filamentous hemagglutinin, and pertactin) to assess immunogenicity
- In adults at week 4, BRRs in the Tdap-1018 3000 µg group were significantly higher (based on lower 95% CI, >0%) than in the Boostrix group for anti-PT (difference in BRRs, 29.6% [95% CI, 7.9%-50.1%]) and anti-PRN (22.2% [95% CI, 8.2%-40.9%]) antibodies and were similar for anti-FHA (14.8% [95% CI, −2.6% to 33.9%]) antibodies (**Figure 3**)
  - Adolescent immunogenicity results are pending further analysis

**Figure 3. Summary of Pertussis BRR by Vaccination Group Through Week 4 for Adults (mITT population)[a]**




[a]Database not locked. anti-FHA indicates anti-filamentous hemagglutinin antibodies; anti-PRN, anti-pertactin antibodies; anti-PT, anti-pertussis toxin antibodies; BRR, booster response rate; mITT, modified intention-to-treat; Tdap-1018, tetanus-diphtheria-pertussis booster vaccine combined with the CpG 1018 adjuvant.

## CONCLUSIONS

1. In the current phase 1 trial, both dose levels of Tdap-1018 were generally well tolerated in adults and adolescents
2. Tdap-1018 3000 µg induced similar or higher anti-pertussis antibodies than Boostrix in adults
3. Tdap-1018 3000 µg induced significantly higher booster responses than Boostrix for anti-PT and anti-PRN and a similar response for anti-FHA in adults

### Acknowledgments

The authors thank all the individuals who participated in the study. The contributions of the investigators and their staff are also gratefully recognized.

Medical writing and/or editorial support was provided by Jared Cochran, PhD, of ApotheCom (Yardley, PA, USA). This assistance was funded by Dynavax Technologies Corporation, Emeryville, CA, USA. Funding for this research was provided by Dynavax Technologies Corporation, Emeryville, CA, USA.

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Presented at IDWeek 2022; October 19-23, 2022; Washington, DC

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