Safety and immunogenicity of the semisynthetic saponin adjuvant TQL1055: preliminary results from a first-in-humans pertussis vaccine trial

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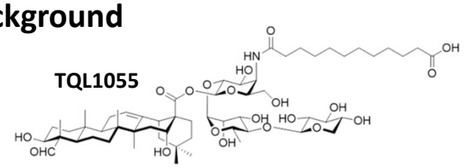
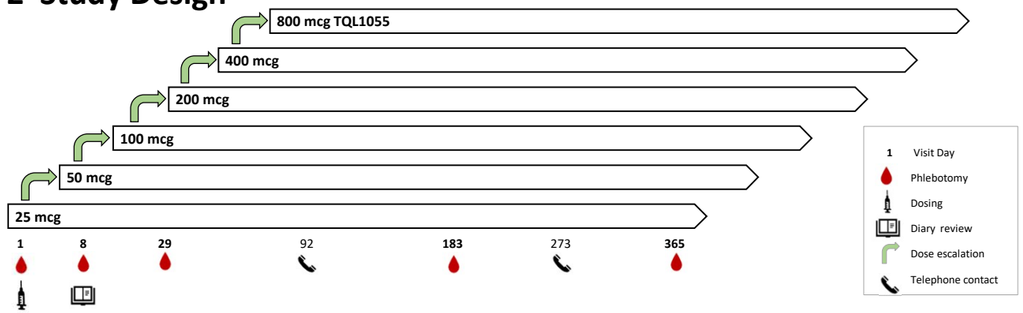
1 Background



↑**1** Acellular pertussis vaccines are better tolerated than whole cell vaccines but require adjuvants.[1] First-generation natural saponins such as QS-21 are potent adjuvants; however, QS-21 can produce prolonged and severe reactions, including injection site necrosis, at doses above 50 mcg. [2] Quenching of this toxicity requires coformulation with liposomes (eg AS01) or other saponins (eg Matrix-M). TQL1055 (above) is a semisynthetic analogue of QS-21, rationally modified to improve tolerability and maintain adjuvant activity.[3] We previously showed that TQL1055 exhibits less toxicity than QS-21 in mice and augments the response to alum-adjuvanted acellular pertussis vaccine (Tdap).[4] Here we present data from a first-in-humans study of TQL1055 field-formulated with Tdap, called pertussis acellular vaccine adjuvanted (PAVA).

2 Study Design



↑**2** A total of 72 healthy Australian adults were enrolled into six sequential groups and randomized to a single intramuscular dose of either PAVA (n=10) or Tdap (n=2). The visit schedule and key procedures are shown above. The TQL1055 dose increased from 25 mcg to 800 mcg, following review of the preceding group's safety data through Day 8. An interim analysis was performed at Day 29. Follow-up is ongoing.

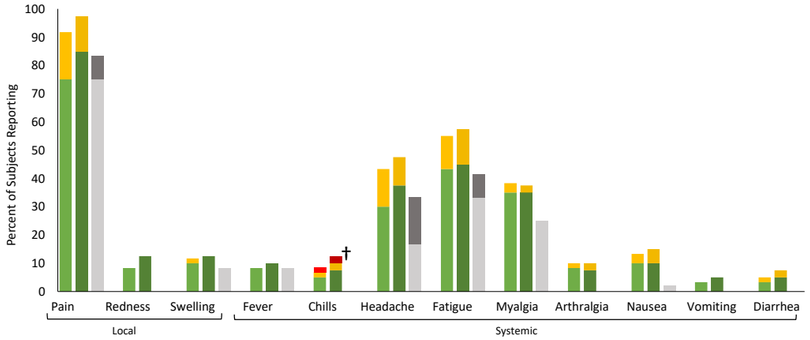
3 Demographics

Group	PAVA 25	PAVA 50	PAVA 100	PAVA 200	PAVA 400	PAVA 800	All PAVA	PAVA 100-800	Tdap
n	10	10	10	10	10	10	60	40	12
Age, years									
Median	32	26	28	39	26	28	**28**	**29**	**27**
Range	22-50	21-50	18-49	19-46	19-44	19-47	**18-50**	**18-49**	**20-47**
Race, n (%)									
White	6 (60)	9 (90)	9 (90)	8 (80)	9 (90)	8 (80)	**49 (82)**	**34 (85)**	**10 (83)**
Asian	3 (30)	1 (10)	0	1 (10)	0	1 (10)	**6 (10)**	**2 (5)**	**2 (17)**
Pacific Islander	1 (10)	0	1 (10)	0	1 (10)	0	**3 (5)**	**2 (5)**	**0**
Other/Missing	0	0	0	1 (10)	0	1 (10)	**2 (3)**	**2 (5)**	**0**
Sex, n (%)									
Female	3 (30)	4 (40)	6 (60)	7 (70)	4 (40)	6 (60)	**30 (50)**	**23 (65)**	**7 (58)**
Male	7 (70)	6 (60)	4 (40)	3 (30)	6 (60)	4 (40)	**30 (50)**	**17 (35)**	**5 (42)**
BMI, kg/m²									
Median	22.3	26.3	24.4	24.6	28.1	25.1	**24.9**	**24.9**	**26.8**

↑**3** Baseline characteristics were similar between the All PAVA group and the Tdap group.

4 Results: Safety and Tolerability

4A: Solicited AEs

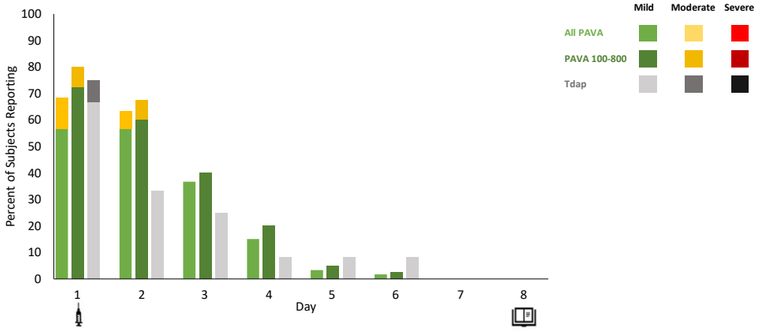


←**4A** Solicited adverse events (AEs) were collected by diary card through Day 8 and graded per USFDA vaccine toxicity guidance.[5] Most solicited AEs were mild. There were no severe solicited AEs related to vaccine.
In all groups, the most frequent local solicited AE was injection site pain and the most frequent systemic solicited AEs were headache, fatigue, and myalgia. Fever was mild and relatively infrequent.

Overall, the solicited AE profile of PAVA appeared similar to that of Tdap.

† One participant in the PAVA 400 group reported severe chills from an unrelated flu-like illness.

4B: Injection Site Pain by Day



←**4B** The local solicited AE of Injection site pain was further analyzed by day. The frequency was highest on Day 1 (the day of dosing) and declined steadily thereafter. By Day 3, all reported injection site pain was mild (ie not interfering with daily activities). By Day 7, no injection site pain was reported. There was no severe injection site pain or necrosis.

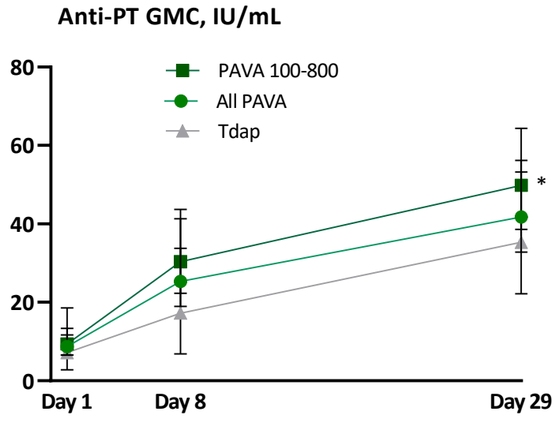
4C: Unsolicited AEs

Group	PAVA 25	PAVA 50	PAVA 100	PAVA 200	PAVA 400	PAVA 800	All PAVA	PAVA 100-800	Tdap
N	10	10	10	10	10	10	60	40	12
Any, n (%)	4 (40)	0	2 (20)	4 (40)	3 (30)	2 (20)	15 (25)	11 (28)	4 (33)
Related	1 (10)	0	0	1 (10)	1 (10)	0	3 (5)	2 (5)	2 (17)
MAAE*	0	0	0	0	2 (20)	1 (10)	3 (5)	3 (8)	0

↑**4C** Unsolicited AEs were relatively infrequent and mostly unrelated to vaccine. Three unrelated medically attended AEs (***MAAEs**) occurred, all associated with suspected SARS-CoV-2 infection. There were no potential immune-mediated disorders, serious AEs, pregnancies or deaths. Addditionally, there were no clinically significant vaccine-related changes in hematology, serum chemistry, or coagulation laboratory values.

5 Results: Immunogenicity

↑**5** Antibodies to pertussis toxin (PT) at Days 1, 8, and 29 were measured by ELISA in international units (IU)/mL using WHO reference standards. The PAVA 100-800 group (n=40) was pooled post hoc. Geometric mean concentrations (GMCs) and 95% confidence intervals (CIs) were calculated at all timepoints. GMCs at Day 29 were compared by Student's t-test.



↑**5** Anti-PT GMCs and 95% confidence intervals are shown above. The GMCs for the All PAVA, PAVA 100-800, and Tdap groups increased from Day 1 to Day 8 and again from Day 8 to Day 29.

* The Day 29 GMC of 49.84 in the PAVA 100-800 group was significantly higher than the GMC of 35.29 in the Tdap group (p = 0.043).

Serum was also collected for analysis of additional vaccine antigens. These analyses are pending.

6 Summary

- **PAVA was well tolerated at doses up to 800 mcg, or 16 times the typical dose of QS-21.**
- **PAVA's overall safety profile was similar to that of Tdap.**
- **Both local and systemic reactions were predominantly mild.**
- **After Day 3, injection site pain was mild and infrequent.**
- **A post-vaccination anti-PT response was observed in all groups.**
- **The PAVA 100-800 group had a significantly higher Day 29 anti-PT GMC than the Tdap group.**
- **These promising preliminary findings warrant continued long-term follow-up and assessment of the antibody response to additional antigens.**

7 Acknowledgments

- **Our team: Melissa Malhame, Jared Wenger, Anna Lampe, Nadia Bracken**
- **Our partners: PI Paul Griffin, Nucleus Network, CNS/Novotech, 360biolabs**
- **Our study participants**

8 References

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