Graves-PCD trial – summary of results

ISRCTN Number: 81162400

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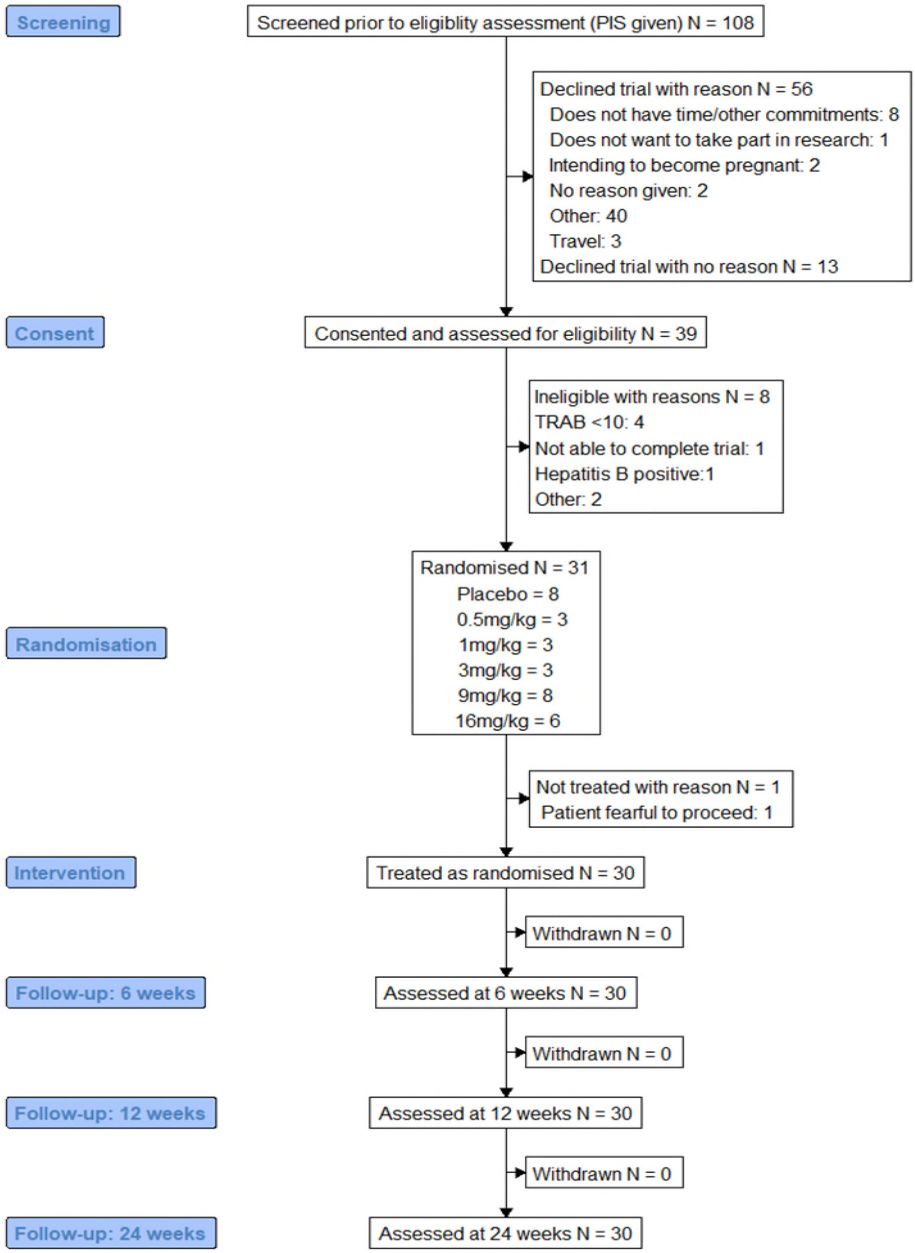
Consort flow diagram



Baseline characteristics

	Randomised group						
	Placebo	**0.5 mg/kg**	**1 mg/kg**	**3 mg/kg**	**9 mg/kg**	**16 mg/kg**	**Total**
N	8 (26.7%)	3 (10.0%)	3 (10.0%)	3 (10.0%)	8 (26.7%)	5 (16.7%)	30 (100.0%)
Age at randomisation (years)	47.1 (17.3)	42.9 (8.1)	51.5 (24.4)	31.2 (13.6)	37.0 (11.2)	38.3 (9.0)	41.4 (14.5)
Height (cm)	166.1 (10.6)	173.7 (13.7)	169.7 (13.3)	174.0 (15.5)	160.2 (5.4)	166.2 (5.3)	166.5 (10.1)
Weight (kg)	73.9 (24.3)	84.4 (23.3)	74.1 (1.9)	76.8 (19.4)	71.8 (12.7)	67.8 (16.4)	73.7 (17.4)
Pulse (bpm)	79.9 (9.0)	64.3 (6.7)	76.3 (22.5)	80.7 (18.6)	77.9 (9.5)	68.8 (6.8)	75.7 (11.8)
BMI (kg/m^2)	26.4 (6.4)	27.5 (3.8)	26.1 (5.0)	25.0 (2.3)	28.1 (5.5)	24.7 (6.8)	26.5 (5.3)
Age at diagnosis (years)	46.9 (17.3)	45.1 (9.5)	44.0 (29.6)	31.1 (13.6)	37.4 (11.9)	38.2 (9.0)	40.7 (14.4)
TSH at diagnosis (U/L)	0.0 (0.02)	0.0 (0.02)	0.0 (0.01)	0.0 (0.02)	0.0 (0.02)	0.0 (0.01)	0.0 (0.02)
FT4 at diagnosis (pmol/L)	74.7 (21.1)	80.6 (12.6)	66.0 (30.0)	100.0 (0.0)	83.8 (24.1)	70.4 (25.2)	78.7 (22.3)
FT3 at diagnosis (pmol/L)	32.1 (9.1)	38.3 (4.9)	34.3 (13.9)	37.6 (6.9)	38.4 (15.1)	36.5 (12.8)	35.9 (11.1)
TRAb at diagnosis (U/L)	33.0 (25.5)	58.7 (33.4)	40.4 (32.7)	34.6 (12.3)	35.6 (26.6)	74.0 (72.0)	44.0 (38.0)
Gender at birth							
Male	2 (25.0%)	2 (66.7%)	2 (66.7%)	1 (33.3%)	1 (12.5%)	0 (0.0%)	8 (26.7%)
Female	6 (75.0%)	1 (33.3%)	1 (33.3%)	2 (66.7%)	7 (87.5%)	5 (100.0%)	22 (73.3%)
Smoking Status							
Smoked within 1 year/current smoker	5 (62.5%)	1 (33.3%)	2 (66.7%)	0 (0.0%)	0 (0.0%)	2 (40.0%)	10 (33.3%)
Hasn't smoked within 1 year	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (62.5%)	1 (20.0%)	7 (23.3%)
Never smoked	2 (25.0%)	2 (66.7%)	1 (33.3%)	3 (100.0%)	3 (37.5%)	2 (40.0%)	13 (43.3%)
Vaping Status							
Vaped within 1 year/current vaper	1 (12.5%)	0 (0.0%)	1 (33.3%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	3 (10.0%)
Hasn't vaped within 1 year	2 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)	3 (10.0%)
Never vaped	5 (62.5%)	3 (100.0%)	2 (66.7%)	3 (100.0%)	7 (87.5%)	4 (80.0%)	24 (80.0%)

Statistics reported are: mean (SD) for continuous data and number (percentage) for categorical data

Primary outcome

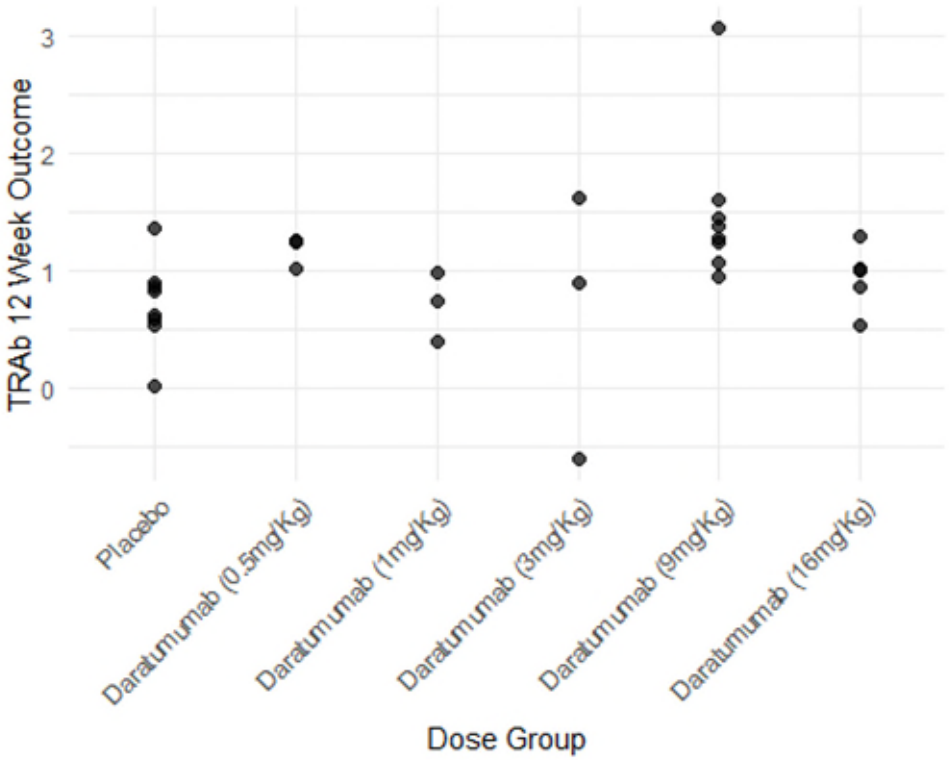


Figure 1 - Primary outcome at 12 weeks by randomised group

The primary analysis, a contrast-based test, testing the null hypothesis of no dose-response, yielded a test statistic for dose-response at 12 weeks of 1.04. The p-value for testing the null hypothesis of no dose-response at 12 weeks is 0.155. Thus, there was not significant evidence to conclude dose-response for TRAb, considering all doses tested.

Safety results

There were 382 adverse events (AEs) reported in the 30 participants or which 173 were consider related to IMP (definitely, probably or possibly) and were defined as adverse reactions (ARs). There was one serious adverse event (SAE) judged to be probably related to IMP.

All except 2 of the ARs were classified as grade 1 severity. There was a single AR classified as grade 2 and a single grade 3 AR. The grade 3 AR was a serious adverse event.

The table below shows the number of ARs by randomised group and severity.

	Randomised dose group (mg/kg)						Total
	0	**0.5**	**1**	**3**	**9**	**16**	
Number of participants	*8*	*3*	*3*	*3*	*8*	*5*	*30*
Number of ARs reported per participant							
0	6	0	0	0	0	0	6
1	1	0	0	0	0	0	1
2	1	1	1	0	0	0	3
3	0	0	0	1	0	0	1
4+	0	2	2	2	8	5	19
Mean	0.38	5.33	3.67	7.00	9.88	8.60	5.77
SD	0.74	3.06	1.53	4.58	3.52	2.41	4.57
Median	0	6	4	6	9	8	6
Min	0	2	2	3	6	6	0
Max	2	8	5	12	16	12	16
Worst grade AR reported per participant							
None	6	0	0	0	0	0	6
1	2	3	3	3	7	4	22
2	0	0	0	0	1	0	1
3	0	0	0	0	0	1	1

There was a single serious adverse event (SAE) – *community acquired pneumonia* - in a participant randomised to the 16mg/kg dose group on 3/7/2023. Onset of the adverse event was 27/01/2024 with resolution on 29/01/2024. The SAE was considered probably related to IMP and was grade 3. The participant was admitted to hospital for a period of 2 days and has now fully recovered.