



Rajendram, R., Taylor, P. N., Wilson, V. J., Harris, N., Morris, O. C., Tomlinson, M., Yarrow, S., Garrott, H., Herbert, H. M., Dick, A. D., Cook, A., Gattamaneni, R., Jain, R., Olver, J., Hurel, S. J., Bremner, F., Drummond, S. R., Kemp, E., Ritchie, D. M., ... Dayan, C. M. (2018). Combined immunosuppression and radiotherapy in thyroid eye disease (CIRTED): a multicentre, 2 × 2 factorial, double-blind, randomised controlled trial. *Lancet Diabetes and Endocrinology*, 6(4), 299-309. [https://doi.org/10.1016/S2213-8587\(18\)30021-4](https://doi.org/10.1016/S2213-8587(18)30021-4)

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Table 1 Characteristics of the Four Trial Groups

Variable	RT + Aza	Sham + Aza	RT + Placebo	Sham + Placebo
Number of patients	31	31	32	32
Age at enrollment	50·4 (10·4)	51·4 (9·53)	46·1 (11·5)	49·2 (11·7)
Age ≥ 60 years (%)	16·1	12·9	18·8	15·6
Disease Duration (months)	6·01 (11·4)	5·01 (4·39)	5·50 (9·41)	7·29 (12·6)
Duration > 6 months	35·5	22·6	34·4	28·1
Ethnicity (% Non Caucasian)	12·9	22·6	40·6	34·4
% Male	29·0	22·5	28·1	25
% Smoker	54·8	48·4	34·4	46·9
Thyroid State (%)				
Euthyroid	9·7	12·9	9·7	6·3
Hyperthyroid	83·9	74·2	80·7	81·3
Hypothyroid	6·5	12·9	9·7	12·5
Previous steroid use (%)	16·1	6·5	12·5	15·6
Study Centre (%)				
Moorfields or Bristol vs the other centres)	83·9	83·9	81·3	84·4
CAS Score				
2-3	17·9	16·7	24·1	9·4
4-5	53·6	70·0	55·2	68·9
6-7	28·6	13·3	20·7	21·9
TES Score				
<22	77·4	83·3	81·3	90·6
>22	22·5	16·7	18·8	9·4

Aza = Azathioprine, RT = Radiotherapy

CAS = Clinical Activity Score TES = Thyroid Eye Score

Table 2 Intention to treat analysis Binary Composite Clinical Outcome, Ophthalmopathy Index and Change in Clinical Activity Score

	Outcome	OR	B	95%CI	P	OR*	B*	95%CI*	P*
Aza	Binary Clinical Composite Outcome ¹ (N=103) [†]	1·99	-	(0·88, 4·51)	0·10	2·56		0·98, 6·66	0·05
RT		1·07	-	(0·47, 2·39)	0·87	0·89		0·36, 2·23	0·80
AzaRT		2·16	-	(0·85, 5·47)	0·11	2·52		0·87, 7·29	0·09
Aza	Ophthalmopathy Index Week 48 ² N=109	-	0·50	(-1·00, 2·00)	0·51	-	0·46	-1·04, 1·95	0·55
RT		-	-0·41	(-1·91, 1·09)	0·59	-	-0·89	-2·34, 0·56	0·23
AzaRT		-	-0·43	(-2·21, 1·35)	0·63	-	-0·78	-2·52, 0·96	0·37
Aza	Change in Clinical Activity Score ³	-	-0·48	(-1·17, 0·21)	0·17	-	-0·54	-1·25, 0·16	0·13
RT		-	-0·08	(-0·78, 0·62)	0·82	-	-0·01	-0·69, 0·68	0·99
AzaRT		(N=107)	-	-0·71	(-1·52, 0·10)	0·09	-	-0·64	-1·46, 0·18

* Adjusted for age group, ethnicity, smoking status, gender, thyroid state, disease duration, study centre, recent steroid use, baseline CAS score, baseline TES score. For Azathioprine and Radiotherapy, this analysis is also adjusted for the other treatment option (but not the combined Azathioprine-Radiotherapy group)

OR= Odds ratio, B = Beta Coefficient

95% CI = 95% confidence interval

p = p value against the null hypothesis of no association

Aza = Randomised to Azathioprine, RT = Randomised to Radiotherapy,

AZART = Randomised to Azathioprine and Radiotherapy

¹ 6 individuals with last data carried forward

² 8 individuals with last data carried forward

³ 10 individuals with last data carried forward

† Absolute values 22/50 patients who received azathioprine improved versus 16/54 who did not receive azathioprine. 19/50 patients who received orbital radiotherapy improved vs 19/54 who did not receive orbital radiotherapy.

Table 3 As per protocol analysis Binary Composite Clinical Outcome, Ophthalmopathy Index and Change in Clinical Activity Score

	Outcome	OR/B	95%CI	P	OR/B*#	95%CI*	P*
Aza	Binary Clinical Composite Outcome [†] Week 48 (N=58) [†]	5.21	(1.62, 16.8)	0.006	6.83	(1.66, 28.1)	0.008
RT		1.49	(0.53, 4.21)	0.45	1.32	(0.36, 4.84)	0.67
AzaRT		7.24	(1.40, 37.4)	0.02	16.1	(2.03, 127.6)	0.009
Aza	Ophthalmopathy Index Week 48 (N=59)	-0.16	(-2.12, 1.80)	0.87	-0.85	(-2.65, 0.95)	0.35
RT		-0.20	(-2.10, 1.69)	0.83	-0.79	(-2.52, 0.94)	0.36
AzaRT		-1.34	(-3.66, 0.99)	0.26	-2.02	(-4.13, 0.09)	0.06
Aza	Change in Clinical Activity Score	-0.63	(-1.37, 0.12)	0.10	-0.54	(-1.29, 0.20)	0.15
RT		-0.03	(-0.79, 0.73)	0.94	0.10	(-0.66, 0.85)	0.80
AzaRT		(N=88)	-0.86	(-1.73, 0.002)	0.05	-0.66	(-1.55, 0.22)

** Adjusted for age group, ethnicity, smoking status, gender, thyroid state, disease duration, study centre, recent steroid use, baseline CAS score, baseline TES score. For Azathioprine and Radiotherapy, this analysis is also adjusted for the other treatment option (but not the combined Azathioprine-Radiotherapy group)

OR= Odds ratio, B = Beta Coefficient

95% CI = 95% confidence interval

p = p value against the null hypothesis of no association

Aza = Randomized to Azathioprine, RT = Randomized to Radiotherapy,

AZART = Randomized to Azathioprine and Radiotherapy

† Absolute Values 15/21 patients who completed protocol on azathioprine improved vs 12/37 who did not receive azathioprine 14/27 patients who completed protocol on orbital radiotherapy improved vs 13/31 who did not receive orbital radiotherapy