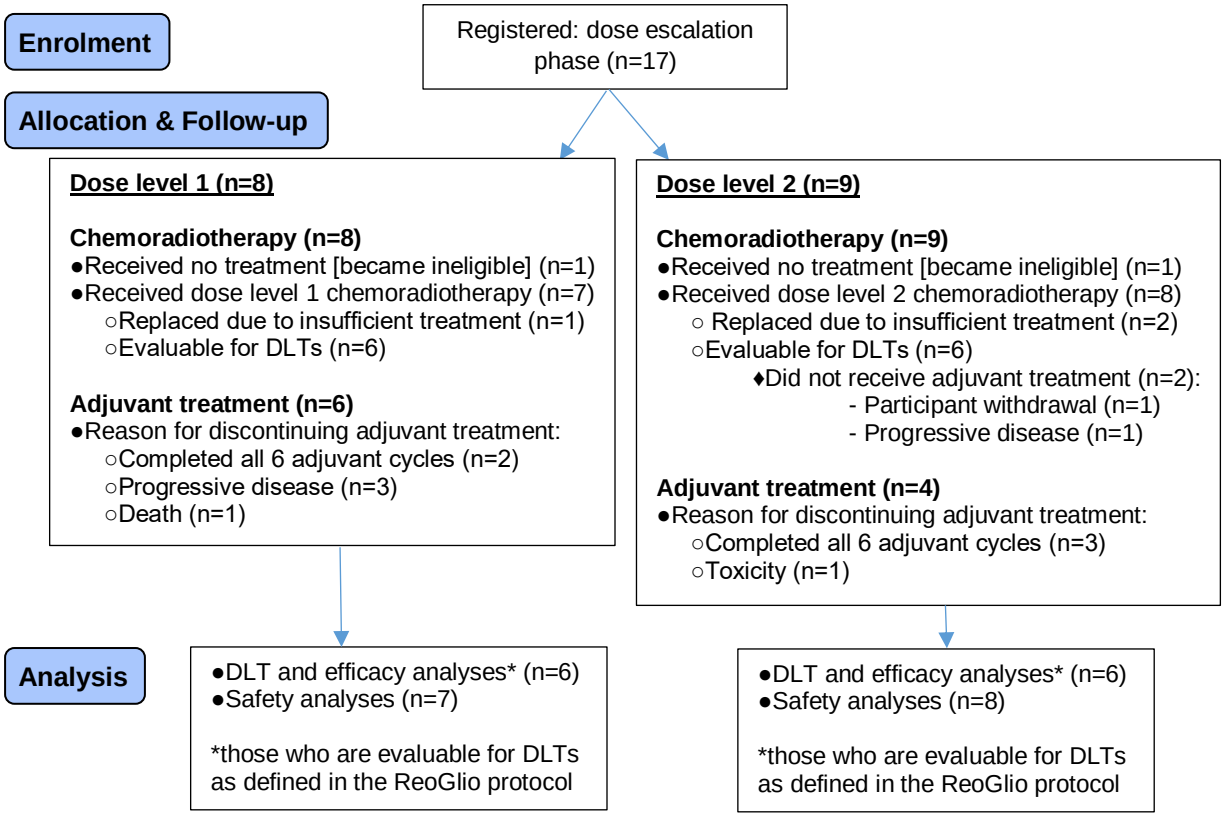
ISRCTN basic results report – ReoGlio ISRCTN70044565

ReoGlio closed to recruitment after the dose escalation phase and results are reported below.

Participant flow



Baseline Characteristics of safety population

	Dose level 1 (n=7)	Dose level 2 (n=8)	Total (n=15)
Participant sex			
Male	5 (71.4%)	4 (50.0%)	9 (60.0%)
Female	2 (28.6%)	4 (50.0%)	6 (40.0%)
Age (years)			
Mean (s.d.)	43.9 (12.2)	52.9 (12.6)	48.7 (12.9)
Median (range)	47 (27, 60)	57 (24, 66)	53 (24, 66)
ECOG performance status			
0	5 (71.4%)	5 (62.5%)	10 (66.7%)
1	2 (28.6%)	3 (37.5%)	5 (33.3%)

	Dose level 1 (n=7)	Dose level 2 (n=8)	Total (n=15)
Concurrent or previous malignancies at other sites			
No	7 (100.0%)	8 (100.0%)	15 (100.0%)
Number of non-measurable lesions			
0	5 (71.4%)	4 (50.0%)	9 (60.0%)
1	2 (28.6%)	3 (37.5%)	5 (33.3%)
2	0 (0.0%)	1 (12.5%)	1 (6.7%)
Number of measurable lesions			
0	2 (28.6%)	3 (37.5%)	5 (33.3%)
1	4 (57.1%)	3 (37.5%)	7 (46.7%)
2	1 (14.3%)	2 (25.0%)	3 (20.0%)
ECG result (msec)			
Normal	3 (42.9%)	5 (62.5%)	8 (53.3%)
Abnormal	0 (0.0%)	1 (12.5%)	1 (6.7%)
N/A (Not clinically indicated)	4 (57.1%)	2 (25.0%)	6 (40.0%)

Outcome Measures

Primary outcome=dose limiting toxicities (DLTs) assessed between day 1 of chemoradiotherapy treatment and up to (but not including) day 1 of planned adjuvant chemotherapy.

Dose level	DLT Type	Description	Treatment received
Dose level 2	Non-haematological toxicity	Hypotension (grade 3)	Received 1 cycle of chemoradiotherapy

Secondary outcome=progression free survival (PFS) calculated from the date of registration to first documented evidence of disease progression or death whichever is sooner. Analysis population, n=12

	Dose level 1 (n=6)	Dose level 2 (n=6)	Total (n=12)
Progression event	5 (83.3%)	5 (83.3%)	10 (83.3%)
No event	1 (16.7%)	1 (16.7%)	2 (16.7%)
Median PFS estimate in months (95% confidence intervals)	6.1 (4.9-9.2)	9.4 (4.2-10.6)	7.8 (4.9-9.7)

Secondary outcome=for participants with measurable disease, response assessed using RANO criteria and defined as the proportion of participants achieving each response category at the time of each follow-up MRI (every 84 days). . Analysis population, n=12

Maximum response	Dose level 1 (n=6)	Dose level 2 (n=6)	Total (n=12)
Complete Response	0 (0.0%)	0 (0.0%)	0 (0.0%)
Partial Response	0 (0.0%)	3 (50.0%)	3 (25.0%)
Stable Disease	3 (50.0%)	1 (16.7%)	4 (33.3%)
Progressive Disease	2 (33.3%)	2 (33.3%)	4 (33.3%)
Missing	1 (16.7%)	0 (0.0%)	1 (8.3%)

Secondary outcome=overall survival (OS) calculated from the date of registration to death. . Analysis population, n=12

	Dose level 1 (n=6)	Dose level 2 (n=6)	Total (n=12)
Died	5 (83.3%)	2 (33.3%)	7 (58.3%)
Alive at analysis	1 (16.7%)	4 (66.7%)	5 (41.7%)
Median OS estimate in months (95% confidence intervals)	12.6 (8.7-14.4)	12.1 (10.2-12.1)	12.1 (10.2-14.4)

Secondary outcome=treatment compliance (dose reductions, delays, omissions and withdrawals). Safety population, n=15

Treatment compliance – during chemoradiotherapy treatment

During chemoradiotherapy treatment has the participant…	Dose level 1 (n=7)	Dose level 2 (n=8)	Total (n=15)
Had a treatment delay?			
Yes	1 (14.3%)	1 (12.5%)	2 (13.3%)
No	6 (85.7%)	7 (87.5%)	13 (86.7%)
Omitted radiotherapy?			
Yes	1 (14.3%)	0 (0%)	1 (6.7%)
No	6 (85.7%)	8 (100%)	14 (93.3%)
Omitted a dose of temozolomide?			
Yes	6 (85.7%)	3 (37.5%)	9 (60.0%)
No	1 (14.3%)	5 (62.5%)	6 (40.0%)
Omitted a dose of GM-CSF?			
Yes	2 (28.6%)	0 (0.0%)	2 (13.3%)

During chemoradiotherapy treatment has the participant…	Dose level 1 (n=7)	Dose level 2 (n=8)	Total (n=15)
No	5 (71.4%)	8 (100.0%)	13 (86.7%)
Omitted a dose of Reolysin?			
Yes	2 (28.6%)	2 (25.0%)	4 (26.7%)
No	5 (71.4%)	6 (75.0%)	11 (73.3%)

Treatment compliance – during adjuvant treatment (n=10)

During adjuvant treatment has the participant…	Dose level 1 (n=6)	Dose level 2 (n=4)	Total (n=10)
Had a cycle delay?			
Yes	3 (50.0%)	2 (50.0%)	5 (50.0%)
No	3 (50.0%)	2 (50.0%)	5 (50.0%)
Omitted a dose of temozolomide?			
Yes	0 (0.0%)	1 (25.0%)	1 (10.0%)
No	6 (100.0%)	3 (75.0%)	9 (90.0%)
Omitted a dose of GM-CSF?			
Yes	1 (16.7%)	1 (25.0%)	2 (20.0%)
No	5 (83.3%)	3 (75.0%)	8 (80.0%)
Omitted a dose of Reolysin?			
Yes	2 (33.3%)	1 (25.0%)	3 (30.0%)
No	4 (66.7%)	3 (75.0%)	7 (70.0%)
Had a dose of temozolomide modified?			
Yes	1 (16.7%)	0 (0.0%)	1 (10.0%)
No	5 (83.3%)	4 (100.0%)	9 (90.0%)

Adverse Events Safety population, n=15

Serious adverse events (SAEs) – summary statistics

	Dose level 1	Dose level 2	Total
Number of patients with one or more SAE	6	4	10
Number of suspected unexpected serious adverse reactions (SUSARs)	0	2	2
Number of SAEs reported (including SUSARs)	12	8	20
Number of SAEs per patient			
Mean (Standard Deviation)	2.0 (0.89)	2.0 (0.82)	2.0 (0.82)
Median (Interquartile Range)	2.0 (1, 3)	2.0 (2, 3)	2.0 (1, 3)
Range	(1, 3)	(1, 3)	(1, 3)

Serious adverse events – number of events by MedDRA code (not mutually exclusive)

MedDRA System Organ Class	Dose level 1 N (%)	Dose level 2 N (%)	Total N (%)
Blood and lymphatic system disorders	1 (6.3)	0 (0.0)	1 (4.2)
Musculoskeletal and connective tissue disorders	1 (6.3)	1 (12.5)	2 (8.3)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	1 (6.3)	0 (0.0)	1 (4.2)
Nervous system disorders	7 (43.8)	1 (12.5)	8 (33.3)
Gastrointestinal disorders	2 (12.5)	0 (0.0)	2 (8.3)
General disorders and administration site conditions	1 (6.3)	0 (0.0)	1 (4.2)
Immune system disorders	0 (0.0)	2 (25.0)	2 (8.3)
Infections and infestations	1 (6.3)	2 (25.0)	3 (12.5)
Vascular disorders	2 (12.5)	2* (25.0)	4 (16.7)
Total	**16 (100.0)**	**8 (100.0)**	**24 (100.0)**

*2 SUSARs occurred in dose level 2, both with MedDRA system organ class=vascular disorders

Adverse events – maximum CTCAE grade experienced for events occurring in more than 20% of patients

Adverse Event Name	Duration of trial		
	Dose level 1 (n=7)	Dose level 2 (n=8)	Total (n=15)
Fatigue			
0	1 (14.3%)	2 (25.0%)	3 (20.0%)
1	3 (42.9%)	2 (25.0%)	5 (33.3%)
2	1 (14.3%)	2 (25.0%)	3 (20.0%)
3	1 (14.3%)	1 (12.5%)	2 (13.3%)
4	1 (14.3%)	1 (12.5%)	2 (13.3%)
Nausea			
0	1 (14.3%)	2 (25.0%)	3 (20.0%)
1	3 (42.9%)	2 (25.0%)	5 (33.3%)
2	1 (14.3%)	3 (37.5%)	4 (26.7%)
3	1 (14.3%)	1 (12.5%)	2 (13.3%)
4	1 (14.3%)	0 (0.0%)	1 (6.7%)
Fever			
0	4 (57.1%)	1 (12.5%)	5 (33.3%)
1	2 (28.6%)	2 (25.0%)	4 (26.7%)
2	0 (0.0%)	3 (37.5%)	3 (20.0%)
3	1 (14.3%)	1 (12.5%)	2 (13.3%)
4	0 (0.0%)	1 (12.5%)	1 (6.7%)
Headache			
0	1 (14.3%)	4 (50.0%)	5 (33.3%)
1	4 (57.1%)	3 (37.5%)	7 (46.7%)
2	1 (14.3%)	0 (0.0%)	1 (6.7%)
4	1 (14.3%)	1 (12.5%)	2 (13.3%)
Lymphocyte count decreased			
0	3 (42.9%)	3 (37.5%)	6 (40.0%)
1	1 (14.3%)	1 (12.5%)	2 (13.3%)
2	1 (14.3%)	2 (25.0%)	3 (20.0%)
3	1 (14.3%)	1 (12.5%)	2 (13.3%)
4	1 (14.3%)	1 (12.5%)	2 (13.3%)
Alopecia			
0	3 (42.9%)	4 (50.0%)	7 (46.7%)

Adverse Event Name	Duration of trial		
	Dose level 1 (n=7)	Dose level 2 (n=8)	Total (n=15)
1	2 (28.6%)	1 (12.5%)	3 (20.0%)
2	0 (0.0%)	1 (12.5%)	1 (6.7%)
3	1 (14.3%)	1 (12.5%)	2 (13.3%)
4	1 (14.3%)	1 (12.5%)	2 (13.3%)
Seizure			
0	2 (28.6%)	5 (62.5%)	7 (46.7%)
1	3 (42.9%)	0 (0.0%)	3 (20.0%)
2	1 (14.3%)	2 (25.0%)	3 (20.0%)
3	1 (14.3%)	1 (12.5%)	2 (13.3%)
Vomiting			
0	2 (28.6%)	5 (62.5%)	7 (46.7%)
1	3 (42.9%)	1 (12.5%)	4 (26.7%)
2	1 (14.3%)	1 (12.5%)	2 (13.3%)
3	0 (0.0%)	1 (12.5%)	1 (6.7%)
4	1 (14.3%)	0 (0.0%)	1 (6.7%)
Flu like symptoms			
0	4 (57.1%)	4 (50.0%)	8 (53.3%)
1	2 (28.6%)	2 (25.0%)	4 (26.7%)
2	1 (14.3%)	1 (12.5%)	2 (13.3%)
3	0 (0.0%)	1 (12.5%)	1 (6.7%)
Skin and subcutaneous tissue disorders			
0	4 (57.1%)	4 (50.0%)	8 (53.3%)
1	2 (28.6%)	2 (25.0%)	4 (26.7%)
2	1 (14.3%)	1 (12.5%)	2 (13.3%)
4	0 (0.0%)	1 (12.5%)	1 (6.7%)
White blood cell decreased			
0	3 (42.9%)	5 (62.5%)	8 (53.3%)
1	1 (14.3%)	0 (0.0%)	1 (6.7%)
2	1 (14.3%)	1 (12.5%)	2 (13.3%)
3	1 (14.3%)	1 (12.5%)	2 (13.3%)
4	1 (14.3%)	1 (12.5%)	2 (13.3%)
Constipation			
0	5 (71.4%)	4 (50.0%)	9 (60.0%)

Adverse Event Name	Duration of trial		
	Dose level 1 (n=7)	Dose level 2 (n=8)	Total (n=15)
1	1 (14.3%)	0 (0.0%)	1 (6.7%)
2	1 (14.3%)	2 (25.0%)	3 (20.0%)
3	0 (0.0%)	1 (12.5%)	1 (6.7%)
4	0 (0.0%)	1 (12.5%)	1 (6.7%)
Neutrophil count decreased			
0	4 (57.1%)	5 (62.5%)	9 (60.0%)
1	1 (14.3%)	0 (0.0%)	1 (6.7%)
2	0 (0.0%)	1 (12.5%)	1 (6.7%)
3	1 (14.3%)	1 (12.5%)	2 (13.3%)
4	1 (14.3%)	1 (12.5%)	2 (13.3%)
Alanine aminotransferase increased			
0	7 (100.0%)	4 (50.0%)	11 (73.3%)
2	0 (0.0%)	2 (25.0%)	2 (13.3%)
3	0 (0.0%)	1 (12.5%)	1 (6.7%)
4	0 (0.0%)	1 (12.5%)	1 (6.7%)
Anemia			
0	4 (57.1%)	7 (87.5%)	11 (73.3%)
1	1 (14.3%)	0 (0.0%)	1 (6.7%)
2	1 (14.3%)	0 (0.0%)	1 (6.7%)
3	0 (0.0%)	1 (12.5%)	1 (6.7%)
4	1 (14.3%)	0 (0.0%)	1 (6.7%)
Platelet count decreased			
0	6 (85.7%)	5 (62.5%)	11 (73.3%)
2	0 (0.0%)	1 (12.5%)	1 (6.7%)
3	0 (0.0%)	1 (12.5%)	1 (6.7%)
4	1 (14.3%)	1 (12.5%)	2 (13.3%)
Rash maculo-papular			
0	5 (71.4%)	6 (75.0%)	11 (73.3%)
1	1 (14.3%)	0 (0.0%)	1 (6.7%)
2	0 (0.0%)	1 (12.5%)	1 (6.7%)
3	1 (14.3%)	0 (0.0%)	1 (6.7%)
4	0 (0.0%)	1 (12.5%)	1 (6.7%)
Abdominal pain			

Adverse Event Name	Duration of trial		
	Dose level 1 (n=7)	Dose level 2 (n=8)	Total (n=15)
0	7 (100.0%)	5 (62.5%)	12 (80.0%)
1	0 (0.0%)	2 (25.0%)	2 (13.3%)
3	0 (0.0%)	1 (12.5%)	1 (6.7%)
Anorexia			
0	6 (85.7%)	6 (75.0%)	12 (80.0%)
2	1 (14.3%)	1 (12.5%)	2 (13.3%)
3	0 (0.0%)	1 (12.5%)	1 (6.7%)
Arthralgia			
0	6 (85.7%)	6 (75.0%)	12 (80.0%)
2	0 (0.0%)	2 (25.0%)	2 (13.3%)
4	1 (14.3%)	0 (0.0%)	1 (6.7%)
Aspartate aminotransferase increased			
0	7 (100.0%)	5 (62.5%)	12 (80.0%)
2	0 (0.0%)	2 (25.0%)	2 (13.3%)
3	0 (0.0%)	1 (12.5%)	1 (6.7%)
Bone pain			
0	5 (71.4%)	7 (87.5%)	12 (80.0%)
1	1 (14.3%)	1 (12.5%)	2 (13.3%)
4	1 (14.3%)	0 (0.0%)	1 (6.7%)
Confusion			
0	5 (71.4%)	7 (87.5%)	12 (80.0%)
1	1 (14.3%)	0 (0.0%)	1 (6.7%)
2	0 (0.0%)	1 (12.5%)	1 (6.7%)
3	1 (14.3%)	0 (0.0%)	1 (6.7%)
Cough			
0	6 (85.7%)	6 (75.0%)	12 (80.0%)
1	1 (14.3%)	1 (12.5%)	2 (13.3%)
4	0 (0.0%)	1 (12.5%)	1 (6.7%)
Depression			
0	6 (85.7%)	6 (75.0%)	12 (80.0%)
2	1 (14.3%)	1 (12.5%)	2 (13.3%)
4	0 (0.0%)	1 (12.5%)	1 (6.7%)
Dyspepsia			

Adverse Event Name	Duration of trial		
	Dose level 1 (n=7)	Dose level 2 (n=8)	Total (n=15)
0	6 (85.7%)	6 (75.0%)	12 (80.0%)
1	1 (14.3%)	1 (12.5%)	2 (13.3%)
4	0 (0.0%)	1 (12.5%)	1 (6.7%)
Hypocalcemia			
0	6 (85.7%)	6 (75.0%)	12 (80.0%)
1	1 (14.3%)	0 (0.0%)	1 (6.7%)
2	0 (0.0%)	1 (12.5%)	1 (6.7%)
3	0 (0.0%)	1 (12.5%)	1 (6.7%)
Myalgia			
0	6 (85.7%)	6 (75.0%)	12 (80.0%)
1	1 (14.3%)	1 (12.5%)	2 (13.3%)
4	0 (0.0%)	1 (12.5%)	1 (6.7%)
Paresthesia			
0	6 (85.7%)	6 (75.0%)	12 (80.0%)
1	0 (0.0%)	1 (12.5%)	1 (6.7%)
4	1 (14.3%)	1 (12.5%)	2 (13.3%)
Skin infection			
0	7 (100.0%)	5 (62.5%)	12 (80.0%)
2	0 (0.0%)	2 (25.0%)	2 (13.3%)
4	0 (0.0%)	1 (12.5%)	1 (6.7%)