Re-irradiation for progressive Diffuse Intrinsic Pontine Glioma (ReRAD) : A Canadian Pediatric Brain Tumour Consortium Phase II study

Chantel Cacciotti, Susan Chafe, Sebastien Perreault, Timothy Hassall, Tao Wang, Karen Tsui, Anirban Das, Ute Bartels, Craig Erker, Nicholas G Gottardo, Paul Wood, Juliette Hukin, Adam Fleming, Donna Johnston, Samuele Renzi, Sonia Skamene, Lynette Bowes, Vineetha Warriyar Kolalore Vijayan, Rahma Alharti, Xing-Chang Wei, Derek S. Tsang, Natalie Logie, Eric Bouffet, Douglas Strother*, Lucie Lafay-Cousin*

BACKGROUND

- The median survival for diffuse intrinsic pontine glioma (DIPG) remains under one year from initial therapy.
- At progression, re-irradiation (rRT) has been used at various doses and schedules making conclusions on benefits difficult.
- Safety and effectiveness data of rRT are limited

METHODS

Prospective international study

Eligibility criteria

- Localized progressive DIPG
- Previously treated with focal radiotherapy (RT) < 60Gy
- At least 180 days elapsed from last day of primary RT
- Agree not to use concomitant or adjuvant anti cancer therapy with rRT

Treatment protocol

- Focal Reirradiation at **30.6 Gy** in 17 fractions (1.8Gy) if time from completion of first RT ≤ 18 months
- Focal Reirradiation at **36 G**y in 20 fractions (1.8Gy) if time from completion of first RT > 18 months

OBJECTIVES

Primary objective

Estimate the post rRT progression free survival (PFS2) and overall survival (OS) of patients with progressive DIPG treated with second course of radiotherapy

Hypothesis *rRT is considered effective in prolonging life if the survival time is 6 months or longer for at least 35% of the patients*

Secondary objectives

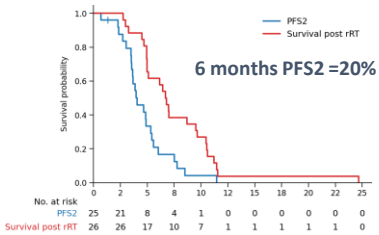
- Describe the overall response to therapy (combined clinical symptoms + MRI findings) and report subjective quality of life at 2 and 6-8 weeks post rRT
- Describe the use of Dexamethasone from diagnosis of recurrence to the best response after rRT

RESULTS

26 patient enrolled from 15 international institutions (Canada, Australia, New Zealand)

Patient characteristics	N=26
Sex (M/F)	16/10
Median age at initial diagnosis (years)	5.7 (range 3.0-11.7)
Median dose of initial RT (Gy)	54 (39-55.8)
Median time from initial RT to rRT (mos)	9.3 (7-26.3)
Dose of rRT 30.6 Gy 36 Gy 25.2 Gy	 23 (88.5%) 2(7.7%) 1 (3.8%)

Progression free survival (PFS2) & Survival post rRT

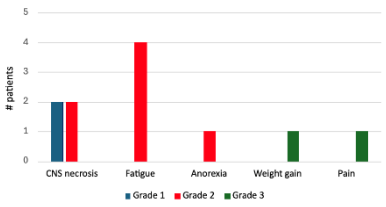


- **Median survival time from first day of rRT: 6.6 months (2.1-24.2)**
- **14 (53.8 %) patients survived ≥ 6 months post rRT**
- **2 yrs OS from initial diagnosis: 30.7% (17.2-54.7)**

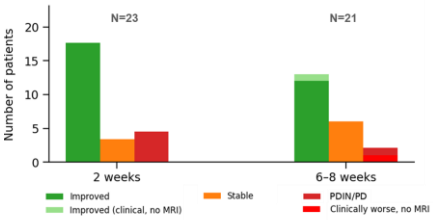
Use of Dexamethasone during and after rRT

Median starting dose of DXM (mg)	2 (1-16)
Median max daily dose (mg)	4.3 (2-16)
Median duration of max dose (days)	12 (1-46)
Number of patients completely weaned off DXM post rRT	12 (46%)

Adverse events description and grade

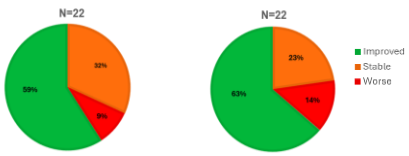


Overall response to therapy (Clinical + MRI)



Subjective evaluation of Quality of Life

Week 2 post rRT **Weeks 6-8 post rRT**



- Despite study requirements, 9/26 patients (35%) subsequently enrolled on other clinical trials or pursued anti tumoral interventions (median time of 4 months post rRT)
- 7 /17 of the patients who only received rRT (41%) survived ≥ 6 months

CONCLUSION:

26 patients with progressive DIPG were prospectively treated with a second course of radiotherapy, delivered at a dose of 30.6 Gy in 88.5%, indicating rRT

- **Is safe, resulting in prolonged survival ≥ 6 months**
- **Is associated with improved to stable overall status within the first 6-8 weeks**

Future comparison with Dordaviprone (ONC 201), recently approved for progressive H3K27M DMG, should be investigated in term of impact on OS and Quality of Life

UNIVERSITY OF CALGARY CUMMING SCHOOL OF MEDICINE

Alberta Children's Hospital

MEAGAN'S WALK