**KPCRTF State Funded Projects Reporting Template**

**University of Louisville**
**Phase 2 Trial of Eflornithine/DFMO as Maintenance Therapy**
**Program Director: Dr. Michael Huang**

**Reporting Period: April 1, 2021 to June 30, 2021**

***Below please provide a brief summary of the status of the Project listed as well as for each Objective listed below. Include any barriers, how and if they were overcome, and successes achieved.***

Please provide a short overall summary of the status of your project here.

Please see the progress report for the DFMO KPCRTF Trust Fund Project that expired in June 30, 2021 for the full historical perspective of the challenges in opening this study. The study, which is assigned the ClinicalTrials.gov identifier NCT04696029, and is referred to as the Beat Childhood Cancer (BCC) BCC016 trial opened in February 2021. The study has now opened at 3 of an initial planned 15 sites: 1) Levine Children's Hospital/Atrium Health in Charlotte, NC, 2) Norton Children's Cancer Institute, and 3) St. Joseph's Children's Hospital in Tampa, FL. The remaining 12 other sites listed below are currently at different stages of activating the study at their local institutions. We intend to expand to a planned total of 30 sites in the near future.

1) Cardinal Glennon Children's Medical Center, St. Louis, MO
2) Arnold Palmer Hospital for Children, Orlando, FL
3) Medical University of South Carolina, Charleston, SC
4) Connecticut Children's Medical Center, Hartford, CT
5) Children's Mercy Hospital, Kansas City, MO
6) Dell Children's Blood and Cancer Center, Austin, TX
7) Penn State Milton S. Hershey Medical Center & Children's Hospital, Hershey, PA
8) Arkansas Children's Hospital, Little Rock, AR
9) Hackensack University Medical Center, Hackensack, NJ
10) UCSF Benioff Children's Hospital Oakland, Oakland, CA
11) St. Luke's Mountain States Tumor Institute, Boise, ID
12) Rady Children's Hospital, San Diego, CA

Primary Objective:
Evaluate the efficacy of DFMO as a single agent in preventing relapse in patients with de novo molecular high risk and very high risk medulloblastoma, and relapsed/refractory medulloblastoma based upon progression free survival (PFS) from time of enrollment.

Please provide a brief summary of the status of this objective here as well as the other objectives below.
To date, 2 patients have been enrolled, 1 additional patient is undergoing eligibility screening, and another 2 are expected to finish standard therapy soon and be eligible for the study. Our projected accrual in the first year of study opening is 20 patients.

Secondary Objectives:

1. Evaluate the efficacy of DFMO as a single agent in patients with de novo molecular high risk and very high risk medulloblastoma, and relapsed/refractory medulloblastoma based upon Overall Survival (OS) and Response Rate (for patients with non-bulky residual disease present)..

2. Develop a complete safety and tolerability profile of DFMO in pediatric subjects with medulloblastoma.

3. Measure Cerebrospinal Fluid (CSF) penetration after DFMO administration in pediatric subjects with medulloblastoma.

Exploratory Objectives:

1. Evaluate the cancer stem cell (CSC) ODC/LIN28 pathway and targeted pathways by genomic analysis to further correlate with response to treatment.

2. Evaluate circulating tumor deoxyribonucleic acid (ctDNA) from patient plasma samples as a biomarker of tumor disease burden and treatment response.

| **Deliverables (check appropriate time period when each deliverable is completed)** | **Month 1-3** | **Month 4-6** | **Month 7-9** | **Month 10-12** | **Month 13-15** | **Month 16-18** | **Month 19-21** | **Month 22-24** | √ |
|---|---|---|---|---|---|---|---|---|---|
| Notify DPH when IRB Approval is received or if not required<br><br>Evaluate the efficacy of DFMO as a single agent<br><br>Develop a complete safety and tolerability profile of DFMO<br><br>Measure CSF penetration after DFMO administration<br><br>Evaluate the cancer stem cell ODC/LIN28 pathway and targeted pathways by genomic analysis to further correlate with response to treatment<br><br>Evaluate circulating tumor DNA from patient plasma samples as a biomarker of tumor disease burden and treatment response | | | √ | | | | | | |

As this study is projected to accrue patients over 4-5 years, well beyond the timeline for the state funding, the below deliverables are more appropriate measures for the first 2 years of this multi-year study. The last 2 listed deliverables above are exploratory in nature and won't be evaluated until the study is completed and the data analyses for the primary and secondary objectives are completed.

| **Deliverables (check when completed)** | **Month 1-3** | **Month 4-6** | **Month 7-9** | **Month 10-12** | **Month 13-15** | **Month 16-18** | **Month 19-21** | **Month 22-24** | √ |
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| Interim Safety Analysis to determine the safety and tolerability of DFMO in the first 10 enrolled patients | | | | | | | | | |
| Measure CSF penetration of DFMO in the first 10 enrolled patients | | | | | | | | | |
| Expected patient accrual of 20 patients in first year of study | | | | | | | | | |
| Interim Futility Analysis after first 2 years of study to determine if DFMO is clearly beneficial or harmful | | | | | | | | | |

Quarterly Reports are due:

- July 15, 2021
- October 15, 2021
- January 15, 2022
- April 15, 2022
- July 15, 2022

Reports should be returned to:
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