Precision Radiotherapy for Incurable Brain Tumors: Phase 1b Dose & Regimen Optimization Study of Iopofosine I 131 in Inoperable Relapsed or Refractory Pediatric High-Grade Glioma, Interim Data Assessment

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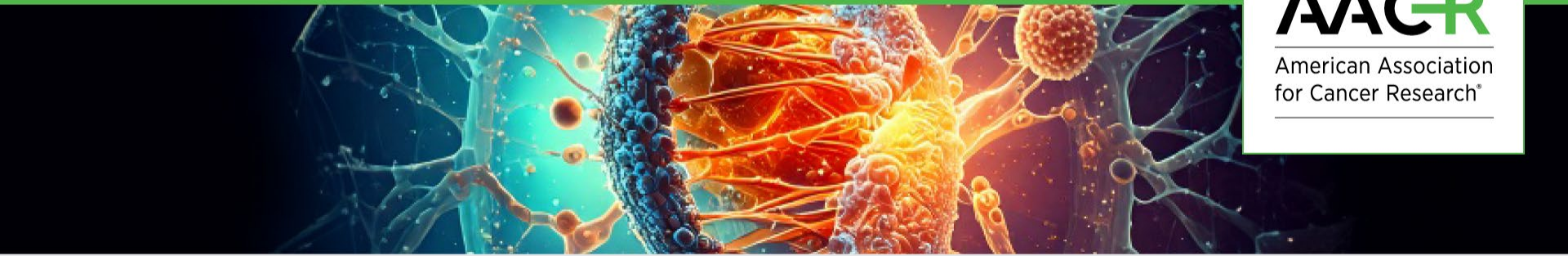
CELLECTAR BIOSCIENCES



AACR American Association for Cancer Research®

DISCOVERY AND INNOVATION IN PEDIATRIC CANCER: FROM BIOLOGY TO BREAKTHROUGH THERAPIES
September 25-28, 2025 | Westin Copley Place | Boston, MA

Disclosure Information

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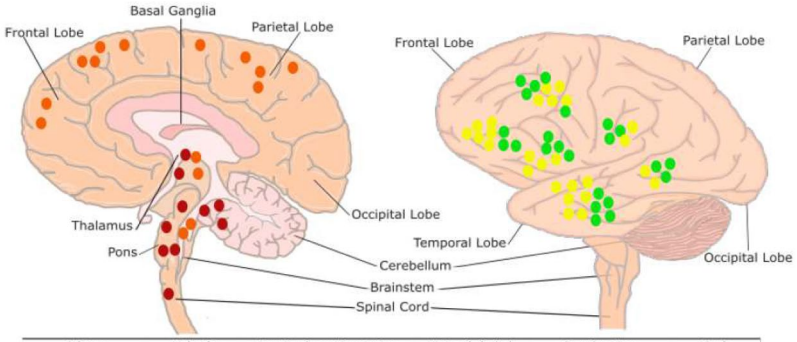
I have the following relevant financial relationships to disclose:
Employee of Cellectar Biosciences Inc.

Pediatric High Grade Glioma



Subtype	Molecular characteristics	Associated somatic mutations	Histopathological classification	Growth pattern	Grade according to WHO
Diffuse Midline Gliomas H3 K27-altered	H3.1K27M	HIST1H3B, *PI3K, ACVR1, ATRX*	Astrocytic morphology with oligodendroglial-like features	Midline structure (thalamus, brainstem, cerebellum, pons), spinal cord	4
	H3.3K27M	H3F3A, *FGFR1, TP53, PPMD1, PDGFRalpha, CCND2, TOP3A, EZHIP, EGFR*			4
Diffuse paediatric-type high-grade glioma, H3-wildtype and IDH wildtype	H3K27WT	*MYCN, EGFR, PDGFRA*, H3-wildtype, IDH-wildtype	Astrocytic morphology with oligodendroglial-like features	Cerebral hemispheres and midline structures	4
Infant-type hemispheric glioma	NTRK family	NTRK family, *ALK, ROS, MET*	Astrocytic morphology	Cerebral hemispheres	4
Diffuse hemispheric glioma, H3 G34- mutant	H3.3G34R/V	H3F3A, *TP53, ATRX, FBXW7, MGMT promoter methylation*	Neuro-glial heterogeneity	Cerebral hemispheres	4

- Pediatric high grade gliomas (pHGGs) are rare but aggressive tumors (5 year survival rates <20%)[1,2]
- Median overall survival remains poor: ranging from 10 to 73 months from initial diagnosis depending on glioma subtype, tumor location, and age at diagnosis
- First line treatment includes resection, local radiotherapy and chemotherapy most will relapse
- In recurrent pHGG, PFS and OS with subsequent treatment is ~3.5 and 5.6 months, respectively
- Not your parents glioma - endemic molecular heterogeneity marks pediatric HGGs, with distinct clinical behaviors and responses to treatment

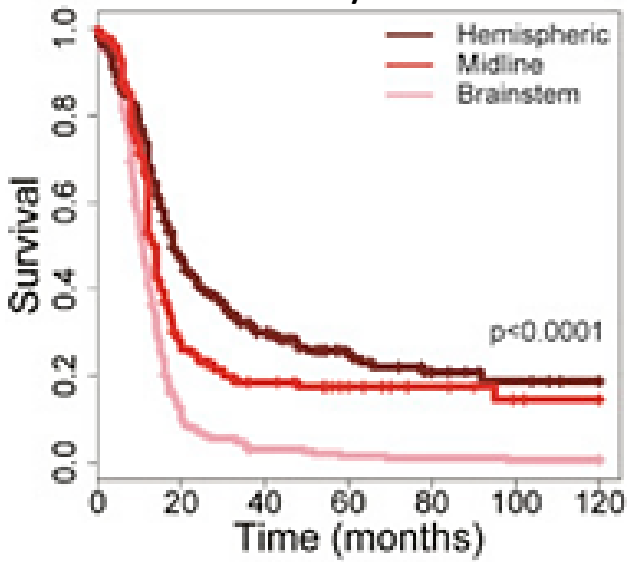
1. Funakoshi Y, Hata N, Kuga D, et al. Pediatric Glioma: An Update of Diagnosis, Biology, and Treatment. Cancers (Basel). 2021;13(4):758.
2. Hall CP, Cronk JC, Rubens JA. STINGing the immune system: lessons learned through a model of G34-mutant pediatric high-grade glioma. J Clin Invest. 2022;132(22):e164420.

Pediatric High Grade Glioma: Overall Survival

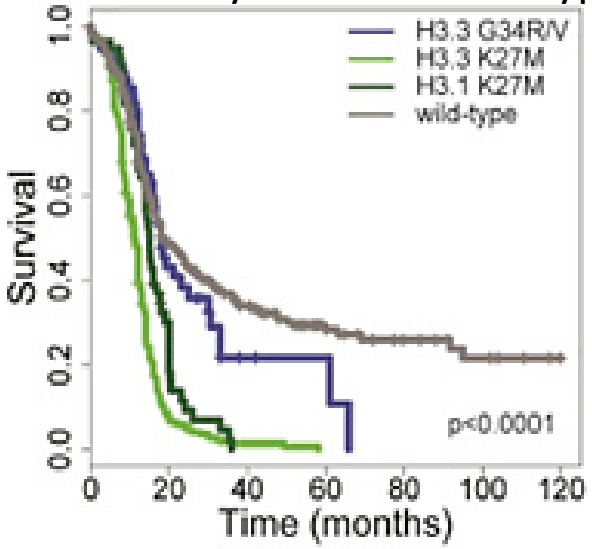
All data from initial diagnosis:

- Average survival (months)
  - DIPG = 10
  - DMG = 13
  - DHG = 18
  - H3.3K27M = 11
  - H3.3G34R/V = 18
  - H3.1/3.2K27M = 15

Survival by Location



Survival by Molecular Subtype



Need for new treatments

1. Mackay, A.; Burford, A.; Carvalho, D.; Izquierdo, E.; Fazal-Salom, J.; Taylor, K.R.; Bjerke, L.; Clarke, M.; Vinci, M.; Nandhabalan, M. Integrated molecular meta-analysis of 1,000 pediatric high-grade and diffuse intrinsic pontine glioma. Cancer Cell **2017**, 32, 520–537.e5..

Iopofosine I 131: A Novel Radiopharmaceutical

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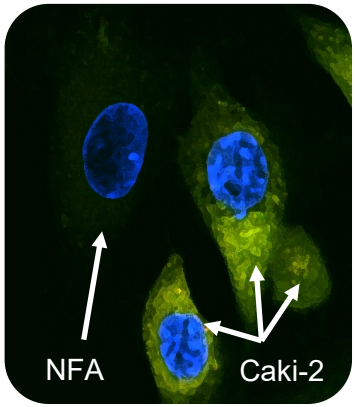
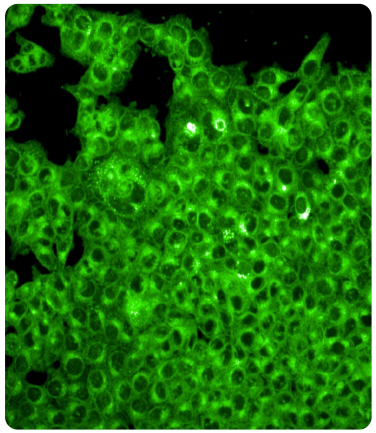
- Iopofosine I 131 is a novel targeted radiopharmaceutical
  - Utilizes a novel target ligand: phospholipid ether (LCFA mimetic)
  - Composed of a phospholipid ether covalently bound to ^{131}I, a beta-emitting radioisotope
  - Broad cancer type targeting and uptake into all tumor cell
  - Demonstrated antitumor activity in murine models of neuroblastoma
  - Crosses the blood-brain barrier

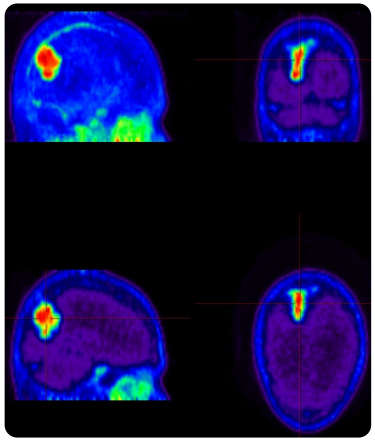
SPECIFIC UPTAKE



UNIFORM DELIVERY



SPECIFIC TARGETING



Lipid Rafts: Novel Approach to Targeting Cancer

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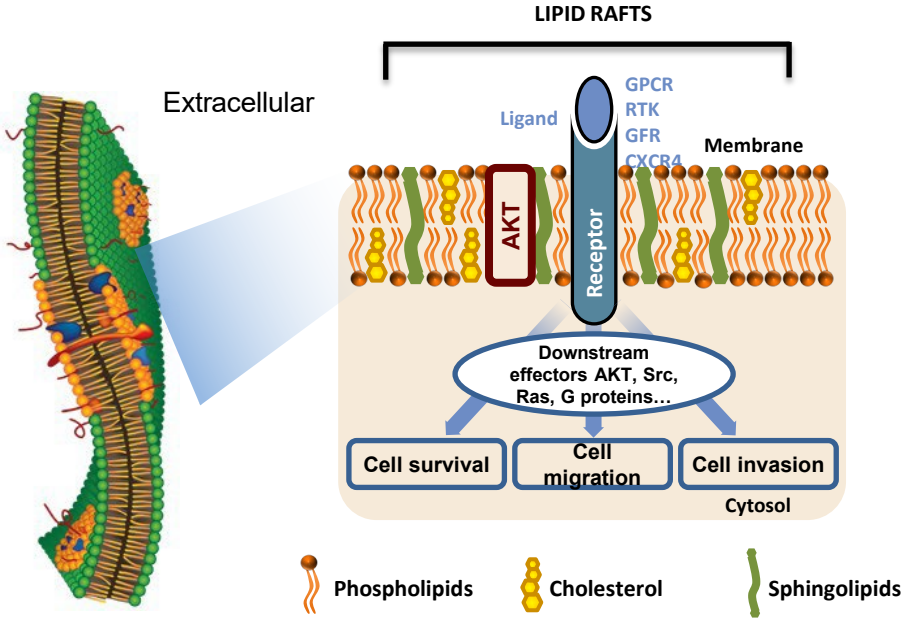
- Highly ordered, tightly regulated microdomains, enriched in cholesterol and sphingolipids
- Signaling hubs: coalesce GPI- anchored proteins, signaling proteins and receptors
- Facilitators of (anaerobic) beta-oxidation
- Upregulation and stabilization in cancer:
  - Normal cells = nanostructures (~25nm)
  - Cancer cells = coalesced raft (100uM)
  - Stabilized (days vs microseconds)



Phospholipid Drug Conjugate (PDC) Platform:

The Role of Lipid Rafts as a Universal Target in Cancer

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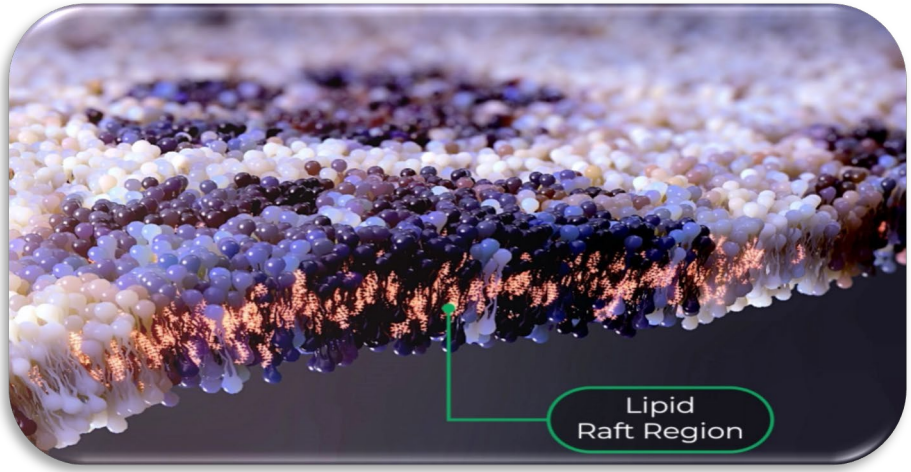


Lipid Rafts:

Specialized microdomains within the plasma membrane play a significant role in cancers by facilitating processes like cell signaling, proliferation, survival, invasion, metastasis, and drug resistance. The enriched presence of cholesterol, sphingolipids, and specific proteins in these microdomains enhances the ability of tumor cells to thrive in challenging environments

Lipid Rafts Play an Influential Role in Cancer

Enhanced oncogenic signaling

- Concentrate and stabilize growth factor receptors

Survival and resistance to apoptosis

- Help cancer cells survive and escape programmed cell death

Cancer invasion and metastasis

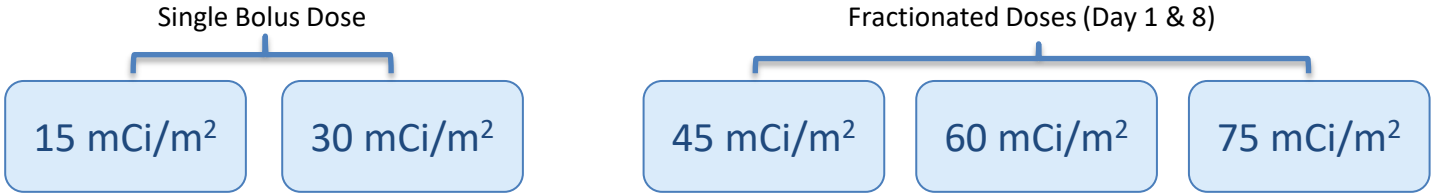
- Facilitate cancer cell migration, invasion, and metastasis

Targeting cancer

- High prevalence on tumor cells vs. healthy tissue
- Stabilize for approximately 10 days in tumor cells compared to milliseconds for healthy tissue
- Uniformly present across tumor cells and tumor types

CLOVER-2: Study Design, Part A

- Primary objective of Part A - determine the safety and tolerability of iopofosine I 131 in children, adolescents, and young adults with relapsed or refractory malignant solid tumors and recurrent or refractory malignant brain tumors
- Dose escalation schema:

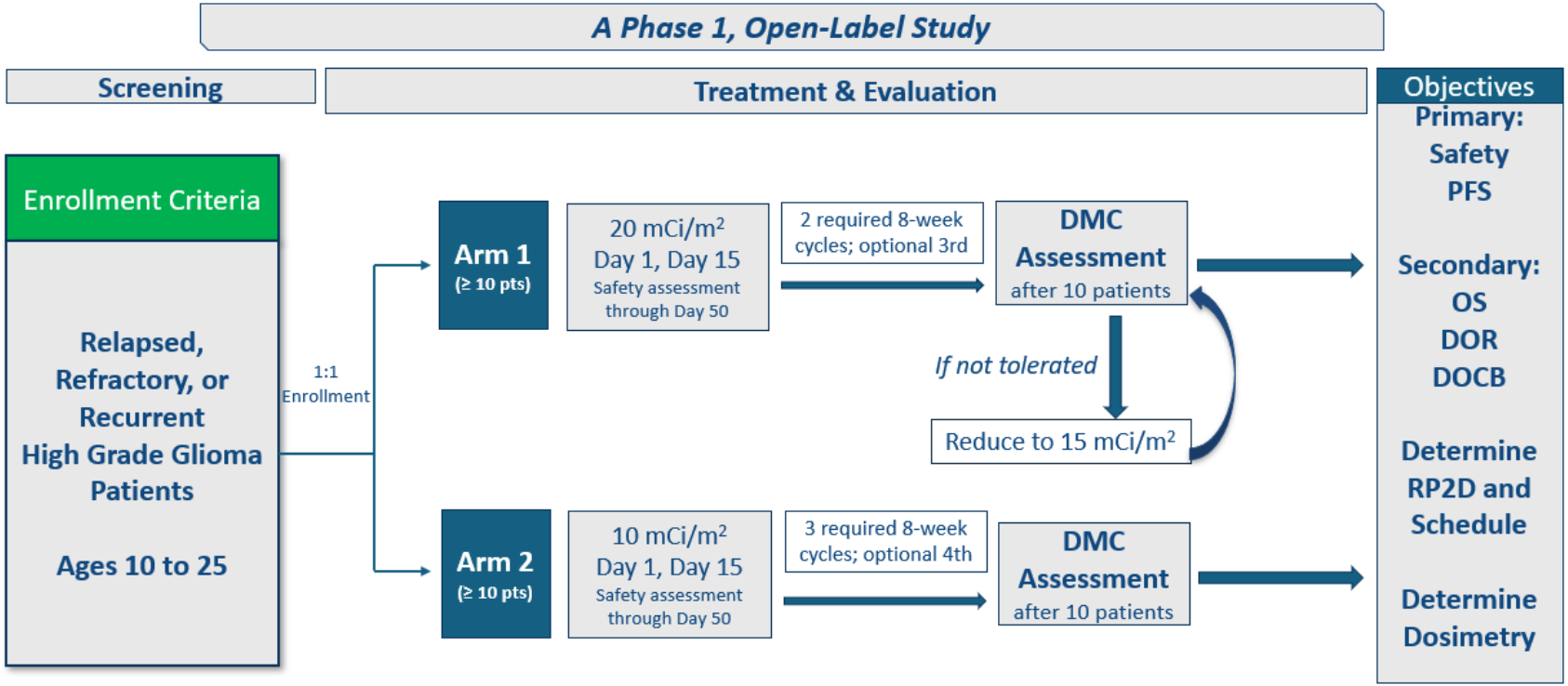


Patients eligible for multiple cycles upon Physician request and DMC approval

- MTD for patients ≥ 10 years old is 60 mCi/m^2 fractionated on Day 1 and 15.
- Primary AEs were cytopenias (anemia, leukopenia, neutropenia, thrombocytopenia), nausea/vomiting, headache

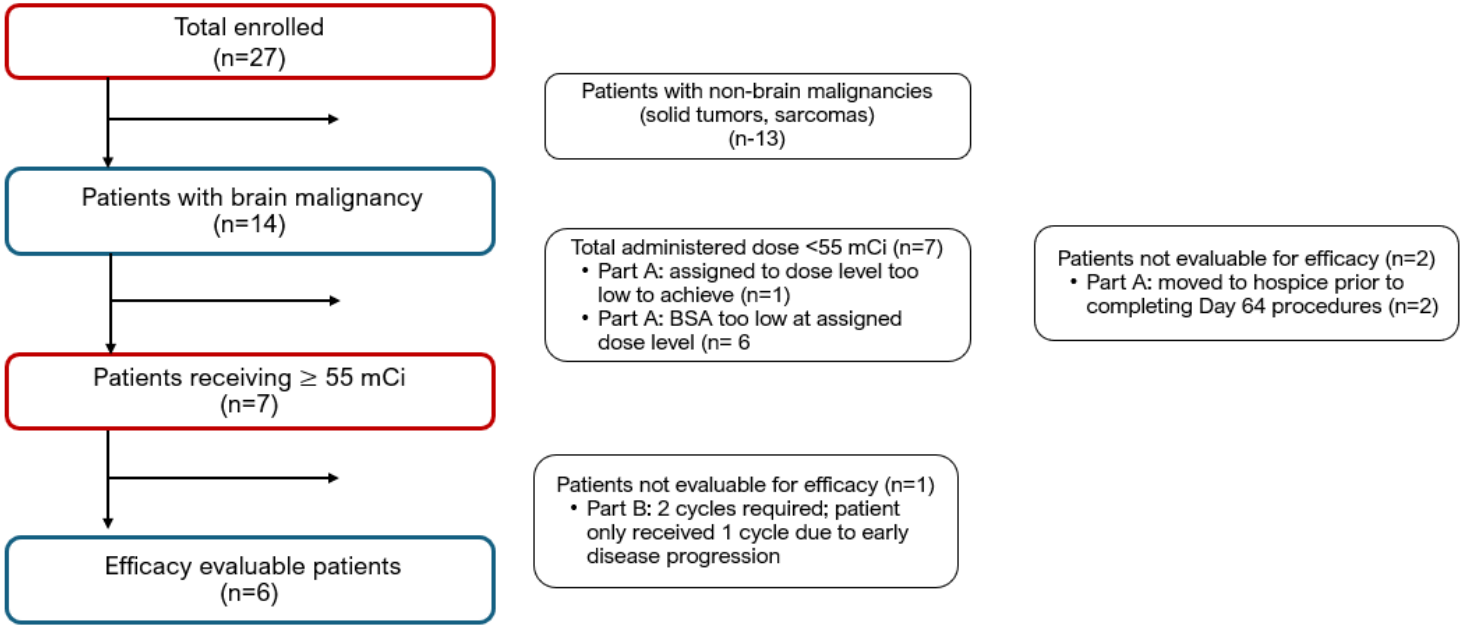
CLOVER-2

CLOVER-2: Study Design, Part B



Abbreviations: DMC = Data Monitoring Committee; DOCB = Duration of Clinical Benefit; DOR = Duration of Response; OS = Overall Survival; PFS = Progression Free Survival, RP2D = Recommended Phase 2 Dose

CLOVER-2: Patient Disposition

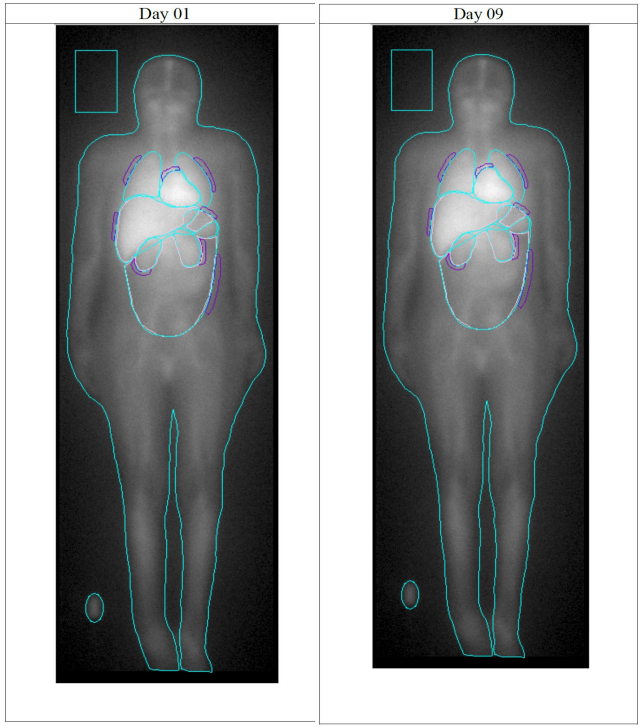


CLOVER-2 pHGG: Patient Characteristics

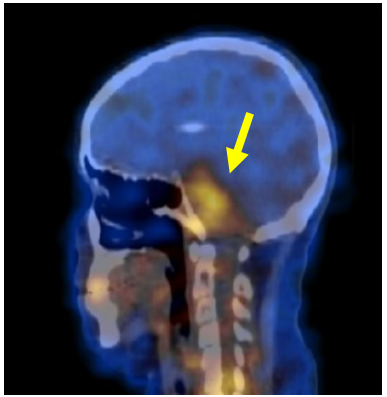
Characteristic	All patients with brain malignancy (n=14)	< 55 mCi TAD iopofosine I 131 (n=7)	≥ 55 mCi TAD iopofosine I 131 (n=7)
Diagnosis, n (%)			
DHG	1 (7)	0	1 (14)
DIPG	4 (29)	3 (43)	1 (14)
DMG	1 (7)	0	1 (14)
Ependymoma	6 (43)	2 (29)	4 (57)
GBM	1 (7)	1 (14)	0
Medulloblastoma	1 (7)	1 (14)	0
Sex, n (%)			
Male	9 (64)	5 (71)	4 (57)
Female	5 (36)	2 (29)	3 (43)
Median age, y (range)	13 (5-25)	12 (5-14)	14 (11-25)
Mean prior interventions	4.4	4.7	4.1
Efficacy Evaluable, n (%)			
Part A[1]	8 (57)	5 (71)	3 (43)
Part B[2]	3 (21)	0	3 (43)

Abbreviations: DHG: diffuse hemispheric glioma; DIPG: diffuse intrinsic pontine glioma; DMG: diffuse midline glioma; GBM: glioblastoma multiforme; TAD: total administered dose
1. Part A patients evaluable for efficacy if completed day 64 procedures following iopofosine I 131 administration; 2. Part B patients evaluable for efficacy if completed 2 cycle of iopofosine I 131

Iopofosine I 131: Dosimetry



Dosimetry in pediatric DIPG patient



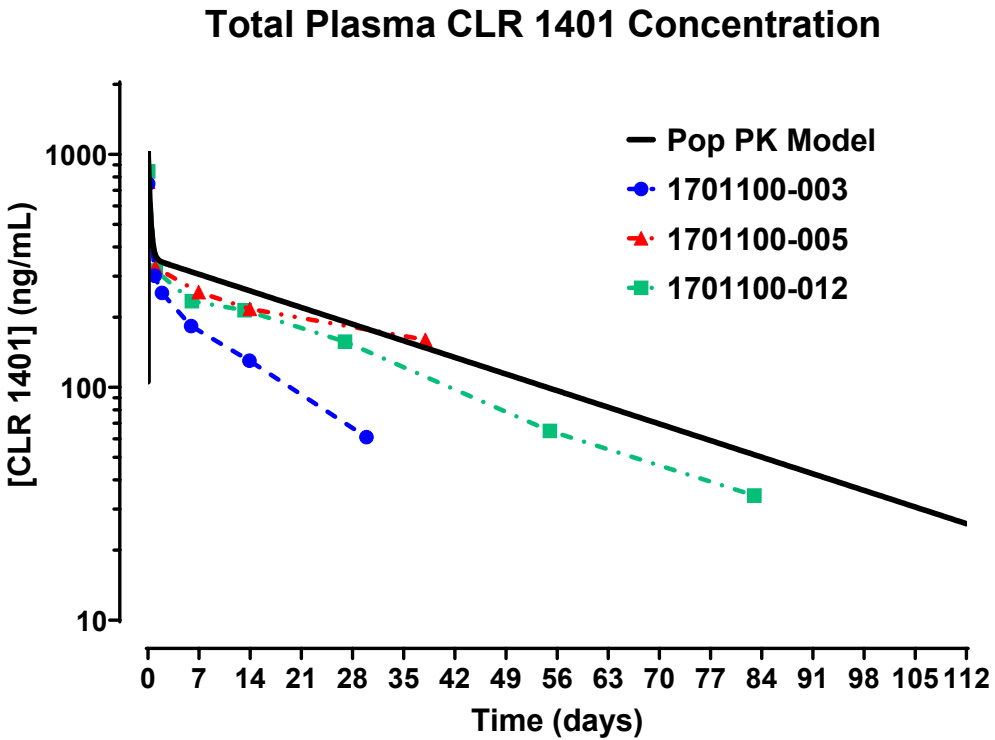
CLR 131 targeting in pediatric DIPG patient

- Whole body planar images were obtained at 5 timepoints (2, 24, 48, 120, 310 hours) following iopofosine I 131 administration
- For every ~25mCi administered to patients, results in between 3-5 Gy to the tumor
- Kidney and red marrow received 1.8 Gy and 0.68 Gy, respectively

CLOVER-2

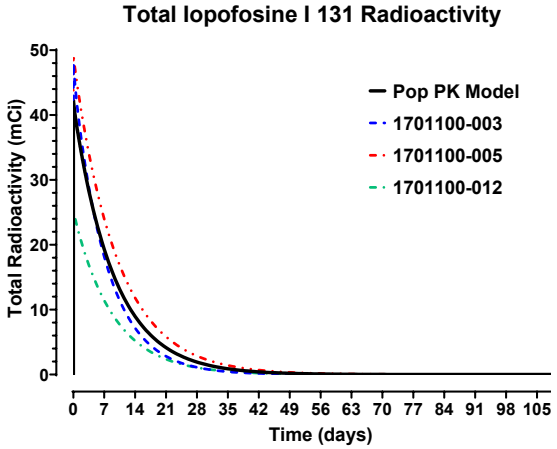
CLOVER-2 Brain Malignancies: Pharmacokinetics

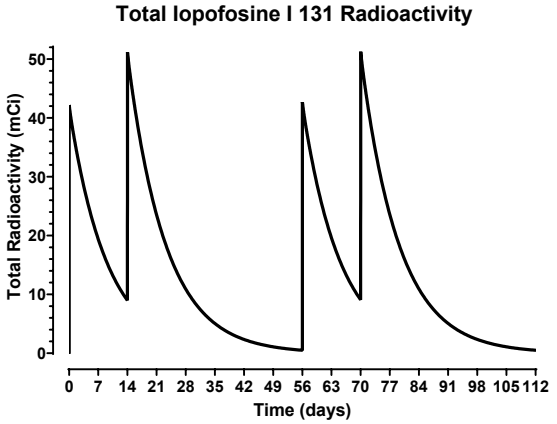
- CLR 1401 is the carrier molecule for Iopofosine I 131
- Plasma concentrations of total CLR 1401 were measured and population PK modeling performed
- CLR 1401 has a long terminal half-life of about 29 days, and limited volume of distribution



CLOVER-2 Brain Malignancies: Pharmacokinetics

- Single 20mCi/m^2 dose used to create pop PK model estimating total body radioactivity in mCi:
  - Single dose
  - Multi-dose & multiple cycles
- Mean circulating half-life was 6.3 days
- Less than 15% of the injected activity is expected to remain in circulation 2 weeks following dose
- Multiple doses shows slight accumulation: no accumulation with multiple cycles





CLOVER-2 pHGG: Efficacy Analysis

Efficacy Result (evaluable patients)	< 55 mCi TAD iopofosine I 131 (n=5)	≥ 55 mCi TAD iopofosine I 131 (n=6)	Part B ≥ 55 mCi TAD iopofosine I 131 (n=3)
RAPNO Response, n (%)			
Minor response	0	2 (33)	2 (67)
Stable disease	1 (20)	6 (100)	1 (33)
Mean DOCB[1], months (range)	1.6 (0.9 – 2.8)	5.4 (1.9 – 11.0)	7.9 (1.9 – 11.0)
Mean PFS[2], months (range)	1.8 (1.2 – 2.8)	5.9 (2.1 – 11.2)	8.1 (2.1 – 11.2)
Mean OS, months (range)	6.1 (3.2 – 7.7)	8.1 (4.9 – 14.9)	ongoing[3]

1. Duration of clinical benefit = time from first iopofosine I 131 dose to progressive disease or death
2. Progression free survival = time from arm assignment to progressive disease or death
3. Median follow up is 11.5 month (range 4.9 - 14.9 months)

CLOVER-2 pHGG: Case Study 1

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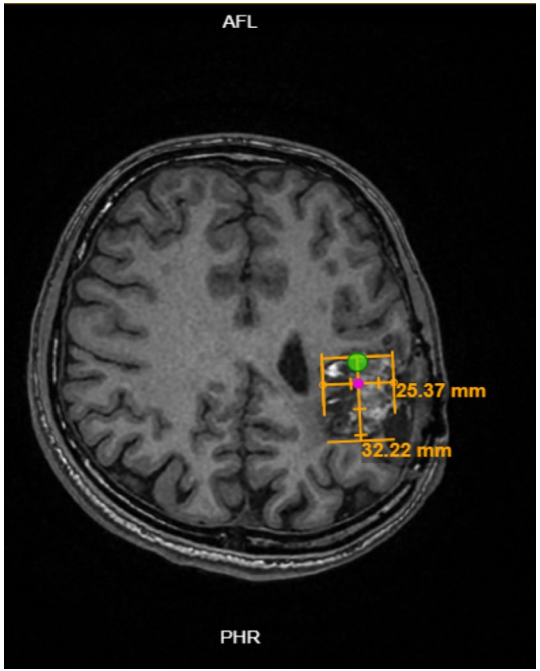
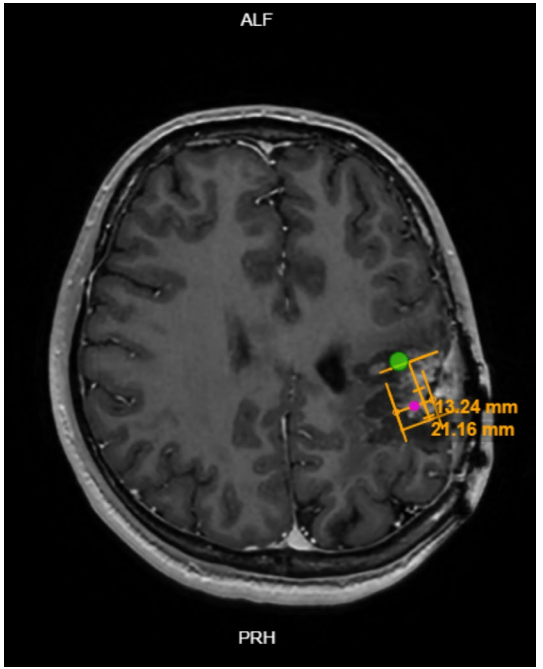
- Patient Background
  - 25 year old male
  - Diffuse hemispheric glioma
  - Mutation: H3 G34R/V
  - 3 prior therapies
- Patient received a total administered dose of 126.6mCi over 4 doses (40mCi/m^2/dose)
- Target lesion reduced by over 50% ~8 months post screening:
  - Reduction of 35% noted ~5 months post treatment
  - PFS = 10.9 months (new lesion ID'ed)
  - Survival = ongoing (>18 months) as of July 25, 2025



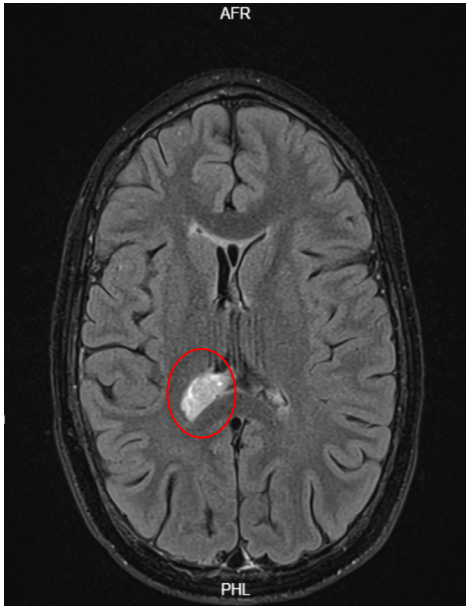
Screening

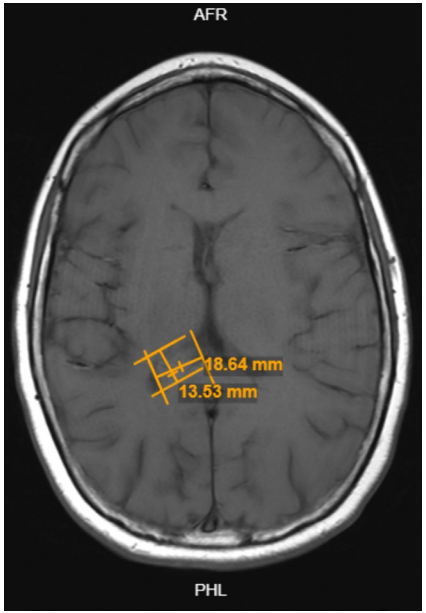


Day 327

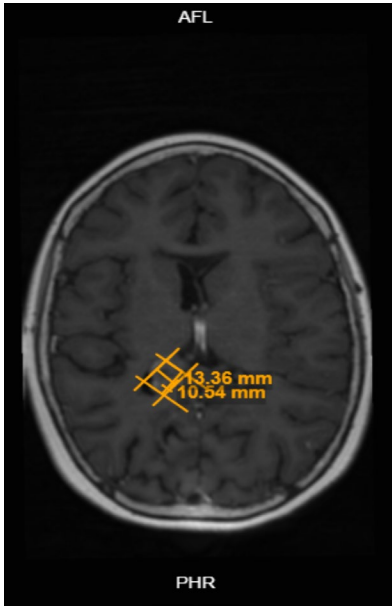
CLOVER-2 pHGG: Case Study 2

- Patient Background
  - 15 year old female
  - Ependymoma
  - Mutation: N/A
  - 8 prior therapies
- Patient received a total administered dose of 58.9mCi over 4 doses (20mCi/m^2/dose)
- Target lesion reduced from 252mm^2 to ~141mm^2
  - PFS = 11.2 months
  - Survival = ongoing (> 17 months) as of July 22, 2025





Screening



Day 270

CLOVER-2 pHGG: Safety Analysis

- Treatment emergent adverse events (TEAE) occurring in at least 10% of patients (n=2)
- Most common grade 3 and 4 TEAEs were restricted to thrombocytopenia, anemia and neutropenia
- Similar to other studies of iopofosine, patients experience minimal non-hematologic side affects
- Heme AEs were considered predictable and manageable
- No treatment related deaths reported

Most common related TEAE (≥ 10% patients), n (%)	Any Grade (n=14)	Grade 3 (n=14)	Grade 4 (n=14)
Hematologic Toxicities			
Anemia	9 (64)	6 (43)	1 (7)
Febrile neutropenia	3 (21)	2 (14)	1 (7)
Lymphocyte count decreased	3 (21)	1 (7)	1 (7)
Neutropenia	9 (64)	1 (7)	8 (57)
Thrombocytopenia	11 (79)	2 (14)	8 (57)
White blood cell count decreased	9 (64)	1 (7)	8 (57)
Non-Hematologic Toxicities			
Constipation	2 (14)	0	0
Fatigue	5 (36)	0	0
Headache	3 (21)	0	0
Infusion-related reaction	2 (14)	0	0
Nausea	5 (36)	0	0
Rhinorrhea	2 (14)	1 (7)	0
Sepsis	2 (14)	2 (14)	0
Vomiting	4 (29)	0	0
Weight decreased	2 (14)	0	0

CLOVER-2 pHGG: Safety Analysis

Supportive care methods	All patients with brain malignancy (n=14)	< 55 mCi TAD iopofosine I 131 (n=7)	≥ 55 mCi TAD iopofosine I 131 (n=7)
Transfusions, n (%)			
Platelets	9 (64)	4 (57)	5 (71)
Red blood cells	7 (50)	2 (29)	5 (71)
Stem Cells[1]	4 (29)	2 (29)	2 (29)
Growth factor injections, n (%)			
Myeloid growth factors	8 (57)	3 (43)	5 (71)
Platelet growth factors	3 (21)	0	3 (43)

1. Part A participants only

Conclusions

- Less than 5% of infused activity accumulating in non-tumor tissue
  - 3 – 5 Gy absorbed dose in the tumor per 25 mCi injected
- Pharmacokinetics demonstrate limited accumulation with fractionated doses
  - Consistent with studies in adult patients
- Heme AEs were considered predictable and manageable
- Total administered doses (TAD) of <55 mCi and ≥ 55mCi show clear dose response
  - TADs closer to 100 mCi demonstrate greater activity
  - Dosing regimen may need to be refined to provide longer durability
- Preliminary data with iopofosine I 131 shows activity and warrants further investigation
  - Responses, durability and survival