STATISTICAL ANALYSIS PLAN

Study Title:	A Multicenter Phase 2 Study of Oncolytic Polio/Rhinovirus Recombinant (lerapolturev, formerly known as PVSRIPO) in Recurrent WHO Grade IV Malignant Glioma Patients
Phase:	II
Protocol No.:	Pro00077024
Protocol Date(s):	Version 8.0: 07 February 2020
Analysis Plan Version and Date:	Final Version 2.0: 27 July 2022
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CONFIDENTIAL AND PROPRIETARY INFORMATION

STATISTICAL ANALYSIS PLAN REVIEW AND APPROVAL

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1. INTRODUCTION

This document describes the statistical methods and data presentations to be used in the planned data summary and analysis of data from Protocol Pro00077024. Background information is provided for the overall study design and objectives. The reader is referred to the study protocol and case report forms (CRFs) for details of study conduct and data collection.

1.1. STUDY OVERVIEW

This is a randomized, multicenter, Phase 2 study of the safety and efficacy of lerapolturev (formerly known as PVSRIPO) in participants with recurrent World Health Organization (WHO) grade IV malignant glioma. Lerapolturev is a recombinant rhinovirus/poliovirus (PV) chimera administered by intratumoral injection. Approximately 122 participants will receive lerapolturev intratumorally via convection enhanced delivery (CED). Prior to protocol version 7, participants were randomized to receive lerapolturev alone or lerapolturev followed by lomustine at week 8-post-infusion, which was stratified by center. From protocol version 7 and beyond, randomization to the lerapolturev + lomustine arm was discontinued and participants are to be enrolled only on the lerapolturev monotherapy arm.

Retreatment with lerapolturev is allowed upon progression or recurrence of tumor in participants who are ≥ 12 months out from the initial and subsequent lerapolturev infusions. In order to qualify, the retreatment eligibility criteria listed in Section 9.2.1 of the protocol must be met. All cases for consideration of lerapolturev retreatment are to be discussed with the study designated neurooncologist/Investigator Steering Committee (ISC) for approval prior to proceeding.

Participants will receive lerapolturev on Day 0 (Study Day 1) during the Infusion Period. Study tests and procedures will be collected post-infusion (Follow-up Period) on Day 1 and Week 1, 2, 4, 8, 16 + every 9 weeks until Week 52. After Week 52, participants will follow-up at the discretion of the treating physician, receiving periodic magnetic resonance imaging (MRIs), but will still be considered on study. While participants are on study, their malignant glioma may not be treated with any modality for cancer other than lerapolturev or a single dose of lomustine (for those randomized to the lomustine arm prior to protocol version 7), or reduced dose of bevacizumab described in "special considerations" in Section 9.1.6 of the protocol. Participants will be considered off study upon initiation of treatment of the tumor with another modality or initiation of hospice care. The study will be considered complete once enrollment has been met, follow-up procedures have been conducted on all participants, and data analysis is concluded.

1.2. SCHEDULE OF EVENTS

Table 1 Schedule of Study Tests and Procedures for Initial lerapolturev Treatment

Description	Screening: Within 6 Weeks	Screening: Within 14 Days Prior to Catheter Placement, but as Close to Biopsy as Possible	Screening: Within 2 Days Prior to lerapolturev	Catheter Placement Biopsy, lerapolturev infusion	Post-Infusion (Follow-up Period)[a]							On-Study Participants (required SOC Visits and Minimum Follow-up)	Off-Study Participants (SOC Visits With Follow-up)
Week					**0**	**1**	**2**	**4**	**8**	**[WEEK 12 VISIT REMOVED IN PROTOCOL V7] 12[b]**	**16 + Every 9 Weeks Until Week 52**	**> 52 (Information Transmitted Routinely as Obtained)**	**From Time Off Study Available For Follow-up (Information Transmitted a Minimum of Every 6 Months [± 1 Month])**
Day		**Within 14 Days Prior to Catheter Placement**	**Within 2 Days Prior to lerapolturev**	**0**	**1**	**7**	**14**	**28**	**56**	**84**	**112**	**> 112**	**Varies**
General Evaluations													
Informed Consent	X												
Clinical assessment including medical history)		X			X[c]	X	X	X	X	X	X	X	X
Physical examination		X			X[c]	X	X	X	X	X	X	X	
Neurological examination		X			X[c]	X	X	X	X	X	X	X	

Description	Screening: Within 6 Weeks	Screening: Within 14 Days Prior to Catheter Placement, but as Close to Biopsy as Possible	Screening: Within 2 Days Prior to lerapolturev	Catheter Placement Biopsy, lerapolturev infusion	Post-Infusion (Follow-up Period)[a]							On-Study Participants (required SOC Visits and Minimum Follow-up)	Off-Study Participants (SOC Visits With Follow-up)
Week					**0**	**1**	**2**	**4**	**8**	**[WEEK 12 VISIT REMOVED IN PROTOCOL V7] 12[b]**	**16 + Every 9 Weeks Until Week 52**	**> 52 (Information Transmitted Routinely as Obtained)**	**From Time Off Study Available For Follow-up (Information Transmitted a Minimum of Every 6 Months [± 1 Month])**
Day		**Within 14 Days Prior to Catheter Placement**	**Within 2 Days Prior to lerapolturev**	**0**	**1**	**7**	**14**	**28**	**56**	**84**	**112**	**> 112**	**Varies**
KPS		X			X[c]	X	X	X	X	X	X	X	
Adverse events				Continuous									
Laboratory Evaluations													
PV immunization booster[d]	X												
CBC with differential		X			X	X	X	X	X	X	X		
CMP		X			X	X	X	X	X	X	X		
PT, aPTT		X											
Serum pregnancy test		X	X						X[e]				
Serum for LSQ, anti-tetanus toxoid IgG	X (pre-boost)												

Description	Screening: Within 6 Weeks	Screening: Within 14 Days Prior to Catheter Placement, but as Close to Biopsy as Possible	Screening: Within 2 Days Prior to lerapolturev	Catheter Placement Biopsy, lerapolturev infusion	Post-Infusion (Follow-up Period)[a]							On-Study Participants (required SOC Visits and Minimum Follow-up)	Off-Study Participants (SOC Visits With Follow-up)
Week					**0**	**1**	**2**	**4**	**8**	**[WEEK 12 VISIT REMOVED IN PROTOCOL V7] 12[b]**	**16 + Every 9 Weeks Until Week 52**	**> 52 (Information Transmitted Routinely as Obtained)**	**From Time Off Study Available For Follow-up (Information Transmitted a Minimum of Every 6 Months [± 1 Month])**
Day		**Within 14 Days Prior to Catheter Placement**	**Within 2 Days Prior to lerapolturev**	**0**	**1**	**7**	**14**	**28**	**56**	**84**	**112**	**> 112**	**Varies**
PV titer[f]	X (pre-boost)	X			X[g]	X[h]	X		X				
Whole blood for immunologic/ other analysis[g]	X												
Whole blood for buffy coat isolation	X[n]												
Stool sample[n]	X[n]								X[n]				
Disease evaluations													
MRI[l]		X						X	X		X	X	X
CT scan				X[j]									
Biopsy[k]				X									
Tumor samples												X[l]	X[l]
Treatment													

Description	Screening: Within 6 Weeks	Screening: Within 14 Days Prior to Catheter Placement, but as Close to Biopsy as Possible	Screening: Within 2 Days Prior to lerapolturev	Catheter Placement Biopsy, lerapolturev infusion	Post-Infusion (Follow-up Period)[a]							On-Study Participants (required SOC Visits and Minimum Follow-up)	Off-Study Participants (SOC Visits With Follow-up)
Week					**0**	**1**	**2**	**4**	**8**	**[WEEK 12 VISIT REMOVED IN PROTOCOL V7] 12[b]**	**16 + Every 9 Weeks Until Week 52**	**> 52 (Information Transmitted Routinely as Obtained)**	**From Time Off Study Available For Follow-up (Information Transmitted a Minimum of Every 6 Months [± 1 Month])**
Day		**Within 14 Days Prior to Catheter Placement**	**Within 2 Days Prior to lerapolturev**	**0**	**1**	**7**	**14**	**28**	**56**	**84**	**112**	**> 112**	**Varies**
lerapolturev				X (+ 1-day window)									
Lomustine									X[m]				

aPTT = activated partial thromboplastin time; CBC = complete blood count; CMP = Comprehensive Metabolic Panel; CT = computed tomography; IgG = immunoglobulin G; KPS = Karnofsky Performance Status; LSQ = lymphocyte subset quantitation; MRI = magnetic resonance imaging; PT = prothrombin time; PV = poliovirus; lerapolturev = polio/rhinovirus recombinant; SAM = Study Administration Manual; SOC = standard of care.

a. Tests and procedures occurring on Day 7 have a ± 3-day window. From Day 14 (Week 2) onward, all tests and procedures have a ± 7-day window.
b. The week 12 clinic visit (± 1 week) and whole blood collection for immunologic/other analysis was removed in protocol v7, as it was associated with follow-up after lomustine use. Participants enrolled under protocol version 7 and after will not have a protocol mandated week 12 visit.
c. Daily after infusion until discharged from hospital; a PE must be documented within 24h (±4h) of discharge.
d. PV booster must occur ≥ 1 week (but ≤ 6 weeks) prior to the initial lerapolturev infusion.
e. Only for women of childbearing potential who are randomized to receive lomustine prior to protocol V7.
f. For screening prior to initial lerapolturev infusion, PV titers are to be drawn after informed consent and prior to PV booster administration. No additional tubes need to be drawn for the PV titer. This analysis can be done from the whole blood drawn for immunologic analysis.

g. Whole blood for immunologic analysis (3mL at Day 1 OR Day 2 post-lerapolturev infusion; thereafter, ~96.5 mL; tube and sample processing and shipping details outlined in laboratory manual portion of the SAM). For participants only at DUMC, an additional 6ml (~102.5 mL total) will be drawn at both the pre-PV boost and post-PV screening visits (before lerapolturev infusion) and again at the Week 1 visit as part of a sub-study at DUMC to explore inflammation-associated biomarkers, immune cell phenotype and innate and adaptive immune competence. After Week 8, only draw 76.5 mL of whole blood for all participants/all centers.
h. Blood sample (6mL) collected on Day 7 (Week 1) post-infusion only for participants enrolled at DUMC consented to sub-study for immune marker analyses.
i. All MRIs in the study include intravenous administration of gadolinium. After week 52, MRIs are to be conducted per the institution's SOC and all images are to be transmitted to the sponsor or their designee no less than every 6 months (± 1 month) after the last images were transmitted.
j. There is a post-catheter placement CT scan and a post-catheter removal CT scan.
k. Biopsy results should be transmitted, or blocks/slides should be shipped to the sponsor or designee per instructions in the laboratory manual portion of the SAM.
l. If any additional samples become available or resections occur anytime during the study (make participant off study) or off-study follow-up period, materials also should be transmitted to the sponsor or their designee, as outlined in the SAM, if possible.
m. For participants randomized to the lomustine cohort prior to protocol v7 received 110 mg/m2 oral lomustine for one cycle at 8 weeks post-lerapolturev infusion. Participants who were on bevacizumab (were treated with bevacizumab in the time since lerapolturev infusion) received 90 mg/m2 oral lomustine for one cycle 8 weeks post-lerapolturev infusion. The lomustine may have been taken the day of or 1 day after the week 8 visit.
n. Stool Sample for OMNIgene Kit (OMNIgene®•GUT (OMR-200)). For newly enrolled participants (i.e., those who have not received lerapolturev under a previous protocol version), a kit will be dispensed at the pre-PV boost screening visit, and they will provide a baseline sample prior to lerapolturev infusion and again after the week 8 visit. For participants who received lerapolturev under a previous version of the protocol, a baseline/pre-lerapolturev sample will not be obtained but the participant will be given a kit to provide a post-lerapolturev infusion stool sample at their next clinic visit.

Table 2. Schedule of Study Tests and Procedures for Lerapolturev Retreatment

Study Procedure	Screening Period	lerapolturev Infusion	Post-Infusion (Follow-up Period)						
	≤ 14 days	Day 0	Day 1	1w (+/- 3d)	2w (+/- 1w)	4w (+/-1w)	8w (+/-1w)	Q9-12w for 52w	> 52 Weeks from Retreatment[b]
Informed Consent[a]	X								
Clinical assessment and medical history	X		X[d]	X	X	X	X	X	X
Physical Exam[c]	X		X[d]	X	X	X	X	X	X
Neurologic Exam	X		X[d]	X	X	X	X	X	X
KPS	X		X[d]	X	X	X	X	X	X
Record Cancer treatments and Concomitant medications[e]	Continuous from signing of ICF onward								
Adverse Events		Continuous							
PV Immunization Booster and Anti-tetanus IgG[f]	X								
CBC w/diff	X		X	X	X	X	X	X	
CMP	X		X	X	X	X	X	X	
PT, aPTT	X								
Pregnancy Test[g]	X								
MRI	X					X	X	X	X
CT Scan		X[h]							
Biopsy		X							
lerapolturev		X							

AEs = adverse events; aPTT = activated partial thromboplastin time; CBC = complete blood count; CMP = comprehensive metabolic panel; CT = computed tomography; IgG = immunoglobulin G; KPS = Karnofsky Performance Status; LSQ = lymphocyte subset quantitation; MRI = magnetic resonance imaging; PT = prothrombin time; PV = poliovirus; SAE = serious adverse events

a. Informed Consent must be renewed prior to initiation of screening activities for lerapolturev retreatment.
b. Follow-up beyond Week 52 post retreatment: participants should be followed per institutional SOC for all assessments after Week 52 post lerapolturev retreatment. Data transfers should occur no > every 3 months (including description of MRI/tumor measurements). If SOC occurs less frequently, data should be entered within 2 weeks (± 1 week) of acquisition.
c. Physical Examination: The screening physical examination should be a complete physical exam of major body systems, per institutional guidelines. Following lerapolturev infusion, physical exams should be focused and symptom-directed. Each exam should be performed in conjunction with a neurological exam and KPS assessment.
d. Post-lerapolturev (re)treatment: Clinical assessment and physical examinations (including neurologic assessment and KPS) should be performed daily until hospital discharge.

e. Cancer Treatments and Concomitant Medications: all start/stop dates, dose, route, frequency, procedures and treatments for glioma or any other cancer treatment are to be recorded from baseline onward, including agents associated with managing lerapolturev anti-tumor inflammatory response (i.e., corticosteroids and bevacizumab) or for any other agents/causes.
f. Polio immunization booster and anti-tetanus toxoid IgG blood test: May be obtained locally and must occur ≥ 1 week (but ≤ 6 months) prior to planned additional lerapolturev infusion(s).
g. Pregnancy Test: A serum-based pregnancy test must be performed for all female participants during screening (≤ 2 days of lerapolturev infusion).
h. CT Scan: Includes a CT to confirm catheter placement prior to lerapolturev infusion (preferably intraoperative) and second CT upon catheter removal to confirm no bleed.

1.3. GLOSSARY OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse Event
AESI	Adverse Event of Special Interest
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Classification
BMI	Body Mass Index
BSA	Body Surface Area
CED	Convection Enhanced Delivery
CI	Confidence Interval
CNS	Central Nervous System
CR	Complete Response
CRF	Case Report Form
CTCAE	Common Terminology Criteria for Adverse Events
DCR	Disease Control Rate
DOR	Duration of Response
DUMC	Duke University Medical Center
EDC	Electronic Data Capture
FAS	Full Analysis Set
HMGB1	High Mobility Group 1 Box
ICE	Intercurrent Events
ICH	International Conference on Harmonization
iRANO	Immunotherapy Response Assessment in Neuro-Oncology
ISC	Investigator Steering Committee
KPS	Karnofsky Performance Status
MedDRA	Medical Dictionary for Regulatory Activities
MR	Minor Response
MRI	Magnetic Resonance Imaging
n	Participants
NE	Not Evaluable
NK	Natural Killer
OMR-200	OMNIgene®•GUT
ORR	Objective Response Rate
OS	Overall Survival
PD	Progressive Disease

PR	Partial Response
PT	Preferred Term
PV	Poliovirus
Lerapolturev	Oncolytic Polio/Rhinovirus Recombinant
SAE	Serious Adverse Event
SAF	Safety
SD	Stable Disease
SD	Standard Deviation
TEAE	Treatment-Emergent Adverse Event
TESAE	Treatment-Emergent Serious Adverse Events
ULN	Upper Limit Normal
WHO	World Health Organization
WHO-DD	WHO Data Dictionary

2. OBJECTIVES

Objective	Endpoint
Primary	
• Assess the anti-tumor response and duration of response among adults with recurrent WHO grade IV malignant glioma treated with lerapolturev	• Objective response rate (ORR) • Duration of response (DOR)
Secondary	
• Assess survival outcomes of adults with recurrent WHO grade IV malignant glioma treated with lerapolturev relative to a criteria matched external (historical) control group	• Landmark Survival • Overall survival (OS)
• Assess the safety of lerapolturev	• The proportion of participants with grade 3, 4, or 5 treatment-related adverse events
• Assess the disease control rate following lerapolturev infusion	• Disease Control Rate (DCR)
Exploratory	
• Describe changes visualized on imaging due to intratumoral inoculation of lerapolturev	• Description of imaging changes
• Assess immunologic responses in peripheral blood and in serum	• Change from baseline in immune function
• Identify genetic predictors of response or failure of response (including in buffy coat) to treatment with lerapolturev	• Identification of genetic markers as predictors of response
• To obtain the quantitative gut microbiome profile via the OMNIgene®•GUT (OMR-200) kit to determine any potential influence in response to lerapolturev	• Identification of quantitative gut microbiome profile as predictors of response
• As part of a smaller sub-study only at Duke University Medical Center (DUMC), to explore inflammation-associated biomarkers, immune cell phenotype and innate and adaptive immune competence pre- and post-poliovirus (PV) boost (prior to infusion) and post-lerapolturev infusion	• Inflammation-associated biomarkers, immune cell phenotype and innate and adaptive immune competence
• Assess anti-tumor responses and outcomes following lerapolturev retreatment(s) or treatment with any other non-protocol specified therapy	• Description of the proportion of participants who achieve complete response (CR), partial response (PR), minor response (MR), stable disease (SD) (along with associated durations) following lerapolturev retreatment

Objective	Endpoint
• Assess anti-tumor responses and outcomes considering site-level experience with lerapolturev treatment	• Description of participant outcomes following lerapolturev infusion in centers based on the number of prior participants infused

3. GENERAL STATISTICAL CONSIDERATIONS

3.1. SAMPLE SIZE AND POWER

The sample size of the study is approximately 122 participants. A formal sample size calculation was not performed. The following table shows the ORR in percent and the corresponding 95% confidence intervals (CI) as a function of the number of objective responses, if for example 120 participants were enrolled.

Table 3 Sample Size Calculation

Number of Participants	Number of objective responses	ORR (%)	95% CI
120	10	8.3%	3.4%, 13.3%
120	12	10.0%	4.6%, 15.4%
120	14	11.7%	5.9%, 17.4%
120	16	13.3%	7.3%, 19.4%
120	18	15.0%	8.6%, 21.4%
120	20	16.7%	10.0%, 23.3%

3.2. HANDLING OF DATA

3.2.1. Strata and Covariates

Participant randomization until protocol amendment 7 was stratified by center.

3.2.2. Multiple Testing and Comparisons

All analyses will be conducted without adjustments for multiple comparisons.

3.2.3. Missing Data and Outliers

Every effort will be made to obtain required data at each scheduled evaluation from all participants who have been randomized. In situations where it is not possible to obtain all data, it may be necessary to impute missing data. These situations are described below. Unless otherwise specified, all other missing data will not be imputed.

3.2.3.1. Missing Severity or Relationship for Adverse Events

Adverse events (AE) with missing severity will have the severity imputed as "Grade 3" for the AE tabulations. Adverse events with missing relationship to study drug will have the relationship imputed as 'Definite' for the AE tabulations if the AE started on or after catheter placement.

3.2.3.2. Imputation of Incomplete Dates

An incomplete date occurs when the exact date an event occurred or ended cannot be obtained from a participant. The database contains data fields for month, day, and year. A date is incomplete if at least one of these three fields is not known. For many of the planned analyses, a complete date is necessary to determine if the event should be included in the analysis (i.e., if the event is treatment-emergent) or to establish the duration of an event. In such cases, incomplete dates will be imputed.

For the purposes of handling partially reported start and stop dates for an event, excluding dexamethasone use, the following algorithm will be applied:

1) For onset date:
   a) If only the day part of the onset date is missing and occurs in the same month and year as the date of dose of study drug, the date of dose of study drug will be used as the onset date. Otherwise, the first day of the month will be used to complete the onset date.
   b) If the day and month parts of the onset date are missing and occur in the same year as the dose of study drug, the date of the dose of study drug will be used as the onset date. Otherwise, January 1st will be used to complete the onset date.
   c) If the onset date is completely missing, the date of the dose of study drug will be used as the onset date.
2) For end date:
   a) If only the day part of the end date is missing, the last day of the month will be used to complete the end date.
   b) If the day and month parts of the end date are missing, December 31st will be used to complete the end date.
   c) If the end date is completely missing, the maximum of the participant's off study date or date of last contact will be used as the end date.

For the purposes of handling partially reported end dates for dexamethasone use, the following algorithm will be applied:

1) If a participant has multiple entries of dexamethasone use and one of them has a start date prior to a subsequent entry and there is no end date to the first entry, the day before the start date of the subsequent record will be used as the end date.
2) If a participant has multiple entries of dexamethasone use and one of them has no end date and no subsequent records, the maximum of either the participant's off study date or the date of last contact will be used as the end date.

If any imputed start date causes the start date to occur after the end date, the end date will be used for the imputation of the start date. If any imputed end date causes the end date to occur prior to the start date of the event, the start date of the event will be used for the imputation of the end date.

3.2.4. Presentations by Study Visit

When data are collected serially over time, individual data presentations may include by-study visit displays. By-study visit displays will only be summarized up to Week 52. Visits will be presented according to the nominal visit as obtained from the CRF. If multiple observations are collected at a scheduled visit, the closet observation to the target day will be chosen. If two observations have equal distance from the target day but one is earlier and the other is later than the target day, the earlier observation will be chosen. Unscheduled assessments will be included in the listings.

3.2.5. Presentations by Worse Case

When data are collected serially over time, individual data presentations may include "worst case on study" displays. In those situations, both scheduled and unscheduled assessments up to 52 weeks will be included.

3.2.6. Definitions and Terminology

Age
Age is age at informed consent and is as captured on the CRF.

Baseline Value
For purposes of analysis, the baseline value is defined as the last non-missing value obtained prior to initiation of study drug. Records with missing time on the date of initiation of study drug will not be considered post-Baseline.

Day 1 (Baseline)
Day 1 is the earliest day that study drug is initiated. Note that this is a change from the protocol where the first day of study drug administration was designated as Day 0.

Study Day
Study Day is defined relative to Baseline (Day 1). Thus, the study day of an event is calculated as:

Study Day = event date – date of Day 1 (+ 1, if event date ≥ date of Day 1).

Study Visit
Study Visit is the nominal visit as recorded on the CRF.

Change from Baseline
Change from baseline for a given endpoint is defined as the Study Day X value minus the Baseline Value.

Days on Study
Days on study is the number of days from Day 1 to the date of study completion as recorded on the Off Study CRF page.

Adverse Event
An AE is any untoward medical occurrence in a participant receiving study drug(s) and which does not necessarily have a causal relationship with this treatment. For this protocol, the definition of AE also includes worsening of any preexisting medical condition. An AE can therefore be any unfavorable and unintended or worsening sign (including an abnormal laboratory finding), symptom, or disease temporally associated with catheter placement or the use of lerapolturev, lomustine (for participants randomized to this arm prior to protocol version 7), bevacizumab, or corticosteroids whether or not related to use of any of these drugs. All adverse events will be recorded on the Adverse Event CRF.

Treatment-emergent Adverse Event (TEAE)
A TEAE will be an AE that occurred during the study on or after catheter placement. Additionally, it is assumed that an Adverse Event which was reported to have started on Day 1 without an associated onset time occurred on or after catheter placement.

Adverse Event of Special Interest (AESI)
An AESI is any grade 3 or grade 4 toxicity considered related (possibly, probably, or definitely) to a protocol treatment (includes surgical biopsy/infusion procedure, lerapolturev, lomustine (for participants randomized to this arm prior to protocol version 7), bevacizumab, corticosteroids) that is not reversible (i.e., does not improve to ≤ grade 2 with exception of neurologic events, which must only improve from highest grade level to next lower grade level) within 2 weeks. This includes any treatment-related life-threatening event or any treatment-related death. Any grade 2 or higher serious autoimmune toxicities—particularly those affecting vital organs (e.g., cardiac, renal, central nervous system (CNS))—will also be considered an AESI if they occur within 2 weeks of any protocol treatment, whether the AE requires intervention.

Exceptions to AESIs are listed in protocol Section 12.8.6. AESIs will be collected on the Adverse Event CRF.

Concomitant Medications
Concomitant medications are those medications taken on or after catheter placement. This definition includes medications started prior to catheter placement but continuing concomitantly with study drug.

Prior Medications
Prior medications are those medications taken and discontinued prior to catheter placement.

Immunotherapy Response Assessment in Neuro-Oncology (iRANO)
iRANO are guidelines that incorporate criteria previously defined by the RANO working committee to define CR, PR, MR, SD, progressive disease (PD), and non-evaluable, for participants with malignant glioma, low-grade glioma, and brain metastases. The key component of iRANO is specific additional guidance for the determination of PD among neuro-oncology participants undergoing immunotherapy. iRANO guidelines require confirmation of progression on follow-up imaging 3 months after initial radiographic progression if:

1. No new or significantly worsened neurologic deficits not due to co-morbid event or concurrent medication AND
2. ≤ 6 months from initiation of immunotherapy

If follow-up imaging confirms progression, the date of actual progression should be backdated to the date of initial radiographic progression. Appearance of new lesions solely does not define progressive disease ≤ 6 months from initiation of immunotherapy. The lesions are added to the total lesion areas for follow-up assessments.

Complete Response (CR)
CR is defined as:

- Disappearance of all enhancing disease for ≥ 4 weeks AND
- No new lesions AND
- Stable/improved T2/FLAIR AND
- No more than physiologic steroids AND
- Stable improved clinically

Partial Response (PR)
PR is defined by:

- ≥ 50% decrease in the sum of biperpendicular diameters of enhancing disease for ≥ 4 weeks AND
- No new lesions AND
- Stable/improved T2/FLAIR AND
- Stable/improved steroids AND
- Stable/improved clinically

Stable Disease (SD)
SD is defined by:

- Does not qualify for CR, PR, PD AND
- No new lesions AND
- Stable/improved T2/FLAIR AND
- Stable/improved steroids AND
- Stable/improved clinically

Progressive Disease (PD)
PD is defined by:

- ≥ 25% increase in the sum of biperpendicular diameters of enhancing disease OR
- New lesions OR

- Significant worsened T2/FLAIR OR
- Significant clinical decline

Immunoprogression/Immunoresponse

In addition to the categories of response defined in iRANO, the protocol had two additional categories of response: immunoprogression and immunoresponse that could be chosen as the time point response or best overall response. Per the CRF completion guidelines, immunoprogression and immunoresponse should be chosen in the following settings:

- Immunoprogression: Marked increase in contrast enhancement possibly due to immunotherapy (this determination is outside the recommended assessment determinations of RANO and is PVSRIPO specific). Immunoprogression will be selected when there is significant probability of, or concern for, immunoprogression over true disease progression.
- Immunoresponse: Marked decrease in contrast enhancement possibly due to immunotherapy (this determination is outside the recommended assessment determinations of RANO and is PVSRIPO specific).

Objective Response Rate (ORR)
ORR is defined as the proportion of participants achieving complete response CR or PR based on iRANO criteria.

Duration of Response (DOR)
DOR is defined as time from CR or PR until confirmed PD or death, censoring at the date of the last imaging without confirmed PD prior to the date the subject is considered off-study.

Landmark Survival
Landmark survival is defined as the proportion of participants alive starting ≥ month 36 after 1st lerapolturev infusion.

Overall Survival (OS)
OS is defined as time from lerapolturev infusion to death from any cause, or last follow-up if participant is alive.

Disease Control Rate (DCR)
DCR is defined as the proportion of participants achieving CR, PR, or SD.

Treatment Period
Treatment period is defined as the period from catheter placement to Week 52.

3.3. TIMING OF ANALYSES

The final analysis will be completed after the last participant completes or discontinues the study and the resulting clinical database has been cleaned, quality checked, and locked.

4. ANALYSIS POPULATIONS

Data analyses will be based on the full analysis (FAS) and safety (SAF) analysis sets.

4.1. FULL ANALYSIS SET

The full analysis set (FAS) includes subjects that were randomized, has an infusion catheter placed, and received the initial dose of lerapolturev. This will be the primary population used for the efficacy analyses. Patients in this population will be analyzed based on assigned treatment. Those participants randomized to lerapolturev + lomustine after protocol version 7 (1068, 1070, 1073, 1074, 1078, 1082, 1083, 4005, and 4008) are considered assigned to the lerapolturev only arm since they did not actually receive lomustine.

4.2. SAFETY SET

The safety (SAF) set includes all enrolled participants who had an infusion catheter placed. This will be the primary population used for the safety analyses. Participants in this population will be analyzed according to the treatment which they receive.

5. STATISTICAL METHODS

Descriptive statistical methods will be used to summarize the data from this study. Unless stated otherwise, the term "descriptive statistics" refers to number of participants (n), mean, median, standard deviation, minimum and maximum for continuous data and frequencies and percentages for categorical data.

Survival estimates will be analyzed with Kaplan-Meier method and summarized with median, twenty-fifth and seventy-fifth percentiles, and 95% confidence intervals (CI), if applicable. All data collected during the study will be included in data listings. Unless otherwise noted, the data will be sorted first by treatment, participant, and then by date within each participant number.
All summary tables and figures will be presented by treatment group and overall. The term "treatment group" refers to treatment with lerapolturev or lerapolturev and lomustine.

Analyses will be implemented using SAS® 9.4 or higher (SAS Institute, Cary, North Carolina, USA). The International Conference on Harmonization (ICH) numbering convention, i.e., ICH-E3, will be used for all tables and listings. Upon completion, all SAS® programs will be validated by an independent programmer within the staff of the third-party vendor doing the primary analysis. The validation process will be used to confirm that statistically valid methods have been implemented and that all data transformations and calculations are accurate. Checks will be made to ensure accuracy, consistency with this plan, consistency within tables, and consistency between tables and corresponding data listings. All documents will be verified by the lead statistician to ensure accuracy and consistency of analyses.

5.1. PARTICIPANT DISPOSITION, DEMOGRAPHIC AND BASELINE CHARACTERISTICS

Participant disposition will be presented for all enrolled participants, where enrolled is defined as participants that signed informed consent. Summaries will be presented based on treatment received. A summary table will be generated by treatment group and overall. The number of participants who were screened, screen failures, and the reason for screen failure will be summarized. Additionally, the number of participants in each analysis population will be summarized. The end of study status and reason the participant was taken off study will be provided. Similarly, the primary reason for death will be presented. Additionally, the number of days on study will be summarized. Participant disposition including treatment group, analysis population, end of study status and reason, and death date and reason will be listed.

Demographic data and baseline characteristics including age at informed consent, gender, race, ethnicity, Karnofsky performance status (KPS) at Baseline and Baseline vital signs (height, weight, and body surface area (BSA)) will be summarized using descriptive statistics. Frequency of KPS scores < 70, 70, 80, 90, and 100 will be summarized by treatment group and overall. Demographic data and baseline characteristics will be listed.

5.2. DISEASE CHARACTERISTICS

Disease characteristics including disease status, description (Unifocal or Multifocal), surgical pathology diagnosis, histologic grade, and the number of prior progressions will be summarized by treatment arm and overall. Number of prior progressions will be derived from prior systemic therapy, prior radiation therapy, and prior surgery collected on the CRF. Disease characteristics will also be listed.

5.3. CONCOMITANT MEDICATIONS

All medication verbatim terms collected will be coded to Anatomical Therapeutic Classification (ATC) and preferred term (PT) using the WHO-DD Version Sep2017.

Concomitant medications, including bevacizumab and dexamethasone, will be summarized by presenting the number and percentage of participants by PT and ATC. Participants taking the same medication multiple times will only be counted once for that PT or ATC. Each summary will be ordered by descending order of incidence of ATC class and PT within each ATC class.

The number of participants who receive bevacizumab will be tabulated along with the number of doses administered and dose levels received. Cumulative actual dose will be summarized. A participant's bevacizumab administration record will be included if it occurred after catheter placement and prior to the participant's Week 52 or end of study/last contact date, whichever occurs first. If a participant has bevacizumab listed as a post study systemic monotherapy record, this data will be included in the analysis if the start and stop dates occur prior to any other type of subsequent anticancer therapy (e.g. lomustine, pembrolizumab, irinotecan, nivolumab, carboplatin, etc.).

The number of participants who receive dexamethasone will be tabulated. The days on dexamethasone, cumulative actual dose, and average daily dose will also be summarized. Exposure will only be calculated from catheter placement to Week 52 or until the participant's end of study/last contact date, whichever occurs first.

5.4. BRAIN SURGERY, RADIOTHERAPY AND SYSTEMIC THERAPY

Brain surgery data will be listed. The number and percentage of participants with prior brain surgery will be summarized; data to be included in the summary are extent of resection, histologic diagnosis, CNS site, and CNS side.

The prior and subsequent radiotherapy will be listed. The number and percentage of participants with prior radiotherapy will be summarized; data to be included in the summary are CNS site, radiation therapy type, total dose delivered, and treatment response. If a participant experiences more than one prior radiotherapy, the worst-case will be used for numerical summaries and all cases will be presented for categorical summaries. A participant will only be included in a single category once.

All verbatim terms collected of subsequent systemic therapy will be coded to Anatomical Therapeutic Classification (ATC) and PT using the WHO-DD Version Sep2017.

The prior systemic therapy will be summarized by presenting the number and percentage of participants by PT and ATC. Participants taking the same medication multiple times will only be counted once for that PT or ATC. Each summary will be ordered by descending order of incidence of ATC class and PT within each ATC class. Additionally, the total number of cycles will be summarized. If a participant experiences more than one prior systemic therapy, the worst-case will be used for numerical summaries and all cases will be presented for categorical summaries. A participant will only be included in a single category once. All prior and subsequent systemic therapies will be presented in a participant listing.

5.5. TISSUE BIOMARKERS

Tissue biomarker and core biopsy data will be listed. The following information will be summarized for the subject's most recent visit prior to initiation of study drug:

- EGFR IHC
- EGFRvIII IHC
- MGMT IHC
- MGMT promoter methylation
- IDH1 R132H
- IDH1 molecular diagnostics
- IDH1 mutation type
- IDH2 molecular diagnostics

- IDH2 mutation type
- TERT molecular diagnostics
- TERT mutation type
- PVR IHC

5.6. EXPOSURE

The number of participants who received study drug and total dose received will be summarized. The number of participants who did not receive one cycle of lomustine at the required dose level will be calculated and the reason for not receiving lomustine as required will be summarized for those randomized to the lomustine arm prior to protocol version 7.

5.7. EFFICACY

5.7.1. Primary Efficacy Endpoints

The primary efficacy endpoints are ORR and DOR. ORR is defined as the proportion of participants achieving CR or PR based on iRANO criteria. DOR is defined as the time from CR or PR until confirmed PD.

5.7.1.1. Statement of Estimand

The **population for the trial** is defined through appropriate inclusion/exclusion criteria to reflect the targeted participant population for approval. The analysis population is based on the FAS set.

The **treatments** of interest are lerapolturev or lerapolturev + lomustine.

The **variable** of interest for ORR is the binary response value for a participant. For DOR, the variables of interest are the time from first response to progression/death/censoring, and a binary censoring value.

The ability to evaluate treatment effect using the variables may be impacted by **intercurrent events** (ICEs). Death, use of additional cancer treatments, and premature discontinuation of study may all impact the interpretation of treatment effect. For ORR, a composite strategy will be used to address intercurrent events (ICEs) of potential death, study discontinuations, and start of additional cancer treatments, meaning occurrence of any of these events prior to a participant achieving CR or PR will mean the participant is considered a non-responder. DOR will use a composite strategy as well, treating death as an event that ends response, and study discontinuations or the start of additional cancer treatments medications will be censored under the strategy.

The **population level summary measures** are the ORR and the Kaplan Meier estimated median DOR, and associated confidence intervals in each treatment group.

5.7.2. Primary Efficacy Analysis

The number of participants in each category of best overall response (CR, PR, SD, PD, immunoresponse, immunoprogression, non-evaluable (NE)), ORR, and DCR will be summarized. ORR and DCR along with their associated exact 95% two-sided confidence intervals (CIs) using Clopper Pearson method will be computed within each treatment group.

The number of participants with disease progression or death and the number of censored participants will be summarized. DOR will be summarized using Kaplan-Meier methods, and the descriptive statistics of median, 25% and 75% percentiles along with their 95% CIs will be calculated. The Kaplan-Meier survival curve will also be plotted.

Supportive data listings will also be provided.

5.7.3. Secondary Efficacy Endpoints

The secondary efficacy endpoints for the study are:

- Overall survival (specifically landmark survival)
- Disease control rate

5.7.4. Secondary Efficacy Analysis

OS, including landmark survival rates (focusing at ≥ month 36), will be summarized using Kaplan-Meier method to estimate the median, 25% and 75% percentiles along with their 95% CIs.

In addition to the quartile summary from Kaplan-Meier method, Kaplan-Meier estimates will be provided for the survival rates at 12, 24, and 36 months along with their 95% CIs for OS.

Analysis of DCR will be conducted in a similar manner to ORR in Section 5.7.2.

5.8. SAFETY

Values for all safety variables will be listed by participant and visit (as applicable). Safety summaries by visit will use scheduled visits up to Week 52.

5.8.1. Adverse Events

Adverse events will be mapped to a Medical Dictionary for Regulatory Activities (MedDRA) version 20.1 by system organ class and preferred term. If a participant experiences multiple events that map to a single preferred term, the greatest severity and strongest assessment of relation to a study drug will be assigned to the preferred term for the appropriate summaries. AEs will be collected from Day 1 through 30 days after the participant is considered off-study. AE severity will be assessed according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03. If CTCAE grading does not exist for an AE, the severity of the AE will be graded as mild (1), moderate (2), severe (3), life-threatening (4), or fatal (5).

The number of participants for the following groups will be summarized by treatment group and overall:

- Any treatment-emergent AE (TEAE)
- Any treatment-emergent serious AEs (TESAEs)
- Any treatment-emergent AESIs
- Any TEAE related to a study drug or catheter
- Any TESAE related to a study drug or catheter
- Any TEAE with grade ≥ 3
- Any TEAE with grade ≥ 3 related to study drug or catheter

The occurrence of TEAEs and TEAEs related to study drug or catheter will be summarized by preferred term, system organ class, and severity. Should an event have a missing severity or relationship, it will be classified as having the highest severity and/or strongest relationship to study medication. Separate summaries of TESAEs, TESAEs related to study drug or catheter, treatment-emergent AESIs, TEAEs with grade ≥ 3, and TEAEs with grade ≥ 3 related to a study drug or catheter will be generated by preferred term and system organ class. All adverse events reported will be listed for individual participants showing both verbatim and preferred terms. All adverse events that occurred prior to catheter placement will be excluded from the tables but will be included in the listings.

Missing onset dates will be imputed as previously outlined in Section 3.2.3.2 as required to determine treatment-emergent events.

5.8.2. Clinical Laboratory Assessments

Toxicities for clinical labs will be characterized according to CTCAE version 4.03 (when possible) and shift in grade from baseline to the worst post-baseline value will be summarized. Both scheduled and unscheduled assessments will be used to identify the worst post-baseline values.

The following categories of abnormal hepatic laboratory values will be evaluated for any occurrence among all post baseline assessments.

- Alanine Aminotransferase (ALT) and/or Aspartate Aminotransferase (AST) > 3 x upper limit normal (ULN), ALP < 2 x ULN, and Total Bilirubin≥ 2 x ULN
- AST > 3, 5, 8, 10, and 20 x ULN, and 5 x ULN for more than 5 weeks
- ALT > 3, 5, 8, 10, and 20 x ULN, and 5 x ULN for more than 5 weeks
- Total Bilirubin > 1.5 or ≥ 2 x ULN

Listings of all laboratory data with normal reference ranges, and CTCAE grades (when possible) will be provided.

5.8.3. Vital Signs

For vital sign parameters (systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, body temperature, body surface area and weight) the observed values and change from baseline will be summarized using descriptive statistics at each visit. The maximum post-baseline values and the change from baseline will also be summarized.

A listing of all vital sign data will be provided.

5.8.4. KPS

The observed values and the change from baseline in the Karnofsky performance status score will be summarized using descriptive statistics at each visit by treatment group. The maximum post-baseline values and the change from baseline will also be summarized.

A listing of KPS data will be generated.

6. PROTOCOL DEVIATIONS

Protocol deviation summaries and listing are not covered by this SAP but will be presented in the clinical study report.

7. CHANGES IN THE PLANNED ANALYSES

1. The interim analysis noted in the protocol was not conducted.
2. The decision to stop the lerapolturev + lomustine arm was made prior to the database being updated to reflect this change. Thus, the randomization arm in Electronic Data Capture (EDC) is incorrect for the following participants:
   - 1068, 1070, 1073, 1074, 1078, 1082, 1083, 4005, 4008 show as randomized to lerapolturev + lomustine but were assigned to lerapolturev only

   The treatment arm will be updated to reflect the changes for analysis purposes.
3. Participants 1012 and 1020 were randomized to lerapolturev + lomustine and participants 1033 and 1058 were randomized to lerapolturev. However, these participants screen failed prior to treatment. These subjects will be considered screen failures for the analysis.
4. 1098 was randomized to lerapolturev but the participant's randomization and treatment assignment were not collected in error. The decision to stop the lerapolturev + lomustine arm was made prior to 1098's enrollment; thus, the assigned arm is lerapolturev with the date the investigator signed off on the participant as eligible (21-Nov-2019) will be used as the randomization date.
5. Comparison to the external control will not be done for any efficacy analyses. Accordingly, the differences between the two groups with respect to demographics (Section 14.6 of the protocol) will not be performed.

6. Day 0 is the earliest day that study drug is initiated but will be designated as Day 1 based on implementation standards for the analysis.
7. Central imaging review was not completed and, therefore, results from this will not be presented.
8. Safety summaries for each cohort randomized prior to protocol version 7 and well as those retreated with lerapolturev (Section 14.6 of the protocol) will not be done.
9. Safety summaries for events related to bevacizumab or corticosteroids will not be done.
10. The exploratory analyses described in Section 14.7 of the protocol will not be done.

8. REVISION HISTORY

Date	Revision	Rationale
27 July 2022	Added derivation of incomplete/missing dates for dexamethasone use	To allow for accurate dexamethasone summary calculations of days on drug, cumulative dose, and average daily dose.
	Updated analysis of dexamethasone	To update exposure summaries included in the analysis based on the data collected.
	Updated analysis of bevacizumab	To update exposure summaries included in the analysis based on the data collected.
	Changed ITT to full analysis set	To create a population of subjects who were randomized, had a catheter placed, and received the initial dose of lerapolturev.
	Changed population used for the efficacy analysis and other additional summaries	To only include subjects that were in the FAS population in efficacy and select summaries.
	Updated participant information in the changes in planned analysis section	Updated/added participant information to clarify randomization/assigned treatment and the treatment received.
	Added clarity to definition of duration of response	Updated to only consider scans collected before the patient was considered off-study
	Added clarity to definition of Baseline	Updated to consider records with missing time as post-Baseline
	Updated analysis of tissue biomarkers	Updated to specify the records used for the analysis

9. REFERENCES

10. PROGRAMMING CONVENTIONS

- Page orientation, margins, and fonts: Summary tables, listings, and figures will appear in landscape orientation. There should be a minimum of a 1.0" boundary on the left and right edges. The top and bottom margins are 1.0" for tables and listings but may vary for figures. Output should be printed in Courier New with a point size of 8. Titles may be printed using a larger font (e.g., Arial point size 10).
- Identification of analysis population: Every summary table and figure should clearly specify the analysis population being summarized. Listings will be prepared for all participants.
- Group headers: In the summary tables, the group headers will identify the summary group and the sample size for the indicated analysis population. Of note, the header's sample size does not necessarily equal the number of participants summarized within any given summary module; some participants in the analysis population may have missing values and thus may not be summarized.
- Suppression of percentages corresponding to null categories: When count data are presented as category frequencies and corresponding percentages, the percent should be suppressed when the count is zero to draw attention to the non-zero counts.
- Presentation of sample sizes: Summary modules should indicate, in one way or another, the number of participants contributing to the summary statistics presented in any given summary module. As mentioned above, this may be less than the number of participants in the analysis population due to missing data.
    - In the quantitative modules describing continuous variables (and thus presenting sample size, means, and standard deviations), the sample size should be the number of non-missing observations. The number of missing observations, if any, will be noted.
    - For categorical variables that are presented in frequency tables, the module should present the total count in addition to the count in each category. Percentages should be calculated using this total as the denominator, and the percentage corresponding to the sum itself (that is, 100%) should be presented to indicate clearly to a reviewer the method of calculation. The number of missing observations, if any, will be noted.
- Sorting: Listings will be sorted by treatment group, participant number and date, if applicable. If a listing is sorted in a different manner, a footnote will indicate as such.
- General formatting rules: Rounding for all variables will occur only as the last step, immediately prior to presentation in listings, tables, and figures. No intermediate rounding will be performed on derived variables. The standard rounding practice of rounding numbers ending in 0-4 down and numbers ending in 5-9 up will be employed.
- Numerical Values: The presentation of numerical values will adhere to the following guidelines:
    - Raw measurements will be reported to the number of significant digits as captured electronically or on the CRFs.

- Standard deviations will be reported to one decimal place beyond the number of decimal places the original parameter is presented.
- Means will be reported to the same number of significant digits as the parameter.
- Calculated percentages will be reported with no decimals.

- Dates will be formatted as DDMMMYYYY. Partial dates will be presented on data listings as recorded on CRFs.
  - Time will be presented according to the 24-hour clock (HH:MM).

11. PROPOSED TABLES, LISTINGS, AND FIGURES

Summary Tables

Accountability and Baseline Characteristics

14.1.1.1 Participant Disposition, All Enrolled Participants
14.1.2.1 Demographics and Baseline Characteristics, Full Analysis Set
14.1.3.1 Disease Characteristics, Full Analysis Set
14.1.3.2 Summary of Prior Anti-Cancer Therapy, Full Analysis Set
14.1.3.3 Summary of Tissue Biomarkers, Full Analysis Set
14.1.4.1 Concomitant Medications, Full Analysis Set
14.1.4.2 Bevacizumab Administration, Full Analysis Set
14.1.4.3 Dexamethasone Use, Full Analysis Set
14.1.5.1 Summary of Study Drug Exposure, Safety Set

Efficacy

14.2.1.1 Summary of Best Overall Tumor Response and Duration of Response, Full Analysis Set
14.2.2.1 Summary of Overall Survival, Full Analysis Set

Safety

14.3.1.1 Overall Summary of Treatment-Emergent Adverse Events, Safety Set
14.3.1.2 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Greatest Severity, Safety Set
14.3.1.3 Treatment-Emergent Adverse Events Related to Study Drug or Catheter by System Organ Class, Preferred Term, and Greatest Severity, Safety Set
14.3.1.4 Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term, Safety Set
14.3.1.5 Treatment-Emergent Serious Adverse Events Related to Study Drug or Catheter by System Organ Class and Preferred Term, Safety Set
14.3.1.6 Treatment-Emergent Adverse Events of Special Interest by System Organ Class and Preferred Term, Safety Set
14.3.1.7 Treatment-Emergent Adverse Events with Grade $\geq$ 3 by System Organ Class and Preferred Term, Safety Set
14.3.1.8 Treatment-Emergent Adverse Events with Grade $\geq$ 3 and Related to Study Drug or Catheter by System Organ Class and Preferred Term, Safety Set
14.3.4.1 Summary of Grade Shifts in Laboratory Abnormalities – Hematology, Safety Set
14.3.4.2 Summary of Grade Shifts in Laboratory Abnormalities – Chemistry, Safety Set
14.3.4.3 Number of Participant with at Least One ALT, AST, or Total Bilirubin Above Upper Limit of the Normal Range Post-Baseline, Safety Set
14.3.4.4 Summary of Vital Signs by Visit, Safety Set
14.3.4.5 Summary of Karnofsky Performance Status Score by Visit, Safety Set

Summary Figures

Efficacy

14.2.1.2 Duration of Response – Kaplan Meier Curve, Full Analysis Set
14.2.2.2 Overall Survival – Kaplan Meier Curve, Full Analysis Set

Data Listings

16.1.7.1 Participant Enrollment
16.2.1.1 Participant Disposition
16.2.2.1 Inclusion/Exclusion Criteria
16.2.3.1 Analysis Sets
16.2.4.1 Demographics and Baseline Characteristics
16.2.4.2 Medical History
16.2.4.3 Disease Status
16.2.4.4.1 Prior Radiation Therapy
16.2.4.4.2 Post-Study Radiation Therapy
16.2.4.5.1 Prior Systemic Therapy
16.2.4.5.2 Post-Study Systemic Therapy
16.2.4.6.1 Prior and Concomitant Medications
16.2.4.7.1 Tissue Biomarkers and Core Biopsies
16.2.5.1.1 Lerapolturev Infusion
16.2.5.1.2 Lomustine Administration
16.2.5.1.3 Catheter Placement
16.2.6.1 Lesion Description
16.2.6.2 Lesion Assessment
16.2.6.3 Lesion Response
16.2.6.4 Brain Surgery
16.2.6.5 Follow-Up
16.2.6.6 Overall Survival
16.2.7.1 Adverse Events
16.2.7.2 Death
16.2.8.1 Laboratory Values – Hematology
16.2.8.2 Laboratory Values – Chemistry
16.2.8.3 Laboratory Values – Coagulation
16.2.8.4 Anti-Polio Virus Titer
16.2.8.5 COVID-19 Impact
16.2.9.1 Vital Signs
16.2.10.1 Karnofsky Performance Status