Treatment Evaluation and Data Monitoring

1. Purpose

1.1 To describe the procedures for obtaining and submitting patient data during active treatment, after treatment and long-term follow-up phases of the PaTK02 clinical trial.

2. Procedure

2.1 General Data Monitoring Procedures

2.1.1 Sponsor will centrally monitor the status of patient treatment and follow up, and notify the site of any issues through the generation of query reports. Data will also be monitored during central or in-person monitoring visits.

2.2 Treatment Phase Specific Procedures

2.2.1 Treatment Phase

2.2.1.1 For the **Test Arm** the treatment phase begins the day of first Adv-tk injection and extends through approximately 30 days after last dose of valacyclovir. For the **Control Arm** the treatment phase begins the first day of chemoradiation and extends through approximately 3 weeks after surgery. Patients in the test arm will receive three courses of AdV-tk injection plus valacyclovir as described in protocol. The AdV-tk injection procedure is described in the Vector Storage and Administration SOP.

2.2.1.2 The **Treatment Evaluation (TA) form** will be used to record evaluations during chemoradiation treatment, during re-staging prior to surgery and approximately 3 weeks after surgery. This form includes a section for recording information on treatment compliance, a checklist of assessments (H&P, laboratories, etc.), and a section for recording medications. If there were any complications, these must be recorded on an Adverse Event form.

2.2.1.3 The procedure for reporting adverse events including serious adverse events (SAEs) is described in the Adverse Event Reporting SOP.

2.2.1.4 Deviations from the protocol specified treatment or follow-up including withdrawals before or during treatment will be reported on the Variance Form.

2.2.2 Post-Treatment Follow-Up Phase

2.2.2.1 For the **Test Arm** the Post-Treatment Phase begins about 30 days after last dose of valacyclovir, for the **Control Arm** the Post-Treatment Phase begins approximately 3 weeks after surgery. This evaluation will occur every 3-4 months after surgery for 2 years and then approximately every 6 months for 3 years, then yearly.

2.2.2.2 Post-Treatment evaluations include clinical assessment, imaging, quality of life and CA-19-9 as described in the protocol.

2.2.2.3 The **Post-Treatment Evaluation (AT) form** will be used to record these evaluations and for cause specific office visits during this time period. The form includes a checklist of evaluations and a page to record new medical problems.

2.2.3 **Disease Progression or Death**

2.2.3.1 If a patient develops clinical progression or death occurs, the **Progressive Disease or Death Form** must be completed.

2.2.3.2 Record the details of the determination of progression in **section I** of a **Progressive Disease or Death Form**. Attach copies of the supporting documentation (e.g. clinical note, pathology report, imaging).

2.2.3.3 If death occurs, **section II** of a **Progressive Disease or Death Form** should be completed with the date and cause of death. If an autopsy is performed, please attach a copy of the report, or detail the findings.