A. CLINICAL TRIAL INFORMATION:

1. **Clinical trial identification (including title of the trial and protocol number):**

TITLE OF STUDY:

A Phase 2 Randomized, Double-Blind, Placebo-Controlled Clinical Trial to Determine the Safety and Efficacy of GL-0817 (with Cyclophosphamide) for the Prevention of Recurrence in HLA-A2+ Patients with High-Risk Squamous Cell Carcinoma of the Oral Cavity

Sponsor Protocol Number: GL0817-01

2. **Identifiers (including EU trial number, other identifiers):**

EudraCT Number: 2016-001256-22

3. **Sponsor details (including scientific and public contact points):**

Gliknik Inc.
801 W. Baltimore Street
Suite 501A
Baltimore, Maryland 21201 USA
(+1) 410-685-0662

4. **Paediatric regulatory details (including information whether the clinical trial is a part of a Paediatric Investigation Plan):**

This trials is not part of a Pediatric Investigation Plan.

5. **Result analysis stage (including information about intermediate data analysis date, interim or final analysis stage, date of global end of the clinical trial).**

The data provided in this report are the results of the primary endpoint analysis, 2-year disease-free interval since randomization.

6. **General information about the clinical trial (including information about main objectives of the trial, trial design, scientific background and explanation of rationale for the trial; date of the start of the trial, measures of protection of subjects taken, background therapy; and statistical methods used):**

This study was a phase 2 clinical trial of the 47-mer synthetic peptide GL-0817, directed against the cancer testis antigen, MAGE-A3, in combination with the vaccine adjuvants Hiltonol (poly-ICLC), Sargramostim (Leukine) and low-dose cyclophosphamide.

This was a multi-center, randomized, double-blind clinical trial to assess the safety and efficacy of GL-0817 as a means to prevent disease recurrence in patients considered at high-risk following surgery and adjuvant chemoradiotherapy. SCCOC patients, who had undergone primary gross total resection with histopathological evidence of high-risk disease and subsequent adjuvant radiation therapy with concomitant cisplatin, were evaluated for expression of the HLA-A2 blood phenotype and tumor MAGE-A3 expression (the latter for correlative purposes only).

Following chemo-radiotherapy, 80 HLA-A2+ patients deemed cancer free by CT scan (or CT-PET or MRI) or had positive imaging with negative biopsy within 6 weeks of randomization and meeting all

other eligibility criteria, were to be randomly assigned to active treatment/placebo at a 1:1 ratio and assigned to treatment using a stratified randomization based on global location and radiation technique (intensity modulated RT - yes or no).

Subjects assigned to active treatment were to be vaccinated with GL-0817 along with the adjuvants Poly-ICLC (Hiltonol®) and GM-CSF (Sargramostim, Leukine®) 3 times at 3-week intervals followed by 7 doses at 3-month intervals beginning at the Week 18 visit. In addition, these patients were to receive intravenous low dose systemic Cyclophosphamide (CY) 1 day prior to the first 3 vaccinations. Subjects assigned to the control arm were to receive placebo CY (normal saline solution) followed by Poly-ICLC/GM-CSF/placebo vaccine injections on the same schedule as the GL-0817 cohort.

The first vaccination was administered 4-8 weeks (28 to 56 days) following the completion of radiotherapy. This time interval was chosen to be as early as possible while allowing for adequate patient recovery and immune system reconstitution. Initiation of vaccinations 4-8 weeks (28-56 days) following chemo-radiotherapy would also allow for interpretation of the radiographic studies and for biopsies of suspicious lesions if necessary. A diagram of the study schedule is provided below.

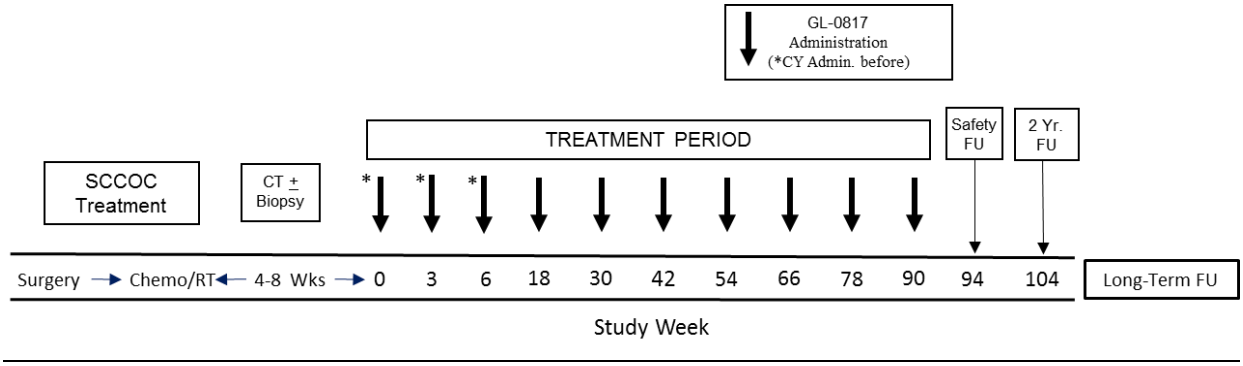


Figure 1 Schema for Study GL0817-01

The objectives of the trial were as follows:

Primary Objective

To compare the disease-free interval of all randomized subjects in the primary analysis population by treatment arm at 2 years following randomization.

Secondary Objectives

- Compare disease-free survival (DFS), overall survival (OS)
- Compare disease-free interval in a per protocol analysis
- Safety Assessment

Exploratory Objectives

- Correlation of MAGE-A3 expression and clinical efficacy
- Correlation of immune biomarker response with clinical efficacy,
- Assessment of risk profiling in predicting likelihood of SCCOC clinical recurrence

7. Population of subjects (including information with actual number of subjects included in the clinical trial in the Member State concerned, in the Union and in third countries; age group breakdown, gender breakdown).

B. SUBJECT DISPOSITION:

1. Recruitment (including information on the number of subjects screened, recruited and withdrawn; inclusion and exclusion criteria; randomization and blinding details; investigational medicinal products used)

A total of 249 patients were screened. The majority failed for the initial screen for the HLA-A2 status for which 35% was the anticipated rate for HLA-A2 positivity. A total of 80 subjects were enrolled and 77 received at least one vaccination.

	Screened	Randomized	Withdrawn
Number of Subjects	249	80	41

Table 1 Patient Disposition

Patient Disposition	GL-0817 (N=40)	Placebo (N=40)
Enrolled	40 (100%)	40 (100%)
Completed the Treatment Period	18 (45.0%)	21 (52.5%)
Discontinued Treatment	22 (55.0%)	19 (47.5%)
Primary Reason for Discontinuing Treatment:		
Death	4 (10.0%)	0
Adverse event	0	1 (2.5%)
Subject withdrew consent	3 (7.5%)	1 (2.5%)
Request of investigator	0	0
Treatment failure / Disease Progression	12 (30.0%)	16 (40.0%)
Non-compliance	1 (2.5%)	0
Protocol violation	0	0
Pregnancy	0	0
Sponsor requests subject to be withdrawn	0	0
Failed to return / lost to follow-up	1 (2.5%)	0
Other	1 (2.5%)	1 (2.5%)

2. **Pre-assignment Period**

Potential study subjects first signed consent for HLA screening. Those patients confirmed as HLA-A2+ entered the second screening period for which the following eligibility criteria applied:

Inclusion Criteria:

1. Age > 18 years
2. Histologic diagnosis of squamous cell carcinoma of the oral cavity
3. Subjects must have undergone primary gross total resection (no re-resected patients are allowed) with fulfillment of at least 1 of the following histologic criteria for high-risk disease:
    - Histologic involvement of 2 or more regional lymph nodes
    - Any involved lymph node with histologic extracapsular extension (ECS)
    - Close (<3mm) or positive surgical margins on microscopic evaluation with no gross residual tumor
4. No evidence of locoregional disease or distant metastases at screening. Subjects must have negative scans (CT, CT-PET or MRI) for locoregional recurrence, brain or lung metastases. A negative biopsy will be mandated in patients with a positive scan. Other evaluations should be performed as clinically indicated.
5. No history of distant metastases.
6. Tumor tissue from surgery or biopsy must be available to determine MAGE-A3 expression for correlative studies.
7. Following surgery, the patient received external beam radiotherapy (58-66 Gy in 2 Gy fractions, 5 days per week) with concomitant cisplatin starting within 8 weeks of surgery. The cumulative dose of cisplatin the subject received must be > 150 mg/m2. Protocol therapy must be initiated within a period of 4-8 weeks (28-56 days) following the end of RT.
8. The patient is, in the investigator's opinion, adequately recovered from the effects of surgery and chemoradiotherapy to participate in this study.
9. Blood HLA-A2 phenotype
10. ECOG Performance Status < 1
11. Laboratory values obtained ≤ 14 days prior to randomization:
    - Absolute neutrophil count (ANC) ≥ 1500/μL (without intervention, e.g., G-CSF)
    - Platelets ≥ 75,000/μL (without intervention, e.g., transfusion)
    - Hemoglobin ≥ 8.0 g/dL (Note: The use of transfusion or other intervention to achieve Hgb ≥8.0 g/dl is acceptable).
    - Alkaline phosphatase ≤ 2.5 x upper limit of normal (ULN)
    - AST and ALT ≤ 2 x ULN
    - Creatinine < 2 x ULN
    - Bilirubin < 1.5x ULN (except for patients with Gilbert's disease, for whom the upper acceptable limit of serum bilirubin is 3 mg/dL)
12. A female subject is eligible to enter the study if she is:
    - not pregnant or nursing; Female participants must not breastfeed during the study and for a period of 30 days following the last dose.
    - of non-childbearing potential (i.e., women who had a hysterectomy, are postmenopausal which is defined as 1 year without menses, have both ovaries surgically removed or have current documented tubal ligation); or
    - of childbearing potential (i.e., women with functional ovaries and no documented impairment of oviductal or uterine function that would cause sterility). This category includes women with oligomenorrhea [even severe], women who are perimenopausal or have just begun to menstruate. These women must have a negative serum pregnancy test at screening, and agree to one of the following:

  - complete abstinence from intercourse from 2 weeks prior to administration of the 1st dose of study agent until 6 months after the last dose of study agent; or
  - consistent and correct use of 1 of the following highly effective methods of birth control for one month prior to the start of the study agent and 6 months after the last dose:
- combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, transdermal)
- progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable)
- intrauterine device (IUD)
- intrauterine hormone-releasing system (IUS)
- bilateral tubal occlusion
- vasectomized partner (if vasectomized is the sole sexual partner and has received medical confirmation of surgical success)

13. A male subject who is sexually active with a woman of childbearing potential is eligible to enter the study if he agrees to use effective contraception throughout the study and for 6 months after the last dose of study agent.
14. The subject must be capable of understanding the investigational nature, potential risks and benefits of the study and capable of providing valid informed consent. The subject must provide study specific informed consent prior to any protocol procedures that are not a part of standard care, including consent for assessment of HLA-A2 status, mandatory tissue submission for MAGE-A3 analysis and correlative studies.
15. The subject must be willing to return to the study center for vaccinations and study-related follow up procedures including blood and tumor collections and completion of imaging studies as required by the protocol.

Exclusion Criteria:

1. Known HIV or hepatitis B/C infection (testing not required). Subjects who are hepatitis C antibody positive may be enrolled if they are confirmed to have a negative viral load at screening.
2. Subjects with active autoimmune disease or a history of autoimmune disease requiring systemic steroids or other immunosuppressive treatment.
3. Subjects who have used systemic corticosteroids or other immunosuppressants for any condition within 14 days of randomization. Inhaled or topical steroids are permitted.
4. Any medical condition which would, in the investigator's opinion, compromise the patient's ability to mount an immune response, renders the patient a poor candidate for this trial or could confound the results of the study
5. Major surgery or traumatic injury within 28 days randomization
6. Prior splenectomy or organ allograft
7. Any other prior, concurrent or planned chemotherapy, immunotherapy, radiotherapy, device, or investigational therapy for this cancer other than those specified in this study
8. History of other malignancy (i.e. excluding disease under study) within 3 years of randomization. Exceptions include adequately-treated basal cell or squamous cell skin cancer, carcinoma in situ of the cervix or breast, or adequately treated non-metastatic prostate cancer.
9. Known hypersensitivity to GM-CSF, yeast-derived products or any component of the GM-CSF drug product (e.g., mannitol) or poly-ICLC (e.g., carboxymethylcellulose).

1. **Post Assignment Periods.**

As noted previously, Subjects assigned to active treatment were to be vaccinated with GL-0817 along with the adjuvants Poly-ICLC (Hiltonol®) and GM-CSF (Sargramostim, Leukine®) 3 times at 3-week intervals followed by 7 doses at 3-month intervals beginning at the Week 18 visit. In addition, these patients were to receive intravenous low dose systemic Cyclophosphamide (CY) 1 day prior to the first 3 vaccinations. Subjects assigned to the control arm were to receive placebo CY (normal saline solution) followed by Poly-ICLC/GM-CSF/placebo vaccine injections on the same schedule as the GL-0817 cohort.

Following the last vaccination at Week 90, subjects returned for an End of Treatment visits on Week 94 to assess safety followed by the 2-year follow-up visit on Week 104 to assess disease status (efficacy).

C. BASELINE CHARACTERISTICS:

1. Baseline Characteristics (Required) Age;
2. Baseline Characteristics (Required) Gender;
3. Baseline Characteristics (Optional) Study Specific Characteristic.

Baseline characteristics are shown in Table 1.

Table 2 Study GL0817-01 Baseline characteristics of enrolled subjects

Parameter		GL-0817 (N=40)	Placebo (N=40)	Overall (N=80)
Age (yrs)	n	40	40	80
	#missing	0	0	0
	Mean (SD)	57.2 (10.90)	59.4 (10.21)	58.3 (10.55)
	Median	55.5	59.0	58.0
	Q1/Q3	53.0/63.0	54.5/64.0	53.5/64.0
	Minimum/Maximum	29/ 81	35/ 86	29/ 86
Race [n(%)]	N of Patients	40	40	80
	American Indian or Alaska Native	0	0	0
	Asian	0	0	0
	Black or African American	0	0	0
	Native Hawaiian or Other Pacific Islander	0	0	0
	White	40 (100%)	39 (97.5%)	79 (98.8%)
	Other	0	1 (2.5%)	1 (1.3%)
Ethnicity [n(%)]	N of Patients	40	40	80
	Hispanic or Latino	0	0	0
	Not Hispanic or Latino	40 (100%)	40 (100%)	80 (100%)
Gender [n(%)]	N of Patients	40	40	80
	Female	14 (35.0%)	14 (35.0%)	28 (35.0%)
	Male	26 (65.0%)	26 (65.0%)	52 (65.0%)
Global Location [n(%)]	N of Patients	40	40	80
	Eastern Europe	34 (85.0%)	32 (80.0%)	66 (82.5%)
	USA	0	1 (2.5%)	1 (1.3%)
	Western and Central Europe	6 (15.0%)	7 (17.5%)	13 (16.3%)

Parameter		GL-0817 (N=40)	Placebo (N=40)	Overall (N=80)
HLA Status [n(%)]	N of Patients	40	40	80
	Positive	40 (100%)	40 (100%)	80 (100%)
	Negative	0	0	0

D. END POINTS:

1. End point definitions:

The primary clinical endpoint of this study was disease-free interval (DFI) at 2 years, defined as the time from the date of randomization to the date of recurrence (any type – defined as an Overall Response of "Local-Regional Recurrence" or "Distant Recurrence"); subjects who died without recurrence or with whom contact was lost before recurrence were to be censored on the date of last disease evaluation visit. Subjects who died due to primary disease or due to unknown reason were also to be considered events at the time of death for the purpose of this analysis. If recurrent disease was found at a site that could not be sampled (e.g., spinal metastasis), the DFI was defined as time from randomization to the time of radiographic detection of the metastatic lesion. Only data up to 2-year follow-up visit was used to derive the primary endpoint. Patients without recurrence at 2-year follow up were to be considered censored at his timepoint. Death due to other causes without recurrence was treated as a competing risk.

The key secondary endpoint for the study, 2-year disease-free survival from randomization, was defined similarly to 2-year DFI, the only difference being that in case of death the subject is considered to have an event at the date of death. Overall survival was defined as the time from randomization to death from any cause.

2. DFI Statistical Analyses:

The primary endpoint analysis showed no benefit for the addition of GL-0817 treatment over standard of care definitive surgery followed by chemoradiotherapy in the treatment of high-risk head and neck squamous cell cancer (**Figure 2**). There were no differences in DFI, Disease-free survival or overall survival between the treatment arms.

As a result, Gliknik terminated the GL0817-01 trial and long-term follow-up of study subjects was discontinued. The clinical development program for GL-0817 has also been discontinued. There are no ongoing trials and Gliknik will conduct no further trials with this IMP.

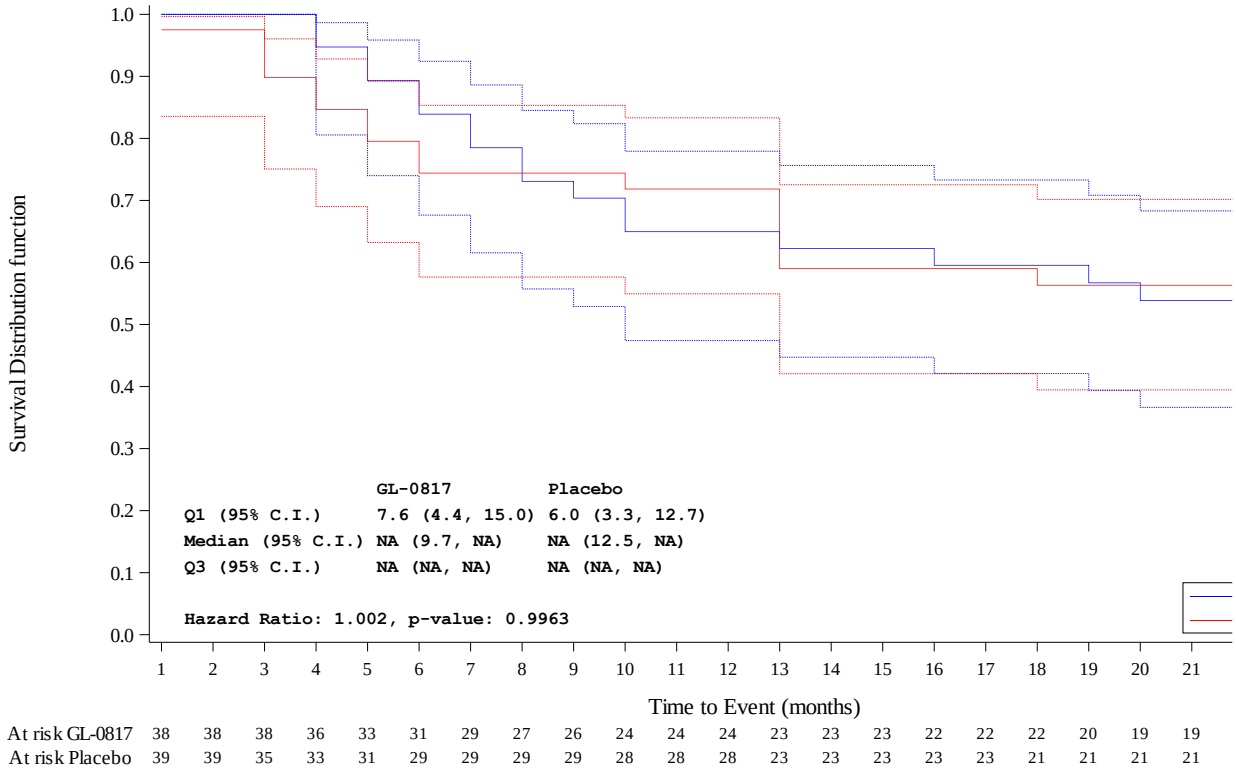


Figure 2 Kaplan-Meier Plot for DFI (ITT Population)

E. ADVERSE EVENTS:

1. Adverse events information

Eighty (80) patients were enrolled to the study GL0817-01 and 77 of them have received at least one dose of GL0817-01/Placebo.

Cumulatively, 1,001 non-serious AEs in 70 subjects and 11 SAEs in 10 subjects were reported in the GL0817-01 study (**Table 3**). Out of these, 881 AEs in 65 subjects were assessed by the Investigator as at least possibly related to GL-0817/ Placebo (i.e., Adverse Drug Reactions [ADRs]). The majority of these ADRs belonged to SOC General disorders and administration site conditions and Investigation:

- *Injection site pain* (267 AEs in 51 subjects)
- *Injection site induration* (83 AEs in 22 subjects)
- *Injection site erythema* (82 AEs in 19 subjects)
- *Injection site swelling* (74 AEs in 17 subjects)
- *Injection site oedema* (47 AEs in 12 subjects)
- *Pyrexia* (85 AEs in 22 subjects)
- *Hyperthermia* (35 AEs in 10 subjects)

- *Body temperature increased* (31 AEs in 10 subjects)

All ADRs were non-serious, and the majority were mild (90.5 %) to moderate (9.2 %) in intensity. Nearly all ADRs recovered without any need for action taken with GL0817-01/ Placebo except for 4 ADRs that resolved after GL-0817/ Placebo interruption. The majority of ADRs (93.5%) were self-limiting and recovered spontaneously without any treatment. Fifty-seven (57; 6.5%) ADRs, mostly of Hyperthermia and Pyrexia, required drug treatment.

2. Serious adverse events (SAE)

A list of all serious adverse events is provided in

Table 4. Cumulatively, 11 SAEs in 10 subjects were reported in the GL-0817-01 study. The most common reported terms were relevant for SOC Neoplasms benign, malignant and unspecified such as *Oesophageal carcinoma* (1), *Malignant neoplasm progression* (1) and *Metastases to lung* (1). Of note, disease progression was not supposed to be reported as an SAE in this study. However, if reported by the Investigator, it was recorded in the safety database.

From the 11 SAEs, 5 SAEs (in 4 subjects) were fatal, 4 SAEs were severe and 2 were life-threatening in intensity. Out of the life-threatening and severe SAEs, 4 resolved, and 2 resolved with sequelae. All SAEs were evaluated as not related to GL0817-01/Placebo either by the Investigator or the Sponsor.

Table 3 GL-0817 or Placebo/GM-CSF/Poly-ICLC Related Adverse Events by MedDRA SOC and Preferred Term (Safety Population)

SOC Term **Preferred Term**	**GL-0817 (N=38) N (%) Y**	**Placebo (N=39) N (%) Y**	**Overall (N=77) N (%) Y**	**P-value***
Any TEAE	34 (89.5%) 390	31 (79.5%) 491	65 (84.4%) 881	0.347
General disorders and administration site conditions	32 (84.2%) 319	28 (71.8%) 418	60 (77.9%) 737	0.272
Injection site pain	27 (71.1%) 123	24 (61.5%) 144	51 (66.2%) 267	0.472
Injection site induration	12 (31.6%) 41	10 (25.6%) 42	22 (28.6%) 83	0.620
Pyrexia	11 (28.9%) 43	11 (28.2%) 42	22 (28.6%) 85	1.000
Injection site erythema	6 (15.8%) 20	13 (33.3%) 62	19 (24.7%) 82	0.112
Injection site swelling	7 (18.4%) 29	10 (25.6%) 45	17 (22.1%) 74	0.584
Injection site oedema	6 (15.8%) 21	6 (15.4%) 26	12 (15.6%) 47	1.000
Injection site pruritus	4 (10.5%) 5	7 (17.9%) 23	11 (14.3%) 28	0.517
Hyperthermia	6 (15.8%) 18	4 (10.3%) 17	10 (13.0%) 35	0.517
Asthenia	4 (10.5%) 8	0	4 (5.2%) 8	0.055
Induration	2 (5.3%) 4	0	2 (2.6%) 4	0.240
Injection site warmth	0	2 (5.1%) 3	2 (2.6%) 3	0.494
Administration site pain	1 (2.6%) 3	0	1 (1.3%) 3	0.494
Administration site swelling	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Fatigue	0	1 (2.6%) 10	1 (1.3%) 10	1.000
Feeling cold	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Injection site inflammation	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Pain	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Swelling	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Swelling face	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Vaccination site pain	0	1 (2.6%) 2	1 (1.3%) 2	1.000
Investigations	9 (23.7%) 15	7 (17.9%) 28	16 (20.8%) 43	0.584
Body temperature increased	5 (13.2%) 8	5 (12.8%) 23	10 (13.0%) 31	1.000
Red blood cell sedimentation rate increased	0	2 (5.1%) 2	2 (2.6%) 2	0.494
Aspartate aminotransferase increased	1 (2.6%) 3	0	1 (1.3%) 3	0.494
Blood bilirubin increased	1 (2.6%) 2	0	1 (1.3%) 2	0.494
Blood pressure increased	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Neutrophil count increased	0	1 (2.6%) 1	1 (1.3%) 1	1.000

SOC Term Preferred Term	GL-0817 (N=38) N (%) Y	Placebo (N=39) N (%) Y	Overall (N=77) N (%) Y	P-value*
Platelet count decreased	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Weight decreased	1 (2.6%) 1	0	1 (1.3%) 1	0.494
White blood cell count increased	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Musculoskeletal and connective tissue disorders	9 (23.7%) 39	6 (15.4%) 10	15 (19.5%) 49	0.401
Myalgia	6 (15.8%) 15	3 (7.7%) 3	9 (11.7%) 18	0.310
Pain in extremity	4 (10.5%) 15	1 (2.6%) 2	5 (6.5%) 17	0.200
Back pain	0	2 (5.1%) 4	2 (2.6%) 4	0.494
Muscular weakness	1 (2.6%) 9	1 (2.6%) 1	2 (2.6%) 10	1.000
Gastrointestinal disorders	3 (7.9%) 4	2 (5.1%) 2	5 (6.5%) 6	0.675
Nausea	1 (2.6%) 1	1 (2.6%) 1	2 (2.6%) 2	1.000
Constipation	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Dysphagia	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Swollen tongue	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Vomiting	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Skin and subcutaneous tissue disorders	2 (5.3%) 4	3 (7.7%) 5	5 (6.5%) 9	1.000
Erythema	2 (5.3%) 2	1 (2.6%) 2	3 (3.9%) 4	0.615
Pruritus	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Psoriasis	0	1 (2.6%) 2	1 (1.3%) 2	1.000
Rash	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Skin exfoliation	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Blood and lymphatic system disorders	1 (2.6%) 3	2 (5.1%) 9	3 (3.9%) 12	1.000
Neutropenia	1 (2.6%) 3	1 (2.6%) 3	2 (2.6%) 6	1.000
Anaemia	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Leukopenia	0	1 (2.6%) 4	1 (1.3%) 4	1.000
Thrombocytopenia	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Metabolism and nutrition disorders	2 (5.3%) 2	1 (2.6%) 1	3 (3.9%) 3	0.615
Decreased appetite	2 (5.3%) 2	0	2 (2.6%) 2	0.240
Dehydration	0	1 (2.6%) 1	1 (1.3%) 1	1.000

SOC Term **Preferred Term**	**GL-0817 (N=38) N (%) Y**	**Placebo (N=39) N (%) Y**	**Overall (N=77) N (%) Y**	**P-value***
Nervous system disorders	0	3 (7.7%) 13	3 (3.9%) 13	0.240
Head discomfort	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Headache	0	1 (2.6%) 10	1 (1.3%) 10	1.000
Somnolence	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Syncope	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Vascular disorders	1 (2.6%) 1	2 (5.1%) 3	3 (3.9%) 4	1.000
Hypotension	1 (2.6%) 1	1 (2.6%) 2	2 (2.6%) 3	1.000
Hypertension	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Ear and labyrinth disorders	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Vertigo	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Psychiatric disorders	1 (2.6%) 2	0	1 (1.3%) 2	0.494
Insomnia	1 (2.6%) 2	0	1 (1.3%) 2	0.494
Renal and urinary disorders	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Proteinuria	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Respiratory, thoracic and mediastinal disorders	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Epistaxis	0	1 (2.6%) 1	1 (1.3%) 1	1.000

Table 4 Serious Adverse Events (SAEs) by MedDRA SOC and Preferred Term (Safety Population)

SOC Term Preferred Term	GL-0817 (N=38) N (%) Y	Placebo (N=39) N (%) Y	Overall (N=77) N (%) Y	P-value*
Any TEAE	6 (15.8%) 6	4 (10.3%) 4	10 (13.0%) 10	0.517
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2 (5.3%) 2	1 (2.6%) 1	3 (3.9%) 3	0.615
Malignant neoplasm progression	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Metastases to lung	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Oesophageal carcinoma	0	1 (2.6%) 1	1 (1.3%) 1	1.000
General disorders and administration site conditions	2 (5.3%) 2	0	2 (2.6%) 2	0.240
Death	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Multiple organ dysfunction syndrome	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Respiratory, thoracic and mediastinal disorders	1 (2.6%) 1	1 (2.6%) 1	2 (2.6%) 2	1.000
Pulmonary embolism	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Respiratory failure	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Gastrointestinal disorders	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Gastric ulcer perforation	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Infections and infestations	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Osteomyelitis	1 (2.6%) 1	0	1 (1.3%) 1	0.494
Metabolism and nutrition disorders	0	1 (2.6%) 1	1 (1.3%) 1	1.000
Hyponatraemia	0	1 (2.6%) 1	1 (1.3%) 1	1.000

F. ADDITIONAL INFORMATION:

1. Global Substantial Modifications:

The protocol was amended twice. A summary of modifications for the amendments is provided below.

Amendment 1 Summary of Modifications and Rationale (24 May 2016):

- The duration between mixing of the adjuvants with GL-0817/Placebo was extended to 60 minutes (formerly 30 minutes) in order to allow more time to administer study drug to trial subjects. The sponsor conducted a study demonstrating that when GL-0817 is mixed with poly-ICLC and GM-CSF, the mixed suspension/solution does not form aggregates, doesn't change appearance over at least one hour and is easily passed through a tuberculin needle.
- Immunogenicity testing was removed from long-term follow-up in the case of tumor recurrence based on feasibility of obtaining a sufficient number of samples for analysis.
- Modification of OSHA reference and addition of one reference (Lu 2004) which had been inadvertently omitted.

Amendment 2 Summary of Modifications and Rationale:

- The informed consent process was modified to provide the option to collect initial consent for HLA testing earlier in the patient's treatment course so HLA-eligible patients can be identified earlier and tracked more closely for study entry while HLA-ineligible patients can be considered for alternate therapies.
- Inclusion criteria were modified to specify anatomical sites in the oral cavity and allow a delay in initiating radiotherapy beyond 8 weeks only to start radiation therapy the following Monday.
- Added exclusion for known hypersensitivity to cyclophosphamide, its metabolites or any other components, or known urinary outflow obstruction per the package insert.
- A new lot of Hiltonol® (poly-ICLC) was released for use in this study. The label concentration of the Active Pharmaceutical Ingredient (Poly-IC) in Hiltonol is changed from 2 to 1.8 mg/ml poly-IC. This change does not constitute a change from the actual historic concentration of poly-IC for most prior lots of Hiltonol®, but rather reflects reporting of 'dry' weight vs 'wet' weight in the calculation of the lyophilized components in Hiltonol. It is not expected that this change should have an impact on dosing, safety or the biologic response to Hiltonol® in humans.
- Tumor staging for this study implemented the 2017 revised staging criteria changes in the American Joint Committee on cancer eighth edition cancer staging manual. Appendix 3 has been added to provide the latest staging criteria and the reference has been added.
- Administrative modifications were made to correct inconsistencies between sections of the protocol.

2. Global Interruptions and re-starts

There were no significant interruptions during the duration of enrollment/treatment period for this study. The last subject / last visit date for the 2-year treatment period was on 17 May 2021.

3. **A declaration by the submitting party on the accuracy of the submitted information.**

Gliknik Inc. hereby declares that to the to the best of its knowledge, the information in this application is accurate.

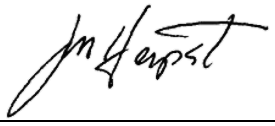
SIGNATURE OF SPONSOR'S REPRESENTATIVE

TITLE OF STUDY:

A Phase 2 Randomized, Double-Blind, Placebo-Controlled Clinical Trial to Determine the Safety and Efficacy of GL-0817 (with Cyclophosphamide) for the Prevention of Recurrence in HLA-A2+ Patients with High-Risk Squamous Cell Carcinoma of the Oral Cavity

Sponsor Protocol Number: GL0817-01

I have read this report and confirm that, to the best of my knowledge, it accurately describes the conduct and results of the study.

	15 September 2021
Jeffrey M. Herpst, RN, OCN Sr. Director, Clinical Development Gliknik Inc.	Date