6. SYNOPSIS

Name of Company:
Enlivex Therapeutics R&D Ltd**.**

Name of Finished Product:
Allocetra-OTS

Name of Active Ingredient(s):
Allocetra-OTS

Title of Study: A Phase 1/2a Study Evaluating Allocetra-OTS as Monotherapy or in Combination with Anti-PD-1 Therapy for the Treatment of Advanced Solid Tumor Malignancy

Protocol Number: ENX-CL-04-002a

Study Phase: 1/2a
Date of first patient, first visit: 04 Oct 2022
Date of last patient, last visit: 30 Jan 2024

Study Centers:
Five sites located in Israel and Spain enrolled study patients.

Publication:
Not applicable

Objectives and Endpoints:

Primary Objectives:

1. To assess the safety and to identify the MTD of Allocetra-OTS as monotherapy when repeatedly administered via IV or IP infusion in patients with advanced solid tumor malignancy (applicable to Stage 1).
2. To assess the safety and to identify the MTD of Allocetra-OTS administered via IV or IP infusion in combination with anti-PD1 therapy (nivolumab or tislelizumab) in patients with advanced solid tumor malignancy (applicable to Stage 2.1 and Stage 2.2).

Secondary Objectives:

1. To assess preliminary efficacy parameters following IV or IP administration of Allocetra-OTS as monotherapy in patients with advanced solid tumor malignancy (applicable to Stage 1).
2. To assess preliminary efficacy parameters following IV or IP administration of Allocetra-OTS in combination with anti-PD1 therapy (nivolumab or tislelizumab) in patients with advanced solid tumor malignancy (applicable to Stage 2.1 and Stage 2.2).

Exploratory Objectives:

1. To assess the effect of Allocetra-OTS with or without anti-PD1 therapy on the immunological profile and applicable tumor biomarkers of patients with advanced solid tumor malignancies.
2. To assess the burden of ascites in cases in which Allocetra-OTS is administered IP.

Primary Endpoint:

1. Stage 1: Characterize the safety of Allocetra-OTS from the first infusion of Allocetra-OTS up to Day 21, based on the DLTs and MTD (or MAD if no MTD is defined) of Allocetra-OTS as monotherapy.
2. Stage 2.1: Characterize the safety of Allocetra-OTS from the first infusion of Allocetra-OTS up to Day 35, based on the DLTs and MTD (or MAD if no MTD is defined) of Allocetra-OTS in combination with nivolumab.
3. Stage 2.2: Characterize the safety of Allocetra-OTS from the first infusion of Allocetra-OTS up to Day 28, based on the DLTs and MTD (or MAD if no MTD is defined) of Allocetra-OTS in combination with tislelizumab.

Secondary Endpoints:

1. Overall Response Rate (ORR)/Best Overall Response Rate (BORR) (percentage of patients who achieve best response of complete response [CR] or partial response [PR]).

2. Clinical benefit rate (CBR) (percentage of patients who achieve best response of CR, PR or stable disease [SD] ≥6 months). (Stage 1 and 2).
3. Duration of response (DoR), defined as the time from first documented evidence of CR or PR until disease progression or death.
4. Time to response (TTR), defined as the time from first infusion of Allocetra-OTS to the first documented CR or PR.
5. Kaplan-Meier estimated median progression-free survival (PFS), defined as the time from the first infusion of Allocetra-OTS to disease progression or death due to any cause, whichever occurs first.
6. Kaplan-Meier estimated median overall survival (OS) defined as the time from the first infusion of Allocetra-OTS to death due to any cause.

All secondary endpoints were applicable to both Stage 1 and Stage 2 (Stage 2.1 and Stage 2.2) of the study, unless otherwise specified.

Exploratory Endpoints:

1. Changes in immune cell/ cytokine profiling in peritoneal fluid (applicable to Stage 1, and Stage 2 for patients receiving Allocetra-OTS IP).
2. Changes in immune cell/ cytokine profiling in peripheral blood (applicable to Stage 1 and Stage 2 for patients receiving Allocetra-OTS IV).
3. Detection of human leukocyte antigen (HLA) antibodies (applicable to Stage 1 and Stage 2).
4. Frequency and amount of peritoneal fluid paracentesis (applicable to Stage 1, and Stage 2 for patients receiving Allocetra-OTS IP).

Changes in applicable tumor specific markers (applicable to Stage 1 and Stage 2).

Study Design:

This was an open-label, non-randomized, multicenter, Phase 1/2a study comprising two stages. The study was designed to evaluate the safety and potential efficacy of Allocetra-OTS in the treatment of advanced solid tumor malignancy as monotherapy (Stage 1), and in combination with an anti-PD-1 therapy (nivolumab or tislelizumab) (Stage 2.1 and Stage 2.2, accordingly).

In all stages, the starting dose of Allocetra-OTS was to be 2.5×10^9 cells. Dose escalation to the maximum administered dose (MAD) of 10×10^9 cells was to proceed using a conventional 3+3 design and decision rules as specified below. These procedures were to apply to Stage 1 (Allocetra-OTS monotherapy) and Stage 2.1 and 2.2 (Allocetra-OTS in combination with anti-PD-1 therapy). Stage 1 dose escalation was to be initiated first. Stage 2 dose escalation was to be triggered based on the demonstration of acceptable safety of Allocetra-OTS monotherapy in the first dose level of Stage 1 (Dose Level 1, 2.5×10^9 cells; see study schema in Section 2).

The route of administration of Allocetra-OTS intravenous (IV) or intraperitoneal (IP) was to be determined according to the tumor location.

At least 3 patients were to be treated with IV Allocetra-OTS prior to initiating IP treatment at each dose level (for both Stage 1 and Stage 2.1 or Stage 2.2, whichever occured first).

Subsequently, dose escalation for each route of administration of Allocetra-OTS (IV/IP) was to proceed, allowing to proceed to Stage 2.1 or Stage 2.2 with one route of administration, once dose level 1 of Stage 1 for that route of administration was complete.

For the purpose of guiding dose escalation decisions, DLT was to be defined as outlined in Section 6.2 of the protocol based on study drug-related events that occur during the DLT evaluation period for Allocetra-OTS monotherapy (Stage 1), and the combined Allocetra-OTS + anti-PD-1 therapy (Stage 2.1 or Stage 2.2).

Initially three patients were to be enrolled on the starting dose of Allocetra-OTS (2.5×10^9 cells). Treatment of the first two patients treated in each stage (in Stage 1; and in Stage 2.1 or in Stage 2.2, whichever occurs first) was to be staggered by an interval of 21 days, allowing to complete a 21-day safety evaluation.

Dose escalation was to proceed if zero of the initial three patients experienced a DLT, and the next three patients were to be enrolled at the next dose level. If one of the initial three patients experienced a DLT, up to three additional patients were to be enrolled at that dose. Dose escalation was to proceed if zero of the next three

patients experienced DLT. All escalations to subsequent dose levels were to be subject to confirmation by the Data Safety Monitoring Board (DSMB).

If two or more of the initial three patients or two or more of the six patients experienced a DLT, that dose level was to be deemed to exceed the maximum tolerated dose (MTD). If the MTD was exceeded in any of the high dose cohorts (10×10^9 cells), an additional cohort was to be enrolled and treated with an intermediate dose (5×10^9 cells).

The aforementioned decision rules were to govern the conduct of dose escalation for both Stage 1 and Stage 2.1 or Stage 2.2. The MTD for each stage and for each route of administration of Allocetra-OTS was to be defined independently.

At the discretion of the Sponsor, once a cohort was completed, and escalation to the subsequent dose level had been confirmed by the DSMB, up to an additional 3 patients could be treated to further characterize the DLT and safety profile at the dose level that had been cleared for safety. This was to be designated as "backfilling" a cohort.

Stage 1: Allocetra-OTS monotherapy

Stage 1 was to commence with a dose escalation of Allocetra-OTS to evaluate the safety of two proposed doses of the investigational product and/or to determine the MTD. Stage 1 was to include four cohorts, as described in Table 1. Dose escalation and definition of the MTD for each route of administration (IV/IP) was to proceed separately.

Table 1: Stage 1 Cohorts

Cohort	**Allocetra-OTS***	
	Dose per Infusion	**Administration Route**
1 (3-6 patients)	2.5×10^9 cells	IV every week x3
2 (3-6 patients)	10×10^9 cells	
3 (3-6 patients)	2.5×10^9 cells	IP every week x3
4 (3-6 patients)	10×10^9 cells	

*Manufacturing approved range for doses is ±20%

After a patient had signed the informed consent form (ICF) and after confirmation of eligibility, the patient was to be enrolled in Stage 1. Patients were to be treated with three Allocetra-OTS infusions with 1-week interval between them (Days 0, 7, and 14). Patients were to be followed up for safety and DLT throughout the treatment period and through one week after the last infusion (Day 21).

Further follow-up was to be carried out as described.

Once the safety profile of Allocetra-OTS monotherapy at the low dose (IV Cohort #1 or IP Cohort #3; 2.5×10^9 cells) was assessed by a review of the 21 days safety data, and/or the MTD for any of the administration routes was determined, Stage 2 (stage 2.1 or 2.2) of the clinical trial was to be initiated at the low dose of Allocetra-OTS (2.5×10^9 cells) at the relevant route of administration, in combination with IV anti-PD-1 therapy (nivolumab or tislelizumab).

Stage 2.1: Allocetra-OTS in combination with anti-PD-1 therapy (nivolumab)

The purpose of Stage 2.1 was to assess administration of Allocetra-OTS administered IV or IP in combination with IV anti-PD1 therapy nivolumab.

Stage 2.1 was to comprise four cohorts, Cohort 5-8, as described in Table 2. Allocetra-OTS was to be infused IV or IP according to the tumor location, with IV nivolumab 240 mg. Dose escalation and definition of the MTD for each Allocetra-OTS route of administration (IV/IP) were to proceed separately.

Patients were to be treated with three IV or IP Allocetra-OTS infusions, once every two weeks (Days 0, 14, and 28), which were to be planned to coincide with the days the patients were scheduled to receive IV nivolumab.

Table 2: Stage 2.1 Cohorts

Cohort	Allocetra-OTS dose*, route of administration, and combination
5 (3-6 patients)	2.5×10^9 cells, IV, with IV nivolumab 240 mg every 2 weeks x 3
6 (3-6 patients)	10×10^9 cells, IV, with IV nivolumab 240 mg every 2 weeks x 3
7 (3-6 patients)	2.5×10^9 cells, IP, with IV nivolumab 240 mg every 2 weeks x 3
8 (3-6 patients)	10×10^9 cells, IP, with IV nivolumab 240 mg every 2 weeks x 3

*Manufacturing approved range for doses was ±20%

After a patient had signed the ICF and after confirmation of eligibility, the patient was to be enrolled in Stage 2.1. Patients were to be monitored for safety and DLT throughout the treatment period (4 weeks) and through one week after the last infusion of Allocetra-OTS (Day 35).

Patients who completed the combination treatments and did not have disease progression were to be offered continued treatment with nivolumab for the duration of the study, until there is evidence of disease recurrence/progression, or per local regulations. Other reasons to discontinue nivolumab treatment could include adverse events or per the Investigator's decision.

Further follow-up was to be carried out as described. An End of Treatment visit was to occur within 30 days of final administration of study treatment.

Stage 2.2: Allocetra-OTS in combination with anti-PD-1 therapy (tislelizumab)

The purpose of Stage 2.2 was to assess administration of Allocetra-OTS administered IV or IP in combination with IV anti-PD1 therapy tislelizumab.

Stage 2.2 was to comprise four cohorts, Cohort 9-12, as described in Table 3. Allocetra-OTS was to be infused IV or IP according to the tumor location, with IV tislelizumab 200 mg. Dose escalation and definition of the MTD for each Allocetra-OTS route of administration (IV/IP) were to proceed separately.

Patients were to be treated with three IV or IP Allocetra-OTS infusions, once every three weeks (Days 0, 21, and 42), which were to be planned to coincide with the days the patients were scheduled to receive IV tislelizumab.

Table 3: Stage 2.2 Cohorts

Cohort	Allocetra-OTS dose*, route of administration, and combination
9 (3-6 patients)	2.5×10^9 cells, IV, with IV tislelizumab 200 mg every 3 weeks x 3
10 (3-6 patients)	10×10^9 cells, IV, with IV tislelizumab 200 mg every 3 weeks x 3
11 (3-6 patients)	2.5×10^9 cells, IP, with IV tislelizumab 200 mg every 3 weeks x 3
12 (3-6 patients)	10×10^9 cells, IP, with IV tislelizumab 200 mg every 3 weeks x 3

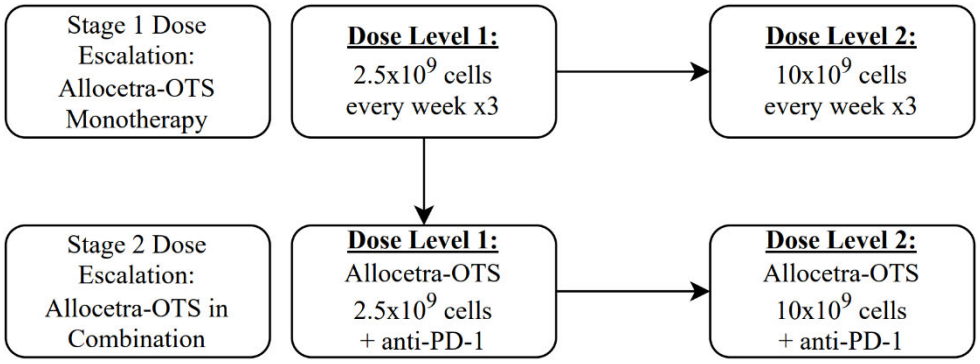
*Manufacturing approved range for doses was ±20%

After a patient had signed the ICF and after confirmation of eligibility, the patient were to be enrolled in Stage 2.2. Patients were to be monitored for safety and DLT throughout 28 days after the first infusion.

Patients who completed the combination treatments and did not have disease progression were to be offered continued treatment with tislelizumab for the duration of the study, until there is evidence of disease recurrence/progression, or per local regulations. Other reasons to discontinue tislelizumab treatment could include adverse events or per the Investigator's decision.

Further follow-up was be carried out as described. An End of Treatment visit was to occur within 30 days of final administration of study treatment.

Figure 1: Dose Escalation Scheme (applicable to IV or IP route of administration)



[1] Dose escalation performed separately for IV and IP Allocetra-OTS

[2] If the MTD was exceeded in any of the high dose cohorts (Dose Level 2), an additional cohort was to be enrolled and treated with an intermediate dose (5×10^9 cells).

Number of Patients (planned and analyzed):

Stage 1: 12-24 patients planned. Nine patients enrolled and treated.

Stage 2.1: 12-24 patients planned. Four patients enrolled and treated.

Stage 2.2: 12-24 patients planned. No patients enrolled.

A total of 13 patients were enrolled and treated up to study termination.

Diagnosis and Main Criteria for Inclusion:

Adult patients with locally advanced, unresectable or metastatic solid tumors, that had relapsed or had been refractory to available approved standard of care therapies specific to their cancer type, based upon standard clinical practice guidelines, with agents that are approved and available to them. Patients who were either not eligible for or had specifically declined additional standard care systemic therapy could also have been enrolled.

For patients who were ineligible for standard of care therapy, the rationale for these patients being deemed intolerant/unsuitable to be treated with SOC therapy had to be well documented. For patients who specifically declined standard of care therapy, documentation that the patient had been informed of these alternatives to treatment on this study were to be documented in the medical record.

Peritoneal tumors or peritoneal spread (peritoneal carcinomatosis) for IP administration of Allocetra-OTS included ovarian/fallopian tube/primary peritoneal cancer, gastric cancer, colorectal cancer, pancreatic cancer, and other rare peritoneal tumors, with no or minimal extraperitoneal disease (as per Investigator discretion). See detailed inclusion/ exclusion criteria in the study protocol.
Test Product, Dose and Mode of Administration: Allocetra-OTS is a cell-based therapeutic comprised of allogeneic non-HLA matched peripheral blood mononuclear cells (PBMCs) induced to an apoptotic state. Allocetra-OTS was to be provided in up to four cryopreservation bags, each containing 2.5×10^9 cells, suspended in a solution containing 50% Plasma-Lyte and 50% CryoStor® CS5 (final Dimethyl Sulfoxide (DMSO) concentration of 2.5%), to a total volume of 100 mL. Allocetra-OTS was to be administered IV or IP as a monotherapy in Stage 1, or in combination with IV nivolumab (in Stage 2.1) or IV tislelizumab (in Stage 2.2). Allocetra-OTS was to be administered at one of the following doses: 2.5×10^9 cells, or 10×10^9 cells. An intermediate dose of 5×10^9 cells could be initiated if the MTD was determined to be exceeded at the highest dose level. Allocetra-OTS was stored at ≤-150°C (in liquid nitrogen). Short-term storage at -80°C could be used, according to the secondary label. Allocetra-OTS administration was done following administration of pre-medication including acetaminophen/paracetamol, diphenhydramine/ dexchlorpheniramine, and hydrocortisone. Prior to its administration, each Allocetra-OTS bag was thawed separately and then infused within 2 hours. IV infusion of Allocetra-OTS was performed via adjusted filter and using a volumetric pump. IP infusion of Allocetra-OTS was performed via a tunnelled IP catheter or via an IP port. In Stage 2.2: on the days of infusion, tislelizumab was to be infused first, followed by an appropriate monitoring period before Allocetra-OTS administration would start.
Reference Therapy, Dose and Mode of Administration, and Lot Number(s): Not applicable

Duration of Treatment:

The study was designed as two consecutive stages, Stage 1 and Stage 2, which was to include Stage 2.1 and Stage 2.2, as described below. Each patient was to be recruited to one of the stages only. The duration of study participation was to be approximately 12 months for each patient in Israel, and approximately 24 months for each patient in Spain.

Stage 1:

Screening: up to 28 days.

Treatment period: approximately 14 days: there were to be three infusions of Allocetra-OTS, on Days 0, 7, and 14.

Dose-limiting toxicity (DLT) evaluation: safety was to be assessed continuously throughout the treatment period and extending to one week after the last infusion (Day 14), i.e., to Day 21.

Main study Follow-up: follow-up was to be carried out following the last infusion of Allocetra-OTS up to disease progression, death, withdrawal of consent, whichever of these events occured earlier, or up to 12 months post first infusion, with safety and efficacy assessments performed at six weeks, then every eight weeks, and with a survival follow-up at 12 months.

Survival follow-up at 6 and 12 months following the first Allocetra-OTS infusion was to be carried out for patients who discontinue the study but have not withdrawn consent.

In Spain only - Long-term follow-up: after completion of the 12 months study, patients were to be followed up for safety for another 12 months. During this long-term follow up, patients were to be contacted via the phone every 4 months to record SAEs that have occurred since last site contact. In case an SAE had occurred, the site was to collect all available SAE-related data and report the SAE to Enlivex or delegate within 24 hours of the site becoming aware of the SAE.

Stage 2.1 Allocetra-OTS and Nivolumab:

Screening: up to 28 days.

Treatment period: approximately four weeks: there were to be three infusions of Allocetra-OTS concomitant with administration of anti-programmed cell death protein 1 (PD-1) therapy (nivolumab). The three Allocetra-OTS infusions were to be planned to coincide with the days the patients are scheduled to receive the anti-PD-1 therapy, i.e., every two weeks.

DLT evaluation: safety was to be assessed continuously throughout the treatment period and extending to one week after the last infusion (Day 28), i.e., to Day 35.

Patients who completed the combination treatments and did not have disease progression were to be offered continued treatment with nivolumab for the duration of the study, until there is evidence of disease recurrence/progression, or per local regulations.

Stage 2.1 dose escalation was to continue until Stage 2.2 is initiated. Once Stage 2.2 was to be initiated, the opening of new cohorts on Stage 2.1 was to be halted, per Sponsor discretion.

Stage 2.2 Allocetra-OTS and Tislelizumab:

Screening: up to 28 days.

Treatment period: approximately six weeks: there were to be three infusions of Allocetra-OTS concomitant with administration of anti-PD-1 therapy (tislelizumab). The three Allocetra-OTS infusions were to be planned to coincide with the days the patients are scheduled to receive tislelizumab anti-PD-1 therapy, i.e., every three weeks.

DLT evaluation: safety was to be assessed continuously throughout 28 days following the first infusion.

Patients who completed the combination treatments and did not have disease progression were to be offered continued treatment with tislelizumab for the duration of the study, until there is evidence of disease recurrence/progression, or per local regulations.

Main study Follow-up period for Stage 2.1 and 2.2: follow-up was to be carried following the last infusion of Allocetra-OTS up to disease progression, death, withdrawal of consent, or up to 12 months post first infusion, whichever of these events occured earlier, with safety and efficacy assessments performed every eight weeks, and with a survival follow-up at 12 months.

Survival follow-up at 6 and 12 months following the first Allocetra-OTS infusion was to be carried out for patients who discontinued the study but had not withdrawn consent.

In Spain only - Long-term follow-up: after completion of the 12 months study, patients were to be followed up for safety for another 12 months. During this long-term follow up, patients were to be contacted via the phone every 4 months to record SAEs that have occurred since last site contact. In case an SAE had occurred, the site was to collect all available SAE-related data and report the SAE to Enlivex or delegate within 24 hours of the site becoming aware of the SAE.

For patients with persistent treatment-related adverse events at the last scheduled follow-up visit, follow-up was to continue pending resolution of the event, or the event is deemed stable and/or irreversible.

Statistical Methods:

This was an open-label, non-randomized, multicenter, Phase 1/2a study, which was not aimed to be powered for efficacy; therefore, no sample size calculation was performed. Cohorts of up to six patients were deemed sufficient to respond to safety and preliminary efficacy objectives.

Replacement of patients who discontinued the study prior to completing full safety evaluation period (21 days for Stage 1, 35 days for Stage 2.1 and 28 days for Stage 2.2) was allowed.

Baseline was defined as last available data prior to first Allocetra-OTS infusion.

The safety population consisted of all patients who received at least one dose of Allocetra-OTS (treated population), including patients withdrawn for any reason from the study. The safety population served as the main analysis set for the safety endpoints in both stages of the study.

Treatment Emergent Adverse Events (TEAEs) were defined as all AEs that start or worsen on or after the start of first Allocetra-OTS infusion.

Adverse events were classified by Medical Dictionary for Regulatory Activities system organ class and preferred term.

Overall responses were assessed according to RECIST v1.1/iRECIST for all patients with response data.

Safety Analysis

The data emerging from this study were to be reviewed periodically by the DSMB and recommendations to be provided to the Sponsor.

Ongoing safety assessments were used to monitor the following events, and alert the DSMB. A safety alert was to be triggered to allow prompt consideration of early stopping or modification of the protocol if one of the following criteria was met:

1. Any death within 30 days of receiving Allocetra-OTS other than for progressive disease (PD).

2. Any death that is at least possibly related to study treatment.

Changes in the Study Conduct:

On September 11th, 2023 the Sponsor decided to terminate further recruitment to the study as a result of strategic reprioritization of the Oncology development program. Patients on the study continued with safety follow-up according to the study protocol.

Study Population Results:

Until the termination of study recruitment, a total of 15 patients were screened for the study, and 13 patients were treated. Screen failures were due to limitations in venous access or contraindication to imaging.

Overall, 7 patients completed 3 IV Allocetra doses, two patients completed 3 IP Allocetra doses, 3 patients completed 3 combined Allocetra + nivolumab doses, and one patient completed 2 combined Allocetra + nivolumab doses and one Allocetra dose (nivolumab held).

[redacted]

All the treated patients received the full Allocetra dose according to the allocated cohort. In one case the 3rd combined treatment of nivolumab + Allocetra was held due to suspected reaction to nivolumab, and only Allocetra was infused.

Efficacy Results:

The study secondary endpoints aimed to assess the efficacy of Allocetra treatment or combined Allocetra + anti-PD1 antibody treatment. [redacted]

The patients included in the study had advanced solid tumors unresponsive to approved therapies. Most of the patients had multiple prior treatment lines, rendering their disease highly refractory to treatment. In protocol version 5, the protocol was modified to limit the number of prior treatment lines, to allow further characterization of treatment responses to Allocetra in patients with slightly less advanced malignant disease, however the study was terminated prior to implementation. Furthermore, only a few patients were treated with the Allocetra high dose by the time the study was terminated – only 4 patients in the intravenous Allocetra cohort, and 2 patients in the intraperitoneal Allocetra cohort. No patients received the combined high dose Allocetra and nivolumab treatment. Under these circumstances, the ability to observe treatment responses was limited.

Safety Results:

Among the 13 patients treated, all patients received the full Allocetra dose according to the allocated cohort – 11 patients received Allocetra intravenous infusions, and 2 patients received intraperitoneal injections.

Of the 11 patients treated intravenously, 7 patients were treated with low dose Allocetra (2.5×10^9 cells) and 4 patients were treated with high dose Allocetra (10×10^9 cells). Four patients treated with Allocetra low dose were also treated with nivolumab concomitantly.

Overall, 4 patients had severe adverse events (30.8%), 9 patients had moderate adverse events (69.2%), and 11 patients had mild adverse events (84.6%). No life threatening events were reported and one death was reported. Two serious adverse events were reported, no related serious adverse events were reported.

The reported events most commonly involved constitutional symptoms or gastrointestinal events, known to afflict patients with advanced refractory malignancies following multiple treatment lines.

The reported death occurred approximately one week following Allocetra treatment, due to exacerbation of dyspnea which started prior to study treatment. The event was not considered related to the study treatment and was consistent with the patient's underlying malignancy.

Among the events reported as probably related or related, mild related events were most commonly reported, in 8 patients (61.5%) and moderate events were reported in 3 patients (23.1%). No severe events were reported as related to study treatment. No events were reported in more than 2 patients (15.4%).

For patients treated with a combination of nivolumab and Allocetra (4 patients), adverse events were conservatively considered as related to both study drugs. All the moderate events considered as related were reported in patients receiving a combination of nivolumab and Allocetra, except for abdominal pain, reported in a patient who received Allocetra intraperitoneally for an advanced peritoneal tumor.

[redacted]

The overall safety profile appears consistent with the expected safety profile of a population with advanced malignancies following multiple prior treatment lines.

Conclusions:

Advanced refractory solid tumors remain a severe unmet clinical need. In the current study, an innovative approach to solid tumor therapy was suggested, utilizing Allocetra cell therapy for the immune modulation of the tumor microenvironment.

The study was designed to assess Allocetra safety and potential efficacy across multiple treatment cohorts, employing Allocetra administration in two treatment doses as a monotherapy, or in combination with anti-PD1 antibody, postulated to potentially provide a combined synergistic effect, potentiating the known activity of anti-PD1 inhibitors. Furthermore, additional treatment cohorts were designed to assess Allocetra treatment in different routes of administration, employing a local intraperitoneal drug delivery for patients with advanced peritoneal tumors, in addition to the more traditional systemic intravenous infusion.

The study was terminated following completion of 3 treatment cohorts comprising intravenous infusion of Allocetra as a monotherapy, low dose and high dose, and combination intravenous infusion of Allocetra low dose with nivolumab. For the intraperitoneal administration of Allocetra, only two patients were treated with high dose Allocetra prior to recruitment termination.

In total, 13 patients were treated on the study with Allocetra, all received to full dosing of Allocetra comprising 3 subsequent treatments, at one or two-week intervals.

The patients included in the study had advanced solid tumors unresponsive to approved therapies. Most of the patients had multiple prior treatment lines, rendering their disease highly refractory to treatment. A protocol modification to limit the number of prior treatment lines was planned, however the study was terminated prior to implementation.

[redacted]

Taking into account the disease history of the patients and malignancies highly refractory to prior treatments, as well as the fact that only a few patients were treated with the Allocetra high dose by the time the study was terminated and no patients received the combined high dose Allocetra and nivolumab treatment, the ability to observe treatment responses was limited, and further clinical studies would be needed to characterize Allocetra efficacy for solid tumors.

The overall safety profile appears to be consistent with the expected safety profile of a severely ill and co-morbid oncologic patient population, commonly involving general constitutional symptoms or gastrointestinal disorders. The number of severe events was acceptable, and none were considered to be related to study treatment. There were few serious adverse events and none were related to treatment.

Taken together, the safety profile combined with inconclusive efficacy results indicates a potential for further clinical studies.

Date of Report: 21 Jan 2025