ENLIVEX THERAPEUTICS – MACROPHAGE REPROGRAMMING AS A PARADIGM SHIFT IN THE TREATMENT OF LIFE-THREATENING INDICATIONS WITH UNMET MEDICAL NEED

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ENLIVEX
immune rebalancing

Off-the-shelf, universal macrophage reprogramming cell therapies for life-threatening diseases

Enlivex is a clinical-stage macrophage reprogramming immunotherapy company developing Allocetra™, a universal off-the-shelf cell therapy designed to reprogram macrophages into their homeostatic state. Resetting non-homeostatic macrophages into their homeostatic state is critical for immune system rebalancing and resolution of life-threatening conditions.

Allocetra harnesses the naturally-occurring activity of apoptotic cells to induce an immunomodulated state. This effect is mediated by the engulfment of Allocetra apoptotic cells by macrophages.

Allocetra for macrophage reprogramming

- **First-ever cell therapy designed to restore macrophage homeostasis, overall immune rebalancing**
- **Provide a highly-differentiated new modality that may offer effective treatment to sepsis and cancer patients who do not respond to standard of care**

Pipeline of reprogrammable macrophage-modulated indications

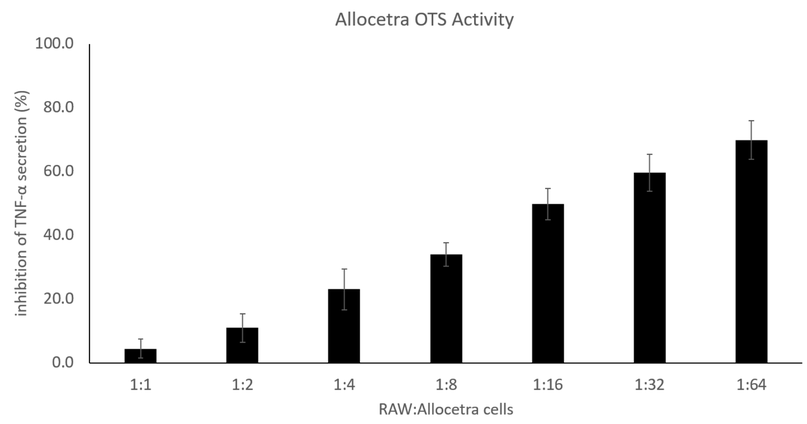
Indication	Pre-Clinical	Phase Ib	Phase IIb
Organ failure associated with sepsis		Completed	Phase II Ongoing
Advanced-stage solid tumors with peritoneal metastases, in combination with chemotherapy		Phase I/II Ongoing	
Advanced-stage solid tumors with peritoneal metastases, stand-alone + in combination with anti-PD1		Phase I/II Ongoing	

Immune system balance: macrophages are key player

- Macrophages are the primary immune cells that regulate immune activity
- They engulf infected as well as cancer cells, and increase/decrease overall immune activity in response to these various challenges
- Some diseases, unfortunately, negatively affect macrophages, and as a result these negatively-reprogrammed macrophages move away from their healthy homeostatic state and are causing excess damage on top of the original disease, instead of orchestrating proper immune response to eliminate the problems and resolve the disease

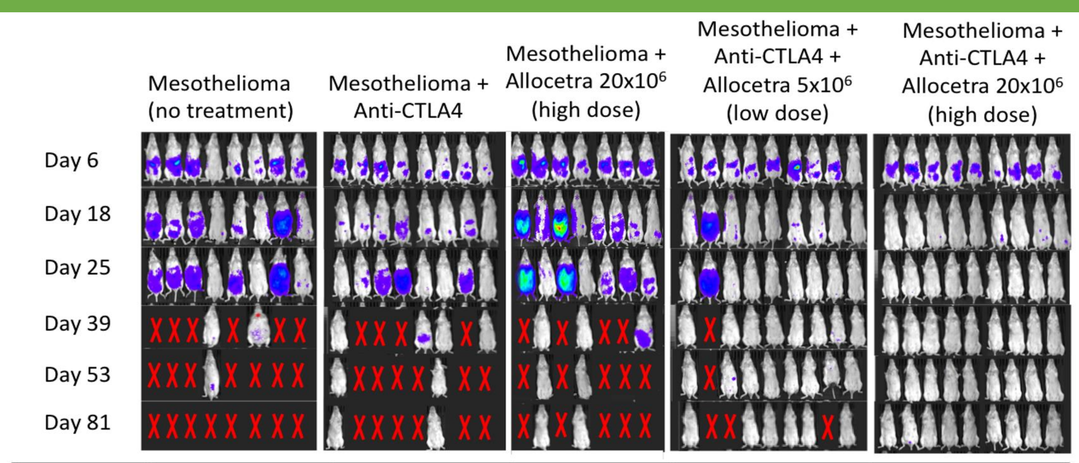
Cells-based potency model: inhibitory effect of Allocetra-OTS on TNF-α secretion by LPS-induced murine macrophages

Incubation of murine macrophage RAW 264.7 cell line with Allocetra-OTS cells leads to a reduction in the LPS-induced TNF-α secretion in a dose-dependent pattern.



$1x10^5$ RAW 264.7 cells were stimulated with LPS at concentrations of 0.1 ng/ml and Allocetra cells were added in different ratios. TNF-α was measured by ELISA. Results are expressed as mean ±SD from 4 independent experiments.

Synergistic effect of Allocetra + anti-CTLA4 in peritoneal mesothelioma solid tumor

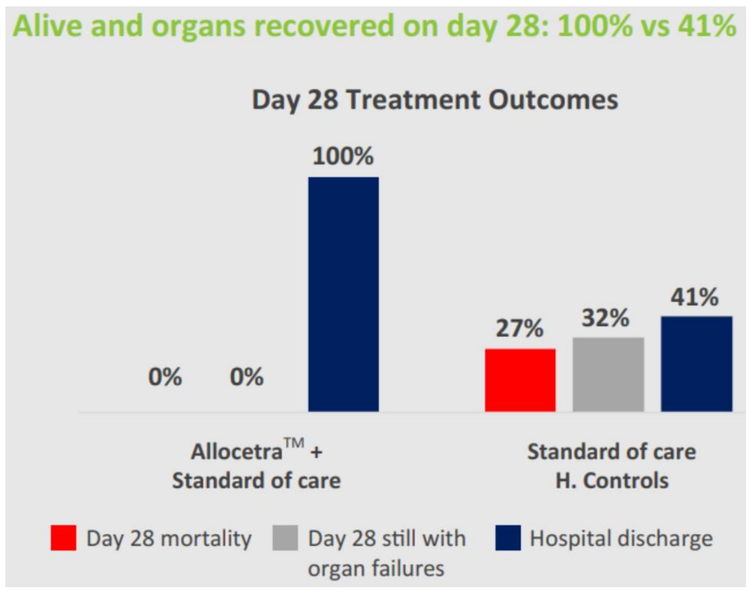


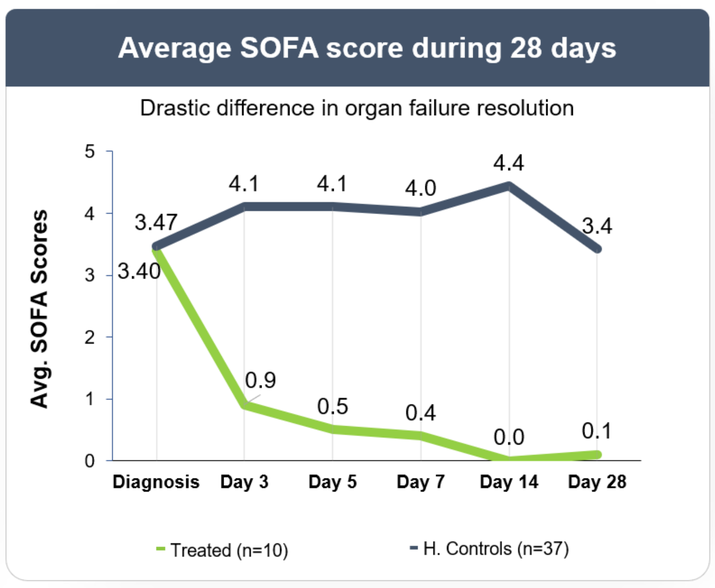
	Mesothelioma (no treatment)	Mesothelioma + Anti-CTLA4	Mesothelioma + Allocetra 20x10⁶ (high dose)	Mesothelioma + Anti-CTLA4 + Allocetra 5x10⁶ (low dose)	Mesothelioma + Anti-CTLA4 + Allocetra 20x10⁶ (high dose)
Mortality	**100%**	**75%**	**71.5%**	**33%**	**0%**
Survival	0%	25%	28.5%	67%	100%
Complete cure	0%	25%	28.5%	67%	100%

Initial cancer spread · Advanced cancer spread · Mouse dead · Mouse alive · IVIS imageing, AB12-137 study

Allocetra macrophage reprogramming leads to improved outcomes for sepsis patients

Ten patients with sepsis were enrolled in a phase Ib clinical study. Enrolled patients were aged 51-83 years, with a Sequential Organ Failure Assessment (SOFA) score ≥2 above baseline and were septic due to presumed infection. Allocetra was administered as a single dose (day +1) or in two doses of $140x10^6$ cells/kg (day +1 and +3), following initiation of standard-of-care (SOC) treatment for septic patients. Organ dysfunction, ICU and hospital stays, and mortality were compared to historical controls treated at the same clinical center.





Clinical track record in infectious diseases and application to solid tumors (no drug-related SAEs to date)

Infectious and inflammatory diseases

- Favorable safety and tolerability profile of Allocetra in 3 completed clinical trials, with 31 fragile, hospitalized patients (sepsis and severe/critical COVID-19)
- Strong indication of clinical effect (29/31 patients with complete recovery and swift hospital discharge)
- Recruitment ongoing in a multi-country, multi-center Phase II clinical trial (sepsis)

Solid tumors

- New clinical collaboration with BeiGene to evaluate the safety and efficacy of Allocetra in combination with tislelizumab, an anti-PD-1 immune checkpoint inhibitor, for the treatment of patients with advanced-stage solid tumors
- Phase I/II Allocetra + chemotherapy (on-going, Israel)
- First cohort patients received 3 injections of Allocetra intraperitoneally with chemotherapy
- Phase I/II Allocetra monotherapy and in combination with anti-PD1 (on-going, Israel)
- First cohort patients received 3 IV injections with Allocetra as a monotherapy, no SAEs
- Q4/2022: Received IND clearance in the US

CONCLUSIONS

- **Allocetra demonstrates a favorable safety profile and preliminary efficacy in pre-clinical and clinical studies**
- **Allocetra offers an innovative, off-the-shelf potential therapeutic modality for the treatment of infectious and inflammatory diseases (e.g., sepsis) as well as cancer**
- **The Allocetra platform may be suitable for the treatment of additional indications in which macrophage non-homeostatic activity is part of the disease pathophysiology**