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SYNERGISTIC ANTI-TUMOR EFFECT OF ALLOCETRA-OTS, A CELLULAR IMMUNE-THERAPY, IN COMBINATION WITH IMMUNE CHECKPOINT INHIBITORS/ CHEMOTHERAPY/CAR T, THROUGH IN-VIVO REPROGRAMMING OF MACROPHAGES

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Background Immune checkpoint inhibitors (ICI) revolutionized solid tumor treatment, however, in many tumors only partial response is achieved. Allocetra-OTS has an immune modulating effect on macrophages¹ and showed an excellent safety profile in patients including patients with sepsis.² Here we investigated the anti-tumoral effect of Allocetra-OTS cellular therapy, in solid tumor animal models.

Methods Allocetra-OTS is manufactured from enriched mononuclear fractions and induced to undergo early apoptosis.

In an immunocompetent model, Balb/c mice were inoculated intraperitoneally (IP) with AB12 (mesothelioma) with pLenti-PGK-V5-Luc-Neo and treated with anti-CTLA4 with or without Allocetra-OTS. Mice were monitored daily for clinical score and weekly using IVIS. Kaplan-Meier log rank test was done for survival. For Allocetra-OTS preparation, enriched mononuclear fractions were collected by leukapheresis from healthy eligible human donors and induced to undergo early apoptosis. To follow tumor growth in vivo, HeLa-CD19 cells were stably transduced with pLenti-PGK-V5-Luc-Neo. For CAR preparation, fresh mononuclear cells (MNC) were transfected with CD19-CAR plasmids. SCID-Bg mice were injected IP with human HeLa-CD19 or HeLa-CD19-luciferase cells, 10×10 allocetraOTS or vehicle, and 10×10 CD19-CAR T cells or mock T cells.

Results In immune competent Balb/c mesothelioma model, anti-CTLA4 standalone therapy significantly improved survival from mean 34±9 to 44.9 ±20 days (p<0.05). Similarly, Allocetra-OTS standalone therapy improved survival to 52.3 ±20 days (p<0.02). However, anti-CTLA4 + Allocetra-OTS combination therapy, ameliorated survival to 86.7±20 days (p<0.0001) with complete cancer remission in 60-100% of mice (figure 1 & 2). Similar anti-tumoral effects of Allocetra-OTS were seen in mesothelioma model in a combination therapy with either anti-PD1 or cisplatin.

In the CAR-T model, SCID-Bg mice were sacrificed or died from tumor progression in 30±5 days (range 27–37). CAR T cell therapy significantly improved survival to 55±11 days (p < 0.05 vs MOCK) but Allocetra-OTS further improved survival to 75±10 (p < 0.001) with 20-40% complete remission.

Conclusions During IP tumor progression, Allocetra-OTS as a standalone therapy or in combination with ICI, cisplatin or CAR-T therapy, significantly reduced tumor size and resulted in complete remission in up to 100% treated mice.

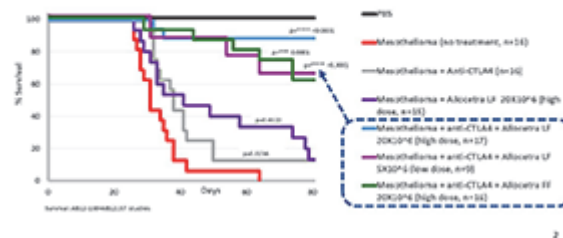
Based on excellent safety profile in > 40 patients treated in prior clinical trials for sepsis and Covid-19, Phase I/II clinical trial of Allocetra-OTS plus chemotherapy has started and first patient already recruited. A second Phase I/II clinical trial of Allocetra-OTS plus anti-PD1, as a second- and third-line therapy in various cancers, is planned for Q4 2022.

REFERENCES

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2. Van-Heerden V, Abitbol A, Mevorach D. Allocetra-OTS for sepsis associated cytokine storm. *Frontiers in Immunology, Front Immunol.* 2021 Sep 30;12:718191.

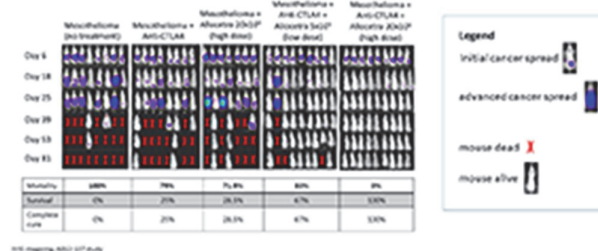
Synergistic effect of Allocetra™ + anti-CTLA4 in peritoneal mesothelioma solid tumor

- Superior survival of the anti-CTLA4+Allocetra combinations, dose response demonstrated
- Weak, although statistically-significant, survival effect of stand-alone anti-CTLA4, Allocetra



Abstract 1380 Figure 1 CTLA4 and Allocetra

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Abstract 1380 Figure 2 CTLA4 and Allocetra

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