Intratumoral RNA-based TLR-7/-8 and RIG-I agonist CV8102 alone and in combination with anti-PD-1 in phase I dose-escalation and expansion trial in patients with advanced solid tumors


Background: CV8102 comprises a single-stranded non-coding RNA complexed with a cationic peptide. It acts as an agonist to TLR-7/-8 and RIG-I (Ziegler et al., J Immunol 2017) to stimulate the innate and adaptive immune system. CV8102 was shown to induce an upregulation of inflammatory cytokines, chemokines and IFN-γ related genes at the injection site along with an activation of T, NK, NKT and migratory dendritic cells in the draining lymph nodes (Heidenreich et al., Int J Cancer 2015). Intratumoral CV8102 demonstrated dose-dependent anti-tumor activity and synergized with systemic PD-1 inhibition in preclinical models. In this phase I trial we are investigating CV8102 as single agent and in combination with anti PD1 antibodies in patients with advanced melanoma, squamous cell carcinoma of skin or head and neck and adenocytic carcinoma.

1. Study Design CV8102-008 – Phase I study of intratumoral CV8102
(dose escalation based on Bayesian design with flexible cohort sizes)

2. Patient Characteristics & Most Frequent Treatment Emergent Adverse Events (TEAEs)*

3. Best Overall Response and Duration by RECIST as assessed by investigators (preliminary data with cut-off March 15th 2019)

4. Single Agent CV8102 (Cohort A) IL-6 and CRP Levels after First Injection

5. CV8102: Single Agent Activity in Three Patients

*TEAEs that occurred in ≥ 4 patients treated with CV8102 anti-PD1/safety population (n=22). Data cut-off Mar 15th 2019. No DLT observed within first 2 weeks of study drug treatment. *13 SAEs occurred in 10 patients and 17 ≥ grade 3 AEs occurred in 9 patients including 1 death due to disease progression (unrelated to CV8102).

*Intratumoral RNA-based TLR-7/-8 and RIG-I agonist CV8102 and expansion cohorts are planned after determination of the phase 2 recommended dose.

Case 004, 100 µg Dose Level

Case 006, 150 µg Dose Level

91-year-old male patient with stage IV hnMEL with large buccal and small lip lesion and a contralateral cervical LNM

- Buccal and lip lesions remained stable for 9 months (study duration)
- Untreated metastatic LN showed ongoing regression

74-year-old female patient with stage IIIC melanoma with multifocal in-transit metastases

- Marked transient rise in serum IL-6 and CRP following the first intratumoral injection
- Partial regression of the injected tumor lesion after 5 injections of CV8102
- Complete regression of in-transit metastases on MRI, complete regression of all skin metastases with minimal residual palpable induration of the injected lesion at week 12
- Patient continued to receive injections at monthly intervals for 9 months without locoregional recurrence
- New intraabdominal soft tissue lesion after 9 months

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