1010P: INTRATUMORALLY ADMINISTERED CV8102 IN PATIENTS WITH ADVANCED SOLID TUMORS: PRELIMINARY RESULTS FROM COMPLETED DOSE ESCALATION IN STUDY 008

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Background: CV8102 is a non-coding, non-capped RNA complexed with a carrier peptide activating the innate (via TLR7/8, RIG-I) and adaptive immune system. An ongoing phase I trial (CV-8102-008) is investigating i.t. CV8102 either as a single agent or in combination with systemic anti-PD-1 antibodies in patients with advanced cutaneous melanoma (MEL), squamous cell carcinoma of the skin (SCC) or head and neck (HNSCC) and adenoid cystic carcinoma (ACC). The dose escalation part of this study has been completed, and preliminary results from this part are reported here.

Methods: Study CV-8102-008 is an open-label, cohort-based, dose escalation and expansion phase 1 study. Eight intratumoral injections of CV8102 are being administered initially over a 12-week period. Primary objective of the dose-escalation part is to determine the maximum tolerated dose and recommended phase 2 dose [NCT03291002].

1. Patient Characteristics & Dose Level Enrollment

(cutoff date June, 21st 2021)

Characteristics	Number of patients (%)		
	Single agent (n=33)	anti-PD-1 combination (n=25)	All (n=58)
Age			
range (yrs)	35-91	36-90	35-91
median (yrs)	69	68	69
Gender			
Male	15 (45)	14 (56)	29 (50)
Female	18 (55)	11 (44)	29 (50)
cMEL			
Stage IIIB	1 (3)	0 (0)	1 (2)
Stage IIIC	4 (12)	5 (20)	9 (16)
Stage IV	9 (27)	15 (60)	24 (41)
HNSCC			
Stage IV	4 (12)	5 (20)	9 (16)
cSCC			
Stage III	1 (3)	0 (0)	1 (2)
Stage IV	5 (15)	0 (0)	5 (9)
ACC			9 (16)
Stage IV	9 (27)	0 (0)	
ECOG PS			
0	17 (52)	18 (72)	35 (60)
1	16 (48)	7 (28)	23 (40)
Pre-treatment with anti-PD-1	19 (58)	22 (88)	41 (71)
Pre-treatment with anti-CTLA4	3 (9)	11 (44)	14 (24)

Due to rounding, percentages presented above may not add up precisely to 100%.

Dose level	Number of treated patients	
	Single agent (n=33)	anti-PD-1 combination (n=25)
25 µg	1	1
50 µg	2	2
100 µg	2	2
150 µg	6	3
200 µg	6	3
300 µg	2	2
450 µg	2	2
RP2D 600 µg	6	4
900 µg	6*	6

*1/6 with DLT and 1/6 related G3 event post DLT evaluation period

2. Most Frequent Treatment Emergent Adverse Events (TEAEs)

(*occurring in ≥ 6 (10%) patients, preliminary data with cutoff date June, 21st 2021)

AE preferred term	Number of patients with ≥1 TEAE (%)*			
	Single agent (n= 33) DL 25-900 µg	anti-PD-1 combination (n= 25) DL 25-900 µg	All (n= 58)	
			G1/G2	≥ G3
Any Adverse Event	33 (100)	25 (100)	58 (100)	22 (38)
Pyrexia	17 (52)	11 (44)	28 (48)	0 (0)
Fatigue	12 (36)	8 (32)	20 (34)	0 (0)
Chills	6 (18)	10 (40)	16 (28)	0 (0)
Headache	9 (27)	3 (12)	12 (21)	0 (0)
Injection site pain	8 (24)	4 (16)	12 (21)	0 (0)
Nausea	8 (24)	3 (12)	11 (19)	0 (0)
Influenza like illness	7 (21)	2 (8)	9 (16)	0 (0)
Urinary tract infection	4 (12)	5 (20)	9 (16)	1 (2) §
C-reactive protein increased	5 (15)	2 (8)	7 (12)	0 (0)
Injection site erythema	2 (6)	5 (20)	7 (12)	0 (0)
Pain in extremity	4 (12)	3 (12)	7 (12)	0 (0)
Anaemia	5 (15)	2 (8)	6 (10)	2 (3) §
Arthralgia	4 (12)	2 (8)	6 (10)	0 (0)
Asthenia	3 (9)	3 (12)	6 (10)	0 (0)
Decreased appetite	3 (9)	3 (12)	6 (10)	0 (0)

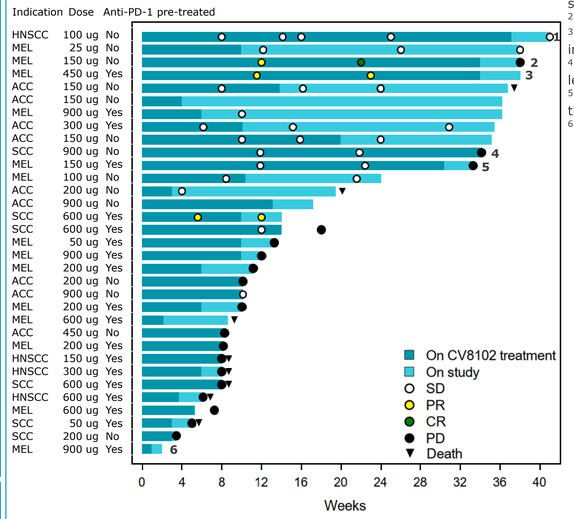
§ assessed as unrelated by investigator

- **≥ Grade 3 AEs considered treatment related per investigator's judgement occurred in 7 (12%) patients:**
  - **Single agent**: transient G3 elevation of liver enzymes (1 pt 150 µg, 2 pts 200 µg, 1 pt 900 µg in context of G2 CRS (DLT per protocol)), G3 immune-mediated pneumonitis (1 pt 900 µg).
  - **Combination with anti-PD-1:** G3 hypertension and G3 elevation of serum lipase (1 pat 100 µg) and G3 elevated serum amylase (1 pat 100 µg).
- **Treatment related SAEs per investigator's judgement**:
  - **Single agent**: G2 CRP increase (1 pt 150 µg DL), G2 tumor pain (1 pt 200 µg DL), G1 chills, pyrexia and vomiting, G2 pyrexia (1 pt 300 µg DL), G2 cytokine release syndrome (1 pt 900 µg DL), G3 immune-mediated pneumonitis (1 pt 900 µg DL).
  - **Combination with anti-PD-1**: G3 Inpatient observation after multiple AEs (1 pt 100 µg DL), G2 cytokine release syndrome (1 pt 300 µg DL), G1 cytokine release syndrome (1 pt 600 µg DL), G1 cytokine release syndrome (1 pt 900 µg DL).
- **Dose limiting toxicities per protocol (occurring within the first 2 weeks of treatment):**
  - G3 increase in ALAT and ASAT in context of G2 cytokine release syndrome in a patient treated with 900 µg single agent CV8102.

3. Overall Response per RECIST 1.1

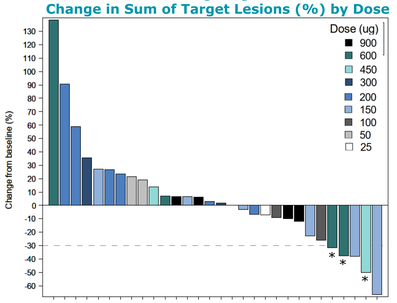
(preliminary data with cutoff June, 21st 2021)

Cohort A – single agent CV8102



[1] Overall stable disease according to RECIST 1.1 for 9 months with shrinkage of the noninjected lesion.
[2] Complete regression of injected and multiple noninjected lesions.
[3] Partial response according to RECIST 1.1 after an early decrease in elevated serum LDH.
[4] SD according to RECIST 1.1 with 50% regression of the injected lesion.
[5] SD according to RECIST 1.1 for > 6 months with shrinkage of the injected and the noninjected lesion.
[6] Early termination due to AE.

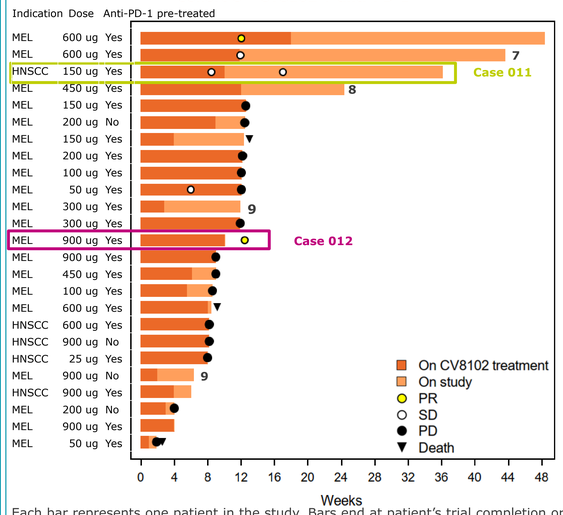
Cohort A - Single Agent CV8102 Change in Sum of Target Lesions (%) by Dose



Each bar represents one patient in the study. All patients with RECIST 1.1 evaluable response are displayed. Change to smallest sum post-dose is depicted.

*Patient with negative change from baseline with progression during previous anti-PD-1 treatment

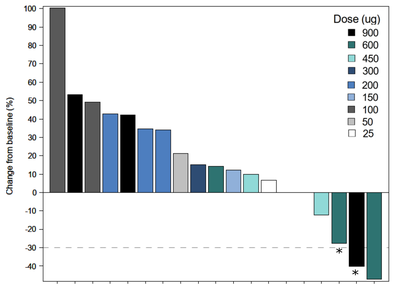
Cohort C – CV8102 + anti-PD-1



Each bar represents one patient in the study. Bars end at patient's trial completion or are cut off at progression or, if indicated, at time of consent withdrawal or early termination due to AE. 'Death': Patients who died have been marked, the mark does not correspond to the time of death.

[7] Partial response of the injected lesion, but patient developed additional lesions.
[8] Mixed response with regression of the injected and several noninjected lesions. Progression of other noninjected lesions.
[9] Withdrawal of consent.

Cohort C - CV8102 + anti-PD-1: Change in Sum of Target Lesions (%) by Dose



Each bar represents one patient in the study. All patients with RECIST 1.1 evaluable response are displayed. Change to smallest sum post-dose is depicted.

*Patient with negative change from baseline with progression during previous anti-PD-1 treatment

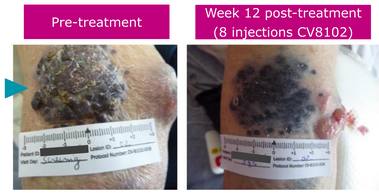
4. Case Reports: Partial or complete response after CV8102 treatment in combination with anti-PD-1

Case report 011, 150 µg DL: Complete histopathological response

- 64-year old male patient with locally advanced HNSCC Stage IVa at study entry
- Previously treated with Pembrolizumab and Nivolumab; best response progression
- Patient received 8 CV8102 injections in combination with biweekly Nivolumab
- RECIST 1.1 evaluation after 9 weeks showed Stable Disease
- Patient underwent salvage tumor resection (including area of injected lesion) due to persistent tumor hemorrhage 11 weeks after last dose
- Histopathological results showed a complete response in the resected specimen with no tumor cells detected

Case report 012, 900 µg DL, partial response

- 84-year-old male patient with stage IV melanoma at study entry.
- Previously treated with Nivolumab for 4 months; best response progression
- The patient received 8 CV8102 intratumoral injections in combination with four weekly Nivolumab
- LDH not elevated
- Overall partial response according to RECIST 1.1 after 12 weeks with regression of the injected and noninjected lesions



5. Conclusion

- CV8102 showed an acceptable safety profile
  - CV8102 was tolerated without DLTs at doses up to 600 µg (single agent and combination with anti-PD-1)
  - In the 900 µg single agent cohort, 1/6 patients experienced a DLT and 1 further patient a potentially related G3 AE after the DLT evaluation period
- Preliminary evidence of efficacy was observed in single agent and anti-PD-1 combination cohorts including anti-PD-1 refractory patients
- 600 µg was selected as recommended phase 2 dose (RP2D) for both, monotherapy and combination with anti-PD1-antibodies
- An expansion part of the trial is ongoing to generate further data on safety and efficacy of the RP2D in melanoma patients

All data presented: Preliminary and unclean data

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