

IMMUNE PROFILING OF PATIENTS WITH ADVANCED MELANOMA INTRATUMORALLY TREATED WITH CV8102 AS A SINGLE-AGENT OR IN COMBINATION WITH ANTI-PD-1 ANTIBODIES – RESULTS OF A PHASE I TRIAL EXPANSION

¹Marina Gonzalez, ¹Peter Wengenmayer, ²Igor Samoylenko, ³Sebastian Ochsenreither, ⁴Erika Richtig, ⁵Ioannis Thomas, ⁶Michael Erdmann, ⁷Celeste Lebbe, ⁸Juan Martin-Liberal, ⁹Patrick Terheyden, ¹⁰Artem Poltoratskiy, ¹¹Marina Sekacheva, ¹²Yuliya Semiletova, ¹³Thomas Eigentler, ¹Beate Schmitt-Bormann, ¹Dominik Vahrenhorst, ¹Sarah-Katharina Kays, ¹³Tobias Seibel, ¹Gianluca Quintini, ¹Birgit Scheel, ¹Martin Falk, ¹Ulrike Gnad-Vogt, ¹Paula Codo*. ¹CureVac AG, Frankfurt am Main, Germany; ²N.N. Blokhin Cancer Research Center, Moscow, Russian Federation; ³Charité Comprehensive Cancer Center, Berlin, Germany; ⁴Medical University of Graz, Graz, Austria; ⁵University Clinic Tübingen, Tübingen, Germany; ⁶University Hospital Erlangen, Erlangen, Germany; ⁷Hôpital Saint Louis, Paris, France; ⁸Catalan Institute of Oncology (ICO), Barcelona, Spain; ⁹University of Lübeck, Lübeck, Germany; ¹⁰National Medical Research Oncology Center n.a. N.N. Petrov, Saint Petersburg, Russian Federation; ¹¹Sechenov University, Moscow, Russian Federation; ¹²Clinic of advanced medical technologies n. a. Nicolay I. Pirogov, Saint Petersburg, Russian Federation; ¹³Charité Medical University, Berlin, Germany

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.^{1, 2} An ongoing expansion of a phase I trial is investigating the intratumoral (i.t.) administration of CV8102 in patients with advanced cutaneous melanoma (cMEL), either as a single agent or in combination with systemic anti-PD-1 antibody therapy. In the initial dose escalation part, the recommended dose for subsequent cohort expansion and phase II was defined as 600 mg. Here we report preliminary immune profiling results.

Methods For the expansion cohorts, 30 anti-PD-1 refractory Melanoma patients received CV8102 in combination with Pembrolizumab or Nivolumab and 10 patients as single agent. Eight i.t. injections of CV8102 were administered over a 12-week period, with optional continuation in case of clinical benefit.

Blood samples for flow cytometry-based immune cell phenotyping and next-generation RNA sequencing (RNAseq) were collected at baseline and multiple time points during the treatment period. For characterization of the tumor microenvironment (TME), core needle biopsies of injected and/or non-injected lesions were taken before, during and after treatment. Changes on various tumor-infiltrating immune cells were assessed by multiplex immunofluorescence (MultiOmyx ^{>TM}) and immune-related gene expression profiling using nCounter® Pan Cancer IO360^{>TM} panel (NanoString).

Results Blood RNAseq analysis showed increase in several transcripts related to systemic immune response activation like interferon alpha and gamma after the first dose.

Paired serial biopsies showed changes in the TME, not only in the immune cell infiltration but also in gene expression profiling.

Comprehensive results of blood RNAseq, immune cell phenotyping, and tissue analysis for the expansion cohorts will be presented, including examples of individual patients.

Conclusions Intratumoral injection of CV8102 activated several pathways of immune response detectable in peripheral blood after the first dose and showed immunological changes in the tumor microenvironment, with increased parameters of immune infiltration in a group of patients.

Trial Registration NCT03291002

REFERENCES

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Ethics Approval The study was approved by central or local ethics committees depending on the country:

In Germany: Central Ethics Committees in Tuebingen, Germany under 785/2016AMG1.

In France: COMITE DE PROTECTION DES PERSONNES SUD-EST I under 2019-49, approval dated 17-May-2019.

In Spain: CEC COMITÉ DE ÉTICA DE INVESTIGACIÓN CLÍNICA CON MEDICAMENTOS del Hospital Universitari Vall d'Hebron, Barcelona, approval date 28-Nov-2019 under the EUdRaCT number.

In Austria: Central Ethics Committee in Graz under 31-426 ex 18/19 approved on 19-Sep-2019.

In the Russian Federation: ETHICS COMMITTEE AT FSBI "NMRC OF ONCOLOGY n.a. N.N. BLOKHIN" OF THE MINISTRY OF HEALTHCARE OF THE RUSSIAN FEDERATION, INTERDISCIPLINARY ETHICS COMMITTEE of Omsk Region, Local Ethics Committee at FSAEI HE "I.M. Sechenov First MSMU" of the Ministry of Healthcare of Russia (Sechenov University, Extract from Minutes □ 03-21 of the scheduled meeting of the Local Ethics Committee dated 03 February 2021), BIOMEDICAL ETHICS COMMITTEE at N.I. PIROGOV CLINIC OF HIGH MEDICAL TECHNOLOGIES (IN-PATIENT AND OUTPATIENT FACILITIES), ST. PETERSBURG STATE UNIVERSITY (EXTRACT FROM MINUTES □ 02/21 of the meeting of the Biomedical Ethics Committee), Ethics Committee at Federal State Budgetary Institution "National Medical Research Center of Oncology named after N. N. Petrov" of the Ministry of Health of the Russian Federation (Extract No. 5/130 from the Minutes of the regular session No. 8 of the Ethics Committee).

Consent Written informed consent from the patient was obtained for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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