2. SYNOPSIS (ADDENDUM 1)

Sponsor: Ultimovacs ASA

Investigational product: UV1

Title of study: A Randomised Phase II, Open-label, Active-controlled, Multicenter Study Investigating the Efficacy and Safety of UV1 Vaccination in Combination with Nivolumab and Ipilimumab as First-line Treatment of Patients with Unresectable or Metastatic Melanoma (UV1-202)

Investigators: This part of the INITIUM study was conducted at 7 sites in 4 countries (2 in Belgium, 1 in Norway, 1 in the UK, and 3 in the US); out of those, 6 sites screened and enrolled patients.

Publications: None at the time of this report.

Period of study: 1 Sept 2022 (date of first informed consent) to 10 April 2024 (date study was prematurely terminated).

Phase of development: Clinical Phase II

Objectives:

To support the Extended Exploratory Cohort of the INITIUM study, an additional 21 patients at selected sites were enrolled in a Single Arm UV1 cohort. This was done to secure that sufficient material was available to identify anti-tumor activity unique for the vaccine responders and thereby to strengthen the support from the mechanistical data to the clinical outcome data derived from all patients in the study. Sample types collected and assessments are described in the main CSR.

For further details see the INITIUM study protocol.

Methodology:
All patients in the single arm UV1 should receive UV1 vaccination in combination with nivolumab and ipilimumab.

Patients in the Single Arm UV1 cohort followed the same treatment schedule, visits, and procedures as in the experimental arm described in the study protocol. In addition, all patients in the Single Arm UV1 cohort performed the biological sampling and procedures as described for the Extended Exploratory Cohort (Appendix 2 main CSR). Patients signed a separate Informed Consent Form (ICF) prior to enrolment in this part of the study.

As in the randomized part of the study, the Single Arm UV1 cohort consisted of 3 phases: Screening, Induction period and a Follow-up period. The Follow-up period included safety, response, and survival follow-up visits. The Response Follow-up visits were performed until

iCPD per iRECIST or until the end of study (whichever came first). The Survival Follow visits were performed every 12 weeks from iCPD per iRECIST until the end of study.

Patients in the Single Arm UV1 cohort were not randomized and were therefore not included in the data used for analysis of primary and secondary endpoints. Only descriptive statistics were used to describe patients in the Single Arm UV1 cohort.

Number of patients (planned and analyzed):

21 patients were enrolled in a single-arm UV1 cohort.

Diagnosis and main criteria for inclusion and exclusion:

- Same criteria as in the randomized part of INITIUM were applied

Duration of treatment:

- Same duration of treatment as for the randomized part of INITIUM were applied

Statistical methods:

- Descriptive analysis only, were applied.

Summary - Conclusions:

Efficacy results:

- Median PFS were not reached
- Median OS were not reached
- 12-months PFS rate assessed by BICR were 60.6%
- 12-months OS rate were 84.8%

Safety results:

- Frequency and severity of AEs were similar to that of the randomized part of INITIUM
- All patients experienced at least 1 AE, and almost all experienced an AE related to treatment with UV1 and/or nivolumab/ipilimumab
- The most frequently reported AEs were fatigue, infusion related reactions and diarrhoea
- The most common SOCs for SAEs were, general disorders and administration site conditions, gastrointestinal disorders, and skin and subcutaneous tissue disorders
- UV1 was generally considered well tolerable.

Conclusions:

- There were no notable differences in safety between UV1 vaccination in combination with nivolumab and ipilimumab in the Single Arm UV1 cohort of INITIUM compared to the randomized part of INITIUM as evaluated by AEs, deaths, vital signs, laboratory assessments, and ECOG status

- UV1 was generally considered well tolerable

- The Single Arm UV1 cohort was terminated earlier than planned due to demonstrated lack of efficacy in the randomized part of INITIUM.