The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: 110551 (MAGE3-AS01B-MEL-001 (MET))

Title: Study of GSK1203486A Antigen-Specific Cancer Immunotherapeutic in patients with unresectable and progressive metastatic cutaneous melanoma
GSK1203486A (MAGE-A3): GlaxoSmithKline (GSK) Biologicals' Antigen-Specific Cancer Immunotherapeutic (ASCI) comprising the recombinant protein ProtD-MAGE-A3/His melanoma antigen, adjuvanted.

Rationale: The aim of the study was to characterize the safety and immunogenicity of the MAGE-A3 product in patients with unresectable and progressive metastatic cutaneous melanoma.
The study was terminated early due to difficulties in recruiting the required population and not on the basis of any other concerns such as safety or absence of clinical activity in the first patients treated.

Phase: II

Study Period: 29 September 2008 to 19 January 2011

Study Design: Open, multicentre with 1 group

Centres: 2 centres in Greece

Indication: Treatment of metastatic cutaneous melanoma in patients with unresectable and progressive metastatic cutaneous melanoma (stage III or stage IV M1a)

Treatment:
MAGE-A3 Group: Patients received 4 cycles of MAGE-A3 product as follows:

- Cycle 1: 6 doses, each given at a 2-week interval,
- Cycle 2: 6 doses, each given at a 3-week interval
- Cycle 3: 4 doses, each given at a 6-week interval
- Cycle 4: 4 doses, each given at a 3-month interval followed by 4 doses, each given at a 6-month interval.

The MAGE-A3 product was administered intramuscularly in the deltoid or lateral regions of the thighs, alternately on the right and left sides.

Objectives:

- The safety of the MAGE-A3 product in patients with MAGE-A3-positive metastatic cutaneous melanoma.
- The clinical activity of the MAGE-A3 product in patients with MAGE-A3-positive metastatic cutaneous melanoma.

Primary Outcome/Efficacy Variable:

- Safety of the ASCI injections assessed in terms of the
  - Occurrence of ASCI-related grade 3/4 adverse events (AEs) according to the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0.
  - Occurrence of serious adverse events (SAEs) during the study.
- Clinical activity: the rate of objective clinical response (complete response (CR) or partial response (PR)).*

*As the study was terminated before the end of recruitment, clinical activity analysis was not performed.

Secondary Outcome/Efficacy Variable(s):*

- The rate of stable disease.
- The rate of mixed response.
- Time to study treatment failure; defined as withdrawal from investigational product because of disease progression or death.
- Progression-free survival, calculated as the time from randomization to either the first progression of the disease or the date of death, whichever occurred first. In case a patient went off protocol treatment, the date of first documented progression (if applicable) would be used as date of progression. Patients still alive with no evidence of disease progression at the time of their last visit or for whom date of first documented progression was not applicable, were to be censored at the time of the last examination.
- Progression-free survival after initial slow progressive disease (SPD), calculated as the time from the time point at which the disease is the most advanced during the treatment to either a new progression of the disease or the date to death, whichever occurred first as another secondary outcome variable of this study. In that case, the largest diameter during the course of treatment would be used as reference measurement. This outcome was defined to take into account the delay to induce an active immune response and the strict rules set up in this study to allow pursuing investigational treatment in case of SPD.
- Documentation of any toxicity (Occurrence of adverse events during the study, including abnormal haematological and biochemical laboratory values).

- Immunogenicity at defined time points:
  - The anti-MAGE-A3 seroconversion and concentration.
  - The anti-protein D seroconversion and concentration.
  - The MAGE-A3 cellular (T-cell) response.

*As the study was stopped before the end of recruitment, secondary outcome variables analysis was not performed.

Statistical Methods:
The analyses were performed on the Total Treated cohort, which included all patients who received at least one dose of MAGE-A3 product.
Analysis of safety
The analysis of safety was performed on the Total Treated cohort.
The percentages of patients with unsolicited AEs, ASCI-related grade 3/4 AEs according to the CTCAE version 3.0 and SAEs, reported after MAGE-A3 product administration and classified by the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms, were tabulated during the study period.

Study Population: Male or female patient at least 18 years old with histologically proven, measurable metastatic cutaneous melanoma expressing MAGE-A3 stage III melanoma or with stage IV M1a melanoma were candidates for inclusion; patients had normal organ functions and documented progressive disease within the 12 weeks before the first administration of study treatment with no other concomitant malignancies and had not received or planned to receive any other anti-cancer therapy. Women of childbearing potential had to follow adequate contraception for 30 days prior to administration of study treatment, to have a negative pregnancy test, and to continue such precautions for 2 months after completion of the injection series. Written informed consent was obtained from the patients before the performance of any protocol-specific procedure.

Number of Patients:	MAGE-A3 Group
Planned, N	34
Enrolled, N (Total Treated cohort)	5
Completed, n (%)	0 (0.0)
Total Number Patients Withdrawn, n (%)	5 (100)
Withdrawn due to Adverse Events n (%)	0 (0.0)
Withdrawn due to Disease Progression n (%)	4 (80.0)
Withdrawn for other reasons n (%)	1 (20.0)
Demographics	MAGE-A3 Group
N (Total Treated cohort)	5
Females: Males	2:3
Mean Age, years (SD)	67.2 (11.17)
Race, n (%)	Not available

Primary Efficacy Results: Number (%) of patients with ASCI-related grade 3/4 adverse events (AEs) according to the CTCAE version 3.0 during the study period (Total Treated cohort)

Grade 3 AEs	MAGE-A3 Group N = 5
Patients with any AE(s), n (%)	0 (0.0)

Secondary Outcome Variable(s): As the study was terminated early, secondary outcome variables analysis was not performed.

Safety Results: Number (%) of patients with unsolicited AE(s) during the study (Total Treated cohort)

Most frequent AEs	MAGE-A3 Group N = 5
Patients with any AE(s), n (%)	5 (100)
Inflammation	1 (20.0)
Injection site pain	3 (60.0)
Injection site reaction	2 (40.0)
Pyrexia	2 (40.0)
Urinary tract infection	1 (20.0)
Diabetes mellitus	1 (20.0)
Hyperglycaemia	1 (20.0)
Myalgia	1 (20.0)
Pain in extremity	1 (20.0)
Exfoliative rash	1 (20.0)

Safety Results: Number (%) of patients with serious adverse events during the study period (Total Treated cohort)	
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]	
All SAEs	MAGE-A3 Group N = 5
Patients with any SAE(s), n (%) [n assessed by investigator as related]	1 (20.0) [0]
Diabetes mellitus	1 (20.0) [0]
Fatal SAES	MAGE-A3 Group N = 5
Patients with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]

Conclusion: During the entire study period, no patient reported any ASCI injection-related grade 3/4 AE as defined by the CTCAE version 3.0. All 5 patients in the MAGE-A3 Group reported at least one unsolicited AE. One patient reported one SAE, which was assessed by the investigator as not related to the study product injection. No fatal SAEs were reported during the study period.

Date updated: 19-September-2014