1. ABSTRACT

Title

A Cross-sectional Survey to Evaluate Patient Knowledge of Safety Messages Included in the Patient Safety Brochure and Patient Alert Card for IMLYGIC®

- **Keywords**

IMLYGIC; talimogene laherparepvec; melanoma; risk minimisation; survey

- **Rationale and Background**

Talimogene laherparepvec (IMLYGIC®) is an oncolytic viral drug approved to treat unresectable and metastatic melanoma. To ensure safe administration and handling, IMLYGIC was authorised with additional risk minimisation measures (aRMMs) in Europe. These aRMMs include a controlled distribution programme, educational material targeted for both HCPs and patients, with the primary aim to inform HCPs and patients and their close contacts about the potential risks associated with IMLYGIC.

For patients, the primary aRMMs are the Patient Safety Brochure and Patient Alert Card. This post-authorisation safety study (PASS, category 3) was initiated to assess the effectiveness of the information provided in the Patient Safety Brochure and Patient Alert Card.

- **Research Question and Objectives**

The primary objective was to evaluate patients' knowledge of the key messages included in the IMLYGIC Patient Safety Brochure among patients who receive IMLYGIC. The secondary objectives were related to both the IMLYGIC Patient Safety Brochure and Patient Alert Card and evaluated the receipt, reading, knowing the purpose of, and use (ie, carrying the Patient Alert Card) among patients who received IMLYGIC.

- **Study Design**

This was a multi-country, non-interventional, cross-sectional survey study.

- **Setting**

The target population was patients' who receive IMLYGIC in Germany and the Netherlands.

- **Subjects and Study Size, Including Dropouts**

Eligible patients must have provided permission to share their responses in aggregate with national competent regulatory authorities. A total of 58 patients were invited to participate, of which 6 patients rejected the invitation. Additionally, 2 completed patient surveys were not provided by the site by the close of the survey and were excluded. Among the remaining 50 invited patients, all 50 patients completed the eligibility questions, giving a survey response rate of 86% (50/58). All respondents were eligible. Of the 50 patients who completed the questionnaire, 36 (72%) completed all of the endpoint questions and comprised the primary analysis set; and all 50 patients (100%) completed at least 1 of the endpoint questions and comprised the secondary analysis set. From herein, the key results will be summarised for the primary analysis set.

Variables and Data Sources

The survey questionnaire was developed to evaluate patients' knowledge of the key messages, and levels of awareness (receipt) and reading, of the Patient Safety Brochure, and receipt, reading, knowing the purpose of, and use of the Patient Alert Card. Success was defined as a knowledge threshold of at least 60% of the sample providing a correct response for each question in each of 8 key domains.

- **Results**

In this study, 58 patients in Germany and the Netherlands were invited to participate in the survey and 50 patients (86.2%) met subject eligibility criteria and were included in the study analysis. Among the respondents, 36 of the 50 patients (72%) completed all the primary endpoint questions (questions 1-17) and represented the primary analysis set; and all 50 patients (100%) completed at least 1 of the endpoint questions, representing the secondary analysis set. From herein, the key results will be summarised for the primary analysis set.

Patients' knowledge was analysed in 8 key domains: 1) risk of disseminated herpetic infection in immunocompromised individuals, 2) risk of spread of the IMLYGIC virus to close contacts, 3) risk of symptomatic herpes infection during or after treatment with IMLYGIC, 4) need to keep injection sites covered with dressings at all times, 5) need to avoid touching or scratching the injection sites, 6) use of IMLYGIC during pregnancy may cause foetal harm, 7) instructions to minimise the risk of exposure of blood and body fluids to close contacts during or after treatment with IMLYGIC, and 8) instructions for safe disposal of used dressings and cleaning materials.

For **Domain #1**, knowledge levels on the risk that you can develop cold sores or a more serious herpes infection during or after treatment with IMLYGIC did not meet the 60% success threshold (47.2%; 95% CI: 30.4-64.5%).

For **Domain #2**, knowledge for the four survey items that were mapped to key messages on the knowledge of risk of spread of the IMLYGIC virus to patient's close contacts ranged from 55.6% to 97.2%. Patients met knowledge levels that exceeded the 60% success threshold for 3 of the 4 survey items: knowledge that close contacts who have direct contact with body fluids of IMLYGIC injection sites may be at risk to develop herpes virus (83.3%; 95% CI: 67.2-93.6%); knowledge that in case of accidental exposure, your close contacts should clean the affected area thoroughly with soap and water and/or a disinfectant (77.8%; 95% CI:60.8-89.9%); and knowledge that people should avoid direct contact with your injection sites or body fluids (97.2%; 95% CI:85.5-99.9%). Although more than half of patients (55.6%; 95% CI:38.7-72.1%) had knowledge that close contacts do not need to avoid hugging you until your treatment with IMLYGIC is completed, patients did not meet the success threshold for this item.

For **Domain #3**, knowledge for the 12 survey items that were mapped to key messages on the knowledge of risk of symptomatic herpetic infection during or after treatment with IMLYGIC ranged from 13.9% to 80.6%. Patients met or exceeded the 60% success threshold for 2 of 12 survey items: knowledge that pain or tingling in a blister around the mouth or genitals is a sign or symptom of a herpes infection (72.2%; 95% CI: 54.8-85.8%), and knowledge to call the doctor who prescribed IMLYGIC right away if you have any signs or symptoms of a herpes infection during or after treatment with IMLYGIC (80.6%; 95% CI: 64.0-91.8%).

Patients did not meet the 60% threshold for 10 of 12 survey items in domain #3: knowledge that diarrhoea is not a sign or symptom of a herpes infection; knowledge that eye pain, light sensitivity, discharge from the eyes, redness of the eye, tearing of the eye, and blurry vision are signs or symptom of a herpes infection; knowledge that weakness in arms or legs is a sign or symptom of a herpes infection; knowledge that extreme drowsiness is a sign or symptom of a herpes infection; knowledge that frequent urination is not a sign or symptom of a herpes infection; knowledge that fever associated with headache is a sign or symptom of a herpes infection; knowledge that mental confusion or memory loss is a sign or symptom of a herpes infection; knowledge that seizures are a sign or symptom of a herpes infection; and knowledge that vomiting is a sign of a herpes infection.

For **Domain #4**, knowledge for three survey items were mapped to key messages on the knowledge regarding keeping the IMLYGIC injection site covered with dressings at all times ranged from 47.2% to 100%. Patients met knowledge levels that exceeded the 60% success threshold for 2 of 3 survey items: knowledge that if you are receiving IMLYGIC, you should keep the IMLYGIC injection sites covered with airtight and watertight dressings (86.1%; 95% CI: 70.5-95.3%) and knowledge that you should tell people who change your dressing to always wear gloves while changing your dressing (100%). Overall, patients did not have knowledge that your close contacts are allowed to change your injection site dressing (47.2%, 95% CI:30.4-64.5%).

For **Domain #5**, there was a single question, and the majority of patients met the knowledge threshold that if they are receiving IMLYGIC, they should avoid touching or scratching the IMLYGIC injection sites (83.3%, 95% CI:67.2-93.6%).

For **Domain #6**, there was a single question and patients did not meet the knowledge threshold that if you receive IMLYGIC and are pregnant or become pregnant, there is risk to your unborn baby and that you need to tell your doctor if you are pregnant or if you plant to become pregnant (47.2%, 95% CI: 30.4-64.5%).

For **Domain #7**, knowledge for 5 survey items mapped to the instructions to minimise the risk of exposure of blood and body fluids to close contacts for the duration of IMLYGIC treatment ranged from 30.6% to 91.7%. Patients met or exceeded the 60% success threshold for 3 of 5 survey items: knowledge that you should avoid sharing injection needles, razor blades, and toothbrushes with close contacts while receiving IMGLYIC (91.7%, 95% CI: 77.5-98.2%); knowledge that you should avoid sharing cutlery, crockery, and drinking vessels with close contacts while receiving IMLYGIC (80.6%, 95% CI:64.0-91.8%); and knowledge that you should avoid kissing if you or your partner has an open mouth sore while receiving IMYLGIC (83.3%, 95% CI:67.2-93.6%). However, patients did not meet the knowledge threshold for 2 questions: knowledge that you should take action to minimize the risk of exposure of your blood and body fluids to your close contacts while being treated with IMLYGIC and for 30 days after your last injection (30.6%, 95% CI:16.3-48.1%); and knowledge that you do not need to avoid sexual intercourse with barrier protection while receiving IMLYGIC (33.3%, 95% CI: 18.6-51.0%).

For **Domain #8**, patients exceeded the 60% success threshold for knowledge that if you are receiving IMLYGIC, you should place all used dressings and injection site cleaning materials in a sealed plastic bag, and throw them away in household waste (86.1%, 95% CI: 70.5-95.3%).

A secondary endpoint evaluated the percentage of patients that reported receiving and reading the IMLYGIC Patient Safety Brochure; and report receipt, reading, and use (ie, carrying) of the IMLYGIC Patient Alert Card. The majority of patients reported receipt of the IMLYGIC patient brochure (83.3%). Of those who received the IMLYGIC patient

brochure, nearly all patients read "all" or "some" of the IMLYGIC Patient Safety Brochure (93.3%).

Only one-third of patients reported receiving the Patient Alert Card (30.6%).In terms of understanding the purpose of the Patient Alert Card, patients had knowledge that the purpose of the Patient Alert Card for IMLYGIC is to let other healthcare professionals that provide care for them to know that they are receiving IMLYGIC (90.9%), to provide contact details for their IMLYGIC prescriber (doctor) in case one of their close contacts or they develop a herpetic lesion (60%). Of those who reported receiving the Patient Alert Card, nearly three-quarters reported "always" or "sometimes" carrying it with them (72.7%).

The exploratory objective evaluated a composite variable on patients' knowledge levels for all 8 primary endpoints. None of the patients responded to all 27 items in the survey correctly. The majority of patients answered between 9-17 items correctly (64.9%, n=24/37).

For the other endpoint that was not mapped to the domains, 97.2% of patients knew that IMLYGIC is a medicine that contains a weakened form of herpes simplex virus type 1.

- **Discussion**

For the 50 patients who participated in this study, knowledge levels of the key messages included in the IMLYGIC Patient Safety Brochure and Patient Alert Card ranged from 13.9% to 100% for individual items. Knowledge levels were comparable to those described in other published aRMMs. Receipt of the Patient Safety Brochure was reported by 82% (n=41/50) of the patients in this survey, and receipt of the Patient Alert Card was reported by 34% (n=17/50) of patients.

- **Marketing Authorization Holder(s)**

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