2. Abstract

2.1 Title

A cross-sectional study to evaluate the effectiveness of additional Risk Minimisation Measures: A Survey among surgeons to assess their knowledge and understanding of selected risks of InductOs (dibotermin alfa/ACS) in Europe.

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2.2 Keywords

InductOs, knowledge, heterotopic ossification, risk minimization

2.3 Rationale and background

The active ingredient of InductOs is dibotermin alfa or recombinant human Bone Morphogenetic Protein 2. Its osteoinductive properties result in the induction of new bone tissue at the site of implantation.

InductOs is approved for:

- single-level lumbar interbody spine fusion as a substitute for autogenous bone graft in adults with degenerative disc disease who have had at least 6 months of non-operative treatment for this condition.
- treatment of acute tibia fractures in adults, as an adjunct to standard care using open fracture reduction and intramedullary unreamed nail fixation.

Additional risk minimisation measures (aRMM) to increase awareness about the identified risk of heterotopic ossification (especially in posterior surgical approaches for lumbar interbody fusion) and the potential risk of medication errors and misuse are available in the form of educational materials. This study was set up to measure the effectiveness of InductOs educational materials.

2.4 Research question and objectives

Primary questions:

- Do physicians administering InductOs understand the potential for heterotopic ossification occurrence after spinal interbody fusion?
- Do physicians administering InductOs know the appropriate measures to be taken to minimize the risk of heterotopic ossification occurrence?

Secondary question:

- Was the knowledge on the risk of heterotopic ossification and minimization measures obtained from the SmPC, educational materials, professional training and literature, or a combination of these?

Objective:

The goal of this study was to assess the awareness of InductOs-using spine surgeons concerning heterotopic ossification in relation to the InductOs Risk Management Plan. A supplementary goal of this study was to gauge the clinician's awareness about the development of heterotopic ossification and the risk minimisation measures; specifically identifying from which source any knowledge was obtained.

2.5 Study design

An anonymous, cross sectional and non-interventional (online) survey of a sample of physicians from Germany, France, Ireland and the United Kingdom who have implanted InductOs in the last 2 years.

2.6 Setting

Participants were chosen from a pool of the four countries comprising the largest InductOs-selling countries (France, Germany, United Kingdom and Ireland). Data was collected from these users in the period October to December 2020.

2.7 Subject and study size

Inclusion criteria

Participants of this study must have met the following inclusion criteria to be eligible to participate in this study:

1. Physicians that have implanted InductOs in a lumbar interbody spine fusion procedure at least once in the 24 months prior to taking this survey

Exclusion criteria

Participants meeting any of the following criteria were not be included in the study:

1. Physicians that participated in the testing of this survey, if there are substantial changes made to the survey post-pilot i.e. changes which, in the view of the research team, make the participants contributions invalid or potentially compromising of the study objectives.
2. Physicians that either themselves work for or have immediate family members who work for Medtronic, third parties involved in this study, or a regulatory agency (EMA, MHRA, HPRA, ANSM, BfARM).

A total of 55 physicians participated in the survey. There was 1 physician from Ireland, and 18 each from France, Germany and the United Kingdom.

2.8 Variables and data sources

Information was collected on three main categories. The first category was used to describe the population and includes variables around demographics, type of practice, and level of experience in using InductOs. The second category of variables was aimed at measuring the awareness on the risk of heterotopic ossification, the educational materials and knowledge about safe use of InductOs presented in the educational materials. The third set

of variables covered the different sources where information on the key messages in the educational materials could have been obtained.

Data was collected using a standardized online questionnaire that has been translated into the local languages of the countries where the survey is being conducted.

2.9 Results

It was found that 19 physicians (35 %) were fully aware of the information regarding heterotopic ossification and the relevant risk minimization.

The majority of physicians will always or frequently use scientific publications (75 % of physicians) or information from peers (78 %) when considering the use of InductOs or when administering InductOs.

2.10 Discussion

The overall awareness of physicians was below the set target with only 35 % of physicians being able to answer 75 % or more of the questions correct.

When considering the use or administration of InductOs, physicians tend to always or frequently use scientific publications (75 % of physicians) or information from peers (78 %). For materials provided by the MAH it is less common to use them always or frequently: SmPC (36 % of physicians), educational materials (38 %), other information from MAH (29 %).

The data obtained in this study do not describe potential clinical effects related to heterotopic ossification. This survey assessed the ability of physicians to provide the correct answer related to heterotopic ossification and the associated risk minimization.

2.11 Conclusion

Based on the available data it is concluded that InductOs-using spine surgeons are not fully aware of the information concerning heterotopic ossification in relation to the InductOs Risk Management Plan.

2.12 Marketing Authorisation Holder

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2.13 Names and affiliations of principal investigators

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