Trastuzumab Deruxtecan Post-Authorisation Safety Study (PASS) – Report Abstract - EUPAS46367

Title	Health Care Professional survey on understanding of key risk minimization measures related to interstitial lung disease (ILD) / pneumonitis with Trastuzumab Deruxtecan treatment
Keywords	Risk minimisation measures (RMMs), educational material (EM), survey
Rationale and background	Trastuzumab Deruxtecan (T-DXd, Enhertu®) is an antibody drug conjugate (ADC) indicated for the treatment of adult patients suffering from various tumour types. ILD and/or pneumonitis have been identified as important risks for patients treated with T-DXd, and fatal outcomes have been observed. To prevent / minimize the occurrence of severe ILD/pneumonitis, the Marketing Authorization Holder (MAH) Daiichi-Sankyo Europe (DSE) proposed additional RMM for ILD/pneumonitis and had developed EM accordingly.
Research question and objectives	The aim of this study was to evaluate the effectiveness of T-DXd's RMMs for the important identified risk of ILD/pneumonitis. The primary objective for this study was: • To assess physicians' awareness, knowledge, and implementation of aRMMs related to the risk, early detection, diagnosis, and management of ILD/pneumonitis. The secondary objectives for this study were: • To measure physicians' awareness of the ILD/pneumonitis risk and its related minimisation measures • To assess the extent to which physicians are aware of having received the educational material (HCP guide and patient card) • To measure physicians' knowledge on the requirement for treatment modifications in case of suspected ILD/pneumonitis • To measure physicians' knowledge on the requirement to monitor specific signs and symptoms that allow early detection of ILD/pneumonitis • To assess whether physicians implement the recommended talking points to patients at the recommended frequency

	• To assess the extent to which physicians implement the distribution of the patient card to their patients
Study design	This was a cross-sectional, multi-national survey conducted among physicians who are prescribers or potential prescribers of T-DXd in a selection of European countries where T-DXd is marketed. An online multiple-choice questionnaire was used to capture the physicians' responses in the survey.
Setting	The survey was conducted among office and hospital-based physicians in European countries approximately 12 months after the distribution of EM for T-DXd. According to the launch sequence of T-DXd planned for 2021-2022, the following 7 European countries were included in the survey: Austria, Denmark, France, Germany, Sweden, Spain, UK.
Subjects and study size	The population to be surveyed in the selected countries comprised physicians who were prescribers or potential prescribers of T-DXd. The physicians were contacted in a random order and invited to participate in the survey until the target number of physicians for that country was reached. Physicians had to meet the following inclusion criterion: • Physicians on the distribution list for the EM In addition, the physician participation was subject to the following exclusion criteria: • Physicians who may have had conflicts of interest with the survey • Physicians who were not actively treating patients for their breast cancer • Physicians who were not aware of T-DXd
Variables and data sources	The following variables were recorded in the survey: 1. Variables related to physician's characteristics and practice information. 2. Variables related to the physician's awareness about the important identified risk of ILD/pneumonitis as well as the physicians' awareness of clinical measures with respect to the identified risk.

	3. Variables related to the physician's knowledge on the requirement to monitor specific signs and symptoms that allow early detection of ILD/pneumonitis and its management - percentages of physicians with correct answers. 4. Variables related to the implementation of the proposed risk minimization measures by the physicians. 5. Other variables. The questionnaire focused on evaluating the participants' knowledge and understanding of the EM related to the important risk of ILD/pneumonitis. It included multiple-choice and closed questions, as appropriate. The original survey questionnaire was validated in a multistep process including input from medical experts of relevant specialties and relevant local languages for its comprehensibility, consistency, and the appropriateness of medical terms.
Results	The final study sample (full analysis set, FAS) used for the analysis consisted of 172 T-DXd prescribers: 154 (89.5%) oncologists and 18 (10.5%) gynaecologists. These are divided among the participating countries as follows: Austria n=18, France n=56, Germany n=44, Spain 23, Nordics (Denmark and Sweden) n=14 and UK n=17 physicians. The majority of the respondents were hospital-based (76.7%), had more than 10 years of experience as practicing physicians (79.1%) and had prescribed T-DXd to at least five patients (67.2%). Overall, 91.6% of physicians were aware of ILD risk for T-DXd, 46.7% were knowledgeable on the risk and management of ILD/pneumonitis and 76.7% responded to the implementation part of the questionnaire successfully (weighted results). This pattern is similar in all participating countries. Taking all the 3 domains together the success rates of the survey respondents with respect to the weighted results were 39.5% for success in all 3 domains, 79.0% success in at least 2 domains.

Discussion	Overall, the results indicate effectiveness of the risk minimisation measures for TDXd according to the pre-defined success thresholds for the domains awareness and implementation. The vast majority of physicians was aware of the ILD risk and the awareness was relatively homogenously distributed across the countries. In addition, most physicians responded correctly to the implementation questions. The results indicate that nearly half of participating physicians had detailed knowledge on the risk of ILD/pneumonitis in conjunction with T-DXd. For the other half, there was primarily one detail (fever) of the ILD risk less recognized leading to an insufficient knowledge score. A separate analysis of the individual responses to the knowledge questions revealed that over 50% of physicians did not consider "fever" to be a typical sign for ILD/pneumonitis. A reason might be that fever is considered a too generic symptom and not typically specifically associated with ILD/pneumonitis sufficiently. When omitting fever as a mandatory answer in a post-hoc analysis, the success threshold for the domain knowledge was clearly met (68.6%).
Conclusion	Overall, the results suggest that the RMMs are effective in all participating countries with respect to physicians' awareness and implementation of aRMMs related to the risk, early detection, diagnosis, and management of ILD/pneumonitis. Although the RMMs seem to be less effective with respect to physicians' knowledge - mainly driven by the observation that "fever" was not considered to be a typical sign for ILD/pneumonitis - it is important to highlight the good knowledge of the physicians regarding this risk in conjunction with T-DXd.
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