Reporting of adverse events in targeted therapy and immunotherapy trials is 'suboptimal'

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A significant number of trials of targeted therapies and immunotherapies in recent years show suboptimal reporting of adverse events, particularly the reporting of recurrent or late toxicities and the duration of the adverse events, researchers have told the ESMO 2016 Congress in Copenhagen.

"Reporting adverse events from clinical trials with new agents is a crucial point, as this will inform physicians and patients regarding the safety profile of that drug and what to expect when starting this therapy in a new patient in everyday clinical practice," said principal investigator Dr Paolo Bossi, from the Head & Neck Unit at the Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan.

In this study, researchers reviewed publications from 81 trials of targeted therapies and immunotherapies approved by the US Food and Drug Administration between 2000-2015 for solid malignancies in adult patients. Each publication was assessed according to a 24-point score card based on the Consolidated Standards of Reporting Trials (CONSORT) guidance.

More than 90% of trials scored poorly in their reporting of recurrent and late toxicities, and in reporting the duration of adverse events; 86% of trials did not adequately report on the time of the adverse event occurrence; and 75% of trials only reported on adverse events that

occurred at a frequency above a fixed threshold.

More than half of the analysed papers showed limitations in the method for presenting adverse events, in describing the toxicities leading to therapy withdrawal, and in the follow-up interval assessment, while dose reductions due to adverse events were not reported in one-third of trials.

"Toxicities of targeted agents and immunotherapy are obviously different from the toxicities we are used to observing and treating due to chemotherapy, and there are some aspects of the toxicities of these newer agents that we are not so well informed about," Dr Bossi said.

He highlighted the issue of duration of an adverse event - the so-called 'third axis' (the other being severity and frequency) in the evaluation of toxicities - which is not regularly considered with a new drug comes to market.

Dr Bossi said that it was encouraging to see a trend towards improved adverse event reporting in recent years. Moreover, there are new instruments available that can help physicians to improve the quality of adverse event reporting and help them discuss potential toxicities with their patients.

"The most important and innovative one is the PRO-CTCAE form, which is the patient-reported outcome version of the common toxicity criteria of adverse events, and which will allow physicians to collect the symptoms as reported by the patients, considering also the severity, intensity and influence of the symptoms on their quality of life."

Commenting on the study, Dr Nathan Cherny from the Shaare Zedek Medical Center in Jerusalem, said, "it ought to be remembered that there is pre-existing evidence that toxicity reporting based upon clinician reports, rather than patient reported data, consistently leads to

underreporting of adverse events and the severity of those events."

"These findings lend further support to the proposal to radically re-evaluate the collection and reporting of adverse event data to give weighting to patient-reported data," Dr Cherny said.

He concluded: "It is worth noting however, that the published reports of studies represent a summary of a dataset that may not necessarily represent the full data set submitted to licensing authorities for purposes of drug approval and registration."

More information: Abstract 320 P 'Systematic review of adverse events reporting in clinical trials leading to approval of targeted therapy and immunotherapy' will be presented by Dr. Paolo Bossi during Poster Session on Clinical trials methodology on 10.10.2016 from 13:00 - 14:00 CEST, Hall E

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