

Assessing an ASCO Decision Aid for Improving the Accuracy and Attribution of Serious Adverse Event Reporting From Investigators to Sponsors

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1. Background

Investigators often send adverse event (AE) reports to sponsors that are incorrectly categorized as serious or misattributed to the investigational drug, contrary to published guidance from the U.S. Food and Drug Administration (FDA). Such errors contribute to a high volume of uninformative Investigational New Drug (IND) safety reports that sponsors submit to FDA and all participating investigators, straining stakeholder resources and impeding the detection of valid safety signals.

2. Goals

To improve the quality of AE reporting, ASCO developed and tested a Decision Aid Tool (DAT). The DAT is an educational tool (one page flowchart) that is designed to improve the accuracy of physician investigator and research staff decision-making about whether an AE should be (1) reported to the sponsor as a serious adverse event (SAE) and (2) attributed to the investigational drug. An effective DAT would reduce the number of uninformative safety reports that are submitted to trial sponsors, the FDA, and participating investigators. Reducing the number of uninformative reports would reduce administrative burden on the FDA, sponsors, trial sites, and clinical research teams, and would increase the efficiency of clinical trials. The time and cost savings associated with increased efficiency would allow for expanded clinical trial participation by individual investigators, research sites, and sponsors. Moreover, reducing uninformative reports would protect patient safety by improving the detection of valid safety signals from clinical trial data.

3. Solutions and Methods

A preliminary study with a cross-over design was conducted to test the DAT. Physician investigators and research staff were randomized to receive clinical case studies. Cases were assessed by participants for seriousness and attribution to the investigational drug, first unassisted and then with the DAT. Participants also completed a feedback survey about the DAT. Effectiveness of reporting and attribution were assessed using logistic regression.

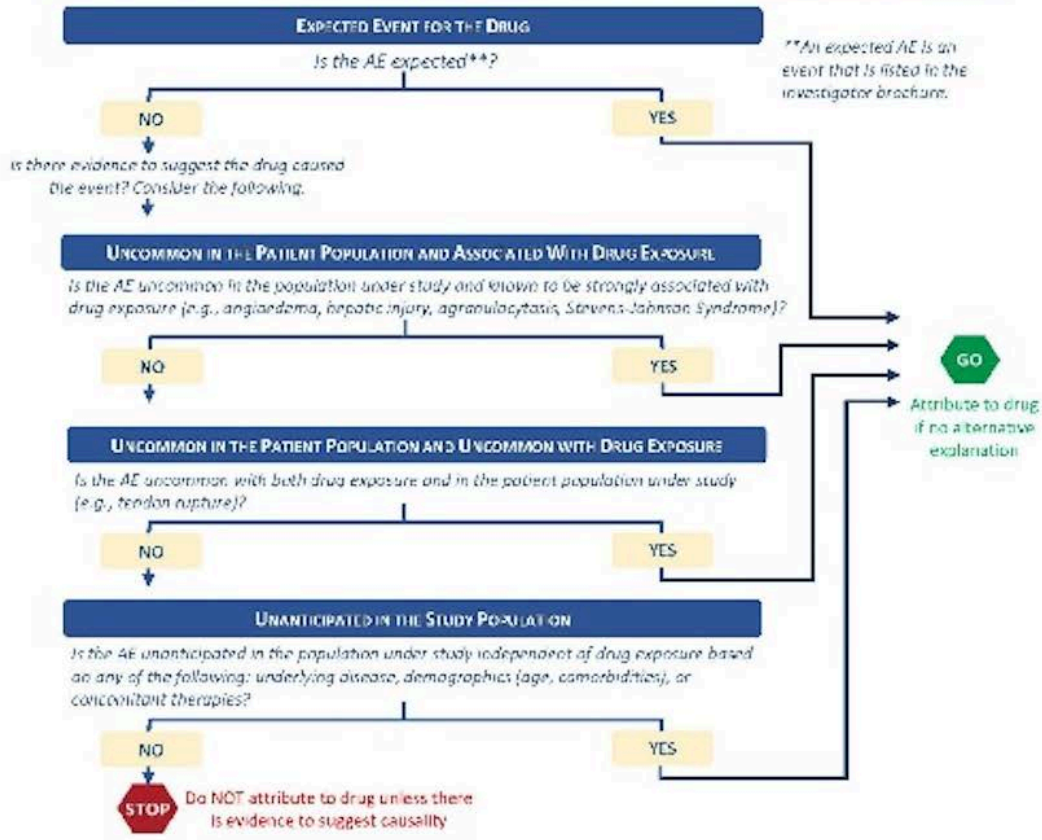
ASCO Adverse Events Reporting Decision Aid[®]

The ASCO Adverse Events Reporting Decision Aid is intended to assist physician investigators and research staff in determining whether an adverse event (AE) should be: (i) reported to the sponsor as a serious AE (SAE) and (ii) attributed to the investigational drug. The Decision Aid is intended to be a general guide for deciding whether an adverse event is caused by an investigational drug. These decisions ultimately require clinical judgement to determine if there is a reasonable possibility that the drug caused the event. The Decision Aid accompanies an ASCO Toolkit that includes other educational resources related to AE reporting. The Toolkit is available via ASCO.org.

SUBMITTING A SERIOUS ADVERSE EVENT TO A TRIAL SPONSOR



ATTRIBUTING AN ADVERSE EVENT TO AN INVESTIGATIONAL DRUG IN AN SAE REPORT



Category: Regulatory – Completed Project

Most of the 29 participants reported that the DAT was helpful (93%), improved their decision-making time (69%) and confidence in reporting (83%), and that they would use it in practice (83%). The DAT significantly increased accuracy of attributing a serious AE to a drug (OR, 3.60; 95% CI: 1.15, 11.4), but did not significantly affect accuracy of determining seriousness (OR, 0.87; 95% CI: 0.31, 2.46). The lack of improvement in determining seriousness is likely due to the fact that seriousness was generally well-understood by the participants prior to exposure to the DAT.

5. Lessons Learned

The DAT shows promise as a method to improve the quality of SAE attribution by investigators and research staff, which may improve the detection of valid safety signals and reduce the administrative burden of uninformative IND safety reports. The DAT and a corresponding educational toolkit are being disseminated to the broader research community and are available on the ASCO Research Community Forum website (asco.org/research-community-forum). A JCO Oncology Practice manuscript highlights the DAT and these findings.