COPENHAGEN 2016 ESMO congress

SPECIAL SESSION
REPORTING CLINICAL TRIALS

Faculty of Principles of Clinical Trials and Systemic Therapy

INTRODUCTION

CHRISTIAN DITTRICH

3rd Medical Department – Centre for Oncology and Haematology
Kaiser Franz Josef-Spital, Vienna, Austria
Applied Cancer Research – Institution for Translational Research Vienna (ACR-ITR VIEnna)

DISCLOSURE

I have no Conflicts of Interest to declare

STANDARDS FOR ACCURATE PUBLICATION AND PRESENTATION OF RESEARCH

International Society for Medical Publication Professionals (www.ismpp.org)	Code of ethics
	Position statement: the role of the professional medical writer
Association of American Medical Colleges (www.aamc.org)	Report of task force on industry funding of medical education
American Medical Writers Association (www.amwa.org)	Code of ethics
	Position statement: the contribution of medical writers to scientific publications
Committee on Publication Ethics (http://publicationethics.org)	Multiple resources for editors
Council of Science Editors (www.councilscienceeditors.org)	White paper on promoting integrity in scientific journal publications
Elsevier (www.elsevier.com/wps/find/editorshome.editors/Introduction)	Publishing ethics resource kit
European Medical Writers Association (www.emwa.org)	Guidelines on the role of medical writers in developing peer reviewed publications
EQUATOR Network (www.equator-network.org)	Reporting guidelines—for example, CONSORT, STROBE, QUOROM/PRISMA, STARD, MOOSE
Federation of American Societies for Experimental Biology (www.faseb.org)	Conflicts of interest in biomedical research—the FASEB guidelines
International Committee of Medical Journal Editors (www.icmje.org)	Uniform requirements for manuscripts submitted to biomedical journals: writing and editing for biomedical publication
Institute of Medicine (www.iom.edu/CMS/3740/47464/65721.aspx)	Conflict of interest in medical research, education, and practice
International Federation of Pharmaceutical Manufacturers and Associations (www.ifpma.org/fileadmin/pdfs/webnews/Revised_Joint_Industry_Position_26Nov08.pdf)	Joint position on the disclosure of clinical trial information via clinical trial registries and databases
International Society for Pharmacoeconomics and Outcomes Research (www.ispor.org/PEguidelines/index.asp)	Pharmacoeconomic guidelines around the world
Pharmaceutical Research and Manufacturers of America (www.phrma.org)	Principles on conduct of clinical trials and communication of clinical trial results
World Association of Medical Editors (www.wame.org/resources /policies)	WAME policy statements prepared by the editorial policy committee, including conflict of interest in peer reviewed medical journals
Wiley-Blackwell (www.wiley.com/bw/publicationethics)	Best practice guidelines on publication ethics: a publisher's perspective

Good publication practice for communicating company sponsored medical research: the GPP2 guidelines
Graf et al; BMJ 339:b4330,2009

ADVERSE EVENT REPORTING IN CANCER CLINICAL TRIAL PUBLICATIONS

Review of publications 2009-2011 (PubMed, Medline, Embase)

Assessment for 14 adverse event-reporting elements derived from CONSORT

---

175 publications: Data on 96,125 patients

96%: AEs reported above a threshold rate or severity

37%: Criteria used for selection of reporting on AEs not specified

88%: AEs of varying severity grouped together

Development of oncology-specific standards for AE reporting required

Sivendran et al; J Clin Oncol 32:83-89,2013

NEW DEVELOPMENTS IN PRO ASSESSMENTS

Discussion about current use of (HR) QoL measures in cancer clinical trials as they include large, multi-domain assessments that attempt to evaluate a broad concept

FDA Criticism about 'static' (HR) QoL measures that include the same questions, irrespective of stage or therapy being studied (Kluetz P, *et al*. AACR 2016):

- Increased flexibility can be obtained to adapt to differing disease and therapy contexts when measuring PRO-CTCAE in combination with physical functioning

EORTC advocates a combination of standardised (HR) QoL measures with validated items from item libraries like PRO-CTCAE, EORTC or other libraries

- This approach ensures evaluation of side effects and their impact on functional health problems reported by patients

SUBGROUP ANALYSES IN RANDOMIZED TRIALS

Review of publications 2011-2013 (Medline via PubMed)

Assessment of prespecification of subgroup analyses, number, subgroup factors, interaction test use, claim for subgroup difference

---

221 publications: Data on 184,500 patients

85% (188): RCTs reported with subgroup analyses

92% (173): Number of subgroup analyses not determined

31% (59): RCTs reported with fully prespecified subgroups

34% (64): Trials reported with interaction tests

54% (102): RCTs reported with claims of subgroup differences

18% (18): Claims of RCTs based on interaction test results

Problems: Large number of subgroups, subgroups without prespecifications, inadequate use of interaction tests

Zhang et al; J Clin Oncol 33:1697-1702,2015
Commentary by Altman DG; Nature Rev Clin Oncol 12;2015

META-ANALYSES

British Journal of Cancer (1996) 74, 496–501

GUEST EDITORIAL

Meta-analyses of randomised trials: when the whole is more than just the sum of the parts

MKB Parmar[1], LA Stewart[1] and DG Altman[2]

META-ANALYSES

VOLUME 25 · NUMBER 29 · OCTOBER 10 2007

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Surrogate End Points for Median Overall Survival in Metastatic Colorectal Cancer: Literature-Based Analysis From 39 Randomized Controlled Trials of First-Line Chemotherapy

Patricia A. Tang, Søren M. Bentzen, Eric X. Chen, and Lillian L. Siu

PFS an appropriate surrogate for OS

VOLUME 25 · NUMBER 33 · NOVEMBER 20 2007

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Progression-Free Survival Is a Surrogate for Survival in Advanced Colorectal Cancer

Marc Buyse, Tomasz Burzykowski, Kevin Carroll, Stefan Michiels, Daniel J. Sargent, Langdon L. Miller, Gary L. Elfring, Jean-Pierre Pignon, and Pascal Piedbois

PFS an acceptable surrogate for OS

THESIS

Stopping early because of benefit is claimed to be ethically justified:

Inacceptable to withhold a more effective remedy from a patient in the control arm

ANTITHESIS

"A good intention is still far from being a good deed"

(Alfred Polgar)

Some initially asked questions may become unanswered but will never more be approached although being important

This may be even more unethical !