Restenosis, statistics, and reasonable inferences: REPLY

Dean J. Kereiakes, Richard E. Kuntz, Laura Mauri, and Mitchell W. Krucoff

J. Am. Coll. Cardiol. published online Dec 22, 2005;
doi:10.1016/j.jacc.2005.10.036

This information is current as of February 10, 2010

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://content.onlinejacc.org/cgi/content/full/j.jacc.2005.10.036v1

JACC
JOURNAL *of the* AMERICAN COLLEGE *of* CARDIOLOGY

Downloaded from content.onlinejacc.org by on February 10, 2010

ARTICLE IN PRESS

Journal of the American College of Cardiology
Vol. 47, No. 2, 2006
ISSN 0735-1097/06/$32.00
© 2006 by the American College of Cardiology Foundation
Published by Elsevier Inc.

REPLY

Although we appreciate the interest by Dr. Ellis and colleagues toward our recent editorial comment (1), we fear a central concept was missed. The argument that more late loss (as long as the absolute measure remains below some arbitrary threshold) is irrelevant as a measure of drug-eluting stent (DES) efficacy is both intuitively flawed and derived by an erroneous extrapolation from *individual* patient-level observations to *mean* late loss values. Across observed levels of mean late loss in recent trials, incremental changes in late loss are associated with increasing restenosis risk (2). The relationship of mean late loss values to clinical restenosis does not follow the S-shaped curve presented by Dr. Ellis and colleagues but instead is curvilinear without an obvious inflection point (2). Furthermore, results of randomized controlled clinical trials comparing the Cypher and Taxus stents for treatment of coronary stenoses in complex patient subsets do not support the "threshold" premise (3–6). Although the ISAR–DIABETES, SIRTAX, REALITY, and ISAR–DESIRE trials reported mean late loss values well below the 0.75 mm "threshold" for clinical significance set by Dr. Ellis and colleagues, the observed binary angiographic restenosis (BAR) and target lesion revascularization (TLR) rates were increased in proportion to increases in late loss (Table 1). If coronary stents are deployed in one million individuals yearly, the relative percent differences in BAR and TLR observed in these trials translate into large socioeconomic differences (≥50,000 more revascularization procedures yearly) and clearly support the premise that "less is better" with respect to late lumen loss in the DES era.

As we predicted in our editorial, when DES with apparent subtle differences in late lumen loss are compared, differences in late clinical/angiographic outcome measures are magnified in those patient cohorts with the greatest propensity for restenosis. Thus, late lumen loss remains a primary measure of stent efficacy, which correlates with late clinical/angiographic outcomes in the DES era.

***Dean J. Kereiakes, MD**
Richard E. Kuntz, MD, MSc
Laura Mauri, MD, MSc
Mitchell W. Krucoff, MD

*The Lindner Center for Research & Education
and The Ohio Heart Health Center
2123 Auburn Avenue
Suite 424
Cincinnati, OH 45219
E-mail: lindner@fuse.net

doi:10.1016/j.jacc.2005.10.036

REFERENCES

1. Kereiakes DJ, Kuntz RE, Mauri L, Krucoff MW. Surrogates, substudies, and real clinical end points in trials of drug-eluting stents. JAM Coll Cardiol 2005;45:1206–12.
2. Mauri L, Orav EJ, Kuntz RE. Late loss in lumen diameter and binary restenosis for drug-eluting stent comparison. Circulation 2005;111: 3435–41.
3. Dibra A, Kastrati A, Mehilli J, et al. Paclitaxel-eluting or sirolimus-eluting stents to prevent restenosis in diabetic patients. N Engl J Med 2005;353:663–70.
4. Windecker S, Remondino A, Eberli FR, et al. Sirolimus-eluting and paclitaxel-eluting stents for coronary revascularization. N Engl J Med 2005;353:653–62.
5. Morica M-C, Serruys PW, Colombo A, et al. Eight-month outcome of the REALITY study: a prospective, randomized, multi-center head-to-head comparison of the sirolimus-eluting stent (Cypher) and the paclitaxel-eluting stent (Taxus). Presented at the 2005 Annual Scientific Session of the American College of Cardiology, Orlando, FL, March 6–9, 2005. Available at: http://www.clinicaltrialresults.org/home.htm. Accessed July 27, 2005.
6. Kastrati A, Mehilli J, von Beckerath N, et al. Sirolimus-eluting stent or paclitaxel-eluting stent vs balloon angioplasty for prevention of recurrences in patients with coronary in-stent restenosis: a randomized controlled trial. JAMA 2005;293:165–71.

Downloaded from content.onlinejacc.org by on February 10, 2010

ARTICLE IN PRESS

Table 1. Randomized Comparative Trials of Cypher Versus Taxus Stents

Trial	Late Lumen Loss (mm)		BAR (%)		TLR (%)	
	Cypher	Taxus	Cypher	Taxus	Cypher	Taxus
ISAR-DIABETES	0.19	0.45	6.9	16.5	6.4	12.0
SIRTAX	0.13	0.25	6.7	11.9	4.8	8.3
REALITY	0.09	0.31	9.6	11.1	5.0	5.4
ISAR-DESIRE	0.10	0.26	14.3	21.7	8.0	19.0

Downloaded from content.onlinejacc.org by on February 10, 2010

Restenosis, statistics, and reasonable inferences: REPLY

Dean J. Kereiakes, Richard E. Kuntz, Laura Mauri, and Mitchell W. Krucoff

J. Am. Coll. Cardiol. published online Dec 22, 2005;
doi:10.1016/j.jacc.2005.10.036

This information is current as of February 10, 2010

Updated Information & Services	including high-resolution figures, can be found at: http://content.onlinejacc.org/cgi/content/full/j.jacc.2005.10.036v1
Rights & Permissions	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://content.onlinejacc.org/misc/permissions.dtl
Reprints	Information about ordering reprints can be found online: http://content.onlinejacc.org/misc/reprints.dtl

Downloaded from content.onlinejacc.org by on February 10, 2010