Reviewer's report

Title: Effects of Abciximab on Key Pattern of Human Coronary Restenosis in Vitro: Impact of the SI/MPL-Ratio

Version: 1 Date: 7 November 2005

Reviewer: Rüdiger Blindt

Reviewer's report:

General
The study by Voisard and colleagues examined the in-vitro effects of abciximab on MAC-1 expression as well as on the migratory and proliferatory potential of HUVEC and coronary endothelial and smooth muscle cells. For this reason, the authors used FACS analysis of MAC-1 expression, a razor-wound migration model, and analysis of proliferation by cell counting. Furthermore, cell viability was quantified by luminescence analysis. The authors state that MAC-1 expression and the migratory potential in all three cell types was not altered by abciximab. Only, cell proliferation was significantly inhibited in the presence of high abciximab concentration. Thus, the study addresses three issues which are relevant for the pathophysiology of restenosis; i.e. inflammation, cell migration, and cell proliferation. Unfortunately, conclusions drawn from the study are limited due to the negative results (MAC-1 expression) or conflicting results to some previous studies which were performed some years ago and which have shown relevant inhibition of smooth muscle migration by abciximab. That implicates serious concerns regarding the techniques which were used to quantify cell migration. Furthermore, there are a some other limitations.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Ad 1: The authors analyzed only the influence of abciximab on MAC-1 expression in endothelial and smooth muscle cells. But, the effects of the substance on inflammatory cells as monocytes might be more relevant. Why did the authors not evaluate inflammatory cells? Furthermore, for an adequate analysis of the role of abciximab on inflammatory processes during restenosis, at least some more investigations of other inflammatory pathways should be performed (e.g. interleukin 6 and 10 expression, effects on chemokine expression, ...)

Ad 2: The authors state that cell migration was not significantly altered by abciximab. In contrast, there were a few other studies that showed significant inhibition of abciximab on SMC migration. (Bendeck MP et al. J Vasc Res. 2001; Baron JH et al. Cardiovasc Res. 2000, Blindt R et al. J Mol Cell Cardiol 2001). The reviewer is concerned regarding the adquate use of the migration model of this study. The razor wound model used for this study may not have enough sensitivity compared to more sensitive assays used in the other studies (e.g. Boyden chamber model).

Ad 3: In consideration of the fact that the effect of abciximab on smooth muscle and endothelial cell migration and proliferation was extensively studied previously and that there might be some problems with the migration model used by the authors, focussing on the first part of the study (abciximab and inflammation) might be favourable. The authors should try to analyse that role of abciximab in this context more detailed. Thus, deeper insight in the pathophysiology of alphavbeta3-integrin blockade and inflammation could be gained.

Ad 4: The authors used a t-test to determine statistical significance. The use of an ANOVA with appropriate post-hoc analysis is more adequate because n of the analysed groups is always >2.
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
Ad 1: The authors should state that the luminiscent assay works by measuring ATP as an indicator of cell viability.

Ad 2: page 6; ‘Durchflußzytometer’ should be translated to English

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests