Journal club

Doubts reduced – end of paclitaxel discussion in sight

Tanja Böhme

Department Cardiology and Angiology, University Heart Center Freiburg-Bad Krozingen, Germany

The importance of using paclitaxel coated drug-eluting devices, especially for the treatment of femoropopliteal lesions, is beyond doubt. However, a meta-analysis [1] of randomized controlled trials led to uncertainty regarding safety beyond 2 years post procedure suggesting an increased risk of all-cause mortality. With the unplanned interim analysis of the SWEDEPAD (Swedish drug eluting trial in peripheral arterial disease) trial [2], the results of the Katsanos analysis are now contrasted with a randomized trial in addition to numerous real-world studies.

The SWEDEPAD trial is a multicentre, randomized, open-label, register-based trial, including 2289 patients (1149 treated with paclitaxel-coated devices and 1140 treated with uncoated devices) at the time of analysis. The study included claudicants (809 patients) and patients with a critical limb ischemia (CLI) (1480 patients). The sole endpoint of the interim analysis was all-cause mortality. Predefined endpoints will be presented with the final analysis.

The mean follow-up was 2.49 years and no patient was lost to follow-up. 1457 patients had a follow-up of 2 years, 789 patients of 3 years, and 282 patients could be followed up for 4 years. The overall mortality rate was 25.1%. The mortality rate did not differ between the treatment groups. During follow-up patients with CLI had a mortality rate of 33.4% in the paclitaxel-coated device group and of 33.1% in the uncoated device group. For claudicants, mortality rate was 10.9% and 9.4%, respectively. Confirming analyses of health insurance data [3] and retrospective analyses [4, 5], this registry-based randomized trial did not show increased mortality after use of paclitaxel-coated devices.

However, this interim analysis is not without limitations. Of course, critics may now argue that paclitaxel devices used within the SWEDEPAD trial had lower dose density than in the trials included in the Katsanos meta-analysis. However, more than 50% of the devices used were devices with a drug density of 3 µg or more paclitaxel per mm^2 balloon surface. Except in the meta-analysis in no other study a dose relationship to the mortality rate was not found [6]; in addition, no mortality signal was found e.g. in oncology where much higher paclitaxel doses are used. Furthermore, due to the low death rate in the claudicant group and the associated wide range of confidence intervals in SWEDPAD, a difference in mortality cannot be completely excluded.

This interim analysis does not make any statement about the clinical outcome except mortality, however, this was not intended in the first place. The aim of Nordanstig et al. was to reduce concerns regarding the saftey of paclitaxel-coated devices. In the meantime, study enrollment – which was temporarily stopped until the results of the interims analysis were available – is ongoing again and it is hoped that full study enrollment and follow-up can be continued. If so, both safety aspects and clinical effectivity will be assessed over a longer period of time.

The SWEDEPAD trial is another step towards ending the paclitaxel safety discussion and is important for physicians and researchers. This is especially true for patients as they were no longer be deprived of an effective therapy. When the FDA and other authorities will react to this published data remains to be seen.

References

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Correspondence address
Dr. Tanja Böhme
Department Cardiology and Angiology
University Heart Center Freiburg-Bad Krozingen
79189 Bad Krozingen
Germany
tanja.boehme@universitaets-herzzentrum.de