Letter by Kounis et al Regarding Article, "Long-Term Efficacy and Safety of Everolimus-Eluting Bioresorbable Vascular Scaffolds Versus Everolimus-Eluting Metallic Stents: A Meta-Analysis of Randomized Trials"

To the Editor:

This significant meta-analysis[1] of 6 high-quality randomized trials reporting clinical outcomes beyond 1 year and comparing everolimus-eluting bioresorbable vascular scaffolds with everolimus-eluting metallic stents in 5392 patients demonstrated that the risk of definite or probable stent/scaffold thrombosis and very late stent/scaffold thrombosis was higher with bioresorbable vascular scaffolds. Specifically, the definite or probable stent/scaffold thrombosis was estimated in the range of 2.1% and 0.8% and very late stent/scaffold thrombosis between 0.8% and 0.2%, respectively, based on DerSimonian–Laird and Peto methods. The authors speculate that this difference could be attributed to the potential malposition, late discontinuity, peristrut low-intensity area, uncovered strut, underdeployment, incomplete lesion coverage, recoil, restenosis, strut thickness, and early discontinuation of dual antiplatelet therapy.

However, they should also have been referred to the components of everolimus bioresorbable vascular scaffolds, the further possible hypersensitivity, and also to July 5th Food and Drug Administration press release and the subsequent approval letter pointing out the recommendations and contraindications[2] that the research and clinical community should be aware of.

The ABSORB bioserorbable scaffold is composed of synthetic aliphatic polyesters, such as poly L-lactide backbone (PLLA), coated by poly-D, L-lactide, and everolimus that serving as antiproliferative agent. Both polymers are eventually degraded into lactic acid and finally into carbon dioxide and water via the Krebs cycle. Acidic degradation products accumulate and decrease the pH of the surrounding tissue, fact that could trigger inflammatory and foreign-body reactions in vivo. This process takes up to 2 years to complete. The lactic acid stimulates molecular lactic acid sensors on sensory neurons innervating the heart and induces similar pain with that encountered in coronary syndromes. Despite the theoretical advantage, PLLA scaffolds have proved to induce extensive inflammatory responses and subsequent neointimal hyperplasia in a porcine model. Although high-molecular-weight PLLA scaffolds are associated with minimal inflammatory reaction, the low-molecular weight, renders them more susceptible to hydrolysis, further resulting in an intense inflammatory reaction.[3]

Furthermore, nuclei of vascular endothelium and endangium of mini-pigs' coronary arteries implanted with PLLA scaffolds have showed positive staining of NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells). NF-κB is a nuclear factor serving as a marker of inflammation, which mediates the expression of numerous inflammatory cytokines and binds to enhancer element of the immunoglobulin κ light chain of activated B cells.[4]

Local foreign-body reactions, synovitis especially in orthopedics, and hypersensitivity reactions have been correlated with the use of PLLA. Systemic hypersensitivity reactions to PLLA acid screws used in orthopedics have been proven by positive skin tests and further necessitating removal of the screws.[5]

The recent Food and Drug Administration safety alert[2] on ABSORB GT1 Bioresorbable Vascular Scaffold System points out that this device is contraindicated in patients with a known hypersensitivity or allergy to everolimus, materials used in the device, such as PLLA, poly-D, L-lactide, contrast media, aspirin, antiplatelet agents, or platinum.

Therefore, strict adherence to Food and Drug Administration recommendations, improvement of current device technology, and efforts for inventing inert materials seem to be of paramount importance so as to avoid such dangerous consequences.

Disclosures

None.

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