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Mortality and cancer after 12 versus 30 months dual antiplatelet therapy: The Korean outcomes registry evaluating antithrombotics (Korea)

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Abstract

© Schattauer 2017. The optimal duration and cancer risks of antiplatelet therapy following percutaneous coronary intervention (PCI) are unclear. We compared cancer and all-cause mortality after dual antiplatelet therapy (DAPT) for the combination of clopidogrel and aspirin (ASA) versus ASA alone over 18 months follow-up in event-free patients at 12 months DAPT from the Health Insurance Review and Assessment (HIRA) dataset via the Korean Outcomes Registry Evaluating Antithrombotics (KOREA). We selected PCI patients who were event free for 12 months and maintained a consistent antiplatelet regimen for 18 more months. The primary endpoints were any cancer and all-cause mortality at 30 months follow-up after PCI. From 320,351 screened post-PCI patient HIRA records, we excluded 294,413 and qualified 25,938, constituting DAPT (n=10,992) and ASA (n=14,946) groups. The Propensity Score Matching (PSM), and Inverse Probability of Treatment Weighting (IPTW) revealed no significant differences in background demographics and clinical characteristics for DAPT versus ASA patients. At 30-months post-PCI, after massive (> 91 %) exclusions, cancer risk was higher for continuous DAPT [455 (4.15 %) vs 606 (4.04 %); HR=1.221; 95 %CI: 1.061-1.405; p=0.005], which remained significant by PSM (p=0.006) or IPTW (p=0.007), while all-cause mortality was similar [136 (1.24 %) vs 192 (1.28 %) HR=0.999; 95 %CI: 0.736-1.135; p=0.993]. This analysis suggests a potential mild excess cancer risk, but no mortality benefit in Korean post-PCI patients treated with DAPT for an additional 18 months beyond conventional 12 months DAPT. These data are not supporting continuing DAPT for more than one year in East Asians. Analysing cancer types and assessing potential cancer association with bleeding are warranted.

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Keywords

Aspirin, Cancer, Clopidogrel, Korean, Mortality, Registry

References

- [1] Mauri L, Kereiakes DJ, Yeh RW, et al.; DAPT Study Investigators. Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. *N Engl J Med* 2014; 371: 2155-2166.
- [2] Serebruany VL. Platelet inhibition with prasugrel and increased cancer risks: potential causes and implications. *Am J Med* 2009; 122: 407-408.
- [3] FDA Drug Safety Communication: FDA reviews long-term antiplatelet therapy as preliminary trial data shows benefits but a higher risk of non-cardiovascular death. Available for download at: <http://www.fda.gov/drugs/drugsafety/ucm423079.htm> Assessed August 16, 2016.
- [4] Food and Drug Administration. Clinical Review on Cancer Risk. Available for download at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/206316Orig1Orig2s000MedR.pdf Assessed August 16, 2016.

- [5] Food and Drug Administration. Briefing document, February 3, 2009 meeting of FDA Cardiovascular and Renal Drugs Advisory Committee on Prasugrel. Available for download at: <http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/cardiovascularandrenaldrugsadvisorycommittee/ucm181185.pdf> Assessed August 16, 2016.
- [6] The FDA ticagrelor review of complete response. Available for download at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/022433Orig1s000MedR.pdf Assessed August 16, 2016.
- [7] NDA 294-886. Cross-discipline Team Leader review on Vorapaxar. April 18th, 2014 Available for download at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/204886Orig1s000SumR.pdf Assessed August 16, 2016.
- [8] Coupland LA, Parish CR. Platelets, selectins, and the control of tumour metastasis. *Semin Oncol* 2014; 41: 422-434.
- [9] Wang Y, Sun Y, Li D, et al. Platelet P2Y12 is involved in murine pulmonary metastasis. *PLoS One* 2013; 8: e80780.
- [10] Kotronias RA, Kwok CS, Wong CW, et al. Cancer Event Rate and Mortality with Thienopyridines: A Systematic Review and Meta-Analysis. *Drug Saf* 2016; Epub ahead of print.
- [11] Park YT, Yoon JS, Speedie SM, et al. Health insurance claim review using information technologies. *Health Inform Res* 2012; 18: 215-224.
- [12] Shin HC, Park YT, Lee YT, Jo EC. Healthcare Utilization Monitoring System in Korea. *Health Inform Res* 2015; 21: 184-190.
- [13] Mezouar S, Darbousset R, Dignat-George F, et al. Inhibition of platelet activation prevents the P-selectin and integrin-dependent accumulation of cancer cell microparticles and reduces tumour growth and metastasis in vivo. *Int J Cancer* 2015; 136: 462-475.
- [14] Sitia G, Aiolfi R, Di Lucia P, et al. Antiplatelet therapy prevents hepatocellular carcinoma and improves survival in a mouse model of chronic hepatitis B. *Proc Natl Acad Sci USA* 2012; 109: E2165-2172.
- [15] Roop RP, Naughton MJ, Van Poznak C, et al. A randomised phase II trial investigating the effect of platelet function inhibition on circulating tumour cells in patients with metastatic breast cancer. *Clin Breast Cancer* 2013; 13: 409-415.
- [16] Clopidogrel Prescribing Information. Available for download at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/020839s042lbl.pdf Assessed August 16, 2016.
- [17] CURE Trial Investigators. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Eng J Med* 2001; 345: 494-502.
- [18] Marciniak TA, Cherepanov V, Golukhova E, et al. Drug Discontinuation and Follow-up Rates in Oral Antithrombotic Trials. *JAMA Intern Med* 2016; 176: 257-259.
- [19] Serebruany VL, Cherepanov V, Cabrera-Fuentes HA, Kim MH. Solid cancers after antiplatelet therapy: Confirmations, controversies, and challenges. *Thromb Haemost* 2015; 114: 1104-1112.
- [20] Bonaca MP, Bhatt DL, Cohen M, et al. Long-term use of ticagrelor in patients with prior myocardial infarction. *N Engl J Med* 2015; 372: 1791-1800.
- [21] Costa F, Valgimigli M. Long-Term Use of Ticagrelor in Patients with Prior Myocardial Infarction. *N Engl J Med* 2015; 373: 1271-1272.
- [22] Serebruany VL. Ticagrelor shift from PLATO to PEGASUS: Vanished mortality benefit, excess cancer deaths, massive discontinuations, and overshooting target events. *Int J Cardiol* 2015; 201: 508-512.
- [23] Palmerini T, Benedetto U, Bacchi-Reggiani L, et al. Mortality in patients treated with extended duration dual antiplatelet therapy after drug-eluting stent implantation: a pairwise and Bayesian network meta-analysis of randomised trials. *Lancet* 2015; 385: 2371-2382.