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The protective role of phosphodiesterase inhibitors in preventing colorectal cancer and advanced colorectal polyps: a systematic review and meta-analysis

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Background: Inflammatory cells within the tumour microenvironment are the driving forces behind colorectal cancer (CRC) tumorigenesis. Understanding the different pathways involved in CRC carcinogenesis paves the way for effective drug repurposing for cancer prevention. Due to its anti-proliferative and anti-inflammatory properties, emerging data from pre-clinical and clinical studies suggest that phosphodiesterase-5 (PDE5) inhibitors might have an anticancer effect.

Methods: This study was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. Prospective registration was performed on PROSPERO (CRD42022372925). A systematic review was performed for studies reporting CRC and advanced colorectal polyp incidence in PDE5 inhibitor “ever-users” and PDE5 inhibitor “never-users”. Meta-analysis was performed using RevMan version 5.

Results: Six studies, comprising of 995,242 patients were included in the final analysis, of which 347,126 were PDE5 inhibitor “ever-users”. Patients who were PDE5 inhibitor “ever-users” had a significantly lower incidence of CRC or advanced colorectal polyps compared to “never-users” [odds ratio (OR) 0.88, 95% confidence interval (CI): 0.79–0.98, P=0.02]. To examine the primary preventative

role of PDE5 inhibitors, subgroup analysis of four studies including patients without a previous history of CRC found that PDE5 inhibitor ever use was associated with a lower incidence of CRC (OR 0.85, 95% CI: 0.75–0.95, P=0.005, I²=64%). There was no significant temporal relationship found between PDE5 inhibitor use and CRC risk as both “current-users” and “previous-users” had a significantly lower incidence of CRC compared to “never-users”.

Conclusions: Our study found a significant anticancer effect of PDE5 inhibitors as shown by a reduced risk of CRC in the context of both primary and secondary CRC prevention.

Keywords: Advanced colorectal polyps; colorectal cancer (CRC); chemoprevention; phosphodiesterase-5 inhibitors; incidence

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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