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First results of the CaPP3 randomised dose non-inferiority trial of cancer prevention with aspirin in Lynch syndrome.

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Background

CAPP2 (Burn et al 2020) showed 600mg aspirin daily for 2-4 years halved the risk of colorectal cancer in Lynch syndrome, the commonest form of hereditary cancer.

Materials and Methods

CaPP3 is an international, dose non-inferiority trial comparing 600mg, 300mg or 100mg aspirin daily (recruitment ratio 4:3:3). 1866 eligible recruits (median age 47) treated for up to 5 years between 2014-2024 and blinded for the first 2 years to record adverse events. Followup is now >5 years for all participants.

Results

Serious adverse events involving bleeding: there were 11(1.5%), 4(0.5%) and 0(0.0%) in the 600mg, 300mg and 100mg groups respectively(Fisher's exact p=0.004)

Cancer Rate: The LS cancer rate in CaPP3 600mg arm matched the rate in the CAPP2 treatment arm. 152 participants developed 183 LS cancers (excluding skin). The 100mg group had the fewest LS cancers.

LS Cancer on trial	100mg	300mg	600mg	Total
No	521 (93.2%)	506 (90.0%)	692 (92.9%)	1719 (92.1%)
Yes	38 (6.8%)	56 (10.0%)	53 (7.1%)	147 (7.9%)
Total	559 (100%)	562 (100%)	745 (100%)	1866 (100%)

Based on Intention-to-Treat, chances of developing an LS cancer 100mg vs 600mg were the same (HR=1.00,95%CI(0.66-1.52)), just outside our predetermined “non-inferiority” threshold of 1.5, similar to the 61% of participants who agreed to stay on their randomisation dose (1.09,95%CI(0.64-1.86)).

Conclusion

Daily aspirin significantly reduces the incidence of LS cancers. The protective effect of 600mg in CaPP3 mirrored that seen in CAPP2. People in the 100mg group had the same cancer risk as the 600mg group but just outside the predefined upper confidence interval. There is now sufficient evidence to recommend an antiplatelet dose of aspirin to prevent cancers in Lynch syndrome.