Treatment optimisation and pharmacogenetics of systemic and intraperitoneal chemotherapy in colorectal cancer

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STELLINGEN

behorend bij het proefschrift

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1. With the available evidence favouring pre-therapeutic *UGT1A1* genotyping in irinotecan patients, it is not ethical to conduct a study randomising between genotype versus non genotyped dosing of irinotecan. [This thesis]
2. *UGT1A1* genotype-guided dosing of irinotecan is the new standard of care in order to improve the individual patient safety. [This thesis]
3. A starting dose dose intensity of 70% in UGT1A1 PMs is sufficient, and must not necessarily be further reduced despite slightly higher SN-38 systemic exposure. [This thesis]
4. Pharmacogenetics may offer an opportunity for patient-tailored therapy also for intraperitoneally administered chemotherapy. [This thesis]
5. The choice of ignoring the high risk of neutropenia in a patient with the *UGT1A1*28* homozygous genotype, while we wait for yet another cohort study or retrospective assessment of large randomized trials, seems unsatisfactory. [Irinotecan Pharmacogenetics: Is It Time to Intervene? McLeod et al. JCO 2004;22(8):1356–9]
6. HIPEC should not be declared ineffective until other promising HIPEC regimens have been tested in randomized controlled trials. [Hyperthermic intraperitoneal chemotherapy (HIPEC) for colorectal and appendiceal peritoneal metastases: lessons learned from PRODIGE 7. Cashin et al. J Gastrointest Oncol 2021;12(Suppl 1):S120–8]
7. Large-scale implementation of genotype-guided treatment using a 12-gene pharmacogenetic panel makes drug therapy increasingly safe. [A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, controlled, cluster-randomised crossover implementation study. Swen et al. The Lancet 2023;401(10374):347–56]
8. The systematic replication of other researchers' work should be a normal part of science. [Replication studies: Improving reproducibility in the empirical sciences. Amsterdam, The Netherlands: KNAW, 2018]
9. The question is not whether we are able to change clinical practice with research, but whether we are changing clinical practice fast enough. [Adjusted from: Angela Merkel]
10. No research outcome is to be feared. It is only to be understood. [Adjusted from Marie Curie, as quoted in: Benarde, Melvin A. Our precarious habitat. New York: WW Norton & Company, 1973]