

Nederlandse Ziekenhuisfarmaciedagen 2025

De hier opgenomen abstracts vormen een selectie, namelijk de drie best beoordeelde abstracts, uit de presentaties tijdens de Nederlandse Ziekenhuisfarmaciedagen op 13 en 14 november 2025 te Arnhem. De digitale versie van deze publicatie op www.npfo.nl bevat alle gepresenteerde abstracts.

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SURVIVAL OF PATIENTS WITH COLORECTAL OR PANCREATIC CANCER WHO RECEIVED UGT1A1 GENOTYPE-GUIDED DOSING OF IRINOTECAN: A MULTICENTER REAL-WORLD STUDY

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Background

Uridine diphosphate glucuronosyl transferase 1A1 (UGT1A1) genotype-guided dosing significantly reduces the incidence of severe toxicity in UGT1A1 poor metabolizer (PM) patients treated with irinotecan [1]. However, the impact of UGT1A1

genotype-guided dosing of irinotecan on survival outcomes remains unknown. This study evaluated whether upfront 30% dose reductions of irinotecan in UGT1A1 PMs affect survival by comparing progression-free (PFS) and overall survival (OS) between PMs treated with an initial 30% dose-reduction and fully dosed intermediate and normal metabolizers (IM/NMs).

Methods

We conducted a retrospective, multicenter cohort study in patients with pancreatic cancer (PC) or colorectal cancer (CRC) treated with UGT1A1 genotype-guided irinotecan dosing at six Dutch hospitals between Aug 2017-Apr 2024. All treatment regimens were eligible for inclusion. Patients were included in the primary analysis if irinotecan was dosed according to UGT1A1 genotype (i.e. 100% dose intensity for IM/NMs and 70% for PMs; \pm 10% deviation allowed) in at least cycle 1. PFS events were defined as either radiological progression (RECIST 1.1), clinical progression or death from any cause. Survival analyses were performed using Kaplan-Meier estimates and multivariable Cox regressions, stratified by tumor type. Safety was also assessed.

Results

In total, 779 patients were included in the primary analysis, 76 (9.8%) of whom were PMs (Figure 1). All baseline characteristics were evenly distributed across UGT1A1 groups. PFS and OS rates were comparable over time between PMs and IM/NMs (stratified log-rank test: PFS: $P = 0.542$; OS: $P = 0.419$) (Figure 2). For patients with PC, median PFS was 9.0 months (95% CI: 6.2-11.8) in PMs and 8.3 months (95% CI: 7.2-9.4) in IM/NMs. For patients with CRC, median PFS was 6.2 months (95% CI: 5.1-7.3) in PMs and 6.0 months (95% CI: 5.3-6.7) in IM/NMs. Median OS was similar between PMs and IM/NMs in both PC and CRC groups. In stratified multivariable Cox regression analyses, the adjusted hazard ratio of PMs vs IM/NMs was 1.015 (95% CI: 0.78-1.32; $P = 0.90$) for PFS and was 1.10 (95% CI: 0.82-1.48; $P = 0.51$) for OS, indicating no significant differences in survival outcomes between 30% dose-reduced PMs and fully dosed IM/NMs. Severe toxicity rates were comparable between PMs and IM/NMs.

Conclusions

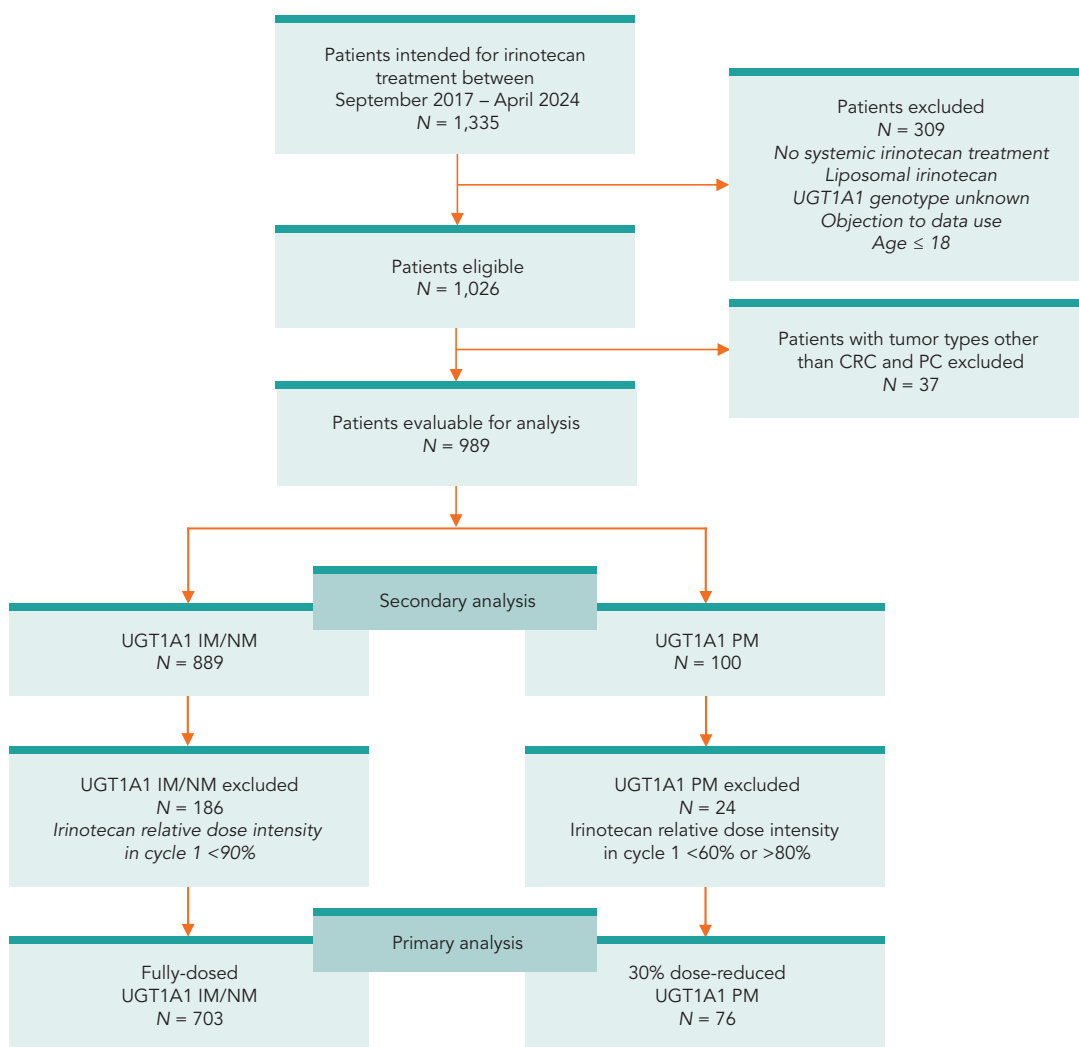
Survival of UGT1A1 poor metabolizers is not affected by an upfront 30% dose reduction of irinotecan. Therefore, UGT1A1 genotype-guided dosing of irinotecan can be confidently performed and should become the new standard-of-care dosing strategy for irinotecan to improve patient safety.

References

1. Hulshof EC, de With M, de Man FM, et al. UGT1A1 genotype-guided dosing of irinotecan: A prospective safety and cost analysis in poor metaboliser patients. *Eur J Cancer*. 2022 Feb;162:148-157.

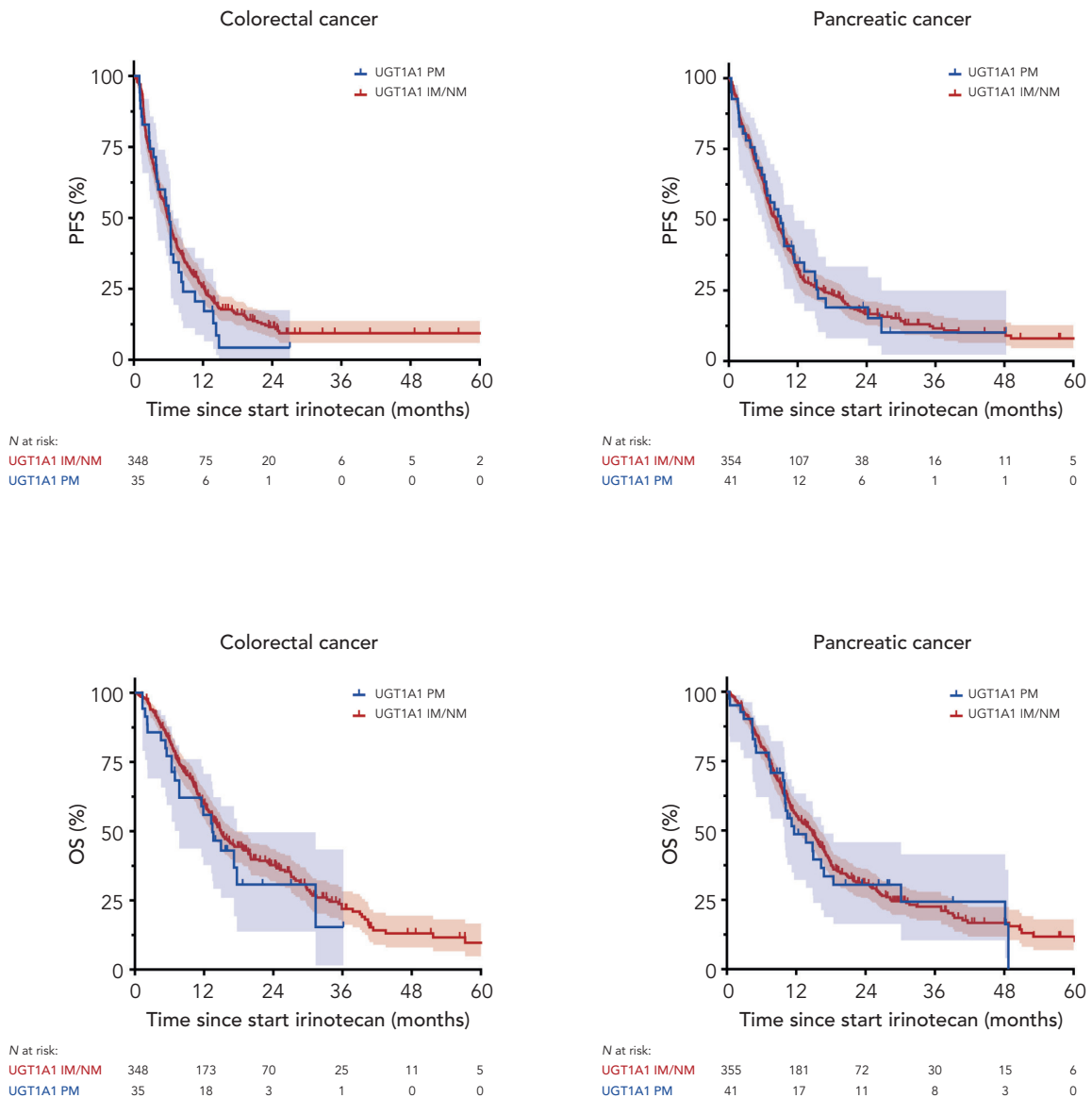
De abstractpresentatie van Sofía Peeters werd bekroond met de prijs voor Best Abstract 2025.

FIGURE 1 CONSORT PATIENT FLOW DIAGRAM



N: number of patients, UGT1A1: uridine diphosphate glucuronosyl transferase 1A1, CRC: colorectal cancer, PC: pancreatic cancer, IM: intermediate metabolizer, NM: normal metabolizer, PM: poor metabolizer.

FIGURE 2 KAPLAN-MEIER PLOTS FOR PFS AND OS OF UGT1A1 PM PATIENTS TREATED WITH A REDUCED IRINOTECAN DOSE AND IM/NM PATIENTS TREATED WITH A FULL IRINOTECAN DOSE FOR COLORECTAL AND PANCREATIC CANCER IN THE PRIMARY ANALYSIS



Censoring is indicated by tick marks. The shaded area represents the 95% confidence interval. A stratified log-rank test (stratified by tumor type) for comparing Kaplan-Meier curves between PM and IM/NM showed a P value of P = .542 for PFS and P = .419 for OS.

PFS: progression-free survival, OS: overall survival, UGT1A1: uridine diphosphate glucuronosyl transferase 1A1, PM: poor metabolizer, IM: intermediate metabolizer, NM: normal metabolizer, N: number of patients.

CEFAZOLIN VERSUS (FLU)CLOXACILLIN FOR METHICILLIN-SUSCEPTIBLE STAPHYLOCOCCUS AUREUS BACTEREMIA: A RANDOMIZED CLINICAL TRIAL

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Background

Staphylococcus aureus (*S. aureus*) bacteremia is a leading cause of mortality worldwide, with more than 1 in 4 afflicted patients dying within 90 days. In the Netherlands, reported mortality rates range from 15-30%. The optimal therapy for methicillin-susceptible *S. aureus* (MSSA) bacteremia remains debated, as guidelines favor antistaphylococcal penicillins over cefazolin due to concerns about the inoculum effect. Meta-analyses of observational studies suggest cefazolin may lower 30-day mortality and has fewer adverse events than antistaphylococcal penicillins, but only a randomized trial can provide reliable evidence. To address this and other questions in *S. aureus* bacteremia, the international *S. aureus* Adaptive Platform (SNAP) trial was initiated in 2022 as an ongoing Bayesian adaptive platform trial.

Methods

Within the SNAP platform, an open-label, randomized 1:1 comparison of cefazolin versus (flu)cloxacillin was conducted in patients ≥ 18 years with MSSA bacteremia, including participation from Dutch centers. The primary outcome was 90-day all-cause mortality, analyzed using a hierarchical Bayesian logistic regression model. Secondary outcomes included acute kidney injury (AKI), defined as an absolute creatinine increase ≥ 26.5 $\mu\text{mol/L}$ within 5 days or a relative increase $\geq 50\%$ from baseline within 14 days and hepatotoxicity within 14 days. Non-inferiority was defined as an adjusted odds ratio (aOR) < 1.2 ($< 2.5\%$ absolute margin if mortality in the (flu)cloxacillin arm was 15%) and superiority as an aOR < 1.0 ; conclusions were drawn if the respective posterior probability exceeded 99%.

Results

The trial was conducted between February 2022 and August 2024, at which time non-inferiority for 90-day mortality was

met, with a concurrent safety signal of increased AKI in the (flu) cloxacillin group. In total, 671 patients (for NL, 22 patients) were randomized to the cefazolin arm and 670 patients to the (flu)cloxacillin arm. 54 patients were lost to follow-up, leaving 1287 patients in the primary outcome analysis. At 90 days, all-cause mortality was 15.0% with cefazolin (97/645) and 17.0% with (flu)cloxacillin (109/642; aOR 0.81; 95% CrI 0.59-1.12), demonstrating non-inferiority (posterior probability 99.2%) but not superiority (89.8%). Cefazolin was superior to (flu)-cloxacillin with respect to AKI (13.9% [92/660] vs. 19.6% [127/648]; aOR 0.67; 95% CrI 0.50-0.89; posterior probability of superiority 99.7%). Hepatotoxicity within 14 days occurred in 13.1% (75/574) of cefazolin recipients and 13.9% (78/562) of (flu)cloxacillin recipients.

Conclusions

Cefazolin was non-inferior to (flu)cloxacillin for 90-day mortality and was associated with less AKI. Cefazolin should be considered the preferred therapy for most adults with MSSA bacteremia.

THE EFFECT OF ALLOPURINOL ON INCIDENT KNEE AND HIP OSTEOARTHRITIS: A POPULATION-BASED COHORT STUDY

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Background

Osteoarthritis (OA) is a leading cause of pain and disability worldwide, yet no disease-modifying OA drugs have been established. Allopurinol, a xanthine oxidase inhibitor commonly used for gout, has been hypothesized to possess disease-modifying properties in OA. This study aimed to investigate the association between allopurinol use and the risk of incident knee or hip OA.

Methods

A retrospective propensity score-matched population-based cohort study was conducted using data from the United Kingdom Clinical Practice Research Datalink. The study included patients aged ≥ 40 years who initiated allopurinol therapy, 1:1 propensity score-matched to non-users. The primary outcome was knee or hip OA incidence. Time-dependent cox proportional hazard models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). Secondary analyses were performed to assess the impact of allopurinol usage patterns and OA incidence.

Results

A total of 214,452 allopurinol users and 214,452 matched non-users were included, with a mean follow-up of 7.6 years

(SD 6.2) and 7.4 years (SD 5.9) respectively. Allopurinol use was significantly associated with a 19% lower hazard of OA (HR: 0.81; 95% CI: 0.74-0.88), and was comparable for both hip (HR: 0.82; 95% CI: 0.69-0.96) and knee OA (HR: 0.80; 95% CI: 0.73-0.88). Longer use (> 1 year) was associated with progressively lower risk (HR: 0.77; 95% CI: 0.71-0.84). High medication adherence ($> 80\%$) showed the strongest risk reduction (HR: 0.18; 95% CI: 0.16-0.20).

Conclusions

Allopurinol use was associated with a 19% reduction in risk of incident knee or hip OA, suggesting disease-modifying properties. Further research is necessary to confirm the preventive role in OA onset.

