cancer patients. The aim of this study was evaluate the plasma concentrations of oxycodone and its demethylates and opioid-induced adverse effects based on cachexia stage in cancer patients receiving oxycodone.

Patients (or Materials) and Methods: Seventy patients receiving oxycodone for cancer pain at Hamamatsu University Hospital were enrolled. Cachexia was evaluated using the Glasgow Prognostic Score (GPS). Predose plasma concentrations of oxycodone, oxymorphone, and noroxycodone were determined at the titration dose. Opioid-induced adverse effects were monitored for 2 weeks after the titration.

Results: Fourteen patients had a GPS of 0, 27 a GPS of 1, and 29 a GPS of 2. Plasma concentrations of oxycodone and oxymorphone but not noroxycodone in patients with a GPS of 2 were significantly higher than that with a GPS of 0. The metabolic ratios of noroxycodone but not oxymorphone to oxycodone in patients with a GPS of 1 and 2 were significantly lower than in those with a GPS of 0. A higher GPS was associated with a higher incidence of somnolence, while the GPS did not affect the incidence of vomiting. Plasma concentrations of oxycodone and oxymorphone were not associated with the incidence of adverse effects.

Conclusion: Cancer cachexia raised the plasma exposures of oxycodone and oxymorphone through the reduction of CYP3A but not CYP2D6. Although the cachexia elevated the incidence of somnolence, alterations in their pharmacokinetics were not associated with the incidence.

Disclosure of Interest: None declared.

PP203—WHOLE BLOOD CANNABINOID PHARMACOKINETIC PARAMETERS IN HEAVY AND OCCASIONAL SMOKERS. DO ORAL FLUID CANNABINOID MEASUREMENTS CORRELATE WITH WHOLE BLOOD DATA IN HEAVY SMOKERS?

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Introduction: Many issues remain to be solved in regard to cannabinoid disposition, elimination time profiles and correlation between oral fluid (OF) and whole blood (WB) concentrations. Delta-9-tetrahydrocannabinol (THC) in OF is usually indicative of a relatively recent cannabis exposure, but the study of other cannabionoids in OF and WB could also be helpful as a confirmatory test when applied for legal purposes.

Patients (or Materials) and Methods: A randomized, blinded, 2-way crossover study was conducted in 48 healthy volunteers (23 heavy and 25 occasional cannabis smokers) who received by smoking each period, in random sequence, a cannabis joint (containing bedrobabolin, 11% THC, and traces of cannabidiol- CBD) or a placebo. WB was collected up to 2.5 hours after smoking. An additional WB sample at 3.5 hours, and OF samples were collected in heavy smokers. Storage at −20°C and liquid-liquid extraction preceded analysis by liquid chromatography-tandem mass spectrometry. THC, 11-hydroxy-THC (11-OH-THC) and 11-nor-9-carboxy-THC (THCCOOH) were measured in WB. THC, THCCOOH, cannabidiol (CBD), and delta-9-tetrahydrocannabinolic acid A (THC-A) were investigated in OF. WB pharmacokinetic parameters of THC and its metabolites were compared in heavy and occasional smokers. Correlations for these parameters between OF and WB were studied in heavy smokers.

Results: Fourteen patients had a GPS of 0, 27 a GPS of 1, and 29 a GPS of 2. Plasma concentrations of oxycodone and oxymorphone but not noroxycodone in patients with a GPS of 2 were significantly higher than that with a GPS of 0. The metabolic ratios of noroxycodone but not oxymorphone to oxycodone in patients with a GPS of 1 and 2 were significantly lower than in those with a GPS of 0. A higher GPS was associated with a higher incidence of somnolence, while the GPS did not affect the incidence of vomiting. Plasma concentrations of oxycodone and oxymorphone were not associated with the incidence of adverse effects.

Conclusion: Cancer cachexia raised the plasma exposures of oxycodone and oxymorphone through the reduction of CYP3A but not CYP2D6. Although the cachexia elevated the incidence of somnolence, alterations in their pharmacokinetics were not associated with the incidence.

Disclosure of Interest: None declared.

PP204—METHADONE KINETICS AND CORRECTED QT TIME DURING HAEMODIALYSIS IN FOUR METHADONE MAINTENANCE TREATMENT PATIENTS WITH END-STAGE RENAL FAILURE

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Introduction: Methadone is known to be associated with prolongation of corrected QT time (QTc). Excretion of methadone is primarily renal in patients with normal renal function. It is unknown to what extent hemodialysis removes methadone. We investigated methadone kinetics and QTc during hemodialysis in methadone maintenance treatment (MMT) patients with end-stage renal disease.

Patients (or Materials) and Methods: The Regional Ethics Committee approved the study. Data are given as median (range). Four patients with end-stage renal failure, 1 female and 3 males, 46 (43–53) years, stabilized on methadone were included. Methadone was measured by UPLC-MMS in serum and hemodialysates collected before morning methadone intake, every 30 minutes during 4 hours hemodialysis and before afternoon dose, and in urine sampled at the end of hemodialysis. ECGs were recorded every 30 minutes during hemodialysis, and QT time was measured in lead v2 using tangential method and QTc was calculated with Bazett’s formula. ECGs were read serially for each patient with blinding of numbering. Several routine biochemical tests were performed before and after hemodialysis.

Results: The daily methadone dose was 100 (60–120) mg. Serum-methadone increased from Cmin of 1124 (547–1581) nmol/L to Cmax of 1806 (1237–2098) nmol/L after 85 (40–120) minutes. The apparent half-life of methadone was 12 (6.3–25) hours. A total of 2.30 (1.25–3.70) % and 0.14 (0.03–0.26) % of daily methadone intake was collected, respectively, in hemodialysate and urine during 4 hours. Renal clearance of methadone was 0.67 (0.31–1.20) mL/min, methadone clearance of hemodialysis was 17.10 (13.67–20.30) mL/min and AUC of dose interval was 253.5 mg min/L. QTc increased from 395 (369–406) ms to 452 (407–479) ms with P = 0.068, Wilcoxon paired comparison. The maximum QTc occurred