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**Introduction:** Docetaxel, cisplatin plus 5-FU (DCF) regimen is a useful chemotherapy against malignant diseases such as advanced head and neck cancer. However, DCF regimen is sometimes withdrawn by severe myelosuppression and nonhematologic toxic effects, including mucositis. Previous animal and clinical studies showed that the degrees of docetaxel-, cisplatin-, and 5-FU–induced toxicities depend on their dosing time. We have reported that the frequency of docetaxel-induced intestinal mucositis was greater after dosing at an active phase than at an inactive phase in mice. The aim of the present study was to determine the influence of dosing schedule of DCF regimen on chemotherapy-induced toxicities in clinical practice.

**Patients (or Materials) and Methods:** Patients with oral squamous cell carcinoma treated with DCF regimen were randomly allocated to the following 2 groups: chemotherapy started from morning (10:30) in the first group and evening (18:30) in the second group. Hematologic and nonhematologic adverse effects were assessed for 14 days after the start of chemotherapy.

**Results:** The most frequently observed mild to severe adverse effects were neutropenia, diarrhea, stomatitis, and nausea. The frequency of grade 3 to 4 neutropenia was 62.5% (5 of 8) in the morning group and 28.6% (2 of 7) in the evening group. Grade 3 to 4 event of stomatitis and grade 3 event of nausea were more detected in the morning group.

**Conclusion:** These findings suggest that chronotherapy of DCF regimen might diminish severe adverse effects in patients with oral squamous cell carcinoma.

**Disclosure of Interest:** None declared.

## PP016—EXPOSURE TO ANTIPSYCHOTICS WITH PRO-ARRHYTHMIC RISK: COMBINING ADVERSE DRUG REACTIONS WITH DRUG UTILIZATION DATA

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**Introduction:** This pilot study, within the ARITMO project, evaluated the population exposure to antipsychotics (APs: ATC group N05A, excluding lithium) with proarrhythmic risk, by analyzing the FDA Database (FDA_AERS) and European drug utilization data (12 countries).

**Patients (or Materials) and Methods:** Cases of QT prolongation and torsades de pointes (TdP) associated with APs were retrieved from the FDA_AERS (2004–2011) database. APs with unexpected signals were defined by disproportionality (Reporting Odds Ratio [ROR], with 95% CI >1, cases >3) and checking in Arizona_CERT (www.azcert.org). Consumption data (2006–2010) were provided from administrative databases from 12 European countries. Data were expressed as DDDs/TID (defined daily doses per thousand inhabitants per day).

**Results:** Thirty-one APs were reported in 1467 cases of TdP/QT prolongation, with 10 unexpected signals: amisulpride (ROR = 25.0; 95%CI, 17.6–35.6), aripiprazole (1.7; 1.3–2.2), bromperidol (88.4; 37.7–207.9), chlorprothixene (10.7; 3.9–29.0), cyamemazine (7.6; 4.3–13.5), fluphenazine (7.9; 3.9–16.0), levomepromazine (5.2; 2.3–11.6), olanzapine (4.7; 4.1–5.3), prothipendyl (21.0; 10.7–41.4), and zuclopenthixol (14.9; 6.9–31.8). In all countries, AP use increased over 5 years from only +0.35 DDD/TID (Norway) to +11.01 (Serbia, preliminary data). The atypical/typical ratio increased in line with expectations. There was variable AP utilization in 2010, from 5.04 (Estonia) to 16.57 (Serbia, preliminary data). The mean use of APs with unexpected signals ranged from 1.72 (Estonia) to 5.45 (Slovenia). Olanzapine was stable but widely used and peaked at 2.9 in Norway. Aripiprazole utilization generally increased. There appeared to be substantial utilization of fluphenazine in Serbia (3.77 in 2010) and cyamemazine in France (2.81 in 2009).

**Conclusion:** Different exposure to AP use among countries implies different levels of population risk. The use of atypical APs is growing (eg, aripiprazole). Olanzapine should be monitored by regulators, due to its appreciable utilization in most countries. Fluphenazine and cyamemazine are specific concerns in Serbia and France, respectively. The study also demonstrates the synergy between drug utilization and adverse event databases to alert health policy personnel of potential future activities to reduce ADRs, especially from drugs with unexpected signals. As a result, help promote higher standards of prescribing in the future.

**Disclosure of Interest:** None declared.

## PP017—SPECTRUM OF OCULAR DIGOXIN TOXICITY IN THE ELDERLY: A CASE REPORT

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**Introduction:** We report a case of digoxin intoxication with severe visual symptoms.

**Patients (or Materials) and Methods:** Digoxin 0.25 mg QD for atrial fibrillation was prescribed to a 91-year-old woman with an estimated creatinine clearance of 18 mL/min. Within 2 to 3 weeks, she developed nausea, vomiting, and dysphagia, and began complaining of snowy and blurry vision, photopsia, dyschromatopsia, aggravated bedtime visual and proprioceptive illusions (she felt as being on a boat), and colored hallucinations. She consulted her family doctor twice and visited the eye clinic once until, 1 month after starting digoxin, impaired autonomy led her to be admitted to the emergency department.

**Results:** Digoxin intoxication was confirmed by a high plasma level measured on admission (5.7 μg/L; reference range, 0.8-2 μg/L). After stopping digoxin, general symptoms resolved in a few days, but visual symptoms persisted. Ophtalmologic care and follow-up diagnosed digoxin intoxication superimposed on pre-existing left eye (LE) cataract, dry age-related macular degeneration (DMLA), and Charles Bonnet syndrome. Visual acuity was 0.4 (right eye, RE) and 0.5 (LE). Ocular fundus was physiologic except for bilateral