Cytarabine + Posaconazol/Voriconazol M6964

Onderbouwend	Stof	Effect	Code
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Overig	Stof	Effect
SPC Cytarabine Sandoz SPC Vyxeos	cytarabine	posaconazol/CYP-remmers niet genoemd
SPC Noxafil, VFend	posaconazol, voriconazol	cytarabine niet genoemd
Alzghari SK. J Oncol Pharm Pract 2017;23:476-80. doi: 10.1177/1078155216664204 comedicatie oa aciclovir, cefepim, pil, dexamethason, docusaat, granisetreon, insuline, levofloxacine, metformine, paracetamol, hydorcocon, hydroxyzine, lorazepam, opioiden	cytarabine + posaconazol	casus: ernstige cytarabinetoxiciteit in de vorm van palmar-plantar erythrodysesthesia (PPE) en aplasie bij vrouw (24) met AML die chemotherapie en oa posaconazol krijgt - inductie cytarabine 100 mg/m^2 per dag 7 dagen, idarubicine 12 mg/m^2 per dag 3 dagen - dag 5 start posaconazol 300 mg/dag - complicaties: blindheid door bloeding, mucositis, neutropene koorts - dag 14 herinductie chemokuur met hoge doses cytarabine (HiDAC) 2 g/m^2 elke 12 uur, 12 doses; posaconazol nog op dag 14+15, vervolgens 3 dagen onderbroken en herstart na voltooien kuur HiDAC - dag 20 weer blindheid in andere oog, tinteling en gevoelloosheid handen en voeten, bleek PPE - overleden door complicaties van ernstige cytopenie. Auteurs: we speculate that posaconazole may inhibit the cytarabine efflux through P-gp inhibition leading to the patient's PPE and subsequent aplasia. Cytarabine is substrate for P-gp and CYP3A4. PPE zelden bij matig-hoge doses cytarabine. Werkgroep Interacties Oncologische middelen: niet onderbouwend, kan ook bijwerking van HiDAC zijn. Toxiciteit cytarabine is zeer divers per dosis.
Maertens JA. J Antimicrob Chemother 2018 Aug 1. doi: 10.1093/jac/dky286. [Epub ahead of print]	posaconazol profylaxe	European guidelines for primary antifungal prophylaxis in adult haematology patients: summary of the updated recommen-dations from the European Conference on Infections in Leukaemia. Azolen aanbevolen bij: - AML/MDS intensieve reductie-remissie chemokuur - allogene HSCT ontvanger, pre- en post-engraftment
Dahlén T. Eur J Haematol. 2016;96:175-80. doi: 10.1111/ejh.12565. P: posaconazol F: fluconazol AML acute myeloid leukaemia MDS myelodysplastic syndromes IFD invasive fungal disease	cytarabine + posaconazol	at day 100, patients receiving P had a significantly lower incidence of total IFD (0.9 vs 10.8%), invasive aspergillosis (0 vs 5.7%) and invasive candidiasis (0 vs 4%). No significant difference in overall survival, neither at day 100 (87% in the P-group vs. 85% in the F-group) nor at end of follow-up (78% vs. 77%). Methode: retrospective cohort study, patients with AML/MDS treated with intensive induction chemotherapy (daunorubicine dag 1-3, cytarabine dag 1-5); 176 patients received F prophylaxis (100 of 200 mg 1dd) and 107 patients P (200 mg 3dd). Auteurs: P prophylaxis decreased the incidence of IFD but did not improve short-term overall survival. Improved treatment efficacy of manifest IFD is likely to explain the lack of survival benefit.

Kung HC. Cancer Med 2014;3:667-73. doi: 10.1002/cam4.225.	cytarabine + posaconazol	single-center, retrospective cohort study of 130 evaluable patients ≥18 y who received either Posaconazole or Fluconazole as prophylaxis during first induction or first reinduction chemotherapy for AML or MDS. Baseline characteristics were well balanced between groups, except that P recipients received reinduction chemotherapy and cytarabine more frequently. IFD occurred in 17/65 (27.0%) in the F group and in 6/65 (9.2%) in the P group. Definite/probable IFDs occurred in 7 (10.8%) and 0 patients (0%), respectively. In multivariate analysis, F prophylaxis and duration of neutropenia were predictors of IFD. Mortality was similar between groups. This study demonstrates superior effectiveness of P over F as prophylaxis of IFD in AML and MDS patients. Such superiority did not translate to reductions in 100-day all-cause mortality.
Osborne WL. Clin Lab Haematol 2004;26:295-6.	cytarabine + voriconazol	casus: progressieve perifere neurologische verslechtering na FLA-regime (fludarabine plus cytarabine) bij man (51) met AML; toxiciteit trad op tijdens 2e kuur FLA, hierbij was voriconazol profylaxe gestart; patiënt uiteindelijk overleden, autopsie toonde geen afwijkingen in myocyten, geen aanwijzing voor myopathie of demyelinisatie; normale zenuwbundels Auteurs: 'suggesting a possible drug interaction' GIC: erg warrig verhaal, te weinig details
Colburn DE. Hematology 2004;9:217-21. = ref.16 uit Alzghari 2017	cytarabine + itraconazol	in vitro studie. Cytarabine is a substrate of CYP3A4; the metabolism was decreased by 51% when combined with itraconazole. Methode: high throughput microtiter assay with isolated human CYP450 isoenzymes.

Opmerkingen
Stockley: niet in.
PubMed: niets op ketoconacol, zie verder bovenstaande tabel.
Hansten: posaconazol sterke remmer CYP3A4 en P-gp.

Risicofactoren	
Mitigerende factoren	

	Interactie	**Actie**	**Datum**
Beslissing WG OncoIA	Nee	Nee	10 april 2019