Sonidegib + CYP3A4-remmers MFB 7321

Onderbouwend	Stof	Effect	Code
SPC + EPAR Odomzo * oa ritonavir, saquinavir, ketoconazol, itraconazol, voriconazol, posaconazol	sonidegib + ketoconazol	toename AUC sonidegib 2.25x (5620 → 12700 ng*h/ml) en Cmax 1.49x (212 → 316 ng/ml) Regime: sonidegib 800 mg 1-malig op dag 5, ketoconazol 200 mg 2dd gedurende 14 dagen; 15 vrijwilligers. Bij combinatie met sterke CYP3A4-remmers* dosering sonidegib verlagen naar 200 mg om de dag. → GIC: door lange t½ zal volledig effect van dosisaanpassing pas na enkele weken optreden. Met simulaties werd voorspeld dat langdurig gelijktijdig gebruik van sterke remmers van CYP3A4 (bijv. > 14 dagen) zal leiden tot een meervoudige verandering in blootstelling aan sonidegib.	3A

Overig	Stof	Effect
EPAR Odomzo p. 49-50	sonidegib	Study X2101 - Phase I dose-escalation study of sonidegib to determine the maximum tolerated dose (MTD) when administered QD (100mg -3000mg) and bid (250, 400 and 750 mg) in a 28-day cycle to adult patients with advanced solid tumours. The MTD was determined to be 800 mg for the once daily regimen and 250 mg for the twice daily regimen. The most common DLT was increased CK. Grade 3 and 4 CK elevations were not observed at dose levels below 800 mg on the QD schedule or 250 mg on the bid schedule in study X2101. Twice-daily dosing with 400- and 750-mg bid dosing resulted in AUC was 18-30% higher than with the equivalent once-daily dose but an increased tendency to cause grade 3 or 4 CK elevations. The 200-mg once-daily regimen was selected for evaluation on the basis that it represented the lowest dose level tested that demonstrated preliminary evidence of anti-tumour activity and Gli-1 inhibition.
Odomzo Prescribing Information http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/205266s000lbl.pdf geraadpleegd 17-11-2015	sonidegib + CYP3A4-remmers	Avoid concomitant administration of sonidegib with strong CYP3A inhibitors, including but not limited to saquinavir, ketoconazole, itraconazole, voriconazole. Avoid concomitant administration of sonidegib with moderate CYP3A inhibitors, including but not limited to atazanavir, diltiazem, and fluconazole. If a moderate CYP3A inhibitor must be used, administer the moderate CYP3A inhibitor for less than 14 days and monitor closely for adverse reactions particularly musculoskeletal adverse reactions.

Opmerkingen
Werkgroep Interacties Oncologische middelen 10-4-19: posaconazol toevoegen aan lijst krachtige CYP3A4-remmers.

Werkgroep Interacties oncologische middelen 27-1-16: ‘eng’ stofje en betreft broze patiënten van gem. > 80jr.

PubMed. Stockley: geen informatie.

Risicofactoren	
Mitigerende factoren	

	Interactie	Actie	Datum
Beslissing WG OncoIA	Ja	Ja	10 april 2019