Simvastatine + Osimertinib M1391

Onderbouwend	Stof	Effect	Code
SPC Tagrisso EPAR	simvastatine + osimertinib	↓ AUC simvastatine 9% en Cmax 23% Werkgroep Interacties Oncologische middelen 2017: deze kleine wijziging valt binnen de ruis. p.51 In this study osimertinib was dosed for 28 days. It should be noted that a new steady state level of CYP3A4 could be reached by 8-10 days and the steady-stated was achieved by Day 15 for osimertinib and AZ5104 in AURA extension and by Day 22 in AURA2. Although the duration of the study is slightly limited is acceptable to investigate whether an investigational drug is an inducer or a time-dependent inhibitor in vivo.	0A

Overig	Stof	Effect
Vishwanathan K. Clin Transl Sci 2020;13:41-6. doi: 10.1111/cts.12688.	simvastatine + osimertinib	retrospective analysis of 2 patients who had liver metastases and high simvastatin exposure (~ 10-fold) prior to osimertinib treatment: *Day 1* — *AUC simva* (ng h/mL) — *Cmax simva* (ng/mL) simva pat1: 700 — 240 simva pat2: 893 — 176 simva pat.other: 97.0 — 30.7 *Day 31* — *AUC simva* (ng h/mL) — *Cmax simva* (ng/mL) simva+osim pat1: 30.7 — 5.8 simva+osim pat2: 41.9 — 19.7 simva+osim pat.other: 96.1 — 23.9 pat1&2: ↓AUC to < 5% of the D1 values and Cmax to ~ 2.5% resp. 11% -at baseline, both patients had abnormal liver function tests, significant liver metastasis, and, after a single simvastatin dose, had higher exposure compared with all other patients - following 31 days of osimertinib, simvastatin exposures and LFTs (such as ALAT, ASAT, bilirubin) normalized to population mean values. Additionally, reductions in liver metastases were observed on computed tomography scans in patients 1 (~ 50%) and 2 (~ 80%). Regime: simvastatin 40 mg 1x on Day 1 and D31, osimertinib 80 mg 1dd on D3-32; open-label study with 52 patients with advanced EGFR-mutated non-small cell lung cancer, plus retrospective analysis of 2 patients who had liver metastases and high simvastatin exposure prior to osimertinib treatment, which changed following treatment. Authors: high simvastatin exposure on D1 likely resulted from impairment of hepatic first pass metabolism due to liver metastases. Reduction in hepatic disease burden due to osimertinib treatment likely resulted in liver function returning to normal levels.

Opmerkingen

Risicofactoren	
Mitigerende factoren	

	Interactie	Actie	Datum
Beslissing WG OncoIA	Nee	Nee	18 januari 2017