

Amgen halts trials on cardiac toxicity



Joanne Fagg

Enrolment into the phase I trial of Amgen's myeloid cell leukemia-1 (MCL-1) inhibitor AMG 397 in various blood malignancies has been placed on hold, the group said [yesterday](#), after a cardiac toxicity signal was seen. No further details on the signal were given, but Amgen also felt the need to stop enrolment into a phase I study of its second MCL-1 inhibitor, AMG 176, in acute myeloid leukaemia. MCL-1 is thought to be highly expressed in many cancers and has been implicated in the development of resistance to therapy. In a [phase I study](#) with AMG 176 in relapsed or refractory multiple myeloma, treatment-emergent adverse events of grade 3 or higher occurred in 62% of patients, the most common of which were neutropenia, anaemia and hypertension. Although no cardiac toxicity has been disclosed here, there were two fatal adverse events in the study, one of which was due to treatment. AstraZeneca and Novartis are also developing projects with this mechanism, but it could be a wasted journey if toxicities turn out to be a class effect.

Inhibitors of MCL-1

Status	Project	Company	Trial
Phase I	AMG 397	Amgen	NCT03465540 (clinical hold)
Phase I	AMG 176	Amgen	NCT02675452 (voluntary hold)
Phase I	MIK665/S64315	Ligand Pharmaceuticals/ Servier/Novartis	NCT02979366 , NCT02992483 , NCT03672695
Phase I	AZD5991	Astrazeneca	NCT03218683
Preclinical	S63845	Ligand Pharmaceuticals/ Servier/Novartis	-
Preclinical	CB-708	Calithera Biosciences	-

Source: EvaluatePharma.

[More from Evaluate Vantage](#)

Evaluate HQ
[44-\(0\)20-7377-0800](#)

Evaluate Americas
[+1-617-573-9450](#)

Evaluate APAC
[+81-\(0\)80-1164-4754](#)

© Copyright 2023 Evaluate Ltd.