

Low-key Astra hold puts spotlight on Novartis and Servier



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A low-key US clinical hold yesterday suggests more problems for the MCL-1 inhibitor drug class. The phase 1 trial of AZD5991, AstraZeneca's inhibitor of this anti-apoptosis regulator, has been put on hold after "asymptomatic elevation in cardiovascular laboratory parameters" was seen in a patient treated in combination with Venclexta, a spokesperson said. Though the elevation resolved, the issue is relevant because two years ago [Amgen halted its rival anti-MCL-1 agent AMG 397 after seeing cardiac toxicity](#). Astra stressed that the patient had other co-morbidities, but nevertheless it is impossible to ignore the possibility of a class effect. The companies most invested in MCL-1 inhibition are probably Novartis and Servier, which have a joint project, MIK665, in phase 1/2. New clinical entrants since *Evaluate Vantage* last analysed the space include projects from Abbvie - though this too has now been scrapped - Prelude Therapeutics and Gilead, while the private group Anji has a preclinical asset. Amgen, meanwhile, has canned AMG 397, though it insists that this was for "strategic" and not "safety" concerns; its second MCL-1 inhibitor, AMG 176, is in two phase 1 trials, one of which is still suspended for lack of safety.

Selected MCL-1 inhibitors

Project	Company	Trial	Note
<i>Phase 1/2</i>			
MIK665/S64315	Novartis/Servier (ex Vernalis)	NCT04629443	Azacitidine combo in AML
		NCT03672695	Venclexta combo in AML
		NCT04702425	VOB560 (Bcl2 inhibitor) combo
<i>Phase 1</i>			
AMG 176	Amgen/Beigene	NCT02675452	Earlier voluntarily halted, now enrolling again
		NCT03797261	Venclexta combo, trial suspended for lack of safety in Sep 2019
AMG 397	Amgen/Beigene	NCT03465540	Put on hold for cardiac tox; now terminated
AZD5991	AstraZeneca	NCT03218683	Trial put on hold after cardiovascular parameter elevations with Venclexta combo
ABBV-467	Abbvie	NCT04178902	Trial terminated for "strategic considerations"
PRT1419	Prelude Therapeutics	NCT04543305	Started Sep 2020
GS-9716	Gilead Sciences	NCT05006794	Started Sep 2021
<i>Preclinical</i>			
ANJ810	Anji Pharmaceuticals	-	-

Source: *Evaluate Pharma & clinicaltrials.gov*.

This story was updated to add comment from AstraZeneca.

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