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Curis hit badly by cancer drug clinical hold

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Mortgaging a successful drug to buy an unproven asset is a dicey strategy, but in fairness to Curis things rarely go this wrong. The death of a patient in a phase I trial of its solid tumour candidate CUDC-427 has prompted the FDA to halt the trial and the company's share price to crash by 26%.

Curis swapped the royalty stream on its sole approved product, basal cell carcinoma drug Erivedge, for rights to Roche's IAP inhibitor CUDC-427 a year ago (*The curious solution to Curis's pipeline conundrum, November 29, 2012*). Perhaps it should have asked itself why Roche was happy to let the project go – and perhaps other developers of early-stage IAP inhibitors should be wary.

Implications

CUDC-427, formerly referred to as GDC-0917, was under investigation in 36 patients with advanced, refractory solid tumours or lymphoma. One patient, whose breast cancer had metastasised to the liver, lungs, bones and ovaries, suffered liver failure a month after treatment with '427 has ceased.

The patient had previously exhibited elevated levels of liver enzymes and bilirubin which did not return to normal after treatment discontinuation. Curis said that other patients had also exhibited changes in liver enzyme levels – this has also been seen in prior trials of the drug – but no others have experienced liver failure.

The partial clinical hold placed on the trial by the FDA means that no new patients may be enrolled until Curis turns further data on patients treated with CUDC-427, and a proposed protocol amendment, over to the FDA. Even before the hold, treatment of all other patients in the study had been discontinued owing to disease progression or patient or physician discretion during the ordinary course of the study, Curis said – in itself, not a good sign.

Curis's success at getting the clinical hold lifted has implications for other groups developing IAP inhibitors. *EvaluatePharma* lists four other such (see table), and interestingly Curis is not the only one to have its development suspended in phase I.

Industry projects targeting IAP		
Product	**Company**	**Development stage**
LCL161	Novartis	Phase II
Birinapant	TetraLogic Pharmaceuticals	Phase II
AT-406/ Debio 1143	Debiopharm	Phase I
CUDC-427	Curis/Roche	Suspended
HGS1029	Pharmascience	Suspended

Last December, GlaxoSmithKline handed rights to HGS1029 back to Pharmascience following its acquisition of Human Genome Sciences, and development of the compound has been in limbo ever since. There is no suggestion that this is due to any danger of serious side-effects from HGS1029, but eyes may now turn to the remaining phase I IAP antagonist, Debiopharm's AT-406, also called Debio 1143. The FDA will surely watch closely for any sign of serious effects on the liver with this product too.

The deal for '427 was not Curis's smartest decision; presumably it believed that it could succeed even after Roche – and before its acquisition, Genentech – had given up. The project could yet turn around, with Curis insisting that it could still find a niche as either monotherapy or in combination. Unfortunately that outcome looks extremely unlikely.

Trial	Trial ID
Genentech's 42-patient phase I dose-escalation trial of GDC-0917 (CUDC-427)	NCT01226277
Curis's 36-patient phase I dose-escalation trial of CUDC-427	NCT01908413

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