

New data Spark haemophilia B gene therapy battle



[Madeleine Armstrong](#)

UniQure's haemophilia B gene therapy candidate AMT-060 was already looking second-best compared with Spark Therapeutics' rival project SPK-9001. New data have done nothing to close the gap - if anything, they have made it wider.

UniQure and Spark are both near the front of the race to develop a haemophilia B cure, one of gene therapy's most active areas (see tables below). But while the companies could steal a march on Baxalta's BAX 335, development of which seems to have stalled with Shire's takeover, at the moment Spark looks like the one to beat.

FIX it

Broadly positive data from a phase I/II study were not enough to save UniQure's stock, which dropped 16% on June 13, the first trading day after its presentation at the European Hematology Association meeting. The group's share price is down 41% from the beginning of the year.

While AMT-060 was on the face of it a success - four out of the five treated patients did not require prophylactic factor IX (FIX) infusions, and all of them ended up with less severe disease than at baseline - it fell short on the amount of FIX activity, which should correlate with blood-clotting ability.

Patient	Before treatment			At six months post AMT-060		
	FIX activity	Haemophilia phenotype	Prophylactic FIX infusions?	FIX activity	Haemophilia phenotype	Prophylactic FIX infusions?
1	<1%	Severe	Yes	6.3%	Mild	No
2	<1%	Severe	Yes	5.4%	Mild	No
3	<1%	Severe	Yes	<2.0%	Moderate	Yes
4	1.5%	Moderate-severe	Yes	6.2%	Mild	No
5	<1%	Severe	Yes	2.9%	Moderate	No

Spark's SPK-9001, meanwhile, had a much more impressive 27-35% range of FIX activity in four patients in its phase I/II study - even better than the 16-30% that the company had previously disclosed ([EHA preview - First blood for Spark, May 20, 2016](#)).

UniQure will hope for more convincing results from the high-dose cohort of the same trial, which is expected to report initial data by the end of 2016.

This is not a given, however. Spark's therapy is administered at a lower dose than UniQure's, but seems to lead to a stronger response. The answer could lie in Spark's approach - while UniQure's product encodes wild-type FIX, Spark's employs a mutated version called Padua FIX. The Padua variant is thought to result in higher FIX activity and therefore improved blood clotting.

Spark's success could therefore be a negative not only for UniQure but also for other groups developing wild-type products, including Dimension Therapeutics.

But caution is needed with such small patient numbers, and FIX activity might not be the be-all and end-all - it is thought that only around 5-10% activity is required to spur a therapeutic effect.

Even so, Spark seems to have the advantage for now. If it can replicate its impressive results in phase III in

more patients its product could become the haemophilia B gene therapy of choice.

Haemophilia B gene therapy pipeline				
Company	Project	Mechanism	Notes	Trial details
Baxalta (Shire)	BAX 335	AAV8-Padua FIX	Phase III to start 2016	NCT01687608
UniQure/Chiesi	AMT-060	AAV5-wild-type FIX	Low-dose phase I/II data presented at EHA ; high-dose data H2 2016	NCT02396342
Spark/Pfizer	SPK-9001	Bio-engineered AAV-Padua FIX	Low-dose phase I/II data presented at EHA	NCT02484092
Dimension Therapeutics/Regenxbio	DTX101	AAVrh10-wild-type FIX	Initial phase I/II data due H2 2016	NCT02618915
Sangamo Biosciences	SB-FIX	In vivo protein replacement using zinc finger nucleases	Phase I trial started in 2016	NCT02695160
Freeline Therapeutics	Haemophilia B Gene Therapy	Self-complementary AAV8 FIX	Claims to have been studied in human trials	Unknown

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