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Roche and Celgene set for battle in acute myelogenous leukaemia

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Last week's pivotal trial success could give Celgene a second AML drug, setting up a battle against Roche's Venclexta and idasanutlin.

Celgene’s positive hit in a pivotal study of CC-486 last week sets up another potential approval in acute myelogenous leukaemia, a disease that had long been without new treatments, but which has enjoyed a flurry of drug launches over the past couple of years.

The space suddenly looks highly competitive, and last year’s approval of Venclexta positions the Roche/Abbvie product to seize significant market share, according to *EvaluatePharma* sellside consensus. Several pivotal trial readouts loom, and for Celgene, which already has a marketed AML drug, Idhifa, Roche’s Mirros study of the MDM2 inhibitor idasanutlin is perhaps the key one to watch.

Indeed, anchored by Venclexta, the Swiss firm looks to be building a strong position in AML. At its pharma investor day in London yesterday it highlighted Mirros as one of the largest trials ever conducted in relapsed/refractory AML; this is due to read out next year, as is Glycomimetics’ phase III study of the E-selectin inhibitor uproleselan.

That said, Celgene’s success came in a novel setting: CC-486 yielded positive topline results in Quazar AML-1, a trial in first-line AML maintenance, meaning the therapy is given while patients are still in complete response after being given induction chemo.

This is just as well, given that the US FDA is showing signs of holding drug makers to a high bar in AML treatment, as Daiichi Sankyo found out in June. The company’s GLT3 inhibitor Vanflyta was slapped with a complete response letter a month after being voted down by an advisory committee.

Vanflyta is approved in Japan for treating relapsed/refractory AML in patients harbouring mutated FLT3. With two FLT3 inhibitors already available for AML in the US, perhaps the FDA saw little reason to approve a third without evidence of an overwhelming safety or efficacy advantage.

Late-stage industry projects targeting AML					
			Indication sales ($m)		
Product	**Company**	**Pharmacology**	**2018**	**2024e**	**Setting/notes**
Marketed					
Venclexta	Roche/Abbvie	BCL-2 inhibitor	NA	851	1L
Xospata	Astellas Pharma	FLT3 & AXL inhibitor	23	520	FLT3mut, r/r
Idhifa	Celgene/Agios	IDH2 inhibitor	72	515	IDH2mut, r/r
Tibsovo	Agios	IDH1 inhibitor	14	358	IDH1mut, r/r
Daurismo	Pfizer	Smoothened inhibitor	0	400	1L
Vyxeos	Jaxx	Pyrimidine analogue & topoisomerase II inhibitor	101	291	1L, therapy-related
Rydapt	Novartis	FLT3 inhibitor	88	88	FLT3mut, 1L
Mylotarg	Pfizer	Anti-CD33 ADC	NA	NA	CD33+ve, 1L & r/r
Approved in Japan only					
Vanflyta	Daiichi Sankyo	FLT3 inhibitor	0	126	FLT3mut, r/r; US CRL Jun 2019
Phase III					
Idasanutlin	Roche	MDM2 inhibitor	0	212	r/r Mirros study reads out early 2020
CC-486	Celgene	DNMT inhibitor	0	134	1L maintenance, Quazar AML-1 trial positive for OS
Uproleselan	Glycomimetics	E-selectin inhibitor	0	181	r/r ph3 data Dec 2020
Crenolanib	Arog (ex Pfizer)	FLT3 inhibitor	0	NA	FLT3mut, studies in 1L & r/r
DFP-10917	Delta-Fly Pharma	Cell cycle inhibitor	0	NA	2/3L & salvage
Pracinostat	Helsinn	HDAC inhibitor	0	NA	1L
Source: EvaluatePharma. 1L=first line; 2L=second line; r/r=relapsed/refractory.					

Celgene's CC-486 applies a tried and tested approach to a novel use. The project is nothing more than the chemotherapy drug azacitidine, formulated for oral delivery.

Celgene markets azacitidine as Vidaza, for subcutaneous or IV delivery, for treating myelodysplastic syndromes. The group, in the process of being acquired by Bristol-Myers Squibb, said Quazar AML-1 had read out positively for its primary endpoint, showing an overall survival improvement versus placebo, but revealed nothing by way of numerical data.

That will have to wait until a medical conference, and December's Ash meeting seems a likely venue. Until then it will be difficult to see how CC-486 might stack up against the AML competition.

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