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With its liquid biopsy approval, Foundation Medicine takes on Guardant

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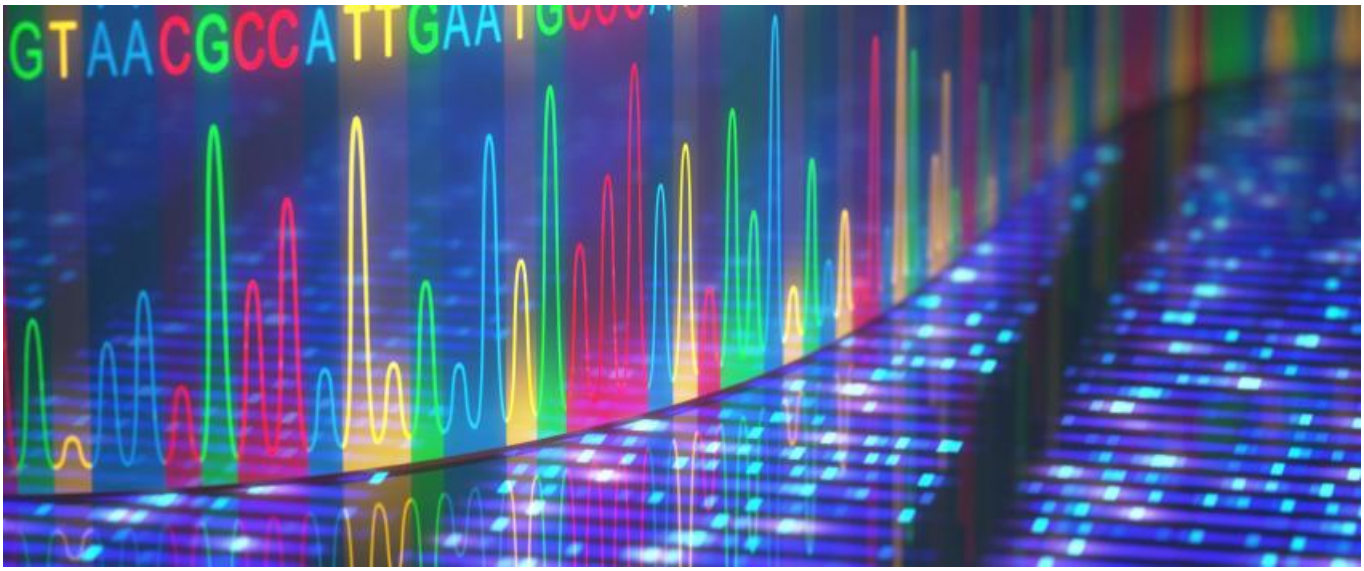

The first pan-cancer approval might have gone to Guardant, but Roche's subsidiary's blood test appears to be able to find more markers.

Though it is possible to launch a diagnostic onto the US market without first obtaining FDA approval, getting the agency's rubber stamp can still provide a major fillip. The FDA approval of Roche's FoundationOne Liquid CDx cancer test, which came at the end of last month, could be a game-changer for the subsidiary that developed it, Foundation Medicine.

"This is a really big moment to have liquid biopsy panels FDA approved – a technology that just years ago there was a lot of uncertainty about," Geoff Oxnard, the global medical lead of Foundation Medicine's liquid franchise, tells *Evaluate Vantage*.

The approval ought to give doctors confidence in the technology – but it is not just Roche's diagnostic that has got a recent boost. Guardant Health's rival test was approved by the FDA three weeks earlier.

Both Guardant's Guardant360 CDx and Roche's FoundationOne Liquid CDx can confirm a cancer diagnosis and identify a patient's tumour from pieces of tumour DNA circulating in the blood. They can also pinpoint the best targeted drug to use and, through repeated testing, track the patient's response to that treatment.

Until last month, many oncologists regarded liquid biopsies as tissue biopsies' poor relation, with guidelines suggesting that they only be used if a surgical biopsy was not possible or did not yield enough tissue. The new approvals, however, put the blood tests on an equal footing with surgical sampling. In fact, Mr Oxnard says, liquid biopsies might take over as first choice.

"The FDA says, use this test, trust it when positive – and, as with all liquid biopsy assays, if it's negative, reflex to tissue as a back-up, because we know that not all cancers shed DNA."

He declines to make a stab at how much sales of FoundationOne Liquid CDx might increase if doctors do indeed use it ahead of surgical biopsies. But there are solid arguments for doing so. At $5,800, the test itself costs the same amount as Roche's equivalent tissue test, FoundationOne CDx. But prioritising a liquid assay would save money as well as being quicker and easier, since a blood draw is much cheaper than a surgical procedure.

Then of course there is the Covid-19 angle: a patient and their healthcare team are at much lower risk of

spreading the contagion if the use of an operating theatre can be avoided.

The market mutates

It is largely undisputed that there is a market for these products. But how do the two approved tests compare?

Guardant360 CDx tests for 98 genetic alterations, including common druggable tumour antigens and microsatellite instability (MSI)-high status. Microsatellites are short repeated sequences of DNA; cancer cells with a lot of them are though to be less able to repair errors in DNA replication. MSI-high status is increasing in importance as a biomarker.

The list of biomarkers for Roche's test is rather longer, clocking in at 311 genes and exons. It also assesses MSI-high status but adds another feature: tumour mutational burden (TMB), which Roche and Bristol Myers Squibb have argued is important for guiding the use of checkpoint inhibitors.

"We've really pushed the emergence of tools like MSI-high and TMB, which is now an on-label genomic biomarker to guide use of pembrolizumab [Keytruda] across cancer types," Mr Oxnard says. "TMB is a different calculation, a new signature. But it's one that we want to be able to use to empower doctors to make informed decisions when they're having that tricky conversation about whether to start a new therapy or not."

Whether this longer list of genes will make FoundationOne Liquid CDx the more compelling choice of approved liquid biopsy is yet to become clear. Mr Oxnard says that this is up to clinicians.

Roche might have a cost advantage: the list price of Guardant360 CDx is thought to be around $1,000 higher than that of Roche's test. But these are out-of-pocket costs; both tests are reimbursed by Medicare, which will cover most of the patients that need them.

Other pan-cancer liquid biopsies are also heading towards the FDA – but slowly. Grail, which intends to list on the Nasdaq in the coming weeks, is targeting 2023 for US registration of its Galleri test, and Thrive Earlier Detection's CancerSeek might obtain approval in a similar timeframe.

For now the market is split between the world's largest diagnostics company and a seven-year-old US group yet to turn a profit. The battle for market dominance should be interesting to watch.

Selected liquid biopsies – progress update				
Company	**Liquid biopsy**	**Type**	**Status in US**	**Company funding ($m)**
Guardant Health	Guardant360	Pan-cancer; helps assign targeted therapy	Approved Aug 7, 2020	$550m VC funding; floated in 2018, current market cap $10.3bn
	Lunar-1	Postsurgical, detects disease recurrence	Sold for research use only	
	Lunar-2	Screening for colon cancer	Clinical trials	
Foundation Medicine (Roche)	FoundationOne Liquid CDx	Pan-cancer; helps assign targeted therapy	Approved Aug 27, 2020	$115m VC funding; bought by Roche for $2.5bn in 2015
Grail	Galleri	Pan-cancer; screening for early detection and identification of tumour origin	Launch as LDT expected in H2 2021	$2.1bn VC funding; has filed for $100m IPO
	DAC	Identification of tumour origin	Launch as LDT expected in 2021	
	Unnamed	Pan-cancer; postsurgical, detects disease recurrence	In development	
Thrive Earlier Detection	CancerSeek	Pan-cancer; early detection	FDA breakthrough device status	$367m VC funding
Natera	Signatera	Pan-cancer; postsurgical, detects disease recurrence	FDA breakthrough device status	$152m in VC funding; floated in 2015, current market cap $5.3bn
Archer DX	Stratafide	Pan-cancer; helps assign targeted therapy	FDA breakthrough device status	$150m VC funding; bought by Invitae in 2020 for $1.5bn
Source: EvaluateMedTech, company websites.				