Evaluate Vantage

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Pharma’s fastest followers revealed

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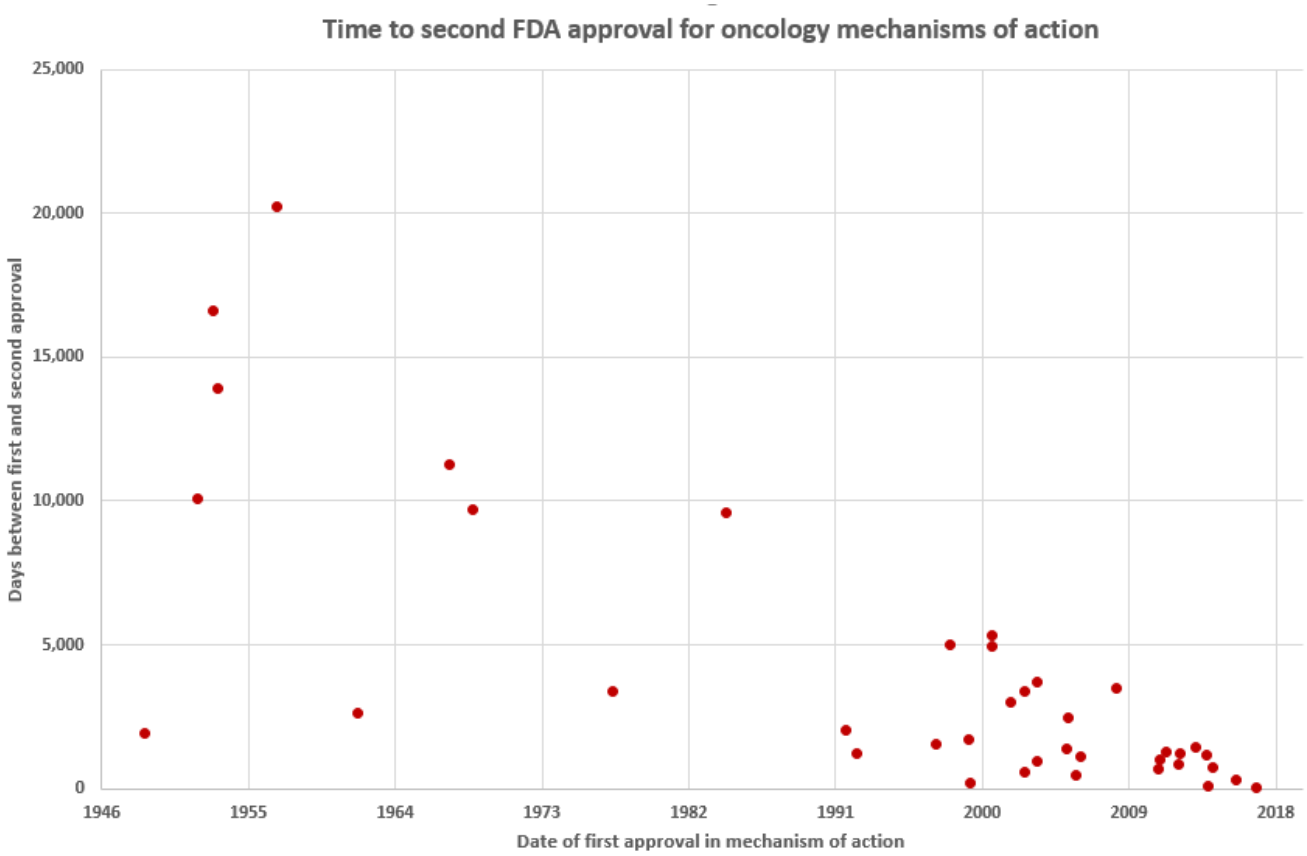
Analysis of me-too drug approvals over time shows trends across therapy areas.

Schemes like US priority review and breakthrough therapy designation aim ultimately to cut approval times, and speed to market has also been improved in recent years by efforts to reduce the FDA’s backlog. But how long does it typically take before a novel mechanism of action sees its second market entrant?

That largely depends on what disease area is being considered, and how hot it is perceived to be. An analysis of *EvaluatePharma* data suggests that in general second-in-class drugs are emerging with increasing speed, though of course being a fast follower does not in itself guarantee success (see charts below).

This can perhaps best be seen in hepatitis C antivirals, where the first-to-market race between the protease inhibitors Victrelis and Incivek was rendered meaningless by Gilead’s subsequent launch of the polymerase inhibitor Sovaldi.

Still, it cannot be denied that antivirals and oncology are two therapy areas where me-too drugs have followed first-in-class launches with increasing speed. This is surely down to the perception that there is enough potential revenue here for more than one product to play for.



Source: EvaluatePharma

Two recent oncology examples are the checkpoint inhibitors and CAR-T therapy. It was just 16 weeks before the anti-PD-1 MAb Keytruda had a direct competitor in the form of Opdivo, and within three years there were two PD-L1-directed drugs on the US market, too. And just seven weeks separate the US approvals of Kymriah and Yescarta – albeit in different haematology uses for now.

Interestingly, Keytruda and Opdivo's fortunes have waxed and waned: the Bristol drug swiftly took away Merck's first-mover advantage, but more recently Keytruda has regained the upper hand, thanks to its dominance in first-line lung cancer.

An even more obvious race to market occurred recently outside oncology, concerning the PCSK9 MAbs Praluent and Repatha, with the former winning by five weeks thanks to a priority review voucher; but it is Repatha that analysts ultimately expect to be the long-term victor in sales terms.

Selected US approvals of oncology drugs and antivirals				
Mechanism of action	**First product**	**Approval date**	**Second product**	**Time lag**
Anti-CD20 MAb	Rituxan, Roche	26 Nov 1997	Arzerra, Glaxosmithkline	12 years
Anti-VEGFR MAb	Avastin, Roche	26 Feb 2004	Cyramza, Lilly	10 years
Proteasome inhibitor	Velcade, Takeda	13 May 2003	Kyprolis, Onyx (Amgen)	9 years
HIV integrase inhibitor	Isentress, Merck & Co	12 Oct 2007	Tivicay, Glaxosmithkline	6 years
Bcr/Abl fusion protein inhibitor	Gleevec, Novartis	10 May 2001	Sprycel, Bristol-Myers Squibb	5 years
BTK inhibitor	Imbruvica, Pharmacyclics (Abbvie)	13 Nov 2013	Calquence, Astrazeneca	4 years
SMO antagonist	Erivedge, Roche	30 Jan 2012	Odomzo, Novartis	42 months
PI3k inhibitor	Zydelig, Gilead	23 Jul 2014	Aliqopa, Bayer	38 months
HDAC inhibitor	Zolinza, Merck & Co	6 Oct 2006	Istodax, Celgene	37 months
Alk inhibitor	Xalkori, Pfizer	26 Aug 2011	Zykadia, Novartis	32 months
Anti-EGFR MAb	Erbitux, Imclone (BMS)	12 Feb 2004	Vectibix, Amgen	32 months
Parp inhibitor	Lynparza, Astrazeneca	19 Dec 2014	Rubraca, Clovis	104 weeks
BRAF inhibitor	Zelboraf, Roche	17 Aug 2011	Tafinlar, GSK (Novartis)	93 weeks
EGFR inhibitor	Iressa, Astrazeneca	5 May 2003	Tarceva, Roche	80 weeks
Anti-PD-L1 MAb	Tecentriq, Roche	18 May 2016	Bavencio, Merck KGaA/Pfizer	44 weeks
Hepatitis C polymerase inhibitor	Sovaldi, Gilead	6 Dec 2013	Harvoni, Gilead	44 weeks
Anti-PD-1 MAb	Keytruda, Merck & Co	4 Sep 2014	Opdivo, Bristol-Myers Squibb	16 weeks
Neuraminidase inhibitor	Relenza, Glaxosmithkline	26 Jul 1999	Tamiflu, Roche	13 weeks
HIV protease inhibitor	Invirase, Roche	6 Dec 1995	Norvir, Abbvie	12 weeks
Anti-CD19 CAR-T	Kymriah, Novartis	30 Aug 2017	Yescarta, Kite (Gilead)	49 days
Multiple tyrosine kinase inhibitor	Nexavar, Bayer	20 Dec 2005	Sutent, Pfizer	37 days
Hepatitis C protease inhibitor	Victrelis, Merck & Co	13 May 2011	Incivek, Lilly	10 days
Source: EvaluatePharma.				

This analysis has been done using *EvaluatePharma's* broad pharmacology classifications, and compares the US approval dates of the first two drugs in each class to reach the market. Not all the data match neatly defined trends.

For instance, oncology is lucrative, but the blockbusters Velcade, Avastin and Rituxan did not see me-too competition for nine, 10 and 12 years respectively. While the first is expected soon to be overtaken by Kyprolis in terms of sales, the last two have proved safe from Cyramza and Arzerra's challenges – thanks basically to being better drugs.

In the middle of the pack lie such strategies as Parp, EGFR and BTK inhibition. Imbruvica's four-year period as the sole BTK inhibitor has given it time to establish a virtually unshakable position, but in EGFR it is a franchise story, with Astrazeneca fighting off Tarceva's threat to its first-mover, Iressa, through the follow-on launch of the highly successful Tagrisso.

The sellside in time expects Tagrisso sales to outstrip those of Tarceva and Iressa combined, so it is clear that first to market only sometimes means best to market.