

Asco 2023 preview - Tigit lives again



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An obscure Roche dataset reignites the Tigit space, and sends up Arcus, Compugen and Iteos.

Despite showing only the vaguest signals of efficacy Tigit blockade remains a major stock price mover. The latest data to have caught investors' imagination come from Roche's Morpheus-liver study, whose results featured among an Asco abstract drop that saw [significant gains for many biopharma companies on Friday](#).

The Roche data – from a trial that until last week had sat firmly under the radar for most – managed to send Iteos stock up 30% even though that Tigit company is not even presenting at Asco; Arcus, which does feature, closed up 26%. However, though Morpheus-liver comes as a positive surprise, those betting on it are perhaps ignoring the earlier lessons of Roche's confusing mid-stage Cityscape trial.

Cityscape had famously misled the markets into thinking that Tigit plus PD-(L)1 blockade had a significant benefit in front-line lung cancer, but the result was [confounded by underperformance of the control arm](#). Morpheus-liver, a multi-cohort phase 1/2 study in first-line liver cancer, appears to suffer from precisely the same effect.

58% risk reduction

The good news for Tigit fans is that combining Roche's anti-Tigit MAb tiragolumab with Tecentriq and Avastin yielded median PFS of 11.1 months, with a reduction in risk of progression or death of a remarkable 58% versus Tecentriq and Avastin alone. ORR also impressed, coming in at 43% versus 11%.

Evercore ISI analysts said the data were hard to ignore, and wrote: "We think it's getting hard to argue there isn't something there." They were especially enthused by an apparent benefit in PD-L1-negative subjects, where ORR was 28% against zero remissions among control subjects; this is unexpected, since Tigit blockade has previously tended to enhance responses only in PD-L1-positives.

However, the big caveat is that control patients seem to be performing worse in Morpheus-liver than expected. Imbrave-150, the phase 3 trial backing Tecentriq plus Avastin's first-line liver cancer use, yielded median PFS of 6.8 months (in Morpheus-liver this was just 4.2 months), and ORR of 28% rather than 11%.

Evercore argues that a cross-trial comparison against Imbrave-150 still yields an impressive result for Morpheus-liver's active arm. The abstract has a 28 November 2022 data cutoff, and the active cohort comprised just 40 patients; data will likely be updated at Asco.

A cross-trial comparison in 1st-line liver cancer

	Morpheus-liver	Imbrave-150	
Cohort	Tiragolumab + Tecentriq + Avastin	Tecentriq + Avastin	
ORR in all-comers	43%	11%	28%
mPFS in all-comers	11.1mth	4.2mth	6.8mth
ORR in PD-L1 -ve	28%	0%	NA
mPFS in PD-L1 -ve	9.1mth	4.2mth	NA

Source: Asco 2023 & Esmo-Asia 2019.

The other big Tigit dataset to watch at Asco will be an update on Arcus/Gilead's Arc-7 study combining domvanalimab with zimberelimab in first-line NSCLC.

This [yielded positive mPFS and ORR data in December](#), but that result was flattered by poor performance of zimberelimab, and BTIG analysts expect an Asco data cut including five more months' follow-up. However, the abstract has not been updated, so Arcus's 26% share price surge can be put entirely down to Roche's Morpheus-liver result.

Also featuring at Asco is Compugen, which will present data from a small study of its [Pvrig inhibitor COM701](#) combined with Bristol Myers Squibb's anti-Tigit MAb BMS-986207 and Opdivo. This uncontrolled trial, in microsatellite-stable endometrial cancer, has shown two partial remissions among nine patients, and Compugen closed up 11% on Friday.

Tigit-relevant Asco 2023 stock movers

Company	Share price chg*	Tigit Asco abstract	Study	Detail
Iteos	+30%	NA	NA	Has GSK-partnered belrestotug in ph2 Libtayo combo
Arcus	+26%	397600	Arc-7	Domvanalimab + zimberelimab in ≥50% PD-L1 expressing 1st-line NSCLC
Compugen	+11%	5595	NCT04570839	COM701 + BMS-986207 + Opdivo in MSS endometrial cancer
Beigene	+4%	NA	NA	Has ociperlimab in ph3 tislelizumab combo
Roche	+1%	4010	Morpheus-liver	1st-line liver cancer, tiragolumab on top of Tecentriq + Avastin

Note: *at close on Friday 26 May.

While all ordinary Asco abstracts are now live, still to be presented are those concerning late-breaking data.

The most industry-relevant Asco late-breakers include Novartis's [Natalee trial of Kisqali](#), [Immunogen's Mirasol](#), [Astrazeneca's Duo-Q](#), [Servier's Indigo](#) and J&J/Legend's Cartitude-4. However, the [EHA meeting managed already to leak the Cartitude-4 data](#), so Natalee looks set to take centre stage.

Selected Asco 2023 late-breakers

Abstract	Project	Mechanism	Company	Trial	Setting
LBA106	Carvykti	Anti-BCMA Car-T	J&J/ Legend	Cartitude-4	2nd to 4th-line multiple myeloma
LBA1013	Toripalimab	Anti-PD-1 MAb	Coherus	Torchlight	1st-line TNBC
LBA100	Keytruda	Anti-PD-1 MAb	Merck & Co	Keynote-671	Stage II-IIIb NSCLC (adj + neoadj)
LBA6002	Sintilimab	Anti-PD-1 MAb	Innovent	Continuum	Nasopharyngeal cancer
LBA5506	Imfinzi	Anti-PD-1 MAb	Astrazeneca	Duo-O	1L Brca- ovarian cancer maintenance
LBA5507	Elahere	Anti-FR α ADC	Immunogen	Mirasol	FR α -high ovarian cancer
LBA3000	Enhertu	Anti-Her2 ADC	Daiichi Sankyo/ Astra	Destiny-Pantumor02	Her2+ solid tumours
LBA3	Tagrisso	EGFR inhibitor	Astrazeneca	Aaura	Stage IB-IIIa EGFR+ NSCLC (adjuvant)
LBA1	Vorasidenib (AG-881)	IDH1 & 2 inhibitor	Servier (ex Agios)	Indigo	IDH1/2+ glioma
LBA500	Kisqali	CDK4/6 inhibitor	Novartis	Natalee	ER+/Her2- breast cancer (adjuvant)

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