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ASCO 2023 – Trop2 Could Validate Merck's Savvy Deal With Kelun

by

In Trop2 Merck & Co. might have got itself an ADC at least as good as Gilead and Astra/Daiichi's leaders, for a fraction of the price.

While *Gilead Sciences, Inc.*, *AstraZeneca PLC* and *Pfizer Inc.* have spent billions acquiring expertise in antibody-drug conjugates, *Merck & Co., Inc.* has trodden a different path. Two low-key deals with China's Kelun brought an early-stage portfolio of ADCs, and the most important of these just yielded its first human data.

That asset is MK-2870, an ADC targeting Trop2 whose Kelun-sponsored lung cancer trial was the subject of poster at the American Society of Clinical Oncology annual meeting 4 June. This will be of interest to those following the industry's two most advanced Trop2-targeting ADCs, Gilead's Trodelvy and *Daiichi Sankyo Co., Ltd.*/AstraZeneca's datopotamab deruxtecan, especially as the data make MK-2870 look at least as good.

The Trop2-targeting space has been tarnished by *Trodelvy's mediocre showing in the Tropics-02 trial*, on the back of which the Gilead drug, acquired in the $21bn takeover of *Immunomedics, Inc.*, secured a US breast cancer indication. But lung cancer could be a bigger use, and this is the primary focus for datopotamab, whose *Tropion-Lung01 study readout is one of the sector's most important first-half catalysts*.

44% response rate

Against this backdrop Kelun today presented an ASCO abstract of a Chinese trial in late-line NSCLC, where 44% of 43 evaluable patients developed investigator-assessed partial remissions.

Tropion-Lung01 tests datopotamab in the less-advanced PD-(L)1-relapsed setting, but a relevant comparator might be an earlier phase 1 trial in various cancers that yielded 24% ORR in its NSCLC cohort. Meanwhile, a basket trial of Trodelvy showed the Gilead drug to have an ORR of

just 17% in NSCLC, a fact that makes MK-2870 look best in class.

But as ever with cross-trial comparisons baseline characteristics differ. The Kelun-sponsored study comprises Chinese hospitals only, and Chinese NSCLC patients tend to have more EGFR-driven disease than those in the west; EGFR mutation-positive NSCLC is more responsive to chemo, which is ultimately what an ADC delivers.

The fact more of Kelun's patients were EGFRm-positive than in the datopotamab trial appears to have driven up efficacy in all-comers. For a fairer comparison, looking only at EGFR wild types gives ORR of 26% for MK-2870 versus 19% for datopotamab – still impressive but realistically an in-line result.

One key to determining how big the market opportunity could be is whether patients might have to be enriched for Trop2 expression. The Kelun study's lead author, Dr Wenfeng Fang, told *Evaluate Vantage* that Trop2 expression had been analysed retrospectively, but said he did not know to what extent it correlated with responses.

For devotees of the ADC space, Kelun's poster revealed MK-2870 (which the company codes SKB-264) to contain a sulfonyl pyrimidine CL2A carbonate linker and belotecan-derivative payload, carrying a drug-to-antibody ratio of 7.4.

Trop2-targeting ADCs in lung cancer: a cross-trial comparison

Company	Project	Trial	Setting	NSCLC data	
Gilead (ex Immunomedics)	Trodelvy	*Immu-132-01 basket study*	Late line NSCLC (n=54)	ORR 17%	mPFS 4.4mth
		Tropics-03, NSCLC cohort	2L NSCLC	Not disclosed	
		Evoke-01	2L NSCLC vs docetaxel	Ends May 2024	
Astrazeneca/ Daiichi Sankyo	Datopotamab deruxtecan	*Tropion-Pantumor01*	Late line NSCLC (n=180)	ORR 24%	mPFS 5-6mth
				ORR 19% in EGFRwt, vs 63% in EGFRm	
		Tropion-Lung01	2L NSCLC vs	Data Q2 2023	

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			docetaxel		
Merck & Co/ Kelun	MK-2870/ SKB-264	NCT04152499	~3L NSCLC (n=43)	ORR 44%	mPFS 6.2mth
				ORR 26% in EGFRwt, vs 60% in EGFRm	
Source: company reports, Asco & clinicaltrials.gov.					

With Merck now behind MK-2870, and datopotamab set to deliver all-important Tropion-Lung01 data, NSCLC might be about to become a key battleground for Trop2-targeting agents.

So where might Trodelvy fit in? The Gilead drug is in Evoke-01, a phase 3 study in a very similar setting to Tropion-Lung01 that is due to end in May 2024. However, readout of an NSCLC cohort from yet another mid-stage multi-tumour Trodelvy trial, Tropics-03, never materialised.

If Trodelvy fails in lung cancer it would underline the disappointment Gilead investors already feel about their company having spent $21bn on Immunomedics. For its part Astrazeneca gave Daiichi $2.4bn up front across two transactions focused on ADCs – but at least that brought in Enhertu, a drug that is already revolutionising treatment of Her2-expressing cancers.

In May 2022 Merck paid Kelun $47m for undisclosed ADC projects later revealed to include MK-2870. It followed that last December with $175m for a further seven preclinical molecules. It would be amazing if Kelun ended up bringing Merck an entire ADC platform, especially as so far the US company's financial exposure has been negligible.

– Jacob Plieth (JacobP@vantageanalysis.com)

This article originally appeared in Evaluate Vantage. Evaluate Vantage and Scrip are part of the same parent company, Norstella.