Evaluate Vantage

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Tiziana takes a deep breath and targets Covid-19

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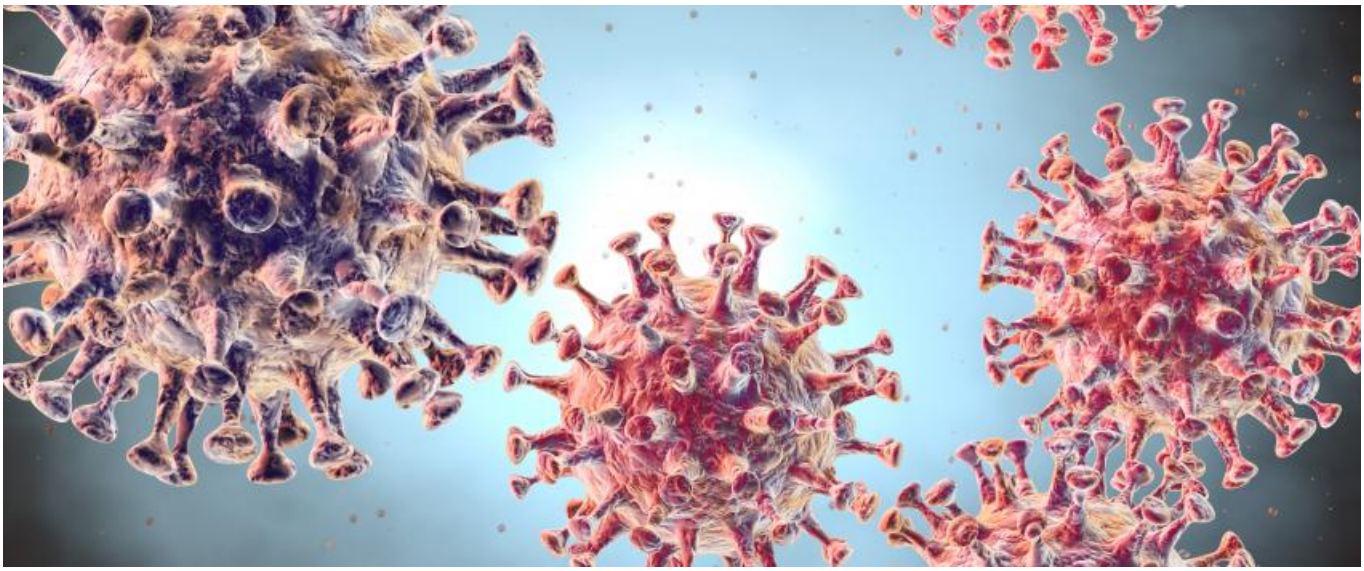

Using drugs that can cause or exacerbate lung infections to treat the novel coronavirus – what could go wrong?

This article has been updated to clarify the mechanism of Eusa Pharma's Sylvant.

The addition last week of Roche's anti-IL-6 receptor antibody Actemra to Chinese guidelines for treating patients with Covid-19 has prompted Tiziana Life Sciences to speed the development of its similarly-acting TZLS-501 for the same use. The group's stock is up 173% on London's AIM so far today.

This could be somewhat overenthusiastic: for one thing, TZLS-501 is still preclinical. For another, both of the approved anti-IL-6R MAbs carry black box warnings of the risk of serious infections in patients with pulmonary disease. Planning to give anti-IL-6Rs to Covid-19 patients is a bold move.

Actemra, long approved for rheumatoid arthritis, has reportedly been used in 20 patients with severe Covid-19 infections in China, lowering body temperatures in all of them within one day. All but one were discharged from hospital within a fortnight.

This approach seems to have been prompted by suggestions that Covid-19 patients might respond to the infection by overproducing inflammatory cytokines such as IL-6 in the phenomenon called cytokine storm. In 2017 Actemra was approved by the FDA to treat cytokine release syndrome caused by Car-T treatment.

A further rationale has been provided by research published on March 3 indicating that viral load is associated with elevated IL-6 levels in severely ill Covid-19 patients. The researchers wrote that IL-6 "should be considered as a therapeutic target in critically ill patients with excessive inflammatory response".

Approved anti-IL-6Rs				
Product	**Company**	**2020e sales ($m)**	**2024e sales ($m)**	**Notes**
Actemra/ Actemra SC	Roche/Chugai	2,408	2,341	BBW of serious infections, including tuberculosis
Kevzara	Sanofi/Regeneron/ Asahi Kasei	355	570	BBW of serious infections, including tuberculosis
Source: EvaluatePharma, drug labels. BBW=black box warning.				

According to the *WSJ*, Regeneron and Sanofi are also repurposing their anti-IL-6R, Kevzara, for the new virus. The partners intend to start a clinical trial of their MAb – which is widely approved for rheumatoid arthritis but not for cytokine release syndrome – in severe Covid-19 as soon as possible.

There is one other approved product that acts on this pathway: Eusa Pharma's Sylvant. This product is a chimeric monoclonal antibody that binds to IL-6 itself, and the company states that this is is a distinct and different mechanism of action from the anti-IL-6 receptor antibodies. Sylvant does not appear to be under investigation for the coronavirus; according to its label Sylvant is not to be given to patients with severe infections.

In a tizzy

The advantage of these approved products, as opposed to novel drugs in development such as Gilead's remdesivir, is that they can be used off-label relatively easily, and their production and distribution ramped up relatively quickly. But there is no getting away from their poor safety profile.

This has not stopped Tiziana, of course. The safety profile of TZLS-501, like its efficacy in Covid-19 or anything else, is unknown, because it is yet to be given to humans. Neither does it have any of the advantages of the approved products.

There is as yet no evidence that any of the dozen or so other IL-6Rs in clinical or preclinical development are being aimed at Covid-19. Perhaps when some of these groups see how nicely Tiziana has done on the markets today they might make their own announcements.

Still, giving an untried drug to severely ill patients, many of whom will be elderly or have comorbidities or both, is taking a big risk. And that would be true even if the molecule did not belong to a class known to be potentially dangerous to patients with lung infections.

The anti-IL-6R pipeline		
	Project	**Company**
Filed		
	Satralizumab	Roche/Chugai
Phase III		
	Olokizumab	UCB
	Clazakizumab	Lundbeck
	BCD-089	Biocad
	BAT1806	Bio-Thera Solutions
Phase I		
	EBI-031	Roche/Sesen Bio
	MEDI5117	Astrazeneca
	MSB11456	Fresenius
	LusiNEX	Mycenax Biotech
	FB704A	Fountain Biopharma
Preclinical		
	Inflammation FynomAbs *	Johnson & Johnson/Mitsubishi Tanabe
	TZLS-501	Tiziana Life Sciences/Light Chain Bioscience
** Also inhibits IL-7a. Source: EvaluatePharma.*		