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Sanofi’s sarilumab bests Humira to set up arthritis showdown

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Sanofi’s IL-6-targeting agent sarilumab had risked being a rheumatoid arthritis also-ran – but not any more. Success in a head-to-head trial against AbbVie’s Humira will not have any impact on its chance of US approval, but should give it an edge in discussions with payers – which will be crucial when Humira biosimilars finally emerge.

In a few years there could also be competition from biosimilar versions of Roche’s Actemra, a fellow IL-6 inhibitor. But this is not Sanofi’s only worry: Johnson & Johnson/GlaxoSmithKline’s IL-6 MAb sirukumab has hinted at best-in-class efficacy in phase II. Glaxo said in December that sirukumab had positive top-line phase III results, but did not give any more details.

Like sarilumab, sirukumab has been tested against Humira, and full data from the Sirround-H study of the latter will be eagerly awaited (*Upcoming events: Sirukumab and serelaxin face phase III readouts, October 30, 2015*).

But for now, Sanofi can claim to have the first IL-6 blocker to show superiority over Humira in RA. The Saril-RA-Monarch trial, which was not included in sarilumab’s regulatory package with the FDA, showed a significant improvement with sarilumab over Humira in the primary endpoint: change from baseline in DAS28-ESR at 24 weeks.

Results from Saril-RA-Monarch		
Endpoint	**Sarilumab**	**Humira**
Change from baseline in DAS28-ESR at 24 weeks	-3.25	-2.22
Patients achieving ACR20	72%	58%

The secondary endpoint of ACR20 response – a 20% improvement in RA signs and symptoms – also favoured Sanofi’s contender with sarilumab showing a significant improvement over Humira. The company did not give values for other secondary outcomes, including ACR50 and 70 responses, but said these too hit significance.

Adverse events were similar between the groups, but neutropenia was more common with sarilumab, at 14% versus 1% with Humira. This side effect has been seen in previous studies of IL-6 inhibitors, according to Sanofi.

ACR20 improvement

As well as showing superiority over Humira, Saril-RA-Monarch also yielded better ACR20 response rates than previously reported with sarilumab (*Why Sanofi’s arthritis biologicals lead could be short-lived, May 21, 2015*).

Sirukumab, meanwhile, has reported an ACR20 response in an impressive 83% of patients in its phase IIb study. However, the usual caveats about cross-trial comparisons apply, and the J&J/Glaxo drug will need to repeat this feat in phase III.

Sanofi now has the upper hand, and with an FDA approval decision expected on October 30, it should have a while to establish sarilumab before sirukumab makes it to the market. Sanofi plans to submit sarilumab for EU approval in the third quarter.

Anti-IL6 agents in late-stage development in RA			
Drug	**Company**	**Status**	**2020E sales ($m)**
Actemra	Roche	Marketed	1,516
Sarilumab	Sanofi/Regeneron	Filed	534
Sirukumab	J&J/GlaxoSmithKline	Phase III	451
ALX-0061	Ablynx/AbbVie	Phase II	22
Olokizumab	UCB/R-Pharm	Phase II	-
Clazakizumab	Alder Biopharmaceuticals	Phase II	-

Currently, *EvaluatePharma* consensus puts 2020 sarilumab sales at $534m, but the data against Humira could give this a boost. The results also set a high hurdle for other groups with IL-6 inhibitors in earlier-stage development.

With pricing pressures continuing, there is no guarantee that the Saril-RA-Monarch outcome will steer prescribers away from biosimilars, who might accept a slightly lower efficacy for a corresponding lower cost. But at least Sanofi has given sarilumab a fighting chance.

Drug	Trial	ID
Sarilumab	Saril-RA-Monarch	NCT02332590
Sirukumab	Sirround-H	NCT02019472

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