Evaluate Vantage

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Upcoming events – Pfizer's abrocitinib and Myovant's relugolix

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Pfizer's abrocitinib heads against Dupixent in atopic dermatitis, while Myovant hopes to raise its Spirits.

Welcome to your weekly roundup of approaching clinical readouts. Pfizer's Jak 1 inhibitor abrocitinib will need to prove itself against the dermatitis stalwart Dupixent in the phase III Jade-Compare trial, data from which are due shortly. It is already known that abrocitinib works in atopic dermatitis, since it met key endpoints in two phase III trials. But the safety profile will need to be closely analysed; Jak inhibitors have had to contend with serious toxicities when used in rheumatoid arthritis.

Abrocitinib is said to be selective for Jak 1, which investigators believe reduces the risk of class-related adverse events such as infections and thromboembolic and other cardiovascular events.

In abrocitinib's previous atopic dermatitis studies, Jade Mono-1 and 2, the rate of serious adverse events was 2-3% in treated patients, and discontinuations were in the 4-6% range, higher than the 2% previously seen with Dupixent. There were no thromboembolic events with Pfizer's Jak, but there seem to be tolerability issues judging by the 10-20% rate of nausea and headache. In Dupixent studies the most frequent adverse events were injection site reactions and conjunctivitis.

In terms of efficacy the higher dose of abrocitinib showed comparable results to Dupixent in its pivotal trials. In the latest study, Jade-Compare, abrocitinib is pitted directly against Dupixent in adults on topical background therapy. Again 100mg and 200mg daily doses of abrocitinib are being tested, and the co-primary endpoints are investigator's global assessment and EASI-75 score at 12 weeks.

On Pfizer's third-quarter call management specifically pointed to a secondary endpoint, pruritus reduction, where the company expects abrocitinib to outperform, as it "inhibits the interleukin-31 that is a major itch mediator, which is not covered by Dupixent."

Displacing Dupixent will be tough given physicians' experience and the potential for a black-box warning for abrocitinib, in common with other Jaks. On Pfizer's side will be convenience: abrocitinib is oral and Dupixent subcutaneous.

In terms of Jak competition Lilly's Olumiant and Abbvie's Rinvoq are in phase III trials in atopic dermatitis and approved, with black box warnings, in rheumatoid arthritis. Meanwhile, Dermira has just been bought by Lilly (*Lilly jumps the gun with Dermira deal, 10 Jan 2020*).

Biggest-selling dermatitis products*				
Product	**Company**	**Mechanism of action**	**Indication sales ($m) 2024e**	**Indication status**
Dupixent	Sanofi	IL-13 and IL-4 antibody	4,138	Marketed
Tradipitant	Vanda Pharmaceuticals	Neurokinin 1 receptor antagonist	463	Phase III
Lebrikizumab	Dermira (Lilly)/Almirall	IL-13 antibody	248	Phase III
Abrocitinib (PF-04965842)	Pfizer	Jak 1 inhibitor	222	Phase III
EDP1066	Evelo Biosciences	Monoclonal microbial	77	Phase I
Olumiant	Lilly	Jak 1 and Jak 2 inhibitor	70	Phase III
**Excludes topical therapies. Source: EvaluatePharma.*				

Myovant looks for Spirit guidance

For Myovant Sciences phase III endometriosis data due by the end of the second quarter will not just be about scoring a clinical win with its GnRH inhibitor relugolix; they will also hopefully show some benefit over the approved market leader, Abbvie's Orilissa.

Relugolix has previously disappointed – relative to expectations – in cross-trial comparisons with Orilissa in uterine fibroids. And on its current development trajectory, even if the Spirit 1 and Spirit 2 trials are successful, the project will hit the market two and a half years after Orilissa. Strong data will be essential if Myovant is to stand any chance of taking market share from the pharma giant.

Relugolix and Orilissa both work by blocking the gonadotrophin hormone and reducing the pain associated with endometriosis, a disorder where tissues that usually line the wall of the uterus grow outside of the womb.

However, where Orilissa is used as a monotherapy, the Spirit trials are testing relugolix in combination with an oestrogen "add-back therapy". One of the biggest side effects of GnRH antagonists is bone loss, which can limit the duration of treatment. Add-back therapy can thus extend the treatment window for what is a chronic disease.

Myovant supporters have highlighted this as an advantage over Orilissa, alongside relugolix's dosing convenience. But Abbvie could hobble this advantage with results from a 681-patient trial comparing Orlissa monotherapy against a combination with hormone add-back. If this trial is positive Leerink analysts say a label extension for Orilissa could follow in the third quarter, six months before relugolix's forecast endometriosis approval.

With so much stacked up against Myovant it is not surprising that 2024 sales forecasts for relugolix in endometriosis are only $278m, compared with $843m for Orilissa, according to *EvaluatePharma*. The Spirit data will have to surprise for Myovant to avoid being an also-ran in the indication.

GnRH products					
Project	**Company**	**Indication**	**Status**	**Sales by indication ($m) 2024**	**Group share (%) 2024**
Orilissa	Abbvie	Endometriosis	Marketed	834	32%
		Uterine fibroids	Filed	657	25%
Relugolix	Myovant Sciences	Endometriosis	Phase III	278	11%
		Uterine fibroids	Phase III	348	13%
Linzagolix	Obseva	Endometriosis	Phase III	158	6%
		Uterine fibroids	Phase III	210	8%
Source: EvaluatePharma.					