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Hay fever vaccines entering new season of innovation

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Today's positive phase II data for private company Circassia for its ragweed allergy vaccine is just the latest in string of clinical advances in field that could be set to revolutionise the multi-billion dollar hay fever and allergy market. The news from Circassia comes hot on the heels of positive phase III data from Alk Abello and Merck & Co's SCH-039641/MK3641 ragweed vaccine, which has prompted the group to predict a filing of the drug early next year.

If successful it could potentially join three other hay fever vaccines due to come to market in 2013, including the group's own grass pollen treatment SCH697243/MK-7243 and Allergy Therapeutic's Pollinex Quattro Ragweed vaccine (see table below). More immediately, Allergy Therapeutics is also gearing up to have its grass vaccine Pollinex Quattro Grass approved in Europe by the end of the summer.

Currently the most widely available treatments for hay fever are coriticosteroids and anti-histamines. The drugs, however, do not treat the underlying causes of hay fever, which is estimated to effect 150m in Europe and the US. The market is also largely generic dominated by over the counter treatments that usually have the side effects of causing drowsiness.

Need for new treatments

While generally considered a minor disorder, hay fever is thought to be increasing in incidence by 5% a year in Europe and the US, it can progress to the more life-threatening allergic asthma. Developers of hay fever vaccines have argued that vaccination stops this progression and therefore should be more widely available.

Hay fever vaccines work on the principle of allergen specific de-sensitisation by damping down the over-active immune response to grass, tree and ragweed pollen. This approach also means that the effects of vaccines can be longer lasting, and some studies have shown benefits stretching out to three years post initial treatment.

There are currently several older hay fever vaccines on the market including Stallergene's Staloral and ALK-Abelló's Grazax, but given their age these drugs tend not to have the ability to either hit as many antigens as the newer drugs in development or generate as strong an immune response. The treatment schedule too is often less convenient, with patients needing to take both Grazax and Staloral many months before the start of the allergy season.

Next in line

But the next allergy vaccine waiting for approval, Allergy Therapeutic's Pollinex Quattro Grass is also a relatively old technology. The drug, which is expected to find out if it has gained approval in Germany by autumn, has suffered a big setback in the US where it is still on a clinical hold.

However, there could be some regulatory progress in the US this year. The FDA has completed a review of the adjuvant used in the vaccine and has agreed to remove the hold once it has agreed clinical trial protocols with Allergy, which were submitted in November. But even if the FDA does agree them Allergy is unlike to continue clinical work in the US until it finds a development partner. The US hold has also affected the group's phase III ragweed vaccine.

Pollinex Quattro Grass could, however, face one big stumbling block when it hits the market in Germany and if it does eventually get approval in the US: The drug is an injected medicine. The majority of treatments currently in phase III trials are transmucosal tablet, which are dissolved in the mouth and taken daily for a period of months.

Technology advances

Both of Merck's phase III allergy vaccines, originally developed by Schering Plough, are tablets. In data shown at the American Academy of Allergy, Asthma & Immunology, the group presented data showing that its ragweed vaccine significantly reduced nasal and eye symptoms in a trial involving 565 patients. Merck is now planning to file both the ragweed and grass vaccine in early 2013; analysts are expecting a launch by the end

of the year for both medicines.

The advances in technology in the allergy vaccines space have been demonstrated by not only by the route of administration but the developments in the allergens themselves.

Although clinical progress of Biomay, Paladin Labs and Stallergenes' STALAIR rBetV1 appears to have slowed, the tablet is the first to use a recombinant allergen as an active substance.

T-cell approach

But perhaps one of the most advanced and interesting new allergy vaccine products is Circassia's ToleroMune Ragweed Allergy Vaccine. The product has been generated using the company's proprietary ToleroMune platform technology, which identifies short peptide sequences called epitopes, typically 10 to 20 amino acids long, from the allergen proteins that are responsible for causing allergic reactions.

When injected, these epitopes mobilise regulatory T-cells, which downregulate components of the allergic response to the allergens. In this way, a sufferer develops tolerance of the antigen, in this case ragweed. The product also does not require adjuvants or other immune stimulators.

But while the results from the new crop of allergy vaccines are promising, and the convenience of the products increasing as they move away from injections, if hay fever vaccines are truly to come into their own and grow market share they need to not only demonstrate better efficacy than the cheap generic alternatives in the market, but also benefits in longer-term symptom control.

Allergic rhinitis vaccine late stage pipeline						
Market status	**Allergy**	**Product**	**Company**	**Routes of Admin.**	**Treatment Regimen**	**Trial IDs**
Filed	Grass	Pollinex Quattro Grass	Takeda/GlaxoSmithKline/ Allergy Therapeutics	Injection	4 injections administered ahead of the peak allergy season	NCT0041414
Phase III	Grass	SCH 697243/ MK-7243	Merck & Co	Transmucosal	1 dissolving tablet sublingually once daily	NCT0055055 NCT0056215 NCT0138537
		Wild-Type Grass Allergy Therapy	Biomay/AllergoPharma	Transmucosal	Daily	NCT0026445 NCT0062370 NCT0084125
	Ragweed	SCH 039641/ MK-3641	Merck & Co/ALK-Abelló	Transmucosal	1 rapidly dissolving tablet, sublingually, once daily prior to and throughout the ragweed pollen season	NCT0078319 NCT0077031
		Pollinex Quattro Ragweed	Takeda/GlaxoSmithKline/ Allergy Therapeutics	Injection	4 injections administered ahead of the peak allergy season	NCT0042378
	Tree	STALAIR rBetV1	Paladin Labs/Stallergenes/ Biomay	Transmucosal	Daily, during approximately 5.5 months	NCT0090191
Phase II	Grass	ToleroMune Grass Allergy	Adiga Life Sciences/Circassia	Injection	1x4 administrations	NCT0116606

		Allergy Vaccine	Sciences/Circassia		4 weeks apart	
		BM32	Biomay	Injection	Every 4 weeks for a total of 3 injections	NCT0144500 NCT0153897
	Ragweed	ToleroMune Ragweed Allergy Vaccine	Adiga Life Sciences/Circassia	Injection	1x4 administrations 2 weeks apart	NCT0087877 NCT0144860
	Tree	Pollinex Quattro Tree	Takeda/Allergy Therapeutics	Injection	Injected weekly	NCT0011862 NCT0011375 NCT0011861
		SLITonePLUS Birch	ALK-Abelló	Transmucosal	-	NCT0119135
		AL0801rB	Merck KGaA	Injection	-	NCT0084151
		AllerT birch pollen	Anergis	Injection	Five subcutaneous injections over 2 months	-