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End in sight for Oncopeptides’ stormy Ocean voyage

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Pepaxto might not be a complete bust in myeloma.

A new cut from a phase 3 trial of Pepaxto might just rehabilitate the blood cancer drug after its effectiveness was called into question in July. The poor finding on overall survival in the Ocean trial has now been attributed by Oncopeptides to patients whose multiple myeloma had previously been treated with a stem cell transplant.

This raises the possibility that Pepaxto's label might be expanded to encompass third to fifth-line treatment, albeit restricted to patients who have not undergone transplant – a better outcome, from Oncopeptides’ perspective, than full withdrawal of the product. Yet another possibility is that the FDA will demand more trials. A panel meeting next month will give a hint as to how this convoluted journey might end.

Pepaxto gained accelerated approved for fifth-line relapsed refractory multiple myeloma in February on the back of the Horizon trial. To make a success of the agent, though, Oncopeptides needs to get it approved for earlier use. Ocean compared the alkylating agent versus Pomalyst in third to fifth-line therapy, and had initially been considered to show only noninferiority to the established drug on progression-free survival, its primary endpoint.

A re-analysis reported in May, incorporating more data points, confirmed that Ocean did hit superiority on PFS, but also brought the less welcome news that overall survival favoured Pomalyst (*Oncopeptides gives with one hand and takes away with the other, July 8, 2021*). Ocean and a number of other trials were put on hold.

Half the market

This weekend a new cut of Ocean data was presented at the International Myeloma Workshop in Vienna. Among patients who had previously received an autologous stem cell transplant the OS readout strongly favoured Pomalyst. Among those with no such treatment history, Oncopeptides’ agent won out, improving PFS by 41% and OS by 22%.

Ocean trial of Oncopeptides' Pepaxto, subgroup analysis			
	Pepaxto	**Pomalyst**	**Hazard ratio**
Total population			
PFS	6.8mth	4.9mth	0.79
OS			1.1
ORR	33%	27%	
Patients without a prior ASCT			
PFS	9.3mth	4.6mth	0.59
OS	21.6mth	16.5mth	0.78
Patients with a prior ASCT			
OS	16.7mth	31.0mth	1.61
ASCT = autologous stem cell transplant. Source: company release.			

The benefit with Pepaxto was greatest in older patients, who are less likely to receive a stem cell transplant. One theory is that the stem cell plus an alkylator like Pepaxto places stress on the patient's bone marrow, leading to worse outcomes.

Pepaxto's safety was less than ideal: it resulted in substantially more grade 3 or 4 haematologic adverse events compared with Pomalyst. These were manageable but more dose modifications were needed with Pepaxto than Pomalyst.

These are matters for the FDA's oncologic drugs advisory committee to weigh when it meets on October 28. The panel is expected to make one of three recommendations: expand Pepaxto's label to include third- and fourth-line use, but only in patients with no prior stem cell transplant; insist on more clinical trials; or yank the drug from market altogether.

According to Jefferies analysts, around 50% and 40% of multiple myeloma patients receive a stem cell transplant as first-line therapy in the US and EU respectively, so should the FDA restrict the label to the non-transplant group Oncopeptides can still expect to reach roughly half the market. A further argument in favour of this course of action is that transplant-ineligible myeloma patients tend to have poorer outcomes than those who can receive stem cells.

The worst-case scenario, that the drug is pulled despite its success in the Horizon trial, is perhaps unlikely – the FDA does not pursue the nuclear option very frequently. But it is certainly possible that more trials might be required, meaning Pepaxto's adoption in earlier lines of therapy would be delayed by months or years.

Pepaxto is currently forecast to have 2026 sales of $552m, according to *Evaluate Pharma*'s sellside consensus. Oncopeptide's investors must confront the depressing thought that even the best case will see Pepaxto sell half as much as originally hoped.