Evaluate Vantage

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HyperAcute Pancreas will go to the wire

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With no call for an early stop to the Impress trial of NewLink Genetics' HyperAcute Pancreas in second-line pancreatic cancer, investors will be left waiting until next year for the results of this binary event.

Expectations on Wall Street that the 700-patient study would show evidence of efficacy and close early were probably low anyway. The continuation now means that the final results will come as a number of other high-profile phase III pancreatic programmes read out in 2016, leaving NewLink in an increasingly crowded market.

Competing for investor attention in 2016 will be data from Merck KGaA/Threshold Pharmaceuticals' Maestro trial of evofosfamide and one or both of Incyte/Lilly's Janus studies of Jakafi. In the former, evofosfamide is being tested in combination with gemcitabine used first line, while separate trials of Jakafi compare it in addition to, and against, capecitabine as second-line therapy.

If this were not enough noise in the market, 2016 could also see the launch of Baxter Laboratories and Merrimack Pharmaceuticals' MM-398 – a liposomal irinotecan – for second-line pancreatic cancer, the project having been filed in the US and EU in recent weeks.

Pancreatic cancer, which has seen few therapeutic breakthroughs in recent years, looks set to be in for a series of events that could dramatically change the treatment landscape.

Not impressive enough

So far, however, pancreatic cancer has been a graveyard for pharmaceutical development, so analysts have learned the hard way to moderate their predictions for success. Mizuho Securities' Peter Lawson is not unusual in assuming only a 35% probability of success for HyperAcute Pancreas.

The Impress trial recruited patients with surgically resected pancreatic cancer, testing HyperAcure Pancreas and gemcitabine with or without chemo and radiotherapy against standard of care alone. Overall survival (OS) is the primary endpoint.

Two interim analyses have taken place. The first, in early 2014, would have needed to show a 45% improvement in median OS to warrant termination for positive efficacy. The second, announced earlier this week, was triggered by the 333rd event, and it too fell short of a similarly high hurdle for an efficacy stop. The study will therefore continue to its planned final analysis at 444 events, where the project will have to show an 18-20% improvement over placebo.

The continuation could be seen as predictive of failure, but generally if immunotherapies show efficacy in the shape of a durable response it is only in a small proportion of patients, if at all.

No change after all

NewLink said on Monday that after communications with the FDA it had not decided to change the trial's statistical analysis plan after all.

It had earlier stated that it was considering an alternative plan that might make use of newly developed approaches that are better suited to immunological therapies. However, to make this change, it would have to forgo the benefit of a special protocol assessment, which gives some assurance that the FDA will not contest how NewLink analyses the data.

NewLink plans to provide a formal update on the timing of the final analysis, as well as the smaller Pillar phase III trial, later this year, but it seems likely the Impress data will become available in late 2015 or early 2016. The 280-patient Pillar tests a different chemotherapy regimen with HyperAcute Pancreas in patients with borderline resectable or unresectable pancreatic cancer.

EvaluatePharma's consensus forecasts see HyperAcute Pancreas achieving $526m in 2020 sales, slightly more than the $500m forecast for the same year for Baxalta/Merrimack's MM-398 and the $396m for Merck KGaA/Threshold's evofosfamide. Consensus data for Jakafi, which is already approved for myelofibrosis, are not available separately for the pancreatic indication.

There are four other phase III agents: Eleison Pharmaceuticals' glufosfamide, Immunomedics' Y-90 clivatuzumab in first-line disease, AstraZeneca's Lynparza in gBRCA-mutated patients and Orient Pharma's nanoplatin, a non-emulsion formulation of cisplatin. Abbvie/J&J's Imbruvica is in large phase II/III trials and there are now a surprising number – around 20 – of agents being tested in phase II.

This recent blooming of activity may or may not come to fruition next year.

Project	Company	Study	Therapy line	Trial ID
Phase III				
HyperAcutePancreas (algentpucel-L)	NewLink Genetics	Impress, 722 patients, on top of gemcitabine	Second line	NCT01072981
		Pillar, 280 patients, on top of chemo	First line	NCT01836432
evofosfamide	Merck KGaA	Maestro, 694 patients, on top of gemcitabine	First line	NCT01746979
Glufosfamide	Eleison Pharmaceuticals	480 patients, vs 5FU	Second Line	NCT01954992
Y-90 clivatuzumab	Immunomedics	Pancrit-1, 440 patients, on top of low-dose gemcitabine	>third line	NCT01956812
Nanoplatin/NC-6004	Orient Europharma/ Nanocarrier	290 patients, on top of gemcitabine	First line	NCT02043288
Jakafi (ruxolitinib)	Lilly/Incyte	Janus 2, 290 patients, vs capecitabine	Second line	NCT02117479
		Janus 1, 310 patients, on top of capecitabine	–	NCT02119663
Lynparza	AstraZeneca	145 patients, vs placebo	gBRCA-mutated, first line	NCT02184195
Phase II/III				
Imbruvica	Pharmacyclics (AbbVie)/J&J	326 patients, on top of gem/Abraxane	First line	NCT02436668

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