Evaluate Vantage

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Upcoming events: Pivotal data for Seattle Genetics and Erytech

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Welcome to your weekly digest of approaching regulatory and clinical readouts. By October, Seattle Genetics will reveal interim data from a phase III trial called Aethera, testing Adcetris in a new indication: Hodgkin's lymphoma patients who have received an autologous stem cell transplant.

Success would open up a new revenue stream for the company and boost confidence that the drug is effective in broader uses. Meanwhile, Erytech expects phase II/III results in the fourth quarter for Graspa, its lead pipeline asset, in acute lymphoblastic leukaemia (ALL). The French company completed its IPO last year, and Graspa could become its first marketed product.

Broadening Adcetris

The Aethera trial is in 329 patients at high risk of relapse after autologous stem cell transplant. Hodgkin's lymphoma patients who relapse after a stem cell transplant – most will have already also failed front-line treatments – have no options left, so any improvement in progression-free survival or, hopefully, the rate of cures will be seen as a big win.

The trial tests the antibody-drug conjugate when given immediately after transplant, and the primary endpoint is an analysis of progression-free survival at two years. The study completed enrolment in September 2012, and the last patient was treated in August 2013.

Concerns about the trial's chances of success have been raised because the company changed the primary endpoint after the study had started. Initially, it was to measure event-driven progression-free survival, but because the pre-specified events did not happen as expected this was switched to a two-year measure.

Analysts at UBS point out that, because landmark analyses are somewhat less robust than event-driven ones, this superficially increases risk. However they remain optimistic about the readout because most post-transplant relapses happen within two years, so the trial should still detect a signal.

In 2011 Adcetris received accelerated approval to treat Hodgkin's lymphoma after transplant failures or in refractory patients not candidates for transplant, as well as relapsed or refractory systemic anaplastic large cell lymphoma. These approvals were based on single-arm phase II studies, and Aethera will be the first controlled phase III study to report on the drug.

The post-transplant setting is commercially modest, at an estimated $100m a year in the US. But demonstrating efficacy in a rigorous study is an important milestone for the drug and Seattle, which hopes to continue to broaden its uses.

Erytech Pharma/Recordati: Graspa

The data due from Erytech are from an open-label, phase III, Europe-based trial in 80 relapsed or refractory ALL patients up to 55 years of age. Graspa, a red blood cell-encapsulated version of the chemotherapy drug L-asparaginase, was pitted against reference L-asparaginase; both were dosed in combination with standard chemotherapy.

L-asparaginase derived from *Escherichia coli* has been used since the 1970s as a cancer treatment in combination with chemotherapy, but is commonly associated with serious allergic reactions. Graspa encapsulates L-asparaginase to reduce its exposure to the immune system, and reduce hypersensitivity.

The phase III trial's primary endpoint comprises two measures: mean duration of asparaginase depletion, on which Graspa needs to show non-inferiority, and toxicity; Graspa needs to show fewer allergic reactions.

A previous phase II trial testing Graspa in combination with chemotherapy found it to have a good safety profile even in elderly patients. The study enrolled 30 patients over 55 years old with newly diagnosed ALL. At the optimal dose 91% of patients reached a complete remission and the median overall survival was 15.6 months.

Should these encouraging findings be repeated the company intends to file for approval in Europe. Graspa has orphan drug designation in Europe and the US for ALL, acute myeloid leukaemia and pancreatic cancer. It is licensed to Recordati in Europe, while Teva has a profit share with Erytech in Israel. It is unpartnered in the US, where early trials started recently.

Erytech floated on the NYSE Euronext last May, raising €17.7m ($23.3m), and its shares are up 62% since the IPO.

Including the ALL and AML indications Credit Suisse analysts who follow Recordati forecast $225m peak global sales for Graspa, 40% of which come from Europe. However, there is competition from Jazz Pharmaceuticals, whose version of the chemotherapy called Erwinaze is derived from a different bacterium to overcome allergic reactions. Erwinaze is on the market in Europe and the US for ALL, and 2020 sales are forecast to reach $315m, according to *EvaluatePharma* consensus.

Study	**Trial ID**
Aethera	NCT01100502
Phase III Graspa trial	NCT01518517

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