Evaluate Vantage

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Upcoming events – Clinical data due for Celldex and Faron

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Welcome to your weekly digest of approaching regulatory and clinical readouts. Celldex is still reeling from the failure of the cancer vaccine Rintepla, and its attention now turns to glembatumumab vedotin, an antibody-drug conjugate that should yield phase II results in triple-negative breast cancer in the second quarter.

Also expected in the coming months are data from Faron's Traumakine in respiratory distress syndrome, a condition with limited treatment options. Phase III European results, alongside data from a Japanese trial, are expected to form the basis of a US filing, a first for the Finnish company.

Celldex turns to Metric

Celldex's Metric study tests 327 advanced triple-negative breast cancer subjects given glembatumumab vedotin, a conjugate developed using Seattle Genetics' technology, using the same toxin and linker as those used in Adcetris.

Glembatumumab targets gpNMB, a glycoprotein whose overexpression promotes invasion and metastasis by several tumour types. High expression in triple-negative breast cancer is associated with poor prognosis and increased risk of recurrence. Metric recruited patients whose tumours had >25% gpNMB expression, and uses Xeloda as the active comparator.

The primary endpoint is PFS, and secondary measures include overall response rate, OS, duration of response and safety. 203 progression events are needed to trigger primary endpoint evaluation.

As for the kind of result that glembatumumab will need to show, Celldex has noted that, historically, Xeloda has shown a PFS of 1.7-2.5 months in patient populations similar to Metric. The study is 85% powered to detect a 36% or better reduction in risk of progression.

In another phase II study, Emerge, of glembatumumab in refractory breast cancer, patients were stratified by gpNMB expression with ≥5% as the lower limit. Glembatumumab failed to confer a survival benefit in all comers, but there was an improvement in patients who had >25% gpNMB expression and triple-negative cancer, with a PFS of 3.5 versus 1.5 for investigators' choice of chemotherapy. However, this group included just 16 of 124 subjects enrolled.

Glembatumumab is now Celldex's lead project, having replaced the cancer vaccine Rintega, which failed two years ago in glioblastoma *(No good reaction to Celldex's Act IV, March 7, 2016).*

The stock has struggled to recover since. Celldex has $139m in cash, enough to fund it through 2019, and wants a partner for glembatumumab outside the US.

Study	Trial ID
Emerge	NCT01156753
Metric	NCT01997333

Interest in Traumakine

Faron's Traumakine is being tested in 300 patients with moderate to severe acute respiratory distress syndrome (ARDS) in a European phase III study known as Interest.

ARDS can be caused by sepsis, pneumonia or workplace inhalation of toxins, and therapy is broadly limited to mechanical intervention in intensive care.

The Interest trial tests once-daily intravenous Traumakine versus placebo, measuring all-cause mortality at day 28, and days free of mechanical ventilation as co-primary endpoints. The target is a 50% reduction in 28-

day mortality between placebo and active treatment.

The study's data monitoring committee recommended that it remain blinded until 90 days' follow-up, so Faron is expected to report three-month mortality alongside 28-day results in the second quarter.

The Interest results are particularly important as the US FDA has proposed that Faron proceed directly to a BLA filing using data obtained from European and Japanese trials. The latter are due to complete recruitment by mid-year, and a US filing is expected in the first half of 2019.

In a phase I/II study three of 37 subjects on Traumakine had died by day 28, versus 32% of 59 control patients, resulting in a statistically significant 81% reduction in 28-day mortality (p=0.01).

Faron listed on the London stock exchange in 2015, raising £10m ($14m), and shares have more than tripled since. Traumakine is the company’s lead asset, but if it makes it to market it might struggle commercially. As an interferon-beta 1a it is similar to Biogen’s Avonex or Merck KGaA’s Rebif, which might hit Traumakine sales if they are used outside their multiple sclerosis labels.

Study	**Trial ID**
Interest	NCT02622724/EudraCT 2014-005260-15
Japanese trial	JapicCTI-163320
Phase I/II	NCT00789685/EudraCT 2008-000140-13

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