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Asco look ahead - Big caps poised for slew of pivotal late stage data

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This year's Asco, the biggest annual cancer confab, looks set to be a particularly bumper year for pivotal late-stage data from a number of the biggest oncology players.

Studies from new and existing therapies are due to be presented in Chicago over the first weekend in June which hold the potential to shape their future, clinically and commercially. Candidates from Bristol-Myers Squibb, Celgene and Roche look set to be in the spotlight, as this review of some of the late-stage studies and their implications reveals.

Keenly awaited

Much of the really interesting data has been reserved for the high profile plenary session, which guarantees the presentations a lot of attention.

One of the most keenly awaited this year is from Bristol-Myers Squibb's ipilimumab, an antibody that stimulates the immune system by targeting and blocking CTLA-4, a T cell surface receptor that is believed to suppress the body's immune response.

The drug has not exactly had an encouraging history, have been turned down by the FDA two years ago with a request for more conclusive survival data (*Confidence in Medarex's ipilimumab dented again, April 28, 2008*). However hopes have been rising over the last few years as more evidence has emerged that this approach, boosting the body's immune system to fight tumours, could well prove to be an important strategy in cancer therapy alongside the targeted agents.

At the plenary session, the results from a phase III study in patients with melanoma will be presented. Considering BMS has already announced it plans to file the drug in the middle of this year, and has made clear that preparations for a commercial launch are already underway, hopes are high for a positive read out.

This study was conducted in a second line setting where options are currently limited, results from a potentially more important first line study are due later this year. Although read across will not be reliable due to trial differences, this presentation is seen as pivotal in helping to determining the future of this drug.

The results of a phase II study of ipilimumab in lung cancer will also be of interest elsewhere at the conference, particularly in terms of future competition to Roche's Avastin, another plenary session candidate.

Therefore a good Asco for ipilimumab is certain to lead to upgrades to analysts sales forecasts, which currently sits at $598m in 2016, according to consensus data from *EvaluatePharma*.

Head-to-head

Another big trial from BMS which is being held back until the day is a head-to-head trial of the tyrosine kinase inhibitors (TKIs), Sprycel and Gleevec, in newly diagnosed chronic phase Philadelphia chromosome positive chronic myelogenous leukaemia. The results to be presented are 12-month efficacy and safety, and are pivotal to BMS' attempts to win approval in first line, and boost demand overall.

Sprycel is expected to outperform, given the presentation status granted and bullish company comments. However, physicians and financial analysts will be looking for evidence of emerging greater efficacy and improved safety with this second generation TKI. Gleevec, which was first launched ten years ago and last year generated sales of almost $4bn, has demonstrated an overall survival (OS) benefit and is well known by doctors, but Sprycel and Tasigna, Novartis' own follow-on to Gleevec, have yet to generate this data, albeit with convincing progression-free survival (PFS) data already available.

Tasigna has already demonstrated impressive initial phase III data in this setting, presented at ASH last year, and extension data beyond one year will be released at Asco.

How comfortable doctors are at using the newer agents over a well known and well studied drug will probably

be debated at the conference, however convincing the evidence as to their advantages is over the incumbent.

As to competition between Tasigna and Sprycel, the former has a black box warning about cardiovascular risks, including sudden death, and food restrictions, which could give Sprycel the edge if efficacy rates appear similar.

With Gleevec losing patent protection in 2015/16 the interplay between these two agents in leukaemia, and the incumbent's ability to maintain share, will be crucial in determining how Novartis copes with the loss of one of its biggest products. The data presented at Asco will certainly help further this debate.

Maintenance therapies

Data from Celgene and Roche is likely to open a big debate about the use of cancer drugs, particularly hugely expensive antibodies, in a maintenance setting. This is when patients with stable disease are treated over the long term in an attempt to prevent recurrence, and ultimately extend survival.

With many believing that the use of these medicines in this setting brings more benefit to the companies through higher sales than to patients, evidence will be sought that terminally ill patients can be offered longer and better lives with this technique.

Two studies on Celgene's Revlimid will be presented in this setting, in multiple myeloma patients who had already undergone a stem cell transplant.

The first, called CALGB 100104, was conducted in 568 patients and this is a second look at interim data, with the trial yet to complete as median time to progression (TTP) has not yet been reached in the drug arm. In the placebo arm estimated median TTP is 25.5 months, allowing the researchers to conclude that Revlimid significantly prolongs TTP in this setting.

A second study, called IFM 2005-02, was unblinded after superior PFS was seen in the drug arm during the first interim look at the data; 68% of patients at three years compared to 35% in the placebo arm were progression free at three years.

These data seem to confirm that Revlimid can prolong PFS in a maintenance setting, as both studies reduced the risk of the disease recurring, by 58% and 54% respectively. However, the question still remains whether this regimen improves overall survival, and will no doubt be a subject for debate. The authors of the latter study noted that two year survival was similar between the two treatment arms, at 95%.

Surival benefit

Another therapy going for a maintenance setting is Roche's Rituxan, with further data from the Prime study due to be released.

Patients with follicular lymphoma who responded to first line therapy were given Rituxan over two years as a maintenance therapy, a total of 1,217 were recruited in all. PFS was significantly prolonged, almost halving the risk of recurrence at two years. Among the drug arm 82% had no progression at two years compared to 66% in the placebo group. However, the Rituxan group has more side effects, particularly infections.

The authors concluded that this study provides evidence for a new standard of care for follicular lymphoma patients; the disease is a form of non-Hodgkin's lymphoma, cancer of the lymphatic system. Still, the abstract makes no mention of survival data, and some commentators have been expecting three-year survival data to be available at the conference, which will make for interesting reading.

Given the cost of this therapy, widespread use of the drug in this setting, particularly in Europe, will probably require evidence of a meaningful survival benefit.

Flagship product

Roche has also managed to win a high profile plenary spot for Avastin, when the results from the phase III GOG 0218 study will be presented. As such, the data is not yet available, but the company has already announced a significant extension of survival was seen.

The extent of the survival benefit here will be key – clearly the longer the better, with a benefit of three to four months being clinically significant, analysts at Citi have commented. Given the known safety and tolerability issues with Avastin, these details will also be crucial.

Roche is presenting data from a number of studies this year on Avastin, that could prove crucial for the years to come, in terms of commercial potential.

For example another study will be presented in colon cancer, showing that patients who continued with an Avastin-based therapy after the disease progressed lived longer: 16.3 months versus 8.5 months for those who did not continue to receive the drug. In these terminally ill patients, quality of life can be as important a

measure as length of life, and it will be interesting to see further detail on this measure.

Also, with the FDA still to grant full approval for Avastin in first-line metastatic breast cancer pending firm evidence that the drug improves overall survival, data in this setting will also be scrutinised. One to watch here is a meta-analysis of three phase III studies conducted in this setting, which primarily measured PFS, leading to the tentative approval, and OS as a secondary measure.

By pooling the data, researchers concluded that Avastin plus chemo improved PFS and although no significant difference in median OS was seen in these trials, the pooled data suggests an early benefit at one year. Not all commentators are convinced this is good enough for a full approval, which would be a huge blow for the Swiss drug maker and its flagship oncology product.

Others on the radar

The above review is far from conclusive, and other late stage data that will no doubt attract attention includes data from Amgen on Prolia, which will hopefully boost confidence in success in what could be the drug's biggest indication, bone metastasis. Positive top line data has already been presented but as always the devil is in the detail, and full results will be closely scrutinised (*Amgen racks up vital Prolia data against Zometa, February 9, 2010*).

Additionally, phase III data from Pfizer on a novel ALK inhibitor, crizotinib, in a sub set of NSCLC patients. The drug could potentially represent a threat to Avastin in lung cancer, so the results are keenly awaited.

Also in lung cancer, OSI Pharmaceuticals is due to present a number of studies of its flagship product, Tarceva, which will now be of interest to Japanese investors following the company's recent takeover by Astellas Pharma.

All of which means Asco 2010 is starting to look like a particularly bumper year for important late-stage data which could influence treatment regimens in many cancers and therefore impact the commercial prospects for related drugs.