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TRIAL WATCH

Pivotal oncology trials: outlook for Q2 2009

Data from several pivotal oncology trials that could help drive important treatment advances are due to be reported in the second quarter of 2009. Among these trials, three are particularly notable: sipuleucel-T (Provenge; Dendreon) in androgen-independent prostate cancer (AIPC), bevacizumab (Avastin; Genentech/Roche) in front-line metastatic breast cancer (MBC) and erlotinib (Tarceva; OSI Pharmaceuticals/Genentech/Roche) in non-small-cell lung cancer (NSCLC).

In April 2009, final survival results are expected from the Phase III trial of sipuleucel-T, which enrolled ~500 patients with metastatic AIPC. These data might bring the long saga of this cell-based cancer vaccine, which is designed to stimulate an immune response against prostate cancer cells, to a conclusion by providing the FDA with the additional efficacy data that was requested in an approvable letter issued in May 2007. In October 2008, an interim analysis showed a 20% reduction in the risk of death in the treatment arm compared with placebo after 24 months, but unfortunately it did not meet the pre-specified end point required for an accelerated biologic license application (BLA) filing. Dendreon has stated that the final analysis needs to show a 22% reduction in the risk of death to demonstrate statistical significance and satisfy the FDA's efficacy requirement. If a greater separation between the survival curves of sipuleucel-T and placebo is found in the final analysis, heralding success in meeting the pre-specified end point, a BLA resubmission should follow and FDA approval might be obtained by the end of the year.

During the second quarter of 2009, Genentech should also release survival data from two Phase III MBC trials of bevacizumab, a monoclonal antibody against vascular endothelial growth factor that is approved or in late-stage development for multiple oncology indications. In 2008, bevacizumab was granted accelerated approval for MBC by the FDA based on data showing a progression-free survival (PFS) benefit in the E2100 Phase III trial. Two additional Phase III studies, known as AVADO and RIBBON-1, compared bevacizumab plus chemotherapy with chemotherapy alone as first-line therapy for MBC in over 1,800 patients, and both showed an improvement in PFS in an interim analysis. Historically, the FDA has required an overall survival benefit as the gold standard for the approval of oncology therapies, and a key question is whether the final results of these two trials will show a statistically significant overall survival benefit. If not, and the FDA were to repeal the accelerated approval, this might provoke uproar from both oncologists and patients, as the drug has demonstrated a significant PFS benefit, which is widely considered to be clinically meaningful. Conversely, if the FDA were to grant full approval of bevacizumab based on a significant PFS benefit and a positive trend towards a survival benefit, this might reflect a shift in the regulatory view of what constitutes an approvable end point for oncology clinical trials.

Finally, updated data from two Phase III trials studying erlotinib, a small-molecule inhibitor of the epidermal growth factor receptor kinase, as a first-line treatment of NSCLC will be presented at the 2009 American Society of Clinical Oncology meeting in May. The SATURN trial studied erlotinib as maintenance monotherapy following chemotherapy, whereas the ATLAS trial studied erlotinib plus bevacizumab as maintenance therapy following treatment with bevacizumab plus chemotherapy. Top-line results showed that both studies met the end point of improving PFS. Overall, these data could support expansion of the use of erlotinib, which is currently the standard of care in the second- and third-line treatment of NSCLC, into the front-line maintenance setting.

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