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ASCO 2016: Pivotal Avelumab Study Shows Positive Results in Metastatic Merkel Cell Carcinoma

Monday, June 06, 2016 - 05:00am

•First pivotal study for Merck KGaA, Darmstadt, Germany, and Pfizer's investigational anti-PD-L1 antibody avelumab shows clinically meaningful tumor responses in pre-treated metastatic Merkel cell carcinoma (MCC) •International, multicenter Phase II study results in metastatic MCC with 88 patients represents largest data set of any anti-PD-L1/PD-1 reported in this patient population •Plan to submit to regulatory authorities based on these results

"Forward-Looking Information and Factors That May Affect Future Results"

Merck KGaA, Darmstadt, Germany, and Pfizer (NYSE: PFE) today announced results from the first pivotal, international, multicenter, open-label, Phase II study of avelumab*, which showed a 31.8% objective response rate (ORR) (28 of 88 patients; 95.9% CI: 21.9–43.1%†), in the pre-planned primary analysis of the study, and a manageable safety profile in patients with metastatic Merkel cell carcinoma (MCC) who were treated with avelumab in second or subsequent lines of therapy. Tumor responses were rapid, with 78.6% of patients (22 of 28) responding within 7 weeks of starting treatment, and durable, with 82.1% of patients (23 of 28) still responding at the time of analysis. No unexpected safety signals were reported. These data will be reported today during an oral presentation at the 52nd American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL.

"To see a tumor response in almost a third of patients in this trial, and for the majority to keep responding after six months, represents a potential breakthrough for this challenging disease," said lead investigator Howard L. Kaufman, M.D., FACS, Rutgers Cancer Institute of New Jersey, USA. "Currently, the only treatment option available for advanced stages of this aggressive type of skin cancer is chemotherapy, where the response rates are not adequate or durable."

Metastatic MCC has a poor prognosis with less than 20% of patients surviving longer than five years.[1] Although chemotherapy is considered a second-line treatment option for metastatic MCC, it is not a standard of care. Current guidelines recommend that these patients participate in clinical trials.[2]

"This is an important milestone for us as this is the largest data set of any anti-PD-L1 or anti-PD-1 reported to date in this patient population," said Luciano Rossetti, Executive Vice President, Global Head of Research & Development in the biopharma business of Merck KGaA, Darmstadt, Germany, which in the US and Canada operates as EMD Serono. "The clinically meaningful tumor response rate for avelumab in metastatic Merkel cell carcinoma where chemotherapy has failed, reinforces our belief in the promise of this molecule, particularly considering the high unmet need in this disease."

In the trial, eight patients (9.1%) achieved complete responses and 20 patients (22.7%) achieved partial responses. The median duration of response has not been reached (95% CI: 8.3 months – not estimable; range, 2.8–17.5+ months). Tumor responses were seen in patients regardless of the status of certain biomarkers (PD-L1 and Merkel cell polyomavirus). The progression-free survival (PFS) rate at 6 months was 40% (95% CI: 29–50%, estimated by the Kaplan-Meier method). Early data also showed an overall survival (OS) rate at 6 months of 69% (95% CI: 58–78%) and a median OS of 11.3 months (7.5–14.0 months); however, these OS data are still maturing since minimum follow-up was 6 months for inclusion in this analysis. Treatment-related adverse events (AEs) occurred in 62 patients (70.5%); the most common were fatigue (23.9%) and infusion-related reactions (17.0%), all of which were Grade 1 or 2. Grade 3 treatment-related AEs were reported in four patients (4.5%). There were no Grade 4 treatment-related AEs or deaths.

“This has been an exciting ASCO for the strategic collaboration between the two companies, between the MCC data and the other encouraging responses observed across a broad range of tumors,” said Chris Boshoff, M.D., PhD., Vice President and Head of Early Development, Translational and Immuno-Oncology at Pfizer Oncology. “The clinical benefits for avelumab as a monotherapy in notably hard-to-treat cancers may be amplified even further when combined with other therapies.”

Avelumab has received multiple regulatory designations in MCC from the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), including Orphan Drug (FDA and EMA), Fast Track and Breakthrough status (FDA). There are plans to submit marketing applications for avelumab to regulatory authorities based on these data.

About JAVELIN Merkel 200

JAVELIN Merkel 200 is an international, multicenter, open-label, Phase II study of avelumab conducted in 88 patients with metastatic MCC. Patients in this study were generally elderly (median age was 72.5 years, range 33–88 years) and pre-treated, with at least one line of chemotherapy (one [59.1%], two [29.5%] or three or more [11.4%] previous treatments). Patients received avelumab 10 mg/kg intravenously once every two weeks. The protocol-defined analysis set for efficacy and safety consisted of all patients who received at least one dose of study treatment. The cut-off date for the planned primary analysis was 6 months after start of study treatment of the last patient. The primary endpoint of the study was confirmed best overall response according to RECIST v1.1 and assessed by an independent review committee. Secondary endpoints were duration of response, PFS, OS, response status by RECIST at 6 and 12 months, safety and tolerability, pharmacokinetics, and immunogenicity of avelumab.

*Avelumab is the proposed nonproprietary name for the anti-PD-L1 monoclonal antibody (MSB0010718C). Avelumab is under clinical investigation and has not been proven to be safe and effective. There is no guarantee any product will be approved in the sought-after indication by any health authority worldwide.

†Multiplicity adjustment accounting for interim analysis to achieve overall 95% confidence level.

References

1. Lemos B, Storer B, Iyer J, et al. Pathologic Nodal Evaluation Improves Prognostic Accuracy in Merkel Cell Carcinoma: Analysis of 5,823 Cases as the Basis of the First Consensus Staging System for this Cancer. Journal of the American Academy of Dermatology. 2010;63:751-761.
2. NCCN Merkel Cell Carcinoma Guidelines Version I. 2016. Available from: www.nccn.org/professionals/physician_gls/PDF/mcc.pdf. Accessed April 2016.

About Avelumab

Avelumab (also known as MSB0010718C) is an investigational, fully human anti-PD-L1 IgG1 monoclonal antibody. By inhibiting PD-L1 interactions, avelumab is thought to enable the activation of T-cells and the adaptive immune system. By retaining a native Fc-region, avelumab is thought to potentially engage the innate immune system and induce antibody-dependent cell-mediated cytotoxicity (ADCC). In November 2014, Merck KGaA, Darmstadt, Germany, and Pfizer announced a strategic alliance to co-develop and co-commercialize avelumab.

Alliance between Merck KGaA, Darmstadt, Germany, and Pfizer Inc., New York, US

Immuno-oncology is a top priority for Merck KGaA, Darmstadt, Germany, and Pfizer Inc. The global strategic alliance between Merck KGaA, Darmstadt, Germany, and Pfizer Inc., New York, US, enables the companies to benefit from each other's strengths and capabilities and further explore the therapeutic potential of avelumab, an investigational anti-PD-L1 antibody initially discovered and developed by Merck KGaA, Darmstadt, Germany. The immuno-oncology alliance will jointly develop and commercialize avelumab and advance Pfizer's PD-1 antibody. The alliance is focused on developing high-priority international clinical programs to investigate avelumab as a monotherapy, as well as in combination regimens, and is striving to find new ways to treat cancer.

About Merck KGaA, Darmstadt, Germany

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Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 50,000 employees work to further develop technologies that improve and enhance life – from biopharmaceutical therapies to treat cancer or multiple sclerosis, cutting-edge systems for scientific research and production, to liquid crystals for smartphones and LCD televisions. In 2015, Merck KGaA, Darmstadt, Germany, generated sales of € 12.85 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. Merck KGaA, Darmstadt, Germany operates as EMD Serono, MilliporeSigma and EMD Performance Materials in the United States and Canada.

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Pfizer Disclosure Notice

The information contained in this release is as of June 6, 2016. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about avelumab (MSB0010718C), including a potential indication for avelumab for the treatment of metastatic Merkel Cell carcinoma, Pfizer's and Merck KGaA, Darmstadt, Germany's immuno-oncology alliance involving anti-PD-L1 and anti-PD-1 therapies, and clinical development plans, including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical study commencement and completion dates and regulatory submission dates as well as the possibility of unfavorable study results; risks associated with interim data; the risk that clinical trial data are subject to differing interpretations, and, even when we view data as sufficient to support the safety and/or effectiveness of a product candidate, regulatory authorities may not share our views and may require additional data or may deny approval altogether; whether and when drug applications may be filed in any jurisdictions for any potential indications for avelumab (including a potential indication for avelumab for the treatment of metastatic Merkel Cell carcinoma), combination therapies or other product candidates; whether and when any such applications may be approved by regulatory authorities, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of avelumab, combination therapies or other product candidates; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2015, and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results," as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

Merck Media: Gangolf Schrimpf, +49 6151 72 9591 Investor Relations: +49 6151 72 3321 or Pfizer Media: Sally Beatty, +1 212 733 6566 Investor Relations: Ryan Crowe, +1 212 733 8160