PS1 Late breaking

Immunotherapy (APC8015) for androgen independent prostate cancer (AIPC): final progression and survival data from a second Phase 3 trial

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Background: APC8015 is an immunotherapy product currently in a pivotal Phase 3 trial for metastatic AIPC. We have reported results from D9901, the first of two independent Phase 3 trials in asymptomatic metastatic AIPC, which showed a significant survival advantage for APC8015 treated subjects in the intent-to-treat (ITT) group compared with placebo. The second trial, D9902A, is the subject of this abstract.

Methods: Subjects with asymptomatic metastatic AIPC were randomized (2:1) to APC8015 or placebo, administered in Weeks 0, 2, and 4. Eligible subjects had tumor progression following hormonal therapy and no cancer-related pain or visceral metastases. Monitoring for the primary endpoint, time to objective disease progression (TTP), was by centrally reviewed serial radiologic imaging. All subjects were followed for overall survival, a secondary endpoint, for 3 years after randomization. An estimate of survival was based on the Kaplan-Meier method (log rank) with corresponding confidence intervals. A hazard ratio (HR) estimating the relative risk of death and non-progression, placebo:APC8015, was calculated using a stratified Cox proportional hazards model (PHR). A survival analysis of 225 subjects from the integrated data from D9901 and D9902A was also undertaken.

Results: Ninety-eight subjects were randomized between May 2000 and March 2003. There was not a statistically significant difference in TTP between APC8015 and placebo. In a survival analysis based on the ITT population, the median survival time was 19.0 months for subjects randomized to APC8015 vs 15.7 months for those randomized to placebo ($P = 0.332$, log-rank; unadjusted HR = 1.27 [95%CI: 0.78, 2.07]). At 36 months following randomization, 32% of subjects in the APC8015 group vs 21% of subjects in the placebo group were alive. The results of a secondary analysis based on a Cox PHR model, which adjusted for predictive baseline characteristics, revealed a statistically significant survival advantage for APC8015 over placebo ($P = 0.023$, Wald test; adjusted HR = 1.91 [95%CI: 1.09, 3.35]). As in D9901, APC8015 was generally well tolerated in D9902A. The integrated analysis of the data from D9901 and D9902A showed a statistically significant survival benefit in the overall ITT population, with a median survival of 23.2 months in the APC8015 group vs 18.8 months in the placebo group ($P = 0.011$, log rank, unadjusted HR = 1.5 [95%CI: 1.10, 2.05]). Correcting for predictive baseline characteristics in the integrated analysis also resulted in a significant survival advantage for APC8015 compared to placebo ($P = 0.0007$), Wald Test; adjusted HR = 1.84 [95%CI: 1.29, 2.60]).

Conclusions: Survival data from D9902A is supportive of the findings of D9901. The integrated analysis coupled with the evidence for D9902A is suggestive of a significant survival benefit of APC8015 over placebo in men with asymptomatic metastatic AIPC.