A randomized phase II study of the telomerase inhibitor imetelstat as maintenance therapy for advanced non-small cell lung cancer

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The study was sponsored by Geron Corporation

background

Imetelstat is a 13-azido-13-deoxythymidine (AZTdeoxy-T) derivative that is a potent and selective telomerase inhibitor. It reduces telomerase activity in cancer cells and normal cells, leading to telomere attrition and cell death. In the current study, imetelstat was administered as maintenance therapy after induction therapy in patients with advanced non-small cell lung cancer (NSCLC).

methods

150 patients were enrolled between July 2012 to April 2013, with 1:1 randomization to imetelstat or bevacizumab (imetelstat vs. control). Patients were eligible if they had advanced NSCLC not progressing after completing 6 cycles of induction therapy. Imetelstat was administered as maintenance therapy, whereas bevacizumab was discontinued after progression or intolerance. The primary endpoints were PFS using Kaplan-Meier methods and changes in tumor burden. Changes in telomere length were assessed in a subset of patients. Safety data was collected, and biomarkers were analyzed.

results

Imetelstat demonstrated minimal activity for PFS, but the effect was not statistically significant. Imetelstat is a 13-azido-13-deoxythymidine (AZTdeoxy-T) derivative that is a potent and selective telomerase inhibitor. It reduces telomerase activity in cancer cells and normal cells, leading to telomere attrition and cell death. In the current study, imetelstat was administered as maintenance therapy after induction therapy in patients with advanced non-small cell lung cancer (NSCLC).

Conclusions

- No clinical meaningful trend toward PFS benefit was seen for imetelstat as maintenance therapy in patients with NSCLC (HR = 0.64, 95% CI: 0.42-0.95, p=0.032).
- An improvement in OS was evident, but it was not statistically significant (HR=0.66, 95% CI: 0.42-1.02, p=0.08).
- No activity in the squamous histological subgroup was evident.
- A time-specified exploratory subgroup analysis of PFS in squamous histology was conducted:
  - In the squamous histology subgroup, OS was maintained.
  - The most frequent reported serious adverse events in the imetelstat arm were hematologic, predominantly grade 1 or 2 neutropenia and thrombocytopenia. Grade 3 or 4 hematologic toxicities (e.g., anemia, neutropenia, leukopenia) were rare.

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AAACR abstract #4660

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