Baseline Serum Clusterin Level in Patients with Poor Prognostic Features was Associated with Response to Custirsen Treatment: Results from the Phase 3 SYNERGY Trial of Docetaxel +/- Custirsen

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BACKGROUND

Clusterin

- Production of the protein clusterin (CLU) is a fundamental cellular repair mechanism that protects normal cells from programed cell death.
- sCLU change for each patient was calculated as a normalized Area Under the Curve (AUC).
- sCLU levels were assessed in serum samples collected at baseline, Day 1 of each cycle, end of treatment, and 6 and 12 months after last treatment.

SURVIVAL RESULTS

- Survival by SCape Score and Arm (N=984)

GOALS OF THE ANALYSIS

To evaluate the effect of custirsen treatment on serum sCLU levels in patients with mCRPC, and to assess the correlation between sCLU levels and survival benefits

METHODS

- Measurement of Serum sCLU (sCLU) Levels
- sCLU levels were assessed in serum samples collected at baseline, Day 1 of each cycle, end of treatment, and 6 and 12 months after last treatment.
- Patients were defined as “poor” versus “good” prognosis by the following 5 features:
  - PSA ≥ 30 ng/mL
  - ≥ 331 IU/L
  - ≥ 150 ng/mL
  - Hemoglobin <120 g/L
  - ≥ 15 mg/dL

- Evaluation of 2-Year Survival Status by Day 140 AUC Levels for sCLU
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- sCLU change for each patient was calculated as a normalized Area Under the Curve (AUC).
- sCLU levels were assessed in serum samples collected at baseline, Day 1 of each cycle, end of treatment, and 6 and 12 months after last treatment.

RESULTS

- sCLU Levels at Baseline: Similar Across Subgroups
- No Trend in 2-Year Survival Status in Custirsen Arm Among Patients with Good Prognosis (Based on Day 140 AUC Levels for sCLU)

CONCLUSIONS

- Custirsen treatment was associated with a survival benefit in patients with poor prognostic features.
- Effect was similar using both SCape and Feature Count (Index) scores.
- Custirsen treatment significantly lowered sCLU levels in both poor and good prognostic patients.
- There was a trend for greater custirsen effect on survival if baseline sCLU levels were ≥ 100 mg/mL, especially in patients with good prognosis.
- Patients in the poor prognostic subgroup treated with custirsen and with reduced Day 140 AUC levels had a trend for higher 2-year survival status.
- Survival benefit for the Custirsen Arm appeared greater in poor prognostic patients who achieved lower Day 140 AUC levels (Landmark Analysis).
- For patients in the poor prognostic subgroup treated with Custirsen, the greater the sCLU decrease (baseline to Day 140 post-treatment), the more survival benefit observed.
- Monitoring for lower sCLU levels may be worthwhile; however sCLU levels within tumor cells may be more important for evaluating survival benefit to custirsen treatment.

We are grateful for the participation of study patients, their families, and the SYNERGY investigators. This research was supported by Genentech Inc., Vancouver, BC, Canada, ClinicalTrials.gov identifier: NCT01168187

REFERENCES

- Presented at 18th ECOG - 47th ESMO
- European Cancer Congress
- 29-23 Sep 2015
- Vienna, Austria

SYNERGY: STUDY DESIGN AND RESULTS

Randomized, open-label, multinational 3-phase 2 study conducted in 140 centers in 12 countries

RESULTS

- Custirsen treatment was associated with a survival benefit in patients with poor prognostic features.
- No trend in 2-year survival status in Custirsen Arm among patients with good prognosis (Based on Day 140 AUC Levels for sCLU)

ACKNOWLEDGEMENTS

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CLINICAL PERSPECTIVE

Custirsen treatment was associated with a survival benefit in patients with poor prognostic features. The effect was similar using both SCape and Feature Count (Index) scores. Custirsen treatment significantly lowered sCLU levels in both poor and good prognostic patients. There was a trend for greater custirsen effect on survival if baseline sCLU levels were ≥ 100 mg/mL, especially in patients with good prognosis. Patients in the poor prognostic subgroup treated with custirsen and with reduced Day 140 AUC levels had a trend for higher 2-year survival status. Survival benefit for the Custirsen Arm appeared greater in poor prognostic patients who achieved lower Day 140 AUC levels (Landmark Analysis). For patients in the poor prognostic subgroup treated with Custirsen, the greater the sCLU decrease (baseline to Day 140 post-treatment), the more survival benefit observed. Monitoring for lower sCLU levels may be worthwhile; however sCLU levels within tumor cells may be more important for evaluating survival benefit to custirsen treatment.