

AGENDA

A multicenter, randomized, double-blind study of dacarbazine with or without Genasense® in chemotherapy-naïve subjects with advanced melanoma and low LDH

Sponsor

Genta Incorporated, Berkeley Heights, New Jersey USA

Study centers

Austria, Czech Republic, France, Germany, Italy, Spain, Switzerland, United Kingdom, Canada, United States, Australia

EADO contact

Dr Claus Garbe, University Medical Center, Tuebingen, Germany; +49 707 1298 7110

Background

In a previous clinical trial of Genasense plus dacarbazine versus dacarbazine alone (Bedikian et al, J Clin Oncol, 2006), patients with normal baseline serum LDH received maximum benefit (including an overall survival benefit) from the addition of Genasense to a standard dacarbazine regimen.

Treatment effect was highly correlated with the ratio of LDH to the upper limit of the normal reference range across all efficacy endpoints: the smaller the ratio of LDH to the upper limit of the normal reference range, the larger the treatment effect.

Rationale

This study is being performed to prospectively determine whether dacarbazine plus Genasense is significantly better than dacarbazine plus placebo in chemotherapy-naïve patients with advanced melanoma and low baseline LDH (LDH less than or equal to 0.8 times the upper limit of normal). The Genasense-dacarbazine regimen is identical to that evaluated in the original study (Bedikian et al, J Clin Oncol, 2006), and, as in the original study, patients must be chemotherapy naïve and have measurable disease.

Outcome measures

- **Primary** - progression-free survival and overall survival
- **Secondary** - response (assessed according to Response Evaluation Criteria in Solid Tumors [RECIST]) and durable response, duration of response, and safety

Study design

- Phase III, multicenter, randomized, double-blind, parallel-group trial
- 300 subjects to be randomized at a 1:1 ratio to treatment with dacarbazine plus Genasense or dacarbazine plus placebo

Subject eligibility

- **Primary inclusion criteria**

- Histologically confirmed diagnosis of melanoma
- Progressive disease that is not surgically resectable, or metastatic Stage IV disease
- $LDH \leq 0.8 \times ULN$
- Chemotherapy naïve
- Measurable disease
- ECOG performance status ≤ 1
- At least 4 weeks and recovery from effects of major prior surgery or other therapy, including immunotherapy, radiation therapy, or cytokine, biologic or vaccine therapy
- Adequate organ function
- At least 18 years of age

- **Primary exclusion criteria**

- Prior cytotoxic chemotherapy, including regional perfusion, or prior Genasense treatment
- Primary ocular or mucosal melanoma
- Bone-only metastatic disease
- History or presence of brain metastasis or leptomeningeal disease
- Significant medical disease other than cancer
- Organ allograft

Administration of study medications

- 21-day cycles for up to 8 cycles of
 - Genasense 7 mg/kg/day by continuous IV infusion for 5 days plus dacarbazine 1000 mg/m² as a 60-minute IV infusion immediately following conclusion of Genasense infusion **OR**
 - placebo (that is, locally available commercial 0.9% Sodium Chloride Injection) by continuous IV infusion for 5 days plus dacarbazine 1000 mg/m² as a 60-minute IV infusion immediately following conclusion of placebo infusion
- Subjects responding or with stable disease after 8 cycles of therapy may, at the Investigator's discretion, continue the same therapy for up to 8 additional cycles

Subject accrual and study duration

Estimated enrollment of the planned 300 subjects in 18 months; patient assessment every 42 days from date of randomization during protocol therapy

Reference

Bedikian AY, Millward M, Pehamberger H, Conry R, Gore M, Trefzer U, et al. Bcl-2 antisense (oblimersen sodium) plus dacarbazine in patients with advanced melanoma: The Oblimersen Melanoma Study Group. *J Clin Oncol.* 2006;24:4738-45.