**Anti-mesothelin Vaccine CRS-207 Plus Chemotherapy as Front-Line Treatment for Pleural Mesothelioma (MPM)**

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### Study Design

- **Introduction**
  - This is an open label study to evaluate the safety and induction of immune response of 214 subjects with advanced-stage epithelial or biphasic MPM.
  - Eligible subjects: 18 years of age and older with measurable, histologically-confirmed epithelial or biphasic MPM.
  - Enrollment: 16 subjects (median age: 70; 10 females; 6 males; 10 subjects with epithelial MPM, 6 with biphasic MPM).

- **Study Objectives**
  - **Primary Objectives**
    - Safety
    - The induction of mesothelin-specific T cell responses measured by IFN-γ ELISPOT and intracellular cytokine staining for 214 subjects
    - Induction of mesothelin-specific T cell responses measured by IFN-γ ELISPOT for 15 subjects
    - Induction of mesothelin-specific T cell responses measured by IFN-γ ELISPOT for 13 subjects
  - **Secondary Objectives**
    - Safety
    - Expression of mesothelin by tumor cell lines
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    - Safety
    - Expression of mesothelin by tumor cell lines
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- **Eligibility**
  - Subjects ≥ 18 years of age with measurable, histologically-confirmed epithelial or biphasic MPM.
  - **Exclusion Criteria**
    - Prior chemotherapy or immunomodulators are not permitted unless given for the purpose of the study.
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### Results

- **Clinical Evaluation**
  - **Objective tumor response (modified RECIST for MPM; Byrne and Nowak 2004)**
    - 9 out of 15 subjects had confirmed durable response evaluations ongoing.
    - 27% (4/15) had stable disease (SD).

- **Safety Evaluation**
  - 15% reported grade 3 or 4 adverse events (AEs).
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- **Time to Progression**
  - Median time to progression (TTP) is 4.3 months.

### Conclusion

- Based on subject data treated to date, CRS-207 appears to be safe to administer in a subcutaneous formulation.
- CRS-207 is live-attenuated, double-deleted (LADD) Listeria monocytogenes (Lm) vaccine.
- Deletion of two key virulence factors reduces pathogenicity 1,000-fold.
- The induction of mesothelin-specific T cell responses as measured by IFN-γ ELISPOT.
- The inhibition of tumor growth compared with HBSS or Ad5 hMeso control.
- A significant decrease of tumor growth compared with HBSS or Ad5 hMeso control.
- Therapeutic vaccination of mice with Lm-hMeso.
- Female BALB/c mice were implanted s.c. with 2×10⁶ CT26 cells on day 0.
- Four days later, mice received a single vaccination with a dose equal to 0.1 LD50 of the indicated strain.
- Lungs were harvested on day 19, fixed in Bouin’s solution, and stained with hematoxylin.

### Figures

- **Figure 1**
  - CRS-207 is live-attenuated, double-deleted (LADD) Listeria monocytogenes (Lm) vaccine.
  - Deletion of two key virulence factors reduces pathogenicity 1,000-fold.
  - The induction of mesothelin-specific T cell responses as measured by IFN-γ ELISPOT.
  - The inhibition of tumor growth compared with HBSS or Ad5 hMeso control.
  - A significant decrease of tumor growth compared with HBSS or Ad5 hMeso control.

### References


Brockstedt et al. PNAS 2004

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### References


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