Clinical Trials of a Plague Vaccine in China

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Plague vaccine used in a phase 2a trial

**Formulation:** natural F1 protein (F1) and recombinant V protein (rV) at a ratio of 1:1

**Buffer:** saline

**Adjuvant:** aluminum

**Manufacturer:** Lanzhou Institute of Biological Products Co., Ltd.

- rV antigen was expressed in E. coli.
- F1 was extracted and purified from a live attenuated Y. pestis strain

<table>
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<tr>
<th>Dose</th>
<th>Antigen / formulation</th>
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<tr>
<td>15.0µg</td>
<td>15.0µg F1 antigen, 15.0µg rV antigen, 1.0ml</td>
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<tr>
<td>30.0µg</td>
<td>30.0µg F1 antigen, 30.0µg rV antigen, 1.0ml</td>
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Immunogenicity results after two dose vaccination in the phase 2a trial

**Conclusions:**

- 30 ug formulation elicited higher level of antibodies than 15 ug formulation
- F1 and rV antibody in both groups are robust by month 12
Animal rule of immunized serum from the phase 2a trial

Stage 1

- Ab group 1 (F1 1:128, V 1:2560)
- Ab group 2 (F1 1:256, V 1:2560)
- Ab group 3 (F1 1:512, V 1:5120)
- Control 1
- Control 2

Mixed serum → Immunized with 1 ml intraperitoneally → 3 hours later, subdermal injection of Y. pestis (141 strain) → 6MLD

Stage 2

- Ab group 1 (F1 1:256, V 1:1280)
- Ab group 2 (F1 1:256, V 1:2560)
- Ab group 3 (F1 1:256, V 1:5120)
- Control 1
- Control 2

Mixed serum → Immunized with 1 ml intraperitoneally → 3 hours later, subdermal injection of Y. pestis (141 strain) → 6MLD
30.0µg F1 and 30.0µg rV antigen, 1.0ml/dose

F1 and V antibody GMT after the vaccination
The safety profiles of the vaccination regimens (M 0/1/6 and M 0/2/6) were similar. Most of adverse reactions observed in this study were mild, the incidence of grade 3 adverse reactions were low.

The most common injection-site adverse reaction was injection-site pain, and the most common systemic adverse reaction was fever.
Animal rule of immunized serum from the phase 2b trial

Ab group1 (F1:32/V:16) → Mixed serum → Immunized with 1ml intraperitoneally → 3 hours later, subdermal injection of Y. pestis (141 strain) → 6 MLD (MLD = 7~10 CFU)

Ab group2 (F1:128/V:64) → 12 mouse / group
Ab group3 (F1:512/V:256) → Ab group4 (F1:2048/V:1024) → Ab group5 (F1:8192/V:4096) → Control group

The survival rate of mice in groups 1, 2, 3, 4 and 5 was increased to 41.7%, 58.3%, 83.3%, 91.7% and 100%, respectively. While, none was survived in the control group.

The survival of mice was significantly related to the levels of F1 and V antibody titers in the serum.
Both immunization regimens (M 0/1/6 and M 0/2/6) could induce high levels of F1 and V antibodies after three-dose vaccination.

The immunization regimen (M 0/1/6) showed an advantage in the antibody persistence compared with the immunization regimen (M 0/2/6).

Under the condition of a non-inferiority margin 0.67 for the GMT ratio, the immunization regimen (M 0/1/6) was non-inferior to the immunization regimen (M 0/2/6).

The incidence of adverse reactions/events after vaccination was low in both groups, and showed good safety profile.

The immunized serum could provide significant protection against the lethal challenge in mice. The survival rate and mean survival time of mice were significantly correlated with the titers of serum F1 and V antibody.
THANK YOU!