Poster

Feasibility of a *Klebsiella pneumoniae* vaccine: a proposal for a first-in-human trial and future challenges.

Maldonado Benito, Rebeca *(1), Infante Viñolo, Juanjo (2), Lugo García, Laura (2)

(1) Pablo de Olavide University, 1 Utrera rd., Seville, Spain.

(2)VAXDYN S.L., 55 Spanish Ave., Seville, Spain.

Tutor académico: Infante Viñolo, Juanjo.

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ABSTRACT

Klebsiella pneumoniae is an opportunistic bacteria causing 650.000 deaths worldwide associated with antibiotic-resistance. *K. pneumoniae* causes a variety of infections, including lower-respiratory, urinary-tract, abdominal, thoracic infections, and sepsis, which can lead rapidly to death due to the high level of antibiotic-resistance. The most vulnerable populations are elderly people with chronic conditions and neonates[1].

The World-Health Organization and other international agencies are calling for the development of solutions alternative to antibiotics to combat the rising incidence of disease caused by *K. pneumoniae* worldwide. One type of the sought solutions are vaccines for rising immunity able to contain the evolution of the infections to invasive disease in the vulnerable population[2]. One of the vaccines under development is K-vax, a chimeric inactivated whole cell bacterial vaccine developed by Vaxdyn, currently in preclinical stage.

Testing vaccines in human trials is a challenge due to the complexity in selecting the trial design and the trial population. One decisive step in the development of K-Vax is to design its future clinical study. In this work, we have reviewed the state of the art regarding clinical trials of vaccines with similarities to K-Vax. The designs have been crossed with available preclinical data to define the potential variables of the clinical trial.

Thus, using both preclinical data and a database created through an exhaustive searching and analysis of 34 studies with similar characteristics, our work led to the proposal of a feasible first in human trial for K-Vax. In particular, after evaluating different scenarios, the most suitable study would include a group of at least 90 human volunteers, that could provide safety data to show the lack of reactogenicity and immunogenicity data to establish a correlation of protection and test strain coverage of the adjuvanted vaccine. We consider including a sentinel group first, and the whole trial would be carried out in a randomized way, using placebo, double blinding, and with a dose escalation scheme, where 2 or 3 doses would be tested.

In this work, we have also discussed how the information from the first in human trial could lead to the design of feasible efficacy trials in subsequent clinical stages to overcome the

barriers for marketing the vaccine[3] to prevent disease by *K. pneumoniae* and fulfill the current urgent need.

REFERENCES

[1] Paczosa M.K., Mechas J. (2016) Klebsiella pneumoniae: going on the offense with a strong defense. *Microbiology and Molecular Biology Reviews*, 80: 629-661.
[2]Murray, C. J., Ikuta, K. S., Sharara, F., Swetschinski, L., Aguilar, G. R., Gray, A., ... & Tasak, (2022) N. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *The Lancet*, 399(10325): 629-655.
[3]Douglas, R. G., & Samant, V. B. (2018) The vaccine industry. *Plotkin's Vaccines*, 41.

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