**Safety and efficacy of RCP recombinant spike protein covid-19 vaccine compared to Sinopharm BBIBP: A phase III, non-inferiority trial**

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**Abstract**

**Background:** We conducted a phase III, non-inferiority trial comparing safety and efficacy of RCP recombinant spike protein Covid-19 vaccine to BBIBP (Sinopharm).

**Methods:** Adult Iranian population received RCP or BBIBP in a randomized, double blind and an additional non-randomized open labeled trial arms. Eligible participants signed a written informed consent and received two intramuscular injections three weeks apart. In the randomized arm, an intranasal dose of vaccine or adjuvant-only preparation were given to the RCP and BBIBP recipients at day 51 respectively. Participants were actively followed for up to 4 months for safety and efficacy outcomes. Primary outcome was PCR+ symptomatic Covid-19 disease two weeks after the second dose. The non-inferiority margin was 10% of reported BBIBP vaccine efficacy (HR = 1.36).

**Results:** We recruited 23110 participants (7224 in the randomized and 15886 in the non-randomized arm). We observed 604 primary outcome events during 4 months of active follow-up including 121 and 133 in the randomized and 157 and 193 cases in the non-randomized arms among recipients of RCP and BBIBP respectively. Adjusted hazard ratios for the primary outcome in those receiving RCP compared with BBIBP interval were 0.91 (0.71-1.16) and 0.62 (0.49 – 0.77) in the randomized and non-randomized arms respectively. The upper boundary of 99.1% confidence interval of HR=0.91 (0.67 – 1.22) remained below the margin of non-inferiority in the randomized arm after observing the early stopping rules using O’Brien Fleming method.

**Conclusion:** Our study showed that the RCP efficacy is non-inferior and its safety profile is comparable to the BBIBP.

**Trial registry**: IRCT20201214049709N3

**Keywords:** Razi-Cov-Pars, BBIBP, Non-inferiority design, Recombinant Covid-19 Vaccine, Vaccine efficacy, Phase III clinical trial

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