

## Single-visit rabies pre-exposure prophylaxis regimens in travellers: a randomized controlled non-inferiority trial

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**Background:** Single-visit rabies pre-exposure prophylaxis (PrEP) regimens could facilitate travel readiness, given they generate timely, adequate immune responses after post-exposure prophylaxis (PEP).

**Methods:** Single-visit intradermal and intramuscular PrEP regimens were compared to the standard two-visit intramuscular regimen. Participants were randomized to receive Rabipur® as one intramuscular dose at Do (1-IM regimen), four intradermal doses at Do (1-ID regimen), or one intramuscular dose at Do and one at D7 (2-IM regimen, standard-of-care). On D180, all received simulated PEP according to PrEP regimen. Rabies virus-neutralizing antibodies were assessed via Rapid Fluorescent Focus Inhibition Test at Do, D28, D180, D187, D208 and D270.

**Results:** Overall, 284 participants were included in the per-protocol analysis. Both the 1-IM and 1-ID were non-inferior to the 2-IM regimen, using a non-inferiority margin of -10%. At D187, the proportion of individuals with neutralizing antibodies  $\geq 0.5$  IU/mL was equal between the 1-ID and 2-IM regimen ( $\Delta 0.0$ , 95%CI -3.6;4.6). This proportion was slightly lower in the 1-IM compared with the 2-IM regimen ( $\Delta -1.1$ , 95%CI -6.0;3.6), but remained non-inferior. At D187, geometric mean titres (GMTs) did not significantly differ between the 1-ID (32.49, 95%CI 27.50;38.39) and 2-IM regimens (32.85, 95%CI 26.99;39.97); the 1-IM regimen had significantly lower but still adequate GMTs (19.36, 95%CI 15.27;24.55).

**Conclusion:** Single-visit 1-IM and 1-ID rabies PrEP regimens induce adequate immune responses within 7 days following PEP and are non-inferior to the standard 2-IM regimen, offering more feasible, cost-effective alternatives.