Long-Term Safety and Cell-Mediated Immunity Before and After Booster of Tetravalent Dengue Vaccine TAK-003 in Healthy Adults in Dengue Nonendemic United States

Ian Escudero[1], Vianney Tricou[2], Suely Tuboi[3], Nicholas Roubinis[2], Vasiliki Michaki-Papasaika[2], Michael Hellwig[2], Kelley Moss[1], Shibadas Biswal[1]
[1] Takeda Vaccines, Inc., Cambridge, MA, USA, [2] Takeda Pharmaceuticals International AG, Zurich, Switzerland, [3] Takeda Vaccines, Sao Paolo, Brazil

Background: The cell-mediated immune (CMI) response likely contributes to long-term protection against dengue. The safety and long-term CMI response following TAK-003 vaccination (2-dose schedule) and a single booster dose were evaluated in healthy adults (18-60 years) in the DEN -303 trial. Methods: TAK-003 recipients were enrolled in DEN-303 and followed for 36 months post-first dose. A CMI subset was evaluated for CMI response (magnitude of interferon-gamma ELISPOT to peptide pool). At month 36, participants were randomized to receive TAK-003 booster dose or placebo. CMI response was evaluated at 21, 33 and 36 months post-first dose and 1 and 6 months post-booster. Reactogenicity and booster safety was also evaluated. Results: 50/246 participants enrolled in DEN-303 were included in the CMI subset. 149 participants were randomized in the booster phase (TAK-003=74; placebo=75), with 21 participants from the CMI subset (TAK-003=10; placebo=11). No vaccine related deaths or SAEs occurred during follow up. CMI response persisted at 21, 33 and 36 months in seronegative participants with median magnitude of IFN-γ ELISPOT response to any peptide pool of 696.50 (Q1=316.00, Q3=1421.50), 366.25 (Q1=122.00, Q3=644.50), and 498.75 (Q1=234.00, Q3=1203.00) SFC/106 PBMC, respectively. Median magnitude of IFN-γ ELISPOT response to any peptide pool in seronegative booster recipients were 420.00 (Q1=324.00, Q3=837.50) and 466.25 (Q1=70.50, Q3=1325.50) SFC/106 PBMC, in placebo recipients they were 474.50 (Q1=288.50, Q3=1497.00) and 193.00 (Q1=88.75, Q3=300.25) SFC/106 PBMC at 1 and 6 months post-booster. Conclusion: Long-term safety of TAK-003 was maintained during 42 months of follow-up. TAK-003 elicited CMI responses that persisted over this timeframe