Broad-spectrum humoral and cellular immune responses elicited by a tetravalent dengue vaccine (TAK-003)

Sanja Mandaric[1], Mayuri Sharma[2], Vianney Tricou[1], Eduardo J. M. Nascimento[2], Christina De Maso[2], Melissa Zahralban-Steele[2], Heather Watkins[2], Isamu Tsuji[2], David Dominguez[2], Eric Lloyd[2], Nicolas Folschweiller[1], Shibadas Biswal[2]

[1] Takeda Pharmaceuticals International AG, Zürich, Switzerland, [2] Takeda Vaccines, Inc., Cambridge, MA, USA

Background: TAK-003, a tetravalent dengue vaccine, demonstrated long-term efficacy and safety against symptomatic and hospitalized dengue. A broad spectrum of humoral and cellular immune responses are engaged in developing protection against the dengue virus (DENV). Here, we report the antibody and T-cell responses elicited by TAK-003 in baseline seropositive and seronegative participants from clinical studies.

Materials and methods: Immune response data were from the DEN-301 (NCT02747927) and DEN-313 (NCT02948829) studies. DEN-301 and DEN-313 enrolled children and adolescents aged 4–16 years from similar dengue-endemic regions and timeframes; enrollment began in 2016 and 2017, respectively. Dengue serostatus was tested at baseline (seropositivity: reciprocal neutralizing antibody [NAb; MNT50] titer ≥10 for ≥1 serotype). DEN-301 sera were assessed for anti-DENV binding antibody response, NAb response, complement-fixing antibody (CFA) response, and non-structural protein 1 (NS1) antibody response. DEN-313 peripheral blood mononuclear cells were assessed for DENV-specific T-cell response.

Results: Vaccination elicited sustained antibody and cellular responses against all four DENV serotypes. Tetravalent binding antibodies with high avidity, type-specific and cross-reactive NAbs as well as CFA and anti-NS1 antibody responses were observed, regardless of baseline serostatus. Additionally, multifunctional tetravalent T-cell responses were detected, irrespective of baseline serostatus.

Conclusions: TAK-003 elicited sustained antibody and cellular tetravalent responses, including type-specific and cross-reactive NAbs as well as multifunctional T-cell responses, irrespective of baseline serostatus. Sustained long-term efficacy and safety of TAK-003 are likely due to the diversity of the TAK-003–driven immune responses.

Funding: Takeda