procedures coded as trauma and non-trauma. As a proxy for patients with penetrating trauma, SIR for patients coded as trauma who had a surgical wound class noted as dirty was compared to SIR for patients coded as trauma with surgical wound code classed as contaminated or clean-contaminated.

**Results.** For the CMS model, there was a statistically significant difference (p = 0.0003) between SIR for trauma (SIR = 3.451) and non-trauma (SIR = 1.071) procedures. There was also a statistically significant difference (p=0.0014) between trauma procedures with dirty surgical wound class (SIR = 6.608), compared to those with wounds categorized as contaminated or clean-contaminated (SIR = 2.235).

**Discussion.** Victoria Divino, PhD, Seqirus (Consultant) Maarten Postma, Dr., Seqirus (Consultant) Stephen J. Pelton, MD, Seqirus (Consultant) Joaquin F. Mould, Seqirus (Employee) Mitchell DeKoven, PhD, Seqirus (Consultant) myron J. levin, MD, GSK group of companies (Employee, Research Grant or Support)

97. Tetravalent Dengue Vaccine (TAK-003) Development Program: A Bird’s Eye View
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Session: O-21. Innovations and Advancements in Vaccines

**Background.** Dengue fever is a mosquito-borne viral disease endemic in 128 countries. An unmet clinical need remains for an effective vaccine that can be used more broadly than the vaccine presently available. A clinical development program has evaluated the long-term safety, immunogenicity, and vaccine efficacy (VE) of TAK-003, a live attenuated tetravalent dengue vaccine with a DENV-2 backbone engineered to elicit immune responses to all 4 dengue serotypes.

**Methods.** 18 clinical trials in 13 countries have involved 28,175 seropositive/seronegative participants aged from 1.5-60 years from endemic/non-endemic regions. In the ongoing pivotal phase III study, 4-16-year-old healthy children (N=20,099) were randomized 2:1 to receive two doses of TAK-003 or placebo, 3 months apart for an evaluation of VE and safety over a multi-year period stratified pre-vaccination dengue serostatus. Active surveillance throughout the trial detected symptomatic dengue. The trial will continue up to 4-4.5 years post 2nd dose, and for another 25 months after a booster dose. Data up to 3 years after the second vaccination are currently available.

**Results.** Safety and immunogenicity data from Phase I/II studies established the final formulation and dosing schedule. Overall VE in the pivotal phase III study was 80.2% [95% CI: 73.3–85.3] against virologically confirmed dengue (VCD) at 12 months post 2nd dose. At 18 months, VE was 66.2% [95% CI: 49.1–77.5] in dengue-naive and 73.3% [95% CI: 68.5–81.9] in dengue–pre-exposed participants. VE against dengue-1 VCD was 85.9% [94.0–93.6] at 3 years post 2nd dose.

**Conclusion.** TAK-003 is immunogenic against all 4 dengue serotypes and continues to be efficacious, well-tolerated, and with no evidence of disease enhancement in seronegative population up to 3 years post-vaccination.

Disclosures. Vianney Tricou, D Phil; Takeda Pharmaceuticals International AG (Employee) Shibadas Biswal, MD; Takeda Vaccines Inc. (Employer) Sanjay S. Patel, PhD; Takeda Pharmaceuticals International AG (Employee) Olaf Zent, MD, Takeda Pharmaceuticals International AG (Employee) Martina Ruschaer, PhD; Takeda Pharmaceuticals International AG (Employee) Gonzalo Perez, MD; Takeda group of companies (Employee) Walid Kandeil, MD; Takeda Pharmaceuticals International AG (Employee) Nicolas Folschweiller, PhD; Takeda (Employee)

98. COVID-19 Vaccine Breakthrough Hospitalizations and Deaths in the Veterans Health Administration
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Session: O-21. Innovations and Advancements in Vaccines

**Background.** A COVID-19 vaccine breakthrough infection is defined as SARS-CoV-2 RNA or antigen detected ≥14 days after completion of a final vaccine dose.
CDC’s May 25 MMWR report of 10,262 vaccine breakthrough infections in the U.S. is likely an underestimate. Herein, we report Veterans Health Administration (VHA) breakthrough cases, focusing on hospitalizations and deaths.

**Methods.** We extracted COVID-19 vaccine breakthrough infections tested between 1/19/2021 and 4/30/2021 from the VHA Corporate Data Warehouse (including screening tests). We reviewed medical records of cases who died and/or were hospitalized within 14 days of SARS-CoV-2 positive test for clinician documentation of conditions deemed high risk for COVID-19 and to confirm hospitalization or death was related to COVID-19. SARS-CoV-2 whole genome sequencing (Clear Labs platform) and antigen testing (Abbott BinaxNOW) from available patient samples were performed and Pangolin lineage determined.

**Results.** 1,142 COVID-19 vaccine breakthrough infections were identified. 357/1,142 (31.3%) were hospitalized and/or died. 1,085 (95%) were male (Table 1), and median age was 72.5 years (74 years for hospitalized/deceased patients). COVID-19 infection contributed to hospitalization and/or death in 139 (38.9%) cases. The remaining 218 (61.1%) were hospitalized or died of causes apparently unrelated to COVID-19. Smoking and heart conditions were seen most frequently among hospitalized/deceased breakthrough cases (Table 2). Variant B.1.1.7 was predominant, present in 17/27 (63%) total samples sequenced, and 13/21 (61.9%) hospitalized/deceased. (Table 3). Of 21 sequenced hospitalized/deceased cases, SARS-CoV-2-antigen positivity was present in 11 (52.4%).

**Conclusion.** Compared to CDC reported breakthrough infections, VHA cases were more male, older, and hospitalized/died at higher frequency. Further study is needed to determine the contribution of specific underlying conditions, COVID-19 vaccine formulations and variants on hospitalization and death among COVID-19 vaccine breakthrough infections. Sequencing efforts for breakthrough cases should be intensified, particularly for those presenting with more severe infections.

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**Table 1. Demographics of COVID-19 vaccine breakthrough cases, Veterans Health Administration, January – April 2021.**

| Characteristic          | Total Cases (%) | Hospitalized and/or Deceased Cases |
|-------------------------|-----------------|-----------------------------------|
| Age Group               | N=1,142         | N=957                             |
| Under 64                | 29 (2.5)        | 9 (0.5)                           |
| 45-64                   | 232 (18.6)      | 46 (3.2)                          |
| 65-84                   | 760 (66.5)      | 230 (16.5)                        |
| 85 and older            | 143 (12.2)      | 68 (6.0)                          |
| Sex                     |                 |                                   |
| Female                  | 579 (50.5)      | 249 (27.7)                        |
| Male                    | 563 (49.5)      | 308 (32.5)                        |
| Race/Ethnicity          |                 |                                   |
| Black                   | 246 (21.5)      | 68 (6.0)                          |
| Hispanic                | 100 (8.8)       | 30 (2.6)                          |
| White                   | 729 (63.6)      | 206 (18.7)                        |
| Other*                  | 34 (3.0)        | 12 (0.5)                          |
| Unknown                 | 41 (3.6)        | 9 (0.5)                           |
| Rurality                |                 |                                   |
| Highly Rural            | 9 (0.8)         | 1 (0.1)                           |
| Remain                 | 293 (25.2)      | 71 (7.0)                          |
| Urban                   | 853 (75.2)      | 260 (28.3)                        |

*Other race/ethnicity includes American Indian or Alaskan Native, Asian, Mixed Race, Native Hawaiian or Other Pacific Islander, and Unknown.

**Table 2. High-risk medical conditions among patients hospitalized and/or deceased with COVID-19 vaccine breakthrough infection, Veterans Health Administration, January – April 2021.**

- Cancer
- Chronic Kidney Disease
- Chronic Lung Disease
- Dementia (or Other Neurological Conditions)
- Diabetes
- Heart Disease
- HIV Infection
- Immunocompromised State
- Liver Disease
- Obesity
- Smoking, Current or Former
- Solid Organ or Blood Stem Cell Transplant
- Stroke or Cerebrovascular Disease
- Substance Use Disorders

**Table 3. SARS-CoV-2 variants among patients with breakthrough COVID-19 infection, Veterans Health Administration, January – April 2021.**

- B.1.1.7 (UK)
- B.3 (South Africa)
- B.1.529 (USA - New York)
- B.1.526 (USA - California)
- B.1.351 (South Africa)
- B.1.525 (USA)
- B.1.354 (Brazil)
- B.1.529 (USA - California)

**Conclusion.** The HI response to cccIV4 was greater than LAIV4 in this study of mostly older children. Day 0 HI titers were 1) a significant determinant of GMFR;