

Tolerability of the Dengue Vaccine Qdenga® in German Travellers: a prospective survey (ongoing)



Tomas Jelinek, Juliane Kramm, Maik Wagner

Berlin Center for Travel & Tropical Medicine, Germany



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Conflict of Interest Statement



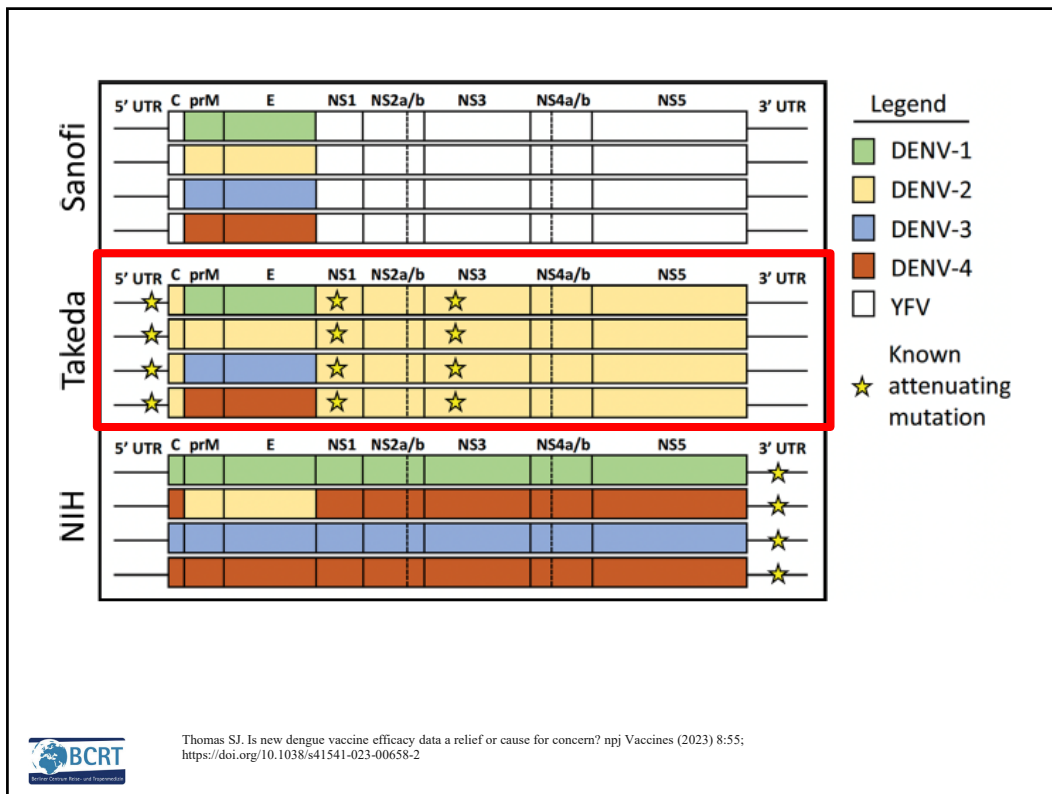
Paid lectures, consultancies, clinical studies for

Abbott, Astella, Astra Zeneca, Bavarian Nordic, Baxter, BioNTech, Boehringer Ingelheim, Clover Pharmaceuticals, Crucell, Dr. Falk Pharma, GSK, Glenmark, Hermes Arzneimittel, Hoffmann LaRoche, India Serum Institute, Medicago, Pfizer, r-biopharm, Sanofi Pasteur, MSD Sharp & Dohme, Sekizui-Virotech, Sigma Tau, Takeda, Themis Bioscience, Valneva

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Vaccination against Dengue: German Experience

- Qdenga® is licensed by EMA in November 2022 for protection against Dengue from the age of 4 years
- Vaccines becomes available in Germany February, 9th, 2023
- Germany the first country where Qdenga® was available
- BCRT was the first institution in Germany using the vaccine
- Indication according to EMA authorisation
- Single shot vaccination before travel regularly applied
- Good acceptance from the start
- Travellers actively seek vaccination, particularly if they/friends already experienced dengue
- BCRT initiated active follow-up: every vaccinee who agrees to being contacted receives a letter asking her/him to complete an anonymous online survey regarding the experience with the vaccine
- Self-reported, uncontrolled data
- Approval by Ethics Committee of Medical Board Berlin
- Use of QuestionStar®



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www.bcr.t.de

Travel preparation

Sun protection, insect protection and a first-aid kit are part of the basic equipment for travel and are entirely sufficient for most short trips. Yet, long-haul journeys generally take us to other climate zones, often tropical, and hence to countries where illnesses which are rare in Germany appear more frequently. However, there is no reason against a tour of Asia, a jungle trip in Costa Rica or a safari in Africa. The important thing is correct preparation. Some vaccinations are even possible for "last minute" trips! However, many vaccinations require time. That is why you should allow us to advise you as early as possible.

Travel medicine and tropical medicine specialists in our numerous travel practices will be happy to advise you with the planning of your stay abroad and provide you with health-related information on travel destinations all over the world, as well as potential illnesses and necessary vaccinations.

You can have all the necessary vaccinations, as well as prescriptions for your first-aid kit and malaria prophylaxis, directly on site. If you travel a lot, you can have your set of vaccinations carried out without any problems in our various BCRT travel clinics: e.g. a first rabies vaccination in our Berlin Travel Clinic, and the second one in our Munich Travel Clinic.

During the opening times of the travel practices you do not need an appointment – you can just come by without any prior arrangement.

Our offer:

- Individual advice on all health-related aspects of travel
- Evaluation of prior illnesses
- Tips on nutrition, hygiene, insect protection, and sun protection
- Advice for pregnant women and for travelling with children
- Preparation of a vaccination plan
- Malaria prophylaxis advice
- Recommendations for the first-aid kit and for medicines abroad
- Advice on interactions between medicines and on contraindications

Payment and reimbursement of costs

In all travel clinics you can pay with an EC bank card or in cash. Health insurance companies are not obliged to reimburse costs for travel medicine services.

[Kostenübernahme](#)

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Basic Statistics

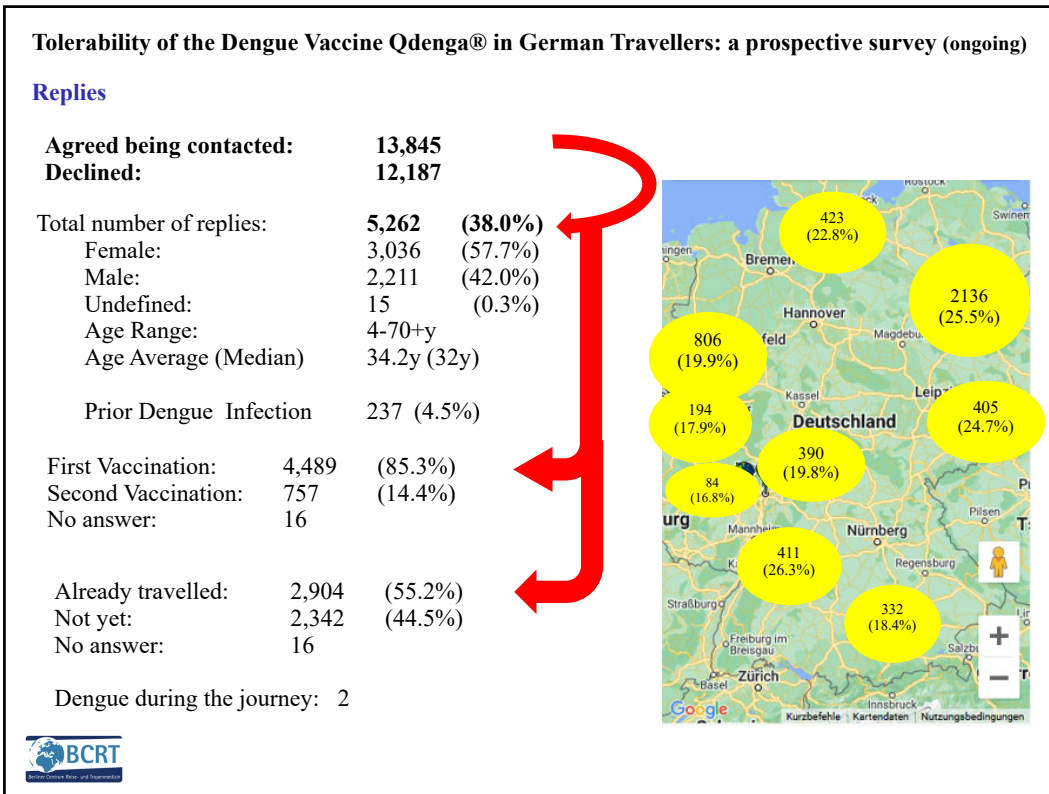
Total number pre-travel visits at BCRT from Feb 2022-Feb 2024: 111,059

Doses Qdenga® applied:	26,032	(23.4%)
Female:	13,384	(51.4%)
Male:	11,255	(44.2%)
Undefined:	1,393	(5.4%)
Age Range:	4-79y	
Age Average (Median)	34.7y (32y)	

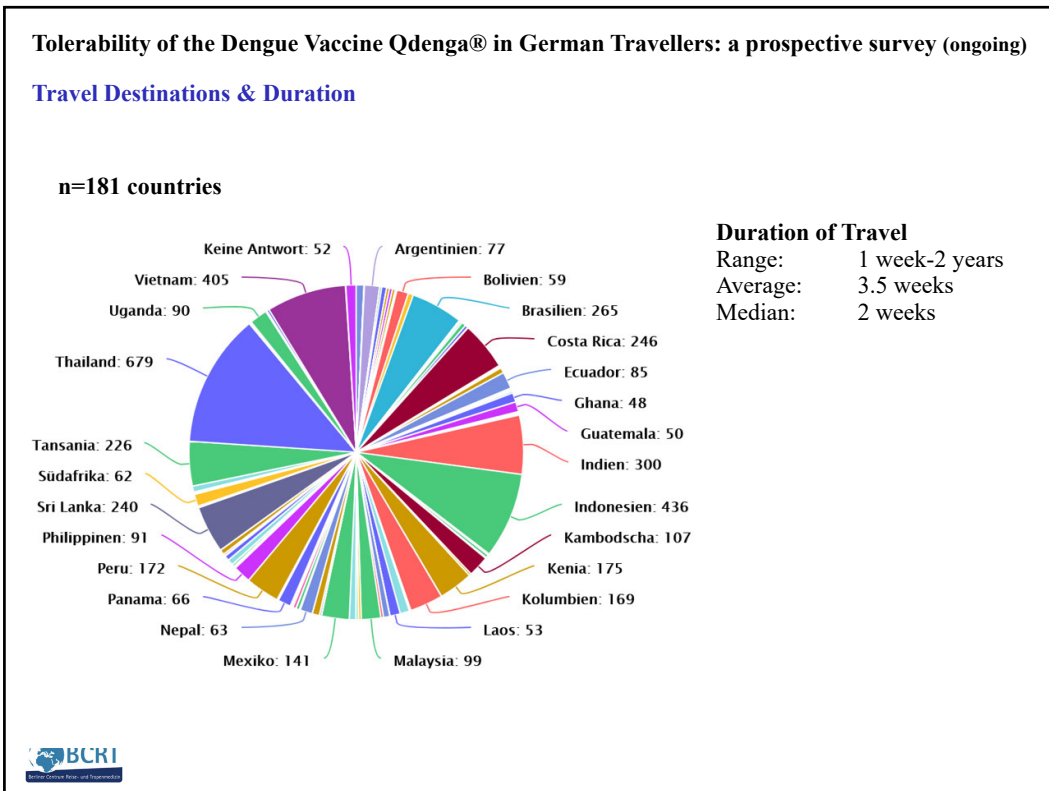
First Vaccination:	15,599	(59.9%)
Second Vaccination:	10,433	(40.1%)

Agreed being contacted:	13,845	(53.2%)
Declined:	12,187	(46.8%)

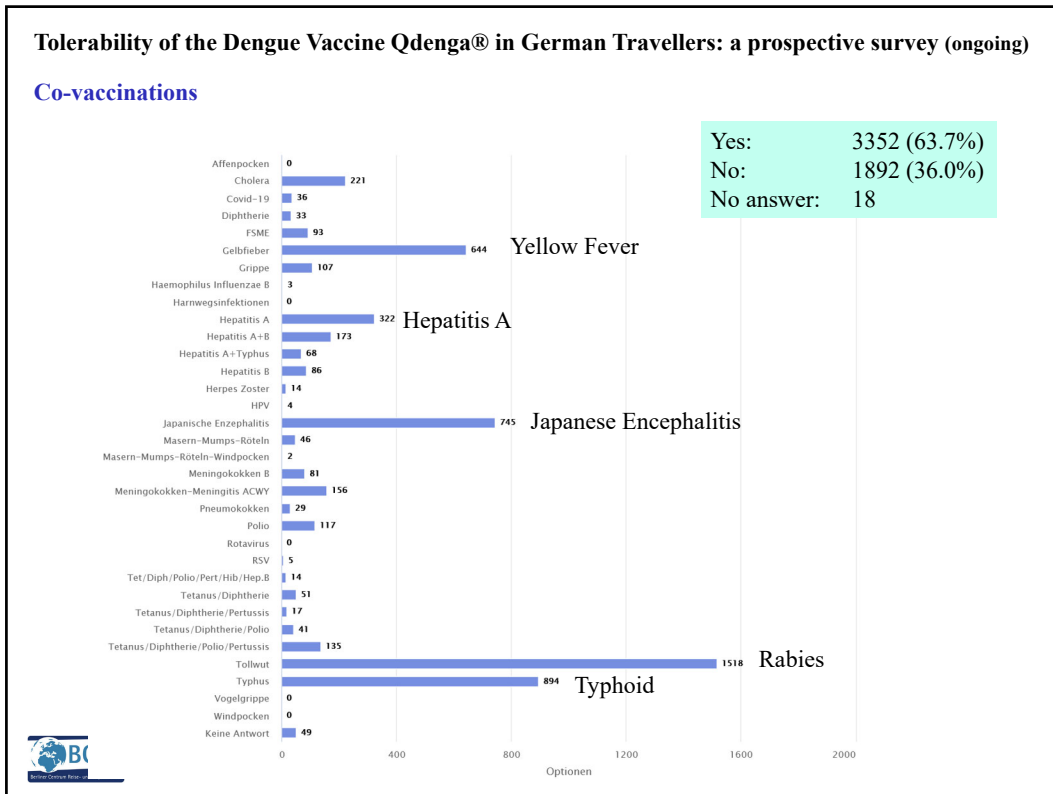
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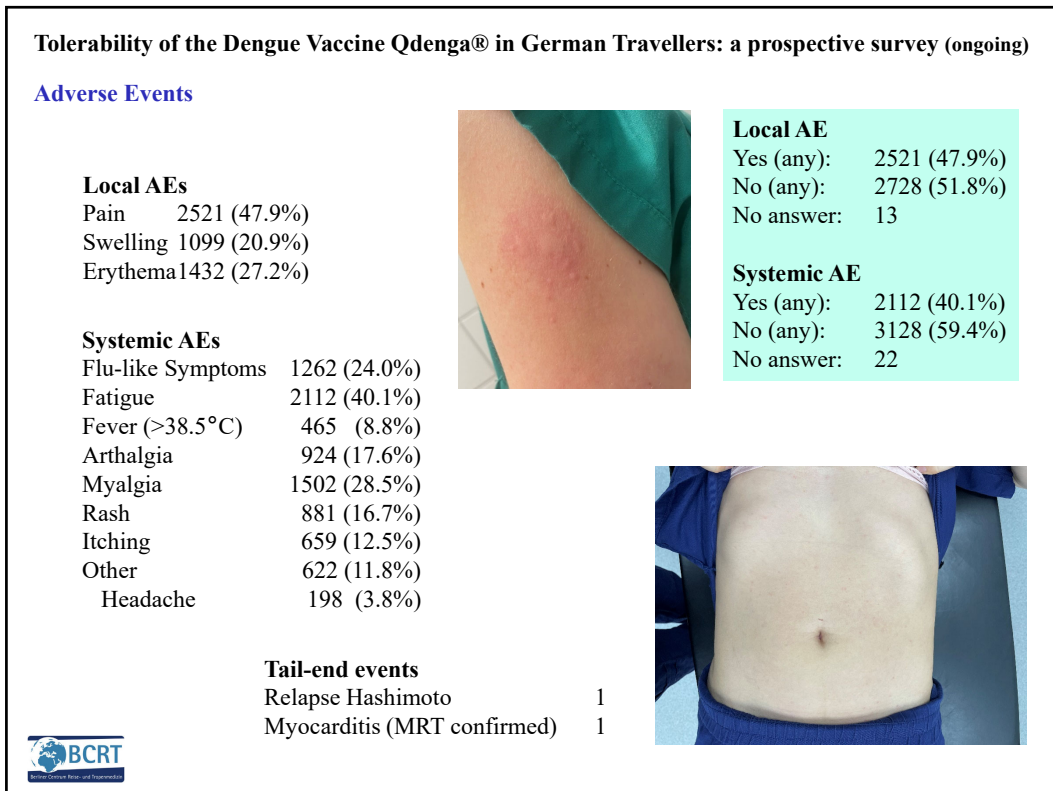
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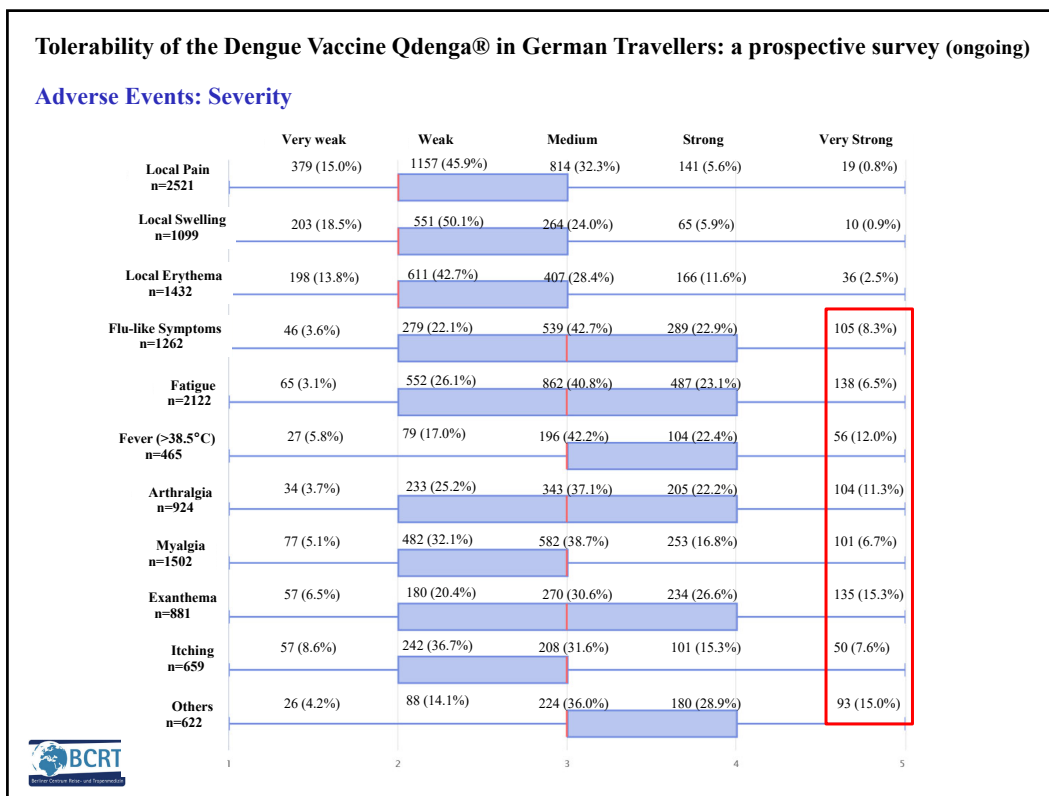
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Potential SAEs

Case 1: Relapse Hashimoto

- Female, 30-40y, travel to Panama for 2 weeks
- First dengue vaccination
- Co-vaccination against yellow fever
- Local pain: medium, 1-3 days
- Flu-like symptoms, fatigue, fever: strong, 4-7 days
- Arthralgia, myalgia: medium, 1-3 days
- Headache: strong, 4-7 days
- "I have Hashimoto since 20 years. With fever after the vaccination, hormonal levels were checked and showed hyperthyroidism for a few days."

Case 2: Myocarditis

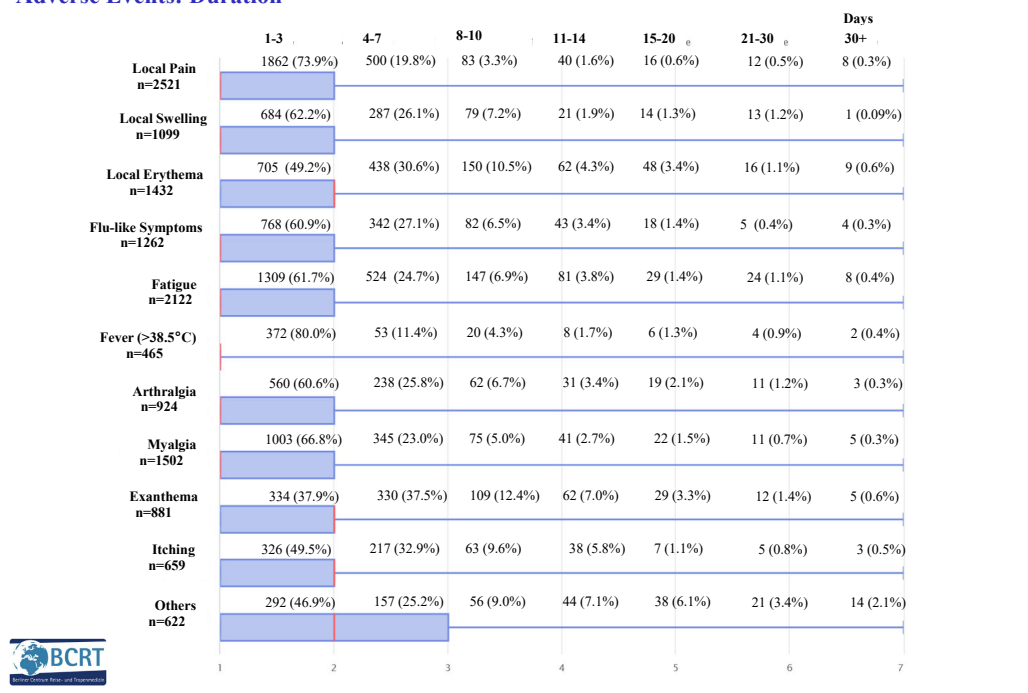
- Male, 30-40y, travel to Cambodia for 12 weeks
- First dengue vaccination
- Co-vaccination against JE
- Local pain and redness: medium, 1-3 days
- Flu-like symptoms, fatigue, fever: strong, 8-10 days
- Arthralgia: medium, 1-3 days
- Headache: very strong, >30 days
- Myocarditis MRT-confirmed 14 days after vaccination

BCRT
Bundeszentrale für gesundheitliche Aufklärung

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Adverse Events: Duration



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Systemic Adverse Events and Prior Dengue Infection

AEs	No Prior Dengue Infection n=5,009	Prior Dengue Infection n=237	P-Value
Local Pain	2054 (41.0%)	114 (48.1%)	0.029
Local Swelling	948 (18.9%)	47 (19.8%)	n.s.
Local Erythema	1008 (20.1%)	72 (30.4%)	0.007
Flu-like Symptoms	1399 (27.9%)	62 (26.2%)	n.s.
Fatigue	2134 (42.6%)	96 (40.5%)	n.s.
Fever >38.5°C	418 (8.3%)	20 (8.4%)	n.s.
Arthralgia	889 (17.7%)	42 (17.7%)	n.s.
Myalgia	1312 (26.2%)	67 (28.3%)	n.s.
Rash	578 (11.5%)	40 (16.9%)	0.026
Itching	351 (7.0%)	31 (13.1%)	0.004
Other	731 (14.6%)	28 (11.8%)	n.s.

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Systemic Adverse Events: First vs. Second Vaccination

AEs	1st Vaccination n=4,489	2nd Vaccination n=757	P-Value
Local Pain	2206 (49.1%)	303 (40.0%)	<0.01
Local Swelling	944 (21.3%)	167 (22.1%)	n.s.
Local Erythema	1251 (27.9%)	198 (26.2%)	n.s.
Flu-like Symptoms	1184 (26.4%)	86 (11.4%)	<0.01
Fatigue	1933 (43.1%)	183 (24.2%)	<0.01
Fever >38.5°C	453 (10.1%)	21 (2.8%)	<0.01
Arthralgia	888 (19.9%)	57 (7.5%)	<0.01
Myalgia	1367 (30.5%)	134 (17.7%)	<0.01
Rash	867 (19.3%)	49 (6.5%)	<0.01
Itching	584 (13.0%)	82 (10.8%)	0.046
Other	593 (13.2%)	42 (5.5%)	<0.01



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Adverse Events and Co-Vaccination

AEs	Any Other Vaccination n=3,352	No Other Vaccination n=1,892	P-Value
Local Pain	1748 (52.1%)	771 (40.8%)	<0.01
Local Swelling	729 (21.7%)	381 (20.1%)	n.s.
Local Erythema	936 (27.9%)	510 (27.0%)	n.s.
Flu-like Symptoms	841 (25.1%)	392 (20.7%)	<0.01
Fatigue	1479 (44.1%)	639 (33.8%)	<0.01
Fever >38.5°C	342 (10.2%)	128 (6.8%)	<0.01
Arthralgia	649 (19.4%)	279 (14.7%)	<0.01
Myalgia	1045 (31.2%)	452 (23.9%)	<0.01
Rash	618 (18.4%)	278 (14.7%)	<0.01
Itching	437 (13.0%)	229 (12.1%)	n.s.
Other	408 (12.2%)	211 (11.6%)	n.s.



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Systemic Adverse Events and Co-Vaccination: Details

AEs	Co-Vaccination												
	None	Cholera	YF	Flu	Hep A	Hep A+B	Jap. Enc.	MMR	Men ACWY	Polio	TdapP	Rabies	Typhoid
Flu-like Symptoms	392 (20.7%)	45 (20.4%)	122 (18.9%)	27 (25.2%)	72 (22.4%)	29 (16.8%)	214 (28.7%)	8 (17.4%)	49 (31.4%)	30 (25.6%)	49 (36.3%)	423 (27.9%)	229 (25.6%)
Fatigue	639 (33.8%)	87 (39.4%)	250 (38.8%)	40 (37.4%)	138 (42.9%)	58 (33.5%)	363 (48.7%)	16 (34.8%)	74 (47.4%)	49 (41.9%)	68 (50.4%)	728 (48.0%)	395 (44.2%)
Fever >38.5°C	128 (6.8%)	17 (7.7%)	38 (5.9%)	9 (8.4%)	25 (7.8%)	8 (4.6%)	89 (11.9%)	1 (2.2%)	15 (9.6%)	8 (6.8%)	16 (11.9%)	166 (10.9%)	87 (9.7%)
Arthralgia	279 (14.7%)	36 (16.3%)	96 (14.9%)	17 (15.9%)	51 (15.8%)	20 (11.6%)	161 (21.6%)	5 (10.9%)	37 (23.7%)	15 (12.8%)	29 (21.3%)	314 (20.7%)	160 (17.9%)
Myalgia	452 (23.9%)	57 (26.0%)	166 (25.8%)	32 (29.9%)	106 (32.9%)	51 (29.5%)	254 (34.1%)	16 (34.8%)	53 (33.9%)	30 (25.6%)	55 (40.7%)	501 (33%)	284 (31.8%)
Rash	278 (14.7%)	38 (17.2%)	57 (8.9%)	18 (16.8%)	48 (14.9%)	22 (12.7%)	139 (18.7%)	3 (6.5%)	34 (21.8%)	23 (19.7%)	31 (23.0%)	321 (21.1%)	169 (18.9%)
Itching	229 (12.1%)	23 (10.4%)	64 (9.9%)	7 (6.5%)	45 (14.0%)	21 (12.1%)	101 (13.6%)	5 (10.9%)	26 (16.7%)	16 (13.7%)	18 (13.3%)	194 (12.8%)	113 (12.6%)
Other	211 (11.6%)	19 (8.6%)	57 (8.9%)	9 (8.4%)	41 (12.7%)	17 (9.8%)	92 (12.4%)	4 (8.7%)	27 (17.3%)	12 (10.3%)	20 (14.8%)	191 (12.6%)	86 (9.6%)
N=	1,892	221	644	107	322	173	745	46	156	117	135	1,518	894



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Case Study: False Positive Dengue Dx after Vaccination

Mail on 27 Feb 2023:

I've been in Vietnam since 23 February and since yesterday I've had a rash all over my upper body, but it doesn't itch, and a slight headache around my eyes. That's why I went to see a doctor today. Communication was very difficult, but they did a blood test and I tested positive for dengue.

The doctor prescribed me methylprednisolone 16mg and Amoxi/Clav 1g. He said something about signs of superinfection.

I am not sure because I was vaccinated against dengue on 17 February, have only been in Vietnam since 23 February and have only seen one mosquito so far. Can the dengue test also be positive due to the live vaccination and the rash a side effect of the vaccination?



PHÒNG KHÁM NỘI TỔNG HỢP SA PA
Địa chỉ: 534 Điện Biên Phủ, phường Phan Sĩ Păng,
thị xã Sa Pa, tỉnh Lào Cai SĐT: 0918084833

KẾT QUẢ XÉT NGHIỆM MIỄN DỊCH

Họ và tên: ██████████ Tuổi / Năm sinh: ██████████
Chỉ định: Kiểm tra Giới tính: Nữ

Xét nghiệm	Kết quả	Tham chiếu
DENGUE NS1	Dương tính	Âm tính
Định lượng CRP	8.1 mg/L	0.0-10.0
Định lượng hs-CRP	>5.0 mg/L	0.0-1.0

09:24 ngày 27/02/2023
Bác sĩ chỉ định: ██████████ Phòng xét nghiệm

Bs. Hà Anh Vân



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Summary and Discussion

- Vaccine generally well tolerated
- Most AEs short-lived
- Most AEs after first vaccination

- Co-vaccination well tolerated, selected vaccine increase AEs
- Systemic AEs typically during 2nd week after vaccination

- Rash as a significant new phenomenon in European vaccinees
- Rash more frequent in those who already had Dengue

- Obvious bias towards reporting of AEs: most non-responders asymptomatic?
- Uncontrolled individual reporting
- NS1 antigen test and antibody tests affected: false positive Dx Dengue possible

- Vaccine can be safely recommended within licensure
- Vaccination should possibly be given at least 2 weeks before the journey



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