

EAACI Clinical Fellowship 2024 Final Report

Project Title: Evaluation of clinical and molecular differences in patients with recurrent angioedema or urticaria receiving standard-dose omalizumab

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Type, duration and location of Fellowship: Long-Term Clinical Fellowship, 1 October 2024-31 March 2025 (6 months), Charité – Universitätsmedizin Berlin, Germany

Host Institution and Supervisor name: Institute of Allergology, Charité - Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology, Berlin, Germany, Prof. Dr. Marcus MAURER

Summary of the Clinical and Academic Activities Undertaken During the Fellowship

It was a distinct honor to be awarded the 2024 Clinical Fellowship by the European Academy of Allergy and Clinical Immunology (EAACI). I had the valuable opportunity to complete this fellowship at Charité - Universitätsmedizin Berlin. During the fellowship period, I was actively engaged in a wide range of clinical activities with a primary focus on urticaria and angioedema patients. My responsibilities included observing and assisting in patient evaluations, performing diagnostic procedures, and participating in multidisciplinary discussions of complex cases alongside leading clinicians and researchers in the field. Working at a center of excellence and reference for urticaria and angioedema (UCARE&ACARE) has greatly contributed to my clinical and academic development in this field.

Clinical Activities and Observations

In addition to the meeting hours mentioned below, I participated in a weekly schedule where, until the end of each day, I assessed clinical patients relevant to my project in outpatient clinics. I also attended patient examinations conducted by allergy specialists and took part in the general evaluations of patients included in various studies.

Monday: Clinical Training and Consultation

Time spent:8:00-8:30

Topic: Each of the researchers at the clinic was responsible for preparing a presentation based on a recently published article and a newly released guideline, in light of the latest evidence in the literature. These sessions allowed for a comprehensive review of current clinical practice and ensured close monitoring of recent developments in the field.

Tuesday: Patient Care Clinical Trials (PCC) Meeting IFA/ITMP

Time spent:12:45-13:45

Topic: This meeting brings together researchers involved in outpatient clinic studies and is organized to review up-to-date information on ongoing research funded either by external sponsors or the clinic itself. The purpose is to outline future plans leading up to the manuscript preparation stage and to facilitate the exchange of recent developments and insights. I also presented my project in German at the meeting held on November 13, 2024.

Wednesday: Preclinic Translational Research (PTR) Meeting

Time spent:12:45-13:45

Topic: This meeting serves as a platform for the evaluation of multicenter national and international studies, during which the most recent data are shared with the clinical team and the principal investigators provide summaries of ongoing research projects.

Thursday: Basic Science/ Solution Discovery (BS) IFA Meeting

Time spent:8:30-10:00

Topic: This is a multidisciplinary meeting conducted in English, distinct from other meetings in that it includes international participants. It provides a platform for the evaluation of ongoing laboratory studies, as well as the presentation of new project proposals through brief five-minute talks. Current laboratory research is discussed in detail, fostering collaboration and exchange of expertise across disciplines. I also presented my project in English during the meeting held on November 21, 2024.

Friday: Outpatient Clinic Visits & Data Collection

Time spent:8:00-16:00

Topic: On the other four days, as with the hours outside of each meeting, I was involved in patient examinations at the outpatient clinic on Fridays. These days were dedicated to prospectively collecting blood samples and clinical data from my project patients, as well as analyzing the data I had gathered.

Apart from these daily routine tasks, I was also involved in the following additional activities

- ACARE Global Angioedema Forum, Copenhagen, Denmark, 04.10.2024-05.10.2024
- The 7th GA²LENetwork Global Urticaria Forum, Berlin, Germany, 04.12.2024-05.12.2024
- Commemorative Event in Honor of Prof. Dr. Marcus Maurer - Scientific Symposium
- EAACI-ESCD Skin Allergy Meeting (SAM), Bilbao, Spain, 27.03.2025-29.03.2025
- Urticaria DACH-TAG Berlin, Germany, 11.04.2025
- GALEN/HAEi ACARE Network's LevelUp Preceptorship on Recurrent Angioedema Berlin, Germany, 12.04.2025

Research Project

Our project, entitled "*Chronic Spontaneous Urticaria with Wheals, Angioedema, or Both: Differences in Clinical Characteristics, Biomarkers, and Treatment Response,*" was selected for a Flash Talk presentation at the EAACI 2025 Congress to be held in Glasgow, United Kingdom.

We retrospectively assessed 340 CSU patients seen in the outpatient clinic of the Urticaria Center of Excellence and Reference (UCARE) Berlin from December 1, 2022 to December 1, 2024. Baseline demographic and disease characteristics, treatment responses, and laboratory parameters were analyzed. Across all CSU patients, 26%, 35%, and 39%, had W, AE, and W+AE, respectively. The W patients, compared with W+AE and AE patients, showed higher rates of atopy (40% vs. 23 and 9%, respectively) and non-response to antihistamines. At the time of referral, AE patients had, compared to W and W+AE patients, the highest median age (59 vs. 41 and 33 years, respectively) and less frequent comorbidities (59% vs. 73% and 72%, respectively). The W+AE patients, compared with W and AE patients, showed lower median blood basophil counts, higher rates of elevated c-reactive protein (23% vs 13% and 10%, respectively), a trend toward a higher male-to-female ratio (2.4 vs 1.74 and 1.93, respectively) and more often non-response to omalizumab (26% vs. 5% and 21%, respectively). Moreover, W+AE patients showed less frequent AE attacks (<24/year) than AE patients (55% vs. 68%) and concomitant chronic inducible urticaria than W patients (17% vs. 32%). Total IgE levels were < 40 kU/mL in 21%, 23%, and 25% of W, AE and W+AE patients, respectively. In the logistic regression analysis, total IgE level <40 kU/L was associated with non-response to omalizumab by 3.5 times in all three CSU phenotypes (p=0.02, [95 % CI: 1.24-9.66]). Despite the clinical and demographic heterogeneity of the three CSU phenotypes, they all share low IgE as a known predictive marker for non-response to omalizumab. Future molecular-based studies may contribute to a better understanding of the pathomechanisms of these phenotypes and improvement of therapeutic strategies.

Additionally, as part of a separate project, we aimed to compare the outcomes of the basophil activation test and the mast cell activation test in our patient cohort. The data analysis for this project is currently in progress. I also contributed as a co-investigator to a study focused on identifying the endotypes of chronic spontaneous urticaria.

Key Achievements

Having the opportunity to observe the diagnostic and therapeutic processes of various diseases—primarily urticaria and angioedema—ranging from history taking and laboratory testing to skin biopsies and allergy tests, was a truly invaluable experience. This was further enriched by the chance to exchange ideas with esteemed colleagues who are leading experts in the field. Both the retrospective review of patient data in German through the hospital system and the fact that most meetings were conducted in German significantly contributed not only to my medical knowledge but also to my personal development. Additionally, close communication with clinical, laboratory, and other healthcare staff further enriched this experience. I had the opportunity to work with ELISA and enzyme kits in a laboratory setting for the first time. This experience allowed me to gain hands-on laboratory skills, including the use of pipettes, preparation of various solutions, and operation of different laboratory instruments. Being actively involved in every step of the project significantly enhanced my motivation and contributed to a more efficient and productive workflow. Starting with a well-structured and thoroughly planned project greatly facilitated the smooth progression of the work and the effective implementation of each step.

Conclusion

The academic experience provided by this fellowship at Charité – Universitätsmedizin Berlin and Institut für Allergologie has been truly invaluable. It significantly broadened my perspective on allergic diseases and clinical research, enabled collaboration with distinguished professionals from various countries, and allowed me to enhance both my English and German language skills. Moreover, it offered a unique platform to exchange diverse approaches within our field. I am deeply grateful to EAACI and the fellowship selection committee for granting me this exceptional opportunity.

Acknowledgements

I would like to express my sincere gratitude to the entire team at Charité – Universitätsmedizin Berlin and Institut für Allergologie and especially to my inspiring supervisor, Prof. Dr. Marcus MAURER, for his unwavering support and dedication. I respectfully and with deep admiration commemorate Marcus Maurer, a distinguished scientist who tragically passed away suddenly. Renowned worldwide, he expanded our horizons through his numerous publications, ideas, and boundless energy in our field. I will never forget his motto "*Never give up*". Over the course of six months, I would like to extend my heartfelt gratitude to Prof. Dr. Markus MAGERL for introducing me to the leading experts in the field and guiding me in planning each step of the project from beginning to end. I am also deeply thankful to Dr. Thomas BUTTGEREIT for his solution-oriented support at every stage of the project's execution, to Prof. Dr. Jörg SCHEFFEL for his unwavering trust and full support in the laboratory phase of the project, Dr. Pavel Kolkhir for sharing his database, and to Dr. Carolina AYALA VERA and Kerim FEDAI for their assistance in facilitating access to data and samples from the Biobank. I would also like to express my gratitude to Prof. Dr. Emek KOCATURK GONCU for continuously motivating me with new projects. I would also like to express my gratitude to my other mentors, Prof. Dr. Ebru DAMADOGLU, Prof. Dr. Gül KARAKAYA, and Prof. Dr. Ali Fuat KALYONCU, for their guidance.