Corresponding Author	Julien Rossignol
List all other authors	Olivier Hermine1° MD, PhD, Orianne Debeaupuis1,2 PharmD, PhD, Gandhi Damaj3 MD, PhD, Johannes Lübke4 MD, Juliana Schwaab4 MD, Marc Heizmann5 MD, Frank Siebenhaar6,7 MD, Polina Pyatilova6,7 MD, Nicole Nojarov6,7 MD, Marek Niedoszytko8 MD, Aleksandra Gorska8 MD, Mattias Mattsson9 MD, Khalid Shoumariyeh10 MD, Stephan de Bra10 MD, Friederike Wortmann11 MD, Nikolas von Bubnoff11 MD, Horia Bumbea12 MD, Delia Soare12 MD, Chiara Elena13 MD, Judit Várkonyi14 MD, Anna Belloni Fortina15 MD, Simge Erdem16 MD, Knut Brockow17 MD, Tobias Michael Franz17 MD, Jens Panse18 MD, Deborah Christen18 MD, Christine Breynaert19 MD, Akif Selim Yavuz20 MD, Luca Malcovati13,21 MD, Michael Doubek22 MD, Vito Sabato23 MD, Ilaria Tanasi24 MD, Massimiliano Bonifacio24 MD, Karin Hartmann25 MD, Axel Rüfer26 MD, Mariarita Sciumè27 MD, Valentina Bellani27 MD, Irena Angelova-Fischer28 MD, Alex Stefan28 MD, Massimo Triggiani29 MD, PhD, Roberta Parente29 MD, Saskia K. Klein30 MD, Michael Makris31 MD, Sotirios Papageorgiou31,32 MD, PhD, Paul van Daele33 MD, Ingunn Dybedal34 MD, Daniel Baffoe34 MD, Theo Gülen35 MD, Madlen Jentzsch36 MD, Olivier Lortholary1 MD, PhD, Mael Heiblig37 MD, PhD, Cristina Bulai Livideanu38 MD, Stéphane Barete39 MD, PhD, Clément Gourguechon40 MD, Sophie Dimicoli-Salazar41 MD, PhD, Olivier Tournilhac42 MD, PhD, Laurent Frenzel1 MD, PhD, Michel Arock43 MD, PhD, Andrzej Mital44 MD, Johannes N. Woltsche45 MD , Hanneke C. Kluin-Nelemans46 MD, PhD, Joanna N.G. Oude Elberink47 MD, Jason Gotlib48 MD, PhD, Martin Sperr49,50 MD, Andreas Reiter4 MD, PhD, Peter Valent49,50 MD, PhD, Wolfgang R. Sperr49,50 MD, PhD, Julien Rossignol1° MD, PhD
Email-Address	julien.rossignol@aphp.fr
Institute/Department	CEREMAST, INSERM U1163, Imagine Institute, Necker-Enfants Malades and Cochin Hospitals, AP-HP, Université Paris Cité
Address of Institute	149 rue de Sevres, Paris, France

Title of Presentation	Outcomes, leukemic transformation, and impact of KIT D816V–selective tyrosine kinase inhibitors in systemic mastocytosis with an associated myeloid neoplasm: an international ECNM registry analysis
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Abstract of Presentation	Background Systemic mastocytosis with an associated hematologic neoplasm (SM-AHN), predominantly of myeloid origin, is the most frequent advanced SM subtype. However, the respective prognostic contributions of the SM and AHN components, the risk of acute myeloid leukemia (AML) transformation, and the impact of KIT D816V–selective tyrosine kinase inhibitors (TKIs) remain insufficiently defined. Methods We analyzed 3,925 SM patients from the ECNM registry (35 centers, 10th data wave, February 2025). Overall survival (OS) was compared between myeloid SM-AHN and SM without AHN, and within SM-AHN by SM component (advanced vs. non-advanced) and AHN subtype. Cumulative incidence of AML transformation was estimated using the Aalen-Johansen method. In the subgroup with an aggressive/leukemic SM component, the association between TKI exposure (midostaurin/avapritinib) and OS/AML transformation was assessed using multivariable Cox, Fine-Gray, and landmark analyses. Results Among 467 patients with myeloid SM-AHN, MDS/MPN was the most frequent AHN (41.1%; CMML 29.6%), and 55.0% had an advanced SM component. OS was markedly shorter in SM-AHN than SM-no-AHN (median 36.1 vs. 340.9 months; P<0.001). Within SM-AHN, advanced SM-AHN had shorter OS than non-advanced SM-AHN (28.3 vs. 70.9 months; P<0.001). In multivariable analysis, the SM component aggressiveness — not AHN subtype (except AML) — independently predicted OS (HR=0.44 for non-advanced; P<0.001). Among 201 patients with an aggressive/leukemic SM component, TKI exposure (n=151) was associated with longer OS (37.9 vs. 17.8 months; P<0.001) and a five-fold lower 36-month AML incidence (5.9% vs. 27.1%; P<0.001; Fine-Gray HR=0.26, P=0.003). Landmark analysis at 24 months confirmed these findings (HR=0.44; P=0.001). Conclusions In the largest myeloid SM-AHN cohort reported, prognosis was driven primarily by the SM component aggressiveness. KIT D816V–selective TKI exposure was associated with improved OS and reduced AML transformation, supporting targeting the SM component with approved KIT-directed therapies. Presenting author: Julien Rossignol