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Title of Presentation	Profiling non-clonal mast cell activation disorders identifies alpha-tryptase-defined profiles
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Abstract of Presentation	Background: Most patients referred for suspected mast cell activation syndrome (MCAS) do not fulfill consensus criteria and are classified as mast cell activation disorder not otherwise specified (MCAD-NOS). Hereditary alpha tryptasemia (HαT), defined by increased germline TPSAB1 α-tryptase allele copy number, is increasingly identified but poorly characterized in this population. We aimed to phenotype non-clonal MCADs, assess HαT prevalence, and identify predictors of omalizumab response. Methods:

	Retrospective multicenter study of 663 patients with suspected non-clonal MCAD (CEREMAST network, France), classified as MCAS (n=36), suspected MCAS with idiopathic anaphylaxis (MCAS-IA, n=43), or MCAD-NOS (n=584). TPSAB1 genotyping was performed by droplet digital PCR. Omalizumab response predictors were assessed by multivariable logistic regression and LASSO models. Results: Only 5.4% fulfilled MCAS criteria. Compared with MCAD-NOS, MCAS featured near-universal anaphylaxis (89% vs 23%, p<0.001) and fewer non-specific symptoms, including asthenia (25% vs 64%) and bone/joint pain (25% vs 58%; all p<0.001). MCAS and MCAS-IA were indistinguishable. HαT was present in 25%—a 4-fold enrichment—but similarly distributed across groups; carriers had fewer non-specific symptoms (p<0.001). Elevated total IgE was associated with MCAS (57% vs 26%, p<0.001) and anaphylaxis (56% vs 22%, p<0.001). Plasma histamine and PGD_2 did not discriminate groups. In multivariable analysis, at least one TPSAB1 α-tryptase allele was the strongest positive predictor of omalizumab response (OR 12.85; 95% CI 2.88-57.36; p<0.001), while bone/joint pain predicted non-response (OR 0.13; 95% CI 0.03-0.72; p=0.019). Conclusions: Consensus-defined MCAS is rare and anaphylaxis-dominated. TPSAB1 α-tryptase alleles identify clinical profiles and predict omalizumab response. Presenting author: Olivier Hermine