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Title of Presentation	Distributions of tryptase genotypes in patients with anaphylaxis with & without clonal mast cell disease – Insights from the PROSPECTOR study
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Abstract of Presentation	Background Tryptase genotype (TG) data from prospective anaphylaxis cohorts are limited. We characterized TG distributions and explored associations with clinical features in real-world patients with anaphylaxis/systemic mast cell activation symptoms. Methods PROSPECTOR (NCT04811365) patients had moderate-to-severe anaphylaxis with: ≥2 organ systems involved (one cardiovascular) and baseline tryptase ≥8 ng/mL, and/or Hymenoptera sting, and/or event-related tryptase elevation with cardiovascular involvement, with no prior systemic mastocytosis/myeloid neoplasm history. Centralized TG (TPSAB1) was determined using droplet digital polymerase chain reaction with post hoc, local follow-up for investigator-diagnosed clonal mast cell disease (cMCD). Patients with available TGs were summarized overall by cMCD status. Results In 380/381 (99.7%) patients, 13 TG configurations were observed. Hereditary alpha-tryptasemia (HaT) and non-HaT TGs were reported in 137/380 patients (36.1%) and 243/380 patients (63.9%), respectively. In 46/381 (12.1%) cMCD patients, 42/46 (91.3%) and 4/46 (8.7%, 4/4 with 3α:2β) had non-HaT and HaT TGs, respectively. In patients with non-HaT TGs with ≥3 β alleles, 35/184 (19%; 21/127 [16.5%] 1α:3β; 14/57 [24.6%]

	0α:4β) had cMCD. These TGs were more frequent in cMCD (35/46 [76.1%]) versus nonclonal patients (149/334 [44.6%]) (univariable logistic regression: OR=3.88; 95% CI=1.90–7.89; p=0.00019). In cMCD patients, no clear differences in clinical phenotype were observed between 1α:3β or 0α:4β versus different TGs. Small samples and unadjusted analyses limit interpretation. Conclusions This analysis provides insights into TG distributions in patients with anaphylaxis. Whether genetic differences reflect susceptibility, a potential cMCD biomarker, or random variation is unclear. Additional research is warranted to clarify these observations, including frequency of β-tryptase-containing alleles.