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Title of Presentation	Clinical manifestations associated with hereditary alpha-tryptasemia: TPSAB1 gene dosage, anaphylaxis & concomitant systemic mastocytosis
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Abstract of Presentation	**Background:** Hereditary alpha-tryptasemia (HAT) is an autosomal dominant genetic trait, caused by increased *TPSAB1* copy number, associated with elevated basal serum tryptase (BST). Despite an estimated prevalence of ~3-8% in the Western population, HAT remains underdiagnosed and *TPSAB1* gene dosage effects are incompletely characterized. **Objectives:** To refine HAT clinical phenotypes and evaluate the impact of gene dosage on BST and clinical manifestations, including anaphylaxis. **Methods:** A retrospective, single-center cohort study was conducted in 62 symptomatic patients with genetically confirmed HAT between 2022 and 2025 using electronic health records and a

	purpose-designed symptom questionnaire. All patients were additionally screened for the *KIT* D816V mutation. **Results:** Patients showed severe multisystem involvement, with cutaneous and gastrointestinal symptoms predominating, most commonly triggered by psychological stress. Symptom burden was not affected by *TPSAB1* number of replications. However, BST increased significantly with two *TPSAB1* replications. Anaphylaxis severity correlated with α-tryptase copy number, with severe reactions (Mueller grade III / IV) most prevalent among patients with four α-copies. Four patients had concomitant Indolent Systemic Mastocytosis (ISM) with *KIT* D816V mutation, representing an independent high-risk subgroup: All patients with HAT and ISM experienced grade IV anaphylaxis and had markedly elevated BST-levels compared to patients with HAT alone. An association between HAT and thyroid dysfunction was observed. **Conclusion:** HAT is associated with a high multisystemic burden. A gene dosage effect was observed with BST and with increased severity of anaphylaxis. Patients with concomitant ISM exhibit a particular severe phenotype, supporting systematic evaluation for systemic mastocytosis in HAT patients with severe anaphylaxis.
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