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Title of Presentation	Modeling Systemic Mastocytosis with Associated Hematologic Neoplasm (SM-AHN): Effects of KitD814V and Jak2V617F in a Hematopoietic Mouse Model
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Abstract of Presentation	In systemic mastocytosis with an associated hematologic neoplasm (SM-AHN), additional oncogenic variants beyond KITD816V are frequently identified. Notably, Jak2V617F is recurrently detected in patients with SM associated with myelodysplastic/myeloproliferative neoplasms, occurring in approximately 11% of all SM-AHN cases. To investigate the potential cooperative effects of KitD814V (homologous to human KIT D816V) and Jak2V617F, we established a novel Scl-CreER;KitD814V;Jak2V617F mouse model in which both mutations are induced in the hematopoietic compartment. Disease pathogenesis and features were determined by serial complete blood counts, serum biomarkers such as murine mast cell (MC) protease-1, and histological evaluation of the skin and viscera to assess MC infiltration and tissue architecture. Preliminary survival analysis demonstrated that mice harboring both KitD814V and Jak2V617F mutations had shorter survival compared to mice with either mutation alone or wild-type controls. Over the course of 12 weeks after induction, complete blood counts indicate a modest rise in the white blood cell compartment (WBC) in KitD814V animals; instead, the double mutant shows a more prominent and

	progressive leukocytosis from weeks 8-12, with neutrophilia and monocytosis being the primary drivers of the WBC differential. Furthermore, the double-mutant mice present marked thrombocytosis, erythrocytosis, and elevated hemoglobin. Skin MC numbers and serum MC protease-1 levels appear comparably elevated in mice harboring KitD814V alone and those co-expressing KitD814V and Jak2V617F compared to wild-type controls. Thus far, these findings suggest that both mutations affect the survival of double-mutant mice despite exerting distinct biological impacts. While KitD814V predominantly drives MC-related characteristics, Jak2V617F largely contributes to the hematologic phenotype.