**Introduction**

Cutaneous T cell lymphoma (CTCL) is a heterogeneous group of extra-nodal non-Hodgkin lymphomas arising from transformation and clonal expansion of skin-homing T cells. An imbalance between Th1/Th2 cells with a Th2 bias is discussed as a possible immune-related mechanism of pathogenesis. Furthermore, pruritus is one of the major symptoms affecting health-related quality of life (HRQoL) of CTCL patients and is associated with high levels of IL31 expression. Epigenetic alterations have been described in the context of CTCL pathogenesis. Resminostat is a potent, orally bioavailable histone deacetylase (HDAC) inhibitor targeting class I, IIb and IV, and is currently in phase II of clinical development. Resminostat showed anti-tumoral in vitro efficacy by inhibiting proliferation of CTCL cell lines. Here, we investigated the molecular mechanism of action of the HDAC inhibitor resminostat in CTCL in vitro using a genome-wide approach.

**Epigenetic mode of action of the HDAC inhibitor resminostat in CTCL cell lines**

- **Resminostat increases global lysine acetylation**
- **Resminostat increases histone H3K27 acetylation on a genome-wide level in a dose-dependent manner**

**Resminostat broadly affects gene expression in CTCL cell lines**

- **HDAC inhibition by resminostat results in up- and down-regulation of gene expression**

**Resminostat affects pathogenesis-relevant targets in CTCL**

- **Resminostat modulates progression-associated genes**
- **Resminostat represses skin-homing receptor genes**
- **Resminostat reduces expression of pruritus markers**

**Conclusions from a genome-wide in vitro study of resminostat in CTCL**

- **Resminostat's effects are translated genome-wide in a dose-dependent manner**
  - HDACi resminostat increases histone H3K27 acetylation levels
  - Significant modulation of gene expression with pleiotropic effects
  - Regulation of both gene induction and repression

- **Resminostat regulates genes associated with CTCL pathogenesis**
  - Modulation of genes associated with CTCL disease progression
  - Switch from unfavorable Th2 to favorable Th1 gene expression
  - Reduced expression of skin-homing receptors
  - Repression of itching mediator (IL31)

- **Data support the clinical development of resminostat in CTCL in a maintenance setting**
- **Current phase II trial: RESMAIN**
  - Resminostat for Maintenance Treatment of Patients with Advanced Stage Mycosis FUNGOIDES (MF) or Sézary Syndrome (SS): NCT02953301

**Abstract 366**

**Poster board PB-029**

**Contact:** matthias.bergmann@4sc.com (www.4sc.com)