INTRODUCTION

MCL1 is a member of the anti-apoptotic BCL2 family of proteins and plays a critical role in mediating cellular homeostasis and promoting cell survival. It is frequently found to be overexpressed or overactivated in both solid tumors and hematologic malignancies.

• Increased expression of MCL1 is associated with a higher grade and poor prognosis in many tumor types.
• MCL1 has been implicated in mediating resistance to chemotherapeutic agents as well as targeted therapies.

RESULTS

PRT1419 is a potent and selective MCL1 inhibitor with robust pro-apoptotic activity and oral bioavailability. It demonstrates synergy in combination with targeted agents, including a BCL2 inhibitor or tyrosine kinase inhibitor, results in complete tumor regressions in the MV4-11 CDX model. Data represent mean ± SD. n = 15.

PRT1419 shows potent anti-proliferative activity in hematologic cancer cell lines. Data represent mean ± SD. n = 15.

PRT1419 shows synergy in combination with targeted agents in vitro and in vivo. Data represent mean ± SD. n = 15.

CONCLUSIONS

• PRT1419 is designed to be a potent, selective and orally active MCL1 inhibitor.
• PRT1419 demonstrates potent oral activity as monotherapy and in combination with standard of care therapies in various tumor types.
• PRT1419 can overcome resistance to multiple targeted therapies, particularly in myeloid malignancies.
• PRT1419 is currently under evaluation as an oral agent in a Phase 1 clinical trial in patients with relapsed/refractory hematologic malignancies (NCT04543305).