Systematic review: hepatosplenic T-cell lymphoma on biologic therapy for inflammatory bowel disease, including data from the Food and Drug Administration Adverse Event Reporting System.

**Abstract**

**BACKGROUND:** Hepatosplenic T-cell lymphoma (HSTCL) is a rare, poorly treatable malignancy associated with therapy for IBD. Current knowledge of HSTCL risk in IBD comes from an era of step-up therapy, before earlier use of biologics or combination therapy was advocated to achieve deep mucosal healing. HSTCL risk among newer biologic classes has also not been evaluated.

**AIMS:** To systematically characterise the association of HSTCL with biologic therapy for IBD.

**METHODS:** We conducted a literature search and query of the Food and Drug Administration Adverse Event Reporting System to summarise HSTCL cases among IBD patients with prior biologic exposure. Demographics and immunosuppression exposure were extracted. Patients were stratified by current regimen (combination therapy, biologic monotherapy or no biologic), and biologic class (anti-TNF, anti-integrin, anti-interleukin 12/23).

**RESULTS:** Sixty-two cases of HSTCL were identified from 2486 abstracts and 181 FDA Adverse Events Reporting System reports. The median age of affected patients was 28 years (range 12–81), and 83.6% were male, 84.7% had Crohn's disease. Five of 62 patients had no reported azathioprine/mercaptopurine exposure. Three patients within the cohort developed HSTCL after exposure to natalizumab, vedolizumab or ustekinumab; all three also had anti-TNF and azathioprine/mercaptopurine exposure. Forty-three of 49 (87.8%) patients with known outcomes died with a median survival of 5 months.

**CONCLUSIONS:** Consistent with existing data, almost all identified HSTCL cases among IBD patients on biologic therapy had azathioprine/mercaptopurine exposure, and all cases on patients exposed to biologics had anti-TNF exposure. These data suggest initiating a patient-centred discussion before starting anti-TNF therapy or other biologics.

PMID: 31990422 [PubMed — as supplied by publisher]

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**Application of an ex-vivo drug sensitivity platform towards achieving complete remission in a refractory T-cell lymphoma.**

PMID: 31988286 [PubMed — in process]

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**The histone deacetylase inhibitor romidepsin spares normal tissues while acting as an effective radiosensitiser in bladder tumours in vivo.**

PMID: 31990422 [PubMed — as supplied by publisher]
Abstract
Muscle-invasive bladder cancer has a 40–60% five-year survival rate with radical treatment by surgical removal of the bladder or radiotherapy-based bladder preservation techniques, including concurrent chemoradiation. Elderly patients cannot tolerate current chemoradiotherapy regimens and so often only receive radiotherapy which is less effective. We urgently need to find effective chemotherapy agents for use with radiotherapy combinations which are non-toxic to normal tissues and tolerated by elderly patients. We have identified HDACi as promising agents to study. Pan-HDAC inhibition, using panobinostat, is a good strategy for radiosensitisation, but more selective agents may be more useful radiosensitisers in a clinical setting, resulting in fewer systemic side effects. Here, we study the HDAC class I-selective agent romidepsin, which we predict to have fewer off-target effects than panobinostat, while maintaining an effective level of tumour radiosensitisation. In vitro effects of romidepsin were assessed by clonogenic assay and showed that romidepsin was effective in the nanomolar range in different bladder cancer cells and radiosensitised these cells. The radiosensitising effect of romidepsin was confirmed in vivo using superficial xenografts. The drug/irradiation combination treatment resulted in significant tumour growth delay but did not increase the severity of acute (3.75 days) intestinal normal tissue toxicity nor late toxicity at 29 weeks. Moreover, we showed that romidepsin treatment impaired both HR and NHEJ DNA repair pathways, suggesting that the disruption of the DNA repair pathways caused by romidepsin is a key mechanism for its radiosensitising effect in bladder cancer cells. The results of this study demonstrate that romidepsin is an effective radiosensitiser in vitro and in vivo and does not increase the acute and late toxicity after ionising radiation. As romidepsin is already in clinical use for the cutaneous T-cell lymphoma, a phase I clinical trial of romidepsin as a radiosensitiser could be considered in muscle-invasive bladder cancer.

PMID: 31987970 [PubMed — as supplied by publisher]