

but whether and how selective epigenetic inhibition counteracts the immune-excluded phenotype to sensitize ICB therapy remain incompletely defined. Here, we aimed to investigate the therapeutic efficacy and mechanistic basis of histone deacetylase 8 (HDAC8), a histone H3 lysine 27 (H3K27)-specific isoform, in HCC development and ICB responsiveness.

Methods The immune-modulatory and anti-tumor effects of HDAC8 inhibition via a HDAC8-selective inhibitor, PCI34051, were determined in orthotopic HCC mouse models. Molecular mechanisms and functional significance of HDAC8 inhibition were conducted by genome-wide H3K27ac ChIP-seq and RNAseq in HCC patient specimens, cancer cell lines, NOD-SCID and humanized mouse models. The efficacy of single or combined therapy with anti-programmed death-1-ligand-1 (anti-PD-L1) and PCI34051 was determined in orthotopic and spontaneous HCC mouse models.

Results Pharmacological inhibition of HDAC8 thwarted HCC tumorigenicity in immunocompetent but not immunodeficient mice. The tumor-suppressive effect of PCI34051 was abrogated by CD8⁺T cell depletion or regulatory T cell adoptive transfer. Chromatin profiling of human HDAC8-expressing HCCs revealed genome-wide H3K27 deacetylation in 1,251 silenced enhancer-target gene pairs that were enriched in metabolic and immune regulators. Mechanistically, down-regulation of HDAC8 increased global and enhancer levels of H3K27 acetylation to reactivate T cell-traffic chemokine production from HCC cells, thus relieving T cell exclusion in both NOD-SCID and humanized mouse models. In the HCC preclinical model, selective HDAC8 inhibition significantly increased tumor-infiltrating CD8⁺T cells and potentiated eradication of established hepatoma by anti-PD-L1 therapy without a sign of toxicity. Importantly, mice treated with HDAC8/PD-L1 co-blockade were protected against subsequent tumor re-challenge with the induction of memory T cells and remained tumor-free for ≥ 15 months.

Conclusions Our study demonstrates that selective HDAC8 inhibition elicits effective and durable ICB responses by co-opting adaptive immunity via enhancer reprogramming, thereby providing a new strategy for effective combined epigenetic immunotherapy.

Clinical gastroenterology

IDDF2020-ABS-0014 COMPARISON OF THE EFFICACY OF PIVIDONE-IODINE AND NORMAL SALINE WASH IN PREVENTING SURGICAL SITE INFECTIONS IN LAPAROTOMY WOUNDS-RANDOMIZED CONTROLLED TRIAL

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Background Povidone-Iodine has been utilized as a broad-spectrum antiseptic irrigation in the wound management processes for many years. However, some recent studies showed that the infection rate in laparotomy wounds decreases more by using normal saline.

The study aims to examine the decreasing infection rate in laparotomy wounds by comparing the effectiveness and safety of povidone-iodine solution with normal saline.

Methods The patients undergoing elective laparotomies were included and randomly assigned to 2 groups. In the first group(90), incision wounds were flushed with 5% povidone-iodine solution. In the second group(90), incisions were flushed with 0.9% normal saline solution. By comparing the infection rates of the wound, outcomes were measured between the two groups.

Results Surgical site infections were seen in 16 of 180(12.5%) patients in povidone-iodine versus 7 in normal saline groups. The difference in the infection rates in the two studied groups($p = 0.6$) has no statistical significance.

Conclusions The infection rate in laparotomy wounds did not increase or decrease when the wound was irrigated with 5% povidone-iodine solution or with 0.9% saline solution.

IDDF2020-ABS-0015 PRUCALOPRIDE IN THE TREATMENT OF CHRONIC GERD

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Background Treatment of persistence of gastroesophageal reflux disease (GERD) symptoms, despite readily available medications and lifestyle advocacy is challenging. Prucalopride, a selective high-affinity serotonin (5-HT₄) receptor agonist, has been a good therapeutic alternative. Data from large randomized, controlled clinical trials indicate that it is effective in chronic constipation and offers a new therapeutic alternative for those whose condition fails to respond to conventional laxatives. Clinical use of Prucalopride in GERD has been of immense use in patients refractory to the conventional pharmacological treatments.

Methods A 45-year-old type 2 diabetic, chronically constipated male gastroesophageal reflux disease-patients presented to our outpatient department with reflux symptoms and an increased number of reflux episodes. Gastroesophageal reflux was detected by multichannel impedance (MII) monitoring. He had been prescribed Pantoprazole and domperidone for his symptoms in the past but did not get relieved. We treated him with prucalopride (2 mg/day). The second MII-monitoring after the initiation of prucalopride 2 mg per day (plus pantoprazole 40 mg per day) showed an overall decrease in reflux episodes.

Results Numbers of all reflux episodes, as well as non-acid reflux episodes, were reduced in the patients. The objective findings were concordant with subjective reports of symptomatic relief. There were no major adverse events during therapy with prucalopride.

Conclusions Administration of prucalopride showed promising results in the treatment of persisting or weakly and/or non-acid reflux episodes in this chronically constipated patient. Therefore, prucalopride can be regarded as a good therapeutic option in the treatment of standard proton pump inhibitor-persistent reflux in the chronically constipated patients.