Budesonide reduces neratinib-induced diarrhea and intestinal inflammation in rats
Faculty Disclosure

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<tr>
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Neratinib: cancer drug causing diarrhea

- Neratinib (Puma Biotechnology): irreversible pan-ErbB tyrosine kinase inhibitor
- FDA approved for extended adjuvant treatment of HER2+ breast cancer
- Severe diarrhea: 40% of patients (no loperamide prophylaxis)¹

Our model

- Albino Wistar rats (90-100% of rats get diarrhea)
- Distal small intestine and colon
- Anatomical derangement
- **Inflammation** – linked with diarrhea

Budesonide

- Corticosteroid used to treat gastrointestinal disorders

Photomicrograph at 400x original magnification stained with Haematoxylin and Eosin (H&E)
Study design

- Male Albino Wistar rats (n=48); vehicle, neratinib only, neratinib + budesonide
- Collected intestinal tissue after 14 or 28 days treatment
- Clinical, histopathological and inflammatory measures
Diarrhea unrelated to serum neratinib concentration

- Budesonide significantly decreased mean number of days with moderate (grade 2) neratinib-induced diarrhea (10.0) vs. neratinib only (15.8)
- Budesonide did not significantly change serum neratinib concentrations
Budesonide decreased histological damage from neratinib in the proximal colon

These results were also observed in the distal ileum
Budesonide reduces apoptosis in the distal ileum

Distal ileum - 28 days: ↑ apoptosis
neratinib vs neratinib + budesonide

Proximal colon - 14 days:
↑ apoptosis neratinib vs vehicle

Data shows mean ± SEM

Neratinib 28 days colon
Example of positively stained cells
Budesonide alters cytokine ratios following neratinib

- Budesonide mitigated neratinib-induced inflammation and decreased diarrhea
- Moderate negative correlation between days with moderate diarrhea & IL-4 (rs=-0.61)
- Protection via altered cytokine ratios
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Cancer Treatment Toxicities Group

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*At time of study

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CANCER TREATMENT TOXICITIES GROUP

Integrating the pathogenesis, prediction and prevention of cancer-related side effects