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## Differential Diagnosis (DDX) of Carcinoid Syndrome Diarrhea (CSD): A Systematic Literature Review (SLR)

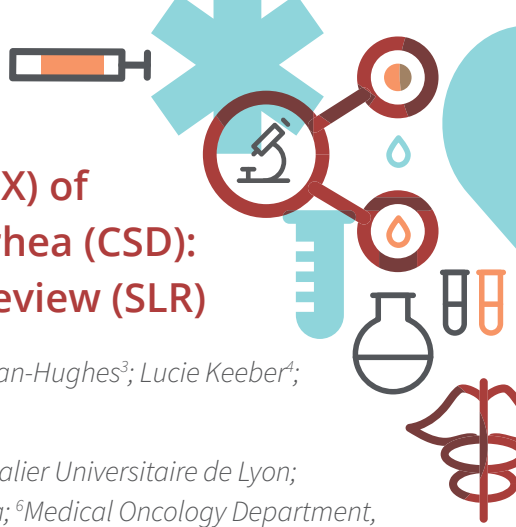
Mohid Khan<sup>1</sup>; Thomas Walter<sup>2</sup>; Amy Buchanan-Hughes<sup>3</sup>; Lucie Keeber<sup>4</sup>; Marion Feuilly<sup>5</sup>; Enrique Grande<sup>6</sup>

<sup>1</sup>University Hospital of Wales; <sup>2</sup>Centre Hospitalier Universitaire de Lyon; <sup>3</sup>Costello Medical; <sup>4</sup>Ipsen Ltd.; <sup>5</sup>Ipsen Pharma; <sup>6</sup>Medical Oncology Department, MD Anderson Cancer Center Madrid

**BACKGROUND:** CSD is related to serotonin secretion by neuroendocrine tumors (NETs). Although CS is often the cause of diarrhea among NET patients, alternative causes should be considered as these may require different treatment. However, there is no guidance on DDX of CSD in NET patients.

**METHODS:** MEDLINE/Embase/Cochrane Library were searched in September 2018 with terms for NETs, CS and diarrhea. Congress abstract books/bibliographies/ClinicalTrials.gov were hand-searched. Two independent reviewers screened articles at title/abstract and full text stage. Relevant studies reported quantitative or qualitative evidence relating to DDX of CSD; framework synthesis was used to synthesize heterogeneous evidence from these studies.

**RESULTS:** 46 publications were included. Most reported on pancreatic enzyme insufficiency (PEI) in NET patients. Other causes include bile acid malabsorption, small intestinal bacterial overgrowth, short bowel syndrome and infection. Diagnostic approaches include fecal elastase (FE) test, hydrogen breath test, SeHCAT scan and stool culture. Other approaches include assessment of patient history, diarrhea characteristics, and trials of treatment modification. There are limited data on effectiveness of approaches; quantitative evidence on FE tests was conflicting. If diarrhea is misdiagnosed, treatment may be deemed ineffective and underlying conditions could remain undetected.



**CONCLUSION:** Evidence on DDx of CSD is limited. PEI is a common topic of discussion, with little data available on other causes of diarrhea in NET patients. While the necessity of DDx of CSD is recognized in the literature, the most effective diagnostic algorithm is unclear.