

## P-6

# The use of Antidepressants is associated with Mesenteric Mass Formation of Ileum Neuroendocrine Tumors

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### BACKGROUND

Serotonin production by ileum neuroendocrine tumors (i-NETs) is considered a critical mediator of the fibrotic reaction in mesenteric mass (MM)/ lymph node metastasis. Antidepressants modify serotonin dynamics: however, their role in MM formation is uncertain. We hypothesized that histories of antidepressant use affect MM formation. This study examined the correlation between antidepressant use and MM formation.

### METHODS

One hundred eighty-two patients who underwent resection of primary i-NET in a single institution between January 2007 and February 2023 were included retrospectively in this study. Use of antidepressants, including SSRI, SNRI, Trazodone, Mirtazapine, Amitriptyline, Bupropion, and St John's Wort prior to referral, was collected from patient records. Mesenteric mass was defined as at least 1 cm diameter from pathological or radiological findings. A multivariable Cox proportional hazards regression model was used to calculate for antidepressant and exposure the hazard ratio of overall mortality from date of resection.

### RESULTS

Out of 182 patients, 42 (23%) had a history of antidepressant use. Specifically, 26 patients used SSRI or SSNI, 10 used non-SSRI/SSNI, and 6 used both SSRI or SSNI and non-SSRI/SSNI. Patients with an antidepressant history had a higher frequency of MM formation than those without (93% vs 75%, p-value = 0.014). In detail, MM formation was observed in 96% of those with SSRI or SSNI, 80% of those with non-SSRI/SSNI, and 100% of those who used both SSRI or SSNI and non-SSRI/SSNI. There was no significant difference in the rate of complete surgical lymph node dissection (78% vs 79%, p-value > 0.9). On multivariate analysis, MM formation (3.3 [1.24-9.0], 0.017), tumor grade 2/3 vs 1 (2.6 [1.35-4.9], 0.004), and hepatic metastasis (4.0 [1.74-9.1], 0.001) were associated with overall survival; however, antidepressant use was not (hazard ratio 1.2 [95% CI 0.57-2.6], p-value = 0.62).

Table. Patient characteristics.

Characteristic	Antidepressant use		P-value <sup>2</sup>
	NO, N = 140 <sup>1</sup>	YES, N = 42 <sup>1</sup>	
Urine 24h 5-HIAA (mg/day)	20 (7, 62)	10 (6, 22)	0.084
Carcinoid syndrome (+)	80 (58%)	18 (43%)	0.077
Flushing (+)	44 (32%)	5 (12%)	<b>0.010</b>
Mesenteric Mass (+)	96 (75%)	37 (93%)	<b>0.014</b>
Tumor Grade (1)	74 (58%)	27 (69%)	0.22
Liver metastasis (+)	78 (57%)	15 (37%)	<b>0.022</b>
Follow-up (months)	54 (26, 91)	35 (9, 69)	<b>0.010</b>
<sup>1</sup> Median (IQR); n (%), <sup>2</sup> Wilcoxon rank sum test; Pearson's Chi-squared test			

## CONCLUSIONS

Antidepressant use was associated with an increase in MM formation in i-NETs. The reasons for this are unclear and deserve further study.

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