

**Supplementary Table 1. Inclusion and Exclusion Criteria for Level 1 (Titles and Abstracts) and Level 2 (Full Text) Screening for Clinical Efficacy**

Criteria	Included	Excluded
Population	<p>Studies in patients with NETs originating from different locations in the body:</p> <ul style="list-style-type: none"> <li>▪ GI NET</li> <li>▪ Lung</li> <li>▪ Pancreas</li> </ul>	<ul style="list-style-type: none"> <li>▪ Studies in patients with non-NET tumors only</li> </ul>
Interventions	<ul style="list-style-type: none"> <li>▪ Long-acting octreotide (depot injection)</li> <li>▪ Octreotide acetate (SC)</li> <li>▪ Comparative trials that include octreotide monotherapy as 1 of the treatment arms</li> </ul>	<ul style="list-style-type: none"> <li>▪ Studies examining interventions other than the drug therapies listed (e.g., radiopharmaceutical therapy and combination therapy, including combination therapy with octreotide, where octreotide monotherapy is not an intervention)</li> </ul>
Outcomes	<p>Efficacy:</p> <ul style="list-style-type: none"> <li>▪ Objective response rate, complete response, unconfirmed complete response, partial response, stable disease rate, progression rate</li> <li>▪ Duration of response</li> <li>▪ Progression-free survival</li> <li>▪ Time to tumor progression</li> <li>▪ OS or any other measure that stands for prolonged survival or control of tumor growth</li> </ul>	<ul style="list-style-type: none"> <li>▪ Health-related quality of life outcomes</li> <li>▪ Biomarker analyses</li> <li>▪ Only baseline diagnostic measures</li> <li>▪ Other outcomes not listed in the inclusion criteria</li> </ul>
Study design	<ul style="list-style-type: none"> <li>▪ All clinical trials, if outcomes of interest are included</li> <li>▪ All prospective or retrospective observational studies</li> <li>▪ Population study using SEER or other databases (e.g., claim databases or EMR databases)</li> <li>▪ Prognostic studies if octreotide is considered a prognostic factor</li> <li>▪ Case-series evaluations</li> </ul>	<ul style="list-style-type: none"> <li>▪ Biomarker analyses</li> <li>▪ Genetic studies</li> <li>▪ Diagnostic studies</li> <li>▪ Health-related quality of life studies</li> <li>▪ Outcomes other than those listed for inclusion</li> <li>▪ Commentaries</li> <li>▪ Editorials</li> <li>▪ Phase 1 studies that do not report OS outcomes</li> <li>▪ Studies in which octreotide combination therapy is used in at least 1 treatment arm and the other treatment arm(s) also includes octreotide, either in combination with another agent(s) or as monotherapy, and there is no placebo or best-of-care arm to which octreotide monotherapy is compared</li> <li>▪ Expert opinion</li> <li>▪ Literature reviews<sup>a</sup></li> </ul>

EMR, electronic medical record; GI, gastrointestinal; NET, neuroendocrine tumor; OS, overall survival; SEER, Surveillance, Epidemiology, and End Results; SC, subcutaneous.

<sup>a</sup> These will be identified during the screening process and used to identify any studies that meet inclusion criteria and were not captured by the literature search.

**Supplementary Table 2. Comparative Studies With Octreotide Monotherapy as 1 Treatment Arm in Studies Assessing Neuroendocrine Tumors**

First Author/ Study	Study Design	No. of Patients	Tumor Type	Treatment and Dose	PR, %	SD, %	PFS, mo	Median OS, mo
<b>Everolimus plus octreotide vs octreotide alone</b>								
Pavel et al. (2011) <sup>[25]</sup> / RADIANT-2	RCT (primary analysis)	429	Low- to intermediate-grade advanced NET with various origin	<ul style="list-style-type: none"> <li>Everolimus 10 mg + LA OCT 30 mg (n=216) vs</li> <li>LA OCT 30 mg (+ PBO) every 28 d (n=213)</li> </ul>	<ul style="list-style-type: none"> <li>4 vs 12</li> <li>Comparison NR</li> </ul>	<ul style="list-style-type: none"> <li>84 vs 81</li> <li>Comparison NR</li> </ul>	<ul style="list-style-type: none"> <li>16.4 (95% CI, 13.7-21.2) vs 11.3 (8.4-14.6)</li> <li>HR, 0.77; 95% CI, 0.59-1.00; 1-sided log-rank test <math>P=.026</math></li> </ul>	—
Anthony et al. (2015) <sup>[26]</sup> / RADIANT-2	RCT (subgroup analysis of previous SSA vs no previous SSA)	429	Progressive advanced NET with small intestine origin	<ul style="list-style-type: none"> <li>Everolimus 10 mg + LA OCT 30 mg (previous SSA use; n=173) vs</li> <li>LA OCT 30 mg (+ PBO) (previous SSA use; n=166) every 28 d</li> </ul>	—	—	<ul style="list-style-type: none"> <li>Previous SSA use: 14.3 (95% CI, 12.0-20.1) vs 11.1 (8.4-14.6)</li> <li>HR, 0.81; 95% CI, 0.60-1.09; <math>P=.077</math></li> <li>SSA naïve: 25.2 (95% CI, 12.0-not reached) vs 13.6 (8.2-22.7)</li> <li>HR, 0.63; 95% CI, 0.35-1.11; <math>P=.054</math></li> </ul>	—
Castellano et al. (2013) <sup>[27]</sup> / RADIANT-2	RCT (subgroup analysis in colorectal NET)	39	Colorectal NET	Everolimus 10 mg + LA OCT 30 mg (n=19 with colorectal NETs) vs LA OCT 30 mg (+ PBO) every 28 days (n=20 with colorectal NETs)	<ul style="list-style-type: none"> <li>67 vs 37</li> <li>Comparison NR</li> </ul>	—	<ul style="list-style-type: none"> <li>29.9 (95% CI, 5.6-not reached) vs 6.6 (95% CI, 3.0-13.0)</li> <li>HR, 0.34; 95% CI, 0.13-0.89; <math>P=.011</math></li> </ul>	—
Fazio et al. (2013) <sup>[28]</sup> / RADIANT-2	RCT (subgroup analysis in lung NET)	44	Low- to intermediate-grade advanced NET with lung origin	Everolimus 10 mg + LA OCT 30 mg (n=33) vs LA OCT 30 mg (+ PBO) (n=11) every 28 d	0 vs 0	—	<ul style="list-style-type: none"> <li>13.63 vs 5.59</li> <li>HR, 0.72; 95% CI, 0.31-1.68</li> <li><math>P=.228</math></li> </ul>	—
Strosberg et al. (2015) <sup>[29]</sup> / RADIANT-2	RCT (subgroup analysis in placebo arm)	196 (foregut, midgut, or hindgut NET) SSA naïve n=41; Previous SSA n=155	Low- or intermediate-grade advanced NET with midgut (74%), foregut (16%), or hindgut (11%) origin	LA OCT 30 mg (plus placebo)	—	—	<ul style="list-style-type: none"> <li>Previous SSA: 11.1 (95% CI, 8.4-14.3)</li> <li>SSA naïve: 13.6 (95% CI, 8.2-22.7)</li> <li>Comparison NR</li> </ul>	<ul style="list-style-type: none"> <li>Previous SSA: 33.5 (95% CI, 27.5-44.7)</li> <li>SSA naïve: 50.6 (95% CI, 36.4-not reached)</li> <li>Comparison NR</li> </ul>

First Author/ Study	Study Design	No. of Patients	Tumor Type	Treatment and Dose	PR, %	SD, %	PFS, mo	Median OS, mo
<b>Interferon-α plus octreotide vs octreotide alone</b>								
Arnold et al. (2005) <sup>[30]</sup>	RCT	105	Progressive metastatic NET with midgut (49.0%), foregut (33.3%), or unknown (17.6%) origin	<ul style="list-style-type: none"> <li>▪ OCT SC 200 µg 3 times daily (n=51) vs</li> <li>▪ OCT SC 200 µg 3 times daily + IFN-α 4.5 × 10<sup>6</sup> IU 3 times daily (n=54)</li> </ul>	<ul style="list-style-type: none"> <li>▪ 2 vs 9.3</li> <li>▪ Comparison NR</li> </ul>	<ul style="list-style-type: none"> <li>▪ 15.7 vs 14.8</li> <li>▪ Comparison NR</li> </ul>	<ul style="list-style-type: none"> <li>▪ 6 vs 6</li> <li>▪ Comparison NR</li> </ul>	—
Kolby et al. (2003) <sup>[31]</sup>	RCT	68	Midgut carcinoid	<ul style="list-style-type: none"> <li>▪ OCT SC 100 µg twice daily or up to 200 µg 3 times daily (n=35) vs</li> <li>▪ OCT + IFN-α 5 × 10<sup>6</sup> units 5 d/wk (n=33)</li> </ul>	—	—	—	— [Mean 5-y survival: 36.6% vs 56.8%; HR, 0.62; 95% CI, 0.33-1.16; <i>P</i> =.132]
<b><sup>177</sup>Lu-Dotatate plus octreotide 30 mg vs octreotide 60 mg</b>								
Strosberg et al. (2017) <sup>[32]</sup>	RCT	229	Midgut NET	OCT 60 mg every 4 wk	18 vs 3; <i>P</i> <.001	—	<ul style="list-style-type: none"> <li>▪ Median PFS, <sup>177</sup>Lu-Dotatate + OCT: not reached vs OCT, 8.4</li> <li>▪ HR, 0.21; 95% CI, 0.13-0.33; <i>P</i>&lt;.001</li> </ul>	<ul style="list-style-type: none"> <li>▪ <sup>177</sup>Lu-Dotatate + OCT: 14 deaths vs OCT: 26 deaths</li> <li>▪ HR, 0.40; <i>P</i>=.004</li> </ul>

CI, confidence interval; HR, hazard ratio; IFN, interferon; LA, long-acting; NET, neuroendocrine tumor; NR, not reported; OCT, octreotide; OS, overall survival; PBO, placebo; PFS, progression-free survival; PR, partial response; RCT, randomized controlled trial; SC, subcutaneous; SD, stable disease; SSA, somatostatin analog.

**Supplementary Table 3. Single-Arm Studies of Octreotide for Neuroendocrine Tumors**

First Author	Study Design	No. of Patients	Tumor Type	Treatment and Dose	Treatment Duration, mo	PR, %	SD, %	PFS, mo	Median OS, mo
Angeletti et al. (1999) <sup>[10]</sup>	CT	7	▪ Metastatic NET with GEP origin	OCT SC 500 µg every day	12 with 10-wk follow-up	14.3	85.7	—	—
Anthony et al. (1993) <sup>[9]</sup>	CT	14	▪ Tumor pathology: NR ▪ Tumor stage: metastatic NET with foregut (21.4%) or midgut (78.6%) origin	OCT SC 500-2000 µg every 8 hours	NR	31	15	—	—
Arnold et al. (1996) <sup>[37]</sup>	CT	103	▪ Moderate or well differentiated metastatic NET with GEP origin	OCT SC 200-500 µg 3 times daily	>6; follow-up to 36 in some patients	0	12.6	—	—
Arnold et al. (1993) <sup>[38]</sup>	CT	85	▪ Tumor pathology: NR ▪ Tumor stage: NR ▪ Tumor origin: GEP	OCT 200 µg 3 times daily	NR	4.4	50	—	—
Bajetta et al. (2005) <sup>[39]</sup>	CT	31	▪ Well-differentiated advanced NET with various origin	LA OCT 30 mg every 28 d	NR	6	52	—	Not reached
Butturini et al. (2006) <sup>[33]</sup>	RCT	21	▪ Well differentiated, nonfunctioning advanced NET with pancreas origin	OCT (100 µg 3 times daily for 2 wk, followed by OCT acetate LAR 20 mg on day 14 and then every 28 d until PD was observed)	IQR, 26-67; median, 49.5	—	28	41	—
Chung et al. (2001) <sup>[40]</sup>	CT	10	▪ Tumor pathology: NR ▪ Progressive, metastatic, carcinoid with mostly (65%) gastrointestinal origin	Adjuvant LA OCT every month (specific dose NR)	26	—	—	—	— (3-y OS: 100%; 5-y OS: 31%)
di Bartolomeo et al. (1996) <sup>[41]</sup>	CT	58	▪ Tumor pathology: NR ▪ Progressive, advanced carcinoid or pNET with various origin	OCT SC <sup>a</sup> 500 µg (n=23) or 1000 µg (n=35)	Median 12	3	47	—	22 (1-32+)
Janson and Oberg (1993) <sup>[42]</sup>	CT	43 (55 total)	▪ Tumor pathology: NR ▪ Progressive, advanced carcinoid or pNET with midgut (78.2%), foregut (1.8%), or unlocalized (20.0%) origin	OCT SC 100 µg twice daily (median starting dose)	Median, 14 (range, 1-58)	—	49	—	—
Panzuto et al. (2006) <sup>[43]</sup>	CT	31	▪ Tumor pathology: NR – Well differentiated, progressive metastatic NET with pancreas (56.0%), intestine (35.5%), or unknown (2.0%) origin	LA OCT 30 mg every 28 d	6-60; median, <sup>b</sup> 26.5	0	47.6	—	—
Ricci et al. (2000) <sup>[44]</sup>	CT	15	▪ Tumor pathology: NR ▪ Metastatic NET ▪ Tumor origin: NR	LA OCT 20 mg every 4 wk	3-12+; median, 7	7	40	—	—

First Author	Study Design	No. of Patients	Tumor Type	Treatment and Dose	Treatment Duration, mo	PR, %	SD, %	PFS, mo	Median OS, mo
Saltz et al. (1993) <sup>[45]</sup>	RCT	34	<ul style="list-style-type: none"> <li>Tumor pathology: NR</li> <li>Advanced incurable NET</li> <li>Tumor origin: NR</li> </ul>	OCT SC 50 µg twice daily to 150-250 µg 3 times daily	1-47; median, 29	0	50	—	—
Shojamanesh et al. (2002) <sup>[34]</sup>	CT	15	<ul style="list-style-type: none"> <li>Tumor pathology: NR</li> <li>Malignant gastrinoma with progressive hepatic metastases with mostly (80%) pancreas origin</li> </ul>	<ul style="list-style-type: none"> <li>OCT SC 100-200 µg every 12 h</li> <li>LA OCT 20-30 mg every mo</li> </ul>	3-54	6	47	—	—
Tomassetti et al. (2000) <sup>[11]</sup>	CT	16	<ul style="list-style-type: none"> <li>Tumor pathology: NR</li> <li>Advanced carcinoid or pNET with mostly (56.25%) ileum origin</li> </ul>	LA OCT 20 mg every 28 d	6-15; mean, 11	0	87.5	—	—
<b>Different octreotide dosing regimens but reporting only overall results</b>									
Al-Efraij et al. (2015) <sup>[46]</sup>	RWE	37	<ul style="list-style-type: none"> <li>Tumor pathology: NR</li> <li>Metastatic, unresectable NET with various origin</li> </ul>	LA OCT (40, 50, or 60 mg every mo) <sup>c</sup> (n=37)	24	—	29 (any dose)	—	—
Laskaratos et al. (2016) <sup>[47]</sup>	RWE	254	<ul style="list-style-type: none"> <li>Tumor pathology: NR</li> <li>Tumor stage: NR</li> <li>Mostly (80%) small bowel origin</li> </ul>	<ul style="list-style-type: none"> <li>LA OCT 20 mg every 28 d (n=198)</li> <li>LA OCT 30 mg every 28 d (n=56)</li> </ul> <p>If patient was OCT naïve, an initial test dose of 50 µg was used.</p>	Mean follow-up: 42	5 (any dose)	—	—	—
Öberg et al. (1991) <sup>[48]</sup>	RWE	22	<ul style="list-style-type: none"> <li>Tumor pathology: NR</li> <li>Metastatic midgut carcinoids</li> </ul>	OCT SC 50 µg twice daily Median 200 µg 3-4 times daily	1-30; median, 12	28	36	—	—
Ramundo et al. (2014) <sup>[49]</sup>	RWE	20	<ul style="list-style-type: none"> <li>Tumor pathology: NR</li> <li>Tumor stage: NR</li> <li>Duodenal-pancreatic origin</li> </ul>	LA OCT 30 mg every 28 d	NR	—	80	—	—
Saglam et al. (2015) <sup>[36]</sup>	RWE	23	<ul style="list-style-type: none"> <li>Tumor pathology: NR</li> <li>Unresectable local advanced or metastatic GEP-NET with pancreas (43.5%), midgut-hindgut (39.1%), or stomach (17.4%) origin</li> </ul>	LA OCT 30 mg every 4 wk	Median follow-up: 47.9 (8.2-111.7)	17.4	60.9	22.4	70.1
Welin et al. (2004) <sup>[35]</sup>	RWE	12	<ul style="list-style-type: none"> <li>Tumor pathology: NR</li> <li>Midgut carcinoid</li> </ul>	OCT SC 160 mg every 2-4 wk (high dose)	12	—	Median, 12 mo: 75	—	37
Wang et al. (2017) <sup>[50]</sup> (abstract)	RWE	NR	<ul style="list-style-type: none"> <li>Tumor pathology: NR</li> <li>Well-differentiated advanced NET with GEP origin</li> </ul>	LA OCT dose and interval NR	NR	—	79.6	—	—

CT, controlled trial; GEP-NET, gastroenteropancreatic neuroendocrine tumor; IQR, interquartile range; LA, long-acting; LAR, long-acting repeatable; mo, month; NET, neuroendocrine tumor; NR, not reported; OCT, octreotide; OS, overall survival; PD, progressive disease; PFS, progression-free survival; pNET, pancreatic neuroendocrine tumor; PR, partial response; RCT, randomized controlled trial; RWE, real-world evidence; SC, subcutaneous; SD, stable disease.

a Results not stratified by dosage.

b Median duration of treatment includes all drug regimens (ie, octreotide and lanreotide; prospective noncomparative analysis).

c Results not stratified by dosage.