

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Strosberg J, El-Haddad G, Wolin E, et al. Phase 3 trial of ¹⁷⁷Lu-Dotatate for midgut neuroendocrine tumors. N Engl J Med 2017;376:125-35. DOI: 10.1056/NEJMoa1607427

¹⁷⁷LU-DOTATATE PHASE 3 TRIAL IN MIDGUT NEUROENDOCRINE TUMORS

SUPPLEMENTARY APPENDIX

TABLE OF CONTENTS

Acknowledgements	2
Supplementary Table S1. Demographic and Baseline Clinical Characteristics of the Patients at Enrollment (Full Analysis Set)	3
Supplementary Table S2. ¹⁷⁷ Lu-DOTATATE Exposure.	4
Safety Assessments	6
Supplementary Figure 1. CONSORT Flow Diagram.	12
Supplementary Figure 2. Relative Change from Baseline in (a) Leukocyte Count.	13
Supplementary Figure 2. Relative Change from Baseline in (b) Lymphocyte Count.	13
Supplementary Figure 2. Relative Change from Baseline in (c) Neutrophil Count.	13
Supplementary Figure 2. Relative Change from Baseline in (d) Platelet Count.	14
Supplementary Figure 3. Creatinine Clearance Over Time in the Study.	14

Acknowledgements

We thank the participating patients and their families, as well as the global network of research nurses, trial coordinators, and operations staff for their contributions, and the investigators whose patients were enrolled in this trial, including: **Belgium:** Eric Van Cutsem; **France:** Catherine Ansquer, Eric Baudin, Frederic Courbon, Francesco Giammarile, Philippe Ruzsniowski, David Taieb; **Germany:** Richard P. Baum, Marianne Pavel, Klemens Scheidhauer, Matthias Weber; **Italy:** Lisa Bodei, Ernesto Brianzoni, Gianfranco Delle Fave, Maria Chiara Grana, Giuliano Mariani, Guido Rindi, Ettore Seregni, Stefano Severi; **Portugal:** Isabel Azevedo; **Spain:** Enrique Grande, Jaime Mora; **Sweden:** Kjell Öberg, Anders Sundin; **United Kingdom:** Adil Al-Nahas, Martyn Caplin, Nick Freemantle, Ashley Grossman, Prakash Manoharan, Nicholas Reed, Rajaventhana Srirajaskanthan; **USA:** Lowell Anthony, Al B. Benson, Jordan Berlin, David Bushnell, Ebrahim Delpassand, Stanley Garbus, Andrew Hendifar, Timothy Hobday, Matthew Kulke, Larry Kvols, David Metz, Erik Mittra, Michael Morse, Meike Schipper, Jonathan Strosberg, Edward Wolin, James Yao.

Funded by Advanced Accelerator Applications; ClinicalTrials.gov number NCT01578239;

EudraCT number 2011-005049-11.

Supplementary Table S1. Demographic and Baseline Clinical Characteristics of the Patients at Enrollment (Full Analysis Set)

Characteristic	¹⁷⁷ Lu-DOTATATE (N = 116)	Octreotide LAR 60 mg (N = 113)
Gender— no. (%)		
Female	53 (46)	60 (53)
Male	63 (54)	53 (47)
Mean age (SD) — yr	63 (±9)	64 (±10)
Mean BMI (±SD) — kg/m²	25 (±5)	26 (±7)
Continent of origin— no. (%)		
USA	66 (57)	69 (61)
EU	50 (43)	44 (39)
Median time since diagnosis — yr	3.8	4.8
Mean KPS (SD)	88.6 (±9.32)	88.0 (±9.56)
Primary tumor site — no. (%)		
Jejunum	6 (5)	9 (8)
Ileum	86 (74)	82 (73)
Small intestine	11 (9)	12 (11)
Appendix	1 (1)	2 (2)
Right colon	3 (3)	1 (1)
Midgut (not otherwise specified)	9 (8)	7 (6)
Site of metastasis — no. (%)		
Liver	97 (84)	94 (83)
Lymph nodes	77 (66)	65 (58)
Mesentery	17 (15)	8 (7)
Bone	13 (11)	12 (11)
Lungs	11 (9)	5 (4)
Peritoneum	7 (6)	10 (9)
Ovaries	1 (1)	9 (8)
Other	15 (13)	10 (9)

Ki67 index — no. (%)		
Grade 1/2	76/40 (66/35)	81/32 (72/28)
SRS, Krenning scale — no. (%)[†]		
Grade 2	11 (10)	12 (11)
Grade 3	34 (29)	34 (30)
Grade 4	71 (61)	67 (59)
Median chromogranin A (quartiles) — µg/l[§]	604 (247–2626)	648 (290 – 2674)
Median 5-HIAA (quartiles)[‡] — mg/24hr[§]	36 (17-126)	44 (21-92)
Median serum alkaline phosphatase (quartiles) — U/l[§]	99 (74-160)	106 (75-152)
Previous treatments—no. (%)[*]		
Surgery	93 (80)	93 (82)
Tumor resection	90 (78)	93 (82)
Tumor ablation	6 (5)	11 (10)
Targeted therapy^{**}	19 (16)	17 (15)
Embolization[#]	18 (16)	13 (12)
Chemotherapy	11 (9)	14 (12)
Interferon	8 (7)	7 (6)
Angiogenesis inhibitor	6 (5)	2 (2)
Radiotherapy (external beam radiation)	4 (3)	6 (5)
PRRT	1 (1)	0 (0)
Investigational drug	1 (1)	1 (1)
¹³¹ I MIBG	0 (0)	2 (2)

5-HIAA denotes 5-hydroxyindoleacetic acid, BMI body mass index, PRRT peptide receptor radionuclide therapy, SD standard deviation, and SRS somatostatin receptor scintigraphy.

[†]Highest grade.

[‡]Available in 82 and 84 patients, in ¹⁷⁷Lu DOTATATE and Octreotide LAR 60 mg group, respectively

^{*}Other than somatostatin analogs (100% at study entry, inclusion criteria)

^{**}Includes everolimus, temsirolimus, sunitinib, imatinib, sorafenib, pazopanib, axitinib and gefitinib

[#]Includes chemo-embolization, radio-embolization and trans-arterial embolization

[§]Normal range: CgA, 19.4 to 98.1 µg/l; 5HIAA, 0 to 15 mg/24hrs; AP, 0 to 150 U/l.

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.