

EVINEC

Safety and efficacy of everolimus as second-line treatment in neuroendocrine neoplasms G3 - an AIO phase II study

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Madrid, 22 October 2023



DECLARATION OF INTERESTS

Marianne Pavel

Compensation as speaker, consultant or advisory board member: AAA, Novartis, IPSEN, Hutchmed, Amgen, Boehringer Ingelheim, Lilly, Recordati, Riemser

Research funding paid to institution in respect of work as a Local or Coordinating Investigator: AAA, Novartis, ITM, IPSEN, AIO Studien GmbH

Stocks- none

Licensing fees or royalties – none

Leadership position for ENETS (president and vice president), ESMO educational Committee, AIO Studien GmbH

Advisor for patient support groups (INCA; Netzwerk NET)

EVINEC | Study Design

Open-label,
prospective, single
arm, multicenter
phase II study

N = 40

Inclusion:

- **NEC G3 or NET G3**
(incl. NET G1/2 that switched to G3)
- Progression during or after **1L platinum-based chemotherapy**
- Measurable disease according to RECIST 1.1
- ECOG status 0 – 2

**Treatment:
Everolimus
10 mg/day**

Endpoints:

- Primary: **Safety**
- Secondary:
ORR, DCR, PFS, OS, QoL
- Exploratory:
Tumor markers
(chromogranin A , neuron-specific enolase)

Recruitment: September 2015 - February 2019
39 patients at 9 study sites in Germany



EVINEC | Patients: Demographics & Baseline Characteristics

N = 39
Enrolled



N = 36
Eligible after
Central Review



N = 30
Per Protocol Set *

		N = 36	
Age (y)	Median	57	
	Range	30 - 77	
Sex (n, %)	M	22 (61.1)	
	F	14 (38.9)	
ECOG status (n, %)	0	24 (66.7)	
	1	11 (30.6)	
	2	1 (2.8)	
Time from initial diagnosis until enrolment (months)	Median	9.1	
	Range	2.1 - 61.5	
Previous chemotherapy (n, %)	Cisplatin/etoposide	23 (63.9)	
	Carboplatin/etoposide	10 (27.8)	
	Carboplatin mono	1 (2.8)	
	FOLFOXIRI	1 (2.8)	
	Other	1 (2.8)	
Disease stage IV at screening (n, %)		36 (100)	

		N = 36 n (%)
Primary tumor location	Pancreas	14 (38.9)
	Unknown primary	6 (16.7)
	Colon	4 (11.1)
	Stomach	2 (5.6)
	Esophagus	1 (2.8)
	Duodenum	1 (2.8)
	Papilla vateri	1 (2.8)
	Appendix	1 (2.8)
	Rectum	1 (2.8)
	Cervix uteri	1 (2.8)
Ki67	Ovary	1 (2.8)
	Prostate	1 (2.8)
	≤ 55%	23 (63.9)
> 55%	13 (36.1)	

* Patients were excluded from the PP set because they received study medication for less than two weeks (n=4) or due to withdrawal of consent (n=2).

EVINEC | Histological Subgroups: Local vs. central review

	Local pathologies N = 39, n (%)	Central review N = 39, n (%)
NET G3	7 (17.9)	13 (33.3)
NEC	32 (82.1)	14 (35.9)
MiNEN	0 (0.0)	9 (23.1)
Other *	0 (0.0)	3 (7.7)

* Other:

- acinar cell carcinoma with neuroendocrine portion < 5%
- MiNEN with NET G1
- Undifferentiated carcinoma

Consistent results between local pathologies and central review:

16/39 samples (41%)

Inconsistent results:

23/39 samples (59%)

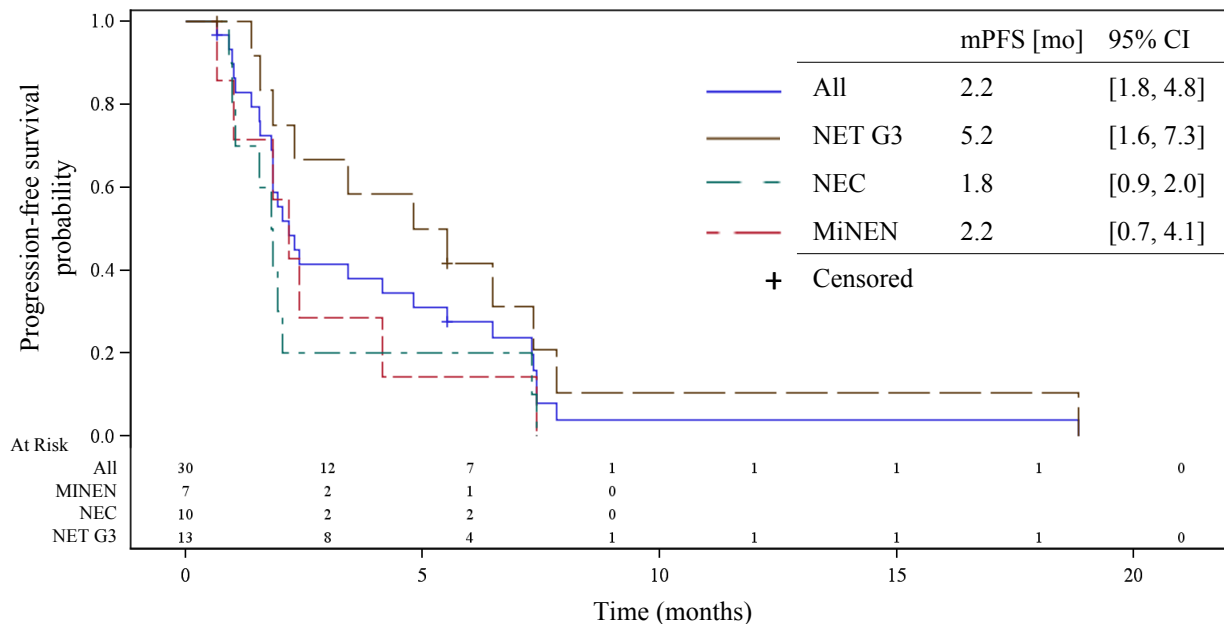
Local pathologies	Central review	N = 39 n (%)
NEC	NET G3	9 (23.1)
	NEC	12 (30.8)
	MiNEN	8 (20.5)
	Other *	3 (7.7)
NET G3	NET G3	4 (10.3)
	NEC	2 (5.1)
	MiNEN	1 (2.6)

EVINEC | Safety Results

Adverse events of special interest

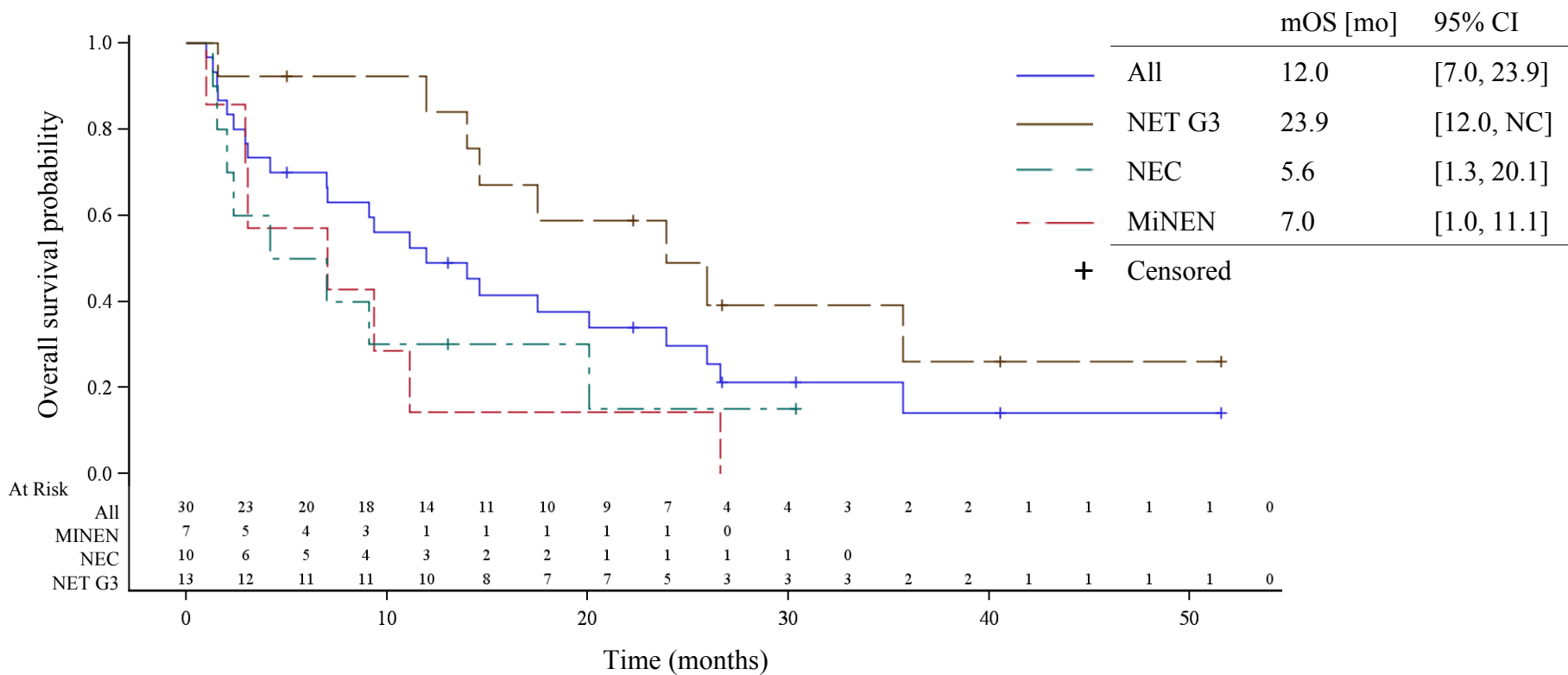
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	All
Infections and infestations	4 (11.1)	5 (13.9)	2 (5.6)	-	-	11 (30.6)
Urinary tract infection	-	3 (8.3)	-	-	-	3 (8.3)
Nasopharyngitis	3 (8.3)	-	-	-	-	3 (8.3)
Bacterial infection	-	1 (2.8)	-	-	-	1 (2.8)
Respiratory tract infection	-	-	-	2 (5.6)	-	2 (5.6)
Bacterial disease carrier	1 (2.8)	-	-	-	-	1 (2.8)
Fungal infection	-	1 (2.8)	-	-	-	1 (2.8)
Fungal skin infection	1 (2.8)	-	-	-	-	1 (2.8)
Gastroenteritis	-	1 (2.8)	-	-	-	1 (2.8)
Influenza	-	1 (2.8)	-	-	-	1 (2.8)
Pneumonia	-	1 (2.8)	-	-	-	1 (2.8)
Sepsis	-	-	1 (2.8)	-	-	1 (2.8)
Pneumonitis	1 (2.8)	1 (2.8)	-	-	-	2 (5.6)
Cerebral hemorrhage	-	-	-	-	1 (2.8)	1 (2.8)
Thrombosis	-	1 (2.8)	-	-	-	1 (2.8)
Hyperglycemia	1 (2.8)	1 (2.8)	1 (2.8)	-	-	3 (8.3)
Hypophosphatemia	2 (5.6)	1 (2.8)	-	-	-	3 (8.3)

EVINEC | Efficacy Results: PFS, Response Rates



		PR Partial remission	SD Stable disease	PD Progressive disease	ORR	DCR
All	N=30	1 (3.3)	13 (43.3)	16 (53.3)	1 (3.3)	14 (46.7)
NET G3	N=13	1 (7.7)	8 (61.5)	4 (30.8)	1 (7.7)	9 (69.2)
NEC	N=10	0 (0.0)	3 (30.0)	7 (70.0)	0 (0.0)	3 (30.0)
MiNEN	N=7	0 (0.0)	2 (28.6)	5 (71.4)	0 (0.0)	2 (28.6)

EVINEC | Efficacy Results: OS



EVINEC | Conclusions

- No new safety signals for EVE after prior platinum-based therapy in NEN G3 were identified; reported adverse events are consistent with those reported in other trials in NET
- The data support efficacy of Everolimus in NET G3 but show insufficient activity in NEC or MiNEN
- More data are warranted from prospective trials in NET G3 to address EVE efficacy compared to other treatments
- Review of pathology specimen by a highly experienced pathologist in the field is strongly recommended in cases of NEN G3



We thank all patients for participation in the study, as well as their caregivers, and all study sites.

AIO trial code: AIO-NET-0112

EudraCT No.: 2012-004550-28

ClinicalTrials.gov identifier: NCT02113800

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The study was sponsored by AIO-Studien-gmbH, Berlin, and supported by a grant from Novartis Pharma GmbH

