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FONDAZIONE IRCCS **ISTITUTO NAZIONALE DEI TUMORI** 

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# AIM

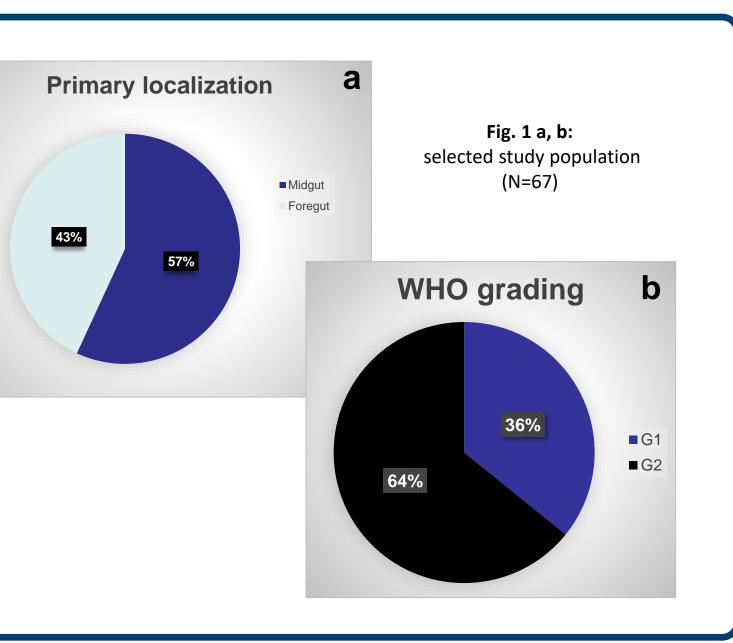
To predict real-life adverse events occurrence in a series of consecutive GEPNET patients treated with PRRT.

## MATERIALS AND METHODS

G1-G2 metastatic GEPNETs patients treated in our centre with PRRT (177Lu-Oxodotreotide, 4 administrations, 7.4 GBq/each) from April 2019 to December 2020 were considered. Patients were all previously treated with SSA followed by radiological disease progression (PD). Haematopoietic, liver and renal toxicities were collected every 14 days during PRRT and graded according to CTCAE v5 (G0, G1-G2, G3-G4). The population was subdivided as midgut/foregut and G1/G2, according to WHO 2019. Patients were categorical grouped according with ECOG-PS, number of metastatic sites, previous treatment lines (1 or  $\geq$ 2) and the therapies received before PRRT (splenectomy, Everolimus, alkylating chemotherapy). To test independence between CTCAE onset and patient characteristics Pearson/Fisher and Wilcoxon's test were assessed. The last was applied to continues variables. Logistic regression with Firth correction (R Puhr, Stat Med 2017) and bootstrap were performed to determine predictability of clinical features and previous therapies for CTCAE onset.

Age	n= 87		
Лean (± SD)	62.8 (± 12.2)		
> 60 ys (n,%)	52 (59.8)		
Gender	n (%)		
Vale	41 (47.1)		
Female	46 (52.9)		
ECOG PS			
)	69 (79.3)		
1_2	18 (20.7)		
Grading (WHO 2019)			
51	33 (37.9)		
52	54 (62.1)		
Primary tumor			
Midgut	56 (64.4)	PRRT administrations	
Foregut	31 (35.6)		87 (100)
Distant metastasis localisation			76 (87.3)
Liver	70 (80.5)		72 (82.7)
Nodal	40 (46)	IV	61 (70.1)
Bone	24 (27.6)	PRRT line of treatment	
Mesenteric .	12 (13.8)	2nd	62 (71.3)
Peritoneal	8 (9.2)	3rd	16 (18.4)
Lung	2 (2.3)	4th or further	9 (10.3)
Other localisations	11 (12.6)	Previous Therapies	
		Surgery	64 (73.6)
Tab 1	L:	Loco-regional (TACE, TARE)	15 (17.2)
Whole study pop	ulation (N=87)	Splenectomy	11 (12.7)
/    -		Alkylating Chemotherapy	16 (18.4)
		mTOR inhibitor (Everolimus)	14 (16.1)
		MetNET protocol	5 (5.7)

# Predictive factors of adverse events onset in GEPNET patients treated with PRRT



		ADVER	SE EVENT	s		-G2, %)*	G3-G	4, n(%)			СТСАЕ, (%)		
		Leukop		-	-	44.8)					44.8)		
		midgu			-	63.3)				-	63.3)		
		foregu			-	36.7) 23.9)	2	(3)		-	36.7) 26.9)		
		midgu	paenia t		-	6.3)		(5) (50)		-	28.9) 28.9)		
		foregu			-	3.7)		(50)			24.1)		
		Anaem			-	58.6)		(1.5)		-	70.1)		
		midgu			-	56.5)	1 (	100)		-	57.5)		
		foregu	t bocytopa	enia		43.5) <b>47.8)</b>	2	(3)			42.5) <b>50.7)</b>		
		midgu		ema	-	65.6)		(2.6)		-	64.7)		
		foregu			-	31.3)		3.5)		-	32.4)		
		-	PT increas	e		31.3)	1 (	1.5)			32.8)		
		midgu foregu			-	47.6) 52.4)	1 (	100)			45.4) 54.5)		
			OT increa	se	-	25.4)	1(	100)		-	25.4)		
		midgu			-	7.1)				8 (4	47.1)		
		foregu			-	2.9)				-	52.9)		
		GGT in			-	17.9) 25)				-	17.9)		
		midgu foregu			-	25) 75)					(25) (75)		
			ilirubin										
		increas	e			25.4)					25.4)		
		midgu foregu			-	7.1) 2.9)					47.1) 52.9)		
			in decrea			(6)					(6)		
		midgu				50)					(50)		
		foregu			2 (	50)				2	(50)		
		INR inc				(9)		1.5)		-	10.5)		
		midgu foregu			-	3.3) 6.6)	1 (	2.6)		-	42.9) 57.1)		
		foregu Creatir	nine cleara	ance		23.9)		-		-	23.9)		
		midgu			-	62.5)					62.5)		
		foregu			6 (3	7.5)				6 (3	37.5)		
		1	lecrease(r	n:58)**	-	75.9)				-	75.9)		
		-	t (n: 31) t (n: 27)		-	47.7) 52.3)				-	47.7) 52.3)		
		irred CTC		-	are ca	lculate				th the	numbe	r of patier cut-off	nts
		irred CTC	CAE. *Perc	-	are ca	lculate				th the	numbe	•	nts
	n=67).	irred CTC	CAE. *Perc	n was as	are ca	lculate l in 58	patient:	s, in acc		th the	numbe	•	eGFR decrease
(	n=67).	rred CTC **eGFR	CAE. *Percalteration	n was as	are ca sessec	lculate l in 58	AST increase in	s, in acc GGT crease inc	corda Bil	th the ance w	numbe ith age	cut-off Creatinine	eGFR
Explan Varia Age Gendo	(n=67).	Urred CTC **eGFR Leukopaenia	CAE. *Perc alteration Neutropaenia	Anaemia 3 0.2547 3 <b>0.003</b>	are ca sessec Thr- paenia	ALT increase	AST increase in 0.4835 1	<b>GGT</b> crease inc 0.7755 0 0.524	Bil rease	Alb decrease	numbe ith age <i>INR</i> <i>increase</i> 0.8753 0.696	Creatinine increase	eGFR decrease 0.0316 0.378
Explan Varia Age	(n=67).	Leukopaenia	CAE. *Percalteration	Anaemia 3 0.2547 3 0.003 2 0.091	are ca sessec <i>Thr-</i> paenia	ALT increase	AST increase in 0.4835 1 0.715	<b>GGT</b> crease inc 0.7755 0 0.524 0.678	Bil rease	th the ance w <i>Alb</i> <i>decrease</i> 0.1586 0.329 0.144	INR increase	Creatinine increase	eGFR decrease 0.0316 0.378 0.322
Explan Varia Age Genda ECOG-	(n=67).	Urred CTC **eGFR Leukopaenia	CAE. *Perc alteration Neutropaenia	Anaemia 3 0.2547 3 0.003 2 0.091 7 0.405	are ca sessec <i>Thr-paenia</i> 0.7569 0.028 0.539 0.131	ALT increase	AST increase in 0.4835 1	<b>GGT</b> crease inc 0.7755 0 0.524 0.678	Bil rease	Alb decrease	numbe ith age <i>INR</i> <i>increase</i> 0.8753 0.696	Creatinine increase	eGFR decrease 0.0316 0.378
Explan Varia Age Genda ECOG- Gradin Liven Noda	(n=67).	Urred CTC **eGFR Leukopaenia	CAE. *Perc alteration <i>Neutropaenia</i> 0.547 0.58 0.77 0.56 0.06 0.59	Anaemia 3 0.2547 3 0.003 2 0.091 7 0.405 9 0.511 2 1	are ca sessec <i>Thr-paenia</i> 0.7569 0.028 0.539 0.131 1 0.627	ALT increase	AST increase in 0.4835 1 0.715 1 1 0.386	<b>GGT</b> crease inc 0.7755 0 0.524 0.678 1 0.328 0.755	Bil rease	Alb decrease 0.1586 0.329 0.144 1 1 0.036	NR increase 0.8753 0.696 0.6 0.407 1 1	Creatinine increase 0.4357 0.011 0.029 1 0.423 0.574	eGFR decrease 0.0316 0.378 0.322 0.118 0.428 1
Explan Varia Age Gendu ECOG- Gradiu Live	(n=67).	Leukopaenia	CAE. *Perc alteration <i>Neutropaenia</i> 0.547 0.58 0.77 0.56 0.06 0.59	Anaemia Anaemia 3 0.2547 3 0.003 2 0.091 7 0.405 9 0.511 2 1 1 0.282	are ca sessec <i>Thr-paenia</i> 0.7569 0.028 0.539 0.131 1	ALT increase	AST increase in 0.4835 1 0.715 1 1	<b>GGT</b> crease inc 0.7755 0 0.524 0.678 1 0.328	Bil rease	Alb decrease 0.1586 0.329 0.144 1 1	numbe ith age <i>INR</i> <i>increase</i> 0.8753 0.696 0.6 0.407 1	Creatinine increase 0.4357 0.011 0.029 1 0.423	eGFR decrease 0.0316 0.378 0.322 0.118 0.428
Explan Varia Age Gendu ECOG- Gradu Liver Noda	(n=67).	Urred CTC **eGFR Leukopaenia	CAE. *Perc alteration <i>Neutropaenia</i> 0.547 0.58 0.7 0.56 0.064 0.59	Anaemia Anaemia 3 0.2547 3 0.003 2 0.091 7 0.405 9 0.511 2 1 1 0.282 5 0.094	are ca sessec <i>Thr-paenia</i> 0.7569 0.028 0.539 0.131 1 0.627 0.34	ALT increase 0.5723 0.298 1 1 0.538 0.792 0.48	AST increase in 0.4835 1 0.715 1 1 0.386 0.053	<b>GGT</b> crease inc 0.7755 0 0.524 0.678 1 0.328 0.755 1	Bil rease	Alb decrease 0.1586 0.329 0.144 1 1 0.036 1	NR increase 0.8753 0.696 0.6 0.407 1 1 1 0.323	Creatinine increase 0.4357 0.011 0.029 1 0.423 0.574 0.438	eGFR decrease 0.0316 0.378 0.322 0.118 0.428 1 0.673
Explan Varia Age Gendu ECOG- Gradu Liver Noda Mesent Periton Bone Lung	(n=67).	Leukopaenia 0.5886 0.219 1 1 1 1 1 0.199 0.692 0.608 0.448	CAE. *Perc alteration <i>Neutropaenia</i> 0.547 0.58 0.77 0.56 0.066 0.59	Anaemia Anaemia 3 0.2547 3 0.003 2 0.091 7 0.405 9 0.511 2 1 1 0.282 5 0.094 3 0.402 1 1	are ca sessec <i>Thr-paenia</i> 0.7569 0.028 0.539 0.131 1 0.627 0.34 0.259 1 0.493	ALT increase 0.5723 0.298 1 1 0.538 0.792 0.48 0.416 0.005 1	AST increase in 0.4835 1 0.715 1 1 0.386 0.053 1 0.547 1	<b>GGT</b> crease inc 0.7755 0 0.524 0.678 1 0.328 0.755 1 1 1 1 1 1	Bil rease	th the ance w <i>Alb</i> decrease 0.1586 0.329 0.144 1 1 0.036 1 0.669 0.113 1	NR increase 0.8753 0.696 0.6 0.407 1 1 0.323 1 0.221 1	Creatinine increase 0.4357 0.011 0.029 1 0.423 0.574 0.438 1 0.574 0.438 1 0.777 1	eGFR decrease 0.0316 0.378 0.322 0.118 0.428 1 0.673 1 0.338 1
Explan Varia Age Gendu ECOG- Gradii Liver Noda Mesent Periton Bone	(n=67).	Leukopaenia 0.5886 0.219 1 1 1 1 1 0.199 0.692 0.608	CAE. *Perc alteration Neutropaenia	Anaemia Anaemia 3 0.2547 3 0.003 2 0.091 7 0.405 9 0.511 2 1 1 0.282 5 0.094 3 0.402 1 1 5 0.102	are ca sessec <i>Thr-paenia</i> 0.7569 0.028 0.539 0.131 1 0.627 0.34 0.259 1	ALT increase 0.5723 0.298 1 1 0.538 0.792 0.48 0.416 0.005	AST increase in 0.4835 1 0.715 1 1 0.386 0.053 1 0.547	S, in acc GGT crease inc 0.7755 0 0.524 0.678 1 0.328 0.755 1 1 1 1 1 1 1 0.047	Bil rease	th the ance w <i>Alb</i> decrease 0.1586 0.329 0.144 1 1 0.036 1 0.669 0.113	NR increase 0.8753 0.696 0.6 0.407 1 1 0.323 1 0.221	Cut-off Creatinine increase 0.4357 0.011 0.029 1 0.423 0.574 0.438 1 0.438 1 0.77	eGFR decrease 0.0316 0.378 0.322 0.118 0.428 1 0.428 1 0.673 1 0.338
Explan Varia Age Gendu ECOG- Gradiu Liveu Noda Mesent Periton Bone Lung PRRT II Chemoth Everolir	(n=67).	Leukopaenia 0.5886 0.219 1 1 1 1 0.199 0.692 0.608 0.448 0.082	CAE. *Perc alteration Neutropaenia	Anaemia Anaemia 3 0.2547 3 0.003 2 0.091 7 0.405 9 0.511 2 1 1 0.282 5 0.094 3 0.402 1 1 1 0.282 5 0.094 3 0.402 1 1 1 0.282 5 0.094	are ca sessec <i>Thr-paenia</i> 0.7569 0.028 0.539 0.131 1 0.627 0.34 0.259 1 0.493 0.504	ALT increase 0.5723 0.298 1 1 0.538 0.792 0.48 0.416 0.005 1 0.718	AST increase in 0.4835 1 0.715 1 1 0.386 0.053 1 0.547 1 0.547 1 0.116	S, in acc GGT crease inc 0.7755 0 0.524 0.678 1 0.328 0.755 1 1 1 1 1 0.047 0.228	Bil rease 0.7576 0.269 1 0.574 1 0.168 1 0.566 1 0.645	Alb decrease 0.1586 0.329 0.144 1 1 0.036 1 0.669 0.113 1 0.398	NR increase 0.8753 0.696 0.6 0.407 1 1 0.323 1 0.221 1 0.221 1 0.062 0.127 0.614	Creatinine increase 0.4357 0.011 0.029 1 0.423 0.574 0.438 1 0.438 1 0.77 1 0.628	eGFR decrease 0.0316 0.378 0.322 0.118 0.428 1 0.673 1 0.673 1 0.338 1 0.714
Explan Varia Age Gendu ECOG- Gradiu Liveu Noda Mesent Periton Bone Lung PRRT II Chemoth	(n=67).	Leukopaenia 0.5886 0.219 1 1 1 1 0.199 0.692 0.608 0.448 0.082 0.759	CAE. *Perc alteration Neutropaenia 0.547 0.58 0.77 0.56 0.06 0.59 0.37 0.77 0.77 0.16 0.31	Anaemia Anaemia 3 0.2547 3 0.003 2 0.091 7 0.405 9 0.511 2 1 1 0.282 5 0.094 3 0.402 1 1 1 0.282 5 0.094 3 0.402 1 1 6 0.102 2 0.315 6 0.74 6 1	are ca sessec thr- paenia 0.7569 0.028 0.539 0.131 1 0.627 0.34 0.259 1 0.493 0.504 0.504 0.504	ALT increase 0.5723 0.298 1 1 0.538 0.792 0.48 0.416 0.005 1 0.718 0.499	AST increase in 0.4835 1 0.715 1 1 0.715 1 1 0.386 0.053 1 0.547 1 0.547 1 0.116 0.715	<b>GGT</b> <b>crease</b> 0.7755 0.524 0.678 1 0.328 0.755 1 1 1 1 1 0.047 0.228 1	Bil rease 0.7576 0.269 1 0.574 1 0.168 1 0.56 1 0.645 0.725	th the ance w Alb decrease 0.1586 0.329 0.144 1 1 0.036 1 0.669 0.113 1 0.398 1	NR increase 0.8753 0.696 0.6 0.407 1 1 0.323 1 0.221 1 0.221 1 0.062 0.127	Cut-off Creatinine increase 0.4357 0.011 0.029 1 0.423 0.574 0.438 1 0.423 0.574 0.438 1 0.77 1 0.628 1	eGFR decrease 0.0316 0.378 0.322 0.118 0.428 1 0.673 1 0.673 1 0.338 1 0.714 0.424
Explan Varia Age Genda ECOG- Gradii Liver Noda Mesent Periton Bone Lung PRRT II Chemotha Everolin MetNu Splenect	(n=67).	Leukopaenia 0.5886 0.219 1 1 1 1 0.199 0.692 0.608 0.448 0.082 0.759 0.65 0.017 Quare/Fis	CAE. *Perc alteration Neutropaenia 0.547 0.58 0.77 0.56 0.06 0.59 0.37 0.77 0.16 0.31 0.73 0.11 0.71	Anaemia Anaemia 3 0.2547 3 0.003 2 0.091 7 0.405 9 0.511 2 1 1 0.282 5 0.094 3 0.402 1 1 6 0.102 2 0.315 6 0.74 6 1 4 1 Wilcoxc	are ca sessec <i>Thr- paenia</i> 0.7569 0.028 0.539 0.131 1 0.627 0.34 0.259 1 0.493 0.504 0.259 1 0.493 0.504 0.765 0.369 0.197 0.006	ALT increase 0.5723 0.298 1 1 0.538 0.792 0.48 0.416 0.005 1 0.718 0.499 1 0.316 0.024 Were a	AST increase in 0.4835 1 0.715 1 0.715 1 0.386 0.053 1 0.547 1 0.116 0.715 0.465 0.588 1 1 applied	GGT crease inc 0.7755 0 0.524 0.678 1 0.328 0.755 1 1 1 1 1 0.047 0.228 1 0.216 0.099 to evalue	Bil rease 0.7576 0.269 1 0.574 1 0.168 1 0.56 1 0.645 0.725 0.158 0.099 1 uate	Alb decrease 0.1586 0.329 0.144 1 1 0.036 1 0.669 0.113 1 0.398 1 0.167 1 1 0.167 1 1 0.167	INR increase 0.8753 0.696 0.6 0.407 1 1 0.323 1 0.221 1 0.062 0.127 0.614 0.081 1 1 sociatic	cut-off <i>Creatinine</i> <i>increase</i> 0.4357 0.011 0.029 1 0.423 0.574 0.438 1 0.77 1 0.628 1 0.274 1 0.274 2 0.274	eGFR decrease 0.0316 0.378 0.322 0.118 0.428 1 0.673 1 0.673 1 0.338 1 0.714 0.424 0.691 0.563 0.424
Explan Varia Age Genda ECOG- Gradii Liver Noda Mesent Periton Bone Lung PRRT II Chemotha Everolin MetNu Splenect	(n=67).	Leukopaenia 0.5886 0.219 1 1 1 0.199 0.692 0.608 0.448 0.082 0.759 0.65 0.017 Quare/Fis ar	CAE. *Percalteration	Anaemia Anaemi	are ca sessec <i>Thr- paenia</i> 0.7569 0.028 0.539 0.131 1 0.627 0.34 0.259 1 0.493 0.504 0.259 1 0.493 0.504 0.765 0.369 0.197 0.006 On test nt vari	ALT increase 0.5723 0.298 1 1 0.538 0.792 0.48 0.416 0.005 1 0.718 0.499 1 0.316 0.024 Were a ables.	AST increase in 0.4835 1 0.715 1 0.715 1 0.536 0.053 1 0.547 1 0.116 0.715 0.465 0.588 1 2 applied T Thr-pae	<b>GGT</b> <b>GGT</b> <b>crease</b> <b>inc</b> 0.7755 0 0.524 0.678 1 0.328 0.755 1 1 1 1 0.047 0.228 1 0.216 0.099 to evalue enia: the	Bil rease 0.7576 0.269 1 0.574 1 0.168 1 0.56 1 0.645 0.725 0.158 0.099 1 uate romb	Alb decrease 0.1586 0.329 0.144 1 1 0.669 0.113 1 0.669 0.113 1 0.398 1 0.167 1 1 1 the as: Docyto	INR increase 0.8753 0.696 0.6 0.407 1 1 0.323 1 0.221 1 0.062 0.127 0.614 0.081 1 sociatic paenia.	Cut-off Creatinine increase 0.4357 0.011 0.029 1 0.423 0.574 0.438 1 0.77 1 0.628 1 0.274 1 0.274 2 0.274 1 0.274 1 0.274 1 0.274 1 0.274 1 0.274	eGFR decrease 0.0316 0.378 0.322 0.118 0.428 1 0.673 1 0.673 1 0.338 1 0.714 0.424 0.691 0.563 0.424 en CTCAE
Explan Varia Age Gendu ECOG- Gradiu Liven Noda Mesent Periton Bone Lung PRRT II Chemothu Everolir MetNu Splenect	(n=67).	Leukopaenia 0.5886 0.219 1 1 1 0.199 0.692 0.608 0.448 0.082 0.759 0.65 0.017 0.65 0.017 0.65 0.017	CAE. *Percalteration	Anaemia Anaemia 3 0.2547 3 0.003 2 0.091 7 0.405 9 0.511 2 1 1 0.282 5 0.094 3 0.402 1 1 6 0.102 2 0.315 6 0.74 6 1 4 1 Wilcoxc epende Neutro- paenia 0.167	are ca sessec <i>Thr- paenia</i> 0.7569 0.028 0.539 0.131 1 0.627 0.34 0.259 1 0.493 0.504 0.765 0.369 0.197 0.006 On test nt vari INR_ increase 0.136	ALT increase 0.5723 0.298 1 1 0.538 0.792 0.48 0.416 0.005 1 0.718 0.499 1 0.316 0.024 Were a ables.	AST increase in 0.4835 1 0.715 1 0.715 1 0.547 1 0.116 0.715 0.465 0.547 1 0.116 0.715 0.465 0.588 1 applied T Thr-pae	S, in acc GGT crease inc 0.7755 0 0.524 0.678 1 0.328 0.755 1 1 1 0.047 0.228 1 0.216 0.099 to evalue enia: the GGT_ increase 0 0.9	Bil rease 0.7576 0.269 1 0.574 1 0.168 1 0.56 1 0.645 0.725 0.158 0.099 1 uate romk	Alb decrease 0.1586 0.329 0.144 1 1 0.669 0.113 1 0.669 0.113 1 0.669 0.113 1 0.167 1 1 0.398 1 0.167 1 1 the as: Docyto	INR increase 0.8753 0.696 0.6 0.407 1 1 0.323 1 0.221 1 0.062 0.127 0.614 0.081 1 1 sociatic paenia.	Cut-off Creatinine increase 0.4357 0.011 0.029 1 0.423 0.574 0.438 1 0.77 1 0.628 1 0.274 1 0.274 2 0.274 0.2	eGFR decrease 0.0316 0.378 0.322 0.118 0.428 1 0.673 1 0.338 1 0.714 0.424 0.691 0.563 0.424 en CTCAE
Explan Varia Age Genda ECOG- Gradii Liver Noda Mesent Periton Bone Lung PRRT II Chemotha Everolin MetNu Splenect	(n=67).	Leukopaenia 0.5886 0.219 1 1 1 0.199 0.692 0.608 0.448 0.082 0.759 0.65 0.017 0.65 0.017 0.65 0.017 0.65 0.017	CAE. *Percalteration	Anaemia Anaemia 3 0.2547 3 0.003 2 0.091 7 0.405 9 0.511 2 1 1 0.282 5 0.094 3 0.402 1 1 6 0.102 2 0.315 6 0.74 6 1 4 1 Wilcoxc epende Neutro- paenia	are ca sessec <i>Thr- paenia</i> 0.7569 0.028 0.539 0.131 1 0.627 0.34 0.259 1 0.493 0.504 0.765 0.369 0.197 0.006 0.197 0.006	ALT increase 0.5723 0.298 1 1 0.538 0.792 0.48 0.416 0.005 1 0.718 0.499 1 0.316 0.024 Were a ables.	AST increase in 0.4835 1 0.715 1 0.715 1 0.547 1 0.116 0.715 0.465 0.547 1 0.116 0.715 0.465 0.588 1 0.548 1 0.548 1 0.547 1 0.116 0.715 0.465 0.588 1 0.588 1 0.588 1 0.588 1 0.588 1 0.588 1 0.588 1 0.588 1 0.588 1 0.588 1 0.588 1 0.588 1 0.588 1 0.553 1 0.547 1 0.16 0.715 0.465 0.588 1 0.588 1 0.553 1 0.553 1 0.547 1 0.547 1 0.547 1 0.547 1 0.556 0.558 1 0.556 0.558 1 0.558 1 0.557 0.557 0.557 0.558 1 0.558 1 0.558 1 0.558 1 0.557 0.558 1 0.556 1 0.558 1 0.558 1 0.550 1 0 0.550 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	S, in acc GGT crease inc 0.7755 0 0.524 0.678 1 0.328 0.755 1 1 1 0.047 0.228 1 0.216 0.099 to evalue nia: the GGT_ increase 0 0.9 6 0.0	Bil rease 0.7576 0.269 1 0.574 1 0.168 1 0.56 1 0.645 0.725 0.158 0.099 1 uate romb	Alb decrease 0.1586 0.329 0.144 1 1 0.669 0.113 1 0.669 0.113 1 0.398 1 0.167 1 1 0.398 1 0.167 1 1 the as: Docyto	INR increase 0.8753 0.696 0.6 0.407 1 1 0.323 1 0.221 1 0.062 0.127 0.614 0.081 1 1 sociatic paenia.	Creatinine increase 0.4357 0.011 0.029 1 0.423 0.574 0.438 1 0.77 1 0.628 1 0.274 1 0.274 1 0.274 1 0.274 1 0.274 1 0.274 1 0.274	eGFR decrease 0.0316 0.378 0.322 0.118 0.428 1 0.673 1 0.673 1 0.338 1 0.714 0.424 0.691 0.563 0.424 en CTCAE
Explan Varia Age Gendu ECOG- Gradin Liven Noda Mesent Periton Bone Lung PRRT II Chemothu Everolin MetNu Splenect Tab 3	(n=67).	Leukopaenia 0.5886 0.219 1 1 1 0.199 0.692 0.608 0.448 0.082 0.759 0.65 0.017 0.65 0.017 0.65 0.017 0.65 0.017	CAE. *Percalteration	Anaemia Anaemia 3 0.2547 3 0.003 2 0.091 7 0.405 9 0.511 2 1 1 0.282 5 0.094 3 0.402 1 1 6 0.102 2 0.315 6 0.74 6 1 4 1 Wilcoxc epende Neutro- paenia 0.167 0.007	are ca sessec <i>Thr- paenia</i> 0.7569 0.028 0.539 0.131 1 0.627 0.34 0.259 1 0.493 0.504 0.765 0.369 0.197 0.006 On test nt vari INR_ increase 0.136 0.011	ALT increase 0.5723 0.298 1 1 0.538 0.792 0.48 0.416 0.005 1 0.718 0.499 1 0.316 0.024 Were a ables.	AST increase in 0.4835 1 0.715 1 0.715 1 0.547 1 0.116 0.715 0.465 0.547 1 0.116 0.715 0.465 0.588 1 applied T Thr-pae	S, in acc GGT crease inc 0.7755 0 0.524 0.678 1 0.328 0.755 1 1 1 1 0.047 0.228 1 0.216 0.099 to evalue enia: the GGT_ increase 0 0.9 6 0.0 5 0.3	Bil rease 0.7576 0.269 1 0.574 1 0.168 1 0.56 1 0.645 0.725 0.158 0.099 1 uate romb	Alb decrease 0.1586 0.329 0.144 1 1 0.669 0.113 1 0.669 0.113 1 0.398 1 0.167 1 1 0.398 1 0.167 1 1 the as: Docyto	INR increase 0.8753 0.696 0.6 0.407 1 1 0.323 1 0.221 1 0.062 0.127 0.614 0.081 1 1 sociatic paenia.	Creatinine increase 0.4357 0.011 0.029 1 0.423 0.574 0.438 1 0.77 1 0.628 1 0.274 1 0.274 1 0.274 1 0.274 1 0.274 1 0.274 1 0.274	eGFR decrease 0.0316 0.378 0.322 0.118 0.428 1 0.673 1 0.673 1 0.338 1 0.714 0.424 0.691 0.563 0.424 en CTCAE
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CONFLICT OF INTEREST and FINANCIAL TRASPERENCY

Eight-seven patients were treated (Tab 1) from April 2019 to December 2020. Twenty were excluded due to ongoing PRRT therefore 67 (31(46.3%) males, 36 (53.7%) female, mean age 63) were selected. Thirty-eight (56.7%) were classified as midgut, 29(43.3%) as foregut, 24 (35.8%) G1 and 43 (64.2%) G2 (Fig 1a,b). Alkylating chemotherapy and Everolimus were the previous treatments in 13 (19.4%) patients, in both cases. Patients were treated with PRRT as third or further lines in 34.3% (23) of the whole population, 48.3% (14) of foregut cohort. All the patients showed at least one G1-G2 CTCAE during PRRT, in particular anaemia, thrombocytopaenia and leukopaenia. G3-G4 were rare events, in particular haematological alterations were reported (Tab2). G3-G4 CTCAE were transitional. No G3-G4 renal toxicities were reported. The results of Chi square/Fisher and Wilcoxon test are shown in **Tab3**. Line of PRRT administration, age, gender and ECOG-PS were the main predictors of CTCAE, according to Firth regression. The mean absolute effect of covariates is shown in **Tab 4.** The model performance, expressed by AUC, was > 65% for anaemia, creatinine and eGFR.

The application of FLIC model can be useful to improve GEPNET decision-making, allowing clinicians to identify the better therapeutic sequence to avoid adverse events PRRTrelated, on the of base of patient characteristics and previous treatment lines. Internal validation confirmed the performance of the model for anaemia, creatinine and eGFR.



The authors have nothing to declare and the didn't receive any founding to develop the study

## RESULTS

## CONCLUSIONS