



Epidemiological study on the current status of patients with type I Gaucher disease in Spain, as assessed by the Therapeutic Goals MAP (Monitor, Action and Progress) Tool©

Estudio MAPPING EG



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► Therapeutic Goals MAP Tool (Monitor, Action & Progress)

- Standardized tool to manage and follow up the disease
- It provides an easy management framework for the identification and mapping of therapeutic goals
- Individual data from patients
- It consists of data from all patients
 - To assess their health status at individual level
 - To study the different management among the centers
 - To strengthen and improve the labour of physicians
- It may permits the evaluating of response to new therapies and to unify diagnostic criteria and therapeutic decisions

► Main variables and therapeutic goals for the study

MAP-Tool	Therapeutic goals (achieved if...)
Haemoglobinaemia	≥ 12 g/dL in men/ ≥ 11 g/dL in women/children
Trombocitemia	$\geq 120 \cdot 10^9$ /L
Splenomegaly	≤ 8 MN**
Hepatomegaly	≤ 1.5 MN**
Bone pain in the last 24 h	≤ 1
Bone Mineral Density	≥ -1
QoL	≥ 70
Additional measure:	
MAP-Tool Index*	Number of therapeutic goals achieved

* MAP-Tool Index: Sum of all the variables from the MAP-tool (0-70) after their transformation:

1. Results expressed in the same direction (the higher the best) and
2. Re-scaled each one into a 0 to 10 scale

** MN = Multiples of Normal

► Study Description

- Epidemiological, cross-sectional, descriptive & multicenter study.
- Gaucher type I disease patients managed in specialized centers in Spain.
- The study was presented for classification to the Spanish Agency of Medicines and Sanitary Products (AEMPS) in mid 2011.
 - Classified as EPA-OD (Post-Authorization study – Other Designs → non prospective follow-up) despite being expected No-EPA.
- As consequence of this classification, study start-up was delayed few months due to Spanish regulations.
- Recruitment Period: June-December 2012.

► Inclusion/exclusion criteria

Inclusion criteria

- Patients with Gaucher disease I who attended the investigator's office for their routine revision
- Patient who signed the Informed Consent.

Exclusion criteria

- Patients who, after the criteria of the investigator, they were considered to have limited cognitive or sensorial abilities or showed psychiatric or linguistic barriers which impair their capacity to respond the CRF.

► Study variables I

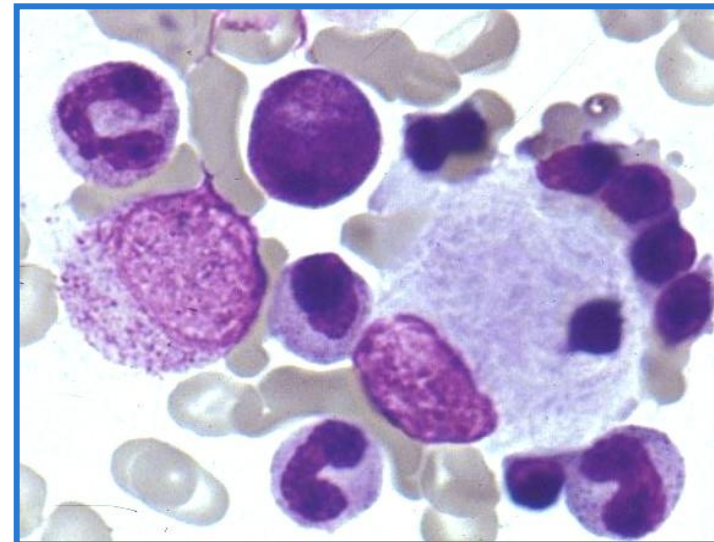
Therapeutic domain	Parameter	
	Adults	Children (≤18 años)
Anaemia	12 (g/dl) for males 11 (g/dl) for females	11 (g/dl) for children ≤18 años
Thrombocytopenia	120 (109/l)	120 (109/l)
Splenomegaly	8 s	8 s
Hepatomegaly	1,5 h	1,5 h
Bone pain in the last 24 h	VAS=1	VAS=1
Bone Mineral Density	Z=0	Z=0
QoL	70	70
Paediatric patients: growth		Mid parental percentile

► Study variables II

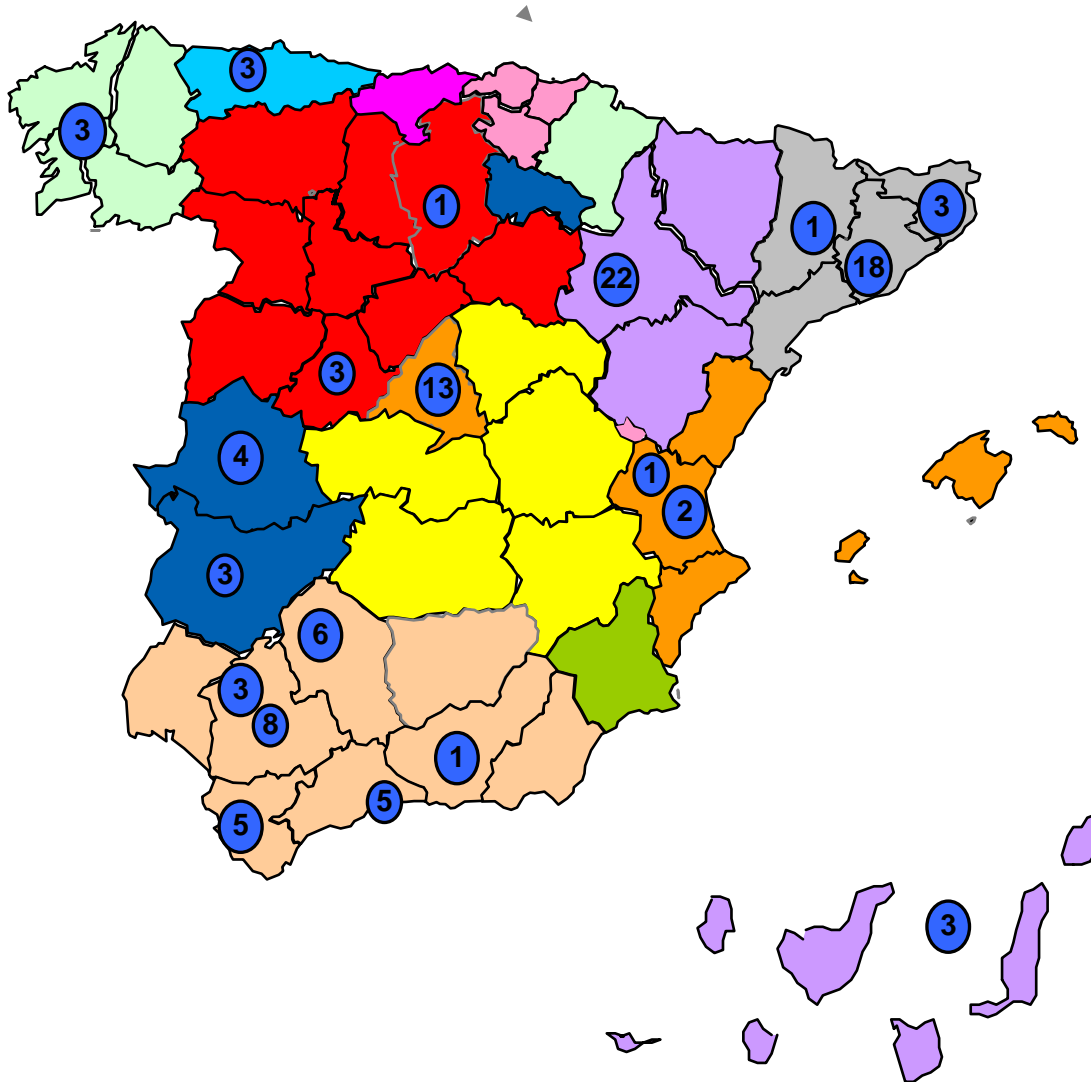
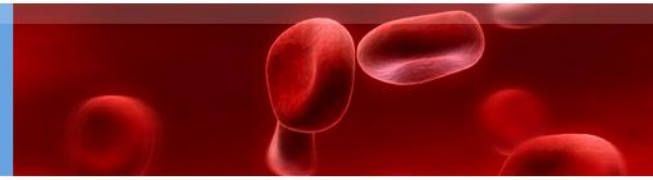
Características generales	Treatment	Other
Gender	Dose (U/kg)	Antibodies
Age	Dose frequency (dose/month)	Co-morbidities
Height (m)	Treatment name	Transfusion dependency
Weight (kg)	Treatment at home	Bleeding tendency
Age symptoms onset (DD/MM/YYYY)	Time since first treatment (months)	Pre-existing bone complication
Age of diagnosis (DD/MM/YYYY)	Co-medication related to GDI	Osteonecrosis
Familial history of Gaucher Disease	Infusion related Reactions	Pulmonary involvement
Gravid and para	Adverse events	Neurological symptoms
Genotype		MRI assessment
CHITO (nmol/mL x h)		Onset of puberty – Tanner scale
CHITO ("mutational status")		Mental status
CCL18 (ng/mL)		

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RESULTS



Centers participants



- 108 patients
- 28 Centers / 35 Investigators recruited patients
- 10/17 Autonomous Communities (CCAA)

Investigators and centers

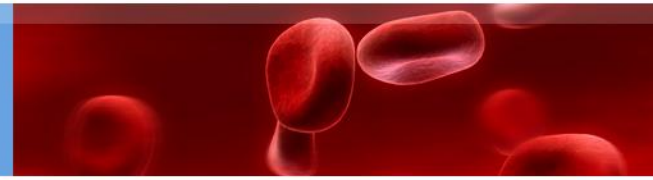


Recruitment according to the known incidence by CCAA:

- Andalucía (28)
- Aragón (22)
- Cataluña (22)



Therapeutic goals

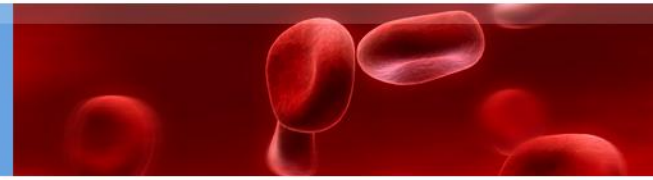


MAP-Tool	Therapeutic goals (achieved if...)
Haemoglobinaemia	≥ 12 g/dL in men/ ≥ 11 g/dL in women/children
Trombocitemia	$\geq 120 \times 10^9$ /L
Splenomegaly	≤ 8 MN**
Hepatomegaly	≤ 1.5 MN**
Bone pain in the last 24 h	≤ 1
Bone Mineral Density	≥ -1
QoL	≥ 70
Additional measure:	
MAP-Tool Index*	Number of therapeutic goals achieved

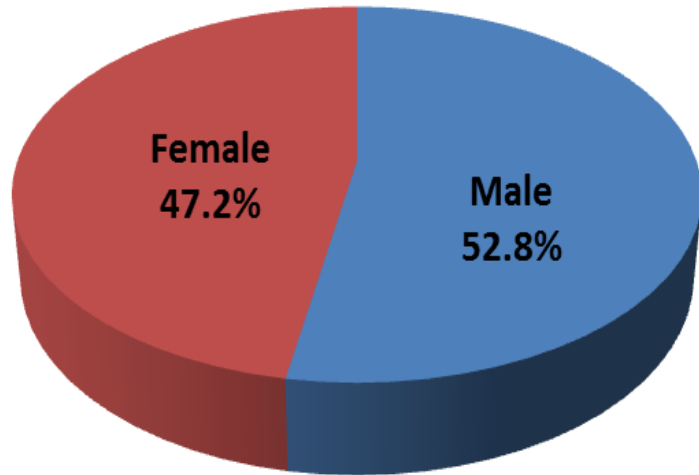
- * MAP-Tool Index: Sum of all the variables from the MAP-tool (0-70) after their transformation:
1. Results expressed in the same direction (the higher the best) and
 2. Re-scaled each one into a 0 to 10 scale

** MN = Multiples of Normal

Full Analysis Set Patient: Characteristics (n=108)



N=108

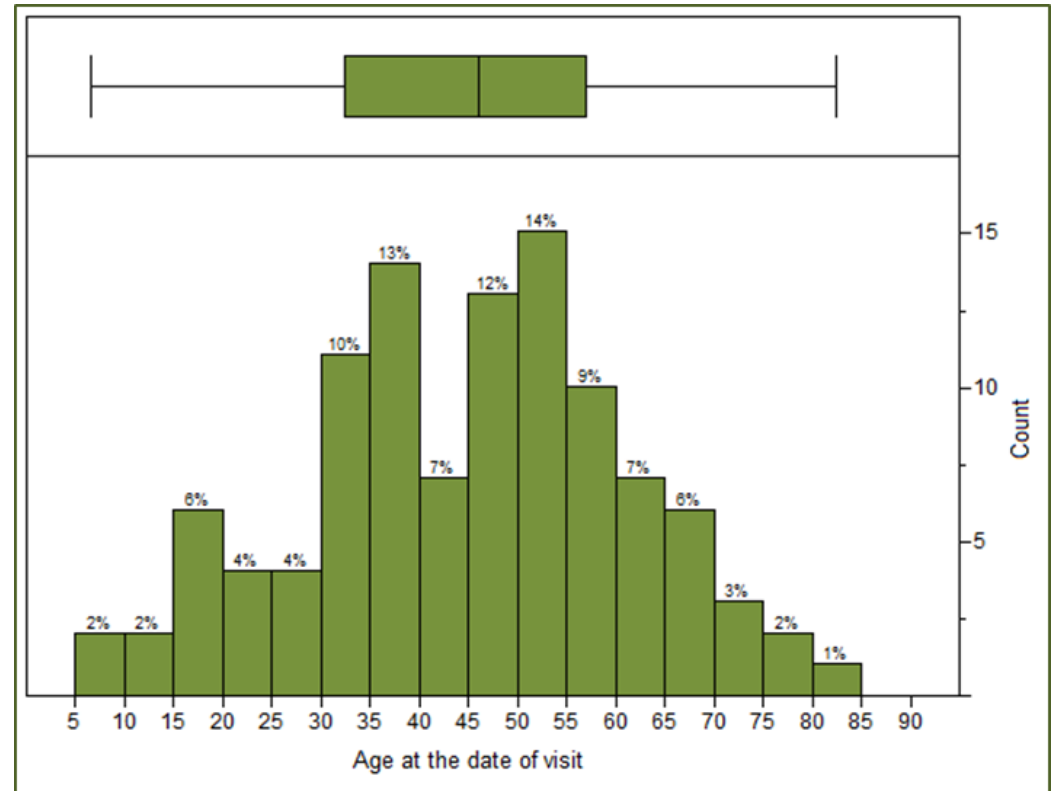


Age Group	n(%)	Count
≤18 years	9 (8.4)	9
19 – 40 years	36 (33.6)	36
40 – 65 years	52 (48.6)	52
>65 years	10 (9.3)	10
Missing	1	1

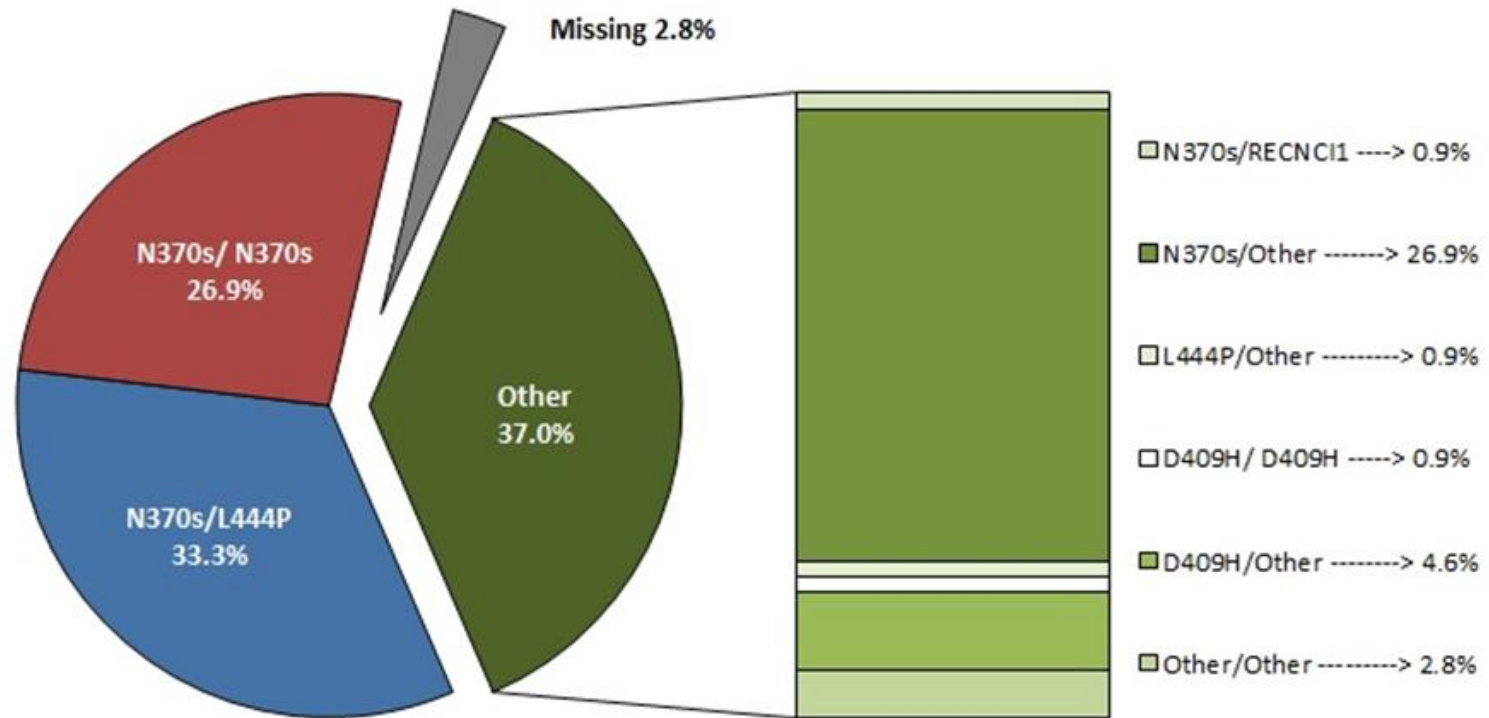
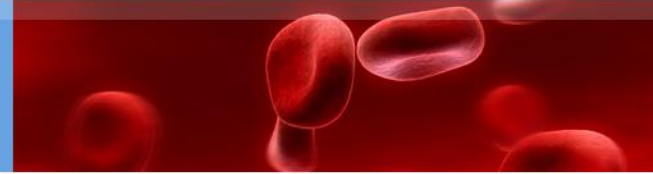
Age (years)

Median: 44.8±16.60

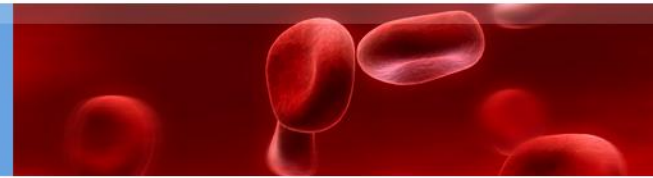
Range: 6,5-82,5



Full Analysis Set Patient: Genotypes (n=108)

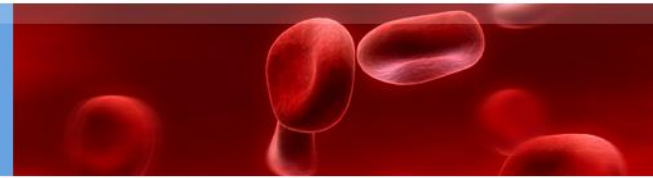


Full Analysis Set Patient: Characteristics (n=108)



		Total N=108
Age onset of symptoms	n X (SD)	20 22.3 (15.7)
Age of diagnosis	n (unknown/missing) X (SD)	105 (3) 27.5 (16.40)
Family history of Gaucher Disease		
Yes	n(%)	46 (42.6)
Pre-existing bone complication		
Yes	n(%)	23 (21.3)
Splenectomy		
Yes	n(%)	27 (25.0)

Full Analysis Set Patient: Treatment I (n=108)

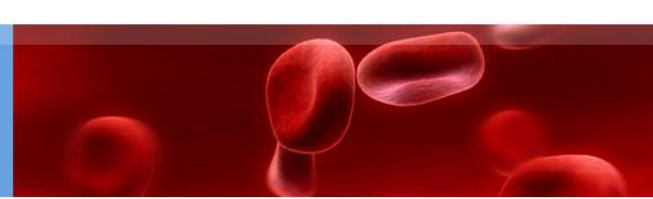


N=108

Treatment			
No		n(%)	13 (12.0)
Yes		n(%)	95 (88.0)
Type of treatment			
	Imiglucerase (IMI)	n(%)	46 (42.6)
	Velaglucerase (VELA)	n(%)	24 (20.4)
	Alglucerase (AL)	n(%)	0 (0.0)
	Miglustat (MI)	n(%)	18 (18.5)
	IMI + MI	n(%)	3 (2.8)
	Other*	n(%)	4 (3.7)
Time since the initiation of the first treatment			
		N (n unknown/missing)	91 (4)
		X (SD)	119 (73.4)
		Med (Q1-Q3)	129 (57 - 168)
		Min - Max	5 - 373
Concomitant medication (related to Gaucher)			
No		n(%)	90 (83.3)
Yes		n(%)	18 (16.7)

* Taliglucerase (3) / Eliglustat (1)

Full Analysis Set Patient: Biomarkers (n=108)

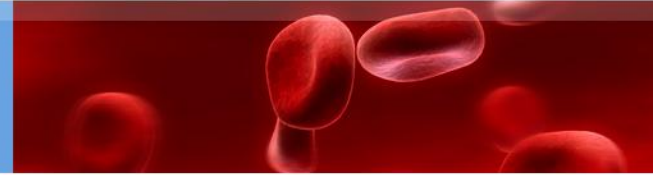


Total: N=108

CCL18 (ng/mL)		
No	n (%)	41 (38.0)
Yes	n (%)	67 (62.0)
	n (n missing)	59 (8)
	X (DE)	467.8 (658.00)
	Med (Q1-Q3)	259.0 (136.0 - 543.0)
	Min - Max	44.0 - 3720.0
CHITO (nmol/mL*h)		
No	n (%)	20 (18.5)
Yes	n (%)	88 (81.5)
	n (n missing)	81 (7)
	X (DE)	3070.5 (7487.53)
	Med (Q1-Q3)	1257.0 (553.0 - 3150.0)
	Min - Max	10.6 - 65497.0

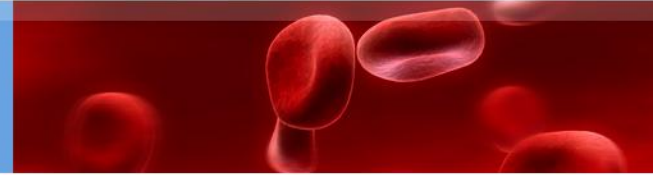
CONFIDENTIAL

Therapeutic goals status and its achievement (n=108)




		All patients
Haemoglobinemia (g/dL)	n (n missing)	108 (0)
	X (DE)	13.6 (1.5)
Goal achievers (♂≥12 & ♀≥11)	n (%)	105 (97.2)
Platelet count (10 ⁹ /L)	n (n missing)	108 (0)
	X (DE)	177 (89.1)
Goal achievers (≥120x10 ⁹ /L)	n (%)	81 (75.0)
Splenomegaly (MN) [only non splenomyzed patients]	n (n missing)	77 (4)
	X (DE)	3.5 (4.5)
Goal achievers (Size ≤ 8 MN)	n (%)	67 (87.0)
Hepatomegaly (MN)	n (n missing)	98 (10)
	X (DE)	1.2 (0.3)
Goal achievers (Size ≤ 1.5 MN)	n (%)	86 (87.8)
Bone pain (in the last 24 hours) [VAS 0-10]	n (n missing)	94 (14)
	X (DE)	1.8 (2.1)
Goal achievers (VAS ≤ 1)	n (%)	50 (53.2)

Therapeutic goals status and its achievement (n=108)

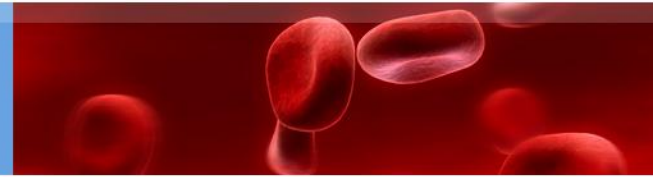


		All patients
Bone pain among patients having pain [VAS > 0]	n (%)	59 (62.8)
	X (DE)	2.9 (1.9)
Bone mineral density (DXA Z-score)	n (n missing)	75 (33)
	X (DE)	-0.7 (1.3)
Goal achievers (Z-score \geq -1)	n (%)	48 (64.0)
Physical Component Score of SF-36 (0 - 100)	n (n missing)	103 (5)
	X (DE)	72.5 (17.4)
Goal achievers (PCS \geq 70)	n (%)	65 (63.1)



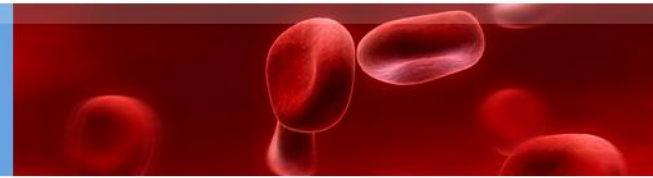
**ANALYSIS BY
TREATMENT - YES/NO
(n=108)**

Patient Characteristics by treatment (n=108)



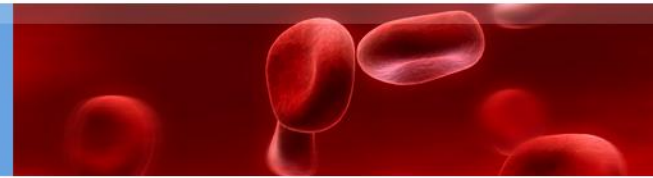
		Treatment		
		No n=13	Yes n=95	p-value
Gender				
Male	n(%)	9 (69.2)	48 (50.5)	n.s.
Female	n(%)	4 (30.8)	47 (49.5)	
Age	n (n missing) X (DE)	13 (0) 48.7 (19.8)	94 (1) 44.3 (16.2)	
Age of symptom onset (years)	n (n missing) X (DE)	7(6) 28.0 (14.8)	81 (14) 21.8 (15.8)	n.s.
Age of diagnosis (years)	n (n missing) X (DE)	12 (1) 39.7 (14.7)	93 (2) 25.9 (16.0)	0.007
Familial history of GD1 (Yes)	n (%)	7 (53.8)	39 (41.1)	n.s.
Pre-existing bone complication (Yes)	n (%)	3 (23.1)	20 (21.1)	n.s.
Splenectomy (Yes)	n (%)	2 (15.4)	25 (26.3)	n.s.

Therapeutic goals status and its achievement by treatment (n=108)




		Without Treatment n = 13	On Treatment n = 95	p-value
Haemoglobinemia (g/dL)	n (n missing)	13 (0)	95 (0)	0.459
	X (DE)	13.3 (1.3)	13.6 (1.5)	
Goal achievers (♂≥12 & ♀≥11)	n (%)	12 (92.3)	93 (97.9)	0.322
Platelet count (10 ⁹ /L)	n (n missing)	13 (0)	95 (0)	0.048
	X (DE)	134 (57.3)	183 (91.2)	
Goal achievers (≥120x10 ⁹ /L)	n (%)	9 (69.2)	72 (75.8)	0.733
Splenomegaly (MN) [only non splenomyzed patients]	n (n missing)	11 (0)	66 (4)	0.965
	X (DE)	3.9 (5.6)	3.5 (4.3)	
Goal achievers (Size ≤ 8 MN)	n (%)	10 (90.9)	57 (86.4)	1.000
Hepatomegaly (MN)	n (n missing)	13 (0)	85 (10)	0.192
	X (DE)	1.3 (0.4)	1.2 (0.3)	
Goal achievers (Size ≤ 1.5 MN)	n (%)	9 (69.2)	77 (90.6)	0.511
Bone pain (in the last 24 hours) [VAS 0-10]	n (n missing)	13 (0)	81 (14)	0.813
	X (DE)	2.3 (2.9)	1.7 (1.9)	
Goal achievers (VAS ≤ 1)	n (%)	6 (46.2)	44 (54.3)	0.584

Therapeutic goals status and its achievement by treatment (n=108)

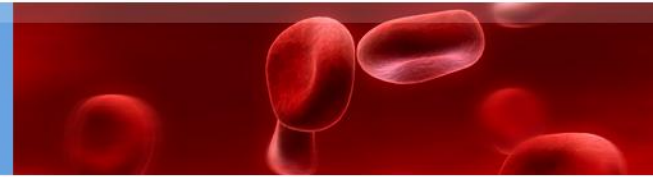


		Without Treatment	On Treatment	p-value
		n = 13	n = 95	
Bone pain among patients having pain [VAS > 0]	n (%)	8 (61.5)	51 (63.0)	0.525
	X (DE)	3.7 (2.8)	2.8 (1.7)	
Bone mineral density (DXA Z-score)	n (n missing)	9 (4)	66 (29)	0.931
	X (DE)	-0.7 (1.6)	-0.8 (1.2)	
	Goal achievers (Z-score \geq -1)	n (%)	5 (55.6)	
Physical Component Score of SF-36 (0 - 100)	n (n missing)	13 (0)	90 (5)	0.823
	X (DE)	74.0 (13.1)	72.3 (17.9)	
	Goal achievers (PCS \geq 70)	n (%)	8 (61.5)	
CCL18 (ng/mL)	n (%)	10 (76.9)	57 (60.0)	0.018
	X (DE)	643.8 (424.7)	436.1 (690.2)	
	Med (Q1-Q3)	515.0 (310.0 - 967.0)	215.0 (131.0 - 448.0)	
	Min – Max	192.0 - 1403.0	44.0 - 3720.0	
CHITO (nmol/mL*h)	n (%)	12 (92.3)	76 (80.0)	0.002
	X (DE)	9456.8 (18033.0)	1959.8 (2214.4)	
	Med (Q1-Q3)	2896.0 (1646.5 - 8491.0)	987.0 (456.0 - 2800.0)	
	Min – Max	1088.0 - 65497.0	10.6 - 8770.0	



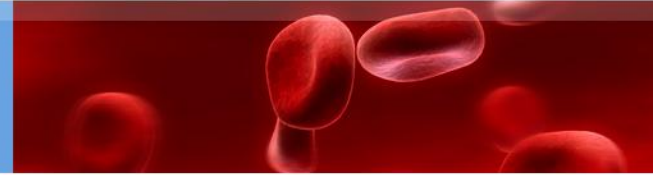
ANALYSIS BY GENDER (n=108)

Patient Characteristics by gender (n=108)



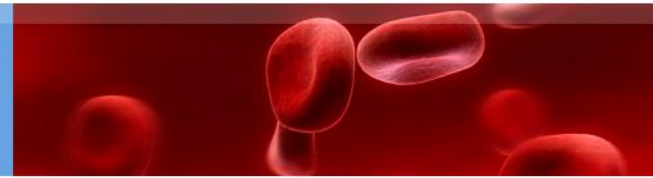
		Gender		p-value
		Male n=57	Female n=51	
Age	n (n missing) X (DE)	56 (1) 42.6 (16.6)	51 (0) 47.2 (16.5)	
Age of symptom onset (years)	n (n missing) X (DE)	48 (9) 21.1 (15.6)	40 (11) 23.7 (16.0)	n.s.
Age of diagnosis (years)	n (n missing) X (DE)	56 (1) 25.6 (15.6)	49 (2) 29.6 (17.2)	n.s.
Familial history of GD1 (Yes)	n (%)	21 (36.8)	25 (49.0)	n.s.
Pre-existing bone complication (Yes)	n (%)	15 (26.3)	8 (15.7)	n.s.
Splenectomy (Yes)	n (%)	16 (28.1)	11 (21.6)	n.s.

Therapeutic goals status and its achievement by gender (n=108)




		Male	Female	p-value
		n = 57	n = 51	
Haemoglobinemia (g/dL)	n (n missing)	57 (0)	51 (0)	n.s.
	X (DE)	14.2 (1.5)	12.9 (1.2)	<0.001
Goal achievers (♂≥12 & ♀≥11)	n (%)	56 (98.2)	49 (96.1)	n.s.
Platelet count (10 ⁹ /L)	n (n missing)	57 (0)	51 (0)	
	X (DE)	174 (92.6)	181 (85.8)	n.s.
Goal achievers (≥120x10 ⁹ /L)	n (%)	40 (70.2)	41 (80.4)	n.s.
Splenomegaly (MN) [only non splenomyzied patients]	n (n missing)	39 (2)	38 (2)	
	X (DE)	4.0 (4.7)	3.0 (4.3)	n.s.
Goal achievers (Size ≤ 8 MN)	n (%)	34 (87.2)	33 (86.8)	n.s.
Hepatomegaly (MN)	n (n missing)	52 (5)	46 (5)	
	X (DE)	1.2 (0.4)	1.1 (0.3)	n.s.
Goal achievers (Size ≤ 1.5 MN)	n (%)	43 (82.7)	43 (93.5)	n.s.
Bone pain (in the last 24 hours) [VAS 0-10]	n (n missing)	47 (10)	47 (4)	
	X (DE)	2.2 (2.3)	1.5 (1.7)	n.s.
Goal achievers (VAS ≤ 1)	n (%)	23 (48.9)	27 (57.4)	n.s.

Therapeutic goals status and its achievement by gender (n=108)

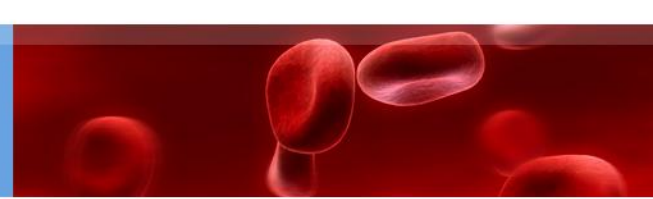


		Male	Female	p-value
		n = 57	n = 51	
Bone pain among patients having pain [VAS > 0]	n (%)	33 (70.2)	26 (55.3)	n.s.
	X (DE)	3.1 (2.2)	2.7 (1.4)	
Bone mineral density (DXA Z-score)	n (n missing)	39 (18)	36 (15)	n.s.
	X (DE)	-0.6 (1.4)	-0.9 (1.1)	
	Goal achievers (Z-score \geq -1)	25 (64.1)	23 (63.9)	
Physical Component Score of SF-36 (0 - 100)	n (n missing)	55 (2)	48 (3)	n.s.
	X (DE)	72.1 (15.7)	73.0 (19.2)	
	Goal achievers (PCS \geq 70)	35 (63.6)	30 (62.5)	
CCL18 (ng/mL)	n (%)	34 (59.6)	33 (64.7)	n.s.
	X (DE)	484.5 (652.4)	452.7 (673.5)	
	Med (Q1-Q3)	249.5 (139.5 - 599.0)	259.0 (131.0 - 461.0)	
	Min – Max	44.0 - 3300.0	69.0 - 3720.0	
CHITO (nmol/mL*h)	n (%)	44 (77.2)	44 (86.3)	n.s.
	X (DE)	3988.1 (10277.7)	2129.9 (2206.6)	
	Med (Q1-Q3)	1300.0 (563.0 - 3150.0)	1218.5 (437.5 - 3200.5)	
	Min – Max	10.6 - 65497.0	15.0 - 8648.0	



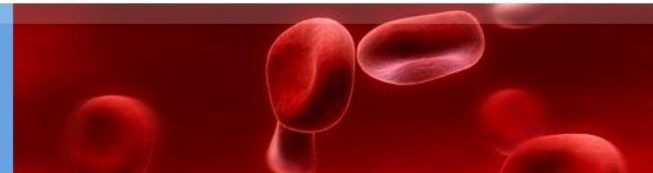
**ANALYSIS BY
SPLENECTOMY YES/NO
(n=108)**

Patient Characteristics by splenectomy (n=108)



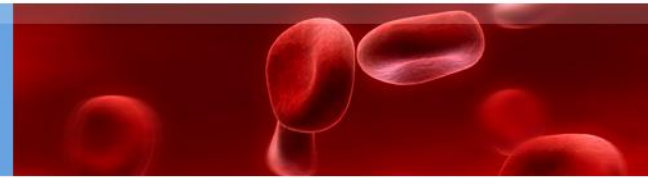
		Splenectomy		
		No n=81	Yes n=27	p-value
Age of symptom onset (years)	n (n missing) X (DE)	61 (20) 22.4 (16.0)	27(0) 21.9 (15.6)	n.s.
Age of diagnosis (years)	n (n missing) X (DE)	78 (3) 27.8 (16.5)	27 (0) 26.6 (16.3)	n.s.
Familial history of GD1 (Yes)	n (%)	40 (49.4)	6 (22.2)	0.0134
Pre-existing bone complication (Yes)	n (%)	16 (19.8)	7 (25.9)	n.s.

Therapeutic goals status and its achievement by splenectomy (n=108)



		Non splenectomized n = 81	Splenectomized n = 27	p-value
Haemoglobinemia (g/dL)	n (n missing)	81 (0)	27 (0)	0.586
	X (DE)	13.6 (1.5)	13.5 (1.3)	
Goal achievers (♂≥12 & ♀≥11)	n (%)	79 (97.5)	26 (96.3)	1.000
Platelet count (10 ⁹ /L)	n (n missing)	81 (0)	27 (0)	<0.001
	X (DE)	148 (50.1)	264 (120.0)	
Goal achievers (≥120x10 ⁹ /L)	n (%)	57 (70.4)	24 (88.9)	0.054
Splenomegaly (MN) [only non splenectomized patients]	n (n missing)	77 (4)	27 (0)	
	X (DE)	3.5 (4.5)	-	
Goal achievers (Size ≤ 8 MN)	n (%)	67 (87.0)	-	
Hepatomegaly (MN)	n (n missing)	75 (6)	23 (4)	0.3225
	X (DE)	1.2 (0.3)	1.2 (0.3)	
Goal achievers (Size ≤ 1.5 MN)	n (%)	67 (89.3)	19 (82.6)	0.468
Bone pain (in the last 24 hours) [VAS 0-10]	n (n missing)	71 (10)	23 (4)	0.365
	X (DE)	1.8 (2.2)	2.0 (1.8)	
Goal achievers (VAS ≤ 1)	n (%)	41 (57.7)	9 (39.1)	0.120

Therapeutic goals status and its achievement by splenectomy (n=108)



		Non splenectomized	Splenectomized	p-value
		n = 81	n = 27	
Bone pain among patients having pain [VAS > 0]	n (%)	43 (60.6)	16 (69.6)	0.643
	X (DE)	2.9 (2.1)	2.8 (1.4)	
Bone mineral density (DXA Z-score)	n (n missing)	58 (23)	17 (10)	0.157
	X (DE)	-0.6 (1.2)	-1.1 (1.5)	
	Goal achievers (Z-score ≥ -1)	39 (67.2)	9 (52.9)	
Physical Component Score of SF-36 (0 - 100)	n (n missing)	78 (3)	25 (2)	0.684
	X (DE)	72.6 (17.8)	72.2 (16.2)	
	Goal achievers (PCS ≥ 70)	49 (62.8)	16 (64.0)	
CCL18 (ng/mL)	n (%)	49 (60.5)	18 (66.7)	0.034
	X (DE)	387.1 (591.9)	704.5 (798.2)	
	Med (Q1-Q3)	215.0 (116.0 - 418.5)	631.0 (152.0 - 877.0)	
	Min – Max	44.0 - 3720.0	131.0 - 3300.0	
CHITO (nmol/mL*h)	n (%)	65 (80.2)	23 (85.2)	0.3529
	X (DE)	3318.5 (8678.4)	2405.3 (2219.0)	
	Med (Q1-Q3)	1143.0 (379.7 - 3150.0)	1729.0 (818.0 - 3505.0)	
	Min – Max	10.6 - 65497.0	15.0 - 8648.0	

Table 5 Complete Data Analysis Set: Therapeutic goals status and its achievement (n=65)



		All patients n = 65	Patients by treatment status			Patients by splenectomy status		
			Without treatment n = 9	On treatment n = 56	p-value	Non splenectomized n = 50	Splenectomized n = 15	p-value
Patients achieving goals								
7	n (%)	10 (15.4)	0 (0.0)	10 (17.9)		10 (20.0)	0 (0.0)	
6	n (%)	15 (23.1)	3 (33.3)	12 (21.4)		14 (28.0)	1 (6.7)	
5	n (%)	24 (36.9)	2 (22.2)	22 (39.3)		18 (36.0)	7 (46.7)	
4	n (%)	10 (15.4)	1 (11.1)	9 (16.1)		6 (12.0)	11 (73.4)	
3	n (%)	4 (6.2)	2 (22.2)	2 (3.6)		1 (2.0)	14 (93.4)	
2	n (%)	2 (3.1)	1 (11.1)	1 (1.8)		1 (2.0)	15 (100)	



OTHER ANALYSIS

Therapeutic goals status and its achievement by splenectomy and Tx (n=108)

		Non Splenectomized		Splenectomized		p-value
		w/o Tx	On Tx	w/o Tx	On Tx	
		n = 11	n = 70	n = 2	n = 25	
Haemoglobinemia (g/dL)	n (n missing)	8	42	1	14	
	X (DE)	13.4 (1.2)	13.9 (1.3)	11	13.4 (1.0)	n.s.
Goal achievers (♂ \geq 12 & ♀ \geq 11)	n (%)	8 (100)	42 (100)	0 (0.0)	14 (100)	n.s.
Platelet count (10 ⁹ /L)	n (n missing)	8	42	1	14	
	X (DE)	112 (38.7)	157 (50.3)	75	214 (63.3)	< 0.001^{1,2}
Goal achievers (\geq 120x10 ⁹ /L)	n (%)	5 (62.5)	30 (71.4)	0 (0.0)	13 (92.9)	n.s.
Splenomegaly (MN) [only non splenomyzed patients]	n (n missing)	8	42	1	14	
	X (DE)	4.9 (6.4)	2.9 (3.7)	-	-	n.s.
Goal achievers (Size \leq 8 MN)	n (%)	7 (87.5)	38 (90.5)	-	-	-
Hepatomegaly (MN)	n (n missing)	8	42	1	14	
	X (DE)	1.5 (0.5)	1.1 (0.2)	1.2	1.4 (0.3)	0.013 ²
Goal achievers (Size \leq 1.5 MN)	n (%)	4 (50.0)	40 (95.2)	1 (100)	10 (71.4)	0.002²
Bone pain (in the last 24 hours) [VAS 0-10]	n (n missing)	8	42	1	14	
	X (DE)	2.4 (3.2)	1.6 (2.1)	2	1.5 (1.6)	n.s.
Goal achievers (VAS \leq 1)	n (%)	4 (50.0)	26 (61.9)	0 (0.0)	8 (57.1)	n.s.

w/o Tx = Without Treatment; On Tx = On Treatment

¹ Significant differences between Splenectomized patients on treatment and Non-splenectomized patients without treatment

² Significant differences between Splenectomized patients on treatment and Non-splenectomized patients on treatment

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Therapeutic goals status and its achievement by splenectomy and Tx (n=108)

		Non Splenectomized		Splenectomized		p-value
		w/o Tx	On Tx	w/o Tx	On Tx	
		n = 11	n = 70	n = 2	n = 25	
Bone pain among patients having pain [VAS > 0]	n (n missing) X (DE)	5 3.9 (3.3)	23 3.0 (2.1)	1 2	8 2.6 (1.2)	n.s.
Bone mineral density (DXA Z-score)	n (n missing) X (DE)	8 -1.1 (1.3)	42 -0.6 (1.1)	1 2	14 -1.4 (1.3)	n.s.
Goal achievers ($\geq 120 \times 10^9/L$)	n (%)	4 (50.0)	29 (69.0)	1 (100)	6 (42.9)	n.s.
Physical Component Score of SF-36 (0 - 100)	n (n missing) X (DE)	8 70.3 (10.0)	42 75.3 (18.3)	1 81.8	14 73.6 (17.2)	n.s.
Goal achievers (Size ≤ 8 MN)	n (%)	5 (62.5)	31 (73.8)	1 (100)	9 (64.3)	n.s.

w/o Tx = Without Treatment; On Tx = On Treatment

¹ Significant differences between Splenectomized patients on treatment and Non-splenectomized patients without treatment

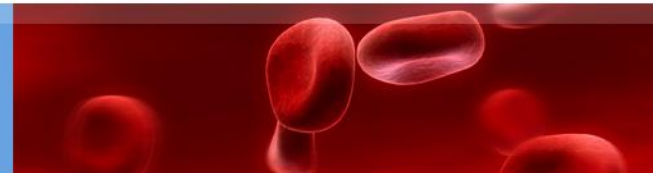
² Significant differences between Splenectomized patients on treatment and Non-splenectomized patients on treatment

Therapeutic goals status and its achievement by gender & age (n=108)

Females

		≤18 years old n = 2	19 – 40 years old n = 17	41 – 65 years old n = 26	>65 years old n = 6
Haemoglobinemia (g/dL)	n (n missing)	2	9	17	3
	X (DE)	13.5 (1.0)	13.1 (0.7)	13.3 (1.0)	12.8 (0.9)
	Goal achievers (♂≥12 & ♀≥11)	2 (100)	9 (100)	17 (100)	3 (100)
Platelet count (10 ⁹ /L)	n (n missing)	2	9	17	3
	X (DE)	260 (24.7)	167 (46.9)	165 (40.7)	134 (49.0)
	Goal achievers (≥120x10 ⁹ /L)	2 (100)	8 (88.9)	14 (82.4)	1 (33.3)
Splénomegaly (MN) [only non splenomyzed patients]	n (n missing)	1	8	13	2
	X (DE)	0.6	2.3 (3.2)	3.5 (5.1)	1.1 (0.0)
	Goal achievers (Size ≤ 8 MN)	2 (100)	9 (100)	16 (94.1)	2 (66.7)
Hepatomegaly (MN)	n (n missing)	2	9	17	3
	X (DE)	1.0 (0.0)	1.1 (0.2)	1.1 (0.2)	1.4 (0.3)
	Goal achievers (Size ≤ 1.5 MN)	1 (100)	7 (87.5)	11 (84.6)	2 (100)
Bone pain (in the last 24 hours) [VAS 0-10]	n (n missing)	2	9	17	3
	X (DE)	2.0 (2.8)	0.9 (1.8)	1.7 (1.9)	2.0 (2.0)
	Goal achievers (VAS ≤ 1)	1 (50.0)	7 (77.8)	9 (52.9)	1 (33.3)

Therapeutic goals status and its achievement by gender and age (n=108)



		Females			
		≤18 years old	19 – 40 years old	41 – 65 years old	>65 years old
		n = 2	n = 17	n = 26	n = 6
Bone pain among patients having pain [VAS > 0]	n (n missing)	1	2	11	2
	X (DE)	4	4.0 (1.4)	2.6 (1.7)	3.0 (1.4)
Bone mineral density (DXA Z-score)	n (n missing)	2	9	17	3
	X (DE)	0.8 (1.1)	-0.7 (1.1)	-1.1 (1.1)	-1.6 (1.1)
Goal achievers (≥120x10 ⁹ /L)	n (%)	2 (100)	7 (77.8)	8 (47.1)	1 (33.3)
Physical Component Score of SF-36 (0 - 100)	n (n missing)	2	9	17	3
	X (DE)	73.5 (30.4)	81.4 (8.8)	71.0 (22.6)	57.5 (23.8)
Goal achievers (Size ≤ 8 MN)	n (%)	1 (50.0)	8 (88.9)	11 (64.7)	1 (33.3)

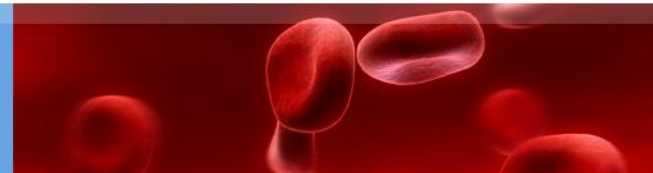
Therapeutic goals status and its achievement by gender & age (n=108)

Males

		≤18 years old	19 – 40 years old	41 – 65 years old	>65 years old
		N=7	N=19	N=26	N=4
Haemoglobinemia (g/dL)	n (n missing)	3	12	16	2
	X (DE)	14.2 (2.4)	14.2 (1.5)	14.3 (1.0)	12.1 (1.6)
	Goal achievers (♂≥12 & ♀≥11)	3 (100)	12 (100)	16 (100)	1 (50.0)
Platelet count (10 ⁹ /L)	n (n missing)	3	12	16	2
	X (DE)	171 (26.7)	123 (53.3)	183 (79.9)	117 (59.4)
	Goal achievers (≥120x10 ⁹ /L)	3 (100)	5 (41.7)	13 (81.3)	1 (50.0)
Splénomegaly (MN) [only non splenomyzed patients]	n (n missing)	3	12	10	-
	X (DE)	2.0 (1.7)	4.8 (5.2)	3.1 (3.9)	-
	Goal achievers (Size ≤ 8 MN)	2 (66.7)	9 (75.0)	13 (81.3)	1 (50.0)
Hepatomegaly (MN)	n (n missing)	3	12	16	2
	X (DE)	1.3 (0.6)	1.4 (0.4)	1.3 (0.3)	1.4 (0.3)
	Goal achievers (Size ≤ 1.5 MN)	3 (100)	11 (91.7)	9 (90.0)	0 (0.0)
Bone pain (in the last 24 hours) [VAS 0-10]	n (n missing)	3	12	16	2
	X (DE)	0.0 (0.0)	2.4 (3.3)	2.0 (2.0)	1.0 (1.4)
	Goal achievers (VAS ≤ 1)	3 (100)	8 (66.7)	7 (43.8)	1 (50.0)

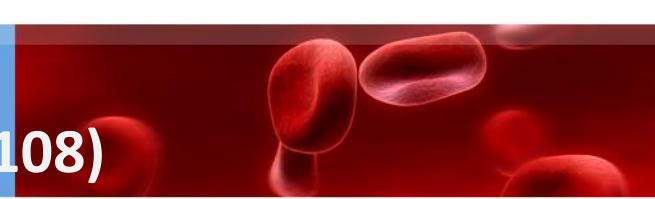
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Therapeutic goals status and its achievement by gender and age (n=108)



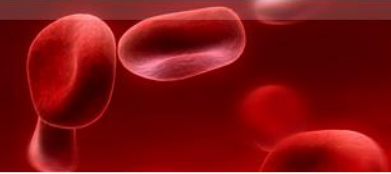
		Males			
		≤18 years old	19 – 40 years old	41 – 65 years old	>65 years old
		N=7	N=19	N=26	N=4
Bone pain among patients having pain [VAS > 0]	n (n missing)	-	7	12	1
	X (DE)	-	4.2 (3.3)	2.7 (1.8)	2
Bone mineral density (DXA Z-score)	n (n missing)	3	12	16	2
	X (DE)	-0.3 (3.1)	-0.6 (0.9)	-1.0 (1.2)	0.7 (1.8)
	Goal achievers (≥120x10 ⁹ /L)	n (%)	2 (66.7)	9 (75.0)	8 (50.0)
Physical Component Score of SF-36 (0 - 100)	n (n missing)	3	12	16	2
	X (DE)	75.8 (12.3)	77.3 (15.2)	73.1 (13.1)	80.9 (1.3)
	Goal achievers (Size ≤ 8 MN)	n (%)	2 (66.7)	10 (83.3)	10 (62.5)

Therapeutic goals status and its achievement by time since diagnosis (n=108)



		Years since diagnosis		
		<10 years	10 – 20 years	≥20 years
		N=16	N=22	N=24
Haemoglobinemia (g/dL)	n (n missing)	16	22	24
	X (DE)	13.7 (1.7)	13.9 (1.1)	13.5 (1.1)
Goal achievers (♂≥12 & ♀≥11)	n (%)	16 (100)	22 (100)	23 (95.8)
Platelet count (10 ⁹ /L)	n (n missing)	16	22	24
	X (DE)	158 (66.8)	159 (51.9)	169 (67.5)
Goal achievers (≥120x10 ⁹ /L)	n (%)	11 (68.8)	17 (77.3)	17 (70.8)
Splenomegaly (MN) [only non splenomyzed patients]	n (n missing)	13	20	14
	X (DE)	4.7 (5.4)	2.6 (3.6)	3.2 (4.3)
Goal achievers (Size ≤ 8 MN)	n (%)	11 (84.6)	19 (95.0)	12 (85.7)
Hepatomegaly (MN)	n (n missing)	16	22	24
	X (DE)	1.4 (0.4)	1.2 (0.3)	1.2 (0.3)
Goal achievers (Size ≤ 1.5 MN)	n (%)	11 (68.8)	19 (86.4)	22 (91.7)
Bone pain (in the last 24 hours) [VAS 0-10]	n (n missing)	16	22	24
	X (DE)	2.0 (2.6)	0.9 (1.4)	2.3 (2.3)
Goal achievers (VAS ≤ 1)	n (%)	9 (56.3)	16 (72.7)	11 (45.8)

Therapeutic goals status and its achievement by time since diagnosis (n=108)



		Years since diagnosis		
		<10 years	10 – 20 years	≥20 years
		N=16	N=22	N=24
Bone pain among patients having pain [VAS > 0]	n (n missing)	10 (62.5)	8 (36.4)	17 (70.8)
	X (DE)	3.3 (2.6)	2.4 (1.4)	3.3 (2.1)
Bone mineral density (DXA Z-score)	n (n missing)	16	22	24
	X (DE)	-1.2 (1.2)	-0.5 (1.2)	-0.8 (1.4)
	Goal achievers ($\geq 120 \times 10^9/L$)	8 (50.0)	15 (68.2)	14 (58.3)
Physical Component Score of SF-36 (0 - 100)	n (n missing)	16	22	24
	X (DE)	78.1 (14.5)	72.6 (18.0)	72.9 (18.0)
	Goal achievers (Size ≤ 8 MN)	13 (81.3)	14 (63.6)	17 (70.8)

Therapeutic goals status and its achievement by treatment initiation (n=108)

		Years since treatment initiation	
		<10	≥10
		N=30	N=24
Haemoglobinemia (g/dL)	n (n missing)	30	24
	X (DE)	13.6 (1.3)	14.1 (1.1)
Goal achievers (♂≥12 & ♀≥11)	n (%)	30 (100)	24 (100)
Platelet count (10 ⁹ /L)	n (n missing)	30	24
	X (DE)	165 (65.7)	173 (54.5)
Goal achievers (≥120x10 ⁹ /L)	n (%)	20 (66.7)	20 (83.3)
Splenomegaly (MN) [only non splenomyzed patients]	n (n missing)	22	19
	X (DE)	4.6 (5.2)	2.1 (3.5)
Goal achievers (Size ≤ 8 MN)	n (%)	18 (81.8)	18 (94.7)
Hepatomegaly (MN)	n (n missing)	30	24
	X (DE)	1.3 (0.3)	1.1 (0.3)
Goal achievers (Size ≤ 1.5 MN)	n (%)	26 (86.7)	21 (87.5)
Bone pain (in the last 24 hours) [VAS 0-10]	n (n missing)	30	24
	X (DE)	2.0 (2.3)	1.3 (2.0)
Goal achievers (VAS ≤ 1)	n (%)	17 (56.7)	16 (66.7)

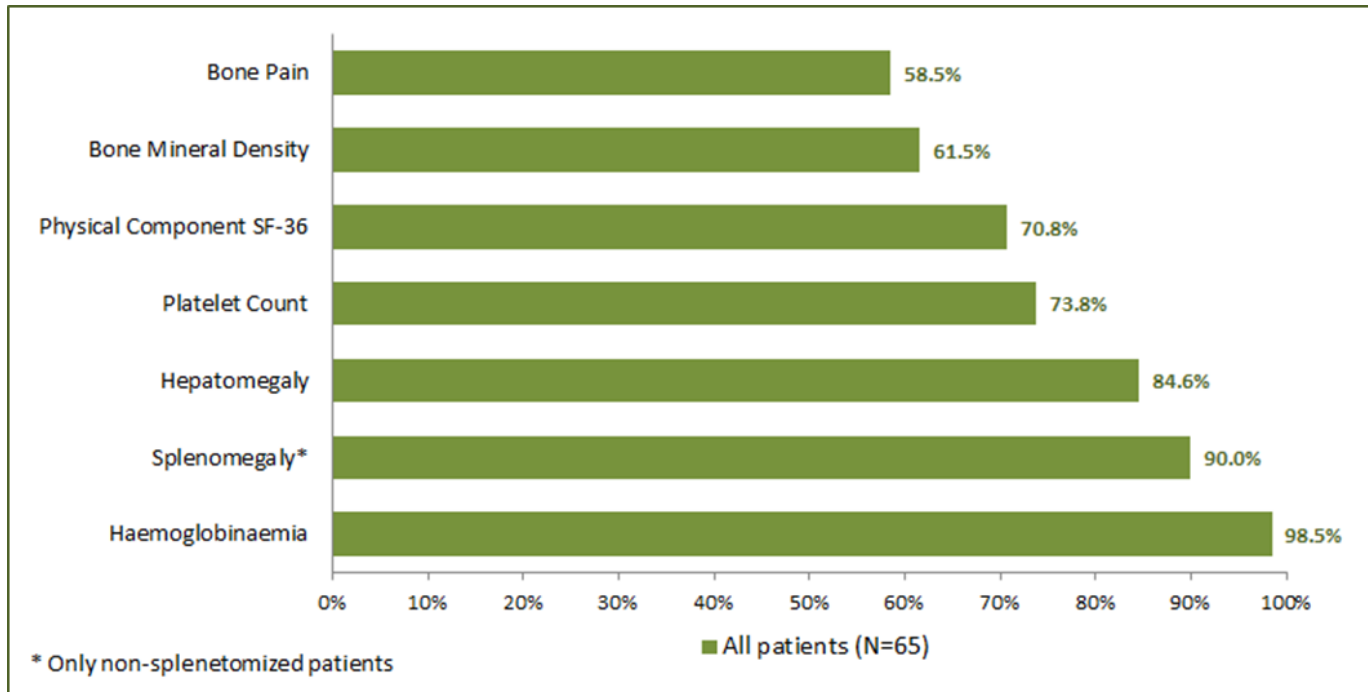
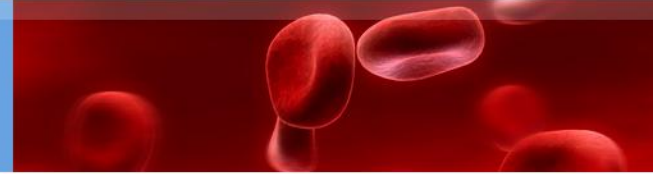
Therapeutic goals status and its achievement by treatment initiation (n=108)

		Years since treatment initiation	
		<10	≥10
		N=30	N=24
Bone pain among patients having pain [VAS > 0]	n (n missing)	20 (66.7)	10 (41.7)
	X (DE)	3.0 (2.2)	3.0 (1.9)
Bone mineral density (DXA Z-score)	n (n missing)	30	24
	X (DE)	-1.2 (1.1)	-0.4 (1.3)
Goal achievers (≥120x10 ⁹ /L)	n (%)	13 (43.3)	19 (79.2)
Physical Component Score of SF-36 (0 - 100)	n (n missing)	30	24
	X (DE)	76.2 (16.7)	75.3 (17.2)
Goal achievers (Size ≤ 8 MN)	n (%)	22 (73.3)	18 (75.0)



FULL CASES ANALYSIS (n=65)

Therapeutic goals status and its achievement (n=65)

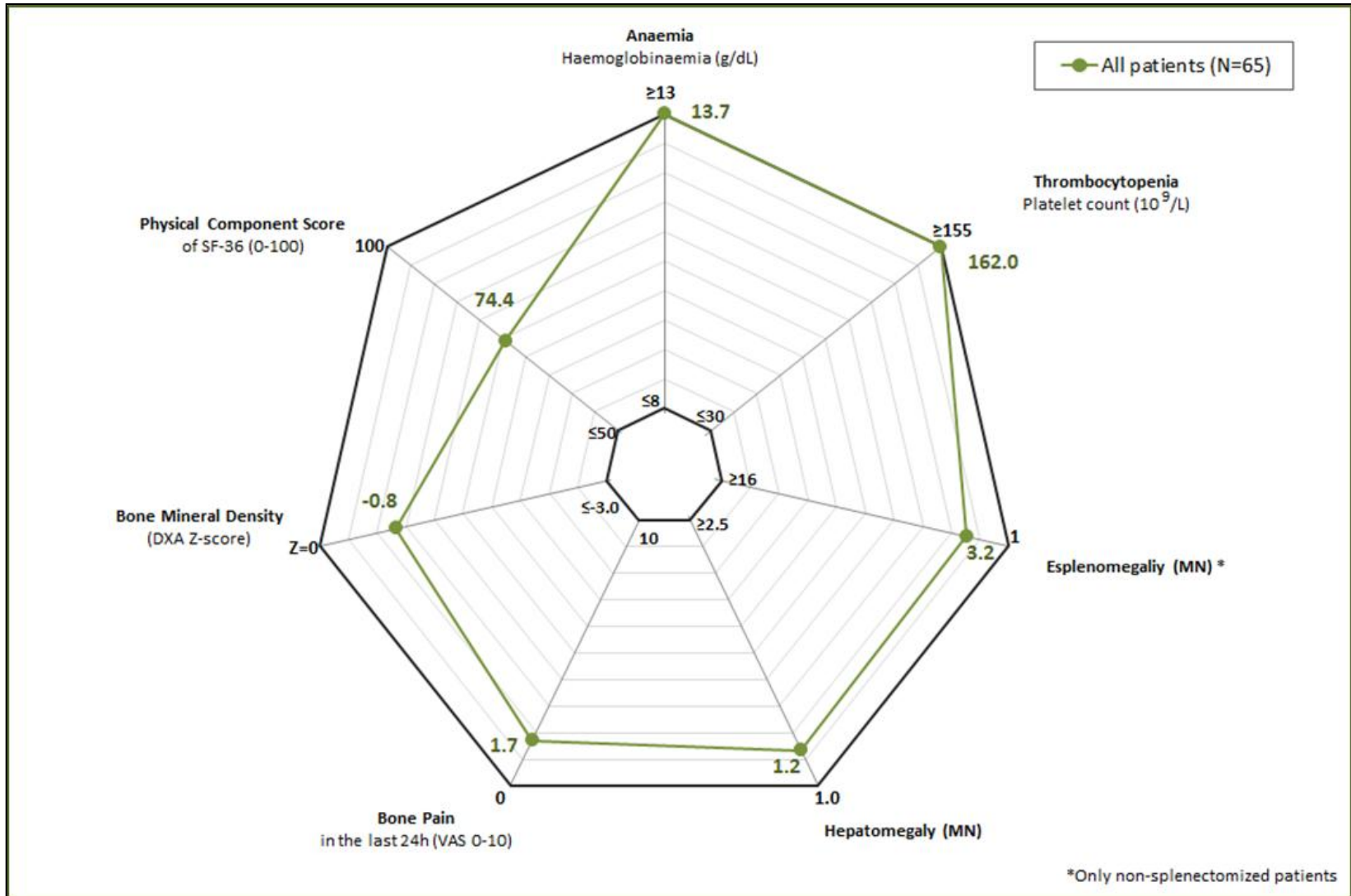
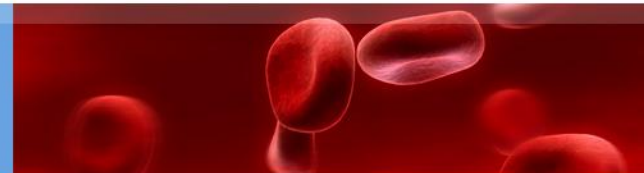



Total n=65

Goals Met	Cumulative	n(%)
7	n(%)	10 (15.4)
6	n(%)	15 (23.1)
5	n(%)	24 (36.9)
4	n(%)	10 (15.4)
3	n(%)	4 (6.2)
2	n(%)	2 (3.1)



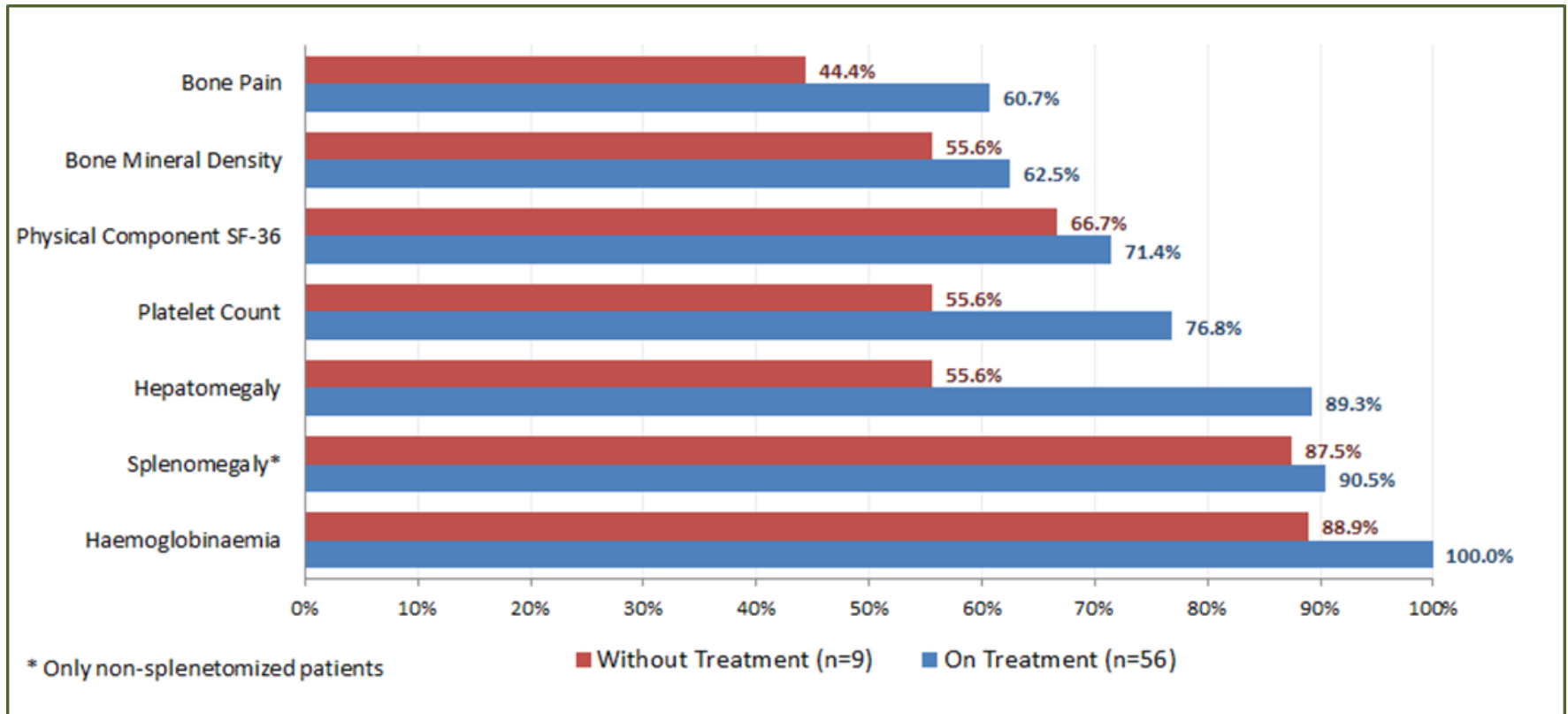
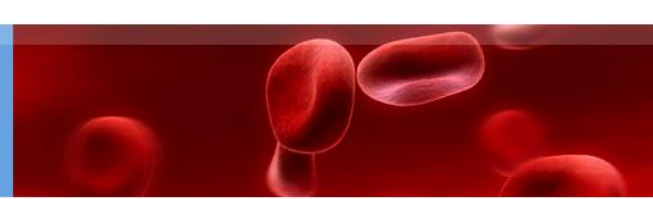
Therapeutic goals status and its achievement (n=65)



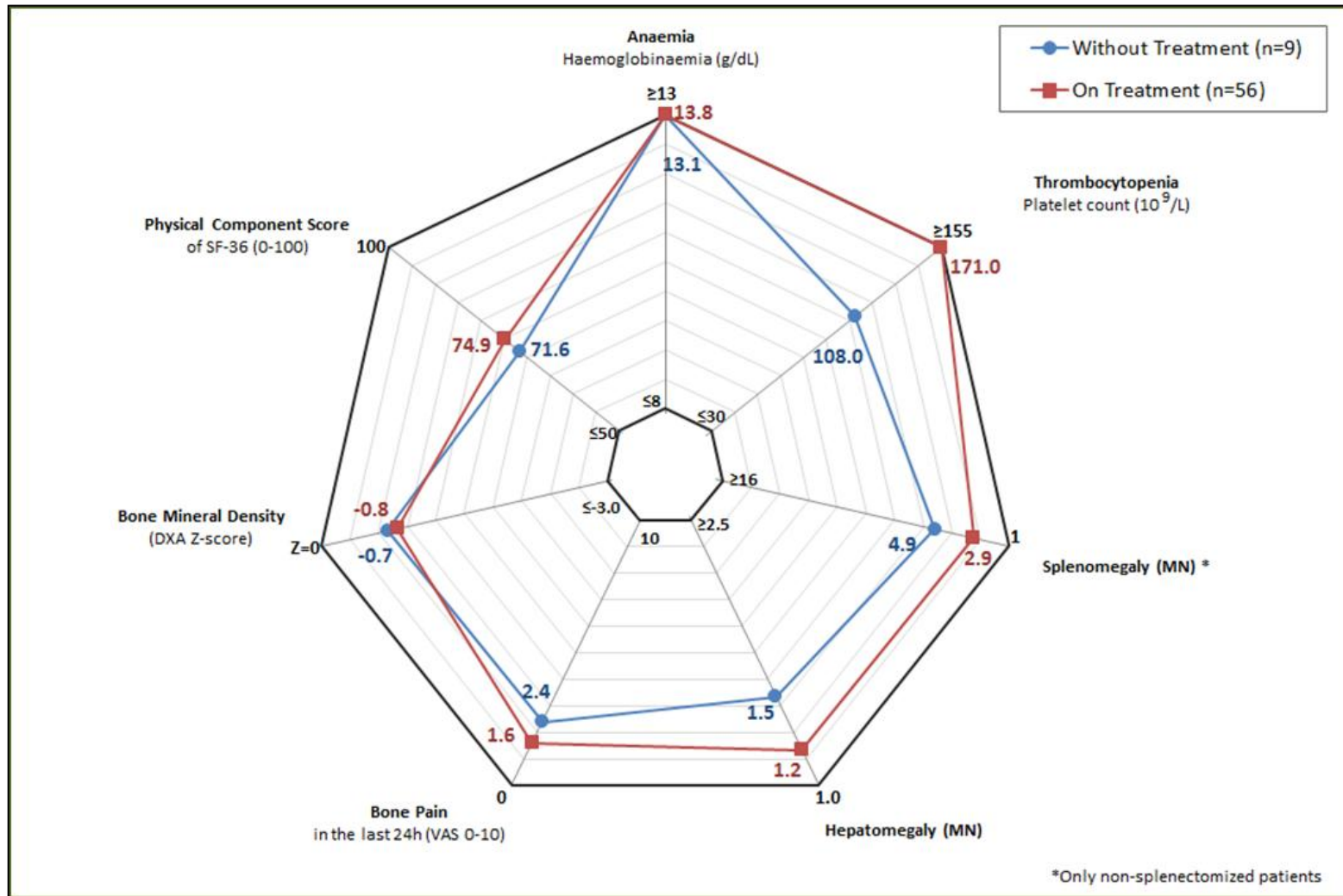
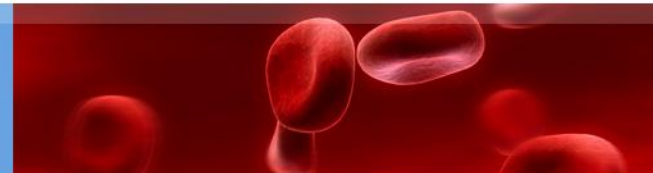



**FULL CASES
ANALYSIS BY
TREATMENT YES/NO
(n=65)**

Therapeutic goals status and its achievement by treatment (n=65)



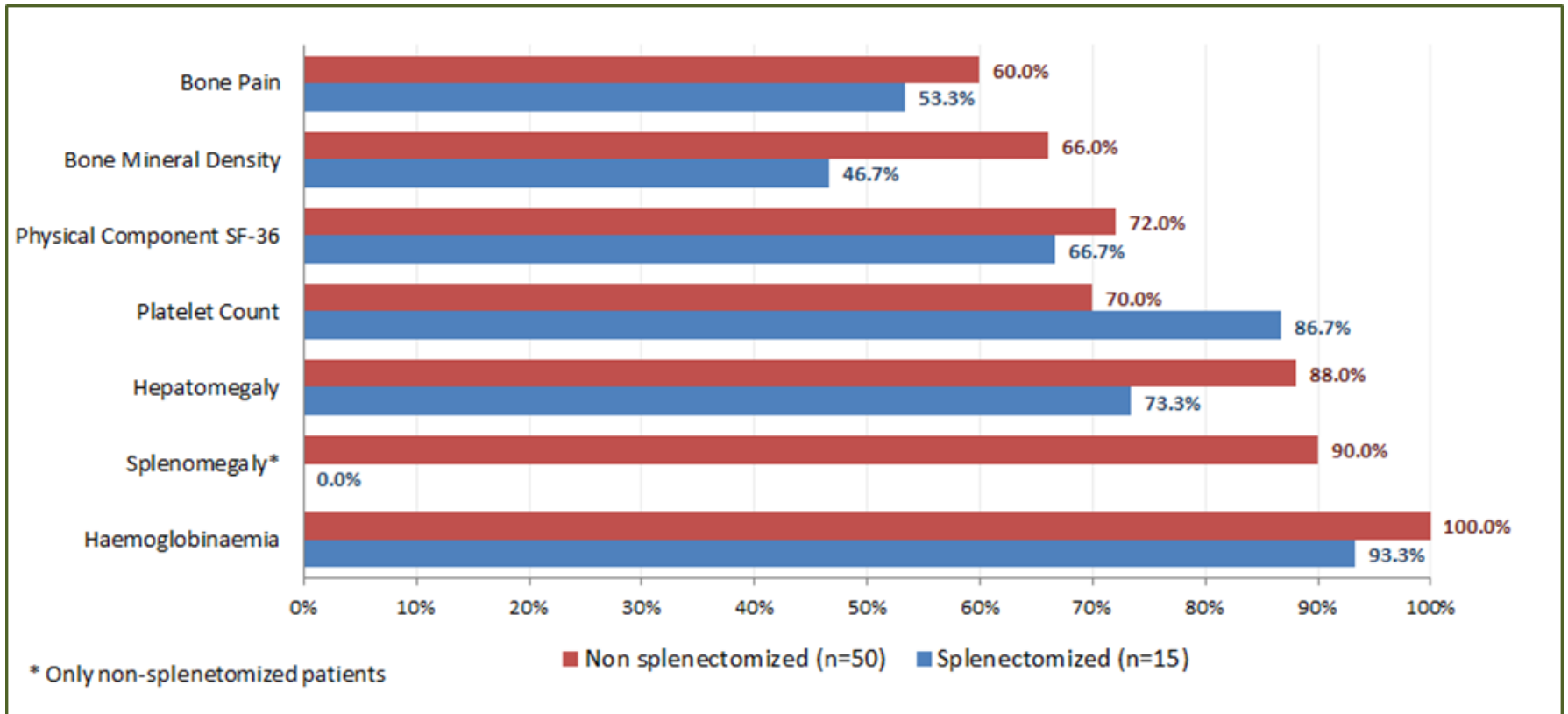
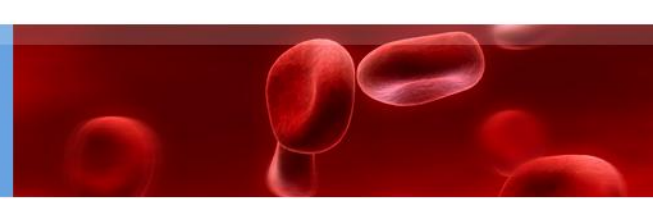
Therapeutic goals status and its achievement by treatment (n=65)



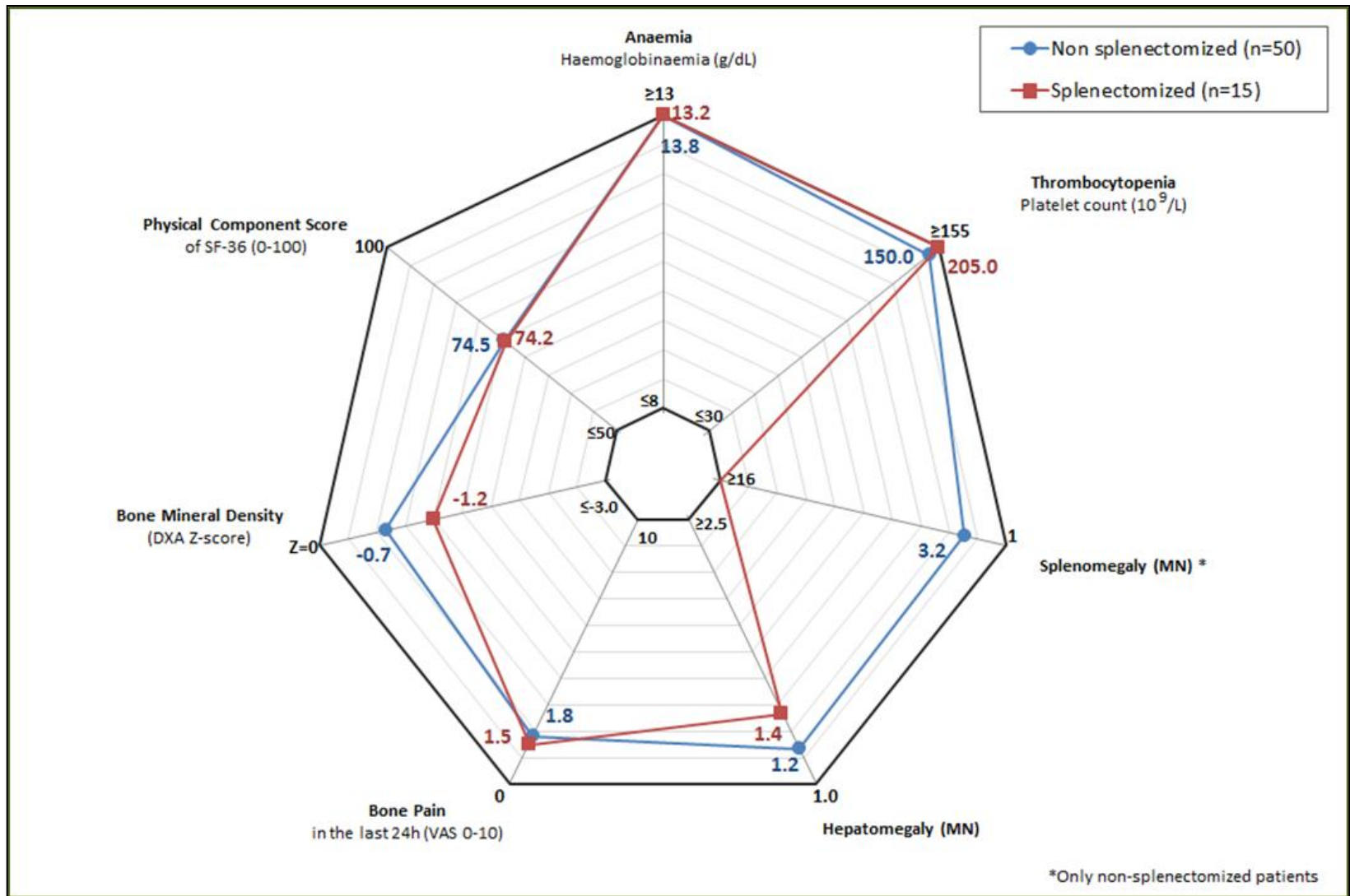


**FULL CASES ANALYSIS
BY SPLENECTOMY
YES/NO
(n=65)**

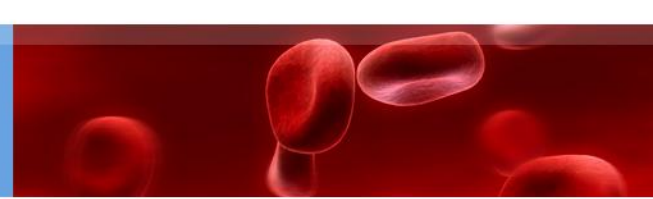
Therapeutic goals status and its achievement by treatment (n=65)



Therapeutic goals status and its achievement by treatment (n=108)



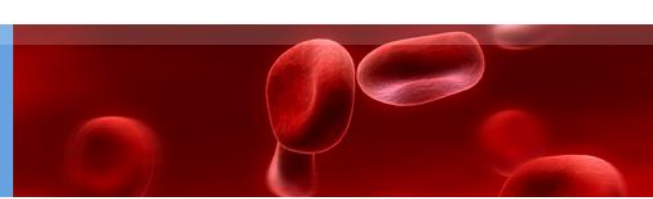
Summary



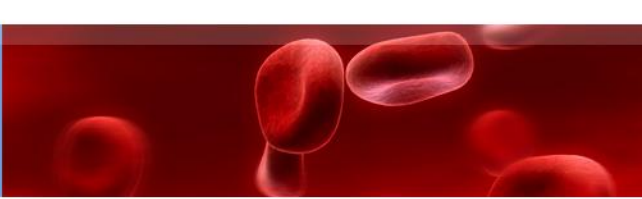
- **MAP tool provides an easy management framework to manage and follow up the disease**
- **On an heterogenous GD I population, data has shown:**
 - Good Hb control (97.2%)
 - Good hepatomegaly control (87.8%)
 - Good splenomegaly control (87.0%)
 - Good plateletets control (75%)

 - Physical component of SF-36 (PCS \geq 70): (63.1%)
 - Bone mineral density (Z-score \geq -1) (64%)
 - Bone pain achievers (VAS \leq 1) (53.2%)

Conclusion



- **MAP tool provides an easy management framework to manage and follow up the disease**
 - **Control is done properly in most objectives**
 - **However only 65 patients registry information on the 7 goals**
 - **33 patients (10 splenectomized) lacking BMD analysis**
 - **Harmonization of data collection between different centers would be necessary**



Gracias