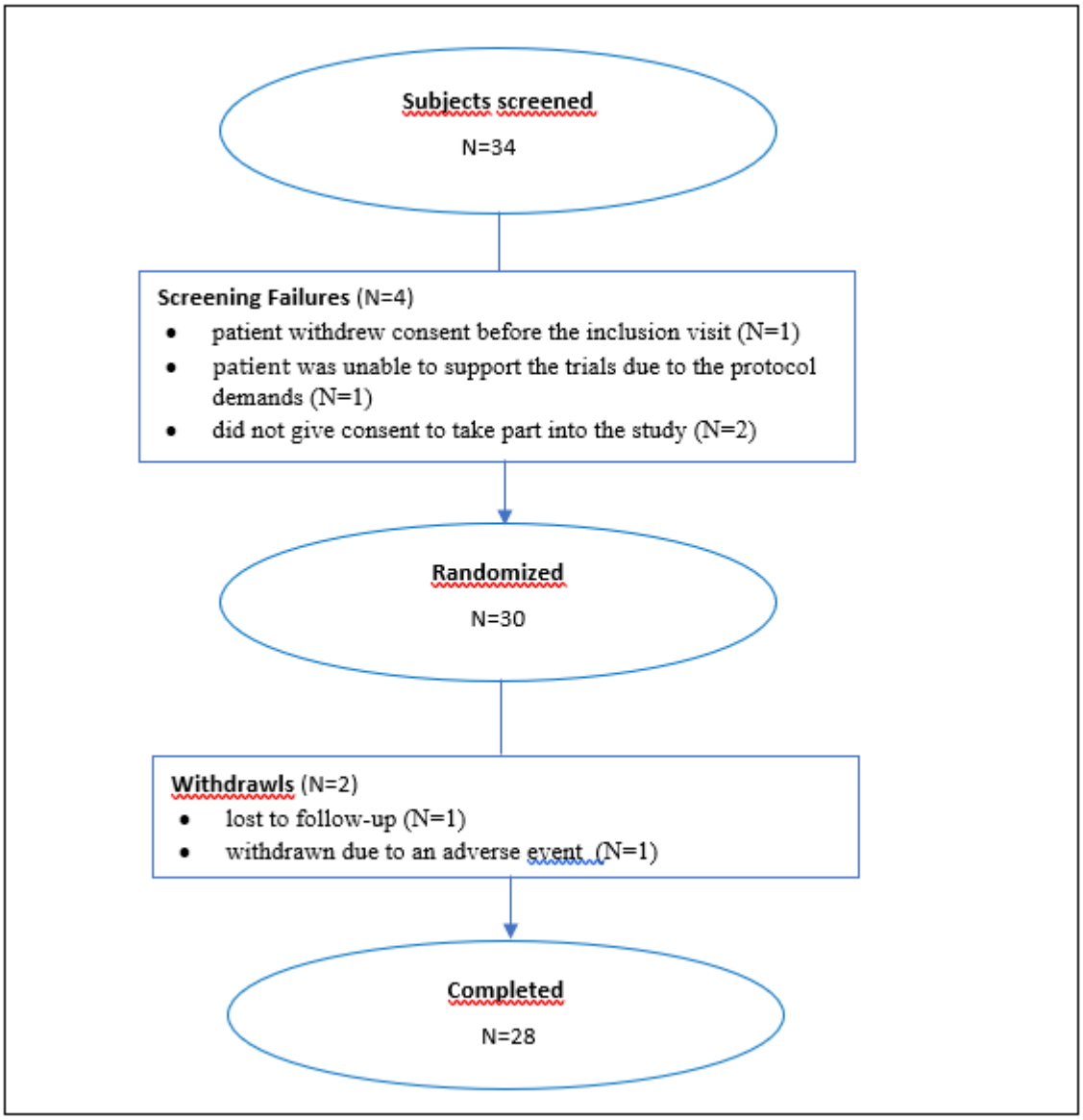
GAN-06 Study Results

1. Participant Flow

In total, 34 patients were screened in 12 study centres in Germany (8 patients), the UK (14 patients), Italy (5 patients) and Australia (7 patients). Out of the 34 screened patients, 4 patients withdrew prior to first administration of study:
1 patient withdrew consent before the inclusion visit, 1 patient was unable to support the trials due to the protocol demands and 2 patients did not give their consents to take part into the study. A total of 28 patients completed the study.

Table 1: flow diagram for participants in this study:



2. Baseline Characteristics

Table 2: Summary of baseline characteristics and demographic data (Safety Population N= 30):

		Number of patients N=30
Age (years)	N	30
	mean±SD	46.2±14.7
	[Min;Max];median	[20.0;73.0];46.0
	Q1;Q3	38.0; 58.0
Female gender	N (%)	15 (50.0%)
Male gender	N (%)	15 (50.0%)
Weight (Kg)	N	30
	mean±SD	78.6±17.1
	[Min;Max];median	[46.7;116.0];80.0
	Q1;Q3	64.0; 90.0
Institutional living	N (%)	1 (3.4%)
Living alone	N (%)	6 (20.7%)
Living with a partner / a family	N (%)	22 (75.9%)
Other	N (%)	0
	ND	1
Professional/school occupation	N (%)	19 (65.5%)
No professional occupation	N (%)	10 (34.5%)
	ND	1
Disability	N	2
Long-term sickness	N	0
Retired	N	5
Sick leave	N	0
Unemployed	N	3

Clinical Study Report, Table 14.1.2-1

The primary efficacy endpoint of this study was the patient satisfaction with the treatment delivery device, as assessed by the LQI scale (factor I: treatment interference) at the end of the 3-month treatment period with each delivery device of Gammanorm® 165 mg/mL (pump or syringe).

At enrolment, patients exhibited high levels of satisfaction regarding IgG replacement therapy by automatic pump at home (FAS population: mean LQI I at 84.0±11.8; PP population: 82.6±11.6). LQI I was lower with the syringe than with the pump since the ratio of Lsmeans was 93.51% [87.58% - 99.84%] in the FAS population and 94.56% [88.53% - 100.99%] in the PP population.

Table 3: Mean LQI I Factors at Baseline and Endpoint: FAS Population (N=29) and PP Population (N=26)

Time of measurement	LQI I FAS Population	LQI I PP Population
Baseline	84.0±11.8	82.6±11.6
Endpoint Pump Sequence	85.3±11.2 (+1.3)	84.6±11.2 (+2.0)
Endpoint Syringe Sequence	80.3±10.5 (–3.7)	80.2±10.1 (–2.4)

Clinical Study Report, Table 10
Numbers in parentheses indicate changes compared to Baseline.

LQI factor II (therapy-related problems) and LQI factor III (therapy setting) were assessed as secondary efficacy endpoints at the end of the 3-month treatment period with each delivery device of Gammanorm® 165 mg/mL (pump or syringe).
At enrolment, the patients showed high levels of satisfaction regarding IgG replacement therapy (FAS population: mean LQI II at 78.4±13.4 and mean LQI III at 91.5±10.8; PP population: mean LQI II at 77.5±13.8 and mean LQI III at 90.7±11.1)

Table 4: Mean LQI factors II and III at Baseline and Endpoint: FAS Population (N=29), PP Population (N=26)

Time of measurement	LQI II FAS	LQI III FAS	LQI II PP	LQI III PP
Baseline	78.4±13.4	91.5±10.8	77.5±13.8	90.7±11.1
Endpoint Pump Sequence	75.1±14.5 (-3.3)	87.6±13.2 (-3.9)	76.0±13.0 (-1.5)	87.5±13.3 (-3.2)
Endpoint Syringe Sequence	75.0±13.6 (-3.4)	88.3±9.7 (-3.2)	74.6±13.5 (-2.9)	87.9±9.7 (-2.8)

Clinical Study Report, Table 12 Numbers in parentheses indicate changes when compared to Baseline.

3. Outcome Measures

3.1 Primary outcome measures

The primary efficacy endpoint of this study was the patient satisfaction with the treatment delivery device, as assessed by the LQI scale (factor I: treatment interference) at the end of the 3-month treatment period with each delivery device of Gammanorm® 165 mg/mL (pump or syringe).
At enrolment, patients exhibited high levels of satisfaction regarding IgG replacement therapy by automatic pump at home (FAS population: mean LQI I at 84.0±11.8; PP population: 82.6±11.6). LQI I was lower with the syringe than with the pump since the ratio of Lsmeans was 93.51% [87.58% - 99.84%] in the FAS population and 94.56% [88.53% - 100.99%] in the PP population.

Table 5: Lsmeans for LQI I Factors at Endpoint: FAS Population (N=29) and PP Population (N=26)

	LQI I FAS Population	LQI I PP Population
Lsmean Endpoint Pump Sequence	84.32 [79.80-89.09]	83.21 [78.60-88.08]
Lsmean Endpoint Syringe Sequence	78.85 [74.74-83.18]	78.68 [74.33-83.29]
Ratio of Lsmeans Syringe / Pump	93.51 [87.58-99.84]	94.56 [88.53-100.99]

Clinical Study Report, Table 11 ; CI= Confidence Interval

3.2 Secondary outcome measures

3.2.1 LQI subscores

The secondary efficacy endpoints were LQI sub-scores (factor II: therapy-related problems; factor III: therapy setting).

For LQI II, the ratio syringe/pump was 99.69% [92.06% - 107.95%] in the FAS population and 99.69% [92.06% - 107.95%] in the PP population. Since the confidence intervals included the value one (100%), there was no difference between the delivery devices.

For LQI III, the ratio syringe/pump was 100.78% [95.79% - 106.02%] in the FAS population and 100.78% [95.79% - 106.02%] in the PP population. Since the confidence intervals included the value one (100%), there was no difference between the delivery devices.

Table 6: Lsmeans for LQI factors II and III at Endpoint: FAS Population (N=29) and PP Population (N=26)

	LQI II FAS	LQI III FAS	LQI II PP	LQI III PP
Lsmean Endpoint Pump Sequence	73.73 [67.84-80.13]	87.00 [82.09-92.20]	73.73 [67.84-80.13]	87.00 [82.09-92.20]
Lsmean Endpoint Syringe Sequence	73.50 [67.75-79.74]	87.67 [82.81-92.82]	73.50 [67.75-79.74]	87.67 [82.81-92.82]
Ratio of Lsmeans Syringe / Pump	99.69 [92.06-107.95]	100.78 [95.79-106.02]	99.69 [92.06-107.95]	100.78 [95.79-106.02]

Clinical Study Report, Table 13

3.2.2 Patient Satisfaction (TSQM Scale)

The ratio syringe to pump was 101.16% [89.84% - 113.92%] in the FAS and 102.99% [90.88% - 116.71%] in the PP population. Since the confidence intervals included the value one (100%), there was no difference between the delivery devices.

Table 7: Lsmeans for TSQM Scores at Endpoint: FAS Population (N=29) and PP Population (N=26)

	TSQM FAS Population	TSQM PP Population
Lsmean Endpoint Pump Sequence	75.90 [69.75-82.60]	75.70 [69.04-82.99]
Lsmean Endpoint Syringe Sequence	76.79 [70.56-83.56]	77.96 [71.10-85.47]
Ratio of Lsmeans Syringe / Pump	101.16 [89.84-113.92]	102.99 [90.88-116.71]

Clinical Study Report, Table 15

3.2.3 Patient preference

Patients were interviewed at V3 to specify which delivery device they prefer. With regard to the FAS population, 19 patients (65.5%, 95% CI [0.46; 0.82]) reported a preference for using the pump

and 10 patients (34.5%, 95% CI [0.18; 0.54]) were in favour of treatment using the syringe. This difference was not statistically significant.

Table 8: Patient preference

		Number of patients N=29
Prefer pump	N(%)	19 (65.5%)
	95% CI	[0.46;0.82]
Prefer syringe	N(%)	10 (34.5%)
	95% CI	[0.18;0.54]

Clinical Study Report, Table 14.2.2.11-1

3.2.4 Residual IgG levels

Residual IgG levels were recorded at V1, V2 and V3 for all patients.

There was no difference between the delivery device on residual IgG levels (Contrast Lsmeans rapid push – Lsmeans pump = -0.22 [-0.66 ; 0.23] in the FAS population and -0.17 [-0.63 ; 0.29] in the PP population

Table 9: Lsmeans of IgG Levels at Endpoint: FAS Population (N=29), PP Population (N=26)

	Mean IgG [g/L]	
Time of measurement	**FAS**	**PP**
Lsmean Endpoint Pump Sequence	9.64 [8.95-10.34]	9.79 [9.08-10.50]
Lsmean Endpoint Syringe Sequence	9.43 [8.74-10.12]	9.62 [8.91-10.33]
Contrast	-0.22 [-0.66-0.23]	-0.17 [-0.63-0.29]

Clinical Study Report, Table 22; CI= Confidence Interval

3.2.5 Burden of Disease (illness) and Burden of Delivery Device

The PRISM test is a tool that enables a quantitative measurement of the patient's perception of the burden felt due to the patient's illness and the burden of the delivery device used.

The burden of delivery device was not impacted by the delivery device in the FAS population (ratio syringe/pump: 84.93 [58.32-123.69]). Similar results were found in the PP population (ratio syringe/pump 89.00 [58.34-135.77]).

Table 10: Lsmeans of PRISM Test at Endpoint: FAS Population (N=29), PP Population (N=26)

	PRISM – Burden of Disease		PRISM – Burden Delivery Device	
Time of measurement	**FAS**	**PP**	**FAS**	**PP**
Lsmean Endpoint Pump Sequence	8.19 [5.31-12.63]	8.79 [5.46-14.14]	9.33 [6.41-13.59]	9.98 [6.69-14.89]
Lsmean Endpoint Syringe Sequence	9.41 [6.18-14.33]	10.32 [6.53-16.32]	7.93 [5.52-11.39]	8.88 [6.00-13.16]

Ratio of Lsmeans Syringe / Pump	114.93 [79.38-166.39]	117.44 [77.3-178.43]	84.93 [58.32-123.69]	89.00 [58.34-135.77]

Clinical Study Report, Table 20; . CI= Confidence Interval

3.2.6 Costs

Direct costs such as expenses for immunoglobulin, pumps, injection kits and nursing time were calculated per treatment period and per month. The mean direct treatment costs for patients of the FAS were 1849.2±577.6 EUR per month (min: 1016.6; max: 1719.3) for the pump and 1798.8±577.0 EUR per month (min: 975.6; max: 2901.6) for the syringe

Table 11: Direct Costs per Month Including Immunoglobulin: FAS Population (N=29), PP Population (N=26)

Direct costs (EUR)	FAS Population		PP Population	
	Pump	Syringe	Pump	Syringe
N	26	27	24	25
Mean±SD	1849.2±577.6	1798.8±577.0	1872.9±592.5	1778.4±569.6
[Min; Max]	[1016.6; 1719.3]	[975.6; 2901.6]	[1016.6; 2996.6]	[975.6; 2901.6]
ND (incl. excluded patients)	3	2	2	1

Clinical Study Report, Table 29; N= Number of patients; SD= Standard Deviation; Min= Minimum; Max = Maximum; ND= Not Determined

The mean direct treatment costs without immunoglobulin were 178.2±102.6 EUR per month (min: 64.4; max: 464.6) for the pump and 100.2±65.8 EUR per month (min: 22.5; max: 283.5) for the syringe (FAS population)

Table 12: Direct Costs per Month Without Immunoglobulin Costs: FAS Population (N=29), PP Population (N=26)

Direct costs (IgG excluded) (EUR)	FAS Population		PP Population	
	Pump	Syringe	Pump	Syringe
N	26	27	24	25
Mean±SD	178.2±102.6	100.2±65.8	178.5±104.9	102.3±67.9
[Min; Max]	[64.4; 464.6]	[22.5; 283.5]	[64.4; 464.6]	[22.5; 283.5]
ND (incl. excluded patients)	3	2	2	1

Clinical Study Report, Table 30; N=Number of patients; SD=Standard Deviation; Min=Minimum; Max=Maximum; ND=Not Determined

Indirect costs were estimated based on the time spent by the patient to prepare the infusion, the infusion itself, and also involved costs of disposal of material. The costs of infectious episodes were not included in the calculation.

The mean total indirect costs for the FAS set were 66.0±20.0 EUR (min: 39.7; max: 109.8) per month during the pump treatment sequence and 63.6±24.8 EUR (min: 28.5; max: 123.8) per

month during the syringe phase. Mean total monthly indirect costs for the PP population were 67.5±20.0 EUR during the pump phase and 63.5±24.0 EUR during the syringe sequence

Table 13: Indirect Costs per Month: FAS Population (N=29), PP Population (N=26)

Indirect costs	FAS Population		PP Population	
(EUR)	Pump	Syringe	Pump	Syringe
N	27	28	25	26
Mean±SD	66.0±20.0	63.6±24.8	67.5±20.0	63.5±24.0
[Min; Max]	[39.7;109.8]	[28.5;123.8]	[39.7;109.8]	[28.5;123.8]
ND (incl. excluded patients)	2	1	1	0

Clinical Study Report, Table 31; N= Number of patients; SD= Standard Deviation; Min= Minimum; Max = Maximum; ND= Not Determined

GAN-06 Study Results

4. Adverse Events

Tabular summary of all anticipated and unanticipated serious adverse events (life-threatening) and anticipated and unanticipated other adverse events (non-life threatening) which will include a description of the adverse event and the number of participants affected. If there were no adverse events associated with your trial then please include a statement to the effect of "There were no adverse events associated with this trial."outcome

4.1 Serious Adverse Events

Table 14 : Number of Patients with Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term - Safety population - N= 30

SOC	Preferred Term	Pump Number of patients N=29	Rapid Push Number of patients N=30	Total Number of patients N=30
INFECTIONS AND INFESTATIONS		0 (0.0%)	2 (6.7%)	2 (6.7%)
	PNEUMONIA	0 (0.0%)	1 (3.3%)	1 (3.3%)
	SEPSIS	0 (0.0%)	1 (3.3%)	1 (3.3%)
	SINUSITIS	0 (0.0%)	1 (3.3%)	1 (3.3%)
NERVOUS SYSTEM DISORDERS		1 (3.4%)	0 (0.0%)	1 (3.3%)
	NERVE ROOT COMPRESSION	1 (3.4%)	0 (0.0%)	1 (3.3%)
VASCULAR DISORDERS		0 (0.0%)	1 (3.3%)	1 (3.3%)
	EMBOLISM	0 (0.0%)	1 (3.3%)	1 (3.3%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS		1 (3.4%)	0 (0.0%)	1 (3.3%)
	ASTHMA	1 (3.4%)	0 (0.0%)	1 (3.3%)
GASTROINTESTINAL DISORDERS		0 (0.0%)	1 (3.3%)	1 (3.3%)
	INTRA-ABDOMINAL HAEMORRHAGE	0 (0.0%)	1 (3.3%)	1 (3.3%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS		0 (0.0%)	1 (3.3%)	1 (3.3%)
	PAIN	0 (0.0%)	1 (3.3%)	1 (3.3%)

Number of Patients with Related Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term - Safety population - N= 30

SOC	Preferred Term	Relationship to treatment	Pump Number of patients N=29	Rapid Push Number of patients N=30	Total Number of patients N=30
VASCULAR DISORDERS		.	0 (0.0%)	1 (3.3%)	1 (3.3%)
	EMBOLISM	Possible	0 (0.0%)	1 (3.3%)	1 (3.3%)

Clinical Study Report, Table 14.3.3-1 and 14.3.3-2

GAN-06 Study Results

4.2 Treatment Emergent Adverse Events

Table 15: Number of patients and number of TEAEs by SOC and PT [Safety Set] Only terms that occurred in more than 5% of the patients

MedDRA SOC	MedDRA Preferred Term	Delivery Device: Pump # of pts. (% of pts.) # of occurences (N=29)	Delivery Device: Syringe # of pts. (% of pts.) # of occurences (N=30)	Any Delivery Device # of pts. (% of pts.) # of occurences (N=30)
Any non-serious TEAE		24 (82.8%) 134	23 (76.7%) 178	27 (90.0%) 312
INFECTIONS AND INFESTATIONS		18 (62.1%) 33	16 (53.3%) 27	24 (80.0%) 60
	BRONCHITIS	7 (24.1%) 9	2 (6.7%) 2	7 (23.3%) 11
	NASOPHARYNGITIS	3 (10.3%) 3	4 (13.3%) 4	7 (23.3%) 7
	LOWER RESPIRATORY TRACT INFECTION	2 (6.9%) 3	3 (10.0%) 3	4 (13.3%) 6
	SINUSITIS	2 (6.9%) 2	4 (13.3%) 6	4 (13.3%) 8
	ORAL CANDIDIASIS		2 (6.7%) 3	2 (6.7%) 3
	PHARYNGITIS	2 (6.9%) 2	1 (3.3%) 1	2 (6.7%) 3
	RHINITIS	1 (3.4%) 1	1 (3.3%) 1	2 (6.7%) 2
	URINARY TRACT INFECTION		2 (6.7%) 2	2 (6.7%) 2
GASTROINTESTINAL DISORDERS		8 (27.6%) 22	5 (16.7%) 9	11 (36.7%) 31
	NAUSEA	4 (13.8%) 10	2 (6.7%) 5	5 (16.7%) 15
	ABDOMINAL DISCOMFORT	1 (3.4%) 1	1 (3.3%) 1	2 (6.7%) 2
	ABDOMINAL PAIN	2 (6.9%) 3		2 (6.7%) 3
	ABDOMINAL PAIN UPPER	1 (3.4%) 1	1 (3.3%) 1	2 (6.7%) 2
	DIARRHOEA	2 (6.9%) 2		2 (6.7%) 2
	VOMITING	1 (3.4%) 1	1 (3.3%) 1	2 (6.7%) 2
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS		9 (31.0%) 31	7 (23.3%) 84	10 (33.3%) 115
	PYREXIA	4 (13.8%) 4	3 (10.0%) 6	5 (16.7%) 10
	CHILLS	3 (10.3%) 7	2 (6.7%) 34	4 (13.3%) 41
	FATIGUE	3 (10.3%) 8	1 (3.3%) 1	3 (10.0%) 9
	FEELING COLD	2 (6.9%) 8	1 (3.3%) 39	2 (6.7%) 47
NERVOUS SYSTEM DISORDERS		5 (17.2%) 16	4 (13.3%) 4	8 (26.7%) 20
	HEADACHE	4 (13.8%) 11	2 (6.7%) 2	6 (20.0%) 13
	DIZZINESS	2 (6.9%) 4	2 (6.7%) 2	3 (10.0%) 6
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS		3 (10.3%) 5	5 (16.7%) 40	8 (26.7%) 45
	BACK PAIN	2 (6.9%) 2	2 (6.7%) 10	4 (13.3%) 12
	ARTHRALGIA	1 (3.4%) 1	2 (6.7%) 12	3 (10.0%) 13
	MYALGIA		2 (6.7%) 16	2 (6.7%) 16
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS		7 (24.1%) 15	4 (13.3%) 4	7 (23.3%) 19

GAN-06 Study Results

MedDRA SOC	MedDRA Preferred Term	Delivery Device: Pump # of pts. (% of pts.) # of occurences (N=29)	Delivery Device: Syringe # of pts. (% of pts.) # of occurences (N=30)	Any Delivery Device # of pts. (% of pts.) # of occurences (N=30)
	COUGH	5 (17.2%) 6	2 (6.7%) 2	5 (16.7%) 8
	OROPHARYNGEAL PAIN	5 (17.2%) 6	1 (3.3%) 1	5 (16.7%) 7
SKIN AND SUBCUTANEOUS TISSUE DISORDERS		2 (6.9%) 4	3 (10.0%) 3	4 (13.3%) 7
VASCULAR DISORDERS		3 (10.3%) 5	1 (3.3%) 1	3 (10.0%) 6
	HYPERTENSION	2 (6.9%) 2	1 (3.3%) 1	2 (6.7%) 3
REPRODUCTIVE SYSTEM AND BREAST DISORDERS		2 (6.9%) 2	1 (3.3%) 1	3 (10.0%) 3
INJURY, POISONING AND PROCEDURAL COMPLICATIONS		1 (3.4%) 1	2 (6.7%) 2	2 (6.7%) 3