

## Chapter 7 Adverse Events

## TABLE OF CONTENTS

Introduction.....	2
Exhibit 7-1A: All AEs Classified and by relatedness to infusion or IS Transplant type ITA.....	4
Exhibit 7-1B: All AEs Classified and by relatedness to infusion or IS Transplant type IAK/SIK.....	15
Exhibit 7-2A1 Adverse Events (AEs) in Days 0-30 Post First Infusion.....	20
Exhibit 7-2A2 Adverse Events (AEs) RELATED TO PROCEDURE in Days 0-30 post First Infusion.....	21
Exhibit 7-2A3 Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION in Days 0-30 post First Infusion.....	23
Exhibit 7-2B1 Any Serious Adverse Event in Days 0-30 post First Infusion.....	25
Exhibit 7-2B2 Serious Adverse Events (SAEs) RELATED TO PROCEDURE in Days 0-30 post First Infusion.....	26
Exhibit 7-2B3 Serious Adverse Events (SAEs) RELATED TO IMMUNOSUPPRESSION in Days 0-30 post First Infusion.....	27
Exhibit 7-3A1 Adverse Events (AEs) in Year 1 post First Infusion.....	28
Exhibit 7-3A2 Adverse Events (AEs) RELATED TO PROCEDURE in Year 1 post First Infusion.....	29
Exhibit 7-3A3 Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION in Year 1 post First Infusion.....	31
Exhibit 7-3B1 Serious Adverse Events (SAEs) in Year 1 post First Infusion.....	34
Exhibit 7-3B2 Serious Adverse Events (SAEs) RELATED TO PROCEDURE in Year 1 post First Infusion.....	35
Exhibit 7-3B3 Serious Adverse Events (SAEs) RELATED TO IMMUNOSUPPRESSION in Year 1 post First Infusion.....	37
Exhibit 7-4A1 Adverse Events (AEs) Any Time Post Islet Transplantation.....	40
Exhibit 7-4A2 Adverse Events (AEs) RELATED TO PROCEDURE in Any Time Post Islet Transplantation.....	41
Exhibit 7-4A3 Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION Any Time Post Islet Transplantation.....	44
Exhibit 7-4B1 Serious Adverse Events (SAEs) in Any Time Post Islet Transplantation.....	48
Exhibit 7-4B2 Serious Adverse Events (SAEs) RELATED TO PROCEDURE in Any Time Post Islet Transplantation.....	49
Exhibit 7-4B3 Serious Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION Any Time Post Islet Transplantation.....	51
Exhibit 7-5 Worst Outcome of Adverse Events (per Recipient).....	55
Exhibit 7-6 ALL Adverse Events Following Islet Transplant In order by Frequency, with Final Outcome..	56
Exhibit 7-7 SAE Criteria.....	63
Exhibit 7-8 Incidence of AEs and SAEs per Recipient by Type of Transplant and Era.....	64
Exhibit 7-9 Neoplasms Reported Post First Islet Transplantation.....	65
Exhibit 7-10A Deaths (By Era and Transplant Type) .....	66
Exhibit 7-10B Deaths( By Cause and Relatedness to Procedure or Immunosuppression).....	67
Exhibit 7-11A Life Threatening Events (By Era).....	68
Exhibit 7-11B Life-Threatening Events (By Relatedness to Infusion or Immunosuppression).....	69
Exhibit 7-11C Life-Threatening Events (in System/Organ Class order) .....	70
Exhibit 7-11D Life-Threatening Events (Outcome by System/Organ Class).....	74

## Introduction

All adverse events reported to the Registry on allo-islet recipients are tallied by relatedness to the infusion procedure or the immunosuppression regimen, as assessed by the local investigator (Exhibit 7-1). For islet-alone, the adverse events most frequently deemed “possibly or definitely related” to the infusion procedure included: peritoneal hemorrhage (n=33), hepatic hematoma, hepatic hemorrhage, or portal vein thrombosis (n=22), increased AST (n=7), blood alkaline phosphatase (n=19), gamma-glutamyl transferase (n=12), abnormal liver function tests (n=121), hematoma/hemorrhage (n=16), and GI/peritoneal hemorrhage (n=19), while those deemed “possibly or definitely related” to immunosuppression included leukopenia/lymphopenia/neutropenia/granulocytes (n=340), diarrhea/GI disorder (n=69), fatigue (n=15), mucosal inflammation (n=15), graft vs host disease (n=2), infection (n=64), pneumonia (n=8), increased blood creatinine (n=11), neoplasm (n=37), renal disorder/failure (n=13), lung disorder/infiltration (n=9), skin disorder (n=11), hypertension (n=8). For IAK/SIK, the adverse events most frequently deemed “possibly or definitely related” to the infusion procedure included: blood disorder/leukopenia/lymphopenia (n=14), gastrointestinal/peritoneal hemorrhage (n=19), infection (10), and renal disorder/failure (n=16).

In the first 30 days following allo-islet transplantation, about 26% of recipients experienced a reportable adverse event (Exhibit 7-2A), which occurred less frequently in IAK/SIK (22) than ITA (28%). The majority were adjudicated by the local investigator as possibly or definitely related to either the infusion procedure or the immunosuppression (IS). The majority were not unexpected, such as abnormal lymphocyte count and increased liver function. Very few were infections. The instances of peritoneal hemorrhage seen in the early era 1999-2002 have been drastically reduced in the recent eras.

About 14% of allo-islet recipients experienced a serious adverse event in the first 30 days (Exhibit 7-2B), which occurred about equally in IAK/SIK as in ITA, and have declined somewhat over the eras. There is likely some lag in reporting.

In the first year after islet transplantation, which includes a majority of the re-infusions that were performed, about 43% of all recipients experienced a reportable adverse event (Exhibit 7-3A), with a decline in the most recent era. About one-third have experienced a serious adverse event within the first year (Exhibit 7-3B), with a significant decline in the most recent era. This pattern is also seen for all adverse events in all follow-up after islet transplantation (Exhibit 7-4).

The outcomes of the reported adverse events have improved over the decade, with fewer patients experiencing long-term sequelae of their adverse events in the most recent era (Exhibit 7-5). Again, there is likely some under-reporting in the most recent era. Many adverse events seen in this population are unrelated to islet transplantation but not unexpected in a cohort of older T1D with significant co-morbidity. Overall, 16% of all recipients failed to recover completely from an adverse event (Exhibit 7-5). This is the worst outcome of all adverse events, including those not related to the islet infusion or immunosuppression. All adverse events are sorted by frequency and classified by outcome in Exhibit 7-6.

Exhibit 7-8 displays trends in AE and SAE incidence according to type of transplant, era and relatedness to the infusion procedure and immunosuppression. While marginally significant differences are noted by era (see above), there may be differences according to immunosuppression strategies and patient characteristics that deserve further investigation.

All adverse events reported to CITR since inception were updated for MedDRA coding in the analysis file for this report. All adverse events reported from the MedDRA classifications were reviewed and either confirmed,

**Introduction (continued)**

revised or left unclassified. Consequently, some adverse events have changed classification from previous Annual Reports.

A total of 46 events in 35 recipients were classified "Neoplasm". There were 23 instances in 19 patients of basal or squamous carcinoma of the skin (Exhibit 7-9B); all recovered (two with sequelae). There were 23 instances in 16 recipients of non-skin cancers, of whom 11 (67%) recovered completely, 1 (6%) recovered with sequelae, and 4 (25%) did not recover. It is difficult with these few cases to determine if any of the reported neoplasms are related to islet transplantation.

There have been 30 or 2.9% deaths; cumulative mortality rates by era are not different (Exhibit 7-10A), of the reported deaths, three were deemed possibly related and two were deemed definitely related to islet transplantation or immunosuppression (Exhibit 7-10B).

Life-threatening events have occurred in 13.7% of islet-alone, and in 20.3% of IAK/SIK recipients ( $p<0.001$ , Exhibit 7-11B). Recent eras have seen a substantial decline in the incidence of life-threatening events ( $p<0.001$ ). Most involved neutropenia and abnormal liver function. The vast majority recovered, 3% died, 3% did not recover, and 7% recovered with sequelae.

**Exhibit 7-1A**  
**All AEs Classified and by relatedness to infusion or IS Transplant type ITA**

**Transplant type ITA**

		Total 1855	Relatedness to Infusion					Relatedness to Immunosuppression						
			0-NR		1-Not related	2-Unlikely related	3-Possibly related	4-Related	0-NR		1-Not related	2-Unlikely related	3-Possibly related	4-Related
			N	%	%	%	%	%	N	%	%	%	%	
<b>TOTAL</b>														
<b>System/Organ Class</b>	<b>Preferred term</b>													
Not coded yet	Not coded yet	88	39.8	19.3	29.5	5.7	5.7	38.6	10.2	13.6	33.0	4.5		
Blood and lymphatic system disorders	Anaemia	32	12.5	34.4	25.0	15.6	12.5	6.3	9.4	12.5	65.6	6.3		
	Blood disorder	3	33.3	66.7	.	.	.	33.3	.	.	33.3	33.3		
	Febrile neutropenia	6	33.3	66.7	.	.	.	33.3	.	.	33.3	33.3		
	Haemolysis	1	.	.	100	.	.	.	.	.	.	100		
	Hypereosinophilia	1	.	100	.	.	.	.	.	100	.	.		
	Leukocytosis	1	100	.	.	.	.	100	.	.	.	.		
	Leukopenia	7	.	71.4	28.6	.	.	.	.	.	71.4	28.6		
	Lymphatic disorder	1	.	100	.	.	.	.	.	100	.	.		
	Lymphopenia	58	22.4	67.2	5.2	5.2	.	22.4	.	.	22.4	55.2		
	Neutropenia	33	33.3	36.4	18.2	12.1	.	33.3	3.0	.	39.4	24.2		
	Platelet disorder	5	.	60.0	40.0	.	.	.	.	40.0	60.0	.		
	Thrombocytopenia	5	40.0	60.0	.	.	.	.	.	.	100	.		
Cardiac disorders	Arrhythmia supraventricular	3	.	33.3	.	33.3	33.3	.	66.7	.	33.3	.		
	Atrioventricular block	1	.	100	.	.	.	.	100	.	.	.		
	Cardiac disorder	2	.	50.0	50.0	.	.	.	50.0	50.0	.	.		
	Myocardial ischaemia	9	.	88.9	.	11.1	.	.	55.6	33.3	11.1	.		
	Myocarditis	2	.	100	.	.	.	.	.	100	.	.		
	Pericardial effusion	2	.	50.0	50.0	.	.	.	.	50.0	50.0	.		
	Pericarditis	1	.	.	100	.	.	.	.	.	100	.		
Ear and labyrinth disorders	Hearing impaired	1	.	100	.	.	.	.	100	.	.	.		
	Tinnitus	1	.	100	.	.	.	.	.	.	100	.		
Endocrine disorders	Basedow's disease	1	.	100	.	.	.	100	.	.	.	.		
	Endocrine disorder	2	.	50.0	.	.	50.0	.	100	.	.	.		
	Hypothyroidism	1	100	.	.	.	.	100	.	.	.	.		

**Exhibit 7-1A (continued)**  
**All AEs Classified and by relatedness to infusion or IS Transplant type ITA**

**Transplant type ITA**

			Total	Relatedness to Infusion					Relatedness to Immunosuppression					
				0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	
				N	%	%	%	%	N	%	%	%	%	
Eye disorders	<b>Eye disorder</b>	10	.	90.0		10.0	.	.	.	40.0		20.0	30.0	10.0
	Retinal detachment	3	.	100	.	.	.	.	.	33.3		66.7	.	.
	Vitreous haemorrhage	6	16.7	16.7		50.0	16.7	.	16.7	16.7		50.0	16.7	.
Gastrointestinal disorders	Abdominal pain	2	100	.	.	.	.	.	100	.	.	.	.	.
	Ascites	5	20.0	20.0		20.0	40.0	.	.	20.0		40.0	.	40.0
	Barrett's oesophagus	1	.	.		100	.	.	.	.	.	.	100	.
	Colitis	5	.	80.0		20.0	.	.	.	20.0	.	.	80.0	.
	Constipation	2	.	100	.	.	.	.	.	.	.	50.0	50.0	.
	<b>Diarrhoea</b>	56	5.4	67.9		21.4	5.4	.	5.4	7.1		3.6	73.2	10.7
	Dysphagia	2	.	50.0		50.0	.	.	.	.	.	.	100	.
	Enteritis	1	.	.		100	.	.	.	.	.	100	.	.
	Gastritis	1	.	.		100	.	.	.	.	.	.	100	.
	<b>Gastrointestinal disorder</b>	13	7.7	53.8		15.4	23.1	.	.	30.8		15.4	46.2	7.7
	Gastrointestinal haemorrhage	2	.	.		.	.	100	.	100	.	.	.	.
	Gastrointestinal obstruction	7	.	71.4	.	.	14.3	14.3	.	14.3		28.6	57.1	.
	Gastrointestinal perforation	2	.	.		.	.	100	.	100	.	.	.	.
	Haemorrhoids	1	.	100	.	.	.	.	.	100	.	.	.	.
	Ileus	2	.	.		.	100	.	.	50.0	50.0	.	.	.
	Mouth ulceration	2	.	50.0	.	.	50.0	.	.	.	.	.	50.0	50.0
	Nausea	9	22.2	33.3		11.1	22.2	11.1	22.2	11.1	11.1	11.1	55.6	.
	Oral pain	1	.	100	.	.	.	.	.	.	.	.	100	.
	Pancreatitis	3	.	33.3		66.7	.	.	.	33.3		66.7	.	.
	<b>Peritoneal haemorrhage</b>	33	.	.		.	6.1	93.9	.	69.7		24.2	6.1	.
	Small intestinal obstruction	1	100	.		.	.	.	100	.	.	.	.	.
	Stomatitis	1	.	100	.	.	.	.	.	.	.	.	100	.
	Vomiting	30	33.3	56.7	.	.	6.7	3.3	26.7	13.3	13.3	36.7	10.0	.

**Exhibit 7-1A (continued)**  
**All AEs Classified and by relatedness to infusion or IS Transplant type ITA**

**Transplant type ITA**

		Total	Relatedness to Infusion					Relatedness to Immunosuppression				
			0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related
			N	%	%	%	%	N	%	%	%	%
General disorders and administration site conditions	Asthenia	1	100	.	.	.	.	100	.	.	.	.
	Chest discomfort	2	.	.	100	.	.	.	.	100	.	.
	Chest pain	6	16.7	16.7	66.7	.	.	16.7	.	66.7	16.7	.
	Death	7	14.3	57.1	.	14.3	14.3	14.3	57.1	14.3	14.3	.
	Fatigue	15	.	66.7	13.3	13.3	6.7	.	13.3	.	86.7	.
	Influenza like illness	1	100	.	.	.	.	100	.	.	.	.
	Injection site reaction	2	.	100	.	.	.	.	50.0	.	50.0	.
	Mucosal inflammation	15	6.7	66.7	26.7	.	.	6.7	.	.	26.7	66.7
	Oedema peripheral	6	.	83.3	16.7	.	.	33.3	.	66.7	.	.
	Pain	61	1.6	47.5	21.3	14.8	14.8	1.6	31.1	19.7	44.3	3.3
	Pyrexia	7	28.6	57.1	14.3	.	.	28.6	.	.	71.4	.
	Ulcer	1	.	.	.	100	.	.	.	.	.	100
Hepatobiliary disorders	Biliary tract disorder	1	.	.	.	.	100	.	100	.	.	.
	Cholecystitis	10	.	70.0	10.0	20.0	.	50.0	40.0	10.0	.	.
	Cholecystitis acute	1	100	.	.	.	.	100	.	.	.	.
	Gallbladder perforation	2	100	.	.	.	.	100	.	.	.	.
	Hepatic haematoma	1	.	.	.	.	100	.	.	100	.	.
	Hepatic haemorrhage	10	80.0	.	.	.	20.0	80.0	20.0	.	.	.
	Portal vein thrombosis	11	9.1	.	.	.	90.9	9.1	72.7	18.2	.	.
Immune system disorders	Autoimmune disorder	1	.	100	.	.	.	.	.	.	100	.
	Cytokine release syndrome	1	100	.	.	.	.	100	.	.	.	.
	Graft versus host disease	2	.	.	.	.	100	.	.	.	.	100
	Hypersensitivity	22	22.7	36.4	22.7	4.5	13.6	13.6	36.4	9.1	18.2	22.7
	Sensitisation	1	.	100	.	.	.	100	.	.	.	.
	Serum sickness	2	100	.	.	.	.	50.0	.	.	.	50.0

**Exhibit 7-1A (continued)**  
**All AEs Classified and by relatedness to infusion or IS Transplant type ITA**

**Transplant type ITA**

		Total	Relatedness to Infusion					Relatedness to Immunosuppression				
			0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related
			N	%	%	%	%	N	%	%	%	%
Infections and infestations	Appendicitis	4	.	.	.	100	.	.	.	.	100	.
	Appendicitis perforated	2	100	.	.	.	.	.	100	.	.	.
	Arthritis bacterial	1	.	100	.	.	.	.	.	.	.	100
	Bacillus infection	2	.	100	.	.	.	.	100	.	.	.
	Clostridium difficile colitis	1	100	.	.	.	.	100	.	.	.	.
	Cystitis	2	.	100	.	.	.	.	.	50.0	50.0	.
	Cytomegalovirus infection	2	.	.	50.0	50.0	.	.	50.0	.	.	50.0
	Ear infection	1	.	100	.	.	.	.	.	100	.	.
	Enterocolitis infectious	1	.	100	.	.	.	.	.	100	.	.
	Gastroenteritis viral	2	.	.	50.0	.	50.0	50.0	.	50.0	.	.
	Gastrointestinal infection	1	.	100	.	.	.	.	.	.	.	100
	H1N1 influenza	1	100	.	.	.	.	100	.	.	.	.
	Herpes simplex	1	100	.	.	.	.	100	.	.	.	.
	Infection	64	4.7	64.1	17.2	7.8	6.3	4.7	15.6	7.8	68.8	3.1
	Laryngitis	1	.	100	.	.	.	.	100	.	.	.
	Metapneumovirus infection	1	.	100	.	.	.	.	100	.	.	.
	Opportunistic infection	1	.	100	.	.	.	.	.	.	.	100
	Periorbital cellulitis	1	.	100	.	.	.	.	.	.	.	100
	Pneumococcal infection	1	100	.	.	.	.	100	.	.	.	.
	Pneumonia	8	25.0	12.5	50.0	12.5	.	25.0	.	.	62.5	12.5
	Pulmonary tuberculosis	1	.	100	.	.	.	.	100	.	.	.
	Pyelonephritis	2	50.0	50.0	.	.	.	50.0	.	.	50.0	.
	Respiratory tract infection	1	.	.	.	100	.	.	.	.	100	.
	Salmonellosis	1	100	.	.	.	.	100	.	.	.	.
	Urinary tract infection	1	100	.	.	.	.	100	.	.	.	.
	Vestibular neuritis	1	.	100	.	.	.	.	.	.	100	.
	Viral encephalitis	1	.	100	.	.	.	.	.	.	100	.

**Exhibit 7-1A (continued)**  
**All AEs Classified and by relatedness to infusion or IS Transplant type ITA**

**Transplant type ITA**

			Total	Relatedness to Infusion					Relatedness to Immunosuppression				
				0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related
				N	%	%	%	%	N	%	%	%	%
Injury, poisoning and procedural complications	Fracture	10	.	80.0		10.0		10.0	.	70.0		30.0	.
	Hepatic haematoma	2	50.0	.		50.0	.	.	50.0	50.0	.	.	.
	Hip fracture	4	50.0	50.0	.	.	.	.	50.0	50.0	.	.	.
	Injury	1	100	.	.	.	.	.	.	100	.	.	.
	Laceration	1	100	.	.	.	.	.	100	.	.	.	.
	Limb injury	1	.	100	.	.	.	.	.	.	.	100	.
	Lower limb fracture	1	100	.	.	.	.	.	100	.	.	.	.
	Post procedural haemorrhage	1	.	.	.	.	.	100	.	100	.	.	.
	Toxicity to various agents	2	.	100	.	.	.	.	.	.	.	.	100
	Transplant failure	1	.	.	.	.	.	100	.	.	.	100	.
	Upper limb fracture	1	100	.	.	.	.	.	100	.	.	.	.
	Wound complication	11	9.1	54.5		9.1		9.1	18.2	9.1	27.3	36.4	27.3
	Wound dehiscence	1	100	.	.	.	.	.	100	.	.	.	.

**Exhibit 7-1A (continued)**  
**All AEs Classified and by relatedness to infusion or IS Transplant type ITA**

**Transplant type ITA**

			Relatedness to Infusion						Relatedness to Immunosuppression					
			Total	0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	
				N	%	%	%			%	%	%		
Investigations	Activated partial thromboplastin time	1	.	.	.	.	.	100	.	.	.	.	100	
	Activated partial thromboplastin time prolonged	1	.	.	.	.	.	100	.	.	.	100	.	
	Alanine aminotransferase increased	9	88.9	.	.	.	11.1	.	88.9	.	11.1	.	.	
	Aspartate aminotransferase increased	7	57.1	.	.	.	14.3	28.6	57.1	14.3	28.6	.	.	
	Bacillus test positive	1	.	100	.	.	.	.	.	100	.	.	.	
	Blood albumin decreased	1	100	.	.	.	.	.	100	.	.	.	.	
	Blood alkaline phosphatase	19	.	.	.	.	89.5	10.5	.	5.3	78.9	10.5	5.3	
	Blood amylase	1	.	.	.	.	.	100	.	.	100	.	.	
	Blood bilirubin	1	.	.	.	.	.	100	.	100	.	.	.	
	Blood creatine phosphokinase	1	.	100	.	.	.	.	.	.	.	.	100	
	Blood creatine phosphokinase increased	2	100	.	.	.	.	.	100	.	.	.	.	
	Blood creatinine increased	11	36.4	45.5	9.1	9.1	.	36.4	.	.	54.5	9.1	.	
	Blood phosphorus decreased	2	100	.	.	.	.	.	50.0	50.0	.	.	.	
	Blood potassium increased	1	100	.	.	.	.	.	100	.	.	.	.	
	Gamma-glutamyltransferase	12	25.0	.	.	.	66.7	8.3	25.0	16.7	8.3	50.0	.	
	Gamma-glutamyltransferase increased	3	66.7	.	.	.	.	33.3	66.7	33.3	.	.	.	
	Glomerular filtration rate	1	.	.	.	.	100	.	.	.	.	100	.	
	Granulocytes abnormal	242	4.1	63.6	25.6	5.4	1.2	3.7	0.8	1.7	62.0	31.8	.	
	Haemoglobin decreased	2	50.0	50.0	.	.	.	50.0	.	.	50.0	.	.	
	Hepatic enzyme increased	4	.	.	.	.	50.0	50.0	.	.	100	.	.	
	International normalised ratio increased	1	100	.	.	.	.	100	.	.	.	.	.	
	Lipase	1	.	.	.	.	100	.	100	.	.	.	.	

**Exhibit 7-1A (continued)**  
**All AEs Classified and by relatedness to infusion or IS Transplant type ITA**

**Transplant type ITA**

		Total	Relatedness to Infusion					Relatedness to Immunosuppression				
			0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related
			N	%	%	%	%	N	%	%	%	%
Liver function test abnormal	Lipase increased	1	.	100	.	.	.	.	.	.	.	100
	Liver function test abnormal	121	9.9	2.5	1.7	60.3	25.6	9.1	20.7	44.6	22.3	3.3
	Low density lipoprotein abnormal	6	66.7	16.7	16.7	.	.	66.7	.	16.7	16.7	.
	Low density lipoprotein increased	13	46.2	38.5	7.7	7.7	.	46.2	.	7.7	46.2	.
	Neutrophil count	6	66.7	33.3	.	.	.	66.7	.	.	33.3	.
	Neutrophil count decreased	18	83.3	11.1	5.6	.	.	83.3	.	.	11.1	5.6
	Transaminases	4	100	.	.	.	.	100	.	.	.	.
	Transaminases increased	3	66.7	.	.	.	33.3	66.7	.	33.3	.	.
	Troponin T	1	.	100	.	.	.	.	100	.	.	.
	Weight decreased	3	33.3	33.3	33.3	.	.	33.3	.	.	66.7	.
Metabolism and nutrition disorders	Decreased appetite	2	.	100	.	.	.	.	.	50.0	50.0	.
	Dehydration	9	11.1	66.7	11.1	11.1	.	11.1	11.1	33.3	44.4	.
	Hyperglycaemia	7	42.9	57.1	.	.	.	42.9	28.6	28.6	.	.
	Hyperkalaemia	13	15.4	76.9	7.7	.	.	15.4	.	7.7	76.9	.
	Hypernatraemia	1	100	.	.	.	.	100	.	.	.	.
	Hypoalbuminaemia	4	25.0	.	50.0	.	25.0	25.0	25.0	50.0	.	.
	Hypocalcaemia	2	100	.	.	.	100	.	.	.	.	.
	Hypoglycaemia	118	39.0	48.3	7.6	3.4	1.7	37.3	49.2	8.5	5.1	.
	Hypokalaemia	14	21.4	28.6	42.9	7.1	.	21.4	7.1	21.4	42.9	7.1
	Hypomagnesaemia	1	.	100	.	.	.	.	.	.	100	.
	Hyponatraemia	23	4.3	43.5	47.8	4.3	.	4.3	26.1	65.2	4.3	.
	Hypophosphataemia	14	42.9	28.6	28.6	.	.	42.9	.	14.3	42.9	.
	Ketoacidosis	91	2.2	91.2	3.3	3.3	.	2.2	82.4	14.3	1.1	.

**Exhibit 7-1A (continued)**  
**All AEs Classified and by relatedness to infusion or IS Transplant type ITA**

**Transplant type ITA**

		Total	Relatedness to Infusion					Relatedness to Immunosuppression				
			0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related
			N	%	%	%	%	N	%	%	%	%
Musculoskeletal and connective tissue disorders	Arthralgia	1	.	.	.	.	100	.	.	.	.	100
	Arthritis	3	.	100	.	.	.	.	33.3	.	.	66.7
	Arthropathy	1	.	100	.	.	.	.	.	100	.	.
	Back pain	1	100	.	.	.	.	100	.	.	.	.
	Muscle necrosis	1	.	100	.	.	.	.	.	.	.	100
	Muscular weakness	8	.	75.0	25.0	.	.	.	12.5	12.5	75.0	.
	Musculoskeletal disorder	5	.	100	.	.	.	.	40.0	.	60.0	.
	Musculoskeletal pain	2	.	.	.	.	100	.	100	.	.	.
	Myositis	1	.	.	100	.	.	.	.	.	100	.
	Rheumatoid arthritis	1	100	.	.	.	.	100	.	.	.	.
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Trigger finger	1	.	100	.	.	.	.	100	.	.	.
	Basal cell carcinoma	6	66.7	33.3	.	.	.	33.3	.	.	33.3	33.3
	Lobular breast carcinoma in situ	1	.	100	.	.	.	.	.	.	100	.
	Lymphoma	1	100	.	.	.	.	100	.	.	.	.
	Metastases	1	.	100	.	.	.	.	.	.	100	.
	Neoplasm malignant	18	.	61.1	33.3	5.6	.	.	5.6	.	94.4	.
	Papillary thyroid cancer	1	.	100	.	.	.	.	.	.	100	.
	Post transplant lymphoproliferative disorder	1	100	.	.	.	.	100	.	.	.	.
	Skin cancer	1	100	.	.	.	.	100	.	.	.	.
	Squamous cell carcinoma	6	66.7	33.3	.	.	.	50.0	.	.	33.3	16.7
	Treatment related secondary malignancy	1	.	100	.	.	.	.	.	.	100	.

**Exhibit 7-1A (continued)**  
**All AEs Classified and by relatedness to infusion or IS Transplant type ITA**

**Transplant type ITA**

			Total	Relatedness to Infusion					Relatedness to Immunosuppression				
				0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related
				N	%	%	%	%	N	%	%	%	%
Nervous system disorders	Ataxia	2	.	50.0	50.0	.	.	.	.	.	100	.	.
	Cerebellar ischaemia	1	.	100	.	.	.	.	.	100	.	.	.
	Cerebral ischaemia	1	.	100	.	.	.	.	.	100	.	.	.
	Cognitive disorder	2	50.0	50.0	.	.	.	.	50.0	.	.	50.0	.
	Convulsion	2	.	100	.	.	.	.	.	50.0	.	50.0	.
	Dizziness	6	16.7	50.0	33.3	.	.	.	16.7	16.7	33.3	33.3	.
	Dyskinesia	1	.	.	.	100	.	.	.	100	.	.	.
	Frontotemporal dementia	1	.	100	.	.	.	.	.	100	.	.	.
	Headache	4	75.0	25.0	.	.	.	.	50.0	.	.	25.0	25.0
	Migraine	2	.	.	100	.	.	.	.	100	.	.	.
	Presyncope	1	100	.	.	.	.	.	100	.	.	.	.
	Serotonin syndrome	1	.	.	100	.	.	.	.	100	.	.	.
	Spinal cord compression	2	100	.	.	.	.	.	100	.	.	.	.
	Syncope	11	27.3	18.2	45.5	.	.	9.1	27.3	.	63.6	9.1	.
Psychiatric disorders	Tremor	5	20.0	60.0	20.0	.	.	.	.	20.0	40.0	40.0	.
	Alcoholism	1	100	.	.	.	.	.	100	.	.	.	.
	Anxiety	1	.	.	100	.	.	.	.	100	.	.	.
	Cognitive disorder	2	50.0	50.0	.	.	.	.	50.0	50.0	.	.	.
	Confusional state	4	50.0	25.0	25.0	.	.	.	50.0	25.0	.	25.0	.
	Insomnia	2	.	50.0	50.0	.	.	.	.	.	50.0	50.0	.
	Mood altered	4	25.0	25.0	50.0	.	.	.	25.0	25.0	50.0	50.0	.
	Psychogenic seizure	2	.	100	.	.	.	.	50.0	50.0	.	.	.
	Psychotic disorder	1	.	100	.	.	.	.	.	.	100	.	.

**Exhibit 7-1A (continued)**  
**All AEs Classified and by relatedness to infusion or IS Transplant type ITA**

**Transplant type ITA**

		Total	Relatedness to Infusion					Relatedness to Immunosuppression				
			0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related
			N	%	%	%	%	N	%	%	%	%
Renal and urinary disorders	Albuminuria	3	.	.	100	.	.	.	.	100	.	.
	Haemoglobinuria	1	.	100	.	.	.	.	100	.	.	.
	Micturition urgency	1	.	100	.	.	.	.	.	.	100	.
	Peyloneprhitis	1	.	100	.	.	.	.	.	.	100	.
	Proteinuria	4	.	75.0	.	25.0	.	.	.	.	75.0	25.0
	Renal disorder	4	25.0	50.0	25.0	.	.	25.0	.	25.0	50.0	.
	Renal failure	9	.	44.4	44.4	11.1	.	.	.	11.1	66.7	22.2
	Tubulointerstitial nephritis	1	.	100	.	.	.	.	.	.	100	.
	Urinary bladder haemorrhage	3	.	33.3	33.3	.	33.3	.	33.3	.	33.3	33.3
Reproductive system and breast disorders	Lactation disorder	1	.	.	100	.	.	.	.	.	100	.
	Ovarian cyst ruptured	1	.	.	100	.	.	.	.	.	100	.
	Sexual dysfunction	7	.	85.7	14.3	.	.	.	14.3	28.6	57.1	.
Respiratory, thoracic and mediastinal disorders	Acute respiratory distress syndrome	1	.	100	.	.	.	.	.	100	.	.
	Aspiration	2	.	50.0	.	50.0	.	.	.	50.0	50.0	.
	Cough	1	.	.	100	.	.	.	.	.	100	.
	Dyspnoea	5	.	80.0	20.0	.	.	20.0	40.0	40.0	.	.
	Haemothorax	2	50.0	.	.	.	50.0	50.0	.	.	50.0	.
	Hypoxia	4	.	50.0	50.0	.	.	75.0	.	25.0	.	.
	Lung disorder	5	.	60.0	20.0	20.0	.	20.0	.	60.0	20.0	.
	Lung infiltration	4	.	100	.	.	.	.	.	50.0	50.0	.
	Pleural effusion	4	50.0	25.0	25.0	.	50.0	.	25.0	25.0	25.0	.
	Pneumonitis	4	25.0	75.0	.	.	25.0	.	.	.	75.0	.
	Pulmonary hypertension	1	.	100	.	.	.	100	.	.	.	.
	Pulmonary oedema	1	100	.	.	.	100	.	.	.	.	.

**Exhibit 7-1A (continued)**  
**All AEs Classified and by relatedness to infusion or IS Transplant type ITA**

**Transplant type ITA**

		Total	Relatedness to Infusion					Relatedness to Immunosuppression				
			0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related
			N	%	%	%	%	N	%	%	%	%
Skin and subcutaneous tissue disorders	Actinic keratosis	1	100	.	.	.	.	.	.	.	.	100
	Acute febrile neutrophilic dermatosis	1	.	100	.	.	.	.	.	.	.	100
	Alopecia	1	100	.	.	.	.	100	.	.	.	.
	Dermatitis	1	100	.	.	.	.	100	.	.	.	.
	Dry skin	1	.	100	.	.	.	100	.	.	.	.
	Exfoliative rash	6	.	100	.	.	.	.	.	16.7	83.3	.
	Pruritus	1	.	100	.	.	.	.	.	.	100	.
	Rash	1	.	100	.	.	.	.	.	.	100	.
	Skin disorder	5	.	40.0	60.0	.	.	.	20.0	80.0	.	.
Surgical and medical procedures	Abdominal hernia repair	2	.	100	.	.	.	.	100	.	.	.
	Breast reconstruction	1	100	.	.	.	.	100	.	.	.	.
	Hospitalisation	1	.	100	.	.	.	100	.	.	.	.
	Hysterectomy	1	.	100	.	.	.	.	.	.	100	.
	Ileostomy	1	100	.	.	.	.	100	.	.	.	.
	Incisional hernia repair	2	50.0	.	.	.	.	50.0	50.0	50.0	.	.
	Laser therapy	1	.	.	100	.	.	.	.	100	.	.
	Nail operation	2	.	100	.	.	.	.	100	.	.	.
	Surgery	4	.	100	.	.	.	.	100	.	.	.
	Toe operation	1	100	.	.	.	.	100	.	.	.	.
Vascular disorders	Haematoma	9	.	11.1	11.1	.	77.8	.	44.4	44.4	11.1	.
	Haemorrhage	7	.	.	.	14.3	85.7	.	85.7	14.3	.	.
	Hypertension	8	.	75.0	25.0	.	.	.	25.0	25.0	50.0	.
	Hypotension	4	.	50.0	.	.	50.0	.	75.0	25.0	.	.
	Thrombosis	3	33.3	66.7	.	.	.	33.3	33.3	.	33.3	.

**Exhibit 7-1B**  
**All AEs Classified and by relatedness to infusion or IS Transplant type IAK/SIK**

<b>Transplant type IAK/SIK</b>			<b>Relatedness to Infusion</b>						<b>Relatedness to Immunosuppression</b>					
			<b>Total</b>	<b>0-NR</b>	<b>1-Not related</b>	<b>2-Unlikely related</b>	<b>3-Possibly related</b>	<b>4-Related</b>	<b>0-NR</b>	<b>1-Not related</b>	<b>2-Unlikely related</b>	<b>3-Possibly related</b>	<b>4-Related</b>	
				<b>N</b>	<b>%</b>	<b>%</b>	<b>%</b>	<b>%</b>		<b>%</b>	<b>%</b>	<b>%</b>	<b>%</b>	
<b>TOTAL</b>			<b>392</b>											
<b>System/Organ Class</b>	<b>Preferred term</b>													
Not coded yet	Not coded yet		23	34.8	43.5	4.3	13.0	4.3	34.8	13.0	21.7	26.1	4.3	
Blood and lymphatic system disorders	Agranulocytosis		1	.	100	.	.	.	.	.	.	.	.	100
	Anaemia		8	12.5	50.0	.	37.5	.	12.5	12.5	37.5	37.5	.	
	Blood disorder		3	.	33.3	.	66.7	.	.	.	33.3	66.7	.	
	Leukopenia		5	.	80.0	20.0	.	.	.	.	.	100	.	
	Lymphopenia		6	.	50.0	33.3	16.7	.	.	.	.	83.3	16.7	
Cardiac disorders	Acute myocardial infarction		1	.	100	.	.	.	.	100	.	.	.	
	Cardio-respiratory arrest		2	.	50.0	50.0	.	.	.	50.0	50.0	.	.	
	Myocardial ischaemia		9	11.1	66.7	22.2	.	.	22.2	44.4	33.3	.	.	
	Pericardial effusion		2	.	100	.	.	.	.	50.0	50.0	.	.	
Endocrine disorders	Endocrine disorder		2	100	.	.	.	.	100	.	.	.	.	
Eye disorders	Eye disorder		4	.	100	.	.	.	.	75.0	.	25.0	.	
	Ocular surface disease		1	.	100	.	.	.	.	.	.	100	.	
	Retinal detachment		1	.	100	.	.	.	.	100	.	.	.	
	Uveitis		1	.	100	.	.	.	.	.	.	100	.	
	Vitreous haemorrhage		1	.	.	.	100	.	.	.	.	100	.	

**Exhibit 7-1B (continued)**  
**All AEs Classified and by relatedness to infusion or IS Transplant type IAK/SIK**

Transplant type IAK/SIK		Total	Relatedness to Infusion					Relatedness to Immunosuppression				
			0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related
			N	%	%	%	%	%	%	%	%	%
Gastrointestinal disorders	Colitis	3	.	66.7	33.3	.	.	.	33.3	33.3	33.3	.
	Diarrhoea	5	20.0	80.0	.	.	.	.	20.0	20.0	40.0	20.0
	Gastritis	1	100	.	.	.	.	.	.	.	100	.
	Gastrointestinal disorder	7	.	71.4	28.6	.	.	.	.	14.3	85.7	.
	Gastrointestinal haemorrhage	3	.	.	.	33.3	66.7	.	33.3	66.7	.	.
	Gastrointestinal obstruction	4	.	50.0	50.0	.	.	.	.	.	100	.
	Mouth ulceration	1	.	.	100	.	.	.	.	.	100	.
	Nausea	2	.	50.0	.	50.0	.	.	.	.	100	.
	Peritoneal haemorrhage	16	.	6.3	.	.	93.8	.	68.8	12.5	18.8	.
	Vomiting	7	.	57.1	42.9	.	.	.	42.9	28.6	28.6	.
General disorders and administration site conditions	Death	7	14.3	71.4	14.3	.	.	.	28.6	57.1	.	14.3
	Mucosal inflammation	3	.	66.7	33.3	.	.	.	.	.	66.7	33.3
	Oedema peripheral	2	50.0	50.0	.	.	.	50.0	.	.	50.0	.
	Pain	11	9.1	36.4	45.5	.	9.1	9.1	9.1	63.6	18.2	.
	Pyrexia	1	100	.	.	.	.	.	.	.	100	.
	Systemic inflammatory response syndrome	3	.	100	.	.	.	.	.	.	66.7	33.3
Hepatobiliary disorders	Cholecystitis	3	.	66.7	.	33.3	.	.	66.7	33.3	.	.
	Hepatic artery stenosis	1	.	100	.	.	.	.	100	.	.	.
	Portal vein thrombosis	2	.	.	.	.	100	.	50.0	50.0	.	.
Immune system disorders	Hypersensitivity	4	.	50.0	50.0	.	.	.	.	50.0	50.0	.

**Exhibit 7-1B (continued)**  
**All AEs Classified and by relatedness to infusion or IS Transplant type IAK/SIK**

Transplant type IAK/SIK		Total	Relatedness to Infusion					Relatedness to Immunosuppression				
			0-NR N	1-Not % related	2-Unlikely % related	3-Possibly % related	4-Related %	0-NR %	1-Not % related	2-Unlikely % related	3-Possibly % related	4-Related %
Infections and infestations	Infection	38	5.3	65.8	26.3	2.6	.	7.9	18.4	39.5	28.9	5.3
	Opportunistic infection	1	.	100	.	.	.	.	.	.	100	.
	Pneumonia	5	20.0	20.0	60.0	.	.	.	.	20.0	60.0	20.0
	Pyelonephritis	1	.	.	100	.	.	.	.	.	100	.
	Renal graft infection	1	.	100	.	.	.	.	.	.	100	.
	Urinary tract infection	1	100	.	.	.	.	.	.	.	100	.
	Urosepsis	1	100	.	.	.	.	.	.	.	100	.
Injury, poisoning and procedural complications	Fracture	2	.	100	.	.	.	.	100	.	.	.
	Injury	1	.	100	.	.	.	.	.	.	100	.
	Wound complication	1	.	100	.	.	.	.	.	.	100	.
Investigations	Activated partial thromboplastin time	1	.	.	.	100	.	.	100	.	.	.
	Blood alkaline phosphatase	2	.	.	.	.	.	100	.	.	100	.
	Blood amylase	1	.	100	.	.	.	.	100	.	.	.
	Blood creatinine increased	8	25.0	62.5	.	12.5	.	25.0	37.5	12.5	25.0	.
	Gamma-glutamyltransferase	1	.	.	.	.	.	100	.	.	100	.
	Glomerular filtration rate	1	.	100	.	.	.	.	100	.	.	.
	Granulocytes abnormal	12	.	83.3	16.7	.	.	.	.	.	100	.
	Lipase	4	.	.	25.0	75.0	.	.	100	.	.	.
	Liver function test abnormal	5	.	20.0	20.0	40.0	20.0	.	40.0	.	60.0	.
	Troponin I	1	.	100	.	.	.	.	100	.	.	.

**Exhibit 7-1B (continued)**  
**All AEs Classified and by relatedness to infusion or IS Transplant type IAK/SIK**

Transplant type IAK/SIK		Total	Relatedness to Infusion					Relatedness to Immunosuppression				
			0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related
			N	%	%	%	%	N	%	%	%	%
Metabolism and nutrition disorders	Dehydration	3	.	66.7	33.3	.	.	.	33.3	.	66.7	.
	Hyperglycaemia	7	.	14.3	.	85.7	.	.	14.3	.	85.7	.
	Hyperkalaemia	2	50.0	50.0	.	.	.	50.0	50.0	.	.	.
	Hypoglycaemia	18	50.0	27.8	11.1	5.6	5.6	22.2	38.9	33.3	5.6	.
	Hypokalaemia	3	66.7	.	33.3	.	.	66.7	.	.	33.3	.
	Hyponatraemia	2	.	50.0	.	50.0	.	.	100	.	.	.
	Hypophosphataemia	3	.	66.7	33.3	.	.	.	33.3	66.7	.	.
Musculoskeletal and connective tissue disorders	Ketoacidosis	9	.	77.8	22.2	.	.	.	77.8	11.1	11.1	.
	Joint range of motion decreased	1	.	100	.	.	.	.	.	100	.	.
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Neoplasm malignant	11	9.1	72.7	18.2	.	.	9.1	.	.	90.9	.
	Papillary thyroid cancer	1	.	100	.	.	.	.	.	.	100	.
	Post transplant lymphoproliferative disorder	3	.	100	.	.	.	.	100	.	.	.
	Squamous cell carcinoma	4	.	100	.	.	.	.	.	.	100	.
Nervous system disorders	Cerebral ischaemia	6	.	50.0	50.0	.	.	.	50.0	50.0	.	.
	Hypoglycaemic seizure	1	.	100	.	.	.	.	100	.	.	.
Psychiatric disorders	Anxiety	2	.	.	100	.	.	.	.	100	.	.
Renal and urinary disorders	Proteinuria	1	.	100	.	.	.	.	.	.	100	.
	Pyelonephritis	1	.	.	100	.	.	.	.	.	100	.
	Renal disorder	4	.	50.0	25.0	25.0	.	.	50.0	25.0	.	25.0
	Renal failure	11	9.1	63.6	27.3	.	.	9.1	9.1	9.1	63.6	9.1
	Renal failure acute	1	.	100	.	.	.	.	100	.	.	.
	Urinary bladder haemorrhage	2	.	50.0	50.0	.	.	.	50.0	50.0	.	.
Reproductive system and breast disorders	Sexual dysfunction	1	.	100	.	.	.	.	.	100	.	.

**Exhibit 7-1B (continued)**  
**All AEs Classified and by relatedness to infusion or IS Transplant type IAK/SIK**

Transplant type IAK/SIK		Total	Relatedness to Infusion					Relatedness to Immunosuppression				
			0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related	0-NR	1-Not related	2-Unlikely related	3-Possibly related	4-Related
			N	%	%	%	%	N	%	%	%	%
Respiratory, thoracic and mediastinal disorders	Acute respiratory distress syndrome	1	.	100	.	.	.	.	.	.	.	100
	Cough	2	.	100	.	.	.	.	.	.	.	100
	Dyspnoea	1	.	.	100	.	.	.	.	100	.	.
	Haemothorax	1	.	.	.	100	.	.	.	100	.	.
	Lung disorder	4	.	50.0	50.0	.	.	.	25.0	25.0	50.0	.
	Pleural effusion	1	.	.	.	100	.	.	.	100	.	.
	Pneumonitis	5	.	100	.	.	.	.	40.0	20.0	20.0	20.0
	Pulmonary hypertension	2	.	100	.	.	.	.	.	100	.	.
Skin and subcutaneous tissue disorders	Acne	1	100	.	.	.	.	100	.	.	.	.
	Decubitus ulcer	2	.	100	.	.	.	.	.	100	.	.
	Exfoliative rash	1	.	100	.	.	.	.	.	.	100	.
Surgical and medical procedures	Nephrectomy	1	100	.	.	.	.	100	.	.	.	.
	Surgery	4	25.0	75.0	.	.	.	25.0	.	50.0	25.0	.
Vascular disorders	Haematoma	5	.	20.0	.	.	80.0	.	60.0	20.0	20.0	.
	Haemorrhage	7	.	42.9	.	.	57.1	.	42.9	57.1	.	.
	Hypertension	5	.	80.0	20.0	.	.	.	40.0	20.0	40.0	.
	Hypotension	1	100	.	.	.	.	100	.	.	.	.
	Peripheral arterial occlusive disease	1	.	100	.	.	.	.	100	.	.	.
	Peripheral ischaemia	4	.	100	.	.	.	.	25.0	50.0	25.0	.
	Thrombosis	2	.	50.0	.	.	50.0	.	100	.	.	.

**Exhibit 7-2A1**  
**Adverse Events (AEs) in Days 0-30 Post First Infusion**

Percent of Recipients with:	Type				Era							
	ITA		IAK/SIK		1999-2002		2003-2006		2007-2010		2011-2014	
	N	%	N	%	N	%	N	%	N	%	N	%
<b>Any AE in Day 0-30</b>	230	28.1	42	21.9	67	32.1	96	35.4	80	32.5	29	10.2
<b>Any AE related to infusion in Day 0-30</b>	128	15.6	22	11.5	45	21.5	58	21.4	37	15.0	10	3.5
<b>Any AE related to IS in Day 0-30</b>	132	16.1	18	9.4	36	17.2	55	20.3	47	19.1	12	4.2
<b>Any AE related to both in Day 0-30</b>	37	4.5	6	3.1	15	7.2	12	4.4	12	4.9	4	1.4
<b>Any AE related to neither in Day 0-30</b>	66	8.1	14	7.3	9	4.3	14	5.2	37	15.0	20	7.0



**Exhibit 7-2A2**  
**Adverse Events (AEs) RELATED TO PROCEDURE in Days 0-30 post First Infusion**

		Overall	Transplant type		Era			
			ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
			N	N	N	N	N	N
System/Organ Class	Preferred term							
Blood and lymphatic system disorders	Anaemia	6	5	1	.	.	1	5
	Lymphopenia	3	2	1	.	.	2	1
	Neutropenia	1	1	.	.	.	.	1
Cardiac disorders	Arrhythmia supraventricular	2	2	.	.	.	2	.
	Myocardial ischaemia	1	1	.	.	.	1	.
Gastrointestinal disorders	Diarrhoea	1	1	.	.	.	.	1
	Gastrointestinal haemorrhage	3	1	2	1	2	.	.
	Gastrointestinal perforation	1	1	.	.	.	1	.
	Ileus	1	1	.	1	.	.	.
	Nausea	4	3	1	.	3	1	.
	Peritoneal haemorrhage	18	12	6	8	5	5	.
	Vomiting	2	2	.	.	.	2	.
General disorders and administration site conditions	Pain	6	6	.	2	1	2	1
Hepatobiliary disorders	Cholecystitis	2	1	1	.	1	1	.
	Portal vein thrombosis	7	7	.	2	3	1	1
Infections and infestations	Infection	2	2	.	1	1	.	.
Investigations	Activated partial thromboplastin time	1	1	.	1	.	.	.
	Activated partial thromboplastin time prolonged	1	1	.	.	.	.	1
	Alanine aminotransferase increased	1	1	.	.	.	1	.
	Aspartate aminotransferase increased	3	3	.	.	.	3	.
	Blood alkaline phosphatase	14	13	1	3	9	2	.
	Gamma-glutamyltransferase	5	4	1	1	3	1	.
	Gamma-glutamyltransferase increased	1	1	.	.	.	1	.
	Granulocytes abnormal	11	11	.	5	5	1	.
	Hepatic enzyme increased	3	3	.	.	.	2	1
	Lipase	3	1	2	1	2	.	.

**Exhibit 7-2A2 (continued)**  
**Adverse Events (AEs) RELATED TO PROCEDURE in Days 0-30 post First Infusion**

		Overall	Transplant type		Era			
			ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
		N	N	N	N	N	N	N
Metabolism and nutrition disorders	Liver function test abnormal	80	78	2	32	38	10	.
	Transaminases increased	1	1	.	.	.	.	1
	Hyperglycaemia	6	.	6	.	.	.	6
	Hypoglycaemia	4	3	1	3	.	1	.
Musculoskeletal and connective tissue disorders	Hypokalaemia	1	1	.	.	1	.	.
	Arthralgia	1	1	.	.	.	.	1
Nervous system disorders	Dyskinesia	1	1	.	.	.	1	.
Respiratory, thoracic and mediastinal disorders	Aspiration	1	1	.	.	.	1	.
	Haemothorax	1	.	1	.	1	.	.
Vascular disorders	Haematoma	6	4	2	1	3	.	2
	Haemorrhage	7	4	3	1	2	1	3
	Hypotension	2	2	.	.	.	2	.
	Thrombosis	1	.	1	1	.	.	.

**Exhibit 7-2A3****Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION in Days 0-30 post First Infusion**

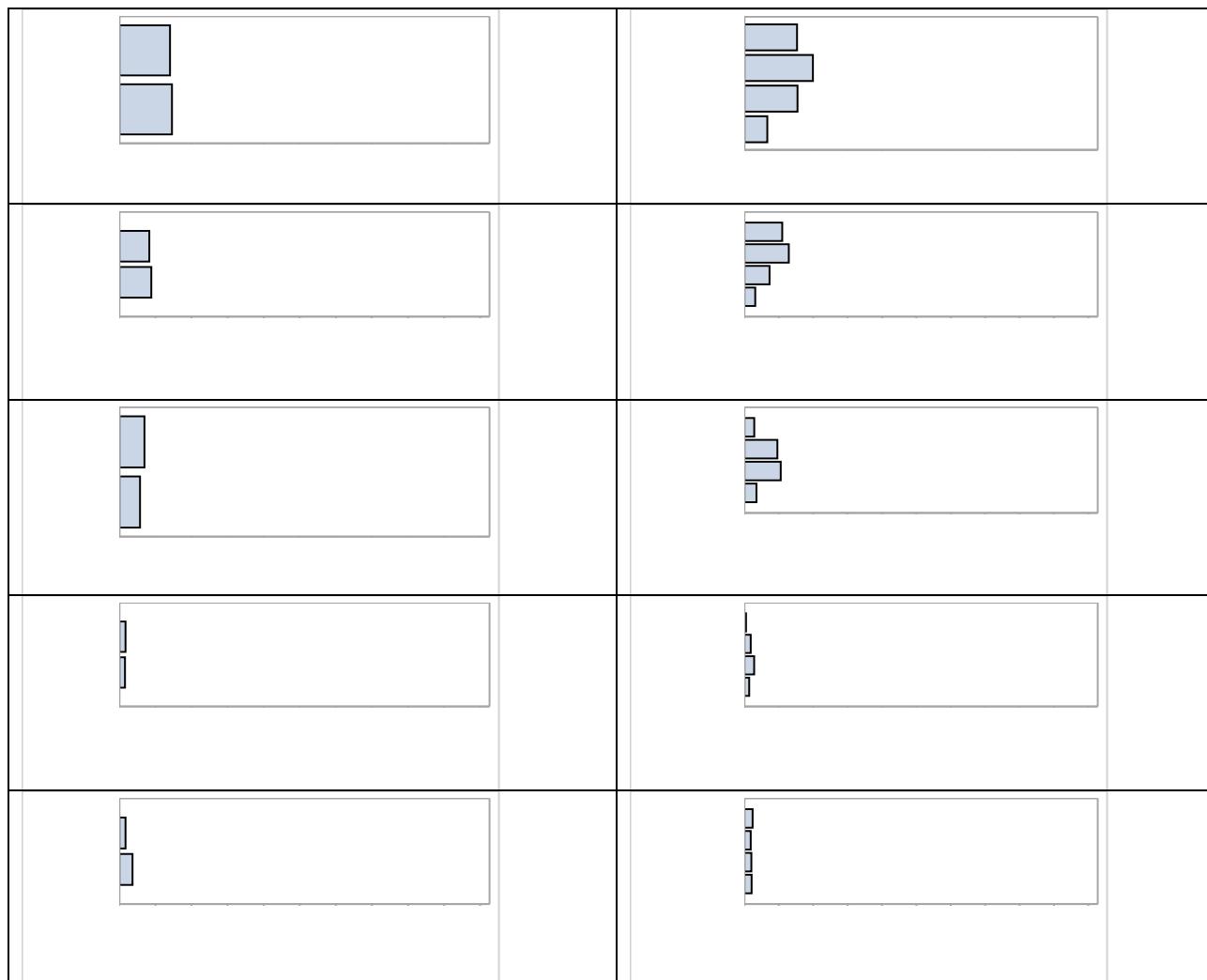
		Overall	Transplant type		Era			
			ITA	IAK/SIK	1999-2002		2003-2006	2007-2010
			N	N	N	N	N	N
<b>System/Organ Class</b>	<b>Preferred term</b>		15	13	2	.	.	13
<b>Blood and lymphatic system disorders</b>	Anaemia		5	4	1	1	2	2
	Blood disorder		1	1	.	.	.	1
	Febrile neutropenia		1	1	.	.	.	1
	Leukopenia		2	1	1	.	.	2
	Lymphopenia		26	24	2	.	10	13
	Neutropenia		5	5	.	.	.	4
	Platelet disorder		1	1	.	.	1	.
<b>Cardiac disorders</b>	Arrhythmia supraventricular		1	1	.	.	.	1
	Myocardial ischaemia		1	1	.	.	1	.
<b>Gastrointestinal disorders</b>	Diarrhoea		6	5	1	.	4	1
	Gastrointestinal disorder		1	1	.	.	1	.
	Nausea		5	3	2	.	3	1
	Peritoneal haemorrhage		2	.	2	2	.	.
	Vomiting		6	5	1	2	.	4
<b>General disorders and administration site conditions</b>	Mucosal inflammation		1	1	.	.	1	.
	Pain		4	4	.	.	2	1
	Pyrexia		1	1	.	.	1	.
<b>Immune system disorders</b>	Hypersensitivity		1	1	.	.	1	.
<b>Infections and infestations</b>	Infection		5	3	2	.	4	1
<b>Injury, poisoning and procedural complications</b>	Toxicity to various agents		2	2	.	.	.	1
<b>Investigations</b>	Activated partial thromboplastin time		1	1	.	1	.	.
	Blood alkaline phosphatase		3	2	1	1	1	1
	Gamma-glutamyltransferase		1	1	.	1	.	.
	Granulocytes abnormal		91	90	1	28	45	17
	Liver function test abnormal		22	20	2	12	5	5
	Neutrophil count		1	1	.	.	.	1
	Neutrophil count decreased		2	2	.	.	.	2
<b>Metabolism and nutrition disorders</b>	Hyperglycaemia		6	.	6	.	.	6
	Hyperkalaemia		1	1	.	1	.	.
	Hypoglycaemia		2	2	.	2	.	.
	Hypokalaemia		2	2	.	.	1	1

**Exhibit 7-2A3 (continued)****Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION in Days 0-30 post First Infusion**

		Overall	Transplant type		Era			
			ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
		N	N	N	N	N	N	N
Musculoskeletal and connective tissue disorders	Arthralgia		1	1	.	.	.	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Neoplasm malignant		2	1	1	.	2	.
Nervous system disorders	Headache		1	1	.	.	1	.
Respiratory, thoracic and mediastinal disorders	Aspiration		1	1	.	.	1	.
	Hypoxia		1	1	.	.	1	.
	Pleural effusion		1	1	.	.	1	.
	Pneumonitis		1	.	1	1	.	.
Skin and subcutaneous tissue disorders	Exfoliative rash		1	1	.	.	1	.
Vascular disorders	Hypertension		1	.	1	.	1	.

**Exhibit 7-2B1**  
**Any Serious Adverse Event in Days 0-30 post First Infusion**

Percent of Recipients with:	Type				Era							
	ITA		IAK/SIK		1999-2002		2003-2006		2007-2010		2011-2014	
	N	%	N	%	N	%	N	%	N	%	N	%
<b>Any SAE in Day 0-30</b>	115	14.0	28	14.6	32	15.3	54	19.9	38	15.4	19	6.7
<b>Any SAE related to infusion in Day 0-30</b>	68	8.3	17	8.9	23	11.0	35	12.9	18	7.3	9	3.2
<b>Any SAE related to IS in Day 0-30</b>	57	7.0	11	5.7	6	2.9	26	9.6	26	10.6	10	3.5
<b>Any SAE related to both in Day 0-30</b>	14	1.7	3	1.6	1	0.5	5	1.8	7	2.8	4	1.4
<b>Any SAE related to neither in Day 0-30</b>	14	1.7	7	3.6	5	2.4	5	1.8	5	2.0	6	2.1



**Exhibit 7-2B2**  
**Serious Adverse Events (SAEs) RELATED TO PROCEDURE in Days 0-30 post First Infusion**

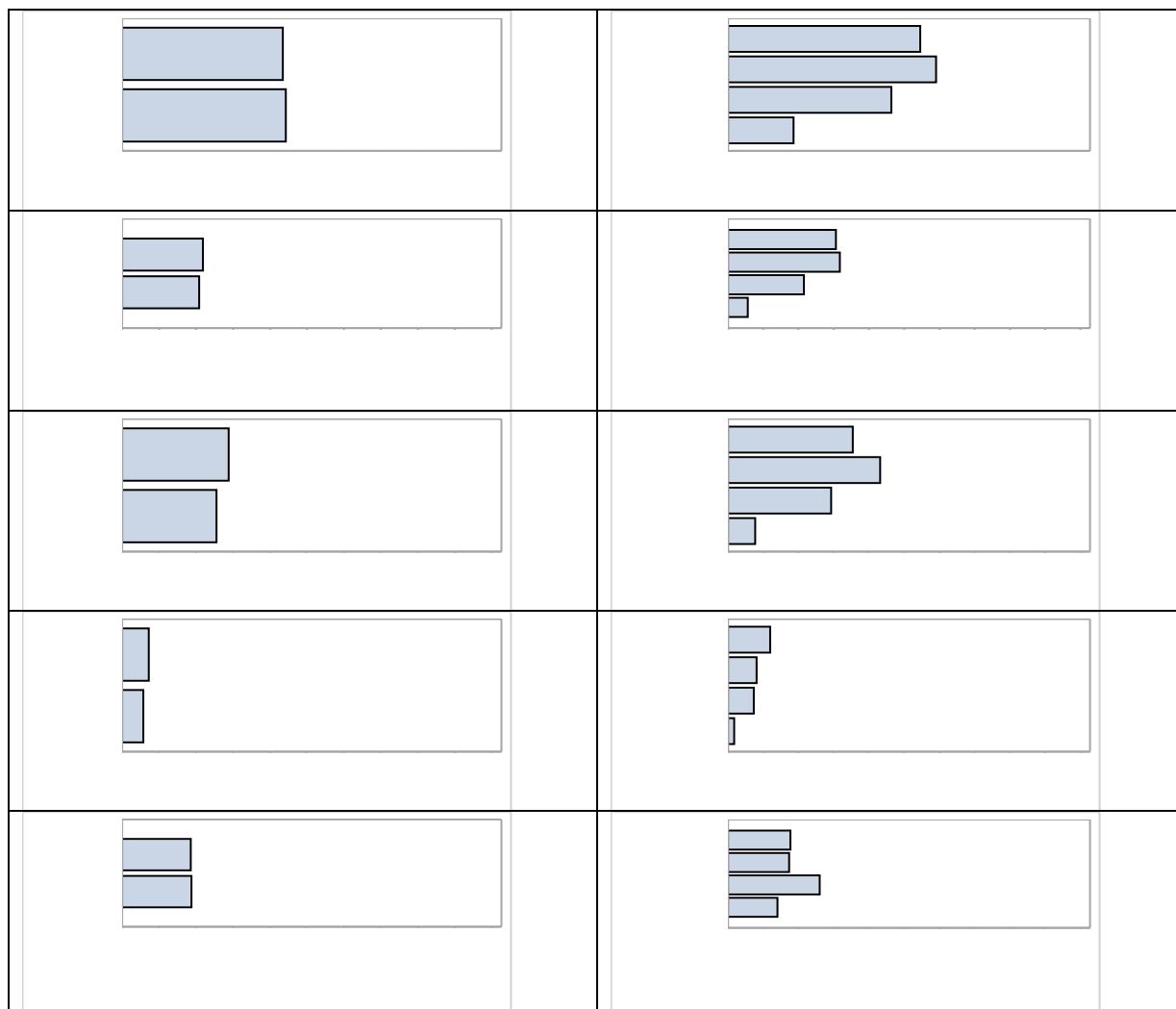
System/Organ Class	Preferred term	Overall	Transplant type		Era			
			ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
		N	N	N	N	N	N	N
Blood and lymphatic system disorders	Anaemia	5	4	1	.	1	4	.
	Neutropenia	2	1	1	.	2	.	.
Cardiac disorders	Arrhythmia supraventricular	1	1	.	.	.	1	.
	Myocardial ischaemia	1	1	.	.	1	.	.
Gastrointestinal disorders	Diarrhoea	1	1	.	.	.	.	1
	Gastrointestinal haemorrhage	3	1	2	1	2	.	.
	Gastrointestinal perforation	1	1	.	.	.	1	.
	Ileus	1	1	.	1	.	.	.
	Nausea	2	2	.	.	1	1	.
	Peritoneal haemorrhage	13	9	4	6	4	3	.
	Vomiting	2	2	.	.	.	2	.
General disorders and administration site conditions	Pain	5	5	.	2	1	1	1
Hepatobiliary disorders	Cholecystitis	2	1	1	.	1	1	.
	Portal vein thrombosis	6	6	.	2	3	1	.
Infections and infestations	Infection	2	2	.	1	1	.	.
Investigations	Blood alkaline phosphatase	8	8	.	2	6	.	.
	Granulocytes abnormal	1	1	.	.	1	.	.
	Hepatic enzyme increased	1	1	.	.	.	.	1
	Liver function test abnormal	27	27	.	12	15	.	.
Metabolism and nutrition disorders	Hyperglycaemia	6	.	6	.	.	.	6
	Hypoglycaemia	2	1	1	1	.	1	.
Musculoskeletal and connective tissue disorders	Arthralgia	1	1	.	.	.	.	1
Respiratory, thoracic and mediastinal disorders	Aspiration	1	1	.	.	.	1	.
	Haemothorax	1	.	1	.	1	.	.
Vascular disorders	Haematoma	6	4	2	1	3	.	2
	Haemorrhage	7	4	3	1	2	1	3
	Hypotension	1	1	.	.	.	1	.
	Thrombosis	1	.	1	1	.	.	.

**Exhibit 7-2B3**  
**Serious Adverse Events (SAEs) RELATED TO IMMUNOSUPPRESSION in Days 0-30 post First Infusion**

System/Organ Class	Preferred term	Overall	Transplant type		Era			
			ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
			N	N	N	N	N	N
Blood and lymphatic system disorders	Anaemia	10	9	1	.	.	8	2
	Blood disorder	1	1	.	.	.	1	.
	Febrile neutropenia	1	1	.	.	.	1	.
	Lymphopenia	6	5	1	.	4	2	.
	Neutropenia	3	3	.	.	.	2	1
	Platelet disorder	1	1	.	.	1	.	.
Cardiac disorders	Arrhythmia supraventricular	1	1	.	.	.	1	.
	Myocardial ischaemia	1	1	.	.	1	.	.
Gastrointestinal disorders	Diarrhoea	4	3	1	.	2	1	1
	Gastrointestinal disorder	1	1	.	.	1	.	.
	Nausea	3	2	1	.	1	1	1
	Peritoneal haemorrhage	1	.	1	1	.	.	.
	Vomiting	5	4	1	1	.	4	.
General disorders and administration site conditions	Mucosal inflammation	1	1	.	.	1	.	.
	Pain	1	1	.	.	.	.	1
	Pyrexia	1	1	.	.	1	.	.
Infections and infestations	Infection	5	3	2	.	4	1	.
Injury, poisoning and procedural complications	Toxicity to various agents	2	2	.	.	.	1	1
Investigations	Granulocytes abnormal	20	20	.	4	9	6	1
	Liver function test abnormal	2	2	.	.	2	.	.
	Neutrophil count	1	1	.	.	.	1	.
	Neutrophil count decreased	1	1	.	.	.	1	.
Metabolism and nutrition disorders	Hyperglycaemia	6	.	6	.	.	.	6
Musculoskeletal and connective tissue disorders	Arthralgia	1	1	.	.	.	.	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Neoplasm malignant	1	1	.	.	1	.	.
Nervous system disorders	Headache	1	1	.	.	.	1	.
Respiratory, thoracic and mediastinal disorders	Aspiration	1	1	.	.	.	1	.
	Pleural effusion	1	1	.	.	.	1	.
	Pneumonitis	1	.	1	1	.	.	.

**Exhibit 7-3A1**  
**Adverse Events (AEs) in Year 1 post First Infusion**

Percent of Recipients with:	Type				Era							
	ITA		IAK/SIK		1999-2002		2003-2006		2007-2010		2011-2014	
	N	%	N	%	N	%	N	%	N	%	N	%
Any AE in 1-year	356	43.5	85	44.3	114	54.5	160	59.0	114	46.3	53	18.6
Any AE related to infusion in 1-year	179	21.9	40	20.8	64	30.6	86	31.7	53	21.5	16	5.6
Any AE related to IS in 1-year	236	28.8	49	25.5	74	35.4	117	43.2	72	29.3	22	7.7
Any AE related to both in 1-year	59	7.2	11	5.7	25	12.0	22	8.1	18	7.3	5	1.8
Any AE related to neither in 1-year	152	18.6	36	18.8	37	17.7	47	17.3	64	26.0	40	14.0



**Exhibit 7-3A2**  
**Adverse Events (AEs) RELATED TO PROCEDURE in Year 1 post First Infusion**

		Overall	Transplant type		Era			
			ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
			N	N	N	N	N	N
<b>System/Organ Class</b>	<b>Preferred term</b>							
<b>Blood and lymphatic system disorders</b>	Anaemia	11	8	3	1	1	8	1
	Blood disorder	2	.	2	1	1	.	.
	Lymphopenia	3	2	1	1	2	.	.
	Neutropenia	4	4	.	.	.	.	4
<b>Cardiac disorders</b>	Arrhythmia supraventricular	2	2	.	.	.	2	.
	Myocardial ischaemia	1	1	.	.	1	.	.
<b>Gastrointestinal disorders</b>	Ascites	2	2	.	1	1	.	.
	Diarrhoea	2	2	.	.	.	1	1
	Gastrointestinal disorder	1	1	.	.	1	.	.
	Gastrointestinal haemorrhage	5	2	3	2	3	.	.
	Gastrointestinal obstruction	1	1	.	.	1	.	.
	Gastrointestinal perforation	2	2	.	1	.	1	.
	Ileus	1	1	.	1	.	.	.
	Mouth ulceration	1	1	.	.	1	.	.
	Nausea	4	3	1	.	3	1	.
	Peritoneal haemorrhage	41	31	10	13	14	11	3
	Vomiting	2	2	.	.	.	2	.
<b>General disorders and administration site conditions</b>	Fatigue	3	3	.	.	3	.	.
	Pain	16	15	1	4	7	4	1
	Ulcer	1	1	.	.	.	1	.
<b>Hepatobiliary disorders</b>	Biliary tract disorder	1	1	.	.	1	.	.
	Cholecystitis	2	1	1	.	1	1	.
	Hepatic haematoma	1	1	.	.	1	.	.
	Hepatic haemorrhage	2	2	.	.	.	.	2
	Portal vein thrombosis	10	8	2	3	5	1	1
<b>Immune system disorders</b>	Hypersensitivity	1	1	.	.	1	.	.
<b>Infections and infestations</b>	Infection	5	4	1	2	3	.	.
<b>Injury, poisoning and procedural complications</b>	Post procedural haemorrhage	1	1	.	.	.	1	.
<b>Investigations</b>	Activated partial thromboplastin time	1	1	.	1	.	.	.
	Activated partial thromboplastin time prolonged	1	1	.	.	.	.	1
	Alanine aminotransferase increased	1	1	.	.	.	1	.
	Aspartate aminotransferase increased	3	3	.	.	.	3	.

**Exhibit 7-3A2 (continued)**  
**Adverse Events (AEs) RELATED TO PROCEDURE in Year 1 post First Infusion**

		Transplant type			Era			
		Overall	ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
		N	N	N	N	N	N	N
	Blood alkaline phosphatase	18	16	2	4	12	2	.
	Blood bilirubin	1	1	.	1	.	.	.
	Gamma-glutamyltransferase	5	4	1	1	3	1	.
	Gamma-glutamyltransferase increased	1	1	.	.	.	1	.
	Glomerular filtration rate	1	1	.	1	.	.	.
	Granulocytes abnormal	16	16	.	8	7	1	.
	Hepatic enzyme increased	4	4	.	.	.	2	2
	Lipase	3	1	2	1	2	.	.
	Liver function test abnormal	98	95	3	41	46	11	.
	Low density lipoprotein increased	1	1	.	.	.	.	1
	Transaminases increased	1	1	.	.	.	.	1
	Dehydration	1	1	.	.	1	.	.
	Hyperglycaemia	6	.	6	.	.	.	6
	Hypoalbuminaemia	1	1	.	.	.	1	.
	Hypoglycaemia	6	4	2	3	1	2	.
	Hypokalaemia	1	1	.	.	1	.	.
	Hyponatraemia	1	1	.	1	.	.	.
	Ketoacidosis	2	2	.	.	.	2	.
	Arthralgia	1	1	.	.	.	.	1
	Musculoskeletal pain	2	2	.	.	.	.	2
Nervous system disorders	Dyskinesia	1	1	.	.	.	1	.
Renal and urinary disorders	Proteinuria	1	1	.	1	.	.	.
	Urinary bladder haemorrhage	1	1	.	.	.	1	.
	Aspiration	1	1	.	.	.	1	.
	Haemothorax	2	1	1	1	1	.	.
	Lung disorder	1	1	.	.	.	1	.
	Pleural effusion	1	.	1	.	1	.	.
	Haematoma	9	5	4	2	5	.	2
	Haemorrhage	10	6	4	1	4	2	3
	Hypotension	2	2	.	.	.	2	.
	Thrombosis	1	.	1	1	.	.	.

**Exhibit 7-3A3**  
**Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION in Year 1 post First Infusion**

System/Organ Class	Preferred term	Overall N	Transplant type		Era			
			ITA N	IAK/SIK N	1999-2002 N	2003-2006 N	2007-2010 N	2011-2014 N
Blood and lymphatic system disorders	Anaemia	21	19	2	4	11	5	1
	Blood disorder	3	1	2	1	1	1	.
	Febrile neutropenia	4	4	.	.	.	4	.
	Leukopenia	6	2	4	.	.	3	3
	Lymphopenia	38	34	4	3	15	16	4
	Neutropenia	19	19	.	.	.	6	13
	Platelet disorder	2	2	.	1	1	.	.
Cardiac disorders	Arrhythmia supraventricular	1	1	.	.	.	1	.
	Myocardial ischaemia	1	1	.	.	1	.	.
Eye disorders	Eye disorder	1	1	.	.	1	.	.
	Vitreous haemorrhage	1	1	.	1	.	.	.
Gastrointestinal disorders	Ascites	1	1	.	1	.	.	.
	Colitis	3	2	1	.	2	1	.
	Constipation	1	1	.	.	.	1	.
	Diarrhoea	26	23	3	2	15	7	2
	Dysphagia	2	2	.	.	2	.	.
	Gastritis	1	1	.	.	1	.	.
	Gastrointestinal disorder	7	4	3	.	7	.	.
	Gastrointestinal obstruction	1	1	.	.	1	.	.
	Mouth ulceration	2	2	.	.	1	1	.
	Nausea	7	5	2	1	4	1	1
	Oral pain	1	1	.	.	.	1	.
	Peritoneal haemorrhage	5	2	3	5	.	.	.
	Stomatitis	1	1	.	.	.	1	.
	Vomiting	10	9	1	2	3	5	.
General disorders and administration site conditions	Chest pain	1	1	.	.	.	1	.
	Death	1	.	1	1	.	.	.
	Fatigue	8	8	.	.	8	.	.
	Injection site reaction	1	1	.	.	1	.	.
	Mucosal inflammation	14	11	3	3	9	2	.
	Oedema peripheral	3	2	1	2	1	.	.
	Pain	20	20	.	4	12	3	1
	Pyrexia	1	1	.	.	1	.	.
	Ulcer	1	1	.	.	.	1	.
Hepatobiliary disorders	Cholecystitis	1	1	.	1	.	.	.
Immune system disorders	Autoimmune disorder	1	1	.	.	.	1	.
	Hypersensitivity	5	4	1	1	2	1	1

**Exhibit 7-3A3 (continued)**  
**Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION in Year 1 post First Infusion**

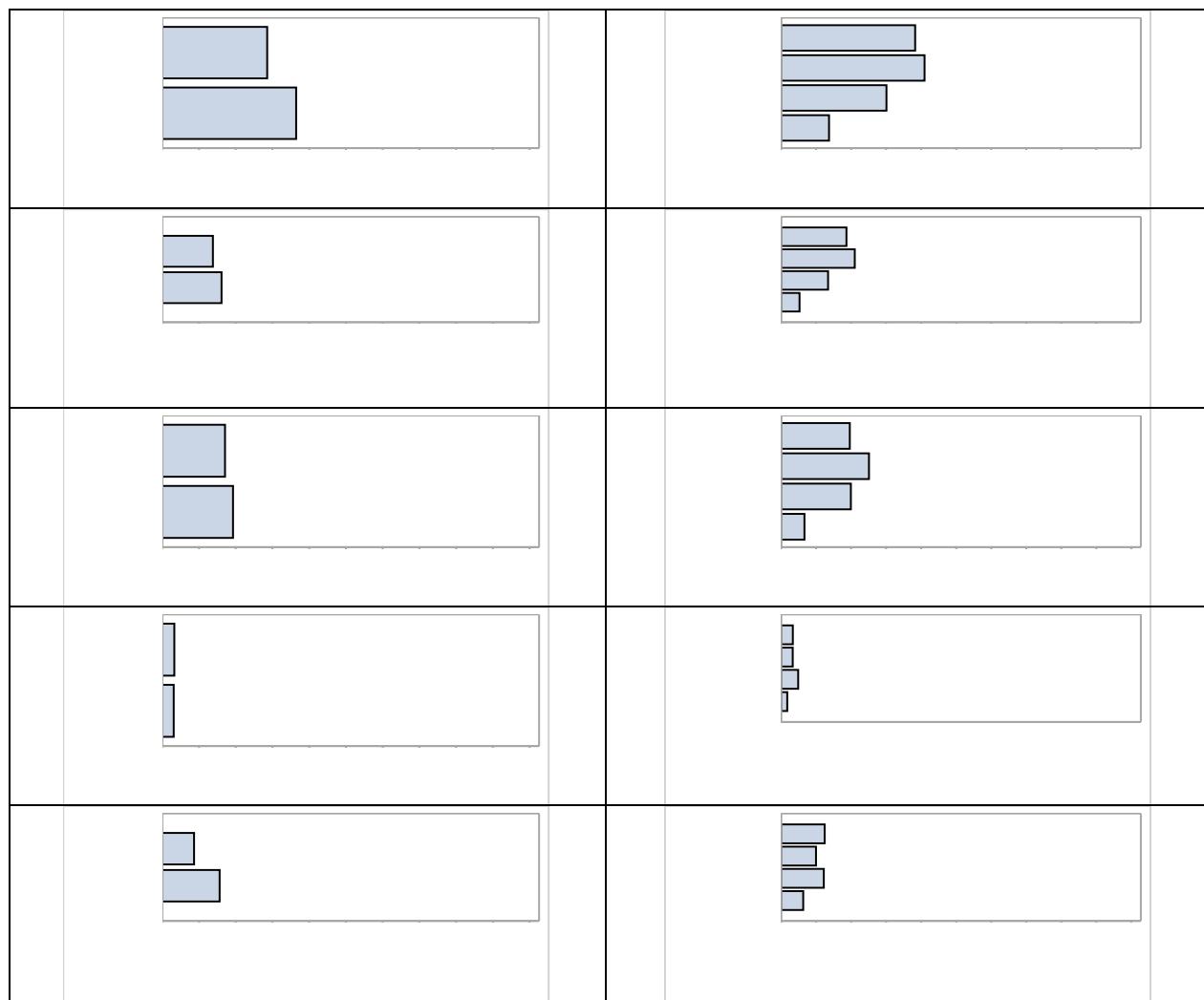
			Transplant type			Era			
			Overall	ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
			N	N	N	N	N	N	N
<b>Infections and infestations</b>	Cystitis		1	1	.	.	.	.	1
	Infection		29	21	8	10	15	4	.
	Pneumonia		3	2	1	.	2	1	.
	Renal graft infection		1	.	1	.	.	.	1
<b>Injury, poisoning and procedural complications</b>	Toxicity to various agents		2	2	.	.	.	1	1
<b>Investigations</b>	Activated partial thromboplastin time		1	1	.	1	.	.	.
	Blood alkaline phosphatase		5	3	2	2	2	1	.
	Blood creatine phosphokinase		1	1	.	.	1	.	.
	Blood creatinine increased		4	4	.	.	2	2	.
	Gamma-glutamyltransferase		1	1	.	1	.	.	.
	Glomerular filtration rate		1	1	.	1	.	.	.
	Granulocytes abnormal		193	184	9	65	97	28	3
	Lipase increased		1	1	.	.	.	.	1
	Liver function test abnormal		25	23	2	14	6	5	.
	Low density lipoprotein abnormal		1	1	.	.	1	.	.
	Low density lipoprotein increased		3	3	.	.	.	.	3
	Neutrophil count		2	2	.	.	.	2	.
	Neutrophil count decreased		3	3	.	.	.	3	.
<b>Metabolism and nutrition disorders</b>	Decreased appetite		1	1	.	.	.	1	.
	Dehydration		4	3	1	.	.	3	1
	Hyperglycaemia		6	.	6	.	.	.	6
	Hyperkalaemia		4	4	.	2	1	.	1
	Hypoglycaemia		3	3	.	2	1	.	.
	Hypokalaemia		3	3	.	.	2	1	.
	Hypomagnesaemia		1	1	.	.	1	.	.
	Hyponatraemia		1	1	.	1	.	.	.
	Hypophosphataemia		5	5	.	1	4	.	.
	Ketoacidosis		1	.	1	.	1	.	.
<b>Musculoskeletal and connective tissue disorders</b>	Arthralgia		1	1	.	.	.	.	1
	Arthritis		1	1	.	.	.	1	.
	Muscle necrosis		1	1	.	.	1	.	.
	Muscular weakness		4	4	.	.	4	.	.
	Musculoskeletal disorder		2	2	.	1	1	.	.
<b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b>	Neoplasm malignant		3	2	1	1	2	.	.
	Papillary thyroid cancer		1	1	.	.	1	.	.
	Treatment related secondary malignancy		1	1	.	.	1	.	.

**Exhibit 7-3A3 (continued)**  
**Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION in Year 1 post First Infusion**

		Overall N	Transplant type		Era			
			ITA N	IAK/SIK N	1999-2002 N	2003-2006 N	2007-2010 N	2011-2014 N
<b>Nervous system disorders</b>	Cognitive disorder	1	1	.	1	.	.	.
	Convulsion	1	1	.	.	.	.	1
	Dizziness	1	1	.	.	1	.	.
	Headache	2	2	.	.	.	1	1
	Tremor	1	1	.	1	.	.	.
<b>Psychiatric disorders</b>	Insomnia	1	1	.	.	1	.	.
	Mood altered	1	1	.	.	1	.	.
<b>Renal and urinary disorders</b>	Micturition urgency	1	1	.	.	1	.	.
	Proteinuria	1	1	.	1	.	.	.
	Renal disorder	2	2	.	2	.	.	.
	Renal failure	9	5	4	5	3	1	.
	Urinary bladder haemorrhage	2	1	1	.	1	1	.
<b>Reproductive system and breast disorders</b>	Ovarian cyst ruptured	1	1	.	.	1	.	.
	Sexual dysfunction	1	1	.	.	1	.	.
<b>Respiratory, thoracic and mediastinal disorders</b>	Acute respiratory distress syndrome	1	.	1	1	.	.	.
	Aspiration	1	1	.	.	.	1	.
	Cough	2	1	1	1	.	1	.
	Dyspnoea	1	1	.	.	1	.	.
	Haemothorax	1	1	.	1	.	.	.
	Hypoxia	1	1	.	.	.	1	.
	Lung disorder	2	2	.	.	1	1	.
	Pleural effusion	1	1	.	.	.	1	.
	Pneumonitis	3	2	1	2	1	.	.
<b>Skin and subcutaneous tissue disorders</b>	Exfoliative rash	4	3	1	1	1	2	.
	Pruritus	1	1	.	.	.	1	.
	Rash	1	1	.	.	.	1	.
<b>Surgical and medical procedures</b>	Hysterectomy	1	1	.	.	1	.	.
<b>Vascular disorders</b>	Haematoma	1	.	1	1	.	.	.
	Hypertension	2	.	2	.	2	.	.

**Exhibit 7-3B1**  
**Serious Adverse Events (SAEs) in Year 1 post First Infusion**

Percent of Recipients with:	Type				Era					
	ITA		IAK/SIK		1999-2002		2003-2006		2007-2010	
	N	%	N	%	N	%	N	%	N	%
<b>Any SAE in 1-year</b>	234	28.6	70	36.5	80	38.3	111	41.0	74	30.1
<b>Any SAE related to infusion in 1-year</b>	113	13.8	31	16.1	39	18.7	57	21.0	33	13.4
<b>Any SAE related to IS in 1-year</b>	140	17.1	37	19.3	41	19.6	68	25.1	49	19.9
<b>Any SAE related to both in 1-year</b>	27	3.3	6	3.1	7	3.3	9	3.3	12	4.9
<b>Any SAE related to neither in 1-year</b>	71	8.7	30	15.6	26	12.4	27	10.0	30	12.2



**Exhibit 7-3B2**  
**Serious Adverse Events (SAEs) RELATED TO PROCEDURE in Year 1 post First Infusion**

System/Organ Class	Preferred term	Overall	Transplant type		Era			
			ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
			N	N	N	N	N	N
Blood and lymphatic system disorders	Anaemia	10	7	3	1	1	7	1
	Lymphopenia	7	5	2	1	4	1	1
	Neutropenia	2	1	1	1	1	.	.
Cardiac disorders	Neutropenia	4	4	.	.	.	.	4
Gastrointestinal disorders	Arrhythmia supraventricular	1	1	.	.	.	1	.
	Myocardial ischaemia	1	1	.	.	1	.	.
	Ascites	2	2	.	1	1	.	.
	Diarrhoea	2	2	.	.	.	1	1
	Gastrointestinal haemorrhage	5	2	3	2	3	.	.
	Gastrointestinal obstruction	1	1	.	.	1	.	.
	Gastrointestinal perforation	1	1	.	1	.	1	.
	Ileus	2	2	.	1	.	1	.
	Nausea	2	2	.	.	1	1	.
	Peritoneal haemorrhage	36	28	8	11	13	9	3
	Vomiting	2	2	.	.	.	2	.
General disorders and administration site conditions	Pain	12	12	.	4	4	3	1
Hepatobiliary disorders	Biliary tract disorder	1	1	.	.	1	.	.
	Cholecystitis	2	1	1	.	1	1	.
	Hepatic haematoma	1	1	.	.	1	.	.
	Hepatic haemorrhage	2	2	.	.	.	.	2
	Portal vein thrombosis	9	7	2	3	5	1	.
Immune system disorders	Hypersensitivity	1	1	.	.	1	.	.
Infections and infestations	Infection	5	4	1	2	3	.	.
Injury, poisoning and procedural complications	Post procedural haemorrhage	1	1	.	.	.	1	.
Investigations	Blood alkaline phosphatase	11	11	.	3	8	.	.
	Granulocytes abnormal	2	2	.	.	2	.	.
	Hepatic enzyme increased	2	2	.	.	.	.	2
	Liver function test abnormal	33	33	.	18	15	.	.
	Low density lipoprotein increased	1	1	.	.	.	.	1

**Exhibit 7-3B2 (continued)**  
**Serious Adverse Events (SAEs) RELATED TO PROCEDURE in Year 1 post First Infusion**

		Overall	Transplant type		Era			
			ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
		N	N	N	N	N	N	N
<b>Metabolism and nutrition disorders</b>	<b>Dehydration</b>	1	1	.	.	1	.	.
	<b>Hyperglycaemia</b>	6	.	6	.	.	.	6
	<b>Hypoglycaemia</b>	4	2	2	1	1	2	.
	<b>Ketoacidosis</b>	2	2	.	.	.	2	.
<b>Musculoskeletal and connective tissue disorders</b>	<b>Arthralgia</b>	1	1	.	.	.	.	1
	<b>Musculoskeletal pain</b>	2	2	.	.	.	.	2
<b>Renal and urinary disorders</b>	<b>Urinary bladder haemorrhage</b>	1	1	.	.	.	1	.
<b>Respiratory, thoracic and mediastinal disorders</b>	<b>Aspiration</b>	1	1	.	.	.	1	.
	<b>Haemothorax</b>	2	1	1	1	1	.	.
	<b>Lung disorder</b>	1	1	.	.	.	1	.
	<b>Pleural effusion</b>	1	.	1	.	1	.	.
<b>Vascular disorders</b>	<b>Haematoma</b>	9	5	4	2	5	.	2
	<b>Haemorrhage</b>	10	6	4	1	4	2	3
	<b>Hypotension</b>	1	1	.	.	.	1	.
	<b>Thrombosis</b>	1	.	1	1	.	.	.

**Exhibit 7-3B3**  
**Serious Adverse Events (SAEs) RELATED TO IMMUNOSUPPRESSION in Year 1 post First Infusion**

System/Organ Class	Preferred term	Overall	Transplant type		Era			
			ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
			N	N	N	N	N	N
Blood and lymphatic system disorders	Anaemia	12	10	2	3	5	3	1
	Blood disorder	1	1	.	.	.	1	.
	Febrile neutropenia	4	4	.	.	.	4	.
	Leukopenia	3	.	3	.	.	.	3
	Lymphopenia	8	6	2	1	5	2	.
	Neutropenia	14	14	.	.	.	2	12
	Platelet disorder	1	1	.	.	1	.	.
Cardiac disorders	Arrhythmia supraventricular	1	1	.	.	.	1	.
	Myocardial ischaemia	1	1	.	.	1	.	.
Eye disorders	Eye disorder	1	1	.	.	1	.	.
Gastrointestinal disorders	Ascites	1	1	.	1	.	.	.
	Colitis	3	2	1	.	2	1	.
	Constipation	1	1	.	.	.	1	.
	Diarrhoea	11	8	3	1	3	5	2
	Dysphagia	1	1	.	.	1	.	.
	Gastrointestinal disorder	5	3	2	.	5	.	.
	Gastrointestinal obstruction	1	1	.	.	1	.	.
	Nausea	5	4	1	1	2	1	1
	Peritoneal haemorrhage	3	2	1	3	.	.	.
	Vomiting	8	7	1	1	2	5	.
General disorders and administration site conditions	Chest pain	1	1	.	.	.	1	.
	Death	1	.	1	1	.	.	.
	Mucosal inflammation	7	6	1	2	4	1	.
	Oedema peripheral	1	.	1	.	1	.	.
	Pain	5	5	.	.	4	.	1
	Pyrexia	1	1	.	.	1	.	.
Hepatobiliary disorders	Cholecystitis	1	1	.	1	.	.	.
Immune system disorders	Autoimmune disorder	1	1	.	.	.	1	.
	Hypersensitivity	4	3	1	1	1	1	1
Infections and infestations	Infection	27	19	8	10	13	4	.
	Pneumonia	3	2	1	.	2	1	.
	Renal graft infection	1	.	1	.	.	.	1
Injury, poisoning and procedural complications	Toxicity to various agents	2	2	.	.	.	1	1

**Exhibit 7-3B3 (continued)**  
**Serious Adverse Events (SAEs) RELATED TO IMMUNOSUPPRESSION in Year 1 post First Infusion**

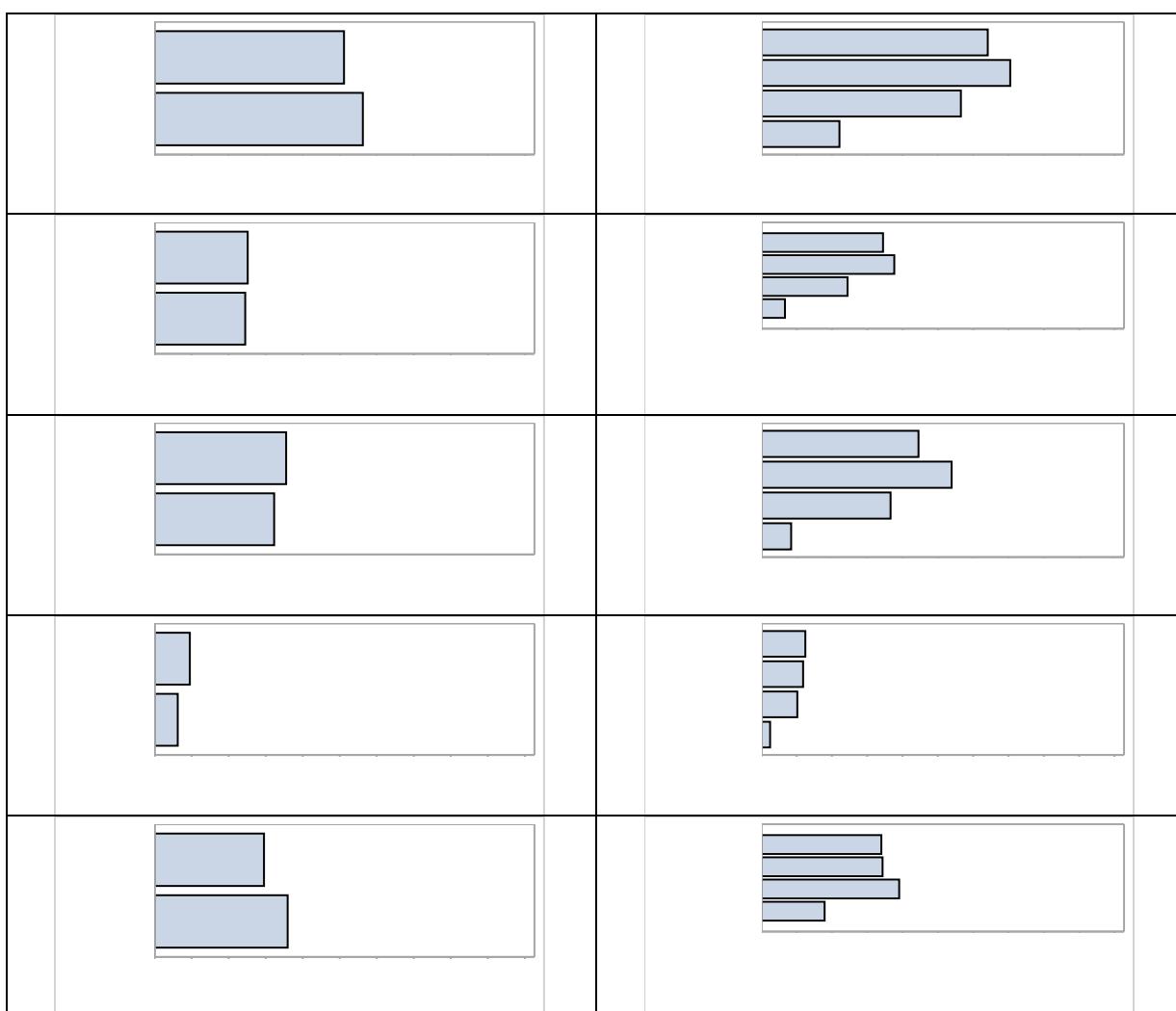
		Transplant type			Era			
		Overall N	ITA N	IAK/SIK N	1999-2002 N	2003-2006 N	2007-2010 N	2011-2014 N
Investigations	Blood alkaline phosphatase	1	1	.	1	.	.	.
	Blood creatine phosphokinase	1	1	.	.	1	.	.
	Blood creatinine increased	4	4	.	.	2	2	.
	Granulocytes abnormal	51	45	6	17	19	12	3
	Liver function test abnormal	3	3	.	1	2	.	.
	Low density lipoprotein increased	1	1	.	.	.	.	1
	Neutrophil count	1	1	.	.	.	1	.
	Neutrophil count decreased	1	1	.	.	.	1	.
Metabolism and nutrition disorders	Dehydration	4	3	1	.	.	3	1
	Hyperglycaemia	6	.	6	.	.	.	6
	Hypoglycaemia	1	1	.	.	1	.	.
	Hypomagnesaemia	1	1	.	.	1	.	.
	Hypophosphataemia	1	1	.	.	1	.	.
	Ketoacidosis	1	.	1	.	1	.	.
Musculoskeletal and connective tissue disorders	Arthralgia	1	1	.	.	.	.	1
	Arthritis	1	1	.	.	.	1	.
	Muscle necrosis	1	1	.	.	1	.	.
	Musculoskeletal disorder	2	2	.	1	1	.	.
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Neoplasm malignant	2	2	.	1	1	.	.
	Papillary thyroid cancer	1	1	.	.	1	.	.
	Treatment related secondary malignancy	1	1	.	.	1	.	.
Nervous system disorders	Cognitive disorder	1	1	.	1	.	.	.
	Convulsion	1	1	.	.	.	.	1
	Headache	2	2	.	.	.	1	1
Psychiatric disorders	Mood altered	1	1	.	.	1	.	.
Renal and urinary disorders	Renal disorder	2	2	.	2	.	.	.
	Renal failure	9	5	4	5	3	1	.
	Urinary bladder haemorrhage	2	1	1	.	1	1	.
Reproductive system and breast disorders	Ovarian cyst ruptured	1	1	.	.	1	.	.
	Sexual dysfunction	1	1	.	.	1	.	.
Respiratory, thoracic and mediastinal disorders	Acute respiratory distress syndrome	1	.	1	1	.	.	.
	Aspiration	1	1	.	.	.	1	.

**Exhibit 7-3B3 (continued)**  
**Serious Adverse Events (SAEs) RELATED TO IMMUNOSUPPRESSION in Year 1 post First Infusion**

		Transplant type			Era			
		Overall	ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
			N	N	N	N	N	N
	<b>Cough</b>	1	.	1	1	.	.	.
	<b>Dyspnoea</b>	1	1	.	.	1	.	.
	<b>Haemothorax</b>	1	1	.	1	.	.	.
	<b>Lung disorder</b>	2	2	.	.	1	1	.
	<b>Pleural effusion</b>	1	1	.	.	.	1	.
	<b>Pneumonitis</b>	2	1	1	2	.	.	.
<b>Skin and subcutaneous tissue disorders</b>	<b>Exfoliative rash</b>	1	1	.	.	.	1	.
	<b>Rash</b>	1	1	.	.	.	1	.
<b>Surgical and medical procedures</b>	<b>Hysterectomy</b>		1	1	.	1	.	.
<b>Vascular disorders</b>	<b>Haematoma</b>	1	.	1	1	.	.	.

**Exhibit 7-4A1**  
**Adverse Events (AEs) Any Time Post Islet Transplantation**

Percent of Recipients with:	Type				Era							
	ITA		IAK/SIK		1999-2002		2003-2006		2007-2010		2011-2014	
	N	%	N	%	N	%	N	%	N	%	N	%
<b>Any AE in ever</b>	419	51.2	108	56.3	134	64.1	191	70.5	139	56.5	63	22.1
<b>Any AE related to infusion in ever</b>	206	25.2	47	24.5	72	34.4	102	37.6	60	24.4	19	6.7
<b>Any AE related to IS in ever</b>	291	35.5	62	32.3	93	44.5	146	53.9	90	36.6	24	8.4
<b>Any AE related to both in ever</b>	78	9.5	12	6.3	26	12.4	32	11.8	25	10.2	7	2.5
<b>Any AE related to neither in ever</b>	242	29.5	69	35.9	71	34.0	93	34.3	96	39.0	51	17.9



**Exhibit 7-4A2**  
**Adverse Events (AEs) RELATED TO PROCEDURE in Any Time Post Islet Transplantation**

			Transplant type			Era			
			Overall	ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
			N	N	N	N	N	N	N
<b>System/Organ Class</b>	<b>Preferred term</b>								1
			12	8	4	1	2	8	
Blood and lymphatic system disorders	Anaemia		12	9	3	3	4	4	1
	Blood disorder		2	.	2	1	1	.	.
	Lymphopenia		4	3	1	1	3	.	.
	Neutropenia		4	4	.	.	.	.	4
Cardiac disorders	Arrhythmia supraventricular		2	2	.	.	.	2	.
	Myocardial ischaemia		1	1	.	.	1	.	.
Endocrine disorders	Endocrine disorder		1	1	.	.	.	1	.
Eye disorders	Vitreous haemorrhage		1	1	.	.	.	1	.
Gastrointestinal disorders	Ascites		2	2	.	1	1	.	.
	Diarrhoea		3	3	.	.	1	1	1
	Gastrointestinal disorder		3	3	.	.	3	.	.
	Gastrointestinal haemorrhage		5	2	3	2	3	.	.
	Gastrointestinal obstruction		2	2	.	1	1	.	.
	Gastrointestinal perforation		2	2	.	1	.	1	.
	Ileus		2	2	.	1	1	.	.
	Mouth ulceration		1	1	.	.	1	.	.
	Nausea		4	3	1	.	3	1	.
	Peritoneal haemorrhage		47	33	14	16	15	12	4
	Vomiting		3	3	.	.	.	3	.
General disorders and administration site conditions	Death		2	2	.	.	1	1	.
	Fatigue		3	3	.	.	3	.	.
	Pain		19	18	1	7	7	4	1
	Ulcer		1	1	.	.	.	1	.
Hepatobiliary disorders	Biliary tract disorder		1	1	.	.	1	.	.
	Cholecystitis		3	2	1	1	1	1	.
	Hepatic haematoma		1	1	.	.	1	.	.
	Hepatic haemorrhage		2	2	.	.	.	.	2
	Portal vein thrombosis		12	10	2	4	5	2	1
Immune system disorders	Graft versus host disease		2	2	.	.	.	.	2
	Hypersensitivity		3	3	.	.	1	2	.
Infections and infestations	Cytomegalovirus infection		1	1	.	.	.	.	1
	Gastroenteritis viral		1	1	.	1	.	.	.
	Infection		9	8	1	2	5	2	.
	Pneumonia		1	1	.	.	.	1	.
	Respiratory tract infection		1	1	.	.	.	1	.

**Exhibit 7-4A2 (continued)**  
**Adverse Events (AEs) RELATED TO PROCEDURE in Any Time Post Islet Transplantation**

			Transplant type		Era			
			Overall	ITA	IAK/SIK	1999-2002	2003-2006	2007-2010
			N	N	N	N	N	N
Injury, poisoning and procedural complications	Fracture		1	1	.	.	.	1
	Post procedural haemorrhage		1	1	.	.	.	1
	Transplant failure		1	1	.	.	.	1
	Wound complication		3	3	.	.	1	2
Investigations	Activated partial thromboplastin time		2	1	1	1	1	.
	Activated partial thromboplastin time prolonged		1	1	.	.	.	1
	Alanine aminotransferase increased		1	1	.	.	.	1
	Aspartate aminotransferase increased		3	3	.	.	.	3
	Blood alkaline phosphatase		21	19	2	5	14	2
	Blood amylase		1	1	.	.	1	.
	Blood bilirubin		1	1	.	1	.	.
	Blood creatinine increased		2	1	1	.	2	.
	Gamma-glutamyltransferase		10	9	1	6	3	1
	Gamma-glutamyltransferase increased		1	1	.	.	.	1
	Glomerular filtration rate		1	1	.	1	.	.
	Granulocytes abnormal		16	16	.	8	7	1
	Hepatic enzyme increased		4	4	.	.	.	2
	Lipase		4	1	3	1	3	.
	Liver function test abnormal		106	103	3	46	49	11
Metabolism and nutrition disorders	Low density lipoprotein increased		1	1	.	.	.	.
	Transaminases increased		1	1	.	.	.	1
	Dehydration		1	1	.	.	1	.
	Hyperglycaemia		6	.	6	.	.	6
	Hypoalbuminaemia		1	1	.	.	.	1
	Hypoglycaemia		8	6	2	3	2	3
	Hypokalaemia		1	1	.	.	1	.

**Exhibit 7-4A2 (continued)**  
**Adverse Events (AEs) RELATED TO PROCEDURE in Any Time Post Islet Transplantation**

			Transplant type		Era			
			Overall	ITA	IAK/SIK	1999-2002	2003-2006	2007-2010
			N	N	N	N	N	N
	<b>Hyponatraemia</b>		2	1	1	1	1	.
	<b>Ketoacidosis</b>		3	3	.	1	.	2
Musculoskeletal and connective tissue disorders	<b>Arthralgia</b>		1	1	.	.	.	1
	<b>Musculoskeletal pain</b>		2	2	.	.	.	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	<b>Neoplasm malignant</b>		1	1	.	.	1	.
Nervous system disorders	<b>Dyskinesia</b>		1	1	.	.	.	1
	<b>Syncope</b>		1	1	.	.	.	1
Renal and urinary disorders	<b>Proteinuria</b>		1	1	.	1	.	.
	<b>Renal disorder</b>		1	.	1	.	1	.
	<b>Renal failure</b>		1	1	.	.	1	.
	<b>Urinary bladder haemorrhage</b>		1	1	.	.	.	1
Respiratory, thoracic and mediastinal disorders	<b>Aspiration</b>		1	1	.	.	.	1
	<b>Haemothorax</b>		2	1	1	1	1	.
	<b>Lung disorder</b>		1	1	.	.	.	1
	<b>Pleural effusion</b>		1	.	1	.	1	.
Surgical and medical procedures	<b>Incisional hernia repair</b>		1	1	.	.	.	1
Vascular disorders	<b>Haematoma</b>		11	7	4	3	6	.
	<b>Haemorrhage</b>		11	7	4	1	4	3
	<b>Hypotension</b>		2	2	.	.	.	2
	<b>Thrombosis</b>		1	.	1	1	.	.

**Exhibit 7-4A3**  
**Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION Any Time Post Islet Transplantation**

System/Organ Class	Preferred term	Overall N	Transplant type			Era			
			ITA N	IAK/SIK N	1999-2002 N	2003-2006 N	2007-2010 N	2011-2014 N	
Blood and lymphatic system disorders	Agranulocytosis	1	.	1	.	1	.	.	.
	Anaemia	26	23	3	5	14	6	1	.
	Blood disorder	4	2	2	1	1	2	.	.
	Febrile neutropenia	4	4	.	.	.	4	.	.
	Haemolysis	1	1	.	.	1	.	.	.
	Leukopenia	12	7	5	.	.	3	9	.
	Lymphopenia	48	42	6	3	20	19	6	.
	Neutropenia	21	21	.	.	.	6	15	.
	Platelet disorder	3	3	.	1	2	.	.	.
	Thrombocytopenia	5	5	.	.	.	5	.	.
Cardiac disorders	Arrhythmia supraventricular	1	1	.	.	.	1	.	.
	Myocardial ischaemia	1	1	.	.	1	.	.	.
	Pericardial effusion	1	1	.	.	1	.	.	.
	Pericarditis	1	1	.	.	1	.	.	.
Ear and labyrinth disorders	Tinnitus	1	1	.	1	.	.	.	.
Eye disorders	Eye disorder	4	3	1	1	3	.	.	.
	Ocular surface disease	1	.	1	.	1	.	.	.
	Uveitis	1	.	1	.	.	1	.	.
	Vitreous haemorrhage	1	1	.	1	.	.	.	.
Gastrointestinal disorders	Ascites	2	2	.	1	1	.	.	.
	Barrett's oesophagus	1	1	.	.	1	.	.	.
	Colitis	5	4	1	.	4	1	.	.
	Constipation	1	1	.	.	.	1	.	.
	Diarrhoea	47	44	3	6	25	14	2	.
	Dysphagia	2	2	.	.	2	.	.	.
	Gastritis	2	1	1	1	1	.	.	.
	Gastrointestinal disorder	13	7	6	.	13	.	.	.
	Gastrointestinal obstruction	7	3	4	.	7	.	.	.
	Mouth ulceration	3	2	1	.	2	1	.	.
	Nausea	7	5	2	1	4	1	1	.
	Oral pain	1	1	.	.	.	1	.	.
	Peritoneal haemorrhage	5	2	3	5	.	.	.	.
	Stomatitis	1	1	.	.	.	1	.	.
	Vomiting	16	14	2	4	4	7	1	.

**Exhibit 7-4A3 (continued)**  
**Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION Any Time Post Islet Transplantation**

		Overall	Transplant type		Era			
			ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
			N	N	N	N	N	N
General disorders and administration site conditions	Chest pain	1	1	.	.	.	1	.
	Death	2	1	1	1	.	1	.
	Fatigue	13	13	.	1	10	2	.
	Injection site reaction	1	1	.	.	1	.	.
	Mucosal inflammation	16	13	3	3	11	2	.
	Oedema peripheral	4	3	1	2	1	1	.
	Pain	31	29	2	7	19	4	1
	Pyrexia	6	5	1	3	2	1	.
	Systemic inflammatory response syndrome	3	.	3	.	1	2	.
	Ulcer	1	1	.	.	.	1	.
Hepatobiliary disorders	Cholecystitis	1	1	.	1	.	.	.
Immune system disorders	Autoimmune disorder	1	1	.	.	.	1	.
	Graft versus host disease	2	2	.	.	.	.	2
	Hypersensitivity	10	8	2	1	4	4	1
	Serum sickness	1	1	.	.	.	1	.
Infections and infestations	Arthritis bacterial	1	1	.	.	1	.	.
	Cystitis	1	1	.	.	.	1	.
	Cytomegalovirus infection	1	1	.	.	1	.	.
	Gastrointestinal infection	1	1	.	.	.	.	1
	Infection	58	45	13	19	27	12	.
	Opportunistic infection	2	1	1	.	.	2	.
	Pneumonia	10	6	4	.	5	5	.
	Pyelonephritis	2	1	1	.	1	.	1
	Renal graft infection	1	.	1	.	.	.	1
	Respiratory tract infection	1	1	.	.	.	1	.
	Urinary tract infection	1	.	1	.	.	.	1
	Urosepsis	1	.	1	.	.	.	1
	Vestibular neuritis	1	1	.	.	.	1	.
	Viral encephalitis	1	1	.	1	.	.	.
Injury, poisoning and procedural complications	Fracture	3	3	.	2	.	1	.
	Injury	1	.	1	.	1	.	.
	Limb injury	1	1	.	.	.	1	.
	Toxicity to various agents	2	2	.	.	.	1	1
	Transplant failure	1	1	.	.	.	.	1
	Wound complication	4	3	1	3	1	.	.
Investigations	Activated partial thromboplastin time	1	1	.	1	.	.	.
	Blood alkaline phosphatase	5	3	2	2	2	1	.
	Blood creatine phosphokinase	1	1	.	.	1	.	.
	Blood creatinine increased	9	7	2	2	5	2	.

**Exhibit 7-4A3 (continued)**  
**Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION Any Time Post Islet Transplantation**

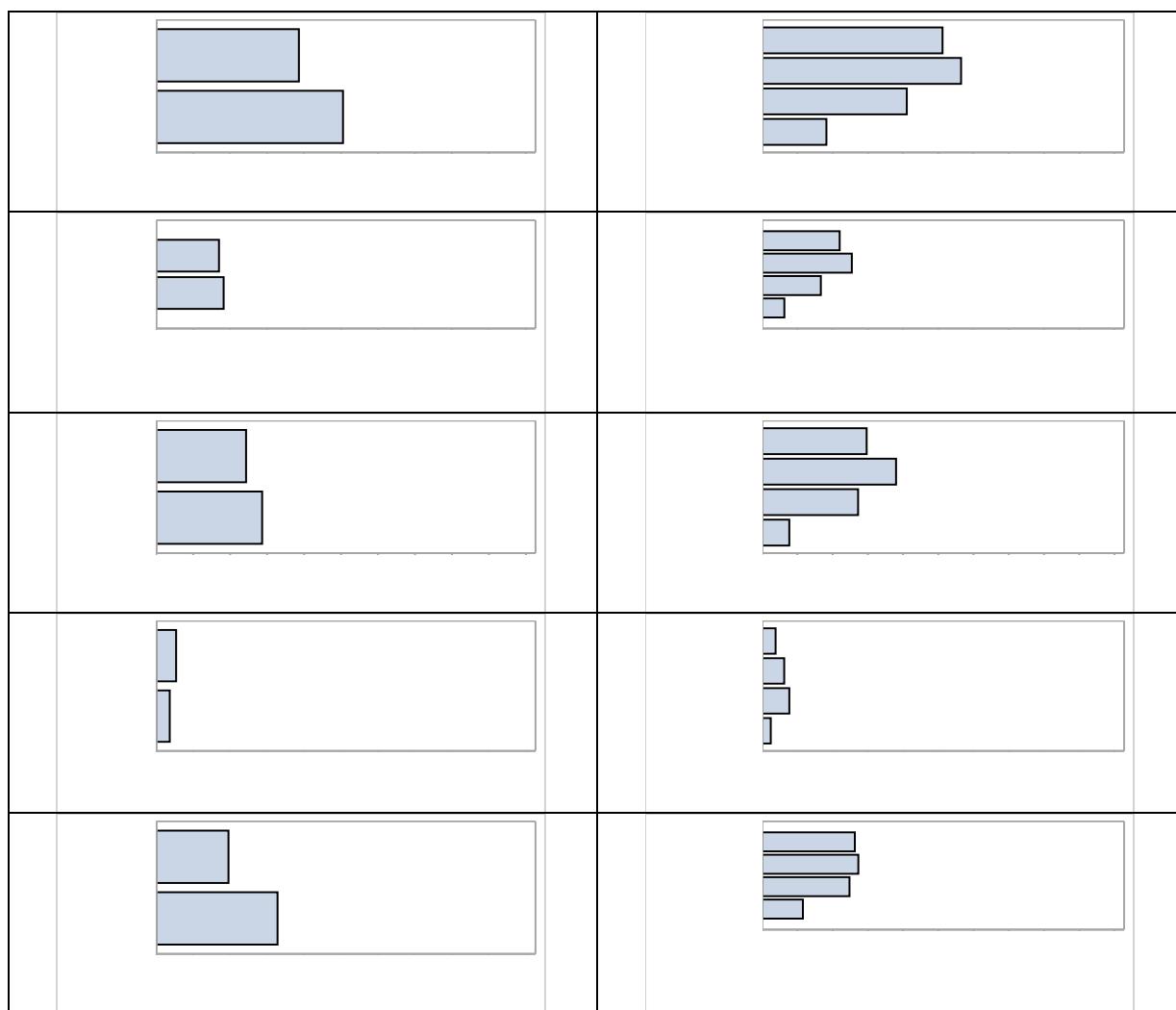
			Transplant type			Era			
			Overall N	ITA N	IAK/SIK N	1999-2002		2003-2006	
						N	N	N	N
	<b>Gamma-glutamyltransferase</b>		6	6	.	.	6	.	.
	<b>Glomerular filtration rate</b>		1	1	.	.	1	.	.
	<b>Granulocytes abnormal</b>		229	217	12	82	115	29	3
	<b>Haemoglobin decreased</b>		1	1	.	.	1	.	.
	<b>Lipase increased</b>		1	1	.	.	.	.	1
	<b>Liver function test abnormal</b>		33	30	3	19	9	5	.
	<b>Low density lipoprotein abnormal</b>		1	1	.	.	1	.	.
	<b>Low density lipoprotein increased</b>		6	6	.	.	1	.	5
	<b>Neutrophil count</b>		2	2	.	.	.	2	.
	<b>Neutrophil count decreased</b>		3	3	.	.	.	3	.
	<b>Weight decreased</b>		2	2	.	.	1	1	.
<b>Metabolism and nutrition disorders</b>	<b>Decreased appetite</b>		1	1	.	.	.	1	.
	<b>Dehydration</b>		6	4	2	1	1	3	1
	<b>Hyperglycaemia</b>		6	.	6	.	.	.	6
	<b>Hyperkalaemia</b>		10	10	.	6	3	.	1
	<b>Hypoglycaemia</b>		7	6	1	3	4	.	.
	<b>Hypokalaemia</b>		8	7	1	.	6	2	.
	<b>Hypomagnesaemia</b>		1	1	.	.	1	.	.
	<b>Hyponatraemia</b>		1	1	.	1	.	.	.
	<b>Hypophosphataemia</b>		6	6	.	1	5	.	.
	<b>Ketoacidosis</b>		2	1	1	1	1	.	.
	<b>Arthralgia</b>		1	1	.	.	.	.	1
	<b>Arthritis</b>		2	2	.	.	1	1	.
<b>Musculoskeletal and connective tissue disorders</b>	<b>Muscle necrosis</b>		1	1	.	.	1	.	.
	<b>Muscular weakness</b>		6	6	.	.	6	.	.
	<b>Musculoskeletal disorder</b>		3	3	.	1	2	.	.
	<b>Myositis</b>		1	1	.	.	1	.	.
	<b>Basal cell carcinoma</b>		4	4	.	.	2	2	.
	<b>Lobular breast carcinoma in situ</b>		1	1	.	.	1	.	.
<b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b>	<b>Metastases</b>		1	1	.	.	1	.	.
	<b>Neoplasm malignant</b>		27	17	10	15	11	1	.
	<b>Papillary thyroid cancer</b>		2	1	1	.	2	.	.
	<b>Squamous cell carcinoma</b>		7	3	4	.	6	1	.
	<b>Treatment related secondary malignancy</b>		1	1	.	.	1	.	.
	<b>Cognitive disorder</b>		1	1	.	1	.	.	.
	<b>Convulsion</b>		1	1	.	.	.	.	1
<b>Nervous system disorders</b>	<b>Dizziness</b>		2	2	.	.	2	.	.
	<b>Headache</b>		2	2	.	.	.	1	1

**Exhibit 7-4A3 (continued)**  
**Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION Any Time Post Islet Transplantation**

		Transplant type			Era			
		Overall N	ITA N	IAK/SIK N	1999-2002 N	2003-2006 N	2007-2010 N	2011-2014 N
Psychiatric disorders	<b>Syncope</b>	1	1	.	.	.	.	1
	<b>Tremor</b>	2	2	.	2	.	.	.
	<b>Confusional state</b>	1	1	.	.	.	1	.
	<b>Insomnia</b>	2	2	.	1	1	.	.
Renal and urinary disorders	<b>Mood altered</b>	2	2	.	1	1	.	.
	<b>Psychotic disorder</b>	1	1	.	1	.	.	.
	<b>Micturition urgency</b>	1	1	.	.	1	.	.
	<b>Peylonephritis</b>	1	1	.	.	.	.	1
Reproductive system and breast disorders	<b>Proteinuria</b>	5	4	1	1	4	.	.
	<b>Pyelonephritis</b>	1	.	1	.	1	.	.
	<b>Renal disorder</b>	3	2	1	2	1	.	.
	<b>Renal failure</b>	16	8	8	11	4	1	.
Respiratory, thoracic and mediastinal disorders	<b>Tubulointerstitial nephritis</b>	1	1	.	.	.	1	.
	<b>Urinary bladder haemorrhage</b>	3	2	1	.	2	1	.
	<b>Lactation disorder</b>	1	1	.	.	1	.	.
	<b>Ovarian cyst ruptured</b>	1	1	.	.	1	.	.
Skin and subcutaneous tissue disorders	<b>Sexual dysfunction</b>	4	4	.	2	2	.	.
	<b>Acute respiratory distress syndrome</b>	1	.	1	1	.	.	.
	<b>Aspiration</b>	1	1	.	.	.	1	.
	<b>Cough</b>	3	1	2	1	1	1	.
Surgical and medical procedures	<b>Dyspnoea</b>	2	2	.	.	2	.	.
	<b>Haemothorax</b>	1	1	.	1	.	.	.
	<b>Hypoxia</b>	1	1	.	.	.	1	.
	<b>Lung disorder</b>	6	4	2	1	3	2	.
Vascular disorders	<b>Lung infiltration</b>	4	4	.	.	.	4	.
	<b>Pleural effusion</b>	1	1	.	.	.	1	.
	<b>Pneumonitis</b>	5	3	2	3	2	.	.
	<b>Acute febrile neutrophilic dermatosis</b>	1	1	.	.	.	1	.
Surgical and medical procedures	<b>Exfoliative rash</b>	6	5	1	2	2	2	.
	<b>Pruritus</b>	1	1	.	.	.	1	.
	<b>Rash</b>	1	1	.	.	.	1	.
	<b>Skin disorder</b>	4	4	.	2	2	.	.
<b>Haematoma</b>	<b>Hysterectomy</b>	1	1	.	.	1	.	.
	<b>Surgery</b>	1	.	1	.	.	1	.
<b>Hypertension</b>	<b>Peripheral ischaemia</b>	1	.	1	.	1	.	.
	<b>Thrombosis</b>	1	1	.	1	.	.	.

**Exhibit 7-4B1**  
**Serious Adverse Events (SAEs) in Any Time Post Islet Transplantation**

Percent of Recipients with:	Type				Era							
	ITA		IAK/SIK		1999-2002		2003-2006		2007-2010		2011-2014	
	N	%	N	%	N	%	N	%	N	%	N	%
<b>Any SAE in ever</b>	316	38.6	97	50.5	107	51.2	153	56.5	101	41.1	52	18.2
<b>Any SAE related to infusion in ever</b>	139	17.0	35	18.2	46	22.0	69	25.5	41	16.7	18	6.3
<b>Any SAE related to IS in ever</b>	199	24.3	55	28.6	62	29.7	103	38.0	67	27.2	22	7.7
<b>Any SAE related to both in ever</b>	44	5.4	7	3.6	8	3.8	17	6.3	19	7.7	7	2.5
<b>Any SAE related to neither in ever</b>	160	19.5	63	32.8	55	26.3	74	27.3	61	24.8	33	11.6



**Exhibit 7-4B2**  
**Serious Adverse Events (SAEs) RELATED TO PROCEDURE in Any Time Post Islet Transplantation**

System/Organ Class	Preferred term	Overall N	Transplant type		Era			
			ITA N	IAK/SIK N	1999-2002 N	2003-2006 N	2007-2010 N	2011-2014 N
Blood and lymphatic system disorders	Anaemia	8	6	2	1	4	2	1
Cardiac disorders	Lymphopenia	2	1	1	1	1	.	.
	Neutropenia	4	4	.	.	.	.	4
	Arrhythmia supraventricular	1	1	.	.	.	1	.
Endocrine disorders	Myocardial ischaemia	1	1	.	.	1	.	.
Eye disorders	Endocrine disorder	1	1	.	.	.	1	.
Gastrointestinal disorders	Vitreous haemorrhage	1	1	.	.	.	1	.
General disorders and administration site conditions	Ascites	2	2	.	1	1	.	.
	Diarrhoea	3	3	.	.	1	1	1
	Gastrointestinal disorder	2	2	.	.	2	.	.
	Gastrointestinal haemorrhage	5	2	3	2	3	.	.
	Gastrointestinal obstruction	2	2	.	1	1	.	.
	Gastrointestinal perforation	2	2	.	1	.	1	.
	Ileus	2	2	.	1	1	.	.
	Nausea	2	2	.	.	1	1	.
	Peritoneal haemorrhage	41	30	11	13	14	10	4
	Vomiting	3	3	.	.	.	3	.
Hepatobiliary disorders	Death	2	2	.	.	1	1	.
	Pain	14	14	.	6	4	3	1
Immune system disorders	Biliary tract disorder	1	1	.	.	1	.	.
	Cholecystitis	3	2	1	1	1	1	.
	Hepatic haematoma	1	1	.	.	1	.	.
	Hepatic haemorrhage	2	2	.	.	.	.	2
	Portal vein thrombosis	11	9	2	4	5	2	.
	Graft versus host disease	2	2	.	.	.	.	2
Infections and infestations	Hypersensitivity	3	3	.	.	1	2	.
	Cytomegalovirus infection	1	1	.	.	.	.	1
	Infection	9	8	1	2	5	2	.
	Pneumonia	1	1	.	.	.	1	.
	Respiratory tract infection	1	1	.	.	.	1	.

**Exhibit 7-4B2 (continued)**  
**Serious Adverse Events (SAEs) RELATED TO PROCEDURE in Any Time Post Islet Transplantation**

			Transplant type			Era			
			Overall N	ITA N	IAK/SIK N	1999-2002 N	2003-2006 N	2007-2010 N	2011-2014 N
Injury, poisoning and procedural complications	Fracture		1	1	.	.	.	1	.
	Post procedural haemorrhage		1	1	.	.	.	1	.
	Transplant failure		1	1	.	.	.	.	1
	Wound complication		3	3	.	.	1	2	.
Investigations	Blood alkaline phosphatase		14	14	.	4	10	.	.
	Blood creatinine increased		2	1	1	.	2	.	.
	Granulocytes abnormal		2	2	.	.	2	.	.
	Hepatic enzyme increased		2	2	.	.	.	.	2
	Liver function test abnormal		36	36	.	19	17	.	.
	Low density lipoprotein increased		1	1	.	.	.	.	1
Metabolism and nutrition disorders	Dehydration		1	1	.	.	1	.	.
	Hyperglycaemia		6	.	6	.	.	.	6
	Hypoglycaemia		5	3	2	1	1	3	.
	Ketoacidosis		3	3	.	1	.	2	.
Musculoskeletal and connective tissue disorders	Arthralgia		1	1	.	.	.	.	1
	Musculoskeletal pain		2	2	.	.	.	.	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Neoplasm malignant								
			1	1	.	.	1	.	.
Nervous system disorders	Syncope		1	1	.	.	.	1	.
Renal and urinary disorders	Renal disorder		1	.	1	.	1	.	.
	Renal failure		1	1	.	.	1	.	.
	Urinary bladder haemorrhage		1	1	.	.	.	1	.
Respiratory, thoracic and mediastinal disorders	Aspiration		1	1	.	.	.	1	.
	Haemothorax		2	1	1	1	1	.	.
	Lung disorder		1	1	.	.	.	1	.
	Pleural effusion		1	.	1	.	1	.	.
Surgical and medical procedures	Incisional hernia repair		1	1	.	.	.	1	.
Vascular disorders	Haematoma		11	7	4	3	6	.	2
	Haemorrhage		11	7	4	1	4	3	3
	Hypotension		1	1	.	.	.	1	.
	Thrombosis		1	.	1	1	.	.	.

**Exhibit 7-4B3****Serious Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION Any Time Post Islet Transplantation**

		Overall N	Transplant type		Era			
System/Organ Class	Preferred term		ITA N	IAK/SIK N	1999-2002 N	2003-2006 N	2007-2010 N	2011-2014 N
Blood and lymphatic system disorders	<b>Agranulocytosis</b>	1	.	1	.	1	.	.
	<b>Anaemia</b>	16	13	3	4	7	4	1
	<b>Blood disorder</b>	1	1	.	.	.	1	.
	<b>Febrile neutropenia</b>	4	4	.	.	.	4	.
	<b>Haemolysis</b>	1	1	.	.	1	.	.
	<b>Leukopenia</b>	4	.	4	.	.	.	4
	<b>Lymphopenia</b>	11	8	3	1	7	2	1
	<b>Neutropenia</b>	15	15	.	.	.	2	13
	<b>Platelet disorder</b>	1	1	.	.	1	.	.
	<b>Thrombocytopenia</b>	5	5	.	.	.	5	.
Cardiac disorders	<b>Arrhythmia supraventricular</b>	1	1	.	.	.	1	.
	<b>Myocardial ischaemia</b>	1	1	.	.	1	.	.
	<b>Pericardial effusion</b>	1	1	.	.	1	.	.
	<b>Pericarditis</b>	1	1	.	.	1	.	.
Eye disorders	<b>Eye disorder</b>	2	2	.	.	2	.	.
	<b>Ocular surface disease</b>	1	.	1	.	1	.	.
	<b>Uveitis</b>	1	.	1	.	.	1	.
Gastrointestinal disorders	<b>Ascites</b>	2	2	.	1	1	.	.
	<b>Barrett's oesophagus</b>	1	1	.	.	1	.	.
	<b>Colitis</b>	5	4	1	.	4	1	.
	<b>Constipation</b>	1	1	.	.	.	1	.
	<b>Diarrhoea</b>	31	28	3	5	12	12	2
	<b>Dysphagia</b>	1	1	.	.	1	.	.
	<b>Gastritis</b>	1	.	1	1	.	.	.
	<b>Gastrointestinal disorder</b>	11	6	5	.	11	.	.
	<b>Gastrointestinal obstruction</b>	5	1	4	.	5	.	.
	<b>Mouth ulceration</b>	1	.	1	.	1	.	.
	<b>Nausea</b>	5	4	1	1	2	1	1
	<b>Peritoneal haemorrhage</b>	3	2	1	3	.	.	.
	<b>Vomiting</b>	14	12	2	3	3	7	1
General disorders and administration site conditions	<b>Chest pain</b>	1	1	.	.	.	1	.
	<b>Death</b>	2	1	1	1	.	1	.
	<b>Fatigue</b>	2	2	.	1	.	1	.
	<b>Mucosal inflammation</b>	9	8	1	2	6	1	.
	<b>Oedema peripheral</b>	2	1	1	.	1	1	.
	<b>Pain</b>	12	10	2	3	8	.	1

**Exhibit 7-4B3 (continued)**  
**Serious Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION Any Time Post Islet Transplantation**

				Transplant type		Era				
				Overall	ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
					N	N	N	N	N	N
		<b>Pyrexia</b>		5	4	1	3	1	1	.
		<b>Systemic inflammatory response syndrome</b>		3	.	3	.	1	2	.
<b>Hepatobiliary disorders</b>		<b>Cholecystitis</b>		1	1	.	1	.	.	.
<b>Immune system disorders</b>		<b>Autoimmune disorder</b>		1	1	.	.	.	1	.
		<b>Graft versus host disease</b>		2	2	.	.	.	.	2
		<b>Hypersensitivity</b>		9	7	2	1	3	4	1
		<b>Serum sickness</b>		1	1	.	.	.	1	.
<b>Infections and infestations</b>		<b>Arthritis bacterial</b>		1	1	.	.	1	.	.
		<b>Cytomegalovirus infection</b>		1	1	.	.	1	.	.
		<b>Gastrointestinal infection</b>		1	1	.	.	.	.	1
		<b>Infection</b>		51	39	12	19	23	9	.
		<b>Opportunistic infection</b>		2	1	1	.	.	2	.
		<b>Pneumonia</b>		10	6	4	.	5	5	.
		<b>Pyelonephritis</b>		2	1	1	.	1	.	1
		<b>Renal graft infection</b>		1	.	1	.	.	.	1
		<b>Respiratory tract infection</b>		1	1	.	.	.	1	.
		<b>Urinary tract infection</b>		1	.	1	.	.	.	1
		<b>Urosepsis</b>		1	.	1	.	.	.	1
		<b>Vestibular neuronitis</b>		1	1	.	.	.	1	.
		<b>Viral encephalitis</b>		1	1	.	1	.	.	.
<b>Injury, poisoning and procedural complications</b>		<b>Fracture</b>		3	3	.	2	.	1	.
		<b>Injury</b>		1	.	1	.	1	.	.
		<b>Limb injury</b>		1	1	.	.	.	1	.
		<b>Toxicity to various agents</b>		2	2	.	.	.	1	1
		<b>Transplant failure</b>		1	1	.	.	.	.	1
		<b>Wound complication</b>		4	3	1	3	1	.	.
<b>Investigations</b>		<b>Blood alkaline phosphatase</b>		1	1	.	1	.	.	.
		<b>Blood creatine phosphokinase</b>		1	1	.	.	1	.	.
		<b>Blood creatinine increased</b>		9	7	2	2	5	2	.
		<b>Granulocytes abnormal</b>		64	56	8	22	26	13	3
		<b>Haemoglobin decreased</b>		1	1	.	.	1	.	.
		<b>Liver function test abnormal</b>		3	3	.	1	2	.	.
		<b>Low density lipoprotein increased</b>		1	1	.	.	.	.	1
		<b>Neutrophil count</b>		1	1	.	.	.	1	.

**Exhibit 7-4B3 (continued)****Serious Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION Any Time Post Islet Transplantation**

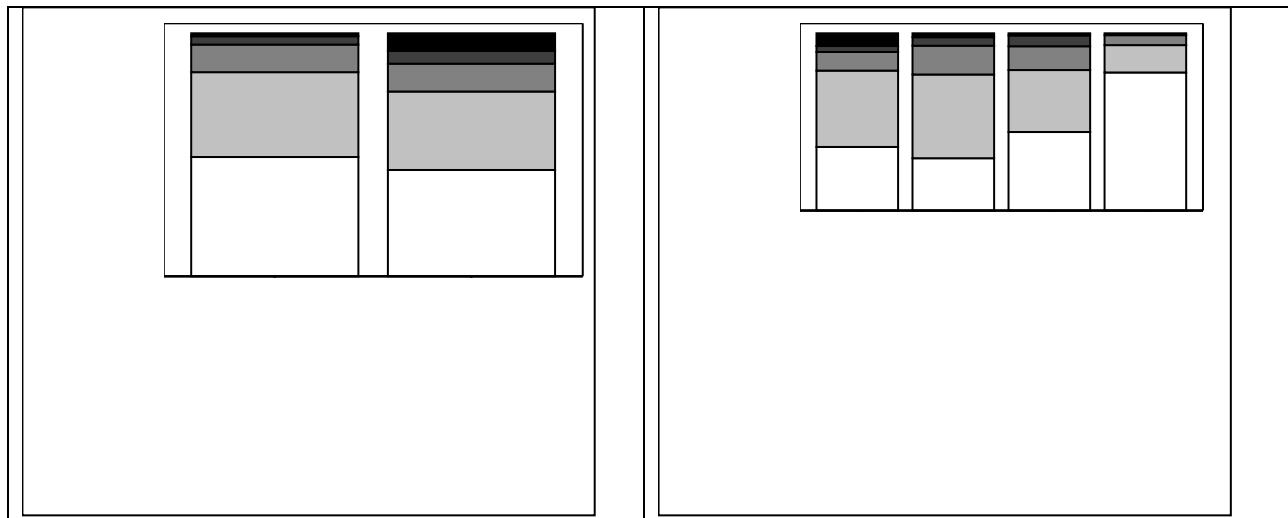
			Transplant type			Era			
			Overall	ITA	IAK/SIK	1999-2002	2003-2006	2007-2010	2011-2014
			N	N	N	N	N	N	N
Metabolism and nutrition disorders	Neutrophil count decreased		1	1	.	.	.	.	1
	Weight decreased		1	1	.	.	.	1	.
	Dehydration	5	4	1	1	.	.	3	1
	Hyperglycaemia	6	.	6	.	.	.	.	6
	Hypoglycaemia	3	2	1	1	2	.	.	.
	Hypokalaemia	1	1	.	.	1	.	.	.
	Hypomagnesaemia	1	1	.	.	1	.	.	.
Musculoskeletal and connective tissue disorders	Hypophosphataemia	1	1	.	.	1	.	.	.
	Ketoacidosis	2	1	1	1	1	.	.	.
	Arthralgia	1	1	.	.	.	.	.	1
	Arthritis	2	2	.	.	1	1	.	.
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Muscle necrosis	1	1	.	.	1	.	.	.
	Musculoskeletal disorder	3	3	.	.	1	2	.	.
	Lobular breast carcinoma in situ	1	1	.	.	1	.	.	.
	Metastases	1	1	.	.	1	.	.	.
	Neoplasm malignant	17	12	5	8	8	1	.	.
Nervous system disorders	Papillary thyroid cancer	2	1	1	.	2	.	.	.
	Squamous cell carcinoma	2	.	2	.	2	.	.	.
	Treatment related secondary malignancy	1	1	.	.	1	.	.	.
	Cognitive disorder	1	1	.	1	.	.	.	.
	Convulsion	1	1	.	.	.	.	.	1
Psychiatric disorders	Headache	2	2	.	.	.	.	1	1
	Syncope	1	1	.	.	.	.	1	.
	Tremor	1	1	.	1	.	.	.	.
	Confusional state	1	1	.	.	.	.	1	.
Renal and urinary disorders	Insomnia	1	1	.	1	.	.	.	.
	Mood altered	2	2	.	1	1	.	.	.
	Psychotic disorder	1	1	.	1	.	.	.	.
	Peylonephritis	1	1	.	.	.	.	.	1
	Proteinuria	2	1	1	.	2	.	.	.
	Pyelonephritis	1	.	1	.	1	.	.	.
Reproductive system and breast disorders	Renal disorder	3	2	1	2	1	.	.	.
	Renal failure	15	7	8	10	4	1	.	.
	Tubulointerstitial nephritis	1	1	.	.	.	.	1	.
	Urinary bladder haemorrhage	2	1	1	.	1	1	.	.
	Lactation disorder	1	1	.	.	1	.	.	.
	Ovarian cyst ruptured	1	1	.	.	1	.	.	.

**Exhibit 7-4B3 (continued)****Serious Adverse Events (AEs) RELATED TO IMMUNOSUPPRESSION Any Time Post Islet Transplantation**

			Transplant type		Era			
			Overall	ITA	IAK/SIK	1999-2002	2003-2006	2007-2010
			N	N	N	N	N	N
	<b>Sexual dysfunction</b>		4	4	.	2	2	.
<b>Respiratory, thoracic and mediastinal disorders</b>	<b>Acute respiratory distress syndrome</b>		1	.	1	1	.	.
	<b>Aspiration</b>		1	1	.	.	.	1
	<b>Cough</b>		2	.	2	1	1	.
	<b>Dyspnoea</b>		1	1	.	.	1	.
	<b>Haemothorax</b>		1	1	.	1	.	.
	<b>Lung disorder</b>		6	4	2	1	3	2
	<b>Lung infiltration</b>		4	4	.	.	.	4
	<b>Pleural effusion</b>		1	1	.	.	.	1
	<b>Pneumonitis</b>		3	1	2	3	.	.
<b>Skin and subcutaneous tissue disorders</b>	<b>Acute febrile neutrophilic dermatosis</b>		1	1	.	.	.	1
	<b>Exfoliative rash</b>		1	1	.	.	.	1
	<b>Rash</b>		1	1	.	.	.	1
<b>Surgical and medical procedures</b>	<b>Hysterectomy</b>		1	1	.	.	1	.
	<b>Surgery</b>		1	.	1	.	.	1
<b>Vascular disorders</b>	<b>Haematoma</b>		1	.	1	1	.	.
	<b>Hypertension</b>		1	1	.	1	.	.
	<b>Peripheral ischaemia</b>		1	.	1	.	1	.

**Exhibit 7-5**  
**Worst Outcome of Adverse Events (per Recipient)**

			Transplant type				Era							
			ITA		IAK/SIK		1999-2002		2003-2006		2007-2010		2011-2014	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
<b>Total</b>	1011	100.0	819	100.0	192	100.0	209	100.0	271	100.0	246	100.0	285	100.0
<b>No AE</b>	486	48.1	402	49.1	84	43.8	75	35.9	80	29.5	109	44.3	222	77.9
<b>Recovered</b>	348	34.4	286	34.9	62	32.3	90	43.1	128	47.2	86	35.0	44	15.4
<b>Sequelae</b>	115	11.4	93	11.4	22	11.5	22	10.5	44	16.2	33	13.4	16	5.6
<b>Disability</b>	38	3.8	28	3.4	10	5.2	7	3.3	13	4.8	15	6.1	3	1.1
<b>Death</b>	24	2.4	10	1.2	14	7.3	15	7.2	6	2.2	3	1.2	.	.



**Exhibit 7-6**  
**ALL Adverse Events Following Islet Transplant In order by Frequency, with Final Outcome**

		Outcome					
		Total	0-Unknown	1-Recover	2-Sequela	3-Disabil	4-Death
		N	%	%	%	%	%
	<b>Total adverse events following islet transplantation</b>	2,074	1.4	83.3	11.7	2.5	1.2

Order by frequency	Adverse event	Total events	Outcome					
			N	0-Unknown Row %	1-Recovered Row %	2-Sequelae Row %	3-Disability Row %	4-Death Row %
1	<b>Granulocytes abnormal</b>	244	.	94.7	4.9	0.4	.	.
2	<b>Hypoglycaemia</b>	135	3.0	94.1	2.2	0.7	.	.
3	<b>Liver function test abnormal</b>	125	0.8	96.0	3.2	.	.	.
4	<b>Ketoacidosis</b>	100	.	98.0	2.0	.	.	.
5	<b>Infection</b>	99	.	78.8	15.2	4.0	2.0	.
6	<b>Pain</b>	72	.	80.6	19.4	.	.	.
7	<b>Lymphopenia</b>	61	1.6	90.2	8.2	.	.	.
8	<b>Diarrhoea</b>	57	.	77.2	19.3	3.5	.	.
9	<b>Peritoneal haemorrhage</b>	48	.	91.7	8.3	.	.	.
10	<b>Anaemia</b>	40	.	97.5	.	2.5	.	.
11	<b>Vomiting</b>	37	.	86.5	13.5	.	.	.
12	<b>Neutropenia</b>	33	.	72.7	27.3	.	.	.
13	<b>Neoplasm malignant</b>	29	3.4	72.4	20.7	3.4	.	.
14	<b>Hypersensitivity</b>	25	4.0	52.0	40.0	.	4.0	.
15	<b>Hyponatraemia</b>	25	.	92.0	8.0	.	.	.
16	<b>Blood alkaline phosphatase</b>	21	.	90.5	9.5	.	.	.
17	<b>Gastrointestinal disorder</b>	20	.	95.0	5.0	.	.	.
18	<b>Renal failure</b>	20	.	60.0	25.0	15.0	.	.
19	<b>Blood creatinine increased</b>	19	.	68.4	31.6	.	.	.
20	<b>Myocardial ischaemia</b>	18	5.6	61.1	22.2	11.1	.	.
21	<b>Neutrophil count decreased</b>	18	.	100.0	.	.	.	.
22	<b>Hypokalaemia</b>	17	.	94.1	.	5.9	.	.
23	<b>Hypophosphataemia</b>	17	.	100.0	.	.	.	.
24	<b>Mucosal inflammation</b>	17	.	82.4	11.8	5.9	.	.
25	<b>Fatigue</b>	15	.	93.3	.	6.7	.	.
26	<b>Hyperkalaemia</b>	15	.	86.7	13.3	.	.	.
27	<b>Death</b>	14	7.1	.	.	.	92.9	.
28	<b>Haemorrhage</b>	14	.	85.7	7.1	.	7.1	.
29	<b>Hyperglycaemia</b>	14	.	57.1	28.6	14.3	.	.
30	<b>Cholecystitis</b>	13	.	92.3	.	7.7	.	.
31	<b>Eye disorder</b>	13	.	61.5	7.7	30.8	.	.
32	<b>Gamma-glutamyltransferase</b>	13	.	84.6	15.4	.	.	.
33	<b>Haematoma</b>	13	.	84.6	15.4	.	.	.

**Exhibit 7-6 (continued)**  
**ALL Adverse Events Following Islet Transplant In order by Frequency, with Final Outcome**

		Total events	Outcome				
			0-Unknown	1-Recovered	2-Sequelae	3-Disability	4-Death
N	Row %	Row %	Row %	Row %	Row %	Row %	Row %
34	Hypertension	13	.	69.2	30.8	.	.
35	Low density lipoprotein increased	13	7.7	69.2	23.1	.	.
36	Pneumonia	13	7.7	61.5	23.1	7.7	.
37	Portal vein thrombosis	13	.	84.6	7.7	7.7	.
38	Dehydration	12	.	91.7	8.3	.	.
39	Fracture	12	.	58.3	41.7	.	.
40	Leukopenia	12	.	83.3	16.7	.	.
41	Wound complication	12	.	100.0	.	.	.
42	Nausea	11	.	90.9	9.1	.	.
43	Syncope	11	.	90.9	.	9.1	.
44	Gastrointestinal obstruction	10	.	60.0	40.0	.	.
45	Squamous cell carcinoma	10	30.0	70.0	.	.	.
46	Alanine aminotransferase increased	9	.	100.0	.	.	.
47	Lung disorder	9	.	77.8	22.2	.	.
48	Pneumonitis	9	.	88.9	.	.	11.1
49	Colitis	8	.	75.0	25.0	.	.
50	Muscular weakness	8	.	62.5	37.5	.	.
51	Sexual dysfunction	8	.	100.0	.	.	.
52	Surgery	8	.	62.5	12.5	25.0	.
53	Aspartate aminotransferase increased	7	.	100.0	.	.	.
54	Cerebral ischaemia	7	14.3	14.3	42.9	14.3	14.3
55	Exfoliative rash	7	.	85.7	14.3	.	.
56	Oedema peripheral	7	.	100.0	.	.	.
57	Pyrexia	7	.	100.0	.	.	.
58	Renal disorder	7	.	85.7	.	14.3	.
59	Vitreous haemorrhage	7	.	42.9	28.6	28.6	.
60	Basal cell carcinoma	6	33.3	50.0	16.7	.	.
61	Blood disorder	6	.	100.0	.	.	.
62	Chest pain	6	.	66.7	33.3	.	.
63	Dyspnoea	6	.	83.3	.	16.7	.
64	Febrile neutropenia	6	.	83.3	16.7	.	.
65	Low density lipoprotein abnormal	6	.	66.7	33.3	.	.
66	Neutrophil count	6	.	100.0	.	.	.
67	Ascites	5	.	100.0	.	.	.
68	Dizziness	5	.	100.0	.	.	.
69	Gastrointestinal haemorrhage	5	.	100.0	.	.	.
70	Lipase	5	.	100.0	.	.	.
71	Musculoskeletal disorder	5	.	60.0	20.0	20.0	.
72	Proteinuria	5	.	20.0	80.0	.	.
73	Skin disorder	5	20.0	80.0	.	.	.
74	Thrombocytopenia	5	.	20.0	80.0	.	.

**Exhibit 7-6 (continued)**  
**ALL Adverse Events Following Islet Transplant In order by Frequency, with Final Outcome**

		Total events N	Outcome				
			0-Unknown Row %	1-Recovered Row %	2-Sequelae Row %	3-Disability Row %	4-Death Row %
75	<b>Urinary bladder haemorrhage</b>	5	.	80.0	20.0	.	.
76	<b>Appendicitis</b>	4	.	50.0	50.0	.	.
77	<b>Cognitive disorder</b>	4	.	75.0	.	25.0	.
78	<b>Confusional state</b>	4	25.0	50.0	25.0	.	.
79	<b>Endocrine disorder</b>	4	.	100.0	.	.	.
80	<b>Headache</b>	4	.	100.0	.	.	.
81	<b>Hepatic enzyme increased</b>	4	.	100.0	.	.	.
82	<b>Hip fracture</b>	4	.	75.0	25.0	.	.
83	<b>Hypoalbuminaemia</b>	4	.	100.0	.	.	.
84	<b>Hypotension</b>	4	.	75.0	25.0	.	.
85	<b>Hypoxia</b>	4	.	100.0	.	.	.
86	<b>Lung infiltration</b>	4	.	25.0	75.0	.	.
87	<b>Mood altered</b>	4	.	25.0	75.0	.	.
88	<b>Pericardial effusion</b>	4	.	100.0	.	.	.
89	<b>Peripheral ischaemia</b>	4	.	50.0	50.0	.	.
90	<b>Platelet disorder</b>	4	.	100.0	.	.	.
91	<b>Pleural effusion</b>	4	.	75.0	25.0	.	.
92	<b>Post transplant lymphoproliferative disorder</b>	4	.	25.0	75.0	.	.
93	<b>Retinal detachment</b>	4	.	50.0	25.0	25.0	.
94	<b>Thrombosis</b>	4	.	75.0	25.0	.	.
95	<b>Transaminases</b>	4	.	100.0	.	.	.
96	<b>Albuminuria</b>	3	.	33.3	66.7	.	.
97	<b>Anxiety</b>	3	.	33.3	33.3	33.3	.
98	<b>Arrhythmia supraventricular</b>	3	.	100.0	.	.	.
99	<b>Arthritis</b>	3	.	.	.	100.0	.
100	<b>Cough</b>	3	.	100.0	.	.	.
101	<b>Gamma-glutamyltransferase increased</b>	3	.	100.0	.	.	.
102	<b>Hepatic haematoma</b>	3	.	66.7	33.3	.	.
103	<b>Hepatic haemorrhage</b>	3	.	100.0	.	.	.
104	<b>Mouth ulceration</b>	3	.	100.0	.	.	.
105	<b>Pancreatitis</b>	3	.	66.7	33.3	.	.
106	<b>Pulmonary hypertension</b>	3	33.3	33.3	33.3	.	.
107	<b>Pyelonephritis</b>	3	.	33.3	66.7	.	.
108	<b>Systemic inflammatory response syndrome</b>	3	.	100.0	.	.	.
109	<b>Transaminases increased</b>	3	.	100.0	.	.	.
110	<b>Tremor</b>	3	.	100.0	.	.	.
111	<b>Weight decreased</b>	3	.	100.0	.	.	.
112	<b>Abdominal hernia repair</b>	2	.	50.0	50.0	.	.
113	<b>Activated partial thromboplastin time</b>	2	.	100.0	.	.	.

**Exhibit 7-6 (continued)**  
**ALL Adverse Events Following Islet Transplant In order by Frequency, with Final Outcome**

		Total events N	Outcome				
			0-Unknown Row %	1-Recovered Row %	2-Sequelae Row %	3-Disability Row %	4-Death Row %
114	<b>Acute respiratory distress syndrome</b>	2	.	.	.	.	100.0
115	<b>Appendicitis perforated</b>	2	.	100.0	.	.	.
116	<b>Aspiration</b>	2	.	100.0	.	.	.
117	<b>Ataxia</b>	2	.	100.0	.	.	.
118	<b>Bacillus infection</b>	2	.	100.0	.	.	.
119	<b>Blood amylase</b>	2	.	100.0	.	.	.
120	<b>Blood creatine phosphokinase increased</b>	2	.	50.0	50.0	.	.
121	<b>Blood phosphorus decreased</b>	2	.	100.0	.	.	.
122	<b>Cardiac disorder</b>	2	.	100.0	.	.	.
123	<b>Cardio-respiratory arrest</b>	2	.	50.0	.	.	50.0
124	<b>Chest discomfort</b>	2	.	50.0	50.0	.	.
125	<b>Constipation</b>	2	.	50.0	.	50.0	.
126	<b>Cystitis</b>	2	.	100.0	.	.	.
127	<b>Cytomegalovirus infection</b>	2	.	100.0	.	.	.
128	<b>Decreased appetite</b>	2	.	100.0	.	.	.
129	<b>Decubitus ulcer</b>	2	.	.	100.0	.	.
130	<b>Dysphagia</b>	2	.	50.0	50.0	.	.
131	<b>Gastritis</b>	2	.	100.0	.	.	.
132	<b>Gastroenteritis viral</b>	2	50.0	50.0	.	.	.
133	<b>Gastrointestinal perforation</b>	2	.	100.0	.	.	.
134	<b>Glomerular filtration rate</b>	2	.	50.0	50.0	.	.
135	<b>Graft versus host disease</b>	2	.	.	100.0	.	.
136	<b>Haemoglobin decreased</b>	2	.	100.0	.	.	.
137	<b>Haemothorax</b>	2	.	100.0	.	.	.
138	<b>Hypocalcaemia</b>	2	.	100.0	.	.	.
139	<b>Ileus</b>	2	.	100.0	.	.	.
140	<b>Incisional hernia repair</b>	2	50.0	50.0	.	.	.
141	<b>Injury</b>	2	.	50.0	50.0	.	.
142	<b>Insomnia</b>	2	.	50.0	50.0	.	.
143	<b>Migraine</b>	2	.	100.0	.	.	.
144	<b>Musculoskeletal pain</b>	2	.	50.0	50.0	.	.
145	<b>Myocarditis</b>	2	.	100.0	.	.	.
146	<b>Opportunistic infection</b>	2	.	100.0	.	.	.
147	<b>Papillary thyroid cancer</b>	2	.	50.0	.	50.0	.
148	<b>Psychogenic seizure</b>	2	.	50.0	50.0	.	.
149	<b>Serum sickness</b>	2	.	50.0	50.0	.	.
150	<b>Spinal cord compression</b>	2	50.0	50.0	.	.	.
151	<b>Toxicity to various agents</b>	2	.	100.0	.	.	.
152	<b>Urinary tract infection</b>	2	.	50.0	50.0	.	.
153	<b>Abdominal pain</b>	1	.	100.0	.	.	.
154	<b>Acne</b>	1	.	100.0	.	.	.

**Exhibit 7-6 (continued)**  
**ALL Adverse Events Following Islet Transplant In order by Frequency, with Final Outcome**

		Total events N	Outcome				
			0-Unknown Row %	1-Recovered Row %	2-Sequelae Row %	3-Disability Row %	4-Death Row %
155	Activated partial thromboplastin time prolonged	1	.	100.0	.	.	.
156	Acute febrile neutrophilic dermatosis	1	.	.	.	100.0	.
157	Acute myocardial infarction	1	.	.	.	.	100.0
158	Agranulocytosis	1	.	100.0	.	.	.
159	Alcoholism	1	.	100.0	.	.	.
160	Arthralgia	1	.	100.0	.	.	.
161	Arthritis bacterial	1	.	.	.	100.0	.
162	Arthropathy	1	.	100.0	.	.	.
163	Atrioventricular block	1	.	.	100.0	.	.
164	Autoimmune disorder	1	.	100.0	.	.	.
165	Bacillus test positive	1	.	100.0	.	.	.
166	Back pain	1	.	100.0	.	.	.
167	Barrett's oesophagus	1	.	100.0	.	.	.
168	Biliary tract disorder	1	.	100.0	.	.	.
169	Blood albumin decreased	1	.	100.0	.	.	.
170	Blood bilirubin	1	.	100.0	.	.	.
171	Blood creatine phosphokinase	1	.	100.0	.	.	.
172	Blood potassium increased	1	.	100.0	.	.	.
173	Breast reconstruction	1	.	100.0	.	.	.
174	Cerebellar ischaemia	1	.	.	100.0	.	.
175	Cholecystitis acute	1	.	100.0	.	.	.
176	Clostridium difficile colitis	1	.	100.0	.	.	.
177	Convulsion	1	.	.	100.0	.	.
178	Cytokine release syndrome	1	.	100.0	.	.	.
179	Dermatitis	1	.	100.0	.	.	.
180	Dyskinesia	1	.	100.0	.	.	.
181	Ear infection	1	.	.	100.0	.	.
182	Enteritis	1	.	100.0	.	.	.
183	Enterocolitis infectious	1	.	100.0	.	.	.
184	Frontotemporal dementia	1	.	100.0	.	.	.
185	Gastrointestinal infection	1	.	100.0	.	.	.
186	H1N1 influenza	1	100.0	.	.	.	.
187	Haemoglobinuria	1	.	100.0	.	.	.
188	Haemolysis	1	.	100.0	.	.	.
189	Haemorrhoids	1	.	100.0	.	.	.
190	Hearing impaired	1	.	.	100.0	.	.
191	Hepatic artery stenosis	1	.	.	.	100.0	.
192	Herpes simplex	1	.	100.0	.	.	.
193	Hypereosinophilia	1	.	100.0	.	.	.
194	Hypernatraemia	1	.	100.0	.	.	.
195	Hypoglycaemic seizure	1	.	100.0	.	.	.

**Exhibit 7-6 (continued)**  
**ALL Adverse Events Following Islet Transplant In order by Frequency, with Final Outcome**

		Total events N	Outcome				
			0-Unknown Row %	1-Recovered Row %	2-Sequelae Row %	3-Disability Row %	4-Death Row %
196	Hypomagnesaemia	1	.	100.0	.	.	.
197	Hypothyroidism	1	100.0	.	.	.	.
198	Hysterectomy	1	.	100.0	.	.	.
199	Ileostomy	1	.	100.0	.	.	.
200	Influenza like illness	1	.	100.0	.	.	.
201	Injection site reaction	1	.	100.0	.	.	.
202	International normalised ratio increased	1	.	100.0	.	.	.
203	Joint range of motion decreased	1	.	100.0	.	.	.
204	Laceration	1	.	100.0	.	.	.
205	Lactation disorder	1	.	100.0	.	.	.
206	Laryngitis	1	.	100.0	.	.	.
207	Laser therapy	1	.	100.0	.	.	.
208	Leukocytosis	1	.	100.0	.	.	.
209	Limb injury	1	.	.	.	.	100.0
210	Lipase increased	1	.	100.0	.	.	.
211	Lobular breast carcinoma in situ	1	.	100.0	.	.	.
212	Lymphatic disorder	1	.	100.0	.	.	.
213	Lymphoma	1	.	100.0	.	.	.
214	Metapneumovirus infection	1	.	.	.	.	100.0
215	Metastases	1	.	100.0	.	.	.
216	Micturition urgency	1	.	100.0	.	.	.
217	Muscle necrosis	1	.	100.0	.	.	.
218	Myositis	1	.	100.0	.	.	.
219	Nephrectomy	1	.	100.0	.	.	.
220	Ocular surface disease	1	.	100.0	.	.	.
221	Oral pain	1	.	100.0	.	.	.
222	Ovarian cyst ruptured	1	.	.	.	100.0	.
223	Pericarditis	1	.	100.0	.	.	.
224	Peripheral arterial occlusive disease	1	.	100.0	.	.	.
225	Peyloneprhitis	1	.	.	.	100.0	.
226	Pneumococcal infection	1	100.0	.	.	.	.
227	Post procedural haemorrhage	1	.	.	.	100.0	.
228	Presyncope	1	.	100.0	.	.	.
229	Pruritus	1	.	.	.	100.0	.
230	Psychotic disorder	1	.	100.0	.	.	.
231	Pulmonary oedema	1	100.0	.	.	.	.
232	Pulmonary tuberculosis	1	.	100.0	.	.	.
233	Rash	1	.	100.0	.	.	.
234	Renal failure acute	1	.	.	.	.	100.0
235	Renal graft infection	1	.	100.0	.	.	.
236	Respiratory tract infection	1	.	100.0	.	.	.

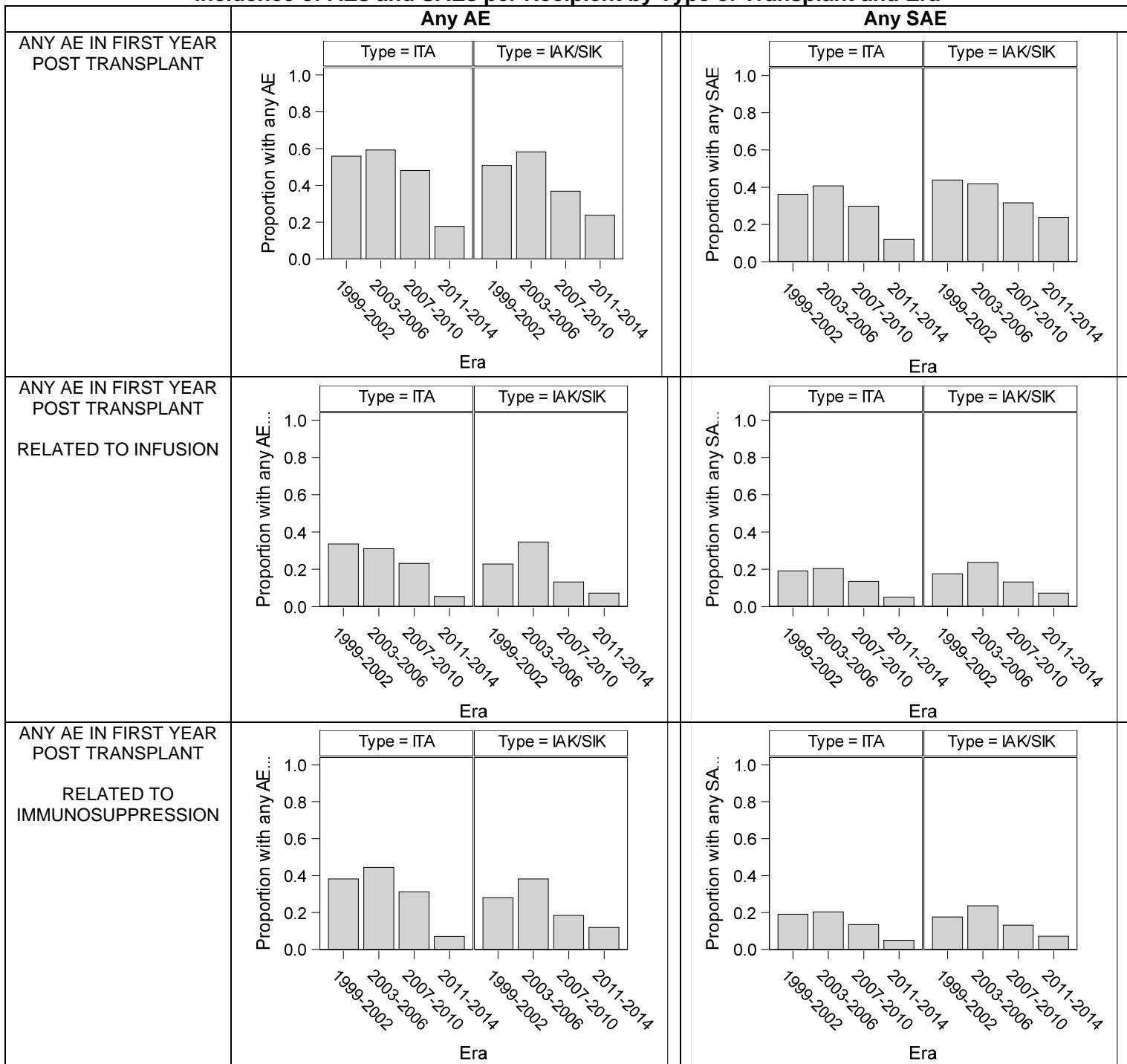
**Exhibit 7-6 (continued)**  
**ALL Adverse Events Following Islet Transplant In order by Frequency, with Final Outcome**

		Total events N	Outcome				
			0-Unknown Row %	1-Recovered Row %	2-Sequelae Row %	3-Disability Row %	4-Death Row %
237	Rheumatoid arthritis	1	.	100.0	.	.	.
238	Salmonellosis	1	.	100.0	.	.	.
239	Sensitisation	1	.	.	100.0	.	.
240	Serotonin syndrome	1	.	.	.	100.0	.
241	Skin cancer	1	100.0	.	.	.	.
242	Small intestinal obstruction	1	.	100.0	.	.	.
243	Stomatitis	1	.	100.0	.	.	.
244	Tinnitus	1	.	.	100.0	.	.
245	Toe operation	1	.	100.0	.	.	.
246	Transplant failure	1	.	100.0	.	.	.
247	Treatment related secondary malignancy	1	.	100.0	.	.	.
248	Trigger finger	1	.	.	100.0	.	.
249	Troponin I	1	.	100.0	.	.	.
250	Troponin T	1	.	100.0	.	.	.
251	Tubulointerstitial nephritis	1	.	100.0	.	.	.
252	Ulcer	1	.	100.0	.	.	.
253	Upper limb fracture	1	.	100.0	.	.	.
254	Urosepsis	1	.	100.0	.	.	.
255	Uveitis	1	.	100.0	.	.	.
256	Vestibular neuritis	1	.	.	.	100.0	.
257	Viral encephalitis	1	.	100.0	.	.	.
258	Wound dehiscence	1	.	100.0	.	.	.

**Exhibit 7-7**  
**SAE Criteria**

	Transplant type				Era							
	ITA		IAK/SIK		1999-2002		2003-2006		2007-2010		2011-2014	
	N	%	N	%	N	%	N	%	N	%	N	%
<b>Total Recipients</b>	819	100.0	192	100.0	209	100.0	271	100.0	246	100.0	285	100.0
<b>Death</b>	10	1.2	14	7.3	15	7.2	6	2.2	3	1.2	.	.
<b>Life Threatening</b>	115	14.0	40	20.8	50	23.9	76	28.0	19	7.7	10	3.5
<b>Hospitalization</b>	244	29.8	85	44.3	96	45.9	133	49.1	74	30.1	26	9.1
<b>Congenital abnormality</b>	2	0.2	1	0.5	1	0.5	1	0.4	.	.	1	0.4
<b>Long term disability</b>	28	3.4	13	6.8	9	4.3	13	4.8	16	6.5	3	1.1
<b>PI Indicated Serious</b>	75	9.2	21	10.9	19	9.1	42	15.5	29	11.8	6	2.1

**Exhibit 7-8**  
**Incidence of AEs and SAEs per Recipient by Type of Transplant and Era**



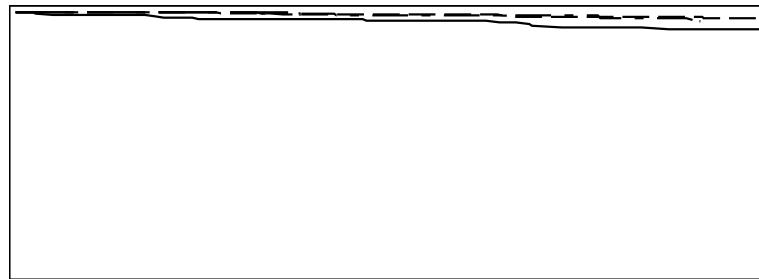
**Exhibit 7-9**  
**Neoplasms Reported Post First Islet Transplantation**

	N	Mean	Std
Total years of follow-up	960	7.7	6.4

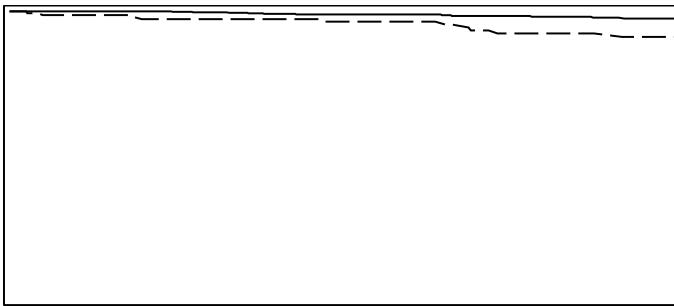
All Neoplasms	Relatedness to Immunosuppression	Outcome								
		Related				Not recovered				
		Total	Unk	Not related	Possibly related	Related	Unk	Recovered	Recovered with seq	Recovering
TOTAL EVENTS	46	4.3	8.7	80.4	6.5	4.3	15.2	69.6	6.5	4.3
Type Pending	6	.	.	100	.	.	16.7	50.0	16.7	16.7
Basal Cell Carcinoma	10	20.0	.	60.0	20.0	20.0	.	70.0	10.0	.
Ductal Carcinoma	2	.	50.0	50.0	.	.	50.0	50.0	.	.
Lung Carcinoma	1	.	.	100	.	.	100	.	.	.
Metastasis	1	.	.	100	.	.	.	100	.	.
Ovarian Cyst	5	.	.	100	.	.	.	100	.	.
Papillary	4	.	.	100	.	.	.	75.0	.	25.0
Post Transplant Lymphoproliferative Disorder	3	.	100	.	.	.	100	.	.	.
Pulmonary Nodules	1	.	.	100	.	.	100	.	.	.
Squamous Cell	13	.	.	92.3	7.7	.	.	92.3	7.7	.

First neoplasm in patient	Related to Immunosuppression	Outcome								
		Related				Not recovered				
		Total	Unk	Not related	Possibly related	Related	Unk	Recovered	Recovered with seq	Recovering
Total first events	35	5.7	5.7	85.7	2.9	5.7	11.4	77.1	2.9	2.9
Classification pending	3	.	.	100	.	.	.	100	.	.
Basal Cell Carcinoma	9	22.2	.	66.7	11.1	22.2	.	77.8	.	.
Ductal Carcinoma	2	.	50.0	50.0	.	.	50.0	50.0	.	.
Lung Carcinoma	1	.	.	100	.	.	100	.	.	.
Ovarian Cyst	5	.	.	100	.	.	.	100	.	.
Papillary	3	.	.	100	.	.	.	66.7	.	33.3
Post Transplant Lymphoproliferative Disorder	1	.	100	.	.	.	100	.	.	.
Pulmonary Nodules	1	.	.	100	.	.	100	.	.	.
Squamous Cell	10	.	.	100	.	.	.	90.0	10.0	.

**Exhibit 7-10A**  
**Deaths (By Era and Transplant Type)**



	<i>Era</i>			
	1999-2002	2003-2006	2007-2010	2011-2014
<i>N</i>	209	271	246	285
%	7.1%	3.0%	2%	0.3%



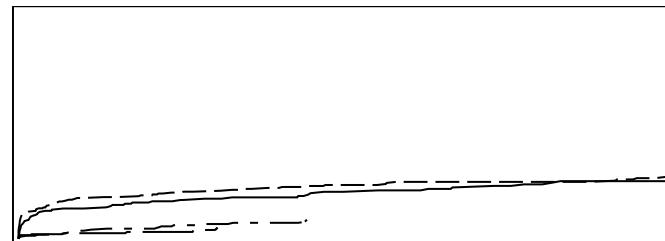
p<0.001

	ITA	IAK/SIK
<i>N</i>	819	192
%	2.2	7.3

**Exhibit 7-10B**  
**Deaths (By Cause and Relatedness to Procedure or Immunosuppression)**

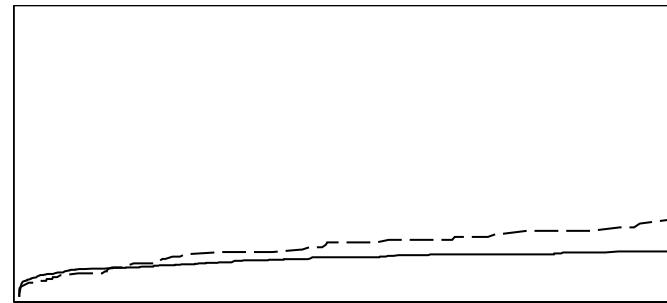
	Type of Transplant	Years post infusion 1	Year of Transplant	Age at Death	MedDRA Primary Cause of Death	Related to Infusion Procedure?	Related to Immunosuppression Therapy?	Active Immuno-suppression
1	ITA	.	2008			Unlikely related	Possibly related	Yes
2	ITA	1.2	2002	44		Missing Information	Missing Information	
3	ITA	1.4	2005	46	Atherosclerotic Coronary Artery Disease	Not related	Not related	Yes
4	ITA	1.7	2008	63	Multiorgan failure of unknown etiology	Possibly related	Possibly related	Yes
5	ITA	1.8	2003	43	Acute Methadone and Diphenhydramine Toxicity	Not related	Not related	Yes
6	ITA	1.9	2012	59	myocardial infarction	Missing Information	Missing Information	
7	ITA	2.1	2009	45		Missing Information	Missing Information	Yes
8	ITA	3.2	2002	45	viral meningitis	Not related	Possibly related	Yes
9	ITA	3.3	2006	58		Missing Information	Missing Information	Yes
10	ITA	3.9	2010	66		Missing Information	Missing Information	
11	ITA	4.4	2001	40	Unknown	Not related	Unlikely related	Yes
12	ITA	4.6	2006	71	Cardiac failure	Related	Not related	Yes
13	ITA	5.3	2003	30	infection	Not related	Unlikely related	
14	ITA	6.5	2000	46	Diabetic Ketoacidosis due to Diabetes Mellitus	Not related	Not related	Yes
15	ITA	8.2	2000	40	Pneumonia	Not related	Not related	Yes
1	IAK/SIK	.	2000			Not related	Not related	
2	IAK/SIK	0.1	2002	52	Infectious pneumopathy	Missing Information	Related	Yes
3	IAK/SIK	0.3	2001	35	CARDIO RESPIRATORY ARREST	Unlikely related	Unlikely related	Yes
4	IAK/SIK	0.9	2001	51	respiratory arrest after therapy withdrawal	Not related	Related	Yes
5	IAK/SIK	1	2000	34	Unknown	Not related	Unlikely related	Yes
6	IAK/SIK	2.3	1999	53	Congestive heart failure	Not related	Not related	
7	IAK/SIK	3.3	2004	46	Brain hemorrhage	Not related	Not related	Yes
8	IAK/SIK	3.4	2000	52		Not related	Not related	Yes
9	IAK/SIK	3.5	2001	52	massive Hemorrhagic Infarct	Not related	Not related	Yes
10	IAK/SIK	3.7	2002	62	Subarachnoid hemorrhage mesencephalic	Not related	Not related	Yes
11	IAK/SIK	4.6	2007	56	severe chronic cardiovascular complications	Not related	Not related	Yes
12	IAK/SIK	6.2	2000	56	Unknown	Not related	Unlikely related	Yes
13	IAK/SIK	6.3	2003	62	pneumonia	Not related	Not related	Yes
14	IAK/SIK	8.8	1999	63	Lung Carcinoma Non-small cell poorly differentiate	Not related	Unlikely related	Yes
15	IAK/SIK	10.2	2003	55	Cardiac decomposition	Missing Information	Missing Information	Yes

**Exhibit 7-11A**  
**Life-Threatening Events (By Era)**



	<i>Era</i>			
	1999-2002	2003-2006	2007-2010	2011-2014
<i>Life-threatening events</i>	50 / 209	76 / 271	16 / 242	9 / 285

**Exhibit 7-11B**  
**Life-Threatening Events (By Transplant Type)**



	<i>Transplant type</i>	
	<i>ITA</i>	<i>IAK/SIK</i>
<i>Life-threatening events</i>	112 / 819	39 192

**Exhibit 7-11C**  
**Life-Threatening Events (in System/Organ Class order)**

Type of Transplant	Related to Infusion Procedure?	Related to Immunosuppression Therapy?	System/Organ Class	MedDRA Preferred Term	Era	Months post infusion 1
<b>IAK/SIK</b>	Not related	Not related	Cardiac disorders	Cardio-respiratory arrest	1999-2002	28.2
	"	"		Myocardial ischaemia	2003-2006	59.8
	"	"	General disorders and administration site conditions	Death	1999-2002	43.9
	"	"	Infections and infestations	Infection	1999-2002	106.8
	"	"	Investigations	Troponin I	2003-2006	57.1
	"	"	Nervous system disorders	Cerebral ischaemia	2007-2010	13.2
	"	"	Vascular disorders	Haematoma	1999-2002	25.8
	<b>Possibly related</b>		Blood and lymphatic system disorders	Anaemia	1999-2002	46.6
			Infections and infestations	Opportunistic infection	2007-2010	12.8
			Investigations	Granulocytes abnormal	1999-2002	3.1
			"	"	2003-2006	3.8
			"	"	2003-2006	2.5
	"	"	"	"	2003-2006	7.9
	"	"	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Neoplasm malignant	1999-2002	105.0
	"	"	Renal and urinary disorders	Proteinuria	2003-2006	28.3
	<b>Related</b>		Respiratory, thoracic and mediastinal disorders	Pneumonitis	1999-2002	0.6
			Blood and lymphatic system disorders	Blood disorder	1999-2002	8.5
			Immune system disorders	Hypersensitivity	1999-2002	10.5
Possibly related	Unlikely related	Blood and lymphatic system disorders	Anaemia	2003-2006	0.9	
<b>Related</b>	Not related	Gastrointestinal disorders	Peritoneal haemorrhage	1999-2002	0.0	
	"	"	"	"	2003-2006	15.2
	"	"	"	"	1999-2002	1.8
	"	"	Vascular disorders	Haematoma	2003-2006	0.0
	"	"	"	Haemorrhage	2011-2014	0.0
	Unlikely related	Gastrointestinal disorders	Gastrointestinal haemorrhage	2003-2006	0.0	
	"	"	Vascular disorders	Haemorrhage	2003-2006	5.4
"	"	"	"	"	1999-2002	0.0
Unlikely related	Not related	Nervous system disorders	Cerebral ischaemia	1999-2002	66.6	
"	<b>Possibly related</b>		Blood and lymphatic system disorders	Lymphopenia	2003-2006	18.6
"			Immune system disorders	Hypersensitivity	2003-2006	34.0
"			Investigations	Granulocytes abnormal	2011-2014	10.0
"			Renal and urinary disorders	Renal failure	1999-2002	8.1
"	Unlikely related	Cardiac disorders	Cardio-respiratory arrest	2003-2006	55.2	
"	"	"	"	Myocardial ischaemia	2007-2010	26.7
"	"	"	"	"	1999-2002	40.0
"	"	Nervous system disorders	Cerebral ischaemia	1999-2002	0.2	

**Exhibit 7-11C (continued)**  
**Life-Threatening Events (in System/Organ Class order)**

Type of Transplant	Related to Infusion Procedure?	Related to Immunosuppression Therapy?	System/Organ Class	MedDRA Preferred Term	Era	Months post infusion 1
<b>ITA</b>	Not related	Not related	Cardiac disorders	Myocardial ischaemia	2003-2006	87.5
	"	"	"	"	2007-2010	0.7
	"	"	Metabolism and nutrition disorders	Hypoglycaemia	2003-2006	26.9
	"	"	"	"	1999-2002	8.7
	"	"	"	"	1999-2002	14.9
	"	"	"	"	2003-2006	11.1
	"	"	"	"	2003-2006	34.9
	"	"	"	"	2003-2006	12.4
	"	"	"	"	2003-2006	-8.1
	"	"	"	"	2011-2014	1.2
	"	"	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Neoplasm malignant	2003-2006	4.4
	Possibly related	Infections and infestations		Infection	2003-2006	20.7
		"	"	"	2003-2006	33.9
		"	Investigations	Granulocytes abnormal	1999-2002	1.9
		"	"	"	1999-2002	2.5
		"	"	"	1999-2002	26.7
		"	"	"	1999-2002	1.4
		"	"	"	1999-2002	4.1
		"	"	"	1999-2002	1.7
		"	"	"	1999-2002	49.2
		"	"	"	1999-2002	0.5
		"	"	"	2003-2006	3.4
		"	"	"	2007-2010	1.8
		"	Metabolism and nutrition disorders	Hypoglycaemia	2003-2006	11.3
		"	"	Hypophosphataemia	2003-2006	2.3
	Related	Neoplasms benign, malignant and unspecified (incl cysts and polyps)		Neoplasm malignant	1999-2002	26.9
		"	Vascular disorders	Hypertension	1999-2002	50.0
		Blood and lymphatic system disorders		Lymphopenia	2003-2006	0.0
		"	"	"	2003-2006	0.0
		"	"	"	2003-2006	-1.2
		"	"	"	2003-2006	0.0
		"	"	"	2011-2014	18.4
		Investigations		Granulocytes abnormal	1999-2002	37.8
		"	"	"	1999-2002	9.8
		"	"	"	2003-2006	0.2
		"	"	"	2003-2006	0.7
		"	"	"	2003-2006	5.2

**Exhibit 7-11C (continued)**  
**Life-Threatening Events (in System/Organ Class order)**

Type of Transplant	Related to Infusion Procedure?	Related to Immunosuppression Therapy?	System/Organ Class	MedDRA Preferred Term	Era	Months post infusion 1
	"	"	"	"	2003-2006	3.6
	"	"	Psychiatric disorders	Insomnia	1999-2002	19.7
	"	"	Renal and urinary disorders	Proteinuria	2003-2006	24.3
	"	Unlikely related	Cardiac disorders	Myocardial ischaemia	2007-2010	4.1
	"		Gastrointestinal disorders	Vomiting	2007-2010	5.6
Possibly related	Possibly related		Cardiac disorders	Myocardial ischaemia	2003-2006	0.0
		"	General disorders and administration site conditions	Death	2007-2010	19.8
	"	"	Investigations	Liver function test abnormal	2003-2006	0.2
	"	"	"	"	2003-2006	0.1
	"	"	Respiratory, thoracic and mediastinal disorders	Aspiration	2007-2010	0.1
		Related	Blood and lymphatic system disorders	Neutropenia	2011-2014	0.1
	"	Unlikely related	Hepatobiliary disorders	Cholecystitis	1999-2002	12.4
	"		Investigations	Blood alkaline phosphatase	1999-2002	0.2
	"	"	"	"	2003-2006	0.1
	"	"	"	"	2003-2006	0.1
	"	"	"	Liver function test abnormal	1999-2002	0.3
	"	"	"	"	1999-2002	0.2
	"	"	"	"	1999-2002	0.2
	"	"	"	"	1999-2002	0.0
	"	"	"	"	2003-2006	0.3
	"	"	"	"	1999-2002	0.2
	"	"	"	"	1999-2002	0.1
	"	"	"	"	1999-2002	0.0
	"	"	"	"	1999-2002	0.1
	"	"	"	"	2003-2006	12.9
	"	"	"	"	2003-2006	0.1
	"	"	"	"	2003-2006	0.1
	"	"	"	"	2003-2006	0.1
	"	"	"	"	2003-2006	0.3
	"	"	"	"	2003-2006	0.3
	"	"	"	"	2003-2006	0.2
	"	"	"	"	2003-2006	0.0
	"	"	Metabolism and nutrition disorders	Ketoacidosis	2007-2010	4.5
Related		Not related	Gastrointestinal disorders	Gastrointestinal obstruction	2003-2006	1.6
"		"	"	Peritoneal haemorrhage	2003-2006	0.0

**Exhibit 7-11C (continued)**  
**Life-Threatening Events (in System/Organ Class order)**

Type of Transplant	Related to Infusion Procedure?	Related to Immunosuppression Therapy?	System/Organ Class	MedDRA Preferred Term	Era	Months post infusion 1
"	"	"	"	"	1999-2002	17.2
"	"	"	"	"	2007-2010	8.2
"	"	"	"	"	2011-2014	16.2
"	"	"	General disorders and administration site conditions	Death	2003-2006	55.1
"	"	"	Hepatobiliary disorders	Portal vein thrombosis	2003-2006	3.3
"	"	"	"	"	2003-2006	0.0
"	"	"	Infections and infestations	Infection	2003-2006	1.6
"	"	"	Investigations	Liver function test abnormal	1999-2002	0.1
"	"	"	Metabolism and nutrition disorders	Hypoglycaemia	2003-2006	2.6
"	"	"	Vascular disorders	Haematoma	2003-2006	0.0
"	Possibly related	Gastrointestinal disorders		Peritoneal haemorrhage	1999-2002	1.1
"	Related	Investigations		Granulocytes abnormal	2003-2006	0.1
"	"	"		Liver function test abnormal	1999-2002	1.1
"	Unlikely related	Gastrointestinal disorders		Peritoneal haemorrhage	1999-2002	1.0
"	"	"		"	2007-2010	6.7
Unlikely related	Possibly related	Infections and infestations		Infection	1999-2002	33.2
"	"	Investigations		Granulocytes abnormal	1999-2002	0.9
"	"	"		"	2003-2006	19.7
"	"	"		"	2003-2006	0.1
"	"	"		"	2003-2006	0.7
"	"	"		"	2003-2006	0.3
"	"	"		"	2007-2010	0.1
"	"	Renal and urinary disorders		Renal failure	2003-2006	3.3
"	Related	Investigations		Granulocytes abnormal	2003-2006	0.1
"	"	"		"	2007-2010	4.8
"	"	"		"	2011-2014	0.1
"	Unlikely related	Blood and lymphatic system disorders		Anaemia	2003-2006	1.9
"	"	Metabolism and nutrition disorders		Hypoglycaemia	2003-2006	0.0
"	"	"		"	2007-2010	16.5

**Exhibit 7-11D**  
**Life-Threatening Events (Outcome by System/Organ Class)**

Life-Threatening Events (Outcome by System/Organ Class)		Total N	Fatal Row%	Not recovered Row%	AEOOUT		Recovered with seq Row%	Unknown Row%
					Recovered Row%	Recovered Row%		
<b>System/Organ Class</b>	<b>Preferred Term</b>							
Blood and lymphatic system disorders	Anaemia	3	.	.	100.0	.	.	.
	Blood disorder	1	.	.	100.0	.	.	.
	Lymphopenia	6	.	.	100.0	.	.	.
	Neutropenia	1	.	.	100.0	.	.	.
Cardiac disorders	Cardio-respiratory arrest	2	50.0	.	50.0	.	.	.
	Myocardial ischaemia	8	.	.	75.0	25.0	.	.
Gastrointestinal disorders	Gastrointestinal haemorrhage	1	.	.	100.0	.	.	.
	Gastrointestinal obstruction	1	.	.	100.0	.	.	.
	Peritoneal haemorrhage	10	.	.	100.0	.	.	.
	Vomiting	1	.	.	100.0	.	.	.
General disorders and administration site conditions	Death	3	100.0	.	.	.	.	.
Hepatobiliary disorders	Cholecystitis	1	.	.	100.0	.	.	.
	Portal vein thrombosis	2	.	.	100.0	.	.	.
Immune system disorders	Hypersensitivity	3	.	.	33.3	33.3	33.3	33.3
Infections and infestations	Infection	5	.	.	60.0	40.0	.	.
	Opportunistic infection	1	.	.	100.0	.	.	.
Investigations	Blood alkaline phosphatase	3	.	.	100.0	.	.	.
	Granulocytes abnormal	31	.	3.2	96.8	.	.	.
	Liver function test abnormal	23	.	.	95.7	4.3	.	.
	Troponin I	1	.	.	100.0	.	.	.
Metabolism and nutrition disorders	Hypoglycaemia	13	.	.	100.0	.	.	.
	Hypophosphataemia	1	.	.	100.0	.	.	.
	Ketoacidosis	1	.	.	100.0	.	.	.
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Neoplasm malignant	3	.	66.7	33.3	.	.	.
Nervous system disorders	Cerebral ischaemia	3	.	33.3	.	66.7	.	.
Psychiatric disorders	Insomnia	1	.	.	100.0	.	.	.
Renal and urinary disorders	Proteinuria	2	.	50.0	50.0	.	.	.
	Renal failure	2	.	.	50.0	50.0	.	.
Respiratory, thoracic and mediastinal disorders	Aspiration	1	.	.	100.0	.	.	.
	Pneumonitis	1	100.0	.	.	.	.	.

**Exhibit 7-11D (continued)**  
**Life-Threatening Events (Outcome by System/Organ Class)**

Life-Threatening Events (Outcome by System/Organ Class)		Total	AEOUT				
			Fatal	Not recovered	Recovered	Recovered with seq	Unknown
Vascular disorders	Haematoma	3	.	.	100.0	.	.
	Haemorrhage	3	.	.	100.0	.	.
	Hypertension	1	.	.	100.0	.	.