Genetics and Precision Medicine Department King Abdullah Specialized Children's Hospital (KASCH) King Abdulaziz Medical City – Riyadh



Protocol for Immune Tolerance Induction for CRIM Negative Pompe Patients in the Naïve Setting

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Reviewed by:

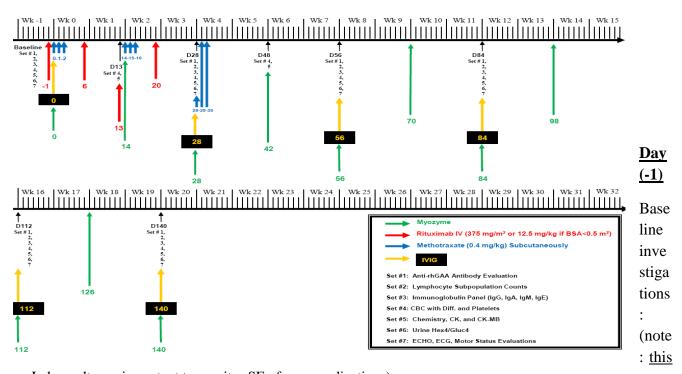
Genetics and Precision Medicine team members

Timeline

- **Myozyme:** Days 0, 14, 28, 42, 56, 70, 84, 98, 112, 126, 140
 - Give every two weeks, unless clinical status and IARs require more administration (see MZM slide)
- **Rituximab:** Days -1, 6, 13, 20
 - Give four doses over 4 weeks
- **Methotrexate:** Days 0, 1,2,14,15,16, 28, 29, 30
 - Give for three consecutive days (1 cycle) every 2 weeks for three cycles.
 - Methotrexate needs to be administered 1 hour to Myozyme infusion on Day 0, 14 and 28.
- **IVIG*:** Days 0, 28, 56, 84, 112, 140
 - *Can be given more or less frequently depending upon immunoglobulin levels, CD19 levels, and clinical status

• Additional notes:

- Changes may be made based on clinical status and antibody titers
- IVIG can be delayed one day, if concerned with volume given in a single day. Also, IVIG can be given more often if indicated clinically.



Lab results are important to monitor SE of your medications)

- Set 1: Anti-rhGAA Antibody Evaluation
- Set 2: Lymphocyte Subpopulation Counts (CD3, CD4, CD8, CD19)
 - Monitor for vaccination (vaccinate only after CD19 recovery)
- Set 3: Immune Status/Immunoglobulin Panel (IgG, IgA, IgM, IgE)
 - Monitor for recovery status (when needed) with diphtheria and tetanus toxoid antibody titers
 - Monitor for IVIG administration
- Set 4: Hematology (CBC with differential, Platelets)
 - Monitor platelet counts for less than 50,000/mm
 - Monitor neutrophil counts for less than 500/mm³
 - Monitor for infections resistant to treatment

- Set 5: Chemistry (ALT, AST, CK, CK-MB)
 - Monitor CK and CK-MB for increases greater than 2x baseline result
 - Monitor AST and ALT for increases greater than 3x baseline result
- Set 6: Urine Oligosaccharides (Hex4/Gluc4).

Day (-1):

Rituximab IV	
• Dose: 375 mg/m²/dose IV; if BSA is lesser than 0.5 m², give 12.5 mg/kg IV.	
• Weightkg, heightcm, BSA	
 Calculated dosemg. Dilution Range: 1 - 4 mg/mL. (Total volume will depend on dilution chosen) 	
Dilution preferred, total volumeml.	
• Infusion rate: 1 mg/kg/hr x 30 min;mg/hr,ml/	hr
2 mg/kg/hr x 30 min;mg/hr,ml/	
3 mg/kg/hr until complete:mg/hr,ml/hr.	
Premedications may include:	
Acetaminophen (10-15 mg/kg) PO; mg PO.	
Diphenhydramine (1mg/kg) IV;mg IV.	
 Methylprednisolone (1mg/kg) IV; mg IV. 	
• Granisetron (10 mcg/kg) IV;mcg IV	
 Nursing: Monitor vital signs Q min. Call MD if any side effect develops. 	
Day (0): Methotrexate, Myozyme®, IVIG	
➤ Methotrexate: (dose 1 of cycle 1)	
To be given 1 hour prior to Myozyme®.	
Given in cycles, each cycle is 3 consecutive days.	
• Dose: 0.4 mg/kg SC or PO once.	
• Weightkg; calculated dose:mg; route	
Premedications may include:	
•	
 Acetaminophen (10-15 mg/kg) PO; mg PO. 	
•	

<u>SE</u>: ulcerative stomatitis, leukopenia, nausea, abdominal distress, malaise, undue fatigue, chills and fever, dizziness, and decreased resistance to infection.

Hold dose for ANC less than 750 OR liver function tests (LFTs) greater than 5x normal.

	• Dose: 20mg/kg IV.
	• Weight: kg: calculated dose mg IV.
	 Dilution Range: 0.5 - 4mg/ml. (Total volume will depend on dilution chosen) Dilution preferred
	Dilution preferred, total volumeini.
Spe	ecial Precautions:
	Stable only in Normal Saline.
	• The diluted Myozyme® solution should be filtered through a 0.2 µm, low protein-binding, in-line
	filter during administration to remove any visible particles.
<u>Int</u>	fusion rate:
	 1 mg/kg/hr x 30 min;mg/hr,ml/hr. 3 mg/kg/hr x 30 min;mg/hr,ml/hr.
	• 5 mg/kg/hr x 30 min:mg/hr,ml/hr.
	• 7 mg/kg/hr until completemg/hr,ml/hr.
	urses: Monitor vital signs during (prior to each rate increase) and up to 1 hour following infusion. If
abr	normal, contact the physician to decrease the rate or temporarily hold the Myozyme® infusion.
CE	La complexication and allowed a magazines, wiels of acusta aconding conjugate on failures, wiels of conding another three and
	anaphylaxis and allergic reactions, risk of acute cardiorespiratory failure, risk of cardiac arrhythmia and deen cardiac death during general anesthesia for central venous catheter placement, infusion reactions, and
	mune mediated reactions.
	<u>IVIG:</u>
	• Dose: 400 - 500 mg/kg.
	• Weight: kg, calculated dose: mg.
	• Please follow the nursing instructions and the infusion rate as per the "IVIG protocol for Pediatrics"
	found in the Hospital IV manual.
Da	y (1): Methotrexate
	Methotrexate: (dose 2 of cycle 1)
	 Dose: 0.4 mg/kg SC or PO once. Weightkg; calculated dose:mg; route
	weightkg, calculated doseing, route
Pro	emedications may include:
	·
	• Acetaminophen (10-15 mg/kg) PO; mg PO.
	• Granisetron (10 mcg/kg) IV;mcg IV.
SE.	t ulgarative etemptitis laukononia nousee abdominal distress malaise undua fatigue abills and favor
	is ulcerative stomatitis, leukopenia, nausea, abdominal distress, malaise, undue fatigue, chills and fever, eziness, and decreased resistance to infection.
uiz	iziness, and decreased resistance to infection.
Ho	old dose for ANC less than 750 OR liver function tests (LFTs) greater than 5x normal.
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<u>Da</u>	y (2): Methotrexate
>	Methotrexate: (dose 3 of cycle 1)
	intenion exate. (dose 5 of cycle 1)
	• Dose: 0.4 mg/kg SC or PO once.
	• Weightkg; calculated dose:mg; route

> Myozyme®: Alglucosidase alfa.

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•	Acetaminophen (10-15 mg/kg) PO;	_ mg PO.
•	Granisetron (10 mcg/kg) IV;	mcg IV.

<u>SE</u>: ulcerative stomatitis, leukopenia, nausea, abdominal distress, malaise, undue fatigue, chills and fever, dizziness, and decreased resistance to infection.

Hold dose for ANC less than 750 OR liver function tests (LFTs) greater than 5x normal.

Day (6):

Rituximab IV

•	Dose: 375 mg/m²/dose IV; if BSA is lesser th	1an 0.5 m², gi	ive 12.5 mg/kg IV.	
•	Weightkg, height	cm, BSA		
•	Calculated dosemg.			
•	Dilution Range: 1 - 4 mg/mL. (Total volume	will depend	on dilution chosen)	
•	Dilution preferred, total	•		
•	Infusion rate: 1 mg/kg/hr x 30) min; _	mg/hr,	ml/hr.
	2 mg/kg/hr mu mu mu mu mu mu mu	min; _	mg/hr,	ml/hr.
	3 mg/kg/hr until complete:	m	g/hr,ml/hr.	
•	Premedications may include:			
	• Acetaminophen (10-15 mg/kg) PO;		mg PO.	
	• Diphenhydramine (1mg/kg) IV;		mg IV.	
	 Methylprednisolone (1mg/kg) IV; 		mg IV.	
	• Granisetron (10 mcg/kg) IV;		mcg IV	

<u>SE:</u> infusion related reactions (i.e. hives, itching, swelling of lips, tongue, throat or face, sudden cough, difficulty breathing, weakness, dizziness, palpitations and chest pain), chills, infections, body aches, tiredness, and low white blood cells.

Nursing:

- Monitor vital signs Q _____ min.
- Call MD if any side effect develops.

Day (13):

Repeat investigations: (note: this lab results are important to monitor SE of your medications)

- Set 4: Hematology (CBC with differential, Platelets)
 - Monitor platelet counts for less than 50,000/mm
 - Monitor neutrophil counts for less than 500/mm³
 - Monitor for infections resistant to treatment
- Set 5: Chemistry (ALT, AST, CK, CK-MB)
 - Monitor CK and CK-MB for increases greater than 2x baseline result
 - Monitor AST and ALT for increases greater than 3x baseline result

<u>Day (13):</u>

Rituximab IV

 Dose: 375 mg/m²/dose IV; if BSA is lesser than 0.5 m², give 12.5 mg/kg IV. Weightkg, heightcm, BSA Calculated dosemg. Dilution Range: 1 - 4 mg/mL. (Total volume will depend on dilution chosen) Dilution preferred, total volumeml.
• Infusion rate: 1 mg/kg/hr x 30 min;mg/hr,ml/hr. 2 mg/kg/hr x 30 min;mg/hr,ml/hr. 3 mg/kg/hr until complete:mg/hr,ml/hr.
 Premedications may include: Acetaminophen (10-15 mg/kg) PO; mg PO. Diphenhydramine (1mg/kg) IV; mg IV. Methylprednisolone (1mg/kg) IV; mg IV. Granisetron (10 mcg/kg) IV; mcg IV
<u>SE:</u> infusion related reactions (i.e. hives, itching, swelling of lips, tongue, throat or face, sudden cough, difficulty breathing, weakness, dizziness, palpitations and chest pain), chills, infections, body aches, tiredness, and low white blood cells.
Nursing:
 Monitor vital signs Q min. Call MD if any side effect develops.
Day (14): Methotrexate, Myozyme®
➤ Methotrexate: (dose 1 of cycle 2)
To be given 1 hour prior to Myozyme®. Given in cycles, each cycle is 3 consecutive days.
 Dose: 0.4 mg/kg SC or PO once. Weightkg; calculated dose:mg; route
Premedications may include:
 Acetaminophen (10-15 mg/kg) PO; mg PO. Granisetron (10 mcg/kg) IV; mcg IV.
<u>SE:</u> ulcerative stomatitis, leukopenia, nausea, abdominal distress, malaise, undue fatigue, chills and fever, dizziness, and decreased resistance to infection.
Hold dose for ANC less than 750 OR liver function tests (LFTs) greater than 5x normal.
➤ <u>Myozyme®</u> : Alglucosidase alfa.
 Dose: 20mg/kg IV. Weight:kg: calculated dosemg IV. Dilution Range: 0.5 - 4mg/ml. (Total volume will depend on dilution chosen) Dilution preferred, total volumeml.

Special Precautions:

- Stable only in Normal Saline.
- The diluted Myozyme® solution should be filtered through a 0.2 µm, low protein-binding, in-line filter during administration to remove any visible particles.

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•	1 mg/kg/hr x 30 min;	mg/hr,	ml/hr.
•	3 mg/kg/hr x 30 min;	mg/hr,	ml/hr.
•	5 mg/kg/hr x 30 min:	mg/hr,	ml/hr.
•	7 mg/kg/hr until complete	mg/hr,	ml/hr.

<u>Nurses:</u> Monitor vital signs during (prior to each rate increase) and up to 1 hour following infusion. If abnormal, contact the physician to decrease the rate or temporarily hold the Myozyme® infusion.

<u>SE:</u> anaphylaxis and allergic reactions, risk of acute cardiorespiratory failure, risk of cardiac arrhythmia and sudden cardiac death during general anesthesia for central venous catheter placement, infusion reactions, and immune mediated reactions.

Day (15): Methotrexate

Methotrexate:	(dose 2	of cycle 1)

•	Dose: 0.4 1	ng/kg SC or PO once.	
•	Weight	kg; calculated dose:	mg; route_

Premedications may include:

•	Acetaminophen (10-15 mg/kg) PO;_	mg PO.
•	Granisetron (10 mcg/kg) IV;	mcg IV.

<u>SE:</u> ulcerative stomatitis, leukopenia, nausea, abdominal distress, malaise, undue fatigue, chills and fever, dizziness, and decreased resistance to infection.

Hold dose for ANC less than 750 OR liver function tests (LFTs) greater than 5x normal.

Day (16): Methotrexate

➤ Methotrexate: (dose 3 of cycle 1)

•	Dose: 0.4 r	ng/kg SC or PO once.	
•	Weight	kg; calculated dose:	mg; route

Premedications may include:

•	Acetaminophen (10-15 mg/kg) PO;	_mg PO.
•	Granisetron (10 mcg/kg) IV;	mcg IV.

<u>SE:</u> ulcerative stomatitis, leukopenia, nausea, abdominal distress, malaise, undue fatigue, chills and fever, dizziness, and decreased resistance to infection.

Hold dose for ANC less than 750 OR liver function tests (LFTs) greater than 5x normal.

<u>Day (20):</u>

Rituximab IV

• Dose: 375 mg/m²/dose IV; if BSA is lesser than 0.5 m², give 12.5 mg/kg IV.
 Weightkg, heightcm, BSA
• Calculated dosemg.
 Dilution Range: 1 - 4 mg/mL. (Total volume will depend on dilution chosen) Dilution preferred total volume ml.
• Dilution preferred, total volumeml.
• Infusion rate: 1 mg/kg/hr x 30 min;mg/hr,ml/h
2 mg/kg/hr x 30 min;mg/hr,ml/h
3 mg/kg/hr until complete:mg/hr,ml/hr.
Durana di addana manin da da
 Premedications may include: Acetaminophen (10-15 mg/kg) PO; mg PO.
Diphenhydramine (1mg/kg) IV;mg IV.
Methylprednisolone (1mg/kg) IV; mg IV.
Granisetron (10 mcg/kg) IV;mcg IV
<u>SE:</u> infusion related reactions (i.e. hives, itching, swelling of lips, tongue, throat or face, sudden cough difficulty breathing, weakness, dizziness, palpitations and chest pain), chills, infections, body ache
tiredness, and low white blood cells.
Nursing:
 Monitor vital signs Q min. Call MD if any side effect develops.
•
<u>Day (28)</u>
Repeat investigations: (note: this lab results are important to monitor SE of your medications)
Set 1: Anti-rhGAA Antibody Evaluation
• Set 2: Lymphocyte Subpopulation Counts (CD3, CD4, CD8, CD19)
 Monitor for vaccination (vaccinate only after CD19 recovery) Set 3: Immune Status/Immunoglobulin Panel (IgG, IgA, IgM, IgE)
 Set 3. Infinding Status/Infinding Jobulin Failer (1gG, 1gA, 1gM, 1gE) Monitor for recovery status (when needed) with diphtheria and tetanus toxoid antibody tites
Monitor for IVIG administration
Set 4: Hematology (CBC with differential, Platelets)
• Monitor platelet counts for less than 50,000/mm ³
• Monitor neutrophil counts for less than 500/mm ³
Monitor for infections resistant to treatment
• Set 5: Chemistry (ALT, AST, CK, CK-MB)
 Monitor CK and CK-MB for increases greater than 2x baseline result
 Monitor AST and ALT for increases greater than 3x baseline result
• Set 6: Urine Oligosaccharides (Hex4/Gluc4).
Day (28): Methotrexate, Myozyme®, IVIG
➤ <u>Methotrexate</u> : (dose 1 of cycle 3)
To be given 1 hour prior to Myozyme®.
Given in cycles, each cycle is 3 consecutive days.
• Dose: 0.4 mg/kg SC or PO once.
 Weightkg; calculated dose:mg; route

Premed	lications may include:
	Acetaminophen (10-15 mg/kg) PO; mg PO. Granisetron (10 mcg/kg) IV; mcg IV.
	erative stomatitis, leukopenia, nausea, abdominal distress, malaise, undue fatigue, chills and fever, as, and decreased resistance to infection.
Hold do	ose for ANC less than 750 OR liver function tests (LFTs) greater than 5x normal.
> <u>M</u>	yozyme®: Alglucosidase alfa.
•	Dose: 20mg/kg IV. Weight:kg: calculated dosemg IV. Dilution Range: 0.5 - 4mg/ml. (Total volume will depend on dilution chosen) Dilution preferred, total volumeml.
•	Precautions: Stable only in Normal Saline. The diluted Myozyme® solution should be filtered through a 0.2 μm, low protein-binding, in-line filter during administration to remove any visible particles.
Infusion •	<u>n rate:</u> 1 mg/kg/hr x 30 min;mg/hr,ml/hr.
•	3 mg/kg/hr x 30 min;mg/hr,ml/hr.
	5 mg/kg/hr x 30 min:mg/hr,ml/hr. 7 mg/kg/hr until completemg/hr,ml/hr.
	Monitor vital signs during (prior to each rate increase) and up to 1 hour following infusion. If al, contact the physician to decrease the rate or temporarily hold the Myozyme® infusion.
sudden	phylaxis and allergic reactions, risk of acute cardiorespiratory failure, risk of cardiac arrhythmia and cardiac death during general anesthesia for central venous catheter placement, infusion reactions, and emediated reactions.
•	IG: Dose: 400 - 500 mg/kg. Weight: kg, calculated dose: mg. Please follow the nursing instructions and the infusion rate as per the "IVIG protocol for Pediatrics" found in the Hospital IV manual.
Day (29): Methotrexate
> <u>M</u>	ethotrexate: (dose 2 of cycle 3)
•	Dose: 0.4 mg/kg SC or PO once.

Premedications may include:

Acetaminophen (10-15 mg/kg) PO;_____ mg PO. Granisetron (10 mcg/kg) IV; ____ mcg IV.

SE: ulcerative stomatitis, leukopenia, nausea, abdominal distress, malaise, undue fatigue, chills and fever, dizziness, and decreased resistance to infection.

Weight _____kg; calculated dose: ____mg; route____.

Hold dose for ANC less than 750 OR liver function tests (LFTs) greater than 5x normal.

Day (30): Methotrexate

Methotrexate: (dose 3 of cycle	23)	
Dose: 0.4 mg/kg SC or PO ofWeightkg; ca		mg; route
Premedications may include:		
Acetaminophen (10-15 mg/kGranisetron (10 mcg/kg) IV;	(g) PO;	_ mg PO. mcg IV.
SE: ulcerative stomatitis, leukopeni dizziness, and decreased resistance to		listress, malaise, undue fatigue, chills and fever,
Hold dose for ANC less than 750 Ol	R liver function tests (L	FTs) greater than 5x normal.
Day (42):		
Repeat investigations: (note: this	s lab results are importa	nt to monitor SE of your medications)
• Set 4: Hematology (CBC w	ith differential, Platelet	s)
 Monitor platelet cou 	ints for less than 50,000	/mm ³
	counts for less than 500 ns resistant to treatment	
	L-MB for increases greated LT for increases greated	ter than 2x baseline result r than 3x baseline result
• Dose: 20mg/kg IV.		
• Weight:kg: calc	culated dose	mg IV.
• Dilution Range: 0.5 - 4mg/m	nl. (Total volume will d	epend on dilution chosen)
Dilution preferred	, total volum	neml.
Special Precautions:		
Stable only in Normal Salin	ne.	
 The diluted Myozyme® sol filter during administration t 		d through a 0.2 μ m, low protein-binding, in-line articles.
Infusion rate:		
• 1 mg/kg/hr x 30 min;		
• 3 mg/kg/hr x 30 min;		
• 5 mg/kg/hr x 30 min:		
 7 mg/kg/hr until complete 	mg/hr,	ml/hr.

<u>Nurses:</u> Monitor vital signs during (prior to each rate increase) and up to 1 hour following infusion. If abnormal, contact the physician to decrease the rate or temporarily hold the Myozyme® infusion.

SE: anaphylaxis and allergic reactions, risk of acute cardiorespiratory failure, risk of cardiac arrhythmia and sudden cardiac death during general anesthesia for central venous catheter placement, infusion reactions, and immune mediated reactions.

Day (56)

Repeat investigations: (note: this lab results are important to monitor SE of your medications)

- Set 1: Anti-rhGAA Antibody Evaluation
- Set 2: Lymphocyte Subpopulation Counts (CD3, CD4, CD8, CD19)
 - Monitor for vaccination (vaccinate only after CD19 recovery)
- Set 3: Immune Status/Immunoglobulin Panel (IgG, IgA, IgM, IgE)
 - Monitor for recovery status (when needed) with diphtheria and tetanus toxoid antibody titers
 - Monitor for IVIG administration
- Set 4: Hematology (CBC with differential, Platelets)
 - Monitor platelet counts for less than 50,000/mm³
 - Monitor neutrophil counts for less than 500/mm³
 - Monitor for infections resistant to treatment
- Set 5: Chemistry (ALT, AST, CK, CK-MB)
 - Monitor CK and CK-MB for increases greater than 2x baseline result
 - Monitor AST and ALT for increases greater than 3x baseline result
- Set 6: Urine Oligosaccharides (Hex4/Gluc4).

Day (56): Myozyme®, IVIG

> N	<u>Ayozyme®:</u>	Alglucosid	lase alfa.
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•	Dose: 20mg/kg IV.			
•	Weight:	_kg: calculated dose	mg IV.	
•	Dilution Range: 0.5	- 4mg/ml. (Total volume will	l depend on dilution chosen)	
•	Dilution preferred_	, total vol	ume ml	

Special Precautions:

- Stable only in Normal Saline.
- The diluted Myozyme® solution should be filtered through a 0.2 µm, low protein-binding, in-line filter during administration to remove any visible particles.

Infusion rate:

•	1 mg/kg/hr x 30 min;	mg/hr,	ml/hr.
•	3 mg/kg/hr x 30 min;	mg/hr,	ml/hr.
•	5 mg/kg/hr x 30 min:	mg/hr,	ml/hr.
•	7 mg/kg/hr until complete	mg/hr,	ml/hr.

<u>Nurses:</u> Monitor vital signs during (prior to each rate increase) and up to 1 hour following infusion. If abnormal, contact the physician to decrease the rate or temporarily hold the Myozyme® infusion.

<u>SE:</u> anaphylaxis and allergic reactions, risk of acute cardiorespiratory failure, risk of cardiac arrhythmia and sudden cardiac death during general anesthesia for central venous catheter placement, infusion reactions, and immune mediated reactions.

> IVIG:

- Dose: 400 500 mg/kg.
- Weight: ______ kg, calculated dose: ______ mg.
- Please follow the nursing instructions and the infusion rate as per the "IVIG protocol for Pediatrics" found in the Hospital IV manual.

Day (70): Myozyme®, IVIG

> Myozyme®: Alglucosidase alfa.

•	Dose: 20mg/kg IV.
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- Weight: _____kg: calculated dose _____mg IV.
- Dilution Range: 0.5 4mg/ml. (Total volume will depend on dilution chosen)
- Dilution preferred______, total volume _____ml.

Special Precautions:

- Stable only in Normal Saline.
- The diluted Myozyme® solution should be filtered through a 0.2 µm, low protein-binding, in-line filter during administration to remove any visible particles.

Infusion rate:

- 1 mg/kg/hr x 30 min; ____mg/hr, ___ml/hr.
- 3 mg/kg/hr x 30 min; ____mg/hr, ___ml/hr.
- 5 mg/kg/hr x 30 min: ____mg/hr, ___ml/hr.
- 7 mg/kg/hr until complete ____mg/hr, ___ml/hr.

<u>Nurses:</u> Monitor vital signs during (prior to each rate increase) and up to 1 hour following infusion. If abnormal, contact the physician to decrease the rate or temporarily hold the Myozyme® infusion.

<u>SE:</u> anaphylaxis and allergic reactions, risk of acute cardiorespiratory failure, risk of cardiac arrhythmia and sudden cardiac death during general anesthesia for central venous catheter placement, infusion reactions, and immune mediated reactions.

Day (84):

Repeat investigations: (note: this lab results are important to monitor SE of your medications)

- Set 1: Anti-rhGAA Antibody Evaluation
- Set 2: Lymphocyte Subpopulation Counts (CD3, CD4, CD8, CD19)
 - Monitor for vaccination (vaccinate only after CD19 recovery)
- Set 3: Immune Status/Immunoglobulin Panel (IgG, IgA, IgM, IgE)
 - Monitor for recovery status (when needed) with diphtheria and tetanus toxoid antibody titers
 - Monitor for IVIG administration
- Set 4: Hematology (CBC with differential, Platelets)
 - Monitor platelet counts for less than 50,000/mm³
 - Monitor neutrophil counts for less than 500/mm³
 - Monitor for infections resistant to treatment
- Set 5: Chemistry (ALT, AST, CK, CK-MB)
 - Monitor CK and CK-MB for increases greater than 2x baseline result
 - Monitor AST and ALT for increases greater than 3x baseline result
- Set 6: Urine Oligosaccharides (Hex4/Gluc4).

Day (84): Myozyme®, IVIG

>	Myozyme®: Alglucosidase alfa	1.		
•	Weight:kg: calcu Dilution Range: 0.5 - 4mg/ml.	(Total volume will depe	end on dilution chosen)	
Spec	ial Precautions:			
	Stable only in Normal Saline The diluted Myozyme® solut filter during administration to	tion should be filtered th	arough a 0.2 μm, low protein-binding, incles.	line
Infu	sion rate:			
•	1 mg/kg/hr x 30 min;			
•	3 mg/kg/hr x 30 min;	mg/hr,	ml/hr.	
•	5 mg ng m n 50 mm			
•	7 mg/kg/hr until complete	mg/hr,	ml/hr.	
			ase) and up to 1 hour following infusionarily hold the Myozyme® infusion.	. If
sudd imm	en cardiac death during general au une mediated reactions. IVIG:	•	piratory failure, risk of cardiac arrhythmia ous catheter placement, infusion reactions,	
	Dose: 400 - 500 mg/kg.	1 1 . 1 1		
	Weight:k			1 .
	Iospital IV manual.	and the infusion rate as p	per the "IVIG protocol for Pediatrics" found	ı ın
me r	iospitai i v manuai.			
Day	(98): Myozyme®			
>	Myozyme®: Alglucosidase alfa	1.		
	Dose: 20mg/kg IV.			
•	Weight:kg: calcu	lated dose	mg IV.	
•	Dilution Range: 0.5 - 4mg/ml.			
•	Dilution preferred	, total volume _	ml.	
Snoc	ial Draggytians			
Spec	<u>ial Precautions</u> : Stable only in Normal Saline	.		
			rough a 0.2 μm, low protein-binding, in-	line
	filter during administration to			iiic
		_	cies.	
T A	<u> </u>		cies.	
Infu	sion rate:	mg/hr		
Infu:	sion rate: 1 mg/kg/hr x 30 min;		ml/hr.	
•	sion rate: 1 mg/kg/hr x 30 min; 3 mg/kg/hr x 30 min;	mg/hr,	ml/hr. ml/hr.	

<u>Nurses:</u> Monitor vital signs during (prior to each rate increase) and up to 1 hour following infusion. If abnormal, contact the physician to decrease the rate or temporarily hold the Myozyme® infusion.

<u>SE:</u> anaphylaxis and allergic reactions, risk of acute cardiorespiratory failure, risk of cardiac arrhythmia and sudden cardiac death during general anesthesia for central venous catheter placement, infusion reactions, and immune mediated reactions.

Day (112):

Repeat investigations: (note: this lab results are important to monitor SE of your medications)

- Set 1: Anti-rhGAA Antibody Evaluation
- Set 2: Lymphocyte Subpopulation Counts (CD3, CD4, CD8, CD19)
 - Monitor for vaccination (vaccinate only after CD19 recovery)
- Set 3: Immune Status/Immunoglobulin Panel (IgG, IgA, IgM, IgE)
 - Monitor for recovery status (when needed) with diphtheria and tetanus toxoid antibody titers
 - Monitor for IVIG administration
- Set 4: Hematology (CBC with differential, Platelets)
 - Monitor platelet counts for less than 50,000/mm³
 - Monitor neutrophil counts for less than 500/mm³
 - Monitor for infections resistant to treatment
- Set 5: Chemistry (ALT, AST, CK, CK-MB)
 - Monitor CK and CK-MB for increases greater than 2x baseline result
 - Monitor AST and ALT for increases greater than 3x baseline result
- Set 6: Urine Oligosaccharides (Hex4/Gluc4).

Day (112): Myozyme®, IVIG

•	Dose: 20mg/kg IV.			
•	Weight:	_kg: calculated dose	mg IV	<i>I</i> .
•	Dilution Range: 0.5	5 - 4mg/ml. (Total volume	e will depend on diluti	on chosen)
•	Dilution preferred	, tota	l volume	ml.

Special Precautions:

• Stable only in Normal Saline.

➤ Myozyme®: Alglucosidase alfa.

• The diluted Myozyme® solution should be filtered through a $0.2~\mu m$, low protein-binding, in-line filter during administration to remove any visible particles.

Infusion rate:

•	1 mg/kg/hr x 30 min;	mg/hr,	ml/hr.
•	3 mg/kg/hr x 30 min;	mg/hr,	ml/hr.
•	5 mg/kg/hr x 30 min:	mg/hr,	ml/hr.
•	7 mg/kg/hr until complete	mg/hr,	ml/hr.

<u>Nurses:</u> Monitor vital signs during (prior to each rate increase) and up to 1 hour following infusion. If abnormal, contact the physician to decrease the rate or temporarily hold the Myozyme® infusion.

<u>SE:</u> anaphylaxis and allergic reactions, risk of acute cardiorespiratory failure, risk of cardiac arrhythmia and sudden cardiac death during general anesthesia for central venous catheter placement, infusion reactions, and immune mediated reactions.

IVIG:		
• Dose: 400 - 500 mg/kg.		
• Weight:	kg, calculated dose:	mg

Please follow the nursing instructions and the infusion rate as per the "IVIG protocol for Pediatrics" found in the Hospital IV manual.

Day (126): Myozyme®

> Myozyme®: Alglucosidase alfa.

•	Dose: 20mg/kg IV.			
•	Weight:	_kg: calculated dose	mg IV.	
•	Dilution Range: 0.5	- 4mg/ml. (Total volume will	l depend on dilution chose	n)
•	Dilution preferred	, total vol	umeı	nl.

Special Precautions:

- Stable only in Normal Saline.
- The diluted Myozyme® solution should be filtered through a 0.2 µm, low protein-binding, in-line filter during administration to remove any visible particles.

Infusion rate:

•	1 mg/kg/hr x 30 min;	mg/hr,	ml/hr.
•	3 mg/kg/hr x 30 min;	mg/hr,	ml/hr.
•	5 mg/kg/hr x 30 min:	mg/hr,	ml/hr.
•	7 mg/kg/hr until complete	mg/hr,	ml/hr.

<u>Nurses:</u> Monitor vital signs during (prior to each rate increase) and up to 1 hour following infusion. If abnormal, contact the physician to decrease the rate or temporarily hold the Myozyme® infusion.

<u>SE:</u> anaphylaxis and allergic reactions, risk of acute cardiorespiratory failure, risk of cardiac arrhythmia and sudden cardiac death during general anesthesia for central venous catheter placement, infusion reactions, and immune mediated reactions.

Day (140):

Repeat investigations: (note: this lab results are important to monitor SE of your medications)

- Set 1: Anti-rhGAA Antibody Evaluation
- Set 2: Lymphocyte Subpopulation Counts (CD3, CD4, CD8, CD19)
 - Monitor for vaccination (vaccinate only after CD19 recovery)
- Set 3: Immune Status/Immunoglobulin Panel (IgG, IgA, IgM, IgE)
 - Monitor for recovery status (when needed) with diphtheria and tetanus toxoid antibody titers
 - Monitor for IVIG administration
- Set 4: Hematology (CBC with differential, Platelets)
 - Monitor platelet counts for less than 50,000/mm
 - Monitor neutrophil counts for less than 500/mm
 - Monitor for infections resistant to treatment
 - Set 5: Chemistry (ALT, AST, CK, CK-MB)
 - Monitor CK and CK-MB for increases greater than 2x baseline result
 - Monitor AST and ALT for increases greater than 3x baseline result
- Set 6: Urine Oligosaccharides (Hex4/Gluc4).

Day (140): Myozyme®, IVIG

- > Myozyme®: Alglucosidase alfa.
 - Dose: 20mg/kg IV.

• Weight:kg: calculated dosemg IV.
• Dilution Range: 0.5 - 4mg/ml. (Total volume will depend on dilution chosen)
• Dilution preferred, total volumeml.
Special Precautions:
Stable only in Normal Saline.
• The diluted Myozyme® solution should be filtered through a 0.2 µm, low protein-binding, in-line
filter during administration to remove any visible particles.
Infusion rate:
• 1 mg/kg/hr x 30 min;mg/hr,ml/hr.
• 3 mg/kg/hr x 30 min;mg/hr,ml/hr.
• 5 mg/kg/hr x 30 min:mg/hr,ml/hr.
• 7 mg/kg/hr until completemg/hr,ml/hr.
Nurses: Monitor vital signs during (prior to each rate increase) and up to 1 hour following infusion. If abnormal, contact the physician to decrease the rate or temporarily hold the Myozyme® infusion. SE: anaphylaxis and allergic reactions, risk of acute cardiorespiratory failure, risk of cardiac arrhythmia and sudden cardiac death during general anesthesia for central venous catheter placement, infusion reactions, and immune mediated reactions.
 IVIG: Dose: 400 - 500 mg/kg. Weight:kg, calculated dose:mg. Please follow the nursing instructions and the infusion rate as per the "IVIG protocol for Pediatrics" found in the Hospital IV manual.