Calaspargase pegol (CalPEG): The new asparaginase

Tamara MacDonald PharmD

IWK/APPHON

Tamara.macdonald@iwk.nshealth.ca

Asparaginase formulations

- Asparaginase products are either derived from E.coli or Erwinia Chrysanthemi bacteria and are either short or long acting.

E.coli:

- Native E.coli asparaginase (Kidrolase): short acting – discontinued
- Pegaspargase (Oncaspar): long acting – phasing out
- Calaspargase pegol (Asparlas): long acting – approved in Canada

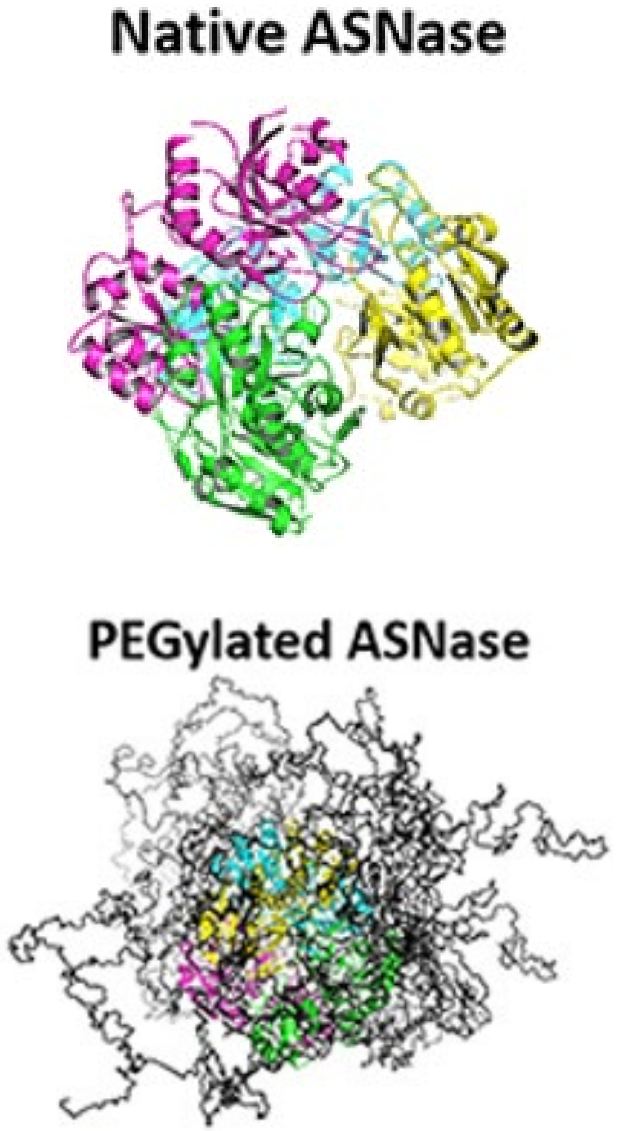
Erwinia Chrysanthemi:

- Erwinase: short acting – phasing out
- Rylaze (recombinant): short acting – approved in Canada

What makes an asparaginase long acting

Polyethylene glycol (PEG)

- What is it:
  - Made up of organic substances (monomers) linked by ethers in chainlike structure.
  - Water soluble and stable (pH & temps).
  - Linked to the asparaginase by esters (linkers) that react to bond the PEG to the asparaginase:
    - Pegaspargase: Succinimidyl succinate SS
    - Calaspargase pegol: Succinimidyl carbonate SC – more stable.
- How does it work:
  - Protects the asparaginase from degradation by proteolytic enzymes – extends half-life.
  - Increases water solubility and stability – causes fewer immunogenic reactions.



Calaspargase pegol vs Pegaspargase

	Pegaspargase (PEG)	Calaspargase pegol (CalPEG)
Linker	Succinimidyl succinate (SS)	Succinimidyl carbonate (SC) – forms more stable bond.
Half-life	5-6 days	16 days
Duration of activity	14 days	21 days
Administration	1-2 hours IV or IM	1-2 hours IV
Shelf-life	5 months	33 months
Approved doses	2500 IU/m2	2500 IU/m2 1-21 years
Asparaginase activity levels	≥ 0.1 IU/mL in > 95% of patients 14 days post-dose	➢ 0.1 IU/mL in 88% of patients 25 days post dose. ➢ We will measure SAA at day 14 vs day 7.
Infusion related reactions/HSR	~20% +/- premedication (+/- steroid) 20% first hour and 80% second hour Fluid bolus	➢ 20-40% (with premedication +/- steroid) possibly due to the linker and increased PEG reagents required to prevent hydrolysis and maintain the integrity of the molecule. ➢ Slow and stepwise increase in rate ➢ Fluid bolus
Incidence of toxicities – thrombosis,hepatotoxicity, pancreatitis	n/a	Higher incidence of hyperlipidemia and hyperglycemia (AALL07P4 and DFCI-01-11) No significant differences b/w PEG and CalPEG incidence of toxicities (AALL1731) Higher rates of toxicity in adolescents over 15 years and in obese patients (don't forget about ACCL1931 –levocarnitine)
Funding	Not funded for IWK $6,879 per vial	**Provincially Funded** for all ($7,441.88)

PEG vs. CALPEG Clinical Trials

	AALL07P4	DFCI 11-001
Primary Objective	Pharmacokinetic comparability	Safety and Pharmacokinetic comparability
CALPEG Population 2500 mg/m2 dose ≥ 16 years	N = 111 N = 42 N = 5	N = 113 N = 6
Pharmacokinetics	CALPEG: Prolonged therapeutic asparaginase activity and asparagine depletion	
Efficacy CALPEG 2100 IU/m2	Comparable Efficacy Outcomes (MRD negativity, EOI CR, EFS, DFS, OS)	
	EOI MRD negative rate 56% vs. 72% (PEG) and 74% (CALPEG 2500 IU/m2) p=0.1	[redacted]
Safety	Grade 3–4 adverse event rates similar	
	CALPEG: Increased hyperbilirubinemia and hyperglycemia	[redacted]

CHILDREN'S ONCOLOGY GROUP

Angiolillo AL, JCO 2014; Sulis ML, PBC 2018; Silverman LB, Blood 2016; Vrooman LM, JCO 2021

Incidence of Asparaginase -Specific Grade 1-4 Adverse Events by Regimen and Course

Protocol-Specified Asparaginase-Specific Adverse Events Restricted to Grades 1-4

	Cal-PEG 2500 IU/m²		Cal-PEG 2100 IU/m²		PEG 2500 IU/m²		
AE and Course	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	***P* Value**
Allergic reaction[a]							
Induction	2/42	4.8	1/69	1.4	4/54	7.4	.26
Consolidation	9/33	27.3	10/49	20.4	10/43	23.3	.77
Interim maintenance I	0/29	0	1/46	2.1	0/39	0	1.00
Delayed intensification I	0/26	0	2/45	4.4	0/38	0	.34
Hyperlipidemia							
Induction	4/42	9.5	2/69	2.9	4/54	7.4	.31
Consolidation	1/33	3.0	1/49	2.0	3/43	7.0	.53
Interim maintenance I	1/29	3.4	1/46	2.2	1/39	2.6	1.00
Delayed intensification I	0/26	0	1/45	2.2	0/38	0.0	1.00
CNS							
Induction	0/42	0	4/69	5.8	0/54	0	.09
Consolidation	0/33	0	0/49	0	0/43	0	1.00
Interim maintenance I	0/29	0	0/46	0	0/39	0	1.00
Delayed intensification I	1/26	3.8	0/45	0	1/38	2.6	.34

a. Allergic reactions limited to events attributed as possibly, probably, or definitely related to Cal-PEG or PEG treatment

Cal-PEG, calaspargase pegol-mknl; PEG, pegaspargase .
Angiolillo AL, et al. *J Clin Oncol*. 2014;32:3874 -3882.

SERVIER

Adverse reactions for ASPARLAS (care of Servier)

Selected Grades ≥3 Adverse Reactions in Patients Receiving ASPARLAS With Multi-agent Chemotherapy (Study DFCI 11-001)[1]

	ASPARLAS 2500 U/m² (n=118)	Pegaspargase 2500 IU/m² (n=119)
Adverse Reaction[a]	**Grades ≥ 3[b]**	
Elevated transaminase	52%	66%
Bilirubin increased	20%	25%
Pancreatitis	18%	24%
Abnormal clotting studies	14%	21%
Diarrhea	9%	5%
Hypersensitivity	8%	7%
Embolic and thrombotic events	8%	8%
Sepsis	5%	6%
Dyspnea	4%	1%
Hemorrhages	4%	4%
Fungal infection	3%	3%
Pneumonia	3%	7%
Arrhythmia	2%	1%
Cardiac failure	2%	1%

Interim analysis of CALPEG toxicity on AALL1732

- Methods
  - Individual and total composite Asparaginase Associated Toxicity (AATs) calculated for:
    - Pancreatitis: Grade 2+ pancreatitis or pancreatic necrosis
    - Thrombosis: Grade 3+ thromboembolic event, any grade stroke or cerebrovascular ischemia
    - Hepatotoxicity: Grade 3+ Bilirubin increased, Grade 4+ Alanine or Aspartate aminotransferase increased or Grade 4+ Hepatic failure

CALPEG-associated toxicity during Induction and Consolidation

Toxicity	Induction	Consolidation
	N=420 (%)	N=286 (%)
Composite Toxicity Outcome	46 (11.0)	29 (10.1)
Pancreatitis (grade 2+)	11 (2.6)	11 (3.9)
Thromboembolic (grade 3+)	10 (2.4)	4 (1.4)
Hepatotoxicity (grade 3+ or 4+)	34 (8.1)	15 (5.2)

PEG vs. CALPEG toxicity

Induction			
Toxicity	**PEG N=1291 (%)**	**CALPEG N=420 (%)**	**P-value**
Pancreatitis	21 (1.6)	11 (2.6)	0.192
Thrombosis	24 (1.9)	10 (2.4)	0.506
Hepatotoxicity	125 (9.7)	34 (8.1)	0.331
Composite Toxicity Outcome	156 (12.1)	46 (11)	0.533

PEG vs. CALPEG toxicity

Consolidation			
Toxicity	**PEG N=1033 (%)**	**CALPEG N=286 (%)**	**P-value**
Pancreatitis	42 (4.1)	11 (3.9)	0.867
Thrombosis	11 (1.1)	4 (1.4)	0.638
Hepatotoxicity	50 (4.8)	15 (5.2)	0.780
Composite Toxicity Outcome	97 (9.4)	29 (10.1)	0.703

Induction

	Composite Toxicity - Yes (n=46)	Composite Toxicity - No (n=374)	P-value
Age (years)			
10-15	18 (7.8%)	213 (92.2%)	
>=15	28 (14.8%)	161(85.2%)	0.022
Sex			
Male	24 (9.3%)	234 (90.7%)	
Female	22 (13.6%)	140 (86.4%)	0.172
Race			
White	37 (13.7%)	232 (86.3%)	
Black or African American	1 (5.3%)	18 (94.7%)	
Other	2 (8.0%)	23 (92.0%)	
Unknown	6 (5.6%)	101 (94.4%)	0.104
Ethnicity			
Hispanic or Latino	20 (11.0%)	162 (89.0%)	
Not Hispanic or Latino	23 (11.4%)	179 (88.6%)	
Unknown	3 (8.3%)	33 (91.7%)	0.864
BMI			
Obese*	20 (17.7%)	93 (82.3%)	
Not Obese	26 (8.6%)	277 (91.4%)	0.008

Consolidation

	Composite Toxicity - Yes (n=29)	Composite Toxicity - No (n=257)	P-value
Age (years)			
10-15	18 (11.2%)	143 (88.8%)	
>=15	11 (8.8%)	114 (91.2%)	0.508
Sex			
Male	17 (9.3%)	165 (90.7%)	
Female	12 (11.5%)	92 (88.5%)	0.554
Race			
White	18 (10.1%)	160 (89.9%)	
Black or African American	1 (7.7%)	12 (92.3%)	
Other	4 (21.1%)	15 (78.9%)	
Unknown	6 (7.9%)	70 (92.1%)	0.393
Ethnicity			
Hispanic or Latino	14 (13.1%)	93 (86.9%)	
Not Hispanic or Latino	14 (9.3%)	137 (90.7%)	
Unknown	1 (3.6%)	437(96.4 %)	0.291
BMI			
Obese*	8 (11.1%)	192 (88.9%)	
Not Obese	21 (9.9%)	64 (90.1%)	0.761

Childrens Hospital of Philadelphia (Dr. Timothy Spear 2024):
PEGasp vs CalPEG toxicity

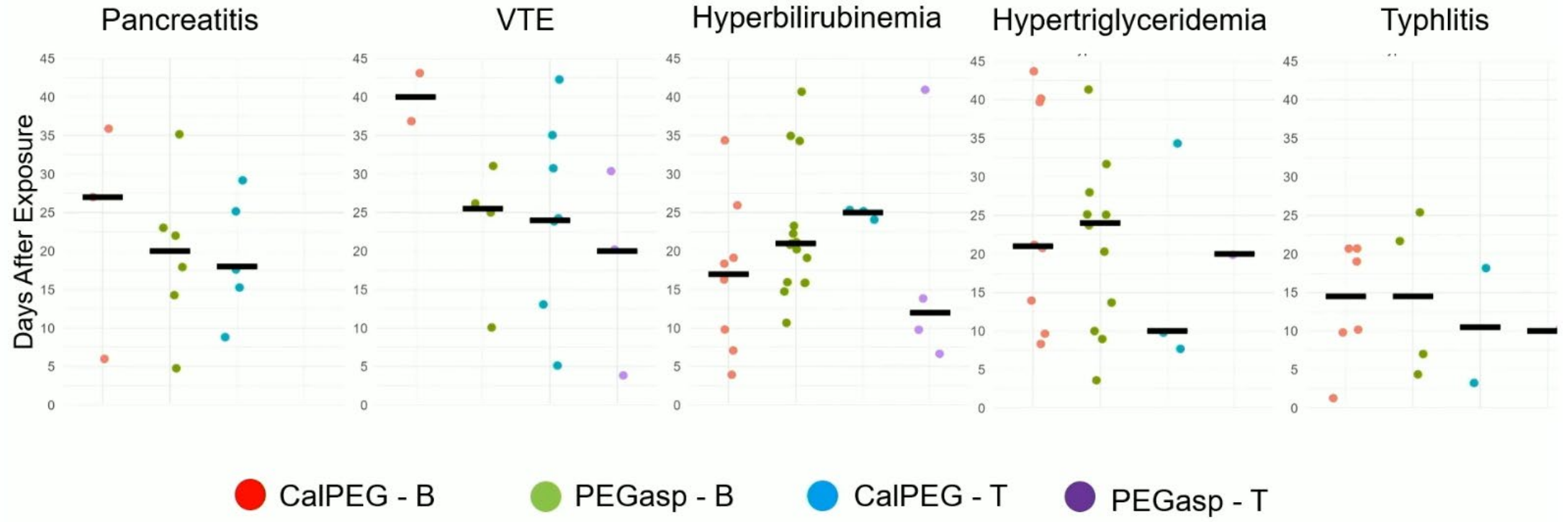
Toxicity	Overall, n (%)	CalPEG, n (%)	PEGasp, n (%)	*P* value
Total	45 (22.0)	17 (20.5)	28 (23.0)	0.68
Allergy	32 (15.6)	14 (16.9)	18 (14.8)	0.68
Silent Inactivation	6 (2.9)	1 (1.2)	5 (4.10)	0.40
Pancreatitis	13 (6.3)	7 (8.4)	6 (4.9)	0.31
Venous Thromboembolism	14 (6.8)	9 (10.8)	5 (4.1)	0.06
Hyperbilirubinemia	30 (14.6)	11 (13.3)	19 (15.6)	0.64
Hypertriglyceridemia	20 (9.8)	11 (13.3)	9 (7.4)	0.16
Typhilitis	13 (6.3)	8 (9.6)	5 (4.1)	0.11

Toxicity Incidence by ALL phenotype

Toxicity	Overall, n (%)	CalPEG, n (%)	PEGasp, n (%)	P value
Total	45 (22.0)	17 (20.5)	28 (23.0)	0.14
B-ALL		10 (15.6)	22 (22.4)	
T-ALL/LLy		7 (38.9)	6 (27.2)	
Allergy	32 (15.6)	14 (16.9)	18 (14.8)	0.11
B-ALL		12 (18.8)	11 (11.2)	
T-ALL/LLy		2 (1.1)	7 (31.8)	
Silent Inactivation	6 (2.9)	1 (1.2)	5 (4.10)	0.37
B-ALL		1 (1.5)	3 (2.5)	
T-ALL/LLy		0 (0.0)	2 (9.0)	
Hyperbilirubinemia	30 (14.6)	11 (13.3)	19 (15.6)	0.90
B-ALL		8 (12.5)	15 (15.3)	
T-ALL/LLy		3 (16.6)	4 (18.8)	

Toxicity	Overall, n (%)	CalPEG, n (%)	PEGasp, n (%)	P value
Pancreatitis	13 (6.3)	7 (8.4)	6 (4.9)	0.006
B-ALL		2 (3.1)	6 (6.1)	
T-ALL/LLy		5 (27.7)	0 (0.0)	
Typhlitis	13 (6.3)	8 (9.6)	5 (4.1)	0.28
B-ALL		6 (9.4)	4 (4.0)	
T-ALL/Lly		2 (1.1)	1 (4.5)	
Hypertriglyceridemia	20 (9.8)	11 (13.3)	9 (7.4)	0.28
B-ALL		7 (10.9)	8 (8.2)	
T-ALL/Lly		4 (22.2)	1 (4.5)	
Venous Thromboembolism	14 (6.8)	9 (10.8)	5 (4.1)	<0.0001
B-ALL		1 (1.6)	3 (3.0)	
T-ALL/LLy		8 (44.4)	2 (9.0)	

Increased time to toxicity with CalPEG



Childrens Hospital of Philadelphia – Dr. Timothy Spear at SIOP: CalPEG

VTE and pancreatitis significantly higher incidence and grade of toxicity in the T cell ALL/LLy patients.

Delay up to 4 weeks for these toxicities.

Likely higher results seen due to small numbers and perhaps the phenotype of T cell ALL being more highly predisposed to clotting.

Dosing of pegylated asparaginase in obesity

- Dose capping at 3,750 units/dose (1 vial) per institutional policy is permissible on COG trials in cases of baseline obesity.
- Note: Obesity has been linked to increased risk of toxicity in patients ≥ 10 years of age.
- Obesity is defined as ≥ 95% BMI for age for patients < 20 y.o or BMI ≥ 30 for patients ≥ 20 y.o
- Monitor asparaginase activity levels in patients who received capped or lower dose of pegaspargase or calaspargase pegol

Switching from PEG-asp to CalPEG

- No indication for CalPEG for children under 1 year in Canada which means PEG-asp still available for now.
- All COG studies that doses of PEG-asp are given greater than 21 days apart a dose of CalPEG will be substituted for each PEG-asp dose 1:1.
- All COG studies that a dose of PEG-asp given less than 21 days apart a single dose of CalPEG will be given on study (e.g AALL1821).
- Off study we will follow one dose of CalPEG substitution for doses of PEG-asp given less than 21 days apart (e.g. T-cell ALL induction).
- Delayed Intensification (DI) cycles extended to 9 weeks (63 days) in high-risk arms to allow for 21 days between calPEG doses.
- As the intended period of asparagine depletion (or asparaginase activity) is 14 days with both PEG-asp and CalPEG regardless of half-life the number of doses of short acting asparaginase or Rylaze (recombinant erwinase) required for patients that have severe reactions or deactivation is 6-7 doses depending on schedule:
  - Rylaze M/W/F 25/25/50 mg/dose x 6 doses OR 25 mg q2 days x 7 doses.

Infusion related/hypersensitivity reactions (IRR/HR) – pegylated asparaginases

- No differences reported for allergic reactions between pegaspargase and CalPEG in 1731 ~17% and 15% respectively.
- AALL07P4 (27%), DFCI (17%), 3 abstracts (4, 9, 42%) IRR/HR to CalPEG.
- Local incidence of pegaspargase reactions ~20%.
- Currently we premedicate each dose of pegaspargase with an antipyretic, antihistamine, antiemetic +/- steroid in an attempt to reduce IRR/HRs.
- Since neutralizing antibodies can occur with any dose of pegaspargase regardless of clinical reaction we monitor serum asparaginase levels with every dose to ensure adequate activity of the drug:
  - Silent inactivation (SI) – no clinical reaction but subtherapeutic asp levels
  - Deactivation – clinical reaction and subtherapeutic asp levels.

Recent chart review of Maritime data on efficacy of premedication with PEG-asp: 2015-2024

- No significant difference in number of reactions between the groups:
  - Premedications do not reduce the number of reactions.
- No difference in the degree or severity of reaction between the groups:
  - Premedications do not reduce the severity of the reaction.
- No difference in incidence of symptoms for rash/flushing, respiratory or cardiovascular:
  - This indicates that antihistamines do not modify/reduce reaction or severity of symptoms to pegaspargase.
  - This is likely due to a non-histamine response to the drug likely cytokine or complement pathway.
- We did see a difference with premedication for GI symptoms and fever but the numbers overall are very low.
- Although not statistically significant we did see a trend toward lower reactions with doses given with steroids. This makes sense for reactions caused by cytokines etc to dampen the immune response.

Demographics

Variable	**No-PM**	**PM**	***p* Value**
Total *n (%)*	57 (45.6)	68 (54.4)	
Age at diagnosis, years *mean (SD)*	6.9 (4.8)	6.9 (4.9)	0.984
Sex *n (%)*			0.578
Male	29 (50.9)	38 (55.9)	
Female	28 (49.1)	30 (44.1)	
Risk *n (%)*			0.173
Standard Risk	26 (45.6)	24 (35.3)	
High Risk	31 (54.4)	44 (64.7)	
Number of pegaspargase doses per patient *mean (SD)*	3.9 (2.2)	4.3 (2.3)	
Reactions *n (%)*	13 (22)	15 (22)	0.920

Reaction severity

Adverse Outcome Category	**No-PM (%)**	**PM (%)**	*Total*
No Reaction	46 (46.5%)	55 (54.4%)	101
Mild Reaction	3 (60.0%)	2 (40.0%)	5
Moderate Reaction	8 (42.1%)	11 (57.9%)	19
Total	57	68	125

Types of Symptoms

Reaction Symptom	Flushing	Rash	GI Reaction	Fever/ Chills	Respiratory Reaction	Other
Incidence						
No-PM	3 (50.0%)	7 (53.8%)	7 (77.8%)	2 (100%)	3 (42.9%)	7 (50.0%)
PM	3 (50.0%)	6 (46.2%)	2 (22.2%)	0 (0.00%)	4 (57.1%)	7 (50.0%)
Total	6	13	9	2	7	14

Effect of Pre-Meds on Reaction Incidence per dose

PM PRIOR TO DOSE (Y/N)	NO REACTION	REACTION	PEARSON CHI-SQUARED STATISTIC	P VALUE
Y n (%)	241 (53.6)	15 (3.3)	0.134	0.714
N n (%)	181 (40.2)	13 (2.9)		

Effect of Steroid on Reaction Incidence per dose

Steroid Prior to Dose (Y/N)	No Reaction	Reaction	Pearson Chi-Squared Statistic	p Value
Y n (%)	239 (53.1)	11 (2.4)	3.2	0.074
N n (%)	183 (40.7)	17 (3.8)		

Silent inactivation, desensitization and switches to Erwinia for Maritime patients: 2015-2024

- No silent inactivation in the patients we have asparaginase levels recorded:
  - Patients maintain their asparaginase levels without clinical reaction.

- 15 patients were switched to Erwinia 9/15 without premeds and 6/15 with premeds. We have successfully desensitized 7 patients which accounts for the lower number of patients switched to Erwinia in the premed group.
- We had 8 patients deactivate with a clinical reaction 5/8 received premedication and 3/8 did not. We do not have consistent levels on patients prior to 2021 which may account for the lower number of reported deactivating patients in the non-premedication group.

United States allergic reaction/premedication experience with CalPEG use 2021 to date

- Outside of clinical trials centers are seeing more allergic reaction with calPEG likely due to the change in the linker/bonds with polyethylene glycol.
- They also report no significant difference in number of reactions with premedication.
- CalPEG was designed to reduce reactions by way preventing the escape of asparaginase from the polyethylene glycol web.
- As asparaginase is not the cause of reaction in the large majority of patients but rather the polyethylene glycol we do not see a reduction in reactions with calPEG infact we see more due to the reactivity of tightly bonded PEG.
- We should however in theory see less deactivations CalPEG as the asparaginase is more protected (1731: SI PEG-asp (4%) and CalPEG (1%).
- The manufacturer (Servier) does recommend premedication with antihistamine, antipyretic, antiemetic +/- steroid. In communication with Servier they do not have any data to support this recommendation.

TABLE 4 Summary of existing data for efficacy of premedication to prevent pegaspargase hypersensitivity reactions (HSR).

References	Patients* (n) Population/Age (years)	Intervention	Outcome	Reduction in HSR from UPM
Cooper et al.[38]	Without UPM: 122 With UPM: 68 Total: 177 (patient overlap) Setting: Single-Institution Population: Pediatric/AYA Age: Mean 9.1 (0.3–24.9)*	• Diphenhydramine • H2-receptor blocker • Hydrocortisone (rechallenge for prior acute reaction)	*Proportion with ERW substitution* • Without UPM: 17.2% • With UPM: 7.4% • RR 0.427 for UPM ($p = .028$) *Proportion with HSR* ("clinically significant", CTCAE v.4.03) • Without UPM: 17.2% • With UPM: 5.9% • RR 0.342 for UPM ($p = .017$)	• Yes
Stock et al.	Without UPM: NR With UPM: NR Total: 295 total Setting: Consortia trial Population: AYA Age: Median 24 (17–39)	• Acetaminophen • Hydrocortisone • diphenhydramine	*Proportion with HSR (CTCAE 3.0 Grade ≥3)* • Without UPM: 10% • With UPM: 4% • No formal statistical analysis	• Yes
Losasso et al.	Without UPM: 42 With UPM (all doses): 34 Total: 76 Setting: Single-Institution Population: Pediatric/AYA Age: NR (1–29)	• Acetaminophen • Diphenhydramine • Methylprednisolone	*Proportion with HSR (CTCAE 4.0 Grade ≥ 3)* • Without UPM: 17% • With UPM: 12% • $p = .55$[b]	• No
Hughes et al.	Without UPM: 121 With UPM: 219 Period 2: 94 Period 3: 125 Total: 277 (patient overlap) Setting: Single-Institution Population: Pediatric Age: NR	*Period 1* • Without UPM *Period 2* • Diphenhydramine • Ranitidine *Period 3* • Diphenhydramine • H2-receptor blocker • Hydrocortisone • Saline piggyback	*Proportion with HSR (Grade NR)* • Period 1: 12.4% • Period 2: 18.1% • Period 3: 12.8% Difference among time periods ($p = .56$)	• No
Babcock et al.	Without UPM: 50 doses UPM: 80 doses Total: 38 patients Setting: Single-Institution Population: Pediatric Age: Median 9 (IQR 4–14)	• Antihistamine • H2-receptor blocker • Corticosteroid	*Proportion with HSR (% doses, Grade NR)* • Without UPM: 6.4% • With UPM: 5.3% • $p = 1.0$	• No
Fajardo et al.	Without UPM: 49 With UPM: 58 Total: 107 Setting: Single-Institution Population: Pediatric Age: Median 6.4 (0.4–16.9)	• Diphenhydramine • H2-receptor blocker	*Proportion with HSR (Grade NR)* • Without UMP: 27% • With UPM: 17% • $p = .25$	• No
Menig et al. (current report)	*CHLA Cohort* Without UPM: 213 With UPM: 69 Total: 282 Setting: Single-Institution Population: Pediatric Age: Mean 8.4 ± 5.4 *SCH Cohort* Without UPM: 58 UPM: 70 Total: 128 Setting: Single-Institution Population: Pediatric Age: Mean 7.6 ± 5.4	*CHLA Cohort* • Diphenhydramine • Hydrocortisone • H2-recpeptor blocker *SCH Cohort* • Diphenhydramine • Hydrocortisone	*Proportion with Grade ≥3 HSR (CTCAE v5.0)* *CHLA Cohort* • Without UPM: 19% • With UPM: 23% • $p = .487$ *SCH Cohort* • Without UPM: 17% • With UPM: 19% • $p = .845$	• No

Things to consider as we switch to CalPEG

Toxicity monitoring with CalPEG

- Change from 3 weeks to 4 weeks for monitoring for pancreatitis, hyperglycemia.
- Be aware that venous thromboembolism can present more frequently and later up to 6 weeks after administration.
- Higher rates of liver toxicity in older and obese children.
- T cell patients may have more pancreatitis and VTE.
- Higher rates of infusion related reactions.

Recommendations for CalPEG administration: Premedication

- One dose of hydrocortisone + ondansetron.
  - Reason: Stop acetaminophen and cetirizine as these medications do not change outcome to patients and we do NOT want to give drugs that don’t change outcome.
  - Hydrocortisone/steroid acts to dampen the immune system including a fever response from an allergic reaction.

Recommendations for CalPEG administration: Rate of infusion

- Change to a *slow step wise rate increase* over the 2 hours.
  - Reason: most IRR (to PEG) occur in first few minutes of the infusion, so we need to slow it down even more at the beginning or dilute the solution (this is very time consuming for pharmacies). Patients who deactivate asparaginase react later into the infusion regardless of rate (these are few patients).
- Continue to run with a fluid bolus
  - Reason: to dilute the drug as it reaches the bloodstream.

Recommendations for CalPEG administration: Serum asparaginase levels

- Continue to draw a day 1 level with the first dose.
  - Reason: to assist is early switch if needed to recombinant Erwinia (Rylaze) during induction.
- Change to measure levels at day 14 with Calaspargase.
  - Reason: We are measuring asparagine depletion by proxy and the gold standard in ALL is 14 days of adequate depletion (SAA trough level >0.1u/mL) regardless of the prolonged half-life of calaspargase.
- We will continue to measure levels on all patients with all doses of calaspargase.
  - Reason: We will continue to premedicate with steroid.

CalPEG chemotherapy orders

- For four weeks following calaspargase pegol: Weekly monitor blood pressure and urine or blood for glucose.
- Monitor for symptoms of pancreatitis (i.e., abdominal tenderness and/or mid-epigastric pain with vomiting).
- Monitor for symptoms of hyperammonemia (i.e., headache, vomiting, confusion, changes in consciousness, ataxia, seizures, and/or gait abnormalities)
- Asparaginase level 14 days following injection on Day 18 _____(date)

- **Premedication to be given 60 minutes prior to calaspargase pegol infusion:**
- Administer hydrocortisone 3 mg/kg/dose (max 100 mg/dose) = _____ mg IV once (Do not give if dexamethasone or prednisone pulse due as part of chemotherapy orders)
- Ondansetron 0.1 - 0.2 mg/kg/dose = _____ mg (max 8 mg) IV/PO once 1 hour prior to infusion

- **Calaspargase pegol** 2500 Units/m^2/dose = _____ Units in 100 mL bag of 0.9% NaCl IV over 2 hours as per guidance below:
- 150 units/m^2/hour = _____ x 10 minutes
- 300 units/m^2/hour = _____ x 20 minutes
- 750 units/m^2/hour = _____ x 30 minutes
- 2000 units/m^2/hour = _____ x 60 minutes
- Day 4_____ ❑ IWK ❑ home
-
- Run IV 0.9% NaCl at 75 mL/m^2/hour = _____ mL/hr during **calaspargase pegol** infusion.

Questions ?