CANADIAN IMMUNIZATION RESEARCH NETWORK

Prospective evaluation of diphtheria-tetanus-acellular pertussis-polio-*Haemophilus influenzae* type b (DTaP-IPV-Hib) and pneumococcal vaccination in children who completed chemotherapy for acute lymphocytic leukemia: A CIRN study

KA Top, B Tapiero, W Vaudry, JM Pernica, A Pham-Huy, S Gantt, SR Rassekh, V Price, L Sung, SK Morris, A McConnell, E Rubin, R Chawla, T Jadavji, SA Halperin

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Canadian Center for Vaccinology
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Background & Rationale

- Acute lymphocytic leukemia is the most common malignancy in children
- Children with ALL are at high risk of vaccine-preventable infections including invasive pneumococcal disease
- Several studies have reported waning of vaccine immunity post-chemotherapy
- Wide variation in practice between centres (2014):
  - 5/11 centres give booster doses of DTaP/Tdap, MMR/V, Hep B to all patients or based on titres
  - 4 centres also administer PCV
  - 5 centres do not give any additional vaccinations

Top et al, Hum Vaccin Immunother, 2016

Objectives

- To estimate the frequency of medically-attended AEFI in children immunized with DTaP-IPV-Hib and PCV13 + PPV23 6-12 months after completing treatment for ALL.

- To assess short and long-term immune responses to PCV13 + PPV23 in children immunized 6-12 months after completing chemotherapy for ALL.

Study Design

- Prospective, multi-centre (open label) trial of DTaP-IPV-Hib and PCV13+PPV23 immunization in children who completed chemotherapy for ALL
- Inclusion criteria:
  - Diagnosed with standard-risk, high-risk or very-high risk ALL
  - Age at diagnosis: >1 year of age
  - Completed chemotherapy 4 to 12 months prior to enrollment
  - No receipt of pneumococcal or tetanus-containing vaccines since completing chemotherapy
- Exclusion criteria:
  - Infant ALL, relapsed ALL, history of underlying primary immunodeficiency, stem cell transplant, recent blood products, hypersensitivity to study vaccine(s)

Study Procedures

- Baseline evaluation:
  - CBC + differential, T and B cell subsets, IgA, IgG, IgM
  - Pneumococcal serotype-specific IgGs (*1, 3, 4*, **6B, 7F, 9V**, 11A, 12F, **14**, 15B, **18C, 19F, 23F**, 33F), tetanus, pertussis toxin, varicella IgGs
- Vaccinations:
  - Visit 1: Administered DTaP-IPV-Hib and PCV13
  - Visit 2 (2 months post-V1): Administered PPV23
- Immunogenicity and safety evaluation:
  - Measured pneumococcal, tetanus and pertussis titers at 2 and 12-15 months post-vaccination
  - Captured adverse events through telephone interviews at 8 and 30 days post-immunization

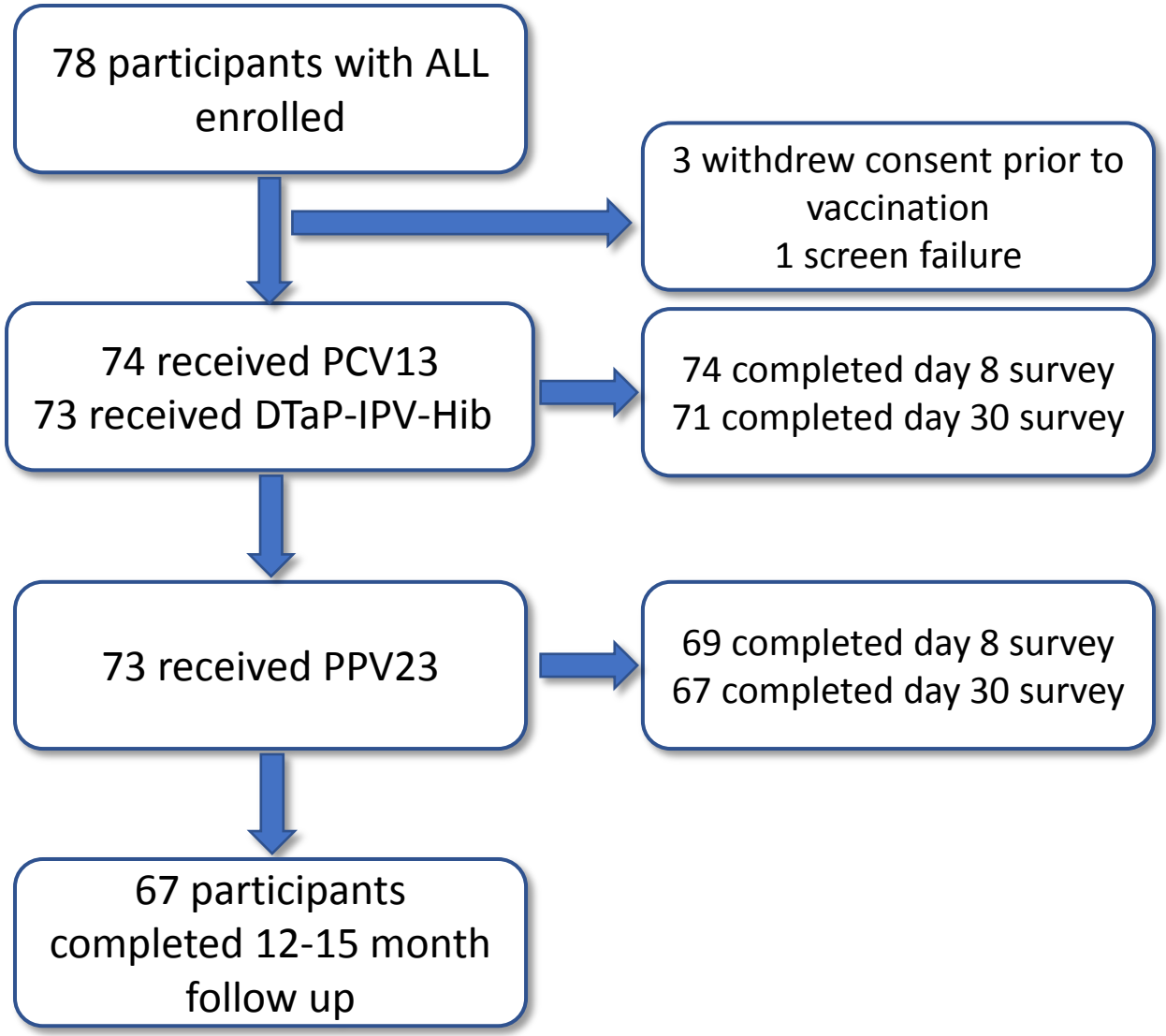
Outcomes and Analysis

- Frequency of medically attended adverse events
- Serotype-specific IgG ≥ 0.35 μg/ml against pneumococcal serotypes at 0, 2 and 12-15 months post-PCV13

- Descriptive analysis conducted using SAS v 9.4.

- Ethics: The study was REB approved at all participating sites.

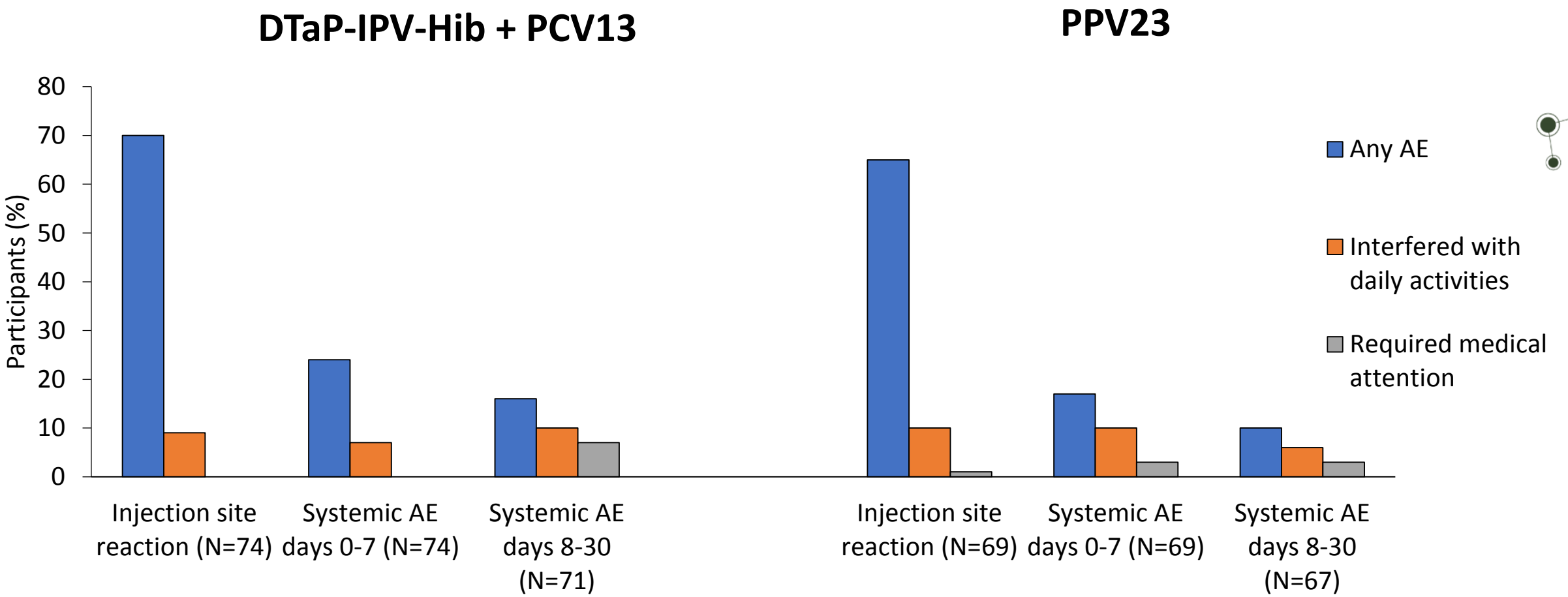
Participant flow chart



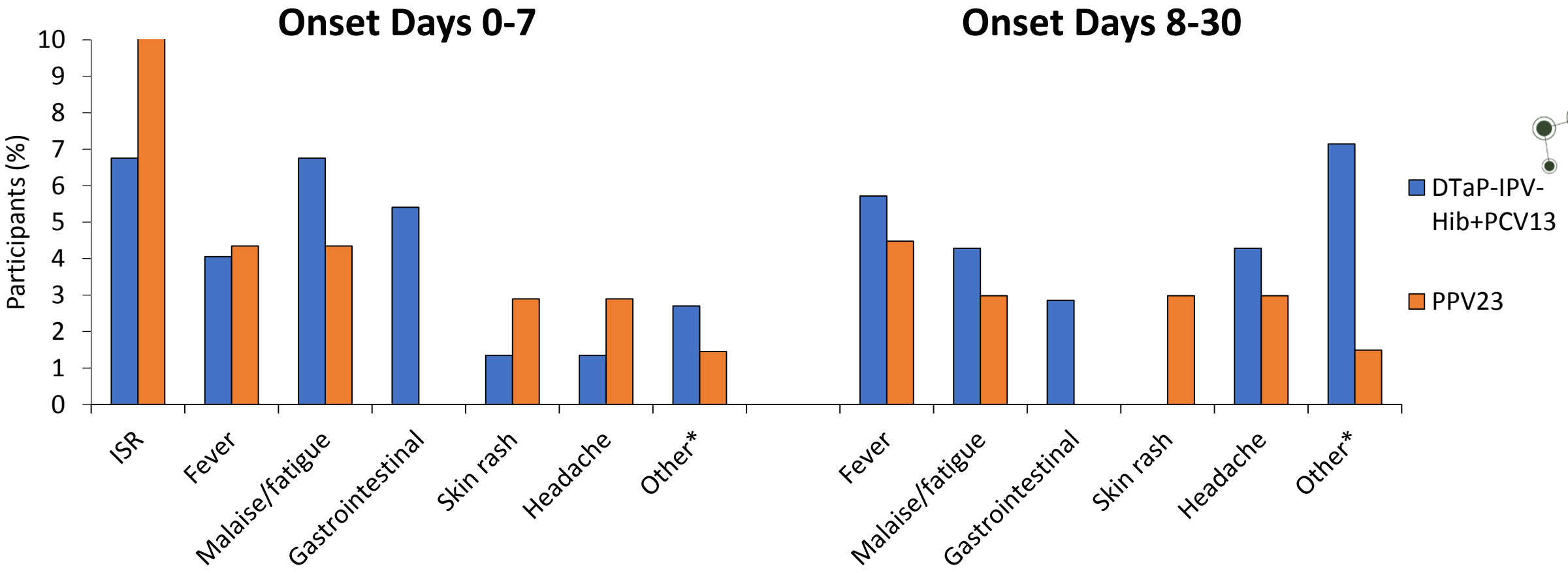
Participant Characteristics

	Participants (N=74)	
Age at ALL diagnosis, yrs, median, IQR	5.0	3.0-8.0
Age at first study visit, yrs, median, IQR	8.1	6.1-11.9
	n	**%**
Sex		
Male	37	50
Female	37	50
Province of residence		
BC	13	18
AB	10	13
SK	2	3
ON	13	18
QC	24	32
NS/NB	12	16
Disease risk category		
Standard risk	40	54
High risk	27	36
Very high risk	6	9
Previous PCV doses		
0	22	31
1-2	7	10
≥3	43	60

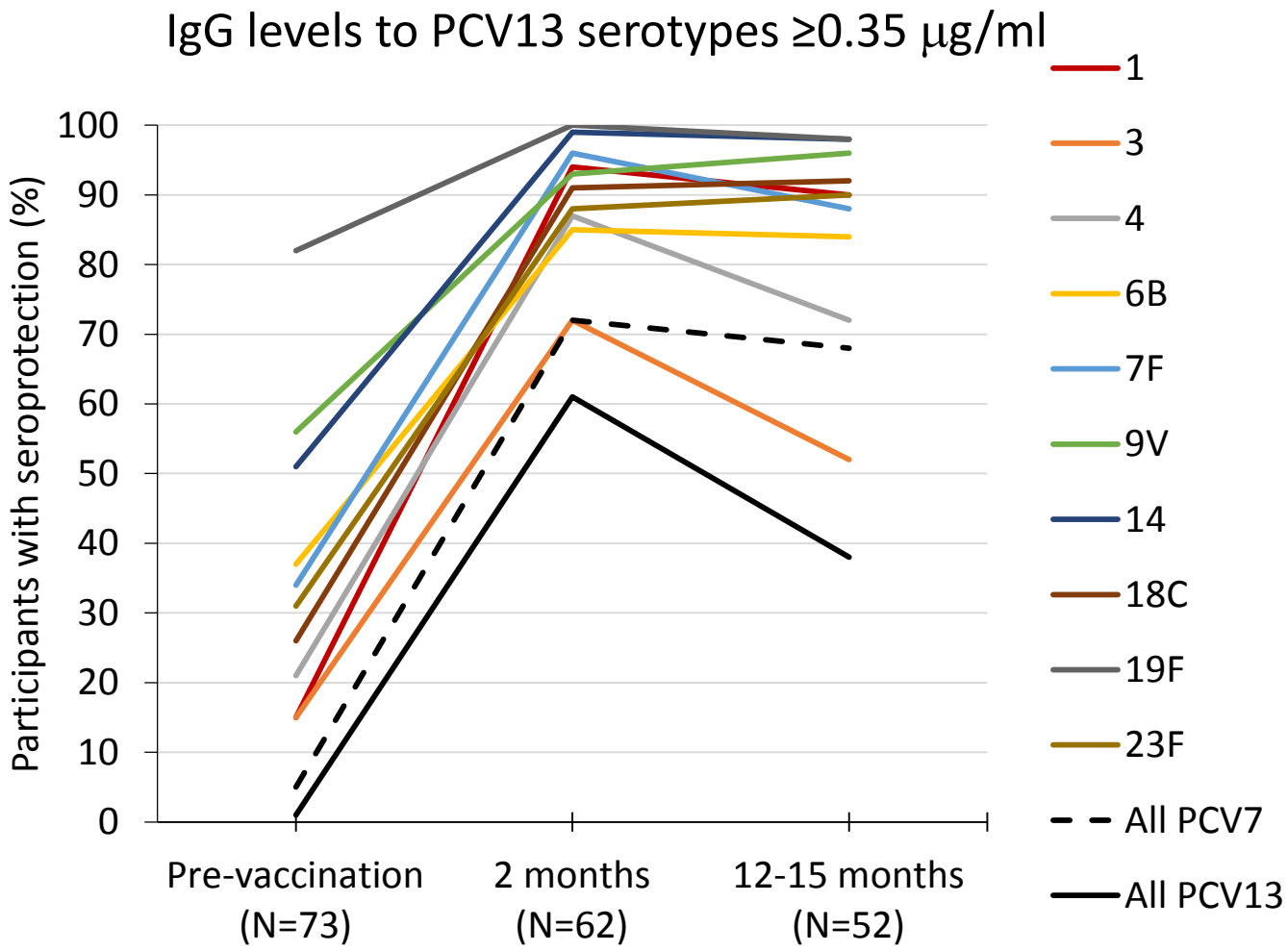
Adverse events following DTaP-IPV-Hib + PCV13 and PPV23

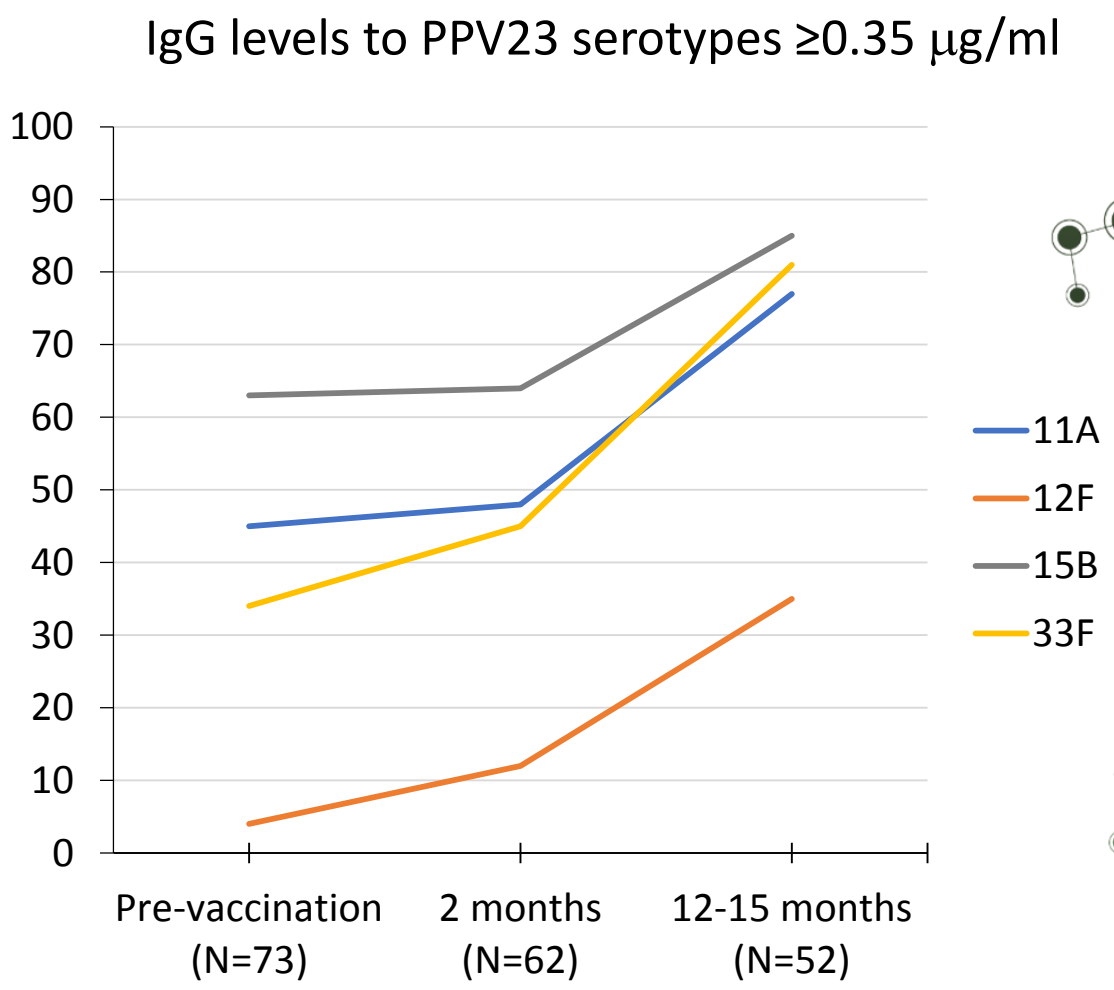


Severe adverse events reported on days 0-7 and 8-30



Immune responses to PCV13 + PPV23 (Preliminary)





Conclusions

- We implemented a post-chemotherapy immunization protocol at Canadian pediatric oncology centres
- Adverse events requiring medical attention were common (6.8%) but none were serious and most were not causally related to vaccination
- Children with ALL appeared to have good serologic responses to PCV13 and PPV23 vaccination up to 12-15 months post-vaccination
- Analyses of responses to DTaP and waning immunity of children with ALL versus age-matched controls is ongoing
- The results will inform immunization guidelines for children with ALL

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Thank you!

Questions?

Extra slides

Adverse events requiring medical attention

Participant	Vaccine(s)	Onset	Symptoms	Type of healthcare visit	Diagnosis	Treatment	Causal association to vaccination
02-019	DTaP-IPV-Hib +PCV13	days 2-3	Skin rash	Outpatient	Erythema multiforme attributed to co-trimoxazole	None	Indeterminate
02-003	DTaP-IPV-Hib +PCV13	days 15-21		Outpatient	Scarlet fever	Cephalexin	Inconsistent
02-010	DTaP-IPV-Hib +PCV13	days 22-30	URI symptoms	Outpatient	Viral URI	Acetaminophen	Inconsistent
02-016	DTaP-IPV-Hib +PCV13	days 8-30	URI symptoms, cough	Outpatient	Upper respiratory infection	None	Inconsistent
03-004	PPV23	days 15-21	Vomiting, abdominal pain, headache, urticarial rash	Outpatient	Allergic reaction	Antihistamine, topical corticosteroids	Inconsistent
10-001	DTaP-IPV-Hib +PCV13	days 15-21		Outpatient	Acute otitis media + pharyngitis	Antibiotics	Inconsistent
10-007	DTaP-IPV-Hib +PCV13	days 22-30	Fever	Outpatient	None	None	Inconsistent
	PPV23	day 0-1	Skin rash on left shoulder	Outpatient	Skin & soft tissue infection	Cephalexin	Inconsistent (vaccine given in R arm)
	PPV23	days 22-30		Outpatient	Viral URI	No	Inconsistent
08-008	PPV23	days 4-7	Injection site reaction, maculopapular rash	Emergency	None	Topical corticosteroids	ISR – consistent, rash - Indeterminate