Laboratory-Confirmed Influenza in Vaccinated Pediatric Hematopoietic Cell Transplant Recipients

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Introduction

Influenza is associated with severe morbidity and mortality among hematopoietic cell transplant (HCT) recipients.

Aim

To compare demographic and clinical characteristics of influenza-positive vs. influenza-negative HCT recipients among a cohort of patients participating in an ongoing influenza vaccine trial.

Methods

Study Participants

- Children 3-17 years
- 3-35 months post-HCT

Part of phase-II, nine-center, randomized-controlled, double-blind immunogenicity and safety clinical trial comparing two doses of either high-dose trivalent or standard-dose quadrivalent inactivated influenza vaccines.

Subjects already enrolled in the preceding study-year (repeaters) were given the option to re-enroll in the following study-year and were considered distinct cases.

Active Influenza Surveillance and Sample collection

During the three-year study period (2016-19), active influenza surveillance was conducted during site-specific influenza seasons and mid-turbinate nasal swabs (MTS) were collected based on influenza-like illness (ILI); and if study visits occurred during influenza season, MTS were also collected regardless of symptoms.

In study year three only, MTS were collected for ILI outside influenza-season.

Retrospective chart reviews were also performed to document lab-confirmed influenza illnesses.

Methods

Sample Testing

Research MTS were tested for influenza using Luminex NxTAG RPP® plus influenza B lineage typing and influenza C (study-year one only) by singleplex PCR.

Results

- 218 HCT recipients were enrolled and received at least one influenza vaccine
  - 48 (22%) were repeaters
- 53% were male and 68% were white
- Median age: 11 years [range:3-18.9]
- Median time post-HCT: 10.9 months
  - 118 (54%) were 3-11 months post-HCT
- 100 (46%) had a history of graft versus host disease(GVHD)

Table 1. *Influenza-positive vs. Influenza-negative Subjects*

Baseline demographics and clinical characteristics	Influenza-positive n=30	Influenza-negative n=188	P-value
Age, median [IQR], years	9 [6-15]	11.6 [7.2-14.4]	0.4
Male	12 (40%)	104 (55%)	0.1
White	20 (67%)	129 (69%)	0.8
Not Hispanic or Latino	26 (87%)	142 (76%)	0.2
Months post-HCT at enrollment, median [IQR]	10.3 [4.1-27.8]	10.9 [4.9-19]	0.7
First vaccine received within 3-11 months post-HCT	18 (60%)	100 (53%)	0.49
Malignant primary disease as indication for HCT	17 (57%)	106 (56%)	0.98
GVHD at enrollment			
History of any GVHD at enrollment	**22/30 (73%)**	**78/184 (42%)**	**0.002**
History of ongoing GVHD at enrollment	**8/16 (50%)**	**19/128 (15%)**	**0.001**
History of resolved GVHD at enrollment	**14/22 (64%)**	**59/169 (35%)**	**0.009**

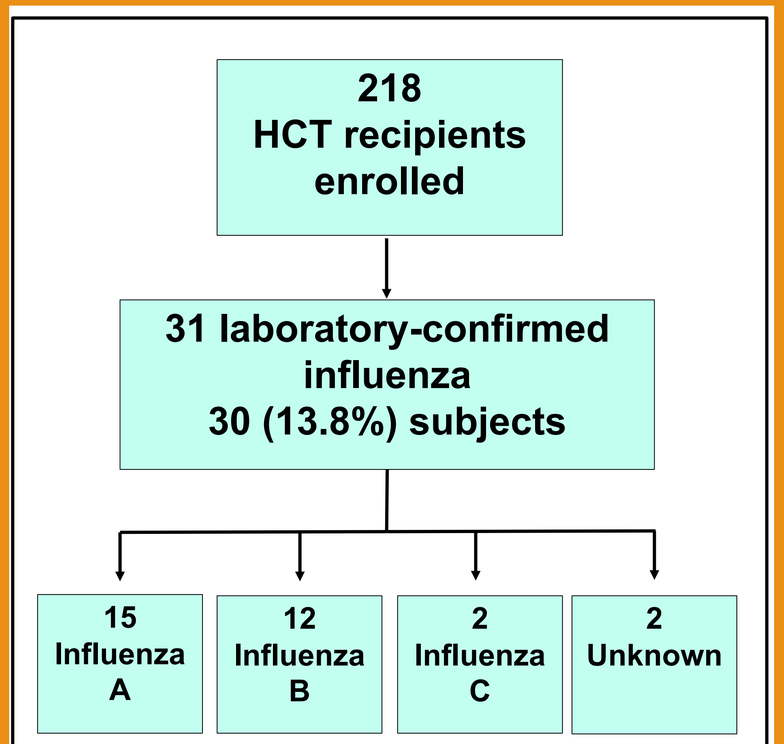

Figure 1. *Total number and types of laboratory-confirmed influenza*

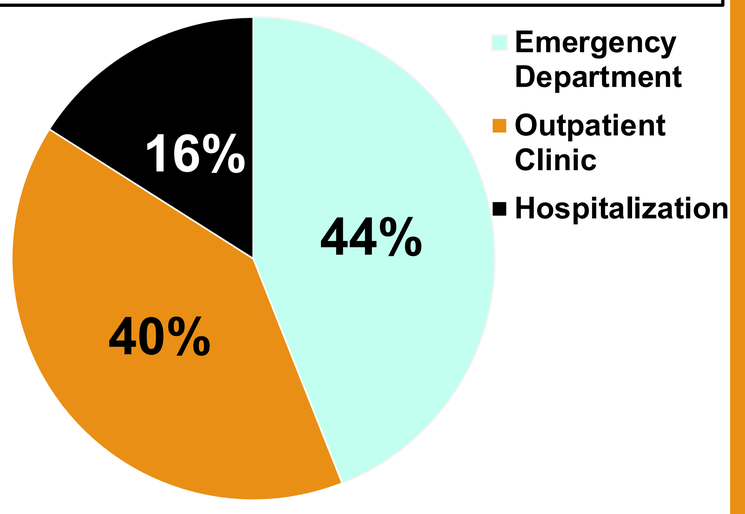

Figure 2. *Clinical setting distribution of laboratory-confirmed influenza*

Conclusions

In our cohort, 14% of pediatric HCT subjects had influenza illness despite receiving influenza vaccination.

Most cases were mild and managed in the outpatient clinic and emergency department.

Influenza-positive subjects were more likely to have a history of any GVHD.

The vaccine assignment in this cohort remains blinded.

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