Figure 1 Unadjusted time to virologic failure

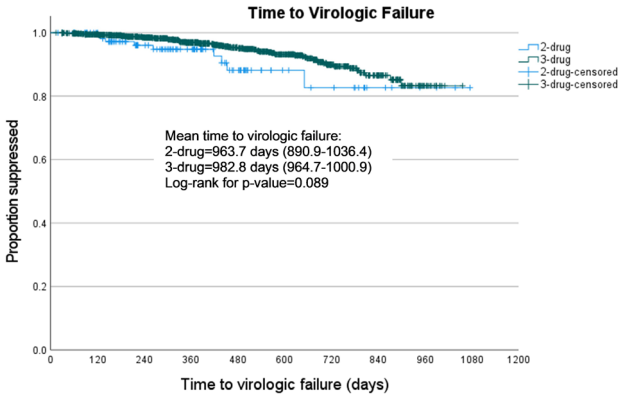

Table 2 Risk of virologic failure

Treatment-experienced suppressed at index	A: 2-drug n=132		B: 3-drug n=1536		P-value
	n	%	n	%	A vs B
Patients with virologic failure	9	7%	65	4%	0.166
Cox Proportional Hazards analysis: Virologic failure risk			**HR 2-drug vs 3-drug**	**CI**	**A vs B**
Unadjusted risk of virologic failure			1.8	0.9-3.7	0.094
Risk of virologic failure adjusted for race, gender, age group, and eGFR at index			2.2	1.1-4.5	**0.032**

Conclusion. This early evaluation showed higher risk of virologic failure among virologically suppressed pts who switched to 2DR vs 3DR STRs after adjusting for differences in baseline characteristics. Future analysis is warranted using a larger sample of 2DR pts with additional adjustment for prior regimen failure.

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78. Non-Invasive Prediction of Invasive Fungal Infection by Plasma-Based Microbial Cell-Free DNA Next-Generation Sequencing (mcfDNA NGS) in Pediatric Patients with Relapsed or Refractory Leukemia

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Session: O-17. Hot Topics in Pediatric Viral and Fungal Infections

Background. Diagnosis of invasive fungal infections (IFIs), a life-threatening complication of cancer therapy or hematopoietic cell transplantation (HCT) can be challenging, and IFI has poor outcomes. Prediction or early non-invasive diagnosis of IFI in high-risk hosts *before* onset of symptoms could reduce morbidity and mortality.

Because non-invasive plasma mcfDNA NGS can detect invasive fungal infections, and may predict bloodstream infections in immunocompromised patients, we hypothesized that mcfDNA NGS might also predict invasive fungal infection before clinical presentation.

Methods. In a prospective study, serial remnant plasma samples were collected from pediatric patients undergoing treatment for relapsed or refractory leukemia. IFI events were classified according to EORTC criteria by 2 independent experts, and episodes empirically treated for suspected IFI, but not meeting 'possible' criteria were classified as 'suspected'. All samples collected within 30 days before clinical diagnosis of non-fungemic IFI were tested for fungal DNA by mcfDNA NGS using a research-use only assay by Karius, Inc. optimized for fungi; because of overlapping clinical syndromes, non-fungal DNA was not considered in this study.

Results. There were 15 episodes of suspected IFI in 14 participants with ≥1 sample available from either diagnostic (within 1 day of diagnosis) or predictive (2 to 30 days prior to diagnosis) periods (5 "suspected", and 4 probable and 6 proven by EORTC definitions).

Of 10 probable or proven IFIs, 6 (60%) had a relevant fungal pathogen identified mcfDNA NGS at diagnosis. In each of these cases the fungal DNA was also detectable prior to clinical onset of IFI (Range 2 to 41 days; Figure 1). In an additional case, manual review of sequence data identified the fungal DNA at diagnosis and during the prior month. Of 5 "suspected" IFI episodes, all were determined by expert review as not representing fungal infection; fungal DNA was identified by mcfDNA NGS in 2/54 (3.7%) of samples from these episodes.

Table 1. Characteristics of Invasive Fungal Infections

Characteristics of Invasive Fungal Infections					
Episode	Site	Causative Organism	Diagnosis mcfDNA NGS+	Predictive mcfDNA NGS+	Prediction Day
Proven					
PQ109 #1	Paranasal sinus	*Alternaria alternata*	Yes	Yes	-25
PQ118	Paranasal sinus	*Mucor velutinosus*	Yes	Yes	-10
PQ120	Hard palate	*Aspergillus flavus/oryzae*	Yes	Yes	-21
PQ206	Paranasal sinus	*Fusarium sp*	Yes	Yes	-2
PQ181	Paranasal sinus	*Curvularia sp.*	No*	No*	
PQ178	Soft tissue	*Curvularia sp.*	No*	No	
Probable					
PQ107	Disseminated	*Histoplasma capsulatum*	Yes	Yes	-41
PQ123	Pulmonary	*Aspergillus flavus/oryzae*	Yes	Yes	-28
PQ109 #2	Pulmonary	*Aspergillus sp.*	No	No	
PQ175	Pulmonary	*Aspergillus sp.*	No	No	
"Suspected"					
PQ124	Pulmonary	Unknown	No	No	
PQ147	Pulmonary	Unknown	No	No	
PQ149	Pulmonary	Unknown	No	No	
PQ174	Pulmonary	Unknown	No	No	
PQ180	Pulmonary	Unknown	No	No	

Diagnosis mcfDNA NGS+, Positive test ≤1 day of diagnosis; Predictive mcfDNA NGS+, Positive test >1 day *before* diagnosis; Prediction Day, Day specific fungal DNA first identified by mcfDNA NGS; *The fungal DNA was identified only by manual review of sequence data.

Conclusion. mcfDNA NGS can identify fungal pathogen DNA before clinical onset of IFI, so might predict IFI in immunocompromised hosts, and may help differentiate fungal infection from other etiologies of lung nodules or infiltrates.

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79. Children with COVID-19 Demonstrate Distinct Serum Cytokines Profiles According to Clinical Presentations

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Session: O-17. Hot Topics in Pediatric Viral and Fungal Infections

Background. Almost 4 million children have tested positive for Coronavirus Disease 2019 (COVID-19) as of June 3 2021, representing 14% of all cases in USA. Children present with diverse clinical findings including the multisystem inflammatory syndrome in children (MIS-C). In this study, we measured serum cytokine concentrations in children with COVID-19 to identify differences in immune profiles according to clinical presentations.

Methods. A total of 133 children 0-21 years of age with COVID-19 were enrolled at Nationwide Children's Hospital, in Columbus, Ohio. Nasopharyngeal swab RT-PCR testing was used for SARS-CoV-2 detection and quantification. Clinical and laboratory information were obtained, and blood samples were collected for measurement of cytokines with a 92-plex inflammation assay (Olink). Normalized cytokine expression levels in patients were compared with serum samples from 66 pre-pandemic age-matched healthy controls.

Results. COVID-19 children included: 1) those identified by universal screening (n=47); 2) moderate disease (ward; n=48); 3) severe disease (PICU; n=20); 4) MIS-C (n=18). Children identified by universal screening were hospitalized for trauma, appendicitis or new onset diabetes among others. Children with symptomatic COVID-19 had significantly higher SARS-CoV-2 viral loads than children with MIS-C or those identified via universal screening. Concentrations of interferon (IFN) related cytokines (IFNg, CXCL9, CXCL10, CXCL11), interleukins (IL6, IL8, IL10, IL17A, IL18, IL24) and other inflammatory cytokines (TGF, TNF, VEGF, MCP, CD40) were significantly increased in children with acute COVID-19 and MIS-C compared with children identified by universal screening and healthy controls. These cytokines were positively correlated with C-reactive protein, D-dimer and disease severity in