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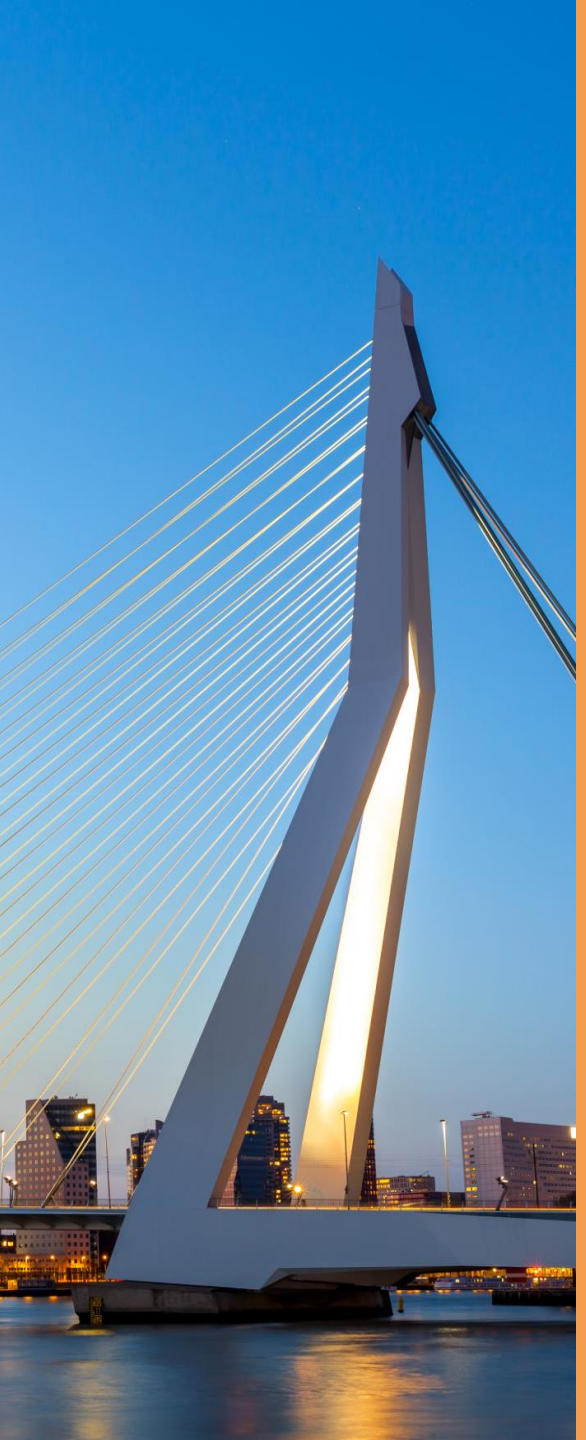


Malignancies and Lymphoproliferations in Children with Primary Immune Deficiency - A Single-Center Experience

Sibel Kaplan Sarikavak

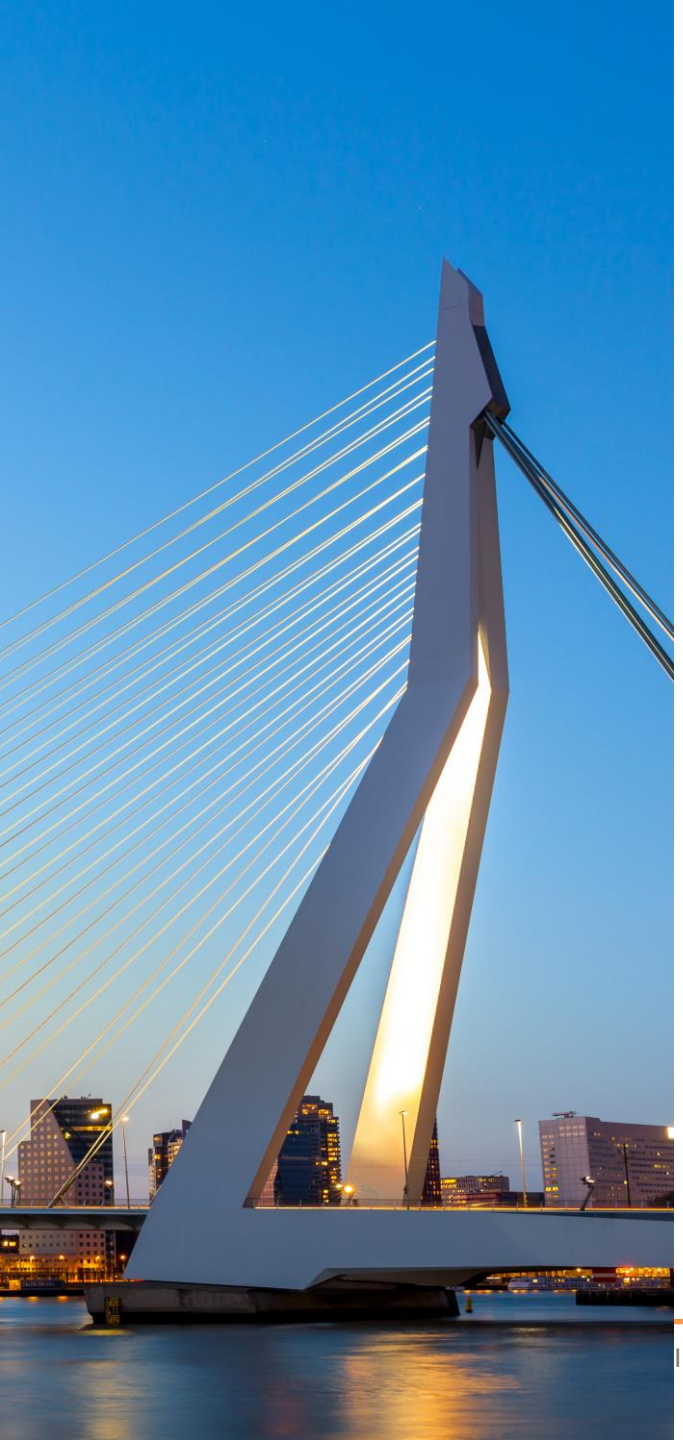
Poster Winners Session

11.10.2023

Introduction

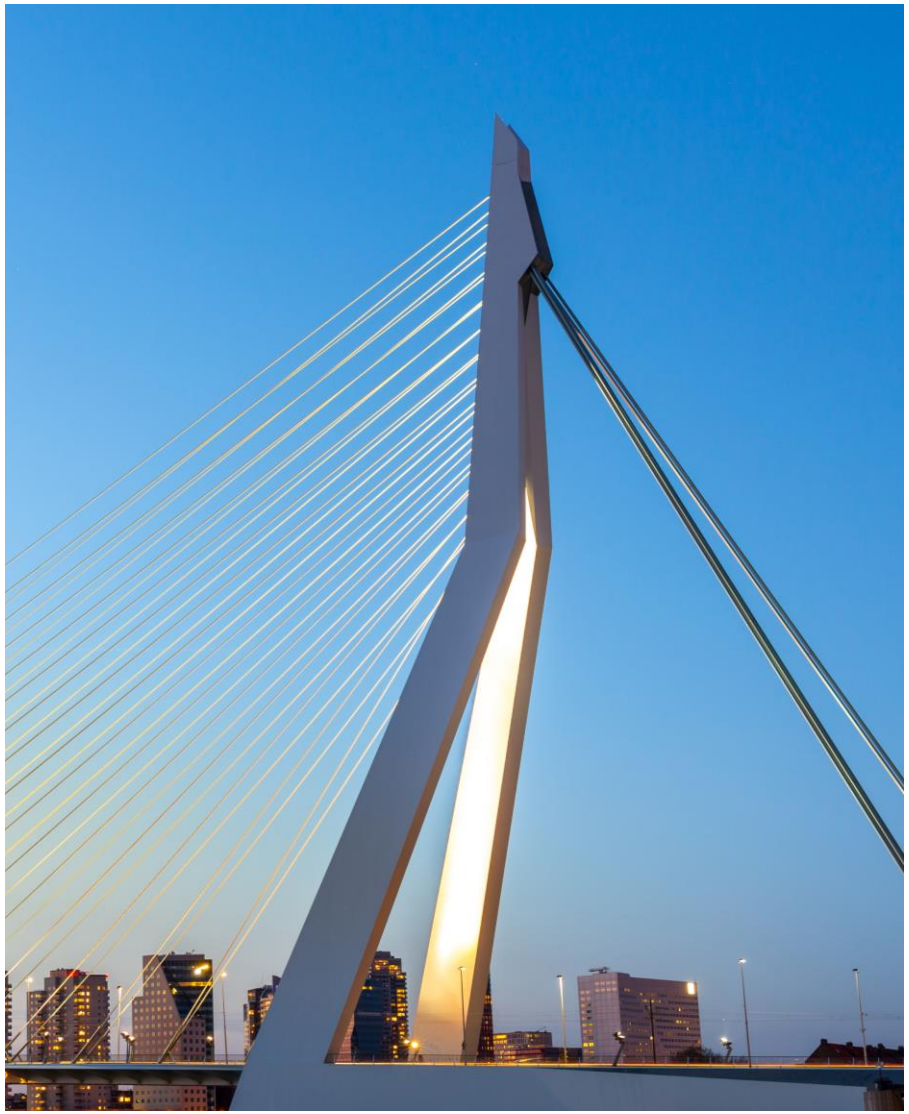
- Primary immune deficiencies (PID) are rare genetic disorders characterized by frequent infections, immune dysregulation, allergy, and malignancy.
- Malignancies occur more frequently and at an earlier age in PID and are the second most common cause of death in patients with PID.
- Benign lymphoproliferations are commonly observed in PIDs, and distinguishing it from malignancy is of great importance.

Jonkman-Berk BM, van den Berg JM, Ten Berge IJ, Bredius RG, Driessen GJ, Dalm VA, et al. Primary immunodeficiencies in the Netherlands: national patient data demonstrate the increased risk of malignancy. Clin Immunol. 2015;156(2):154-62.
Mortaz E, Tabarsi P, Mansouri D, Khosravi A, Garssen J, Velayati A, et al. Cancers Related to Immunodeficiencies: Update and Perspectives. Front Immunol. 2016;7:365.



- In patients with PID, malignancy is most commonly reported to be non-Hodgkin lymphoma, followed by Hodgkin lymphoma and leukemia.
- CVID and AT are the most common immunodeficiencies associated with malignancy.
- We aimed to evaluate the frequency of malignancy and benign lymphoproliferation in PID, the types of PID that cause malignancy/ benign lymphoproliferation, and their prognoses.

Tavakol M, Delavari S, Salami F, Ansari S, Rasouli SE, Chavoshzadeh Z, et al. Diversity of malignancies in patients with different types of inborn errors of immunity. Allergy Asthma Clin Immunol. 2022;18(1):106.
Mayor PC, Eng KH, Singel KL, Abrams SI, Odunsi K, Moysich KB, et al. Cancer in primary immunodeficiency diseases: Cancer incidence in the United States Immune Deficiency Network Registry. J Allergy Clin Immunol. 2018;141(3):1028-35.
Kiykim A, Eker N, Surekli O, Nain E, Kasap N, Aktürk H, et al. Malignancy and lymphoid proliferation in primary immune deficiencies; hard to define, hard to treat. Pediatr Blood Cancer. 2020;67(2):e28091.



Methods:

- Among the 550 patients monitored for PID at the Department of Pediatric Allergy-Immunology in Basaksehir Cam and Sakura City Hospital, 17 PID patients who developed malignancies and/or benign lymphoproliferation included in the study.

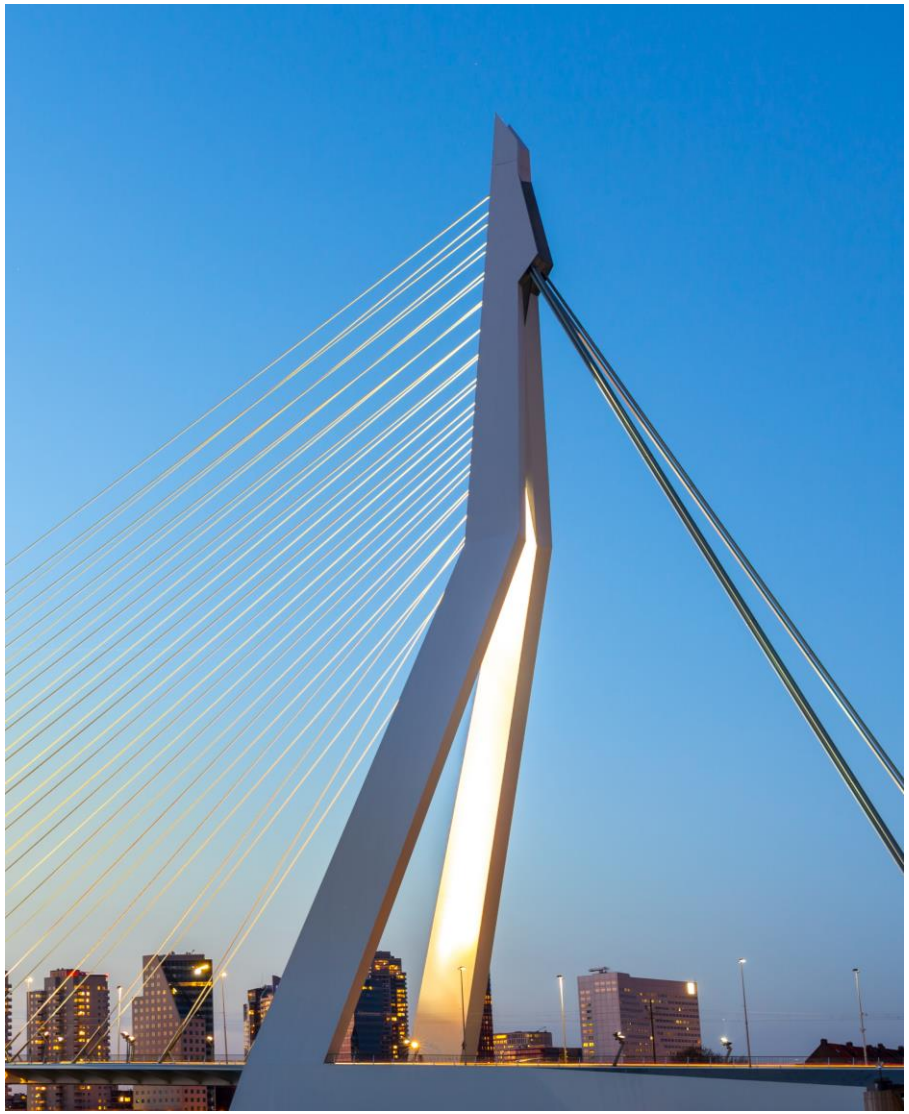
- The diagnoses of PID were made according to the classification of inborn errors of immunity by the International Union of Immunological Societies.

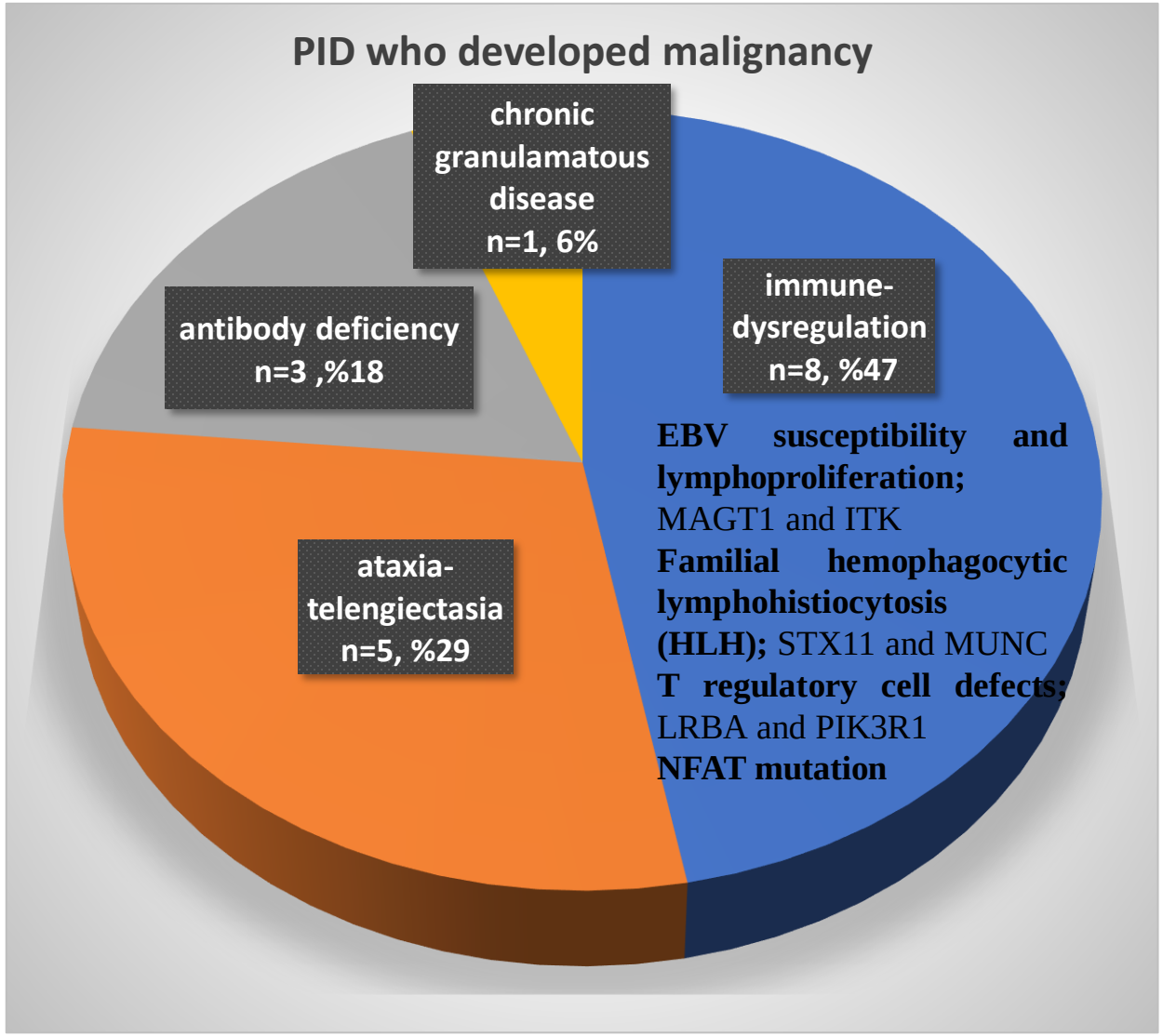
- Demographic information, symptoms, treatment protocols, and response to therapy were recorded.

Tangye SG, Al-Herz W, Bousfiha A, Cunningham-Rundles C, Franco JL, Holland SM, et al. Human Inborn Errors of Immunity: 2022 Update on the Classification from the International Union of Immunological Societies Expert Committee. J Clin Immunol. 2022;42(7):1473-507.

Results:

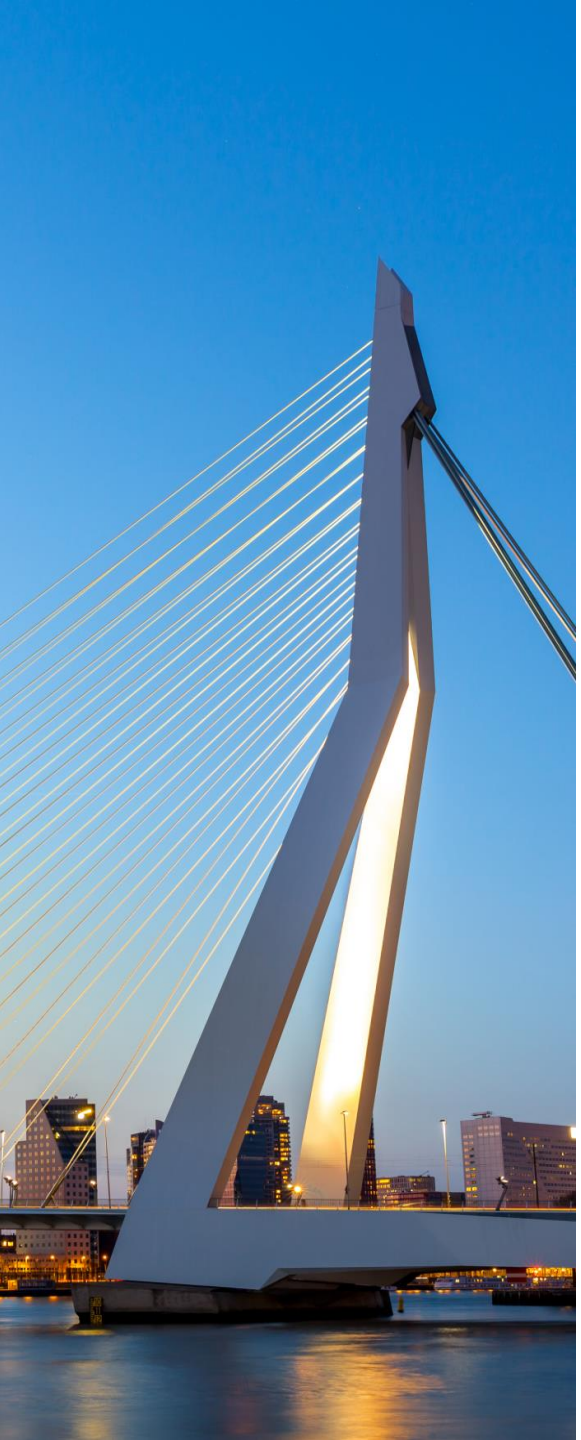
- The study involved 17 patients (3.0% of the total 550 patients) diagnosed with PID and malignancy and/or benign lymphoproliferation. Out of these 17 patients, 10 were male, and 7 were female.
- The mean age at the diagnosis of PID was 5.8 ± 3.8 years.
- The median age of patients at cancer diagnosis was 10 years (2-13 years), and the current median age of the patients was 13 years (2-20 years).



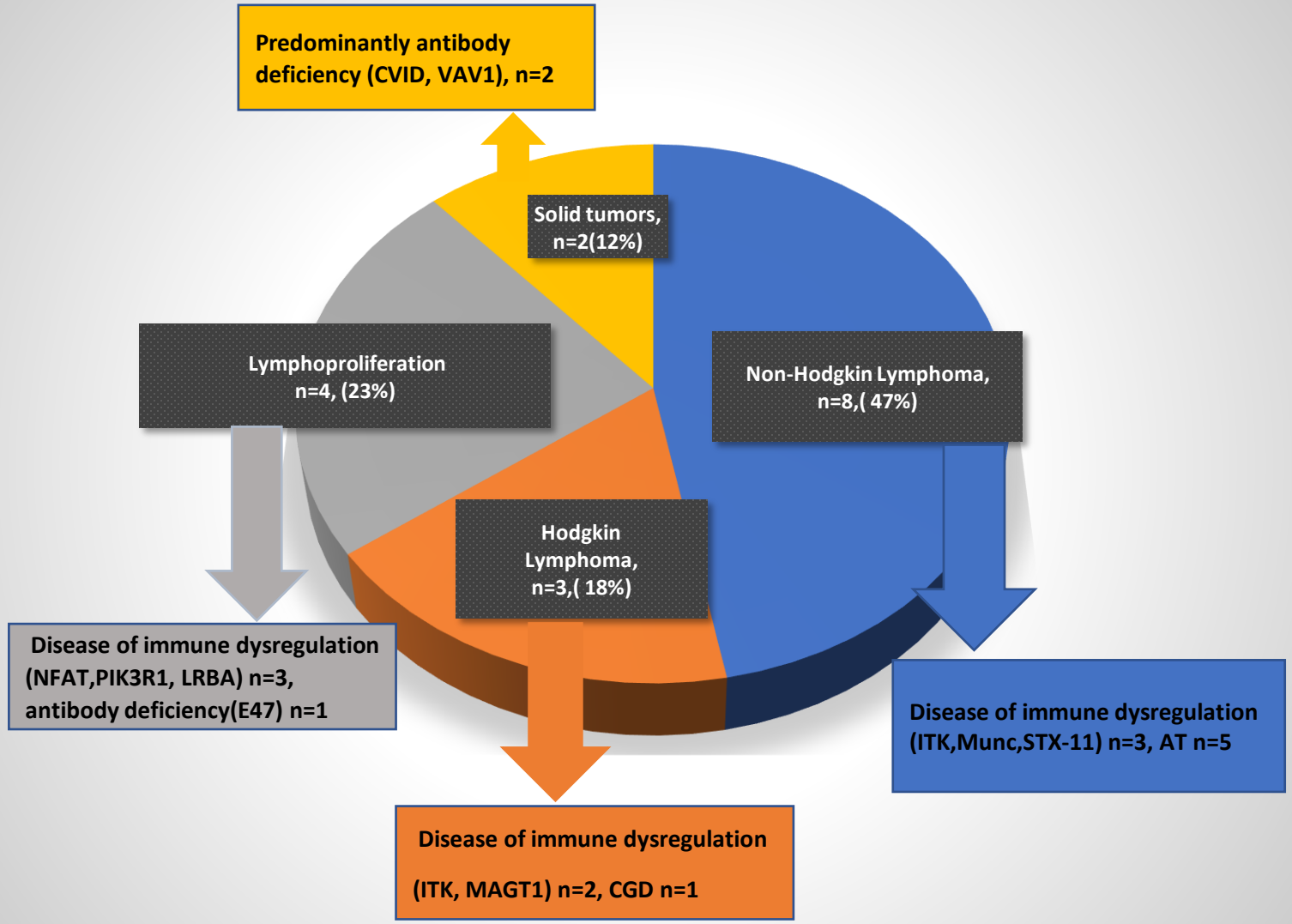

PID who developed malignancy
chronic granulamatous disease n=1, 6%
antibody deficiency n=3 ,%18
immune-dysregulation n=8, %47
ataxia-telengiectasia n=5, %29
EBV susceptibility and lymphoproliferation; MAGT1 and ITK
Familial hemophagocytic lymphohistiocytosis (HLH); STX11 and MUNC
T regulatory cell defects; LRBA and PIK3R1
NFAT mutation

At the time of malignancy/lymphoproliferation diagnosis

		Number(%)
Symptoms	fever	8 (47.0%)
	respiratory distress	7 (41.1%)
	weight loss	7 (41.1%)
	recurrent diarrhea	2 (18.1%)
Physical examination	**lymphadenopathy**	14 (82.3%)
	splenomegaly	9(52.9%)
	hepatomegaly	5(29.4%)
Laboratory analysis	**thrombocytopenia**	6(35.2%)
	anemia	3(17.6%)
	leukopenia	3(17.6%)
	elevated transaminases	5(29.4%)
	EBV PCR (+)	8(47.0%)
	CMV PCR (+)	3(17.6%)



Malignancies and lymphoproliferations



	NO	Age at diag. PID (year)	Age at diagnosis of malignancy	PID disorder	Side of malignancy	Malignancy	EBV	CMV	Therapy	Outcome
MALİGNANCİES	1	2	5,12	AT	Abdomen, Eye	NHL(Burkitt), Rhabdomyosarcoma	-	-	CT, HSCT	**Deceased**
	2	6	10	CGD	Abdomen	HL	-	-	CT, HSCT	Alive
	3	9	10	AT	Bone marrow	NHL(T-ALL)	-	-	CT	Alive
	4	3	4	ITK	Neck	HL	+	-	CT, HSCT	Alive
	5	8	10	STX11 def	Abdomen	NHL	-	-	CT, HSCT	Alive
	6	6	13	AT	Abdomen	NHL(Burkitt)	-	-	CT	Alive
	7	6	11	AT	Bone marrow	NHL(T-ALL)	-	-	CT	Alive
	8	7	12	AT	Head- neck	NHL (DLBCL)	+	-	CT	**Deceased**
	9	6	10	VAV1	Head- neck	Retinoblastoma	-	-	CT,RT	Alive
	10	5	6	CVID (mutation unknown)	Head- neck	Craniopharyngioma	-	-	Surgical resection	Alive

	NO	Age at diag. PID (year)	Age at diagnosis of malignancy	PID disorder	Side of malignancy	Malignancy	EBV	CMV	Therapy	Outcome
LYMPOPROLIFERATION AND MALIGNANCIES	11	5	8	MAGT1	Abdominal	HL	+	-	CT, HSCT	Alive
	12	4	5	ITK	Neck	NHL (DLBCL)	+	+	CT	**HLH** **Deceased**
	13	2	2	MUNC def	Small intestine	NHL(MALT)	+	+	CT	**HLH** **Deceased**
LYMPHOPROLIFERATIONS	14	10	-	NFAT	-	No	+	-	HSCT Rituximab	**Deceased**
	15	7	-	PIK3R1	-	No	+	-	Sirolimus	Alive
	16	8	-	E47 def	-	No	+	-	HSCT Rituximab	Alive
	17	6	-	LRBA	-	No	-	-	Abatacept	Alive

DISCUSSION

Tavakol *et al.*
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Allergy, Asthma & Clinical Immunology

RESEARCH Open Access

Diversity of malignancies in patients with different types of inborn errors of immunity

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- **3056 PID patients**
- **82 patients with malignancy**
- **CVID was the most common type**
- **Lymphoma 67.1%(NHL 43.9%, Hodgkin 23.2 %), leukemia 11 %, solid tumors 18.3 % .**

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DOI: 10.1002/pbc.28091

Pediatric Blood & Cancer

RESEARCH ARTICLE

Malignancy and lymphoid proliferation in primary immune deficiencies; hard to define, hard to treat

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- 17 PATIENTS
- The median age of patients at cancer diagnosis was 12.2 years (2.2 ± 26).
- Lymphoma was the most common malignancy (n=7), followed by adenocarcinoma (n=3), squamous cell carcinoma (n=2), cholangiocarcinoma (n=1), Wilms tumor (n=1), and acute myeloid leukemia (n = 1).
- Lymphoproliferation in 5 Patients
- Cervical and mediastinal lymph nodes

Received: 16 July 2019 | Revised: 30 January 2020 | Accepted: 3 February 2020
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ORIGINAL ARTICLE

WIL

The evaluation of malignancies in Turkish primary immunodeficiency patients; a multicenter study

Sukru Cekic[1] | Ayse Metin[2] | Caner Aytekin[3] | Neslihan Edeer Karaca[4] | Safa Baris[5] | Yasin Karali[1] | Ayca Kiykim[6] | Elif Karakoc Aydıner[5] | Ahmet Ozen[5] | Torehan Aslan[7] | Betul Sevinir[8] | Guzide Aksu[4] | Necil Kutukculer[4] | Sara Sebnem Kilic[1]

- **5 centers, 59 patients**
- **Non-Hodgkin lymphoma was the most common malignancy (n = 32,% 51.6).**
- **AT was the most common PID causing malignancy (n = 19, % 32.2)**
- **DOCK8 deficiency patients had a higher risk**
- **16 patients had (%30.2) EBV PCR(+)**

- While AT and CVID are commonly reported causes of malignancy in the literature, our study highlights that **diseases of immune dysregulation** as the most common cause of lymphoproliferation and malignancy.

- Our work also highlights the importance of **EBV (+)** and monitoring patients for signs of **lymphadenopathy,** hepatosplenomegaly, and cytopenia, especially **thrombocytopenia.**


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