

First-year results of the International Leukemia/Lymphoma Target Board for pediatric relapsed and refractory hematological malignancies

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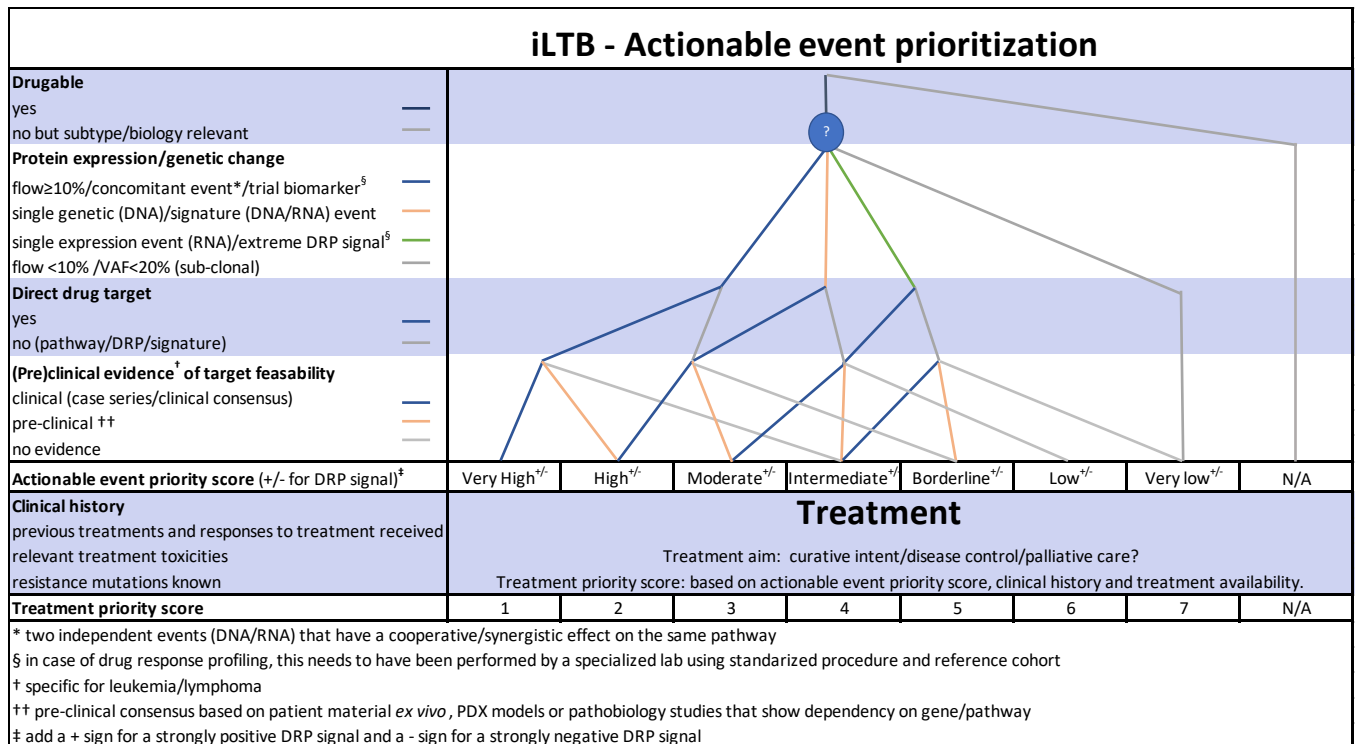
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Supplementary Table S1: Summary of reported actionable events and the respective prioritization discussed in the iLTB

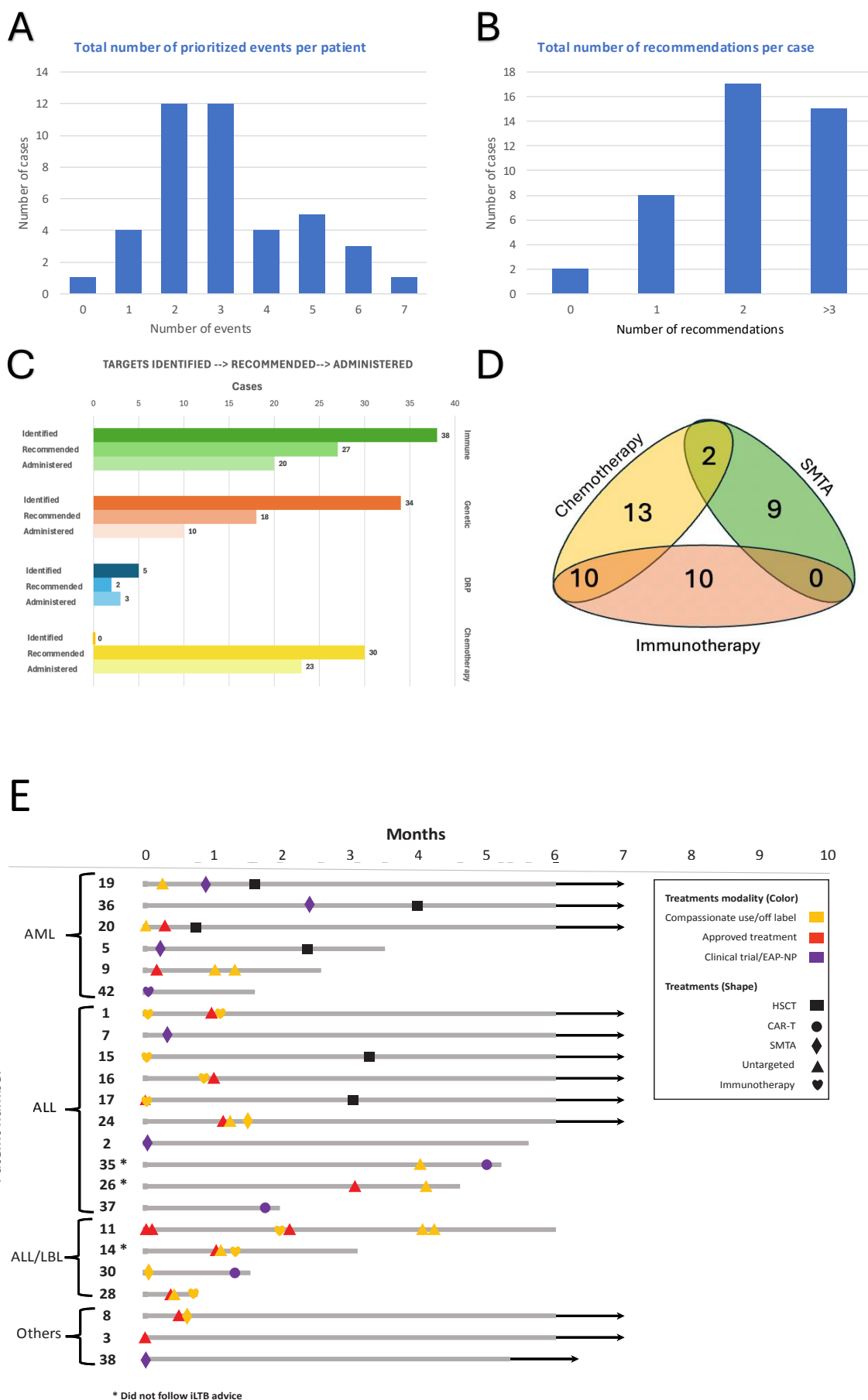
Bold - Highest recommendation by the panel <i>Italic</i> - administered					Treatment priority score					New insight	Recommendation followed
Case number	Disease type	Flow	NGS	DRP	very high	high	moderate	intermediate	borderline/low/very low		
Case 1	BCP-ALL	*	*		CD19 ; CD22; CRLF2 high expression and JAK2 mutation	CD20; CD38				yes	yes
Case 2	BCP-ALL	*	*		CD19; KMT2Ar	CD38				same	yes
Case 3	BPDCN	*	*		CD123	CD38; CDKN2A deletion and CCNE1 overexpression		NRAS mutation		same	yes
Case 4	BCP-ALL	*	*	*	CD22; KMT2Ar				<i>panabinostat sensitivity</i>	yes	yes
Case 5	AML	*	*		CD33; CD123; NUP98r	CD38		NRAS mutation	EV11 overexpression	same	yes
Case 6	AML	*	*		CD33 ; KMT2Ar					same	yes
Case 7	BCP-ALL	*	*		CD19 ; CD22; BCR::ABL1					same	yes
Case 8	B-LBL	*	*		CD19; BCR::ABL1					same	yes
Case 9	AML	*	*		CD33 ; CD123					yes	yes
Case 10	Burkitt leukemia	*	*		CD19; CD20					same	yes
Case 11	T-LBL	*	*		CD7; CD38	JAK3 mutation				yes	yes
Case 12	BCP-ALL	*	*		CD19; CD22	CD20	PTPN11 mutation			same	yes
Case 13	T-ALL	*	*							yes	no
Case 14	T-ALL	*	*					CDKN2A/B deletion	<i>CD38 weak</i>	yes	no
Case 15	BCP-ALL	*	*		CD19 ; CD22	KRAS mutation				same	yes
Case 16	BCP-ALL	*	*		CD19 ; CD22; KMT2Ar	CD38				same	yes
Case 17	BCP-ALL	*	*		CD19 ; CD22	CD20 partial; CD38	IL7R mutation and overexpression			same	yes
Case 18	AML	*	*		CD33 ; KMT2Ar	CD38				same	yes
Case 19	AML	*	*		CD33; KMT2Ar	CD38				same	yes
Case 20	AML	*	*		KMT2Ar	CD38				same	yes
Case 21	AML	*	*		CD33		BCL2 high expression			yes	yes
Case 22	AML	*	*		CD33; KMT2Ar	CD38				yes	yes
Case 23	AML	*	*					CBFA2T3::GLIS2		same	no
Case 24	BCP-ALL	*	*	*	CD19; CD22		<i>FLT3 mutation</i>		venetoclax sensitivity, bortezomib sensitivity	yes	yes
Case 25	AML	*	*		CD33; KMT2Ar					same	yes
Case 26	BCP-ALL	*	*	*	CD22; CD19				fludarabine sensitivity, ruxolitinib sensitivity	same	no
Case 27	AML	*	*		KMT2Ar					same	yes
Case 28	T-LBL	*	*		CD7; CD38	IKZF1::NOTCH1 fusion; CDKN2A/B deletion and PTEN deletion; CDKN2A/B deletion and CCNE1 overexpression		CDKN2A/B deletion		yes	yes
Case 29	T-LBL	*	*		CD7 ; CD38	IKZF2::NOTCH1; CDKN2A/B deletion and PIK3R1 mutation		CDKN2A/B deletion		same	yes
Case 30	T-ALL	*	*		CD7 ; CD38					same	yes
Case 31	T-ALL	*	*		CD7; KMT2Ar					same	NA
Case 32	T-ALL	*	*		CD7					same	yes
Case 33	BCP-ALL	*	*	*	CD19 ; CD22	KRAS mutation		CDKN2A/B deletion	venetoclax sensitivity, MEK inhibitor sensitivity, induction chemotherapy sensitivity	yes	yes
Case 34	BCP-ALL	*	*		CD19 ; CD22	CD20; NRAS mutation		CDKN2A/B deletion		yes	yes
Case 35	BCP-ALL	*	*		CD22	CD20		CDKN2A/B deletion		yes	no
Case 36	AML	*	*		CD33; CD123; KMT2Ar					same	yes
Case 37	BCP-ALL	*	*		CD19 ; CD22; KMT2Ar					same	yes
Case 38	CML	*	*		BCR::ABL1					yes	yes
Case 39	AML	*	*		CD33; KMT2Ar	CD38				same	no
Case 40	T-ALL	*	*		CD7 ; CD38					yes	no
Case 41	T-ALL	*	*		CD7; CD38					yes	yes
Case 42	AML	*	*	*	CD33; CD123 ; KMT2Ar ; FLT3-ITD	CD38			selinexor sensitivity, venetoclax sensitivity	same	yes

Abbreviations: BCP-ALL, B-cell precursor acute lymphoblastic leukemia; AML, acute myeloid leukemia; T-ALL, T-cell acute lymphoblastic leukemia; T-LBL, T lymphoblastic lymphoma; NGS, Next generation sequencing; DRP, Drug response profiling; HSCT, hematopoietic stem-cell transplant; CAR-T, chimeric antigen receptor T-cell immunotherapy. BPDCN: blastic plasmacytoid dendritic cell neoplasm.



Supplementary Figure S1: iLTB actionable event prioritization algorithm.

iLTB actionable event prioritization algorithm. Each actionable event was prioritized using an established algorithm that considered target druggability, somatic genetic alterations, gene overexpression levels, direct drug-target interactions, and supporting clinical evidence. Following this prioritization, a multidisciplinary discussion was conducted, incorporating prior treatment history, observed toxicities, treatment response, and known resistance patterns.



Supplementary Figure S2: Identified events, treatment recommendations, and treatments administered in patients after discussion in the iLTB.

(A) Bar graph representing the number of prioritized events per patient discussed in the iLTB.

(B) Bar graph representing the total number of recommendations per discussed case.

(C) Bar graph representing the identified actionable events, the iLTB panel treatment recommendations, and the administered therapy.

(D) Venn diagram illustrating the treatments and combinations administered. Patients may appear in more than one category if they received multiple treatments. DRP: drug response profile sensitivities.

(E) A swimmer plot of iLTB-enrolled patients with indicated treatment modalities and clinical follow-up. The length of the line represents the time of follow-up after iLTB. An arrow represents that the patient is alive at the last follow-up available at the time of analysis. Symbols represent treatments (shape) and treatment modality (color). Approved treatments refer to therapies that can be administered as standard of care in the respective country.