Centralized Biobanking Supports Hematology Clinical Trials: the new challenge of the University of Torino

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Centralized Biobanking Supports Hematology Clinical Trials: the new challenge of the University of Torino

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Background

Academic and sponsored clinical trials need to rely on laboratory facilities expert in handling biological samples and data. The hematology division of the University of Torino (UNITO) has kicked-off a biorepository system, for specimens' collection, from patients affected by Multiple Myeloma (MM), Non-Hodgkin Lymphoma (NHL) and Waldenström Macroglobulinemia (WM). Herein we present the first overview of sampling and data collection from February 2018 till September 2019.

Methods

Patients were enrolled, after providing informed consent, in 9 longitudinal multi-center clinical-trials. Patients' data were pseudonymized according to the GDPR. The reference laboratory collected data in ACID (Atomicity, Consistency, Isolation, Durability) database (Table1). Samples stock was performed according to trial-established procedures for clinical correlation with genetic and phenotypic analyses: Fluorescent in Situ Hybridization (FISH) to predict cytogenetic risk in MM[1], molecular flow cytometry (MFC) and molecular techniques for both screening and minimal residual disease (MRD) monitoring[2,3,4]. Computerization of the flow management (Figure 1) of the bio-specimen has been implemented via EasyTrack2D® by TwinHelix®, Italy.

Table 1: Bio-specimens data types included in the ACID database

Sample Data	ID Code	
	Materials	Bone Marrow (BM)
		Peripheral Blood (PB)
		CD19+/-, CD138+/-, CD3+
		Urine
		Plasma
		Serum
	Status	In Stock
		Sent
		Deleted
	Box name	
	Position	
	Quantity	Millions of cells
		Volume (mL)
Trial Info	Trial Name	
	Site Name	
	Disease	
Patient Info	Sponsor ID	
	Sex	
	Year of born	

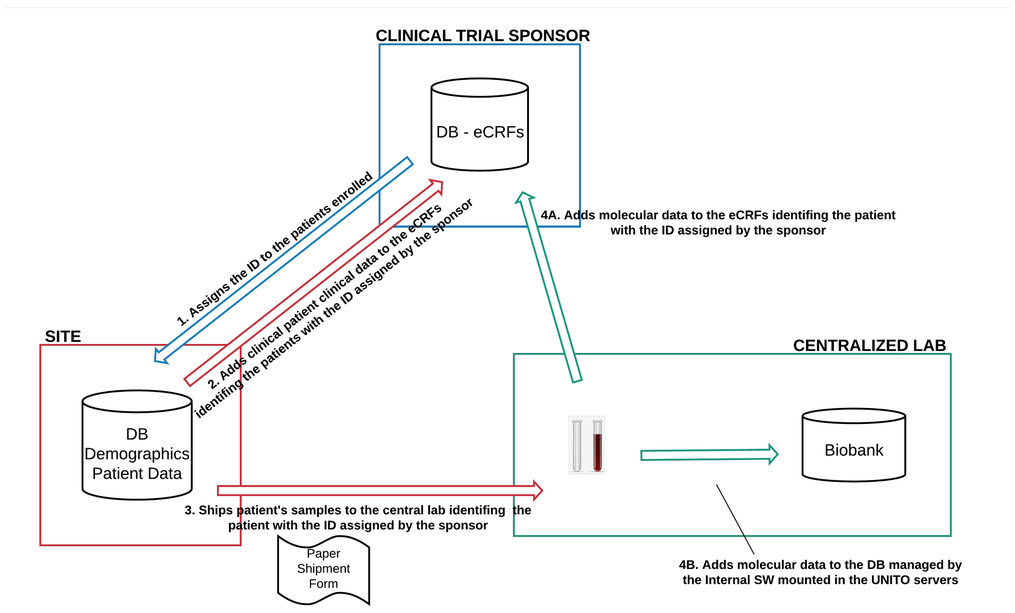

Figure 1: Flow management of bio-specimens. 1: the Clinical trial sponsor assigns the ID to the patient enrolled. 2: the site adds patient's clinical data to the electronic case reports forms (eCRFs). 3: After the biological material withdrawn, the site ships bio-Specimens to the centralized lab. 4: the centralized lab adds molecular data to both e-CRFs (A) and to biobank database (B) by the internal software.

Results

Biospecimens were collected from 919 patients: 643 MM, 156 NHL and 120 WM for totally 22826 vials (Figures 2 and 3). Among these (Figure 4), mononuclear cells (MNCs) from both bone marrow (BM) (3043/8340) and peripheral blood (PB) (5297/8340), plasma (4009), -CD19+/- (533), CD138+/- (518), Serum (2900) and 1106 samples from further tissues: granulocytes, CD3+, Urine, PBMC and cryopreserved cells . Moreover, all samples were organized in dedicated racks and boxes tagged according to each ancillary sub-study (Table 2).

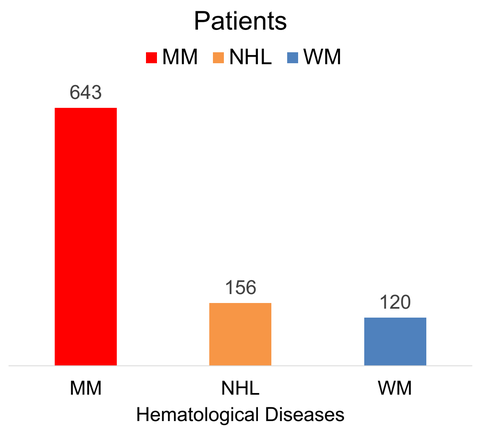

Figure 2: involved patients according to each hematological disease

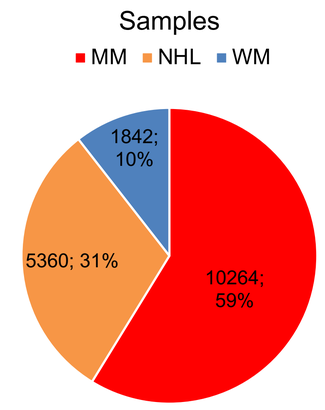

Figure 3: stocked samples according to each hematological disease

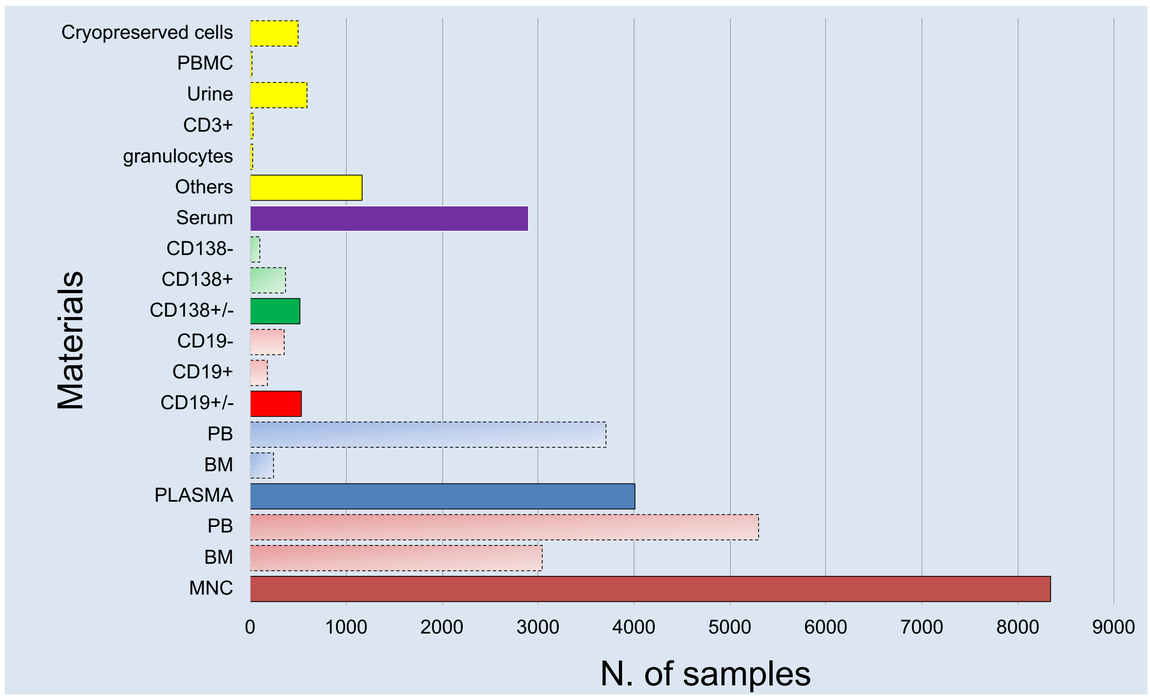

Figure 4: Number of biospecimens collected according to patients' materials

Table 2: Ancillary studies related to each clinical trial involved in the hematological biobank. We recorded 23 sub-studies at September '19 cut-off. Abbreviations. MM: multiple myeloma, MCL: mantle cell lymphoma, DLBCL: diffuse large b-cells lymphoma, WM: Waldenström macroglobulinemia, seq: sequencing, WES: whole exome sequencing. WGS: whole genome sequencing. BM: bone marrow, PB: peripheral blood, NGS: Next Generation Sequencing, MFC: molecular flow cytometry, NGF: next generation flow, PCR: polymerase chain reaction.

Studies from clinicaltrials.gov	Disease	N. of Sub-studies	Sub-studies (sample type)
NCT03848676	MM	1	DNA and RNA-seq for both WES and WGS (CD138+, CD3+)
NCT03829371	MM	4	Bone Disease (BM, PB) Clonal Evolution (CD138+) Immune Dysregulation (PB plasma) Liquid Biopsy (serum)
NCT01208966	MM	1	MRD study by MFC (BM, PB)
NCT01208766	MM	3	MRD assessment by NGS (BM) DNA and RNA seq for both WES and WGS from (CD138+) RNA seq for WGS and Mutational prognostic panels implementation (CD138+)
NCT01800208937	MM	2	MRD assessment by NGS (BM) NGS prognostication panel (BM)
NCT03567876	MCL	2	MRD assessment by real-PCR (BM, PB) MRD assessment by digital-PCR (urine)
NCT201700513723	DLBCL	3	MRD assessment by real-PCR (PB, Plasma) NGS prognostication panel (Plasma) Micro-vesicles (serum)
NCT02858258	MCL	3	MRD assessment by real-PCR (BM, PB) RNA-seq from (BM, PB) MRD assessment by real-PCR (19+/-)
NCT03521516	WM	4	MRD assessment by MFC (BM, PB, urine) MRD assessment by NGS (BM, PB, urine) MRD assessment by real-PCR (BM, PB, urine) MRD assessment by digital-PCR (BM, PB, urine)

Conclusions

We present the first biobank platform at UNITO designed for clinical data merging. This project provides an effective strategy to optimize the sample storage and the selection of biological data retrieved from translational multi-centric clinical trials. A computerized integration with clinical data for precise prognostic analysis is presented in our first reported data ware-housing applied to a phase III centralized open-labeled clinical trial[5].

References

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