

AperTO - Archivio Istituzionale Open Access dell'Università di Torino

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

This is the author's manuscript

Original Citation:

Availability:

This version is available <http://hdl.handle.net/2318/1714234> since 2019-10-23T13:53:03Z

Terms of use:

Open Access

Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.

(Article begins on next page)

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 MM¹, 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
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

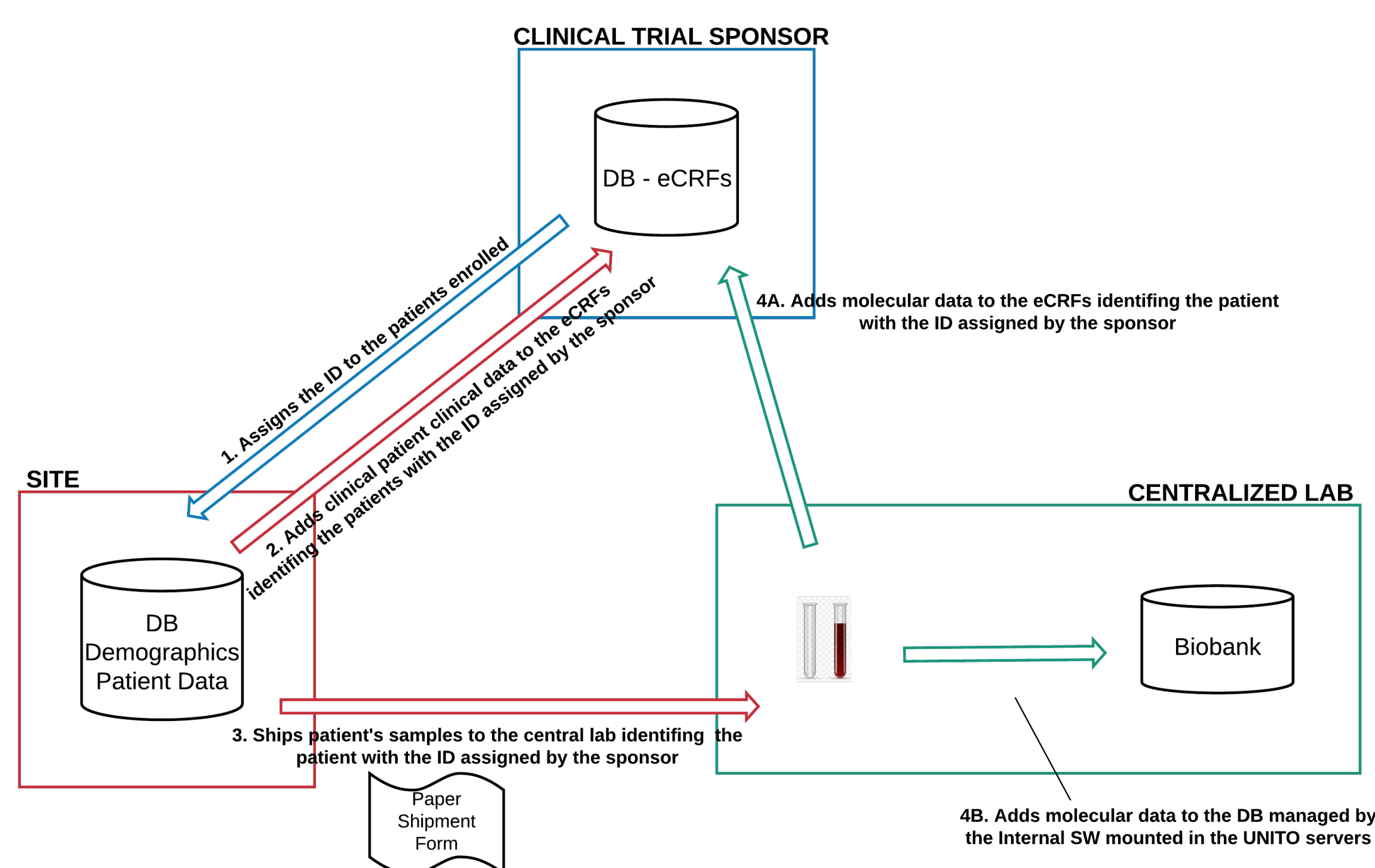


Figure 1: Flow management of bio-specimens. 1: the Clinical trial sponsor assigns the ID to the patient enrolled. 2: the site adds patient's clinical data to the electronic case reports forms (eCRFs). 3: After the biological material withdrawn, the site ships bio-Specimens to the centralized lab. 4: 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).

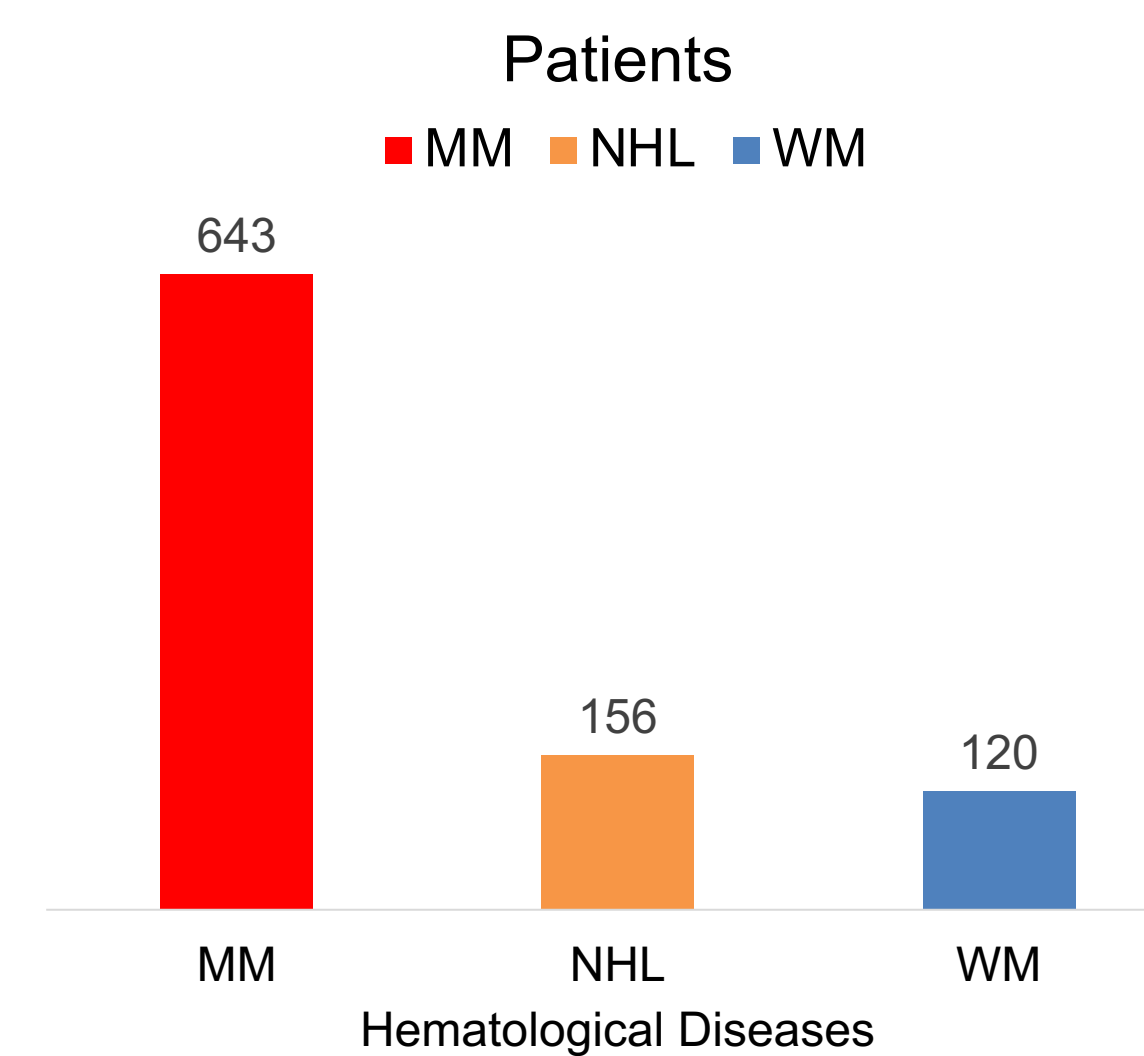


Figure 2: involved patients according to each hematological disease

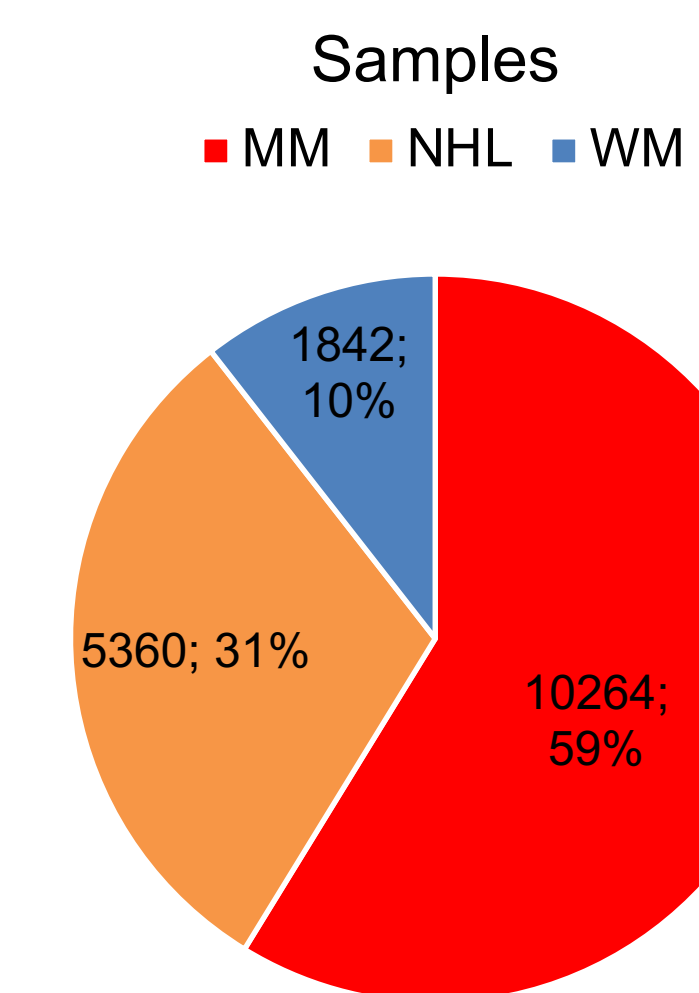


Figure 3: stocked samples according to each hematological disease

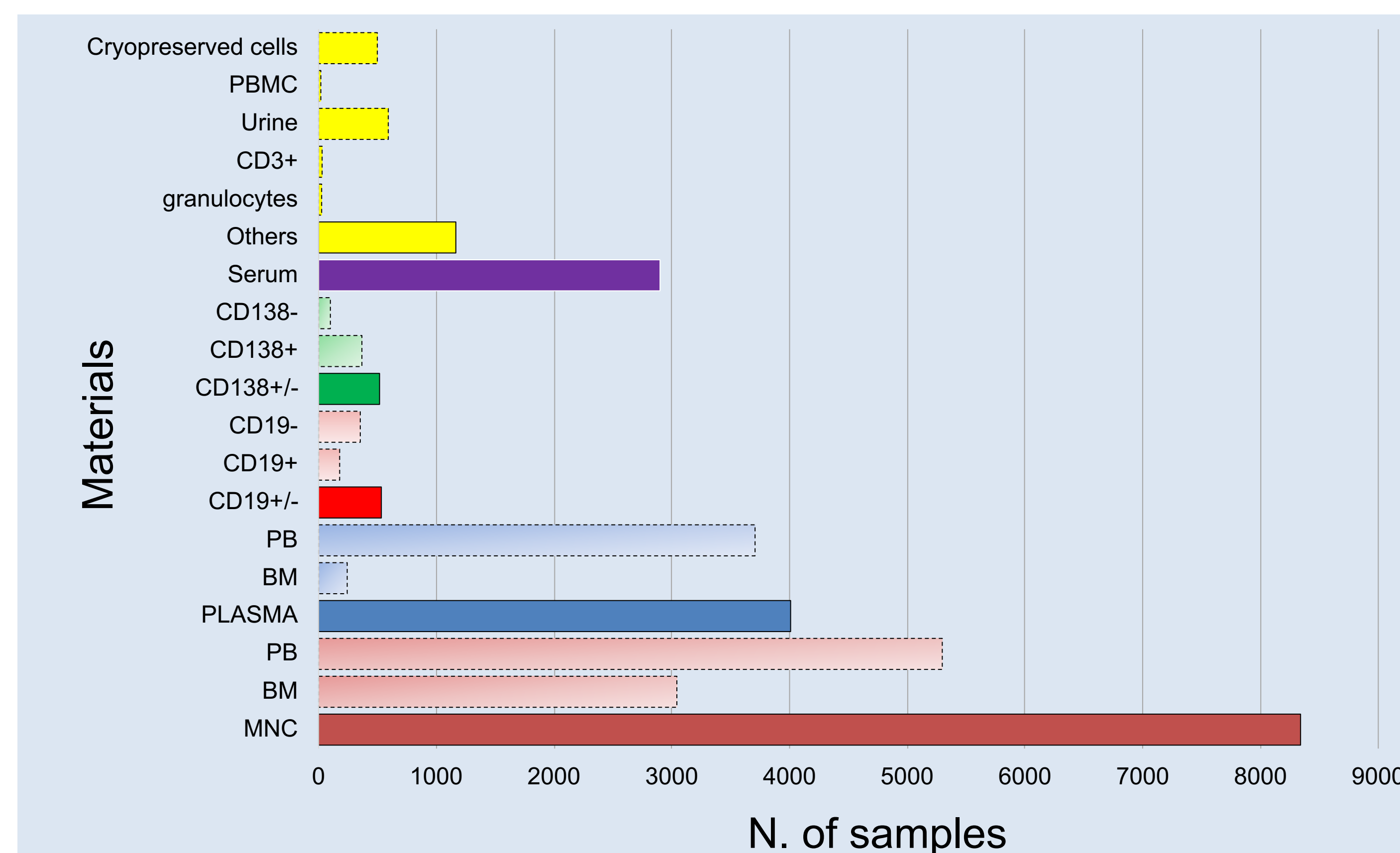


Figure 4: Number of biospecimens collected according to patients' materials

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 warehousing applied to a phase III centralized open-labeled clinical trial⁵.

References

- Palumbo et al., Revised international staging system for multiple myeloma: A report from international myeloma working group. JCO 33: 2863-2869, 2015.
- Cheminant et al., Minimal residual disease monitoring by 8-color flow cytometry in mantle cell lymphoma: An EU-MCL and LYSA study. Haematologica 101:336-345, 2016.
- Drandi et al., Highly sensitive MYD88L252P(L265P) mutation detection by droplet digital PCR in Waldenström Macroglobulinemia, Haematologica, 103(6), 1029-1037, 2018.
- Genuardi et al., Targeted Locus Amplification (TLA): A Novel Next Generation Sequencing (NGS) Technology to Detect New Molecular Markers and Monitoring Minimal Residual Disease (MRD) in Mantle Cell and Follicular Lymphoma, Blood 130 (Suppl 1), 2742-2742.
- Zaccaria et al., Applying Data Warehousing to a Phase III Clinical Trial From the Fondazione Italiana Linfomi Ensures Superior Data Quality and Improved Assessment of Clinical Outcomes, JCO Clinical Cancer Informatics, in press.