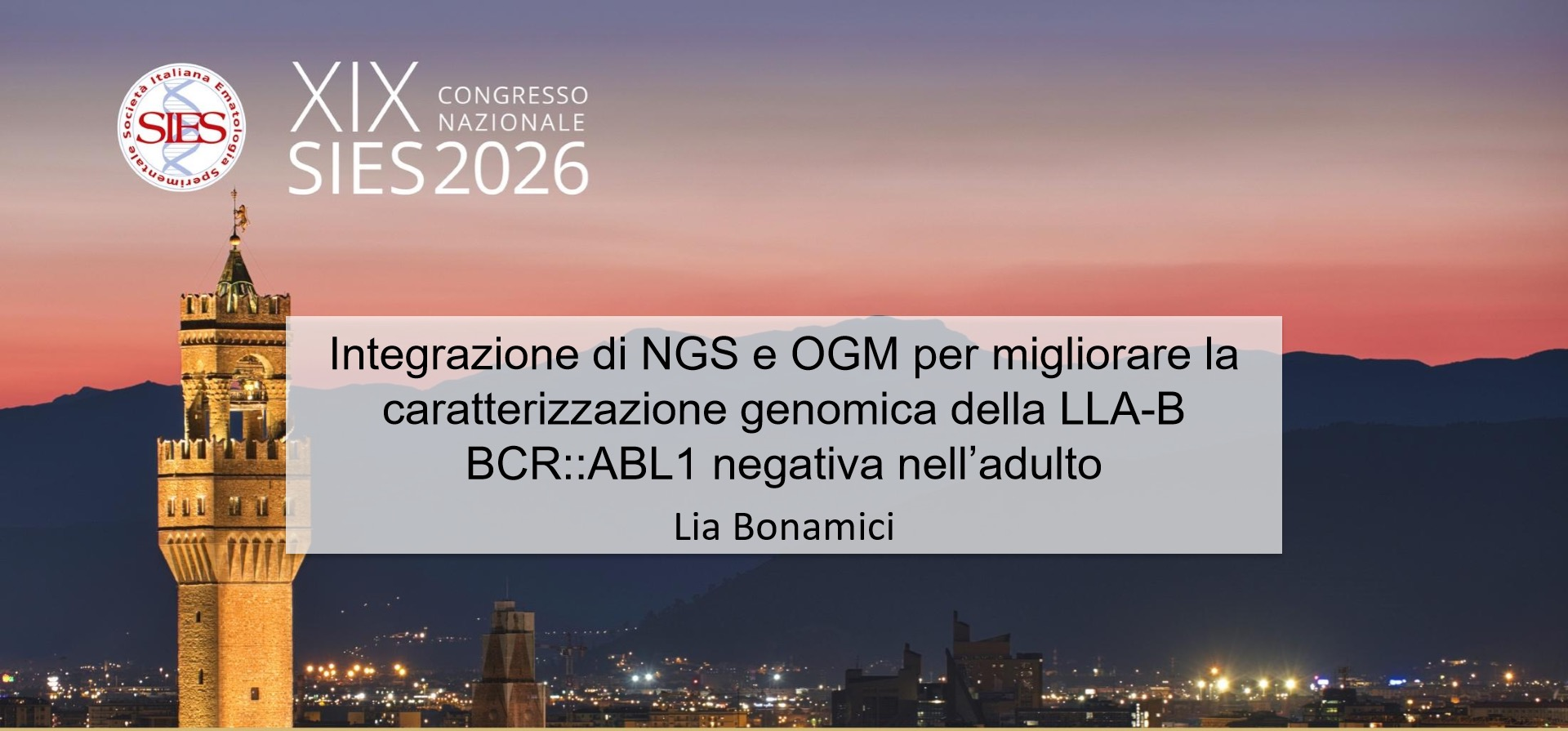


XIX CONGRESSO NAZIONALE SIES 2026

Integrazione di NGS e OGM per migliorare la caratterizzazione genomica della LLA-B BCR::ABL1 negativa nell'adulto

Lia Bonamici

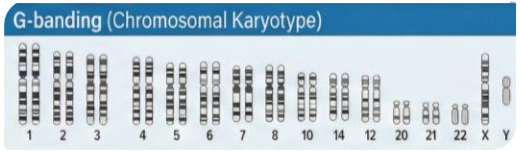
Firenze | 4-6 marzo 2026
Palazzo degli Affari

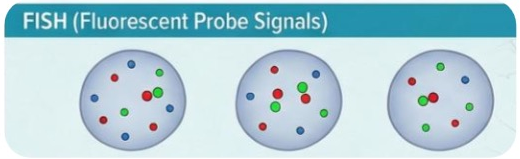
Disclosures of Lia Bonamici

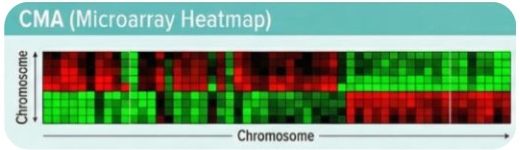
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

ICC 2022 and WHO-HAEM5: Toward a Genetically Driven Classification of B-ALL

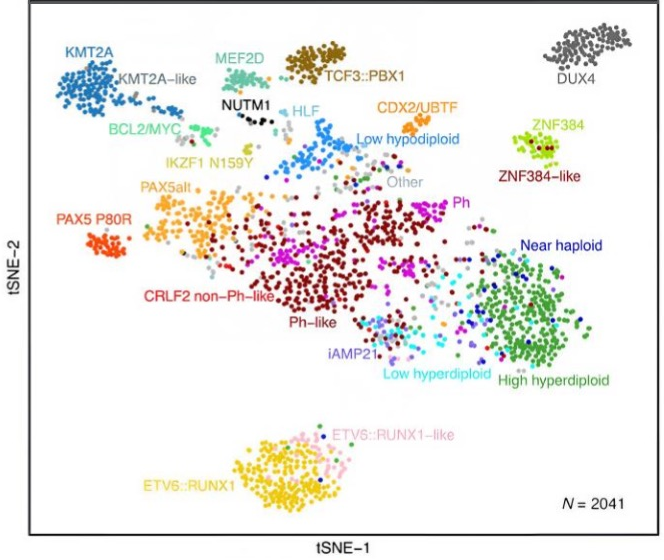
Conventional technologies







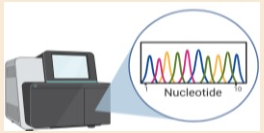
26 distinct molecular subtypes



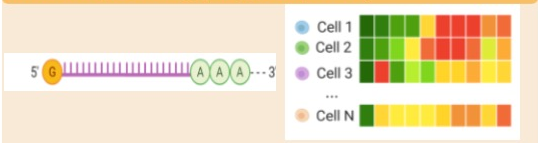
75-80% of adult cases are *BCR::ABL1* negative

Molecular technologies

DNA-sequencing (Targeted, WES, WGS)

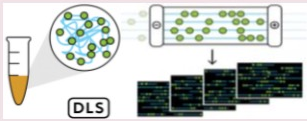


RNA-sequencing (Targeted, WTS)



Promising novel approach

Optical Genome Mapping (OGM)



Adapted from Duffield, A.S. et al. Virchows Arch (2023).

Study design

- Retrospective analysis of 76 *BCR::ABL1*-negative B-ALL adult patients (≥18 years)
- Diagnosed between 2009 and 2025
- 42 patients from ASST Papa Giovanni XXIII, Bergamo
- 34 patients from Azienda Ospedaliero-Universitaria Policlinico, Modena
- Isolated RNA (−80 °C) and cryopreserved MNCs for targeted RNA sequencing and OGM, respectively

Objective

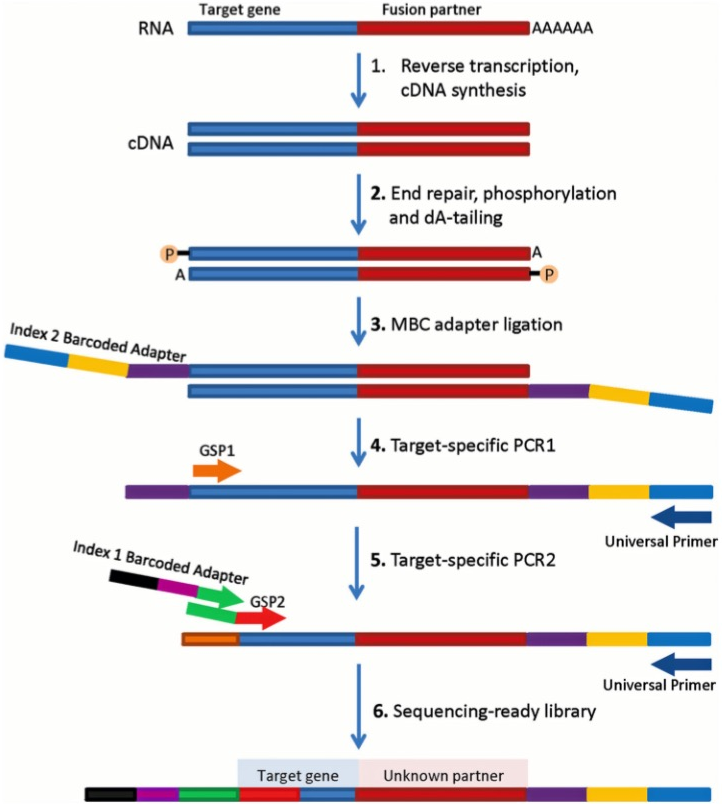
Integration of NGS and OGM to improve genomic characterization of adult BCR::ABL1-negative B-ALL

Patient details

PARAMETER	PATIENTS
Gender (n=76)	
Male	39 (51%)
Female	37 (49%)
Age (n=76)	46 (IQR 27-64)
ECOG performance status (n=69)	
0	42 (60.9%)
1	22 (31.9%)
2	4 (5.8%)
3	1 (1.4%)
Comorbidites (n=68)	
Hypertension	12 (18%)
Cardiac disease	6 (8.8%)
Hepatic disease	5 (7.4%)
Renal disease	4 (5.9%)
Hematologic parameters (n=72)	
Bone marrow blasts	90% (IQR 80-90%)
PB Blasts	62% (IQR 23-80%)
WBC ($\times 10^9$/L)	8.7 (IQR 4.0-28.9)
Hemoglobin (g/dL)	10.5 (IQR 8.15-12.2)
Platelets ($\times 10^9$/L)	66.5 (IQR 30.8–126.8)
CNS involvement (n=72)	2 (2.8%)

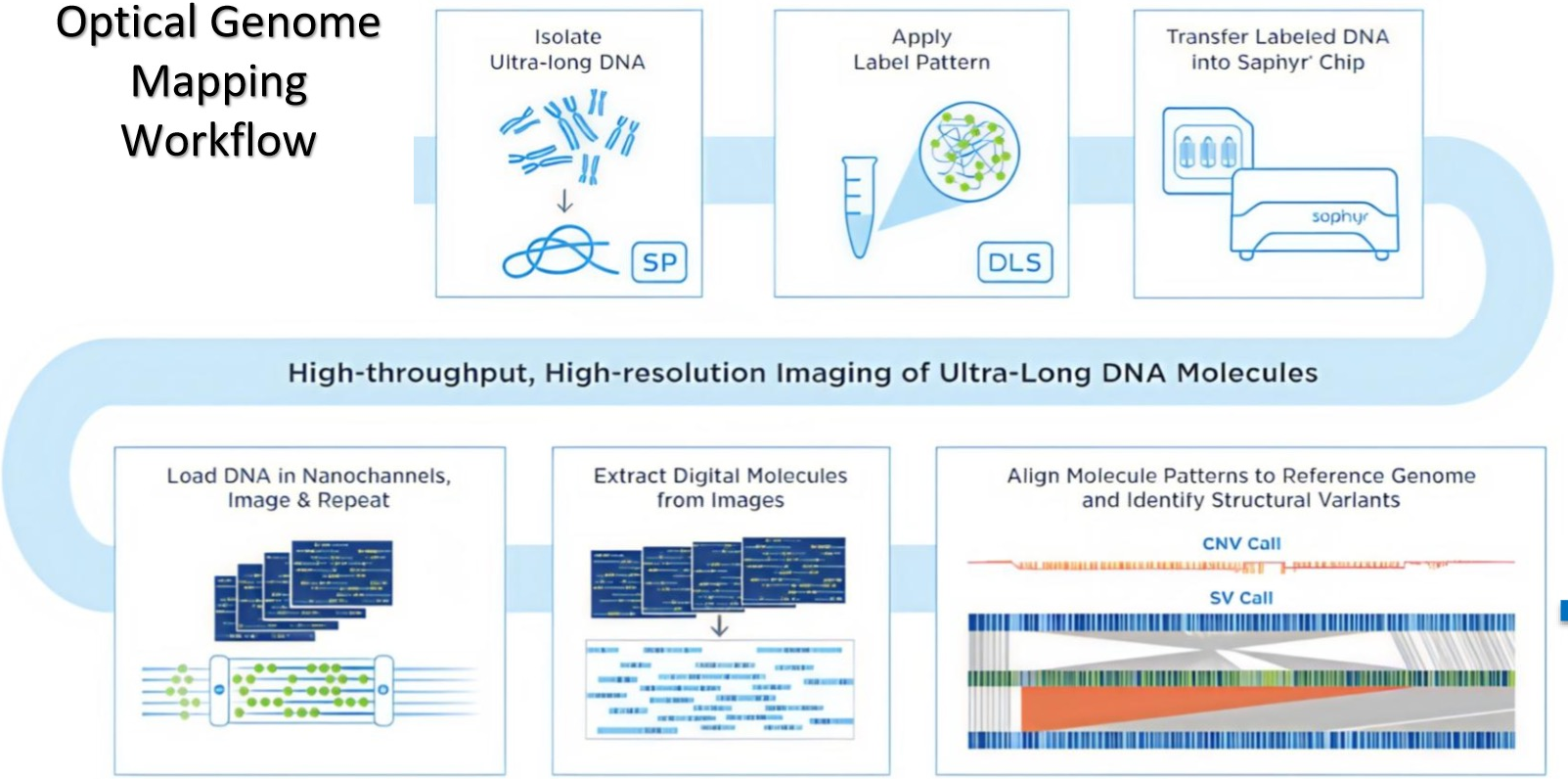
Methods: targeted RNA-sequencing

- ArcherDx® FusionPlex® Acute Lymphoblastic Leukemia (ALL) panel
- 81 genes associated with ALL
- Detection of sequence variants (SNVs & indels)
- Detection of fusion genes with known/unknown partners
- Anchored Multiplex PCR (AMP™)-based library preparation



From Zhu, G. et al.. Mod Pathol. (2019)

Optical Genome Mapping Workflow

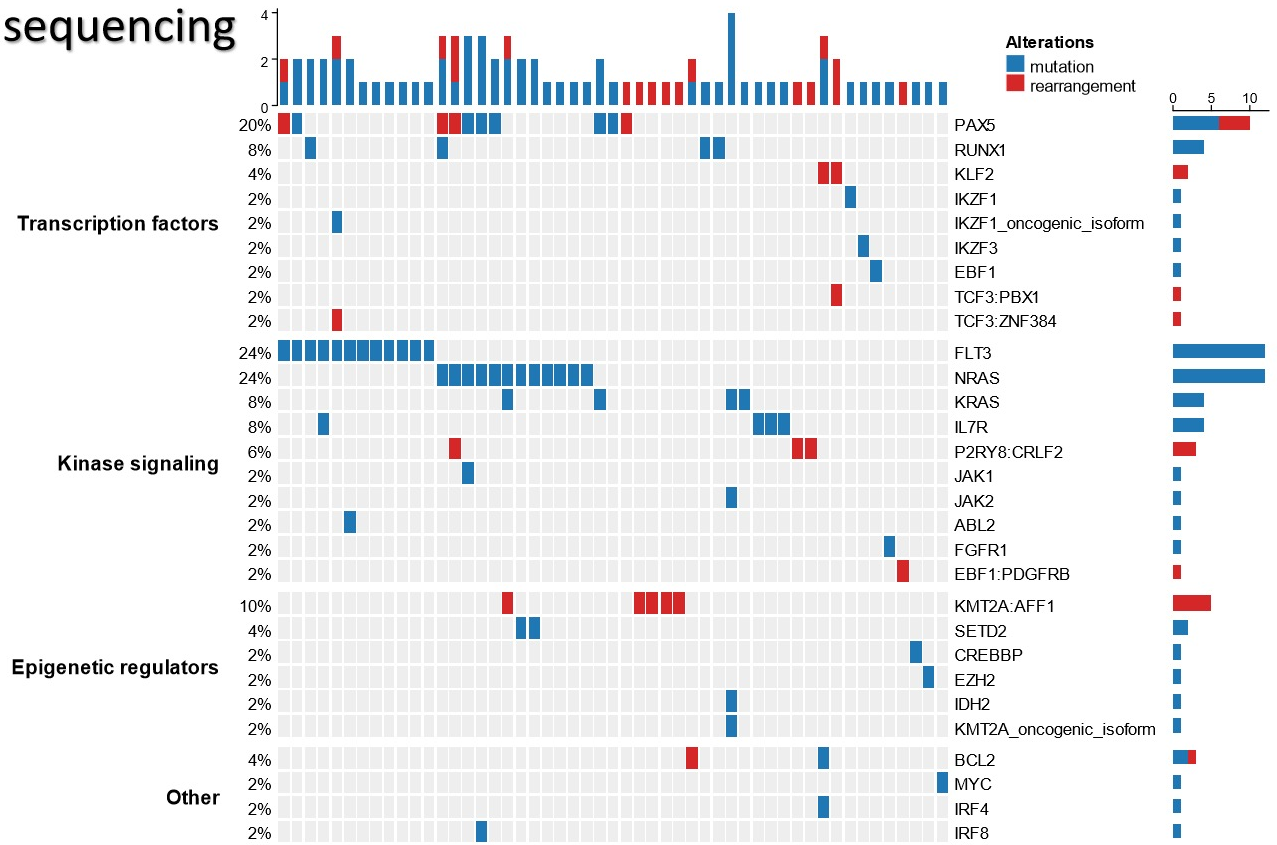


- Aneuploidies
- Insertions
- Deletions
- Duplications
- Translocations
- Inversions

Adapted from Sahajpal NS, et al. Genes. (2021)

Alterations identified by RNA sequencing

- 73/76 cases successfully analyzed
- 51/73 cases harbored ≥1 LP/P variant (69.9% positive yield)
- Median n. of variants per patient: 1 (range, 0-4)
- *FLT3* and *NRAS* most frequently mutated genes
- Kinase signaling most frequently altered pathway (50.6% of alterations)
- *KMT2A* and *PAX5* most frequently rearranged genes



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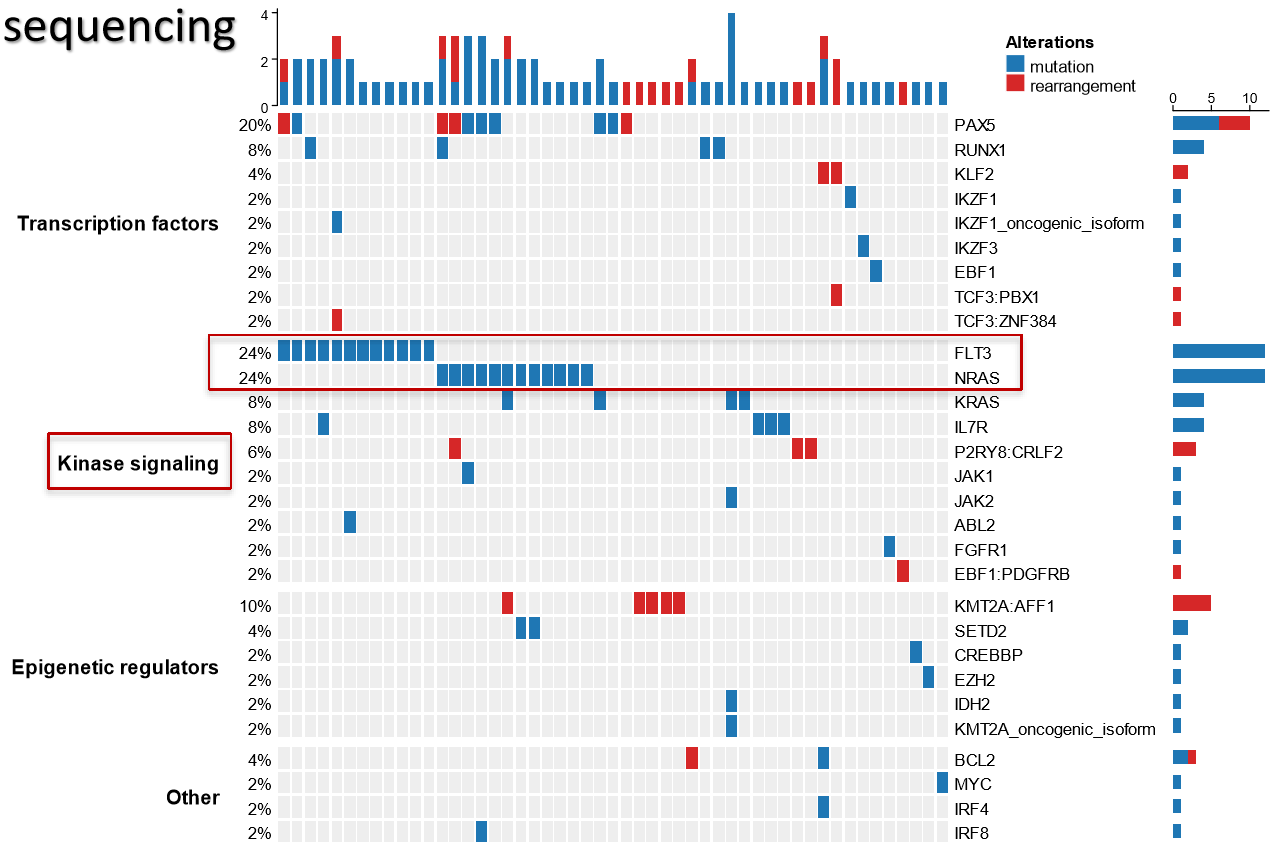

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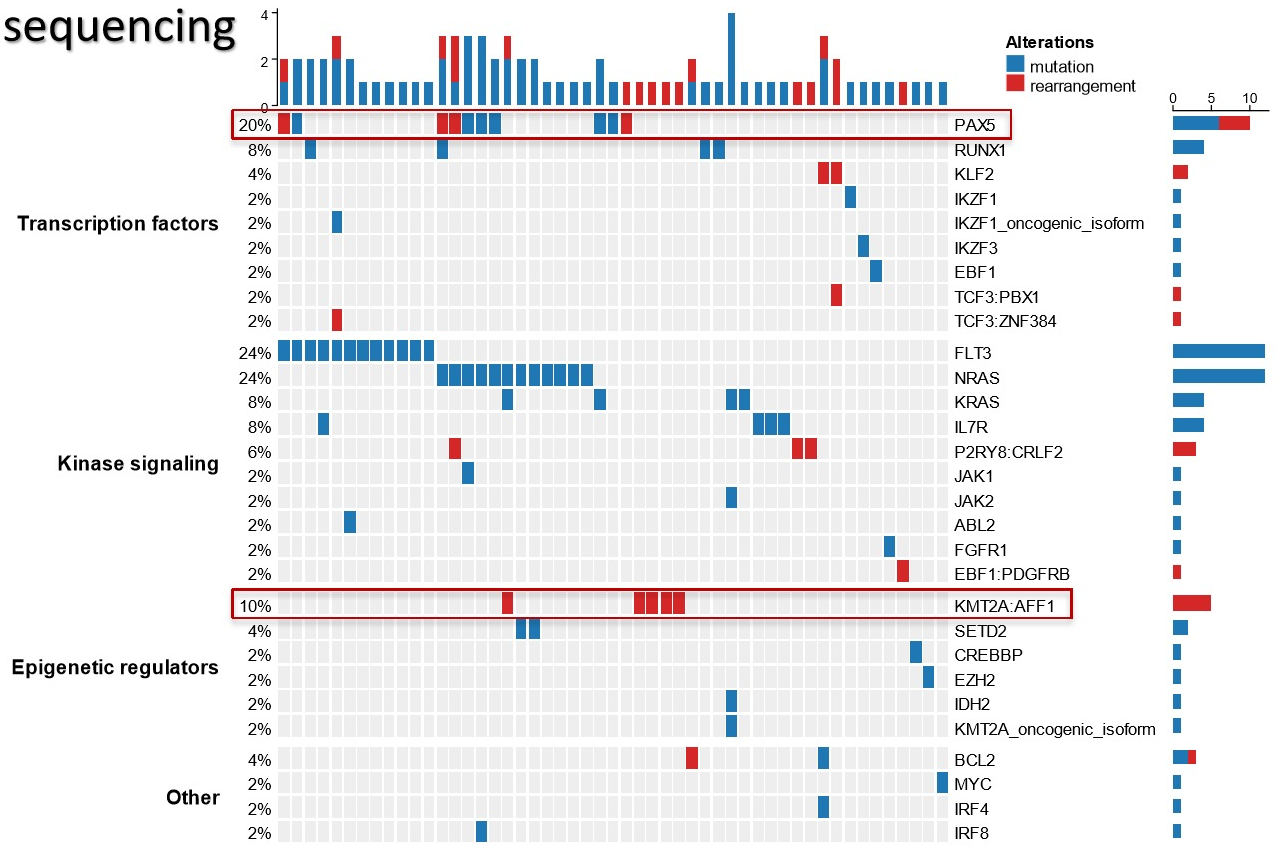
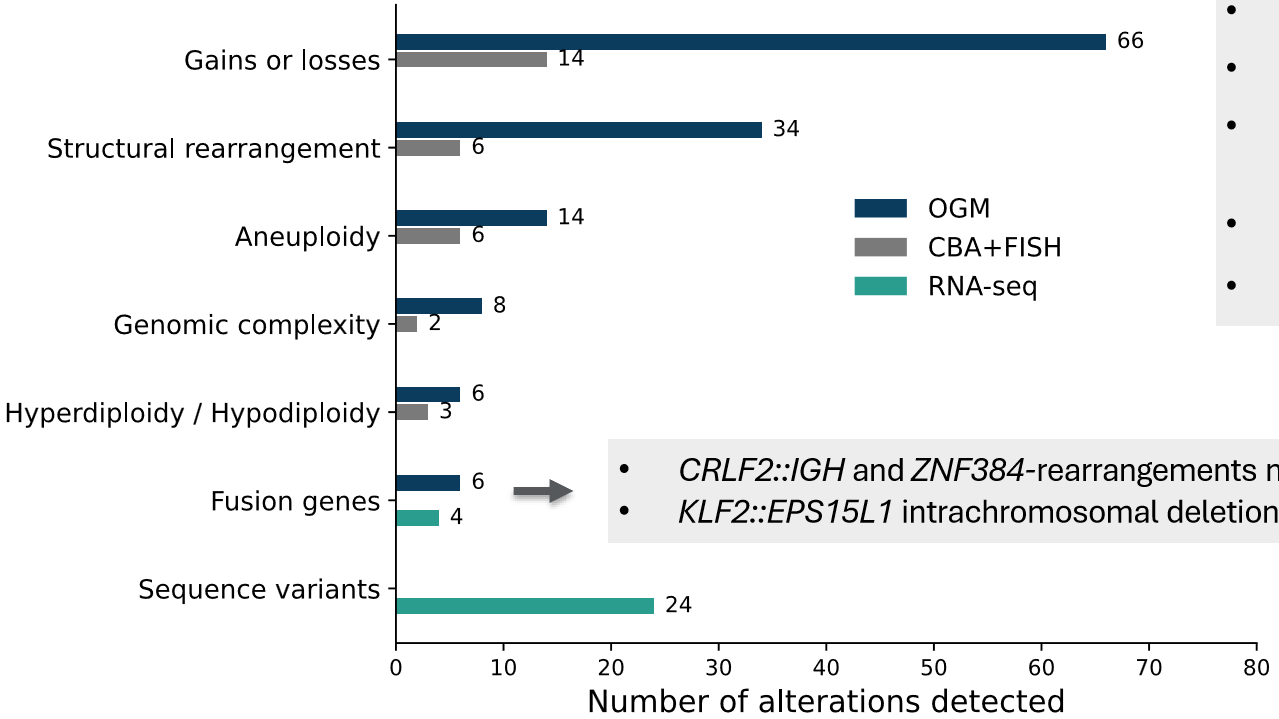


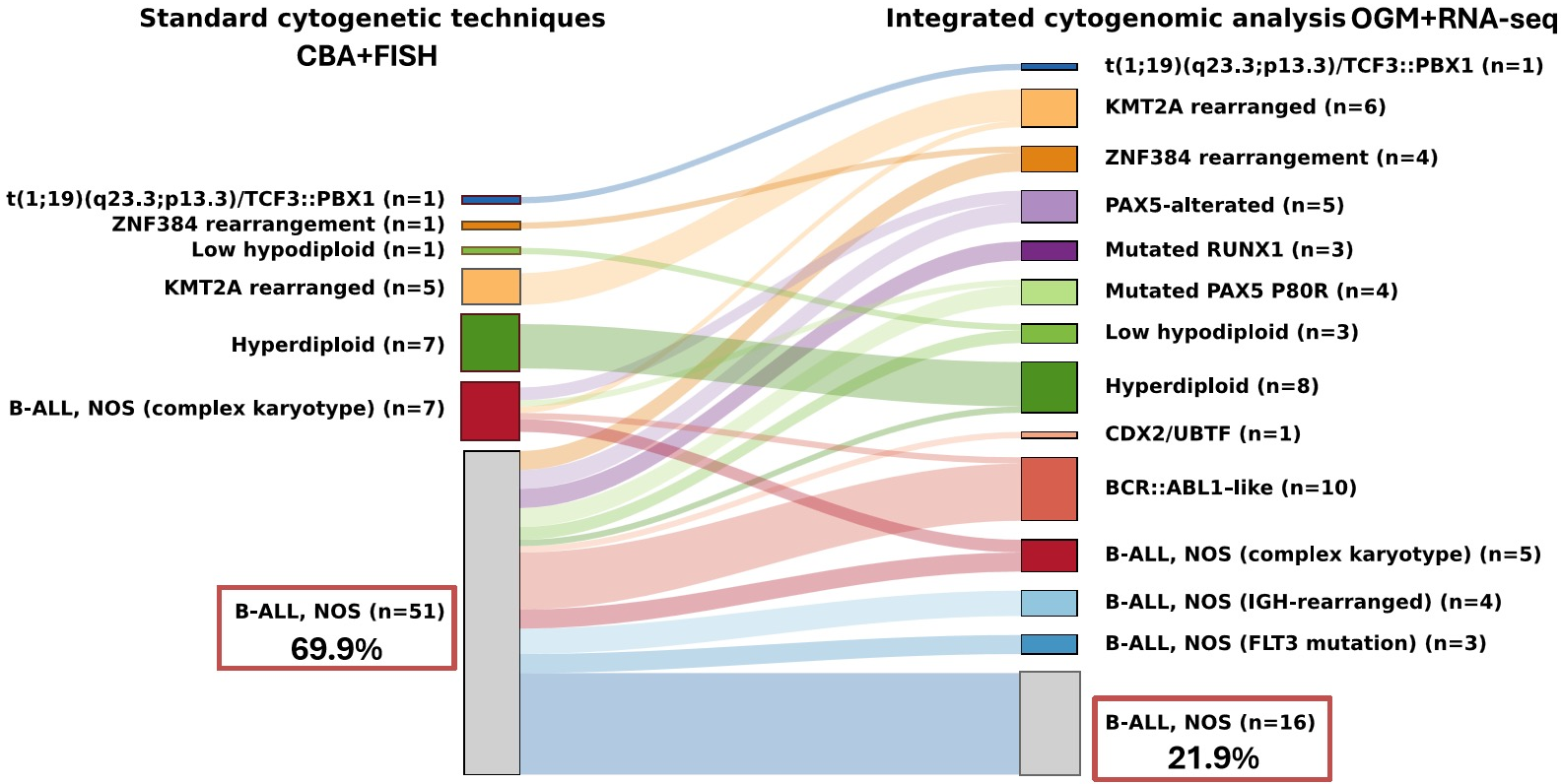
Added value of OGM compared with other methods



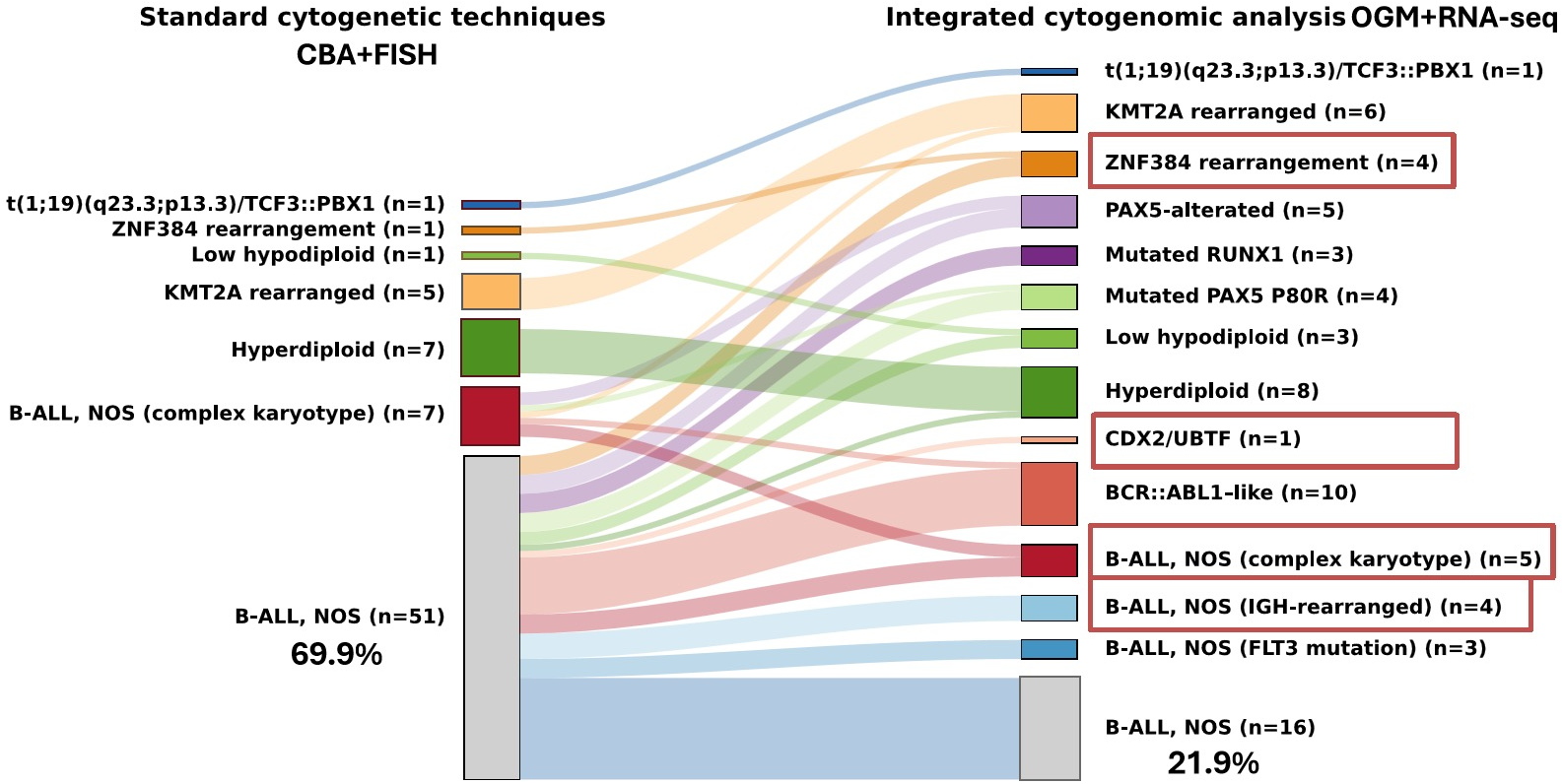
- 32 cases analysed
- Bionano Access v.1.8 software
- 30/32 patients with LP/P alterations (93.8% positive yield)
- Median alterations per patient: 4
- Concordance with CBA/FISH= 88.9%

- *CRLF2::IGH* and *ZNF384*-rearrangements missed by RNA-seq
- *KLF2::EPS15L1* intrachromosomal deletion missed by OGM

Improved B-ALL characterization by integrated genomic profiling

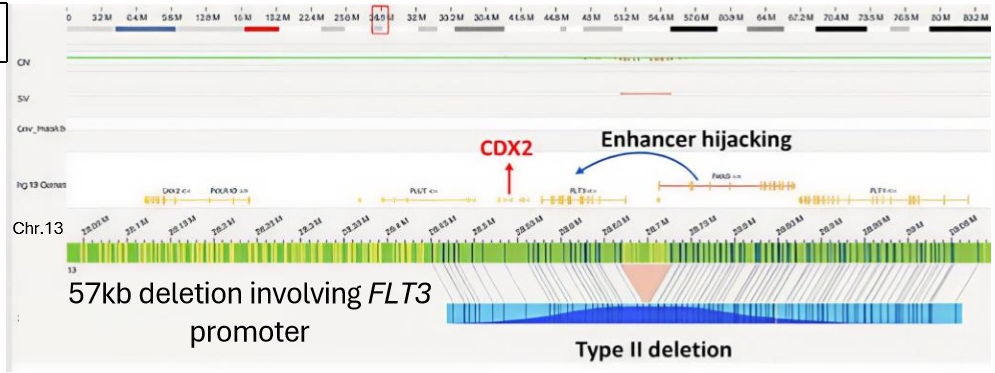


Improved B-ALL Classification by integrated genomic profiling



Structural variant with enhancer hijacking: *CDX2/UBTF*

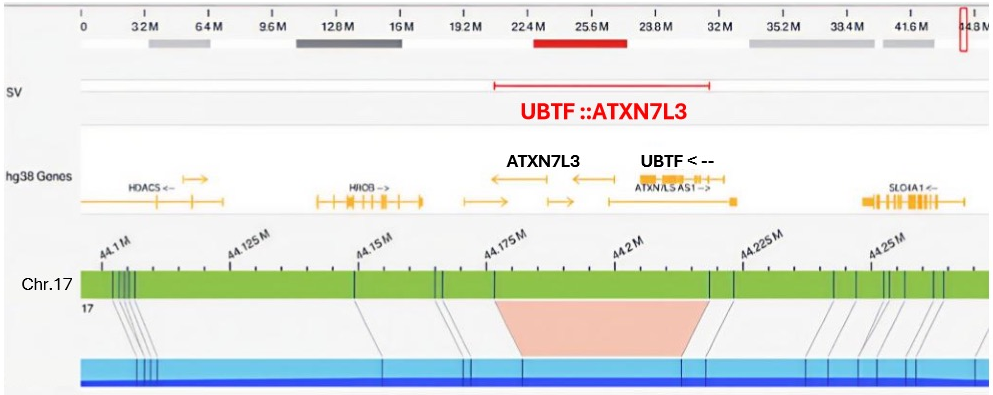
BE-30



- (1-2%) of B-ALL, higher in AYAs and females
- *CDX2* up-regulation
- Poor prognosis

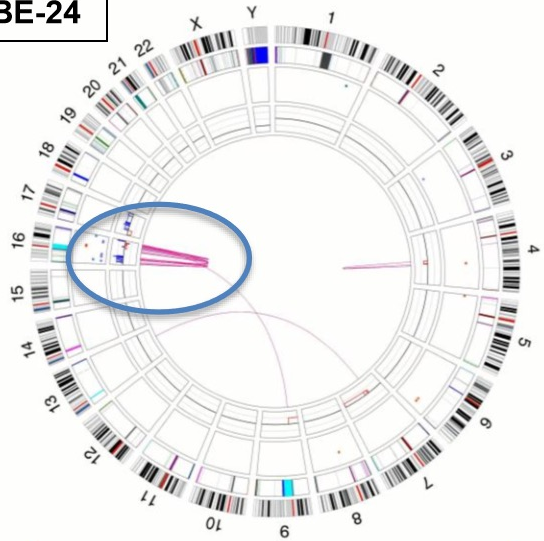
Kimura et al. 2022

putative gene fusion-> UBTF::ATXN7L3



Chromoanagenesis events

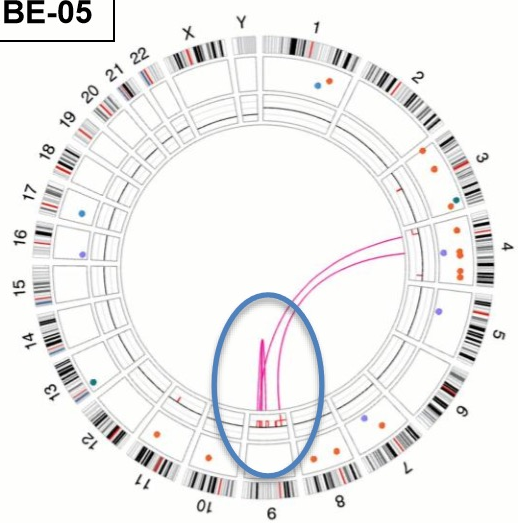
BE-24



Clustered gains and losses with structural variants in one/few chromosomes:

Chromoanasynthesis-like pattern

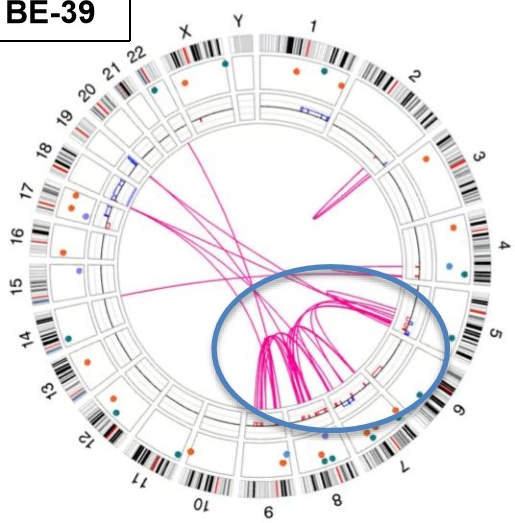
BE-05



Clustered losses with structural variants in one/few chromosomes

Chromothripsis-like pattern

BE-39



Chained translocations involving different chromosomes with related gains and losses

Chromoplexy-like pattern

Conclusions:

→ **OGM:** High concordance with conventional cytogenetics and detection of additional structural alterations

→ **RNA-sequencing:** Relevant information on pathogenic sequence variants and gene fusions with multiple partners

→ **Integration of OGM and RNA-seq:** Enhances genetic characterization of clinically relevant, rare, and cryptic alterations in adult BCR::ABL1-negative ALL patients

Acknowledgements

Diagnostic Hematology Unit (Modena Policlinico)
&
Hematology Unit (Modena and Reggio Emilia University)

- Enrico Tagliafico
- Rossana Maffei
- Ambra Paolini
- Silvia Martinelli
- Benedetta Conte
- Mario Luppi
- Fabio Forghieri
- Giovanni Fera
- Elena Sbadili
- Paola Barozzi
- Giulia Debbia
- Elisabetta Colaci
- Davide Giusti
- Leonardo Potenza
- Francesca Bettelli
- Monica Morselli
- Angela Cuoghi
- Andrea Gilioli
- Andrea Messerotti
- Valeria Pioli

Department of Oncology and Hematology (University of Milan)
&
Department of Oncology and Hematology (ASST Papa Giovanni XXIII, Bergamo)

- Alessandro Rambaldi
- Orietta Spinelli
- Federico Lussana
- Cristian Meli