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BACKGROUND

Prognosis of B-cell precursor acute lymphoblastic leukemia (ALL) has improved in the last two decades through the combination of minimal residual disease (MRD) and oncogenetics based risk stratification, chemotherapy optimization, and more recently the incorporation of various immunotherapy agents. Blinatumomab is a CD19/CD3 bispecific T-cell engager (BiTE) that demonstrated efficacy in several ALL settings for the treatment of adult and pediatric patients.^{1,2,3,4}

AIMS

The ATHENA study aimed to describe the characteristics of pediatric and adult patients with ALL who initiated blinatumomab treatment in France between 2019 and 2022, and to describe treatment pathways following blinatumomab exposure.

METHODS

Study design

This nationwide retrospective cohort study used the French National Hospital discharge database PMSI, which captures claims data from all public and private hospitals in France, and therefore provides comprehensive individual-level data.

Methods

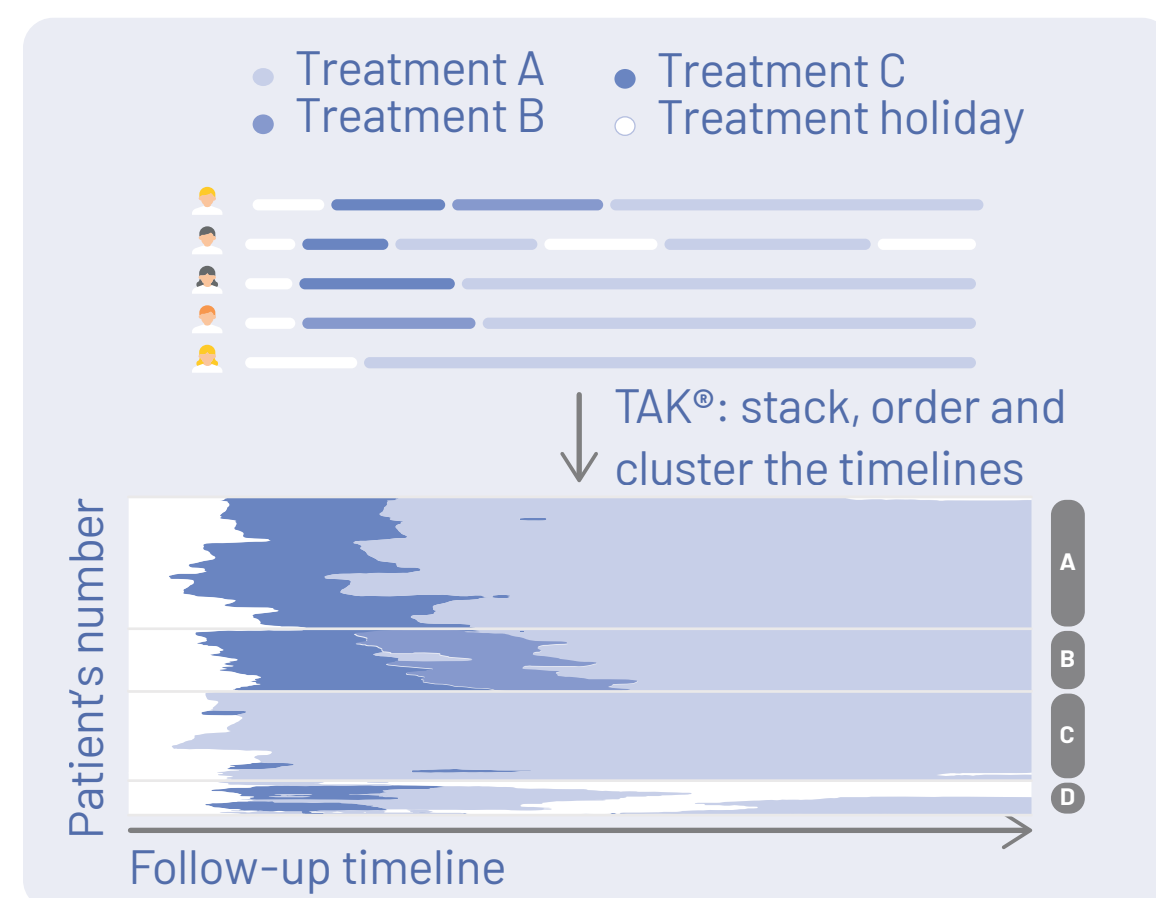
- Population: patients diagnosed with ALL identified by the presence of an ALL code (C91.0 in International Classification of Diseases 10th Revision, ICD-10), treated with blinatumomab, and having received their first blinatumomab administration during the inclusion period.
- Inclusion period: between 01/01/2019 and 12/31/2022.
- Index date: start date of first hospitalization with blinatumomab administration.
- Follow-up: from index date to end of the follow-up period (12/31/2022), in-hospital death, or loss of follow-up.
- Data extraction period: between 01/01/2013 and 12/31/2022 to define medical history and ALL history.
- Outcomes: patient characteristics, blinatumomab use and treatment sequences.

TAK® method

- Time-sequence Analysis through K-clustering^{5,6} (TAK®)
- Artificial intelligence method used to analyze the temporality of treatment sequences with a segmentation of the cohort into groups according to similarity of sequences.

- Two-steps clustering algorithm:

- Model each patient treatment sequence as a timeline.
- Stack timelines, ordered and clustered via Agglomerative Clustering with Hamming distance and ward linkage.



References

¹Kantarjian H, et al. Blinatumomab versus Chemotherapy for Advanced Acute Lymphoblastic Leukemia. N Engl J Med. 2017 Mar 2; 376(9): 836-847.

²Gökbuget N, et al. Blinatumomab for minimal residual disease in adults with B-cell precursor acute lymphoblastic leukemia. Blood. 2018 Apr 5;131(14):1522-1531. Epub 2018 Jan 22. Erratum in: Blood. 2019 Jun 13; 133(24): 2625.

³Gore L, et al. Survival after blinatumomab treatment in pediatric patients with relapsed/refractory B-cell precursor acute lymphoblastic leukemia. Blood Cancer J 2018;8(9):80.

⁴Locatelli F, et al. Effect of Blinatumomab vs Chemotherapy on Event-Free Survival Among Children With High-risk First-Relapse B-Cell Acute Lymphoblastic Leukemia: A Randomized Clinical Trial. JAMA. 2021 Mar 2;325(9):843-854.

⁵Chouaid C, et al. Machine Learning-Based Analysis of Treatment Sequences Typology in Advanced Non-Small-Cell Lung Cancer Long-Term Survivors Treated With Nivolumab. JCO Clinical Cancer Informatics. mai 2022; (6): e2100108.

⁶Tredan O, et al. Innovative Approach for a Typology of Treatment Sequences in Early Stage HER2 Positive Breast Cancer Patients Treated With Trastuzumab in the French National Hospital Database. Cancer Inform. janv 2022; 21: 1176935f2211351.

Abbreviations

ATHENA: Real-world utilization of Blinatumomab in acute lymphoblastic leukemia treatment in France; **CAR-T cells**: Chimeric Antigen Receptor T cells; **GVHD**: Graft Versus Host Disease; **HSCT**: Hematopoietic Stem Cell Transplantation; **MRD**: Minimal Residual Disease; **PMSI**: Programme de Médicalisation des Systèmes d'Information; **R/R**: Relapsed or Refractory.

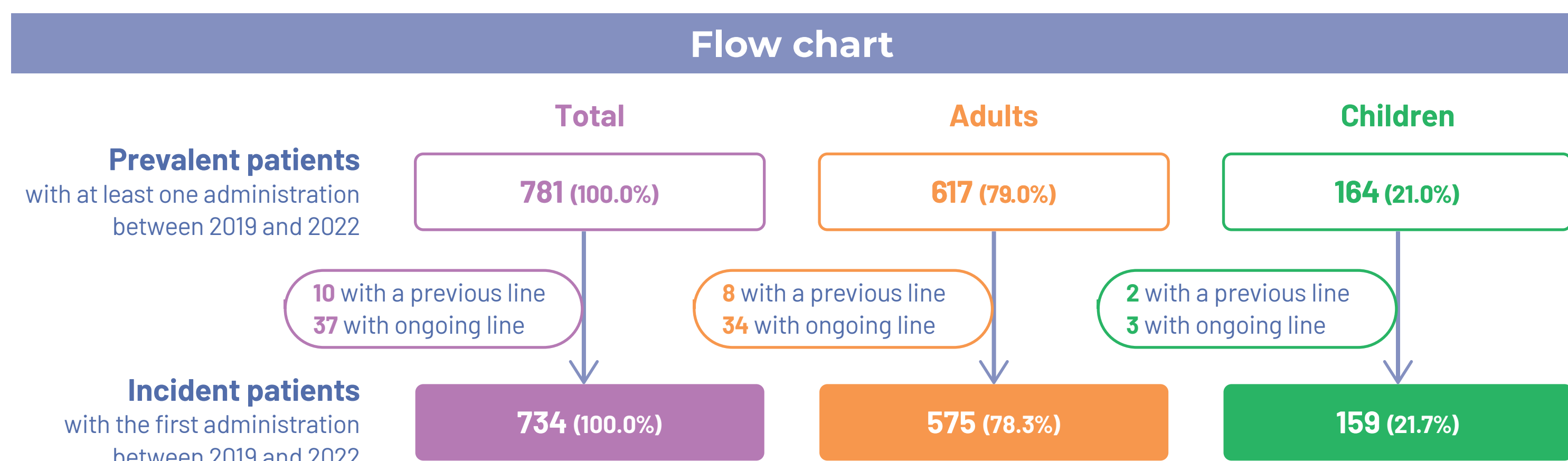
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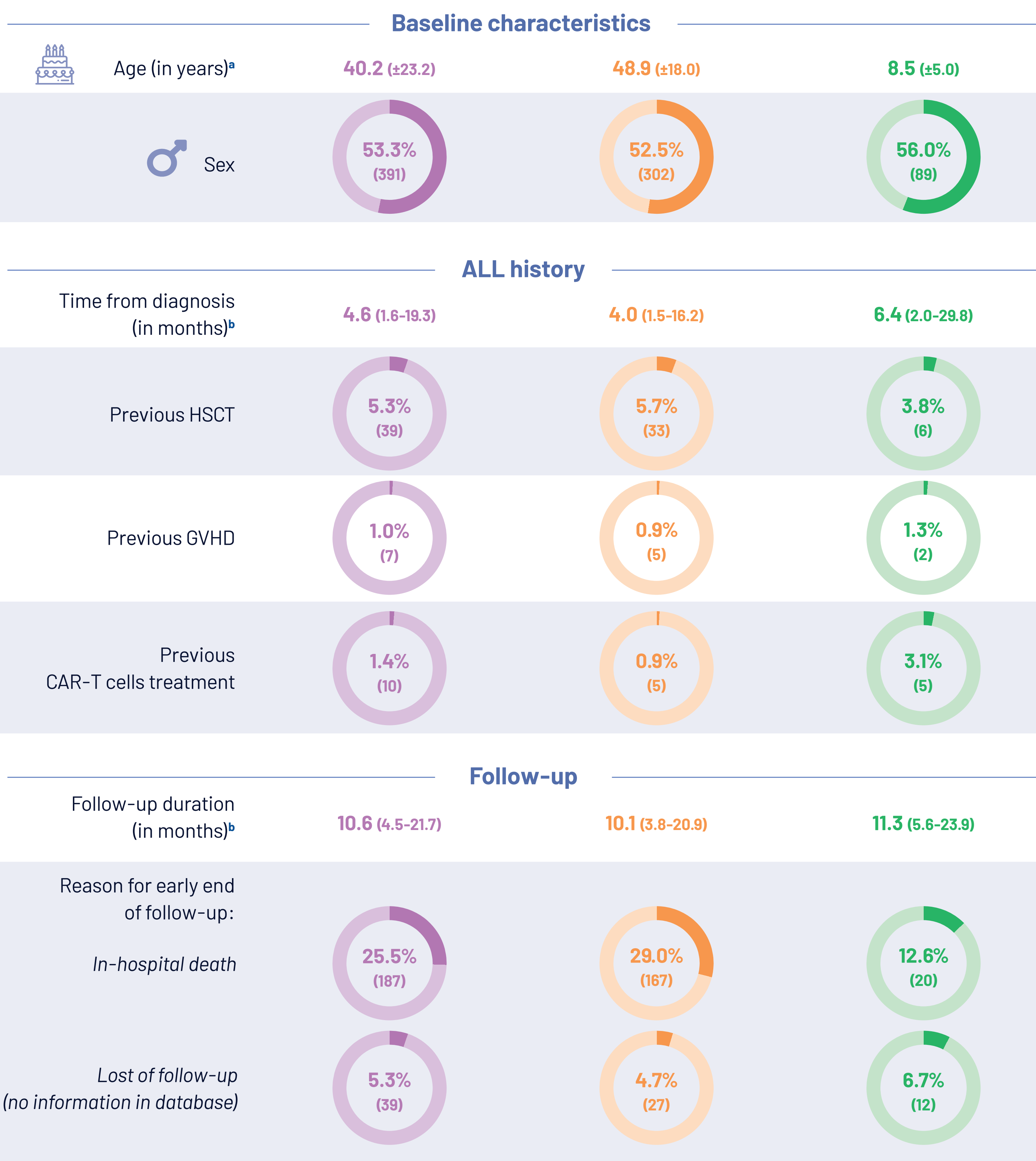
Acknowledgement

We would like to thank the entire Heva team for their contributions to ATHENA study, especially Sacha Hiridjee who performed the data extraction and management, Marie Laurent for her expertise in data scientist analyses and Aurélie Schmidt for team leading.

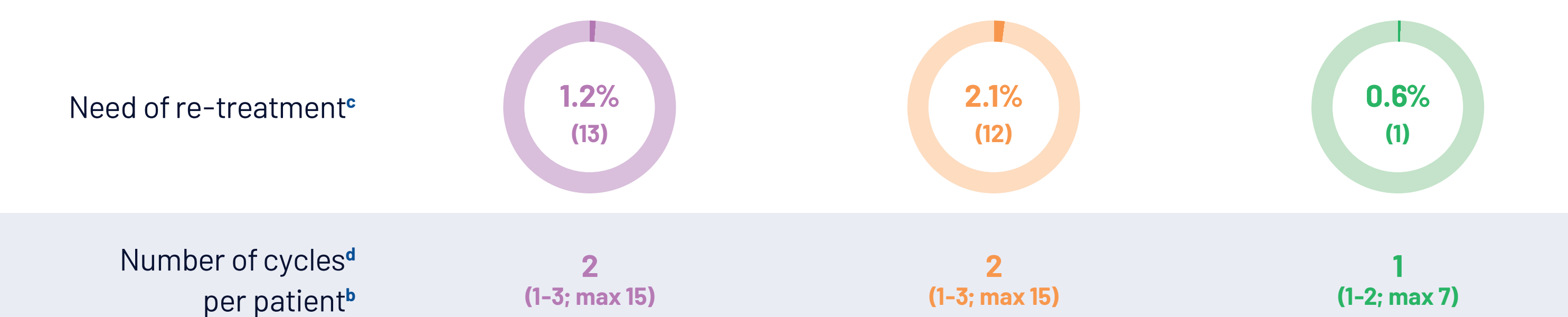
RESULTS



Study population



Blinatumomab use



^aMean (±SD)

^bMedian (Q1-Q3)

^cThe re-treatment was defined by a delay between 2 administrations of blinatumomab > 6 months.

^dThe cycle change was defined by a delay between 2 administrations of blinatumomab > 7 days.

RESULTS

Treatment sequences (using TAK® method)

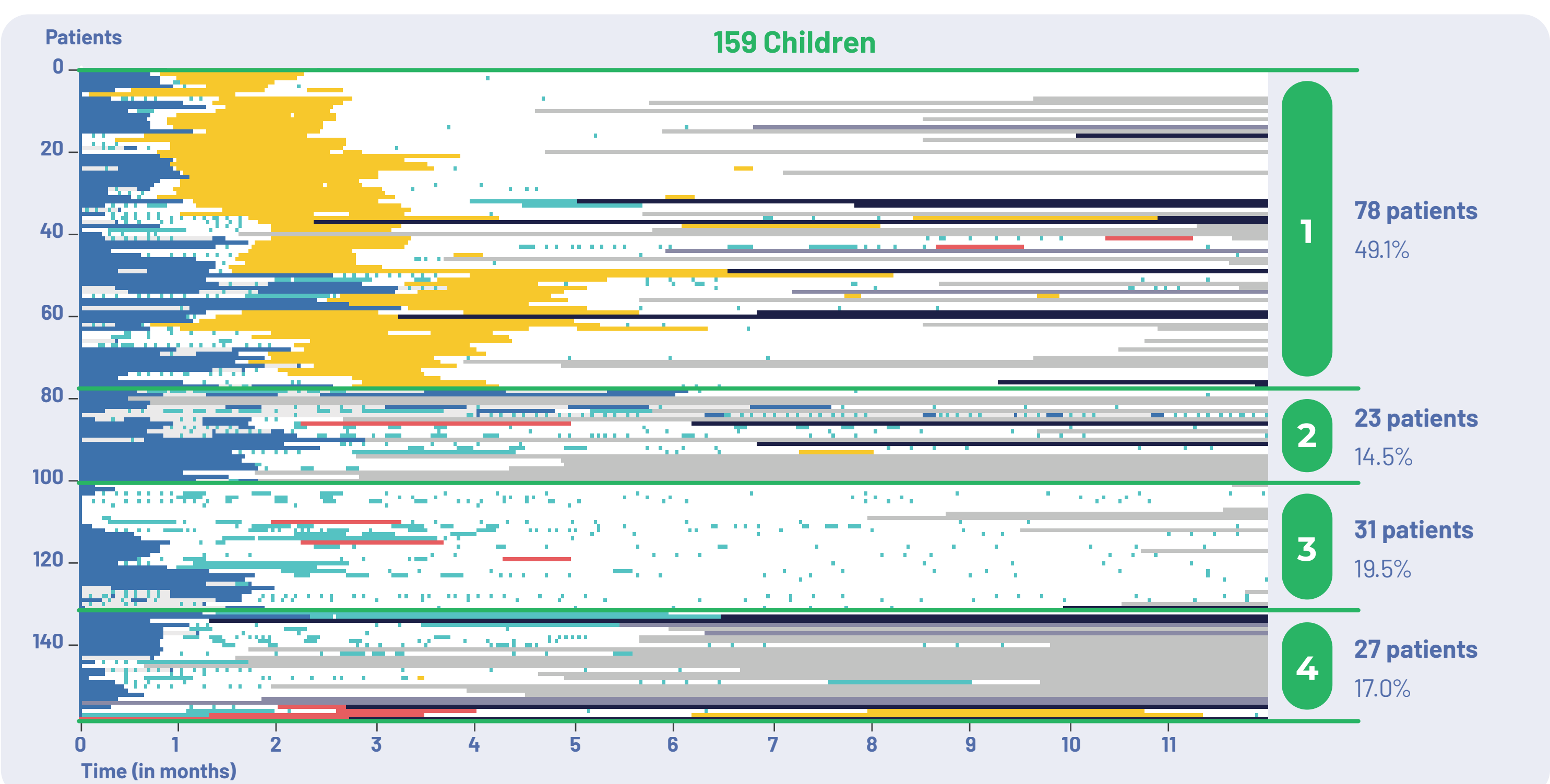
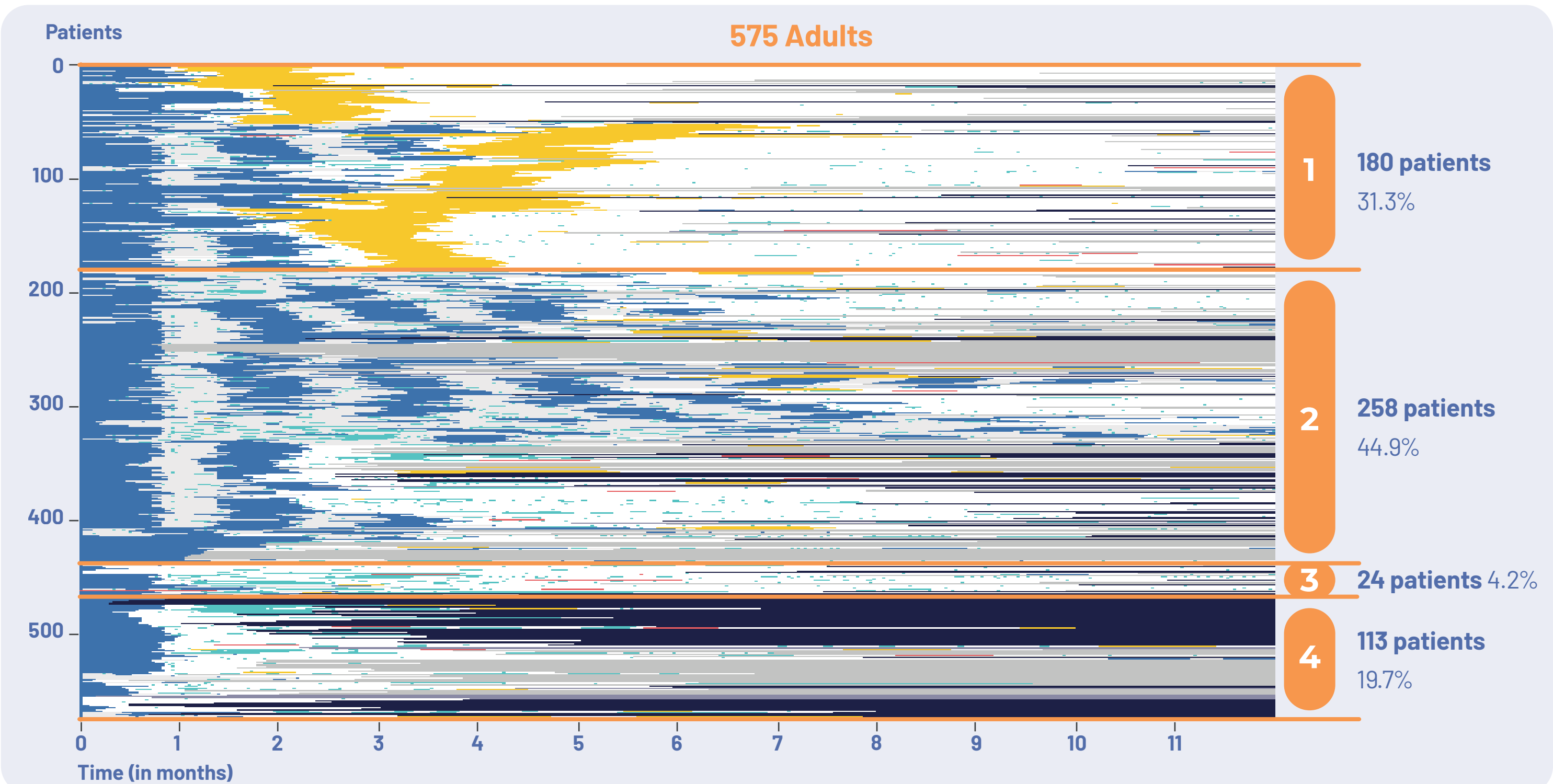
Identification of four different groups consistent with blinatumomab use:

Group 1 "Use in HSCT preparation": adults (31.3%) and children (49.1%).

Group 2 "Use with repeated cycles": adults (44.9%) and children (14.5%).

Group 3 "Short isolated use": adults (4.2%) and children (19.5%).

Group 4 "Short follow-up": adults (19.7%) and children (17.0%); effective clustering on blinatumomab use was unattainable.



In total, 313 (42.6%) patients underwent a HSCT following blinatumomab therapy, of whom 230 (40.0%) were adults and 83 (52.2%) children.

Overall, 8.6% patients (46 adults and 17 children) received both CAR-T cells and blinatumomab therapy: 1.4% of them (5 adults and 5 children) received CAR-T cells before blinatumomab and 7.2% (41 adults and 12 children) after blinatumomab treatment.

CONCLUSION

The present study allows a nationwide assessment of the blinatumomab-based strategies for the treatment of adults and children with ALL.

Blinatumomab may be given as a bridge to HSCT (Group 1: 35%), especially in children; but a significant proportion of patients (Group 2: 38%) received repeated cycles of blinatumomab without HSCT, especially in adults.

Unfortunately, precise distinction between MRD use and R/R use in adults could not be achieved.