EHA EUROPEAN HEMATOLOGY ASSOCIATION
AMGEN
Heva Une filiale de DOCAPOSTE
P424
EHA2024 JUNE 13 - 16 | MADRID

Real-world utilization of blinatumomab in adult and pediatric patients with acute lymphoblastic leukemia in France : Results from the ATHENA Study

Thomas Cluzeau[1,2], Guillaume Oller[3], Arnaud Panes[4], Mallory Cals-Maurette[4], Sophie Bastide[4], Gaëlle Désaméricq[3], Nicolas Boissel[5,6]

1. CHU de Nice, Département d'Hématologie Clinique, Nice, France ; 2. Université de Nice, Nice, France ; 3. Amgen SAS, Courbevoie, France ; 4. Heva, Lyon, France ; 5. Hôpital Saint-Louis, AP-HP, Service d'Hématologie Adolescents et Jeunes Adultes, Paris, France ; 6. Université Paris Cité, URP-3518, Institut de Recherche Saint-Louis, Paris, France

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.

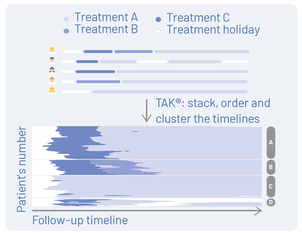
Methods

- 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:

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



References

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

[2]Gökbuget 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.

[3]Gore 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.

[4]Locatelli 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.

[5]Chouaïd 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.

[6]Tredan 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: 11769351221351.

Abbreviations

ATHENA: Re**A**l-world u**T**ilization of Blinatumomab in acute lymp**H**oblastic l**E**ukemia treatme**N**t in Fr**A**nce; **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.

Financial disclosures

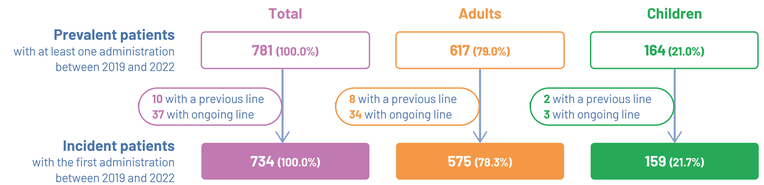
T.C. received honoraria from Amgen. G.O. and G.D. are employees of Amgen SAS and own stocks. A.P., M.CM., S.B. are employees of Heva who received funding from Amgen SAS to perform this work and medical writing. N.B received honoraria from Amgen, Incyte, Jazz Pharma, Novartis, Pfizer, Servier and research grants from Amgen, Novartis, Incyte, Jazz Pharma and Sanofi.

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

Flow chart



Study population

	Total	Adults	Children
Baseline characteristics			
Age (in years)[a]	40.2 (±23.2)	48.9 (±18.0)	8.5 (±5.0)
Sex	53.3% (391)	52.5% (302)	56.0% (89)
ALL history			
Time from diagnosis (in months)[b]	4.6 (1.6-19.3)	4.0 (1.5-16.2)	6.4 (2.0-29.8)
Previous HSCT	5.3% (39)	5.7% (33)	3.8% (6)
Previous GVHD	1.0% (7)	0.9% (5)	1.3% (2)
Previous CAR-T cells treatment	1.4% (10)	0.9% (5)	3.1% (5)
Follow-up			
Follow-up duration (in months)[b]	10.6 (4.5-21.7)	10.1 (3.8-20.9)	11.3 (5.6-23.9)
Reason for early end of follow-up:			
In-hospital death	25.5% (187)	29.0% (167)	12.6% (20)
Lost of follow-up (no information in database)	5.3% (39)	4.7% (27)	6.7% (12)
Blinatumomab use			
Need of re-treatment[c]	1.2% (13)	2.1% (12)	0.6% (1)
Number of cycles[d] per patient[b]	2 (1-3; max 15)	2 (1-3; max 15)	1 (1-2; max 7)

[a]*Mean (±SD)*
[b]*Median (01-03)*
[c]*The re-treatment was defined by a delay between 2 administrations of blinatumomab > 6 months.*
[d]*The cycle change was defined by a delay between 2 administrations of blinatumomab > 7 days.*

RESULTS

Treatment sequences (using TAK® method)

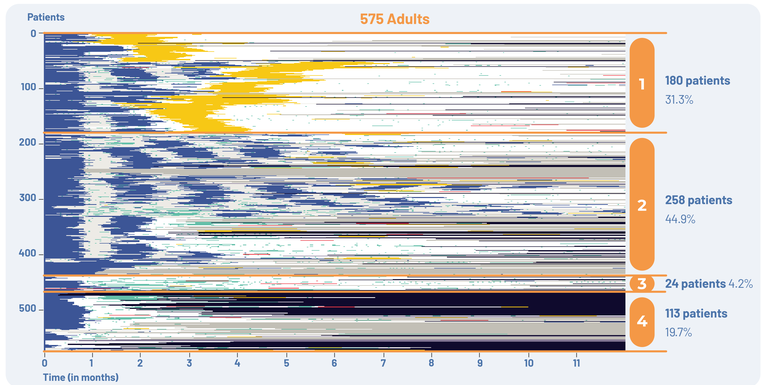
Identification of four different groups consistent with blinatumomab use:

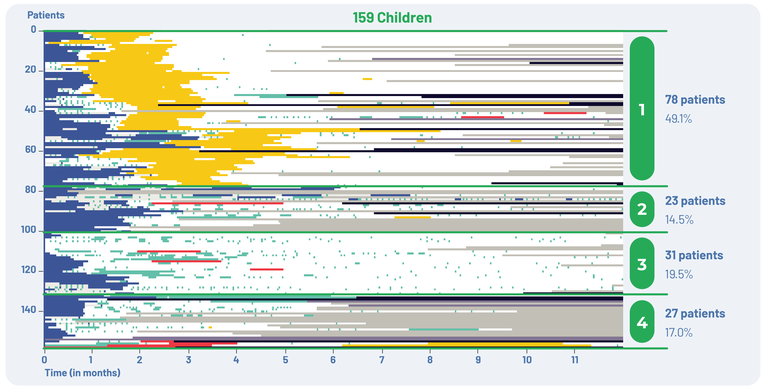
Group 1 "**Use in HSCT preparation**": **adults (31.3%)** and **children (49.1%)**.

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.