Multiple **MY**eloma: an epidemio**LO**gical study using SNII**R**AM **D**atabase

Taux de passage entre les lignes de traitement et prise en charge des patients atteints d'un myélome multiple et ayant initié une première ligne de traitement en 2014 ou 2015
MYLORD, une étude en vie réelle à partir des données du SNDS

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SFH (Société Française d'Hématologie) – 30 mars au 1er avril 2022

Déclaration des conflits d'intérêt

Aurore Perrot

Déclaration des conflits d'intérêt :
Janssen, Amgen, BMS/Celgene, GSK, Takeda, Sanofi

L'étude MYLORD a été financée par JANSSEN-Cilag France

Introduction

Contexte et objectif

MYLORD
Multiple MYeloma: an epidemioLOgical study using SNIIRAM Database

Cohorte de patients traités pour un myélome multiple (MM) en France

Identifiés via la base du Système National des Données de Santé (SNDS)

40 747 patients prévalents de 2014 à 2019, dont 36 241 pour qui l'historique de traitement a été identifié via un algorithme d'IA (ATLAS)

La cohorte la plus étendue et la plus exhaustive de MM en France

Méthodologie et 1er résultats présentés à l'EHA et à l'IMW 2021

Objectif

Décrire le taux de passage entre les lignes de traitement et la prise en charge des patients atteints de MM

Méthodes

Identification des patients et analyses statistiques

Identification des patients

Via la cohorte MYLORD

Inclusion des patients incidents MM en 2014 ou 2015 pour avoir suffisamment de suivi

Suivi jusqu'au 31 décembre 2019 (ou jusqu'au décès)

Analyses statistiques

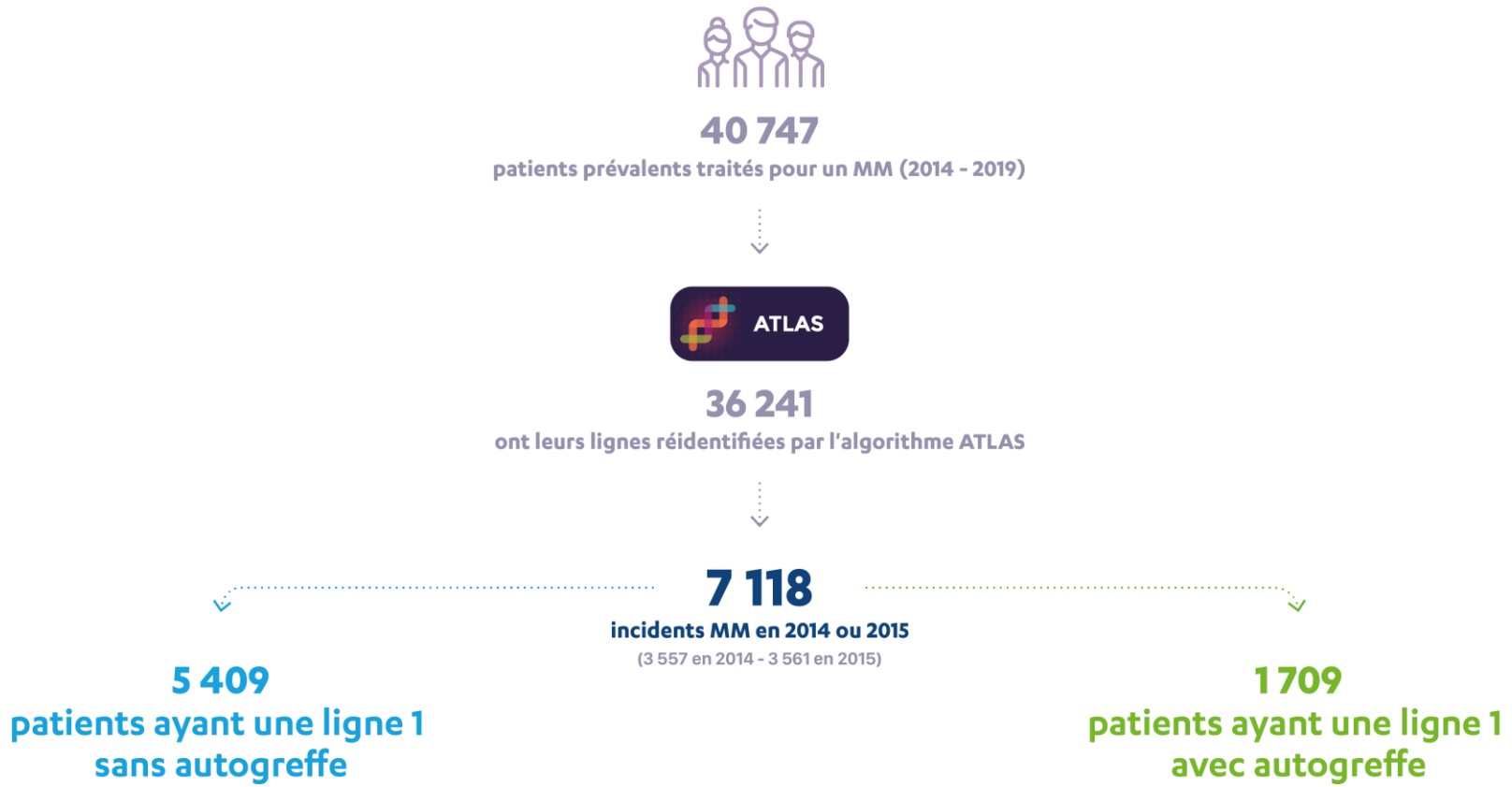
Taux de passage entre les lignes

Séquences de traitement

Analyse de survie (via un Kaplan Meier)

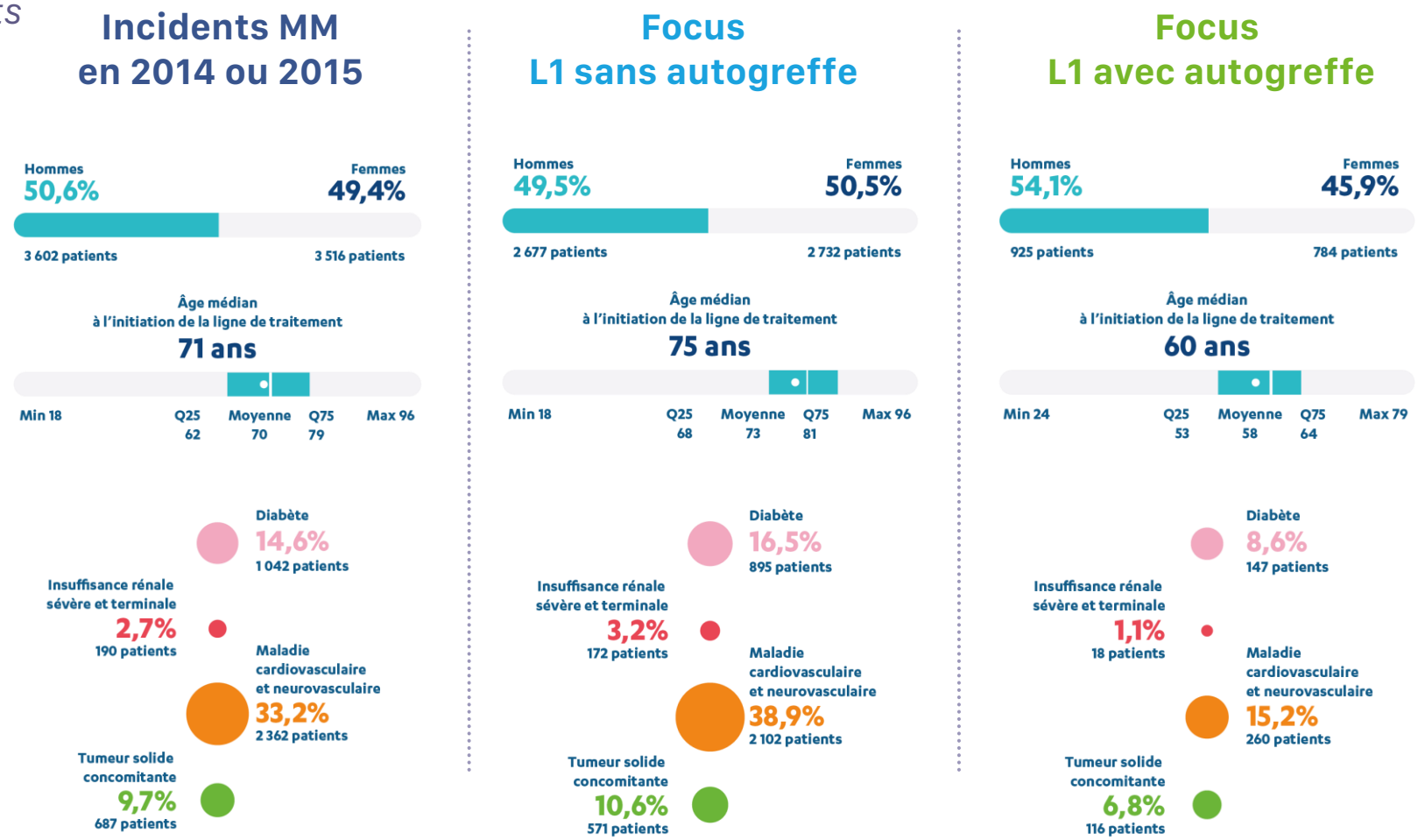
Résultats

Cohorte de patients



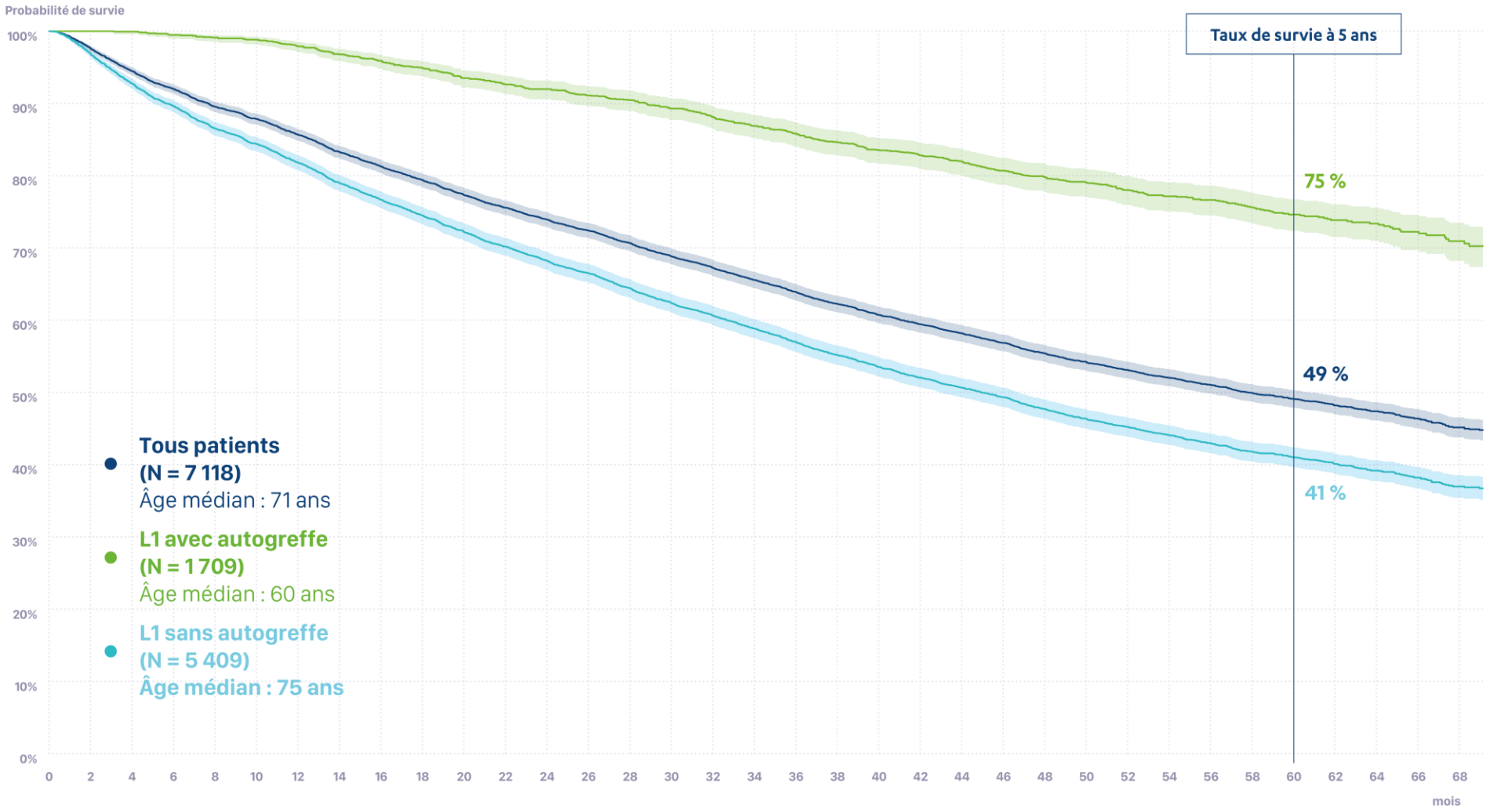
Résultats

Caractéristiques des patients



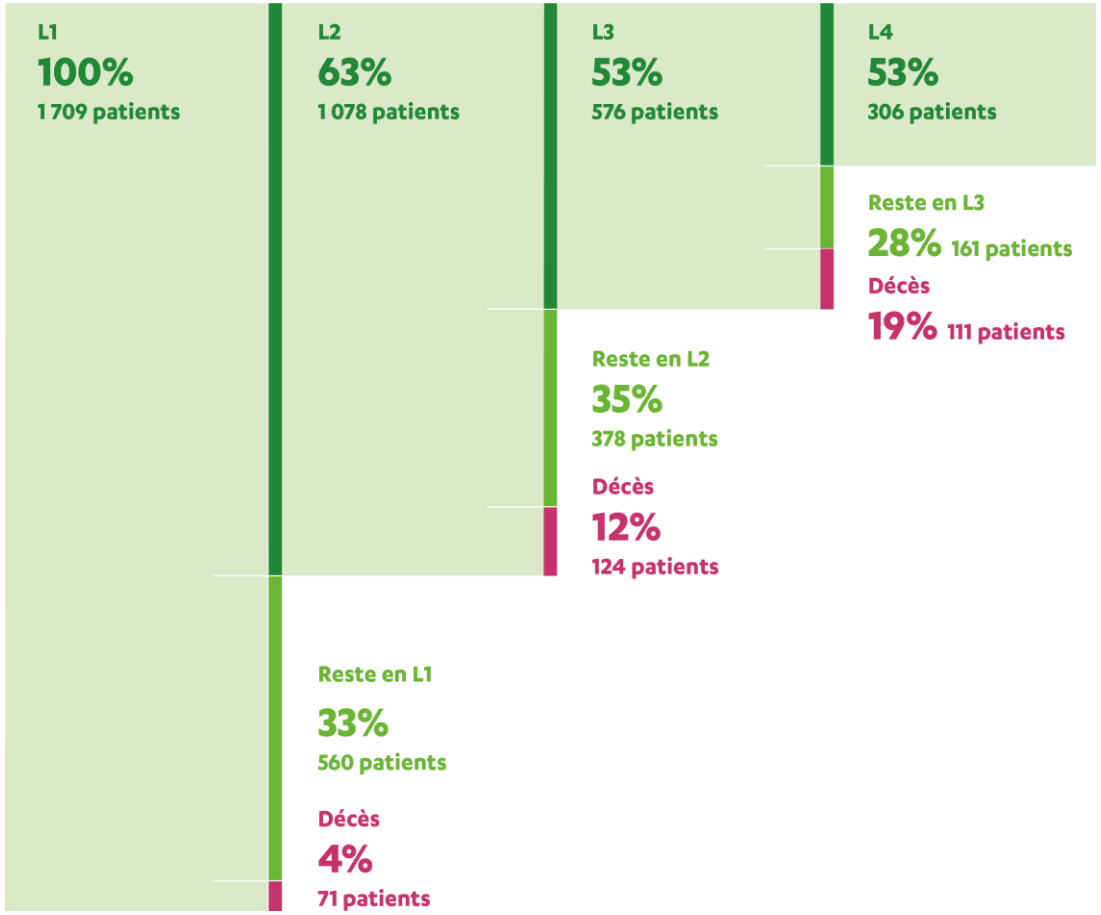
Résultats

Courbe de survie



Résultats

Taux de passage entre les lignes de traitements des patients ayant eu une L1 avec autogreffe



Résultats

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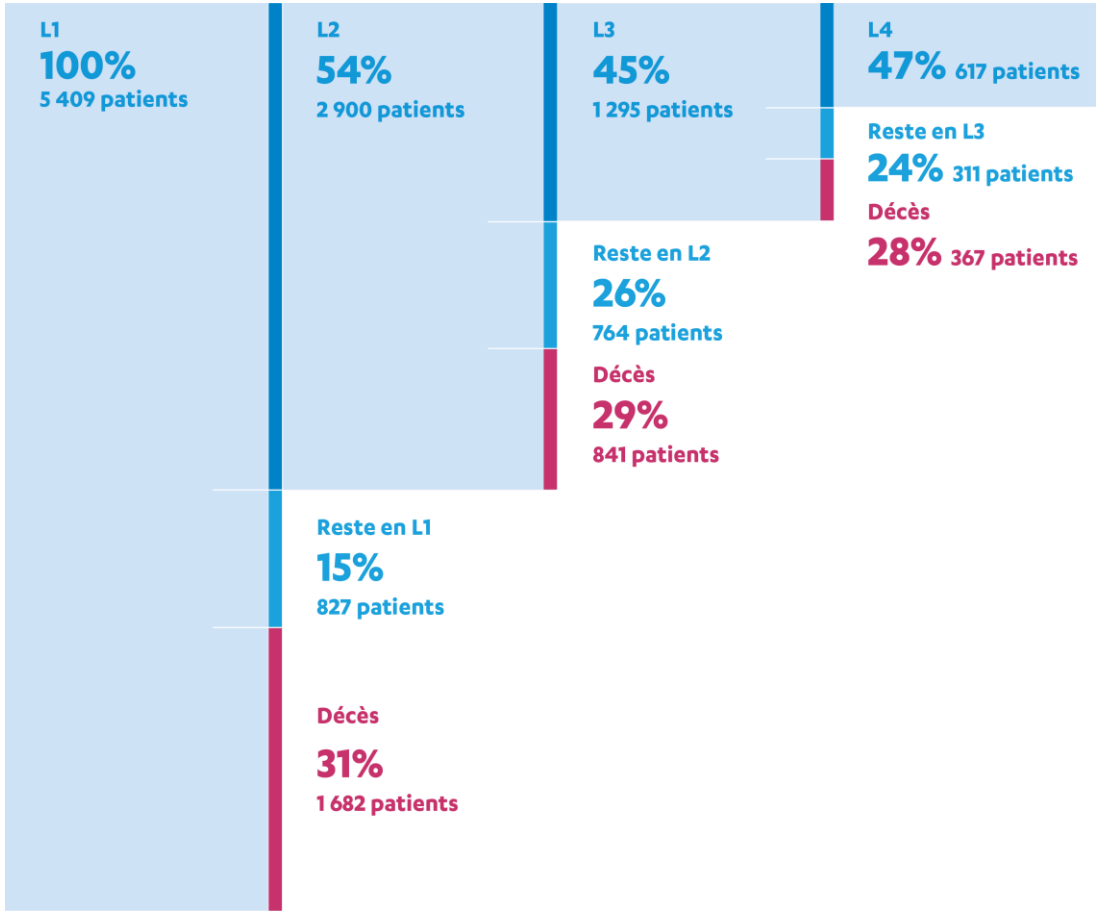

Résultats

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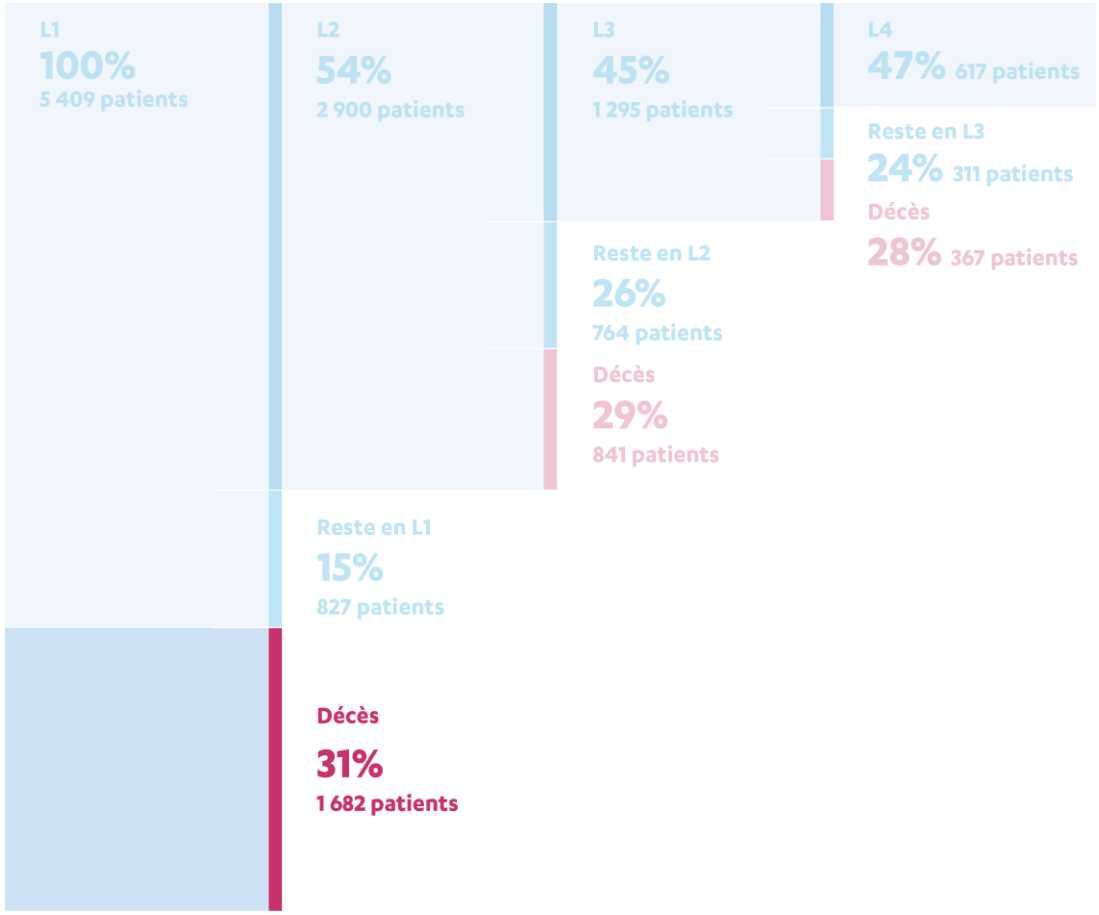
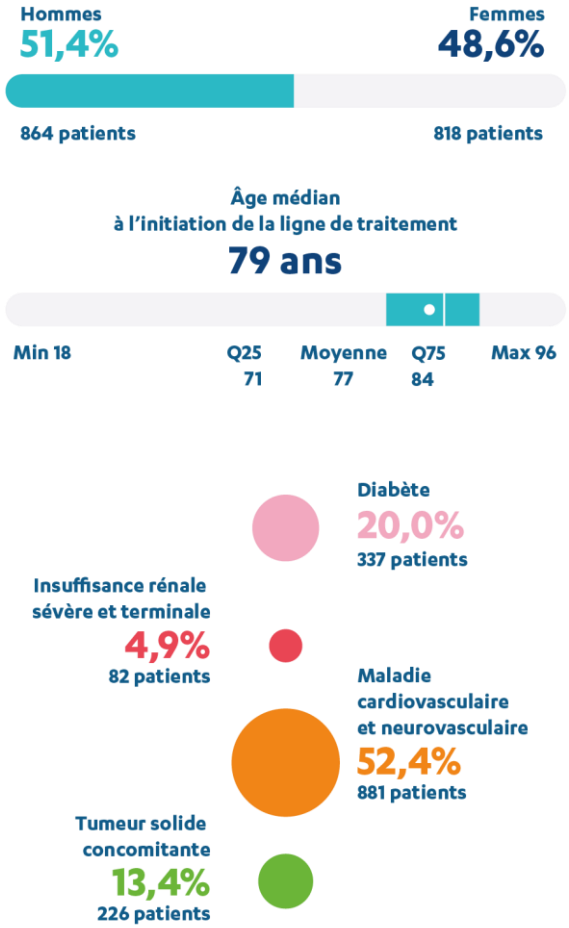


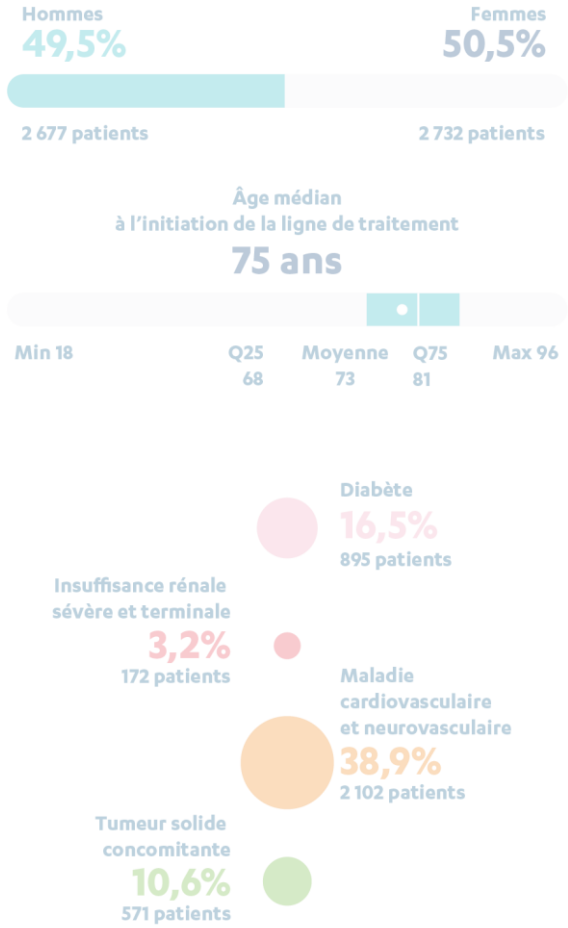
Résultats

Caractéristiques des patients patients ayant eu une L1 sans autogreffe

Patients bénéficiant d'une L1 sans autogreffe et ayant présenté un décès avant passage en L2
N = 1 682

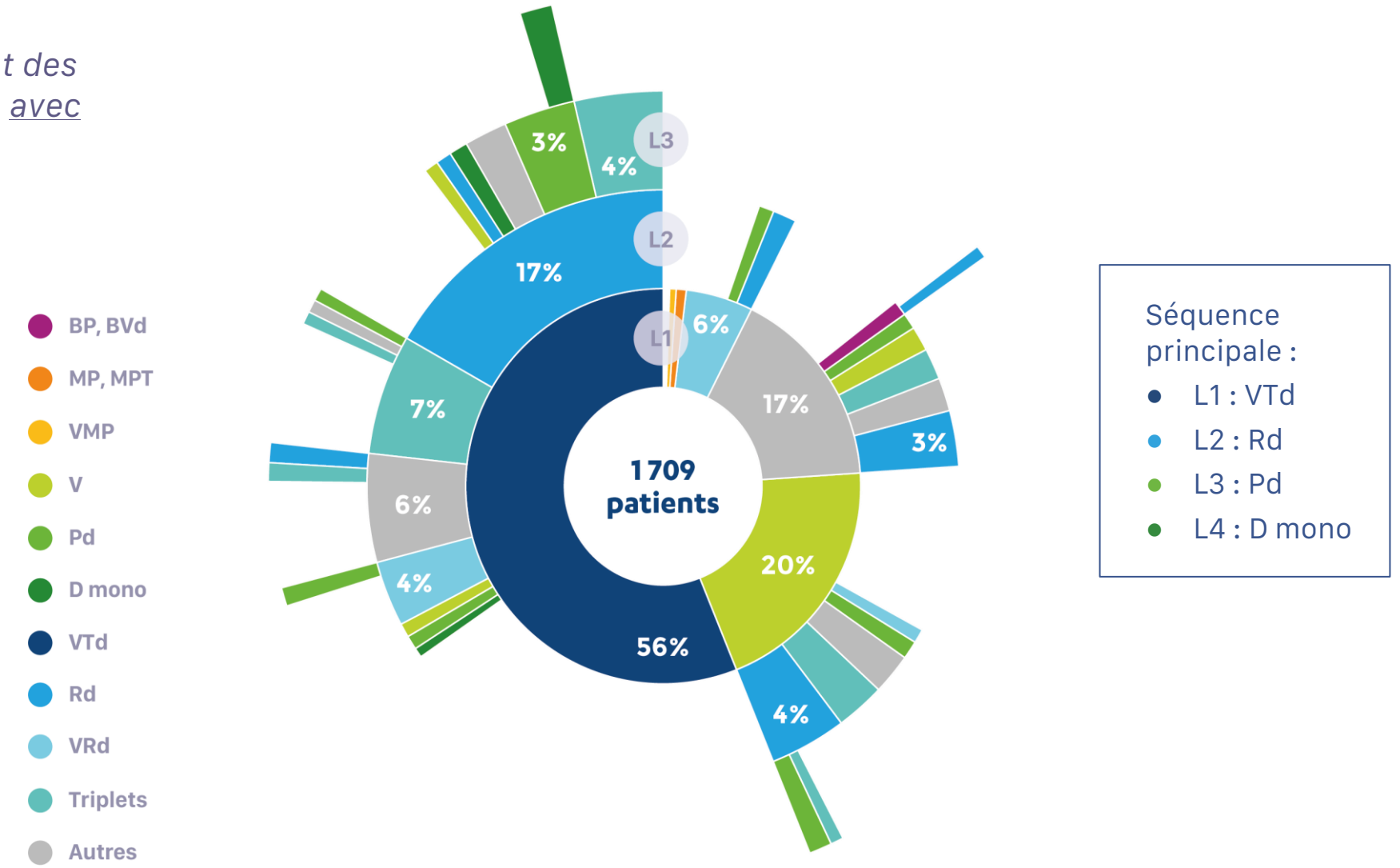


Rappels : patients bénéficiant d'une L1 sans autogreffe
N = 5409



Résultats

Séquences de traitement des patients ayant eu une L1 avec autogreffe



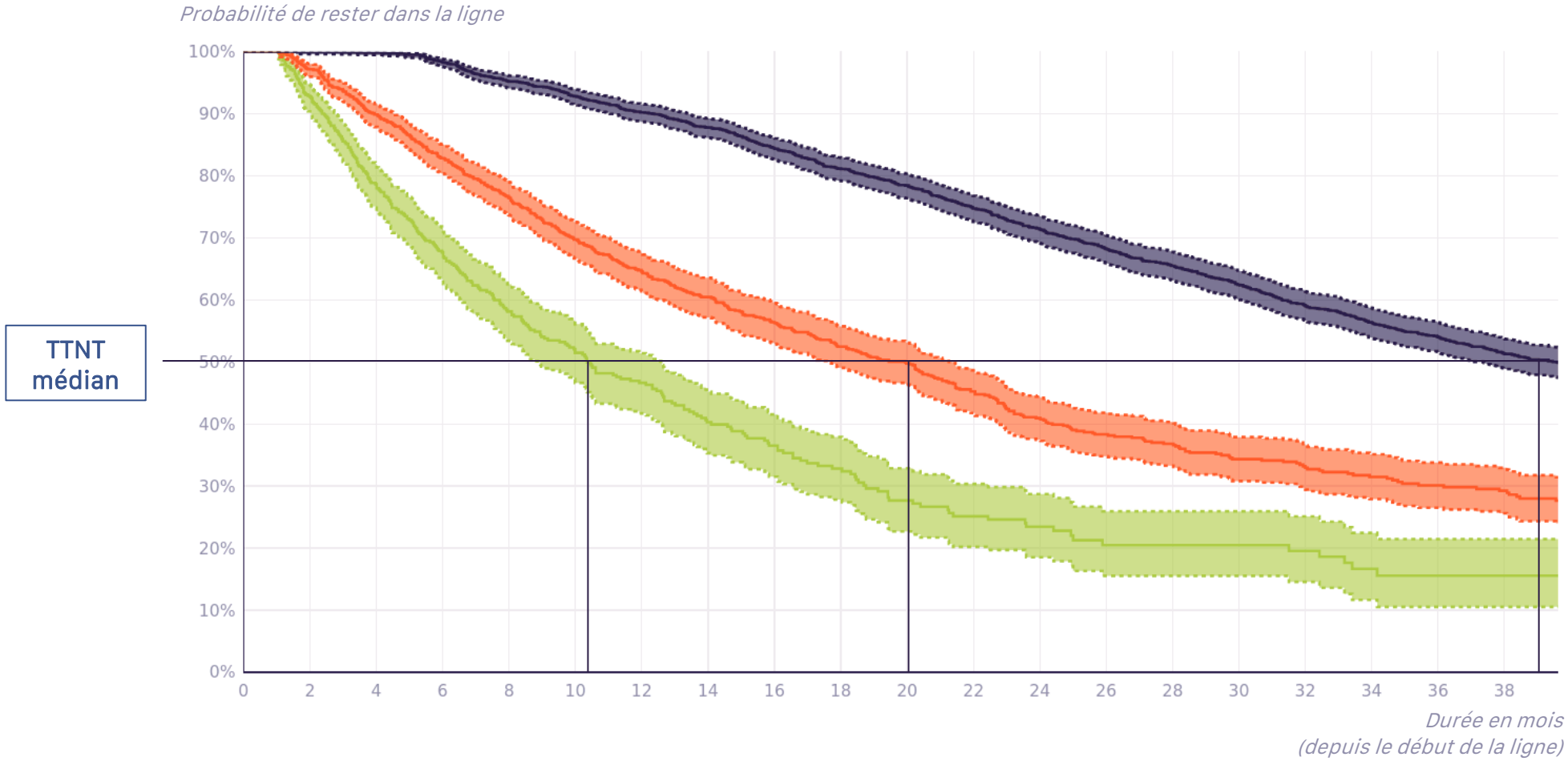
Séquence principale :

- L1 : VTd
- L2 : Rd
- L3 : Pd
- L4 : D mono

Triplets : IRd ; KRd ; DRd ; DVd ; PVd ; DPd ; VRd

Résultats

TTNT des lignes des patients ayant eu une L1 avec autogreffe

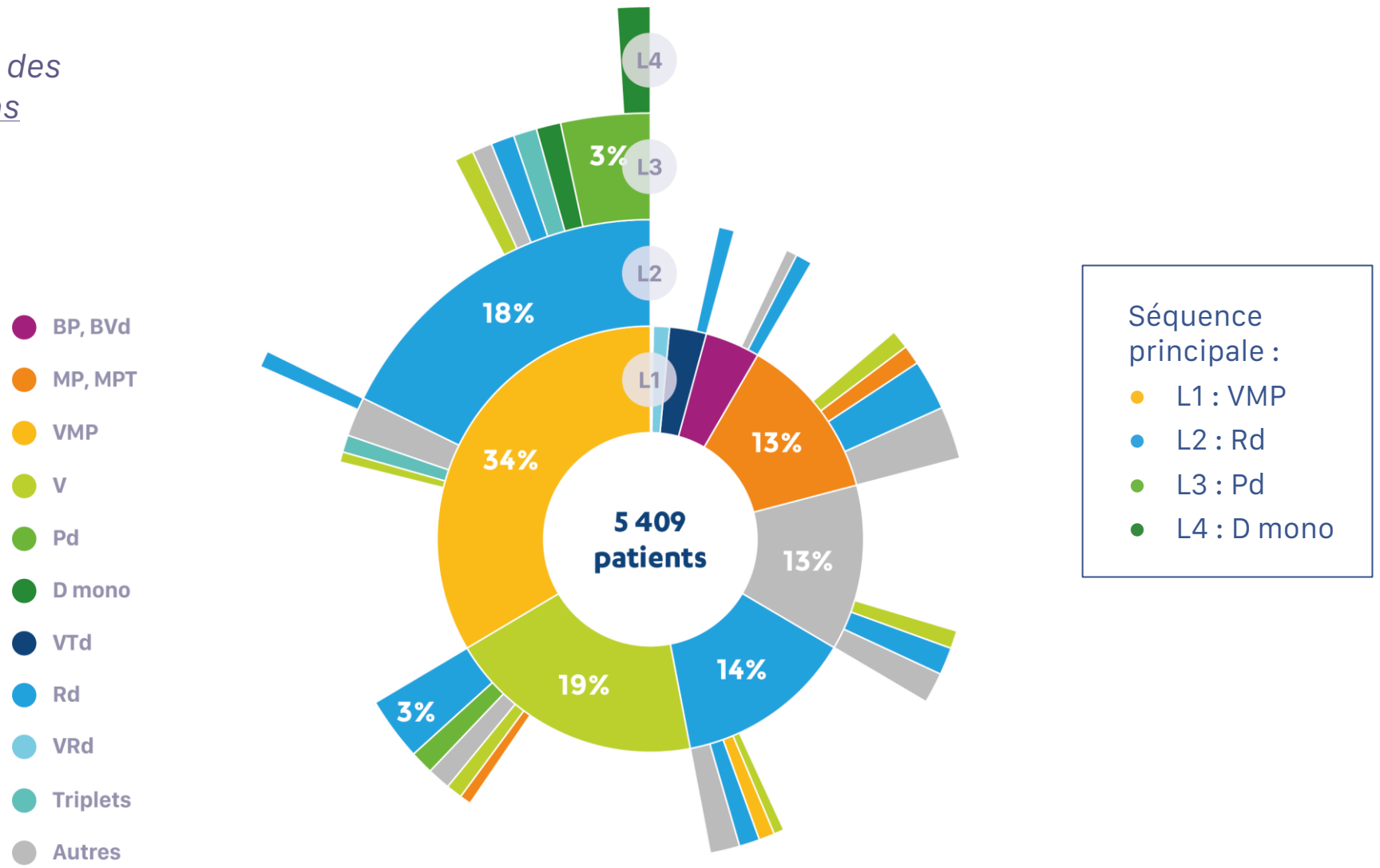


- Ligne 1
- Ligne 2
- Ligne 3

TTNT: Time to Next Treatment

Résultats

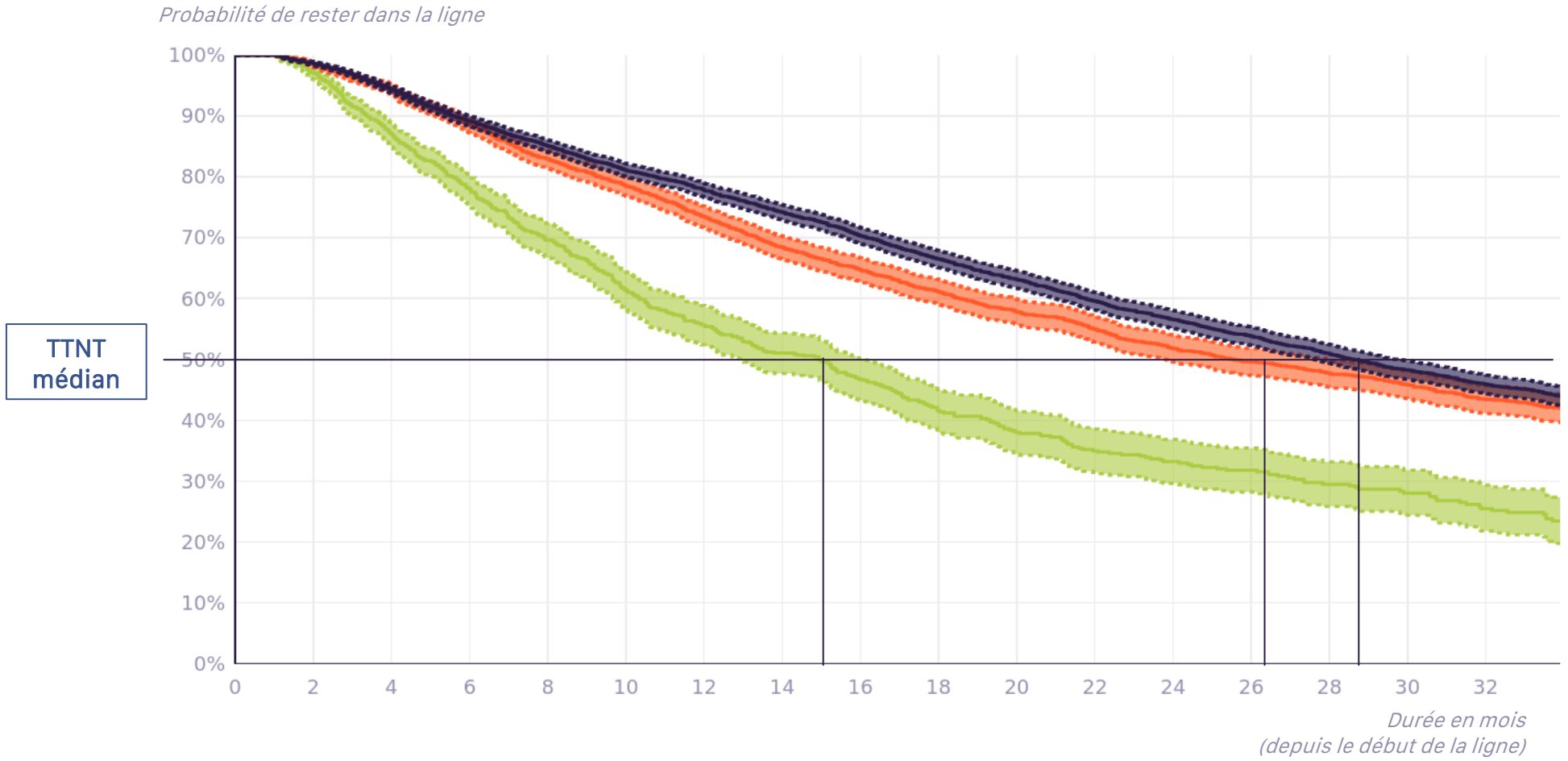
Séquences de traitement des patients ayant une L1 sans autogreffe



Triplets: IRd ; KRd ; DRd ; DVd ; PVd ; DPd ; VRd

Résultats

TTNT des lignes des patients ayant eu une L1 sans autogreffe



- Ligne 1
- Ligne 2
- Ligne 3

TTNT: Time to Next Treatment

Conclusion

- Rôle important des données de vie réelle dans ce paysage thérapeutique qui évolue rapidement

- La cohorte générée via l'étude MYLORD montre un réel potentiel pour obtenir un suivi en vraie vie des patients avec un MM en France (épidémiologie, taux de passage entre les lignes de traitement, séquences thérapeutiques, …)

- Les patients avec un MM qui décèdent après une L1 sont globalement plus âgés et comorbides que ceux pouvant avoir recours à plusieurs lignes de traitement

- De nombreux patients ne peuvent bénéficier que d'un nombre limité de lignes de traitements
  → Il paraît important d'initier de nouveaux traitements le plus tôt possible

Merci pour votre attention

Congrès EHA 2021

MYLORD
Multiple MYeloma: an epidemioLOgical study using SNIIRAM Database

MYLORD EP999

Epidemiology of multiple myeloma: data from the french national health insurance database (SNDS)

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Background

Multiple myeloma (MM) is considered as an incurable hematologic disease. Net cancer-specific survival at 5 years after diagnosis of MM was estimated at 47% between 2005 and 2010 in France[a]. Thanks to significant improvements of the MM therapeutic management in the past decades, the overall survival of MM patients tends to increase, and some patients now achieve long-term remission. This directly impacts the dynamic of MM epidemiology. The world age-standardized MM incidence rate in France was estimated at 4.1 per 100,000 PY in 2020, based on extrapolations from available regional data. For the first time, this study provides updated and comprehensive epidemiological data by line of treatments based on the nationwide French National Health Insurance (NHI) databases, called SNDS ("Système National des Données de Santé"). These databases include hospital records, primary and secondary care, and deaths, for 66 million people.

The objective of the study is to estimate incidence, prevalence of MM and mortality of these patients, each year and for each line from 2014 to 2019, based on secondary use of data from the French NIH databases.

Methods

Design

This is a retrospective observational cohort study of MM patients identified through SNDS from 2014 to 2019. To identify patients with MM, a published algorithm[b] was used as a base and was expanded to consider recent evolutions of MM therapeutic management. The rates were standardized using the age distribution to allow international comparison. Treatment lines were re-constructed through ATLAS, an artificial intelligence algorithm adapted on the Smith-Waterman alignment sequence[c].

Inclusion criteria

Adult patients affiliated to the General health insurance Scheme (covering around 76% of the French population) were included if they presented either:

- a hospital record with MM diagnosis (ICD-10 C90*), or
- a Long-Term Disease (LTD) status with MM diagnosis (ICD-10 C90*), or
- a treatment with lenalidomide or thalidomide paired with at least 2 protein electrophoresis on serum or urine in less than 4 months after the first delivery of the drug

from January 1st, 2006 to December 31st, 2019.

Data since 2006 are used to define prevalent and incident patients. Incident MM patients were defined as patients without MM information (LTD or hospitalization with MM diagnosis codes or MM treatment) during the 2 years prior to index date. Analysis were conducted only on patients treated and alive on January 1st 2014.

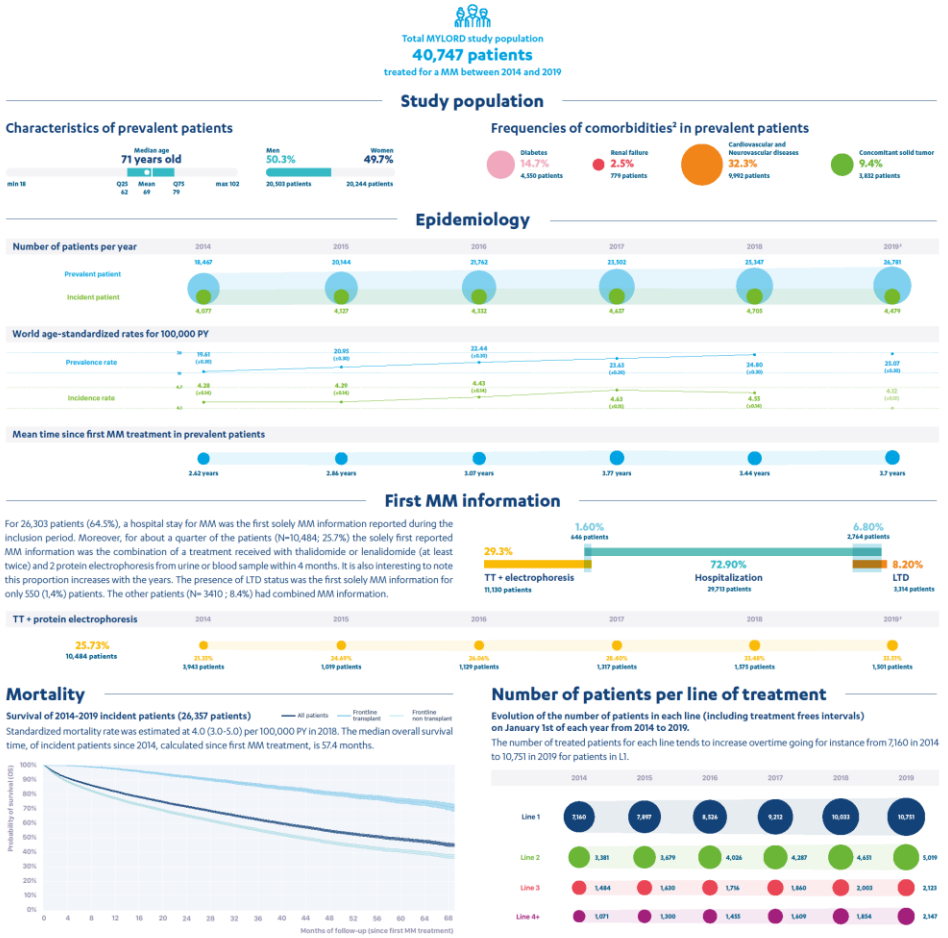
Exclusion criteria

- Patients with only ICD-10 C90.1/C90.2/C90.3 and not treated during the follow-up
- Among patients treated with lenalidomide or thalidomide and paired with at least 2 protein electrophoresis, patients with no hospital stay for MM and with a hospital stay for another reason[1].

Conclusion

This study expands existing epidemiological data on MM patients in France and is the first to present recent nationwide results by line of treatment. Growing prevalence and incidence rates of MM are in accordance with the estimations from French network of cancer registries confirming that the French health insurance databases are a valuable source of data to further study the therapeutic management of MM.

European Hematology Association (EHA), June 9–17 2021



1. Principal diagnosis, related diagnosis or significant associated diagnosis for myelodysplastic syndrome (ICD-10 D46*) and/or follicular lymphoma (ICD-10 C82*) and/or diffuse non-Hodgkin lymphoma (ICD-10 C83*) and/or peripheral and cutaneous T cell lymphoma (with ICD-10 C84*) and/or other non-Hodgkin lymphoma (ICD-10 C85*) and/or osteomyelofibrosis (ICD-10 C47.4) and/or acute panmyelosis with myelofibrosis (ICD-10 C94.4) and/or POEMS syndrome (ICD-10 D47.7) and/or amyloidosis (ICD-10 E85*)
2. Based on the methodology and algorithms developped by the Caisse Nationale d'Assurance Maladie (CNAM)
3. The year 2019 should be interpreted with caution. We are missing some incident patients as 2020 year is requested to accurately identify MM patients

References
a. Monnereau et al. Survie des personnes atteintes de cancer en France métropolitaine 1989-2013. Partie 2 – Hémopathies malignes. Feb 2016
b. Palmaro A et al. Identifying multiple myeloma patients using data from the French health insurance databases. Medicine. 2017. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5371442/
c. M. Prodel, L. Lamarsalle and V. Augusto. ATLAS: A Robust Algorithm for TemporalSequence Alignment of Treatment Lines using Claim Databases. 2019. IEEE. Conference on Computational Intelligence in Bioinformatics and Computational Biology. (CIBCB), Siena, Italy, 2019, pp. 1-8. https://ieeexplore.ieee.org/document/8791467

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https://static.hevaweb.com/web/PDF/61ace9b990b06-janssen-mylord-poster-eha2021-epidemio.pdf

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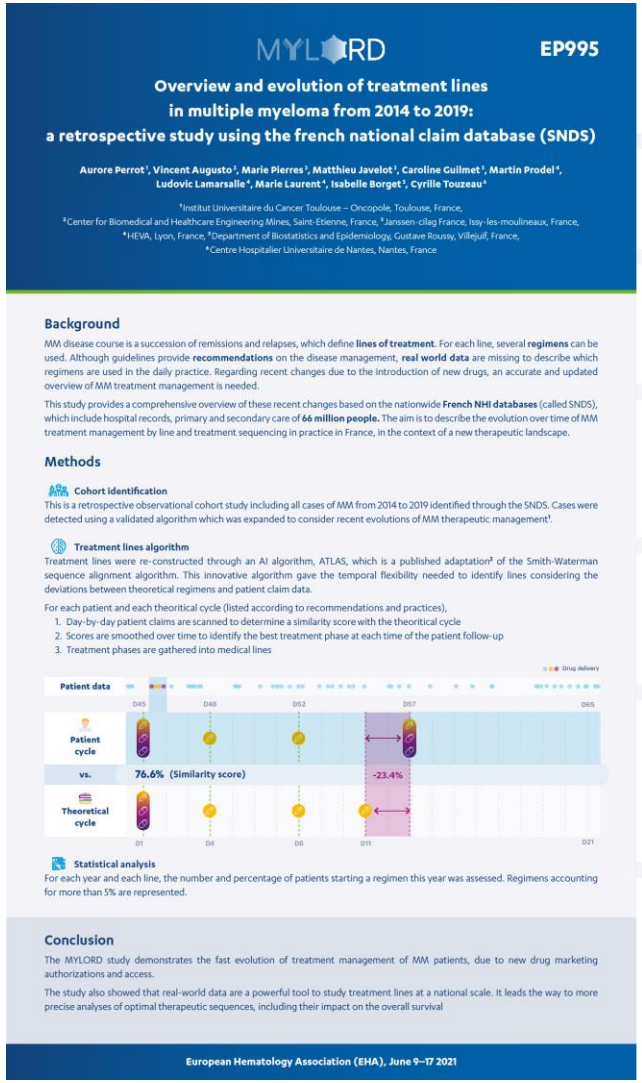

MYLORD

EP995

Overview and evolution of treatment lines in multiple myeloma from 2014 to 2019: a retrospective study using the french national claim database (SNDS)

Aurore Perrot[1], Vincent Augusto[2], Marie Pierres[1], Matthieu Javelot[3], Caroline Guilmet[3], Martin Prodel[4], Ludovic Lamarsalle[4], Marie Laurent[4], Isabelle Borget[2], Cyrille Touzeau[5]

[1]Institut Universitaire du Cancer Toulouse – Oncopole, Toulouse, France, [2]Center for Biomedical and Healthcare Engineering Mines, Saint-Etienne, France, [3]Janssen-cilag France, Issy-les-moulineaux, France, [4]HEVA, Lyon, France, [5]Department of Biostatistics and Epidemiology, Gustave Roussy, Villejuif, France, [6]Centre Hospitalier Universitaire de Nantes, Nantes, France

Background

MM disease course is a succession of remissions and relapses, which define **lines of treatment**. For each line, several **regimens** can be used. Although guidelines provide **recommendations** on the disease management, **real world data** are missing to describe which regimens are used in the daily practice. Regarding recent changes due to the introduction of new drugs, an accurate and updated overview of MM treatment management is needed.

This study provides a comprehensive overview of these recent changes based on the nationwide **French NHI databases** (called SNDS), which include hospital records, primary and secondary care of **66 million people.** The aim is to describe the evolution over time of MM treatment management by line and treatment sequencing in practice in France, in the context of a new therapeutic landscape.

Methods

Cohort identification

This is a retrospective observational cohort study including all cases of MM from 2014 to 2019 identified through the SNDS. Cases were detected using a validated algorithm which was expanded to consider recent evolutions of MM therapeutic management[1].

Treatment lines algorithm

Treatment lines were re-constructed through an AI algorithm, ATLAS, which is a published adaptation[2] of the Smith-Waterman sequence alignment algorithm. This innovative algorithm gave the temporal flexibility needed to identify lines considering the deviations between theoretical regimens and patient claim data.

For each patient and each theoritical cycle (listed according to recommendations and practices),

1. Day-by-day patient claims are scanned to determine a similarity score with the theoritical cycle
2. Scores are smoothed over time to identify the best treatment phase at each time of the patient follow-up
3. Treatment phases are gathered into medical lines

Statistical analysis

For each year and each line, the number and percentage of patients starting a regimen this year was assessed. Regimens accounting for more than 5% are represented.

Conclusion

The MYLORD study demonstrates the fast evolution of treatment management of MM patients, due to new drug marketing authorizations and access.

The study also showed that real-world data are a powerful tool to study treatment lines at a national scale. It leads the way to more precise analyses of optimal therapeutic sequences, including their impact on the overall survival

European Hematology Association (EHA), June 9–17 2021

Results

40,747 patients treated for a MM (2014-2019)

4,508 exclusions (11%)

2,259 (6%) with only 1 day of treatment
1,277 (3%) with only 2 to 4 dates of treatments
972 (2%) with more than 4 dates with treatments but disseminated (less than once every 70 days)

36,239 Patients with lines identified with ATLAS

Distribution of prevalent patients

2014 2015 2016 2017 2018 2019*

Prevalent 16,879 16,291 17,730 21,581 22,904 23,915

Distribution of the most common regimens started each year, by line (in %)

Line 1 with tranplant — 5,287 patients

VTd 54 63 75 67 38 12
VTd 7 9 8 17 49 48
Vd, VCd, V 22 21 9 8 7 8

Line 1 without transplant — 17,858 patients

VMP 34 33 21 21 23 12
Rd 12 15 20 23 32 31
Vd, VCd, V 19 20 19 21 19 18
VTd 2 2 3 4 10 23
MP, MPT 11 9 8 6 3 3

Line 2 — 13,526 patients

In 2019, among the 35% of Triplets, Dara-based regimens represent 16% (DRd: 13%, DVd: 2%, DPd: 1%)

Rd 44 49 50 50 40 30
Triplets 5 9 11 13 21 23
Vd, VCd, V 12 9 7 6 4 1
Pom-Dex 3 4 6 6 6 6
Dara mono 0 0 1 3 4 6
MP, MPT 6 5 4 3 3 1

Line 3 — 7,885 patients

In 2019, among the 32% of Triplets, Dara-based regimens represent 16% (DRd: 7%, DVd: 5%, DPd: 4%)

Rd 30 32 26 25 21 16
Triplets 5 6 8 13 19 22
Vd, VCd, V 16 11 11 9 6 4
Pom-Dex 10 17 23 24 23 17
Dara mono 0 0 5 9 11 13
MP, MPT 8 6 6 3 4 3
BP, BVd 13 9 6 2 2 0

Line 4+ — 5,446 patients

In 2019, among the 29% of Triplets, Dara-based regimens represent 16% (DRd: 6%, DVd: 6%, DPd: 4%)

Rd 15 14 14 12 12 10
Triplets 4 4 7 13 20 29
Vd, VCd, V 11 14 8 7 7 3
Pom-Dex 25 28 23 20 14 12
Dara mono 0 0 21 25 18 14
MP, MPT 9 6 6 4 4 4
BP, BVd 14 14 6 5 4 3

*The year 2019 should be interpreted with caution. We are missing some incident patients as 2020 year is requested to accurately identify MM patients

Treatment sequences of all incident patients from 2014 to 2019

With a transplant and who had 3 lines of treatment

The main course is: **L1: VTd, L2: Rd, L3: Triplets**

Without transplant who had 4 lines of treatment

The main course is: **L1: VMP, L2: Rd, L3: Pom-Dex, L4: Dara mono**

Legend

Rd
Lenalidomide / low-dose dexamethasone

Triplets
IRd: Ixazomib / Lenalidomide / Dexamethasone
KRd: Carfilzomib / Lenalidomide / Dexamethasone
DRd: Daratumumab / Lenalidomide / Dexamethasone
DVd: Daratumumab / Bortezomib / Dexamethasone
PVd: Pomalidomide / Bortezomib / Dexamethasone
DPd: Daratumumab / Pomalidomide / Dexamethasone
VRd: Bortezomib / Lenalidomide / Dexamethasone

VTd
Bortezomib / Thalidomide / Dexamethasone

VRd
Bortezomib / Lenalidomide / Dexamethasone

Vd, VCd, V
Vd: Bortezomib / Dexamethasone
VCd: Bortezomib / Cyclophosphamide / Dexamethasone
V: Bortezomib monotherapy

Pom-Dex
Pomalidomide / Dexamethasone

Dara mono
Daratumumab

VMP
Bortezomib / Melphalan / Prednisone

MPT, MP
MP: Melphalan / Prednisone
MPT: Melphalan / Prednisone / Thalidomide

BP, BVd
BVd: Bendamustine / Bortezomib / Dexamethasone
BP: Bendamustine / Prednisone

Glossary

AI: Artificial Intelligence
ATLAS: Analysis of Treatment Lines using Alignment of Sequences
MM: Multiple Myeloma
NHI: National Health Insurance
MYLORD: Multiple myeloma: an epidemioLOgical study using SNIIRAM Database
SNDS: Système National des Données de Santé

References

1. C. Touzeau, M. Pierres, M. Javelot, C. Guilmet, L. Lamarsalle, F. Raguideau, I. Borget, V. Augusto, A. Perrot, "Epidemiology of multiple myeloma: data from the french national health insurance database (SNDS)", 2021 European Hematology Association (EHA), June 9–17 2021

2. M. Prodel, L. Lamarsalle and V. Augusto, "ATLAS: A Robust Algorithm for Temporal Sequence Alignment of Treatment Lines using Claim Databases," 2019 IEEE Conference on Computational Intelligence in Bioinformatics and Computational Biology (CIBCB), Siena, Italy, 2019, pp. 1-8. https://ieeexplore.ieee.org/document/8791467

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