

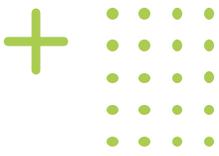
SMMML newsletter

May 25th, 2023

Based on data from April 2023

Monthly updates around multiple myeloma





The goal of this newsletter is to give an overview of what is happening around multiple myeloma in terms of medical developments. This is achieved by monitoring news articles, PR releases and scientific reports on one hand. Conversations from HCPs, digital opinion leaders and other influencers attending congresses, offering their opinion on treatments and commenting on new developments on the other hand.

◆ Who will benefit from this newsletter?

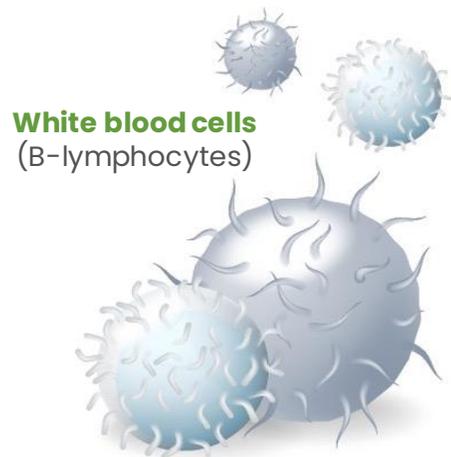
Any professionals interested in keeping up with developments around multiple myeloma:

- Marketers
- Business Analysts
- But also HCPs who want to anticipate the future landscape of MM management

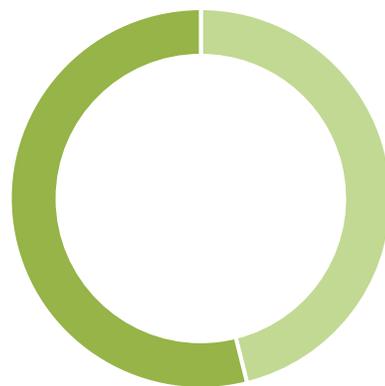


Introduction on Multiple Myeloma

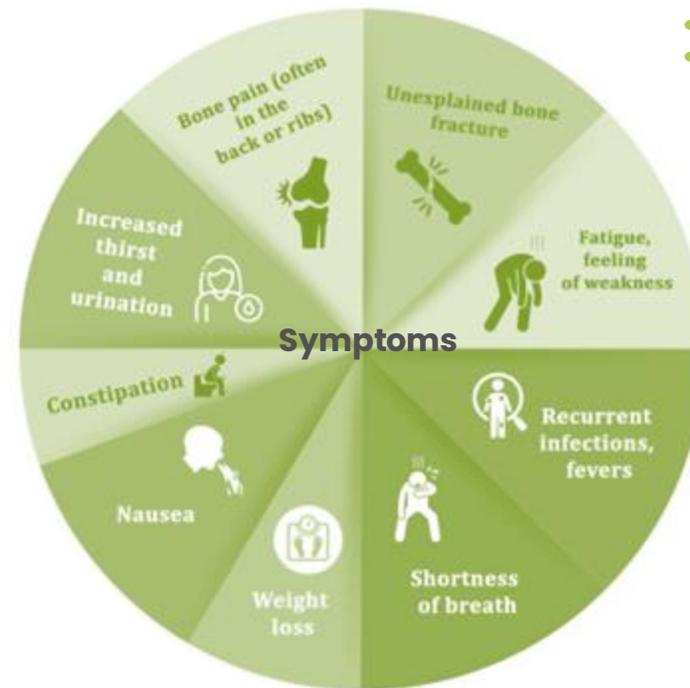
What is Multiple Myeloma?



70
YEARS



■ 5 year survival rate ~50%



Read more on Multiple Myeloma:



→ [Professional version in English](#)

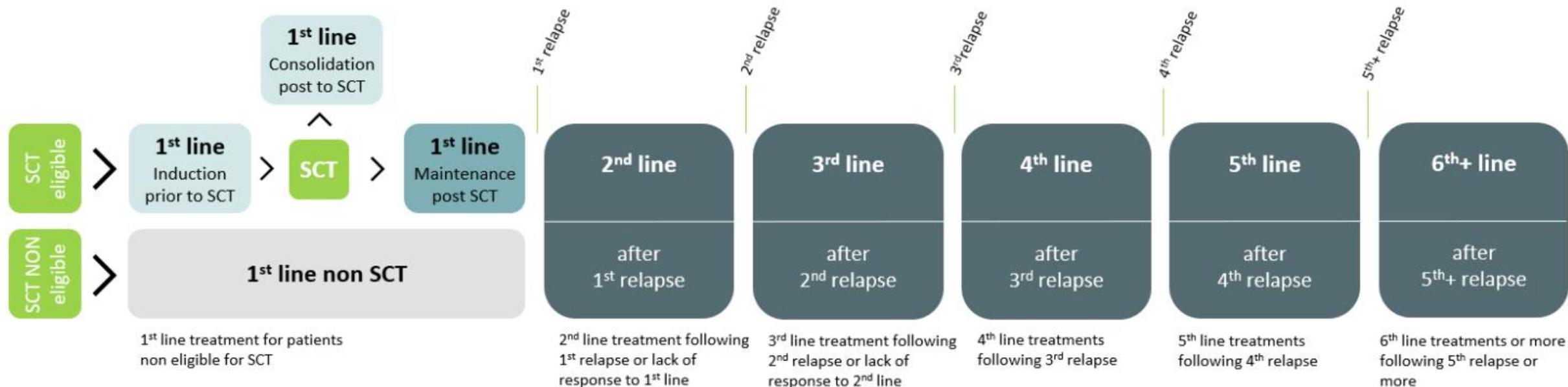
→ [Professional version in French](#)



→ [Consumer version in English](#)

→ [Consumer version in French](#)

MM lines of therapy based on to the following definitions



1st line treatment for patients non eligible for SCT

2nd line treatment following 1st relapse or lack of response to 1st line

3rd line treatment following 2nd relapse or lack of response to 2nd line

4th line treatments following 3rd relapse

5th line treatments following 4th relapse

6th line treatments or more following 5th relapse or more

1st line Induction prior SCT

For stem cell candidates, the first step to gain a response to reduce the tumor burden before SCT. Please note that patients who received more than one SCT are considered to be in "1st line prior to stem cell transplant" for the latest SCT procedure planned. For instance, should a patient receive an induction treatment prior to a 2nd SCT, he should be considered as a 1st line transplant patient.

1st line Consolidation post SCT

1st line therapy **after** stem cell transplant to **deepen the response** achieved by adding a **short course** of full dose therapy.

1st line Maintenance post SCT

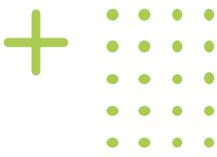
1st line therapy **after** stem cell transplant to **sustain the quality of the response** achieved by adding a long course – from several months up to disease progression – of reduced dose therapy.

Drugs approved by European Medicines Agency (EMA)



Brand name	Active substance	Manufacturer	Class of therapy	EMA Date of authorisation	Line of treatment	Product Monograph
Revlimid®	lenalidomide	BMS	Immunomodulating agents (IMiDs)	14/06/2007	All lines	Click here
Thalidomide BMS® / Thalomid® (US)	thalidomide	BMS	Immunomodulating agents (IMiDs)	16/04/2008	All lines	Click here
Imnovid® / Pomalyst® (US)	pomalidomide	BMS	Immunomodulating agents (IMiDs)	05/08/2013	2L+ (after Revlimid and Velcade)	Click here
Pepaxti® / Pepaxto® (US)	melflufen	Oncopeptides AB	Peptide conjugated alkylator	17/08/2022	Triple class exposed / 3L+ / 4L+ / 5L+	Click here
Velcade®	bortezomib	Janssen	Proteasome inhibitors (PIs)	26/04/2004	1LSCT / 1LNSCT	Click here
Kyprolis®	carfilzomib	Amgen	Proteasome inhibitors (PIs)	19/11/2015	2L+ / 3L+	Click here
Ninlaro®	ixazomib	Takeda	Proteasome inhibitors (PIs)	21/11/2016	2L+	Click here
Farydak®	panobinostat	Novartis + (Secura Bio)	Histone deacetylase inhibitors (HDACis)	28/08/2015	2L+ Relapsed / Refractory	Click here
Darzalex®	daratumumab	Janssen	Monoclonal antibody against CD38 (Mabs)	20/05/2016	All lines	Click here
Empliciti®	elotuzumab	BMS + (AbbVie)	Monoclonal antibody against SLAMF7 (Mabs)	11/05/2016	2L+ / 3L+	Click here
Sarclisa®	isatuximab	Sanofi	Monoclonal antibody against CD38 (Mabs)	30/05/2020	2L+ / 3L+	Click here
Tecvayli®	teclistamab	Janssen	BiTE	21/07/2022	2L+ / 3L+	Click here
Blenrep® / Belamaf® (US)	belantamab mafodotin-blmf	GSK	Antibody-drug conjugates (BCMA)	25/08/2020	2L+ (4L+ after P, IMiD and MAB (L5+ in Italy))	Click here
Nexpovio® / Xpovio® (US)	selinexor	Karyopharm Therapeutics	Nuclear export inhibitor (SINE)	26/03/2021	Penta-refractory (2xPI + 2xIMiDs + 1 Mab)	Click here
Venclyxto® / Venclexta® (US)	venetoclax	AbbVie	B-cell lymphoma 2 (BCL-2)	04/12/2016	2L+ (already used in CLL / AML treatments)	Click here
Abecma®	idecabtagene vicleucel	BMS	Cell-based gene therapy (CAR-T)	18/08/2021	Triple class exposed / 3L+ / 4L+ / 5L+	Click here
Carvykti®	ciltacabtagene autoleucel	Janssen	Cell-based gene therapy (CAR-T)	25/05/2022	L3 / L4+ / L5+	Click here
Aredia®	pamidronate	Novartis	Bisphosphonates for bone disease	31/10/1991	Supportive care / Long-term use (5+ years)	Click here
Zometa®	zoledronate	Novartis	Bisphosphonates for bone disease	20/03/2001	Supportive care / Long-term use (5+ years)	Click here
Prolia® + Xgeva®	denosumab	Amgen	Bisphosphonates for bone disease	26/05/2010 - 13/07/2011	Supportive care	Prolia® / Xgeva®
Mozobil®	plerixafor	Genzyme	Stem cell mobilazor	30/07/2009	Supportive care	Click here

MM treatment history timeline



- IMiDs
- PIs
- IMS
- Mabs
- HDACi
- SINE
- BCMA
- CAR-T

1844
"Rhubarb & orange peel, strengthening plaster to the chest, a pound of blood removed & leeches applied for maintenance therapy".

1947
 Urethane

1958
 Melphalan

1962
 Corticosteroids

1983
 Autologous transplantation

1984
 Vincristine + Adriamycin + Dexamethasone

2013
 pomalidomide (Imnovid®/Pomalyst®)

2012
 carfilzomib (Kyprolis® US)

2010
 bendamustine (Levact®)

2005
 lenalidomide (Revlimid®)

2002
 bortezomib (Velcade®)

1999
 thalidomide

2015
 panabinostat (Farydak®)

2016
 elotuzumab (Empliciti®)
 daratumumab (Darzalex®)
 ixazomib (Ninlaro®)

2020
 belantamab mafodotin (Blenrep® EU, Belamaf® US)

2021
 selinexor (Nexpovio® EU, Xpovio® US)
 isatuximab (Sarclisa®)
 idecabtagene vicleucel (Abecma®)

2022
 melflufen (Pepaxti® EU, Pepaxto® US)
 ciltacabtagene autoleucel (Carvykti®)

20??
 teclistamab (Tecvayli®) ★
 marizomib, anetumab, ravtansine, venetoclax, oprozomib, talquetamab, elranatamab



16+
YEARS

17+
COUNTRIES OVER TIME

UP
TO **90**
HCPs
per wave
per country

UP
TO **4**
WAVES
per year

4,5k
PATIENTS CHARTS
per wave

18k
PATIENTS CHARTS
per year (in EU5)

What's new **MMsyndiTrack™**

Launching of a US pilot wave, Why ?

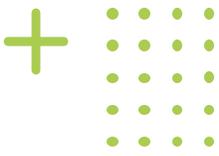
- Needs from clients for MM US data
- Back data for EU5 for 15 years
- MM US market changing fast
- Different needs in the US market for labs (patients' ethnicity treatments gap as an example)

APLUSA's added value

- Quarterly + month to month data collection (our competitors → only quarterly data)
- Market adaptability: adjusting our questionnaires and updating the list of treatments by including market trends on a monthly basis → **new CAR-Ts + BisAbs**
- Patient's full treatment history
- Deliverables with Power BI DID



April 2023



● CONTENTS

01.

News around clinical trials in Phase III

- Phase III Relapse/Refractory: CAR-T

02.

Themes of discussion : HCPs

- SOV Themes of discussion
- Posts driving most engagement

03.

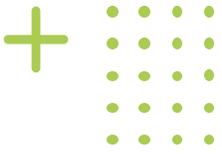
News articles overtime

- Volume of articles per volume of mentions
- Articles per themes

04.

Drug approvals

- Drug approvals



● SCOPE



The scope of the analysis is focused on mentions coming **worldwide**.*



There were a total of **19K** mentions from patients recorded during the listening period from **April 1st, 2023**, to **April 30th, 2023**.



A majority of mentions came from **News (48%), Twitter (40%), Instagram (5%), Forums (3%), Reddit (2%), Blogs (1%)** and **tumblr (1%)**.

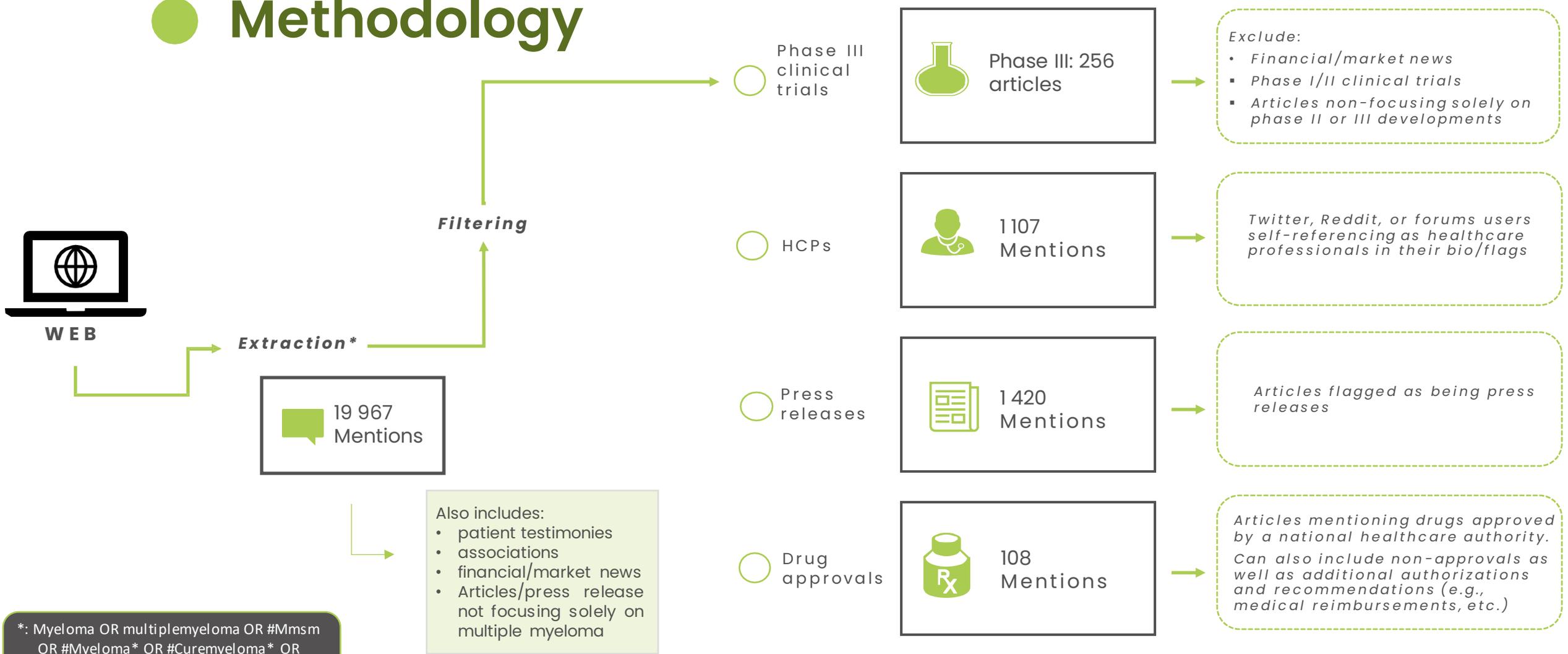


A total of **5K** unique authors were identified.

: Myeloma OR multiplemyeloma OR #Mmsm OR #Myeloma OR #Curemyeloma* OR #Mmmrd OR #mmsm OR title: ("multiple myeloma" OR myeloma)



Methodology



: Myeloma OR multiplemyeloma OR #Mmsm OR #Myeloma OR #Curemyeloma* OR #Mmmrd OR #mmsm OR title: ("multiple myeloma" OR myeloma)

Also includes:

- patient testimonies
- associations
- financial/market news
- Articles/press release not focusing solely on multiple myeloma

Drugs in clinical trials (Phase III) monitored during the listening period



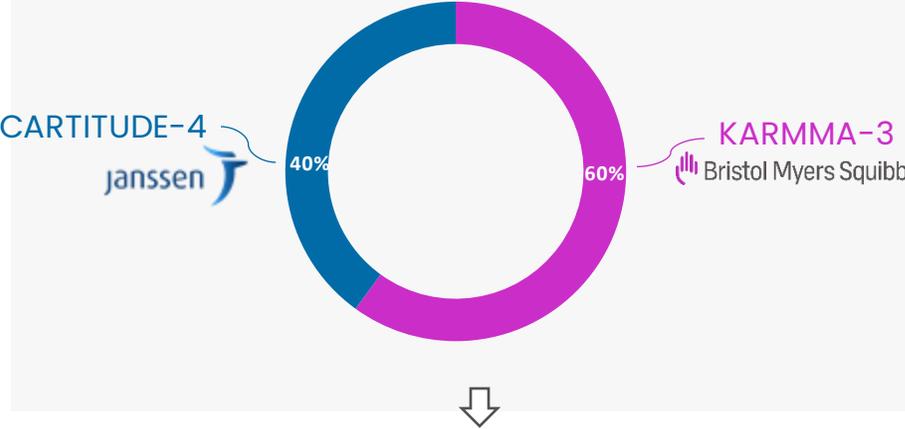
Molecule name	Commercial name	Class	Manufacturer	Trial names + link (ctrl + right click) / line of treatment / Combination being studied
lenalidomide	Revlimid®	immunomodulatory drugs (IMiDs)	BMS	DETERMINATION (RR): lenalidomide (Revlimid), bortezomib (Velcade), and dexamethasone (RVD) MAIA (ND): daratumumab in combination with lenalidomide and dexamethasone ATLAS (Maintenance): Lenalidomide, Carfilzomib, Dexamethasone DRAMMATIC (??): Lenalidomide, Daratumumab EQUATE (ND): daratumumab, bortezomib, lenalidomide and dexamethasone POLLUX (RR): Daratumumab, Lenalidomide, and Dexamethasone TOURMALINE (RR): Ixazomib Plus Lenalidomide and Dexamethasone Myeloma XI (ND): cyclophosphamide, dexamethasone plus lenalidomide with or without carfilzomib AURIGA (Maintenance): Daratumumab Plus Lenalidomide
pomalidomide	Imnovid® / Pomalyst® (US)	immunomodulatory drugs (IMiDs)	BMS	ICARIA-MM (RR): Isatuximab, Pomalidomide, Dexamethasone
bortezomib	Velcade®	Proteasome inhibitors (PIs)	Takeda	DETERMINATION (RR): lenalidomide (Revlimid), bortezomib (Velcade), and dexamethasone (RVD) BOSTON (RR): selinexor plus bortezomib (Velcade) plus low-dose dexamethasone (SVd) EQUATE (ND): daratumumab, bortezomib, lenalidomide and dexamethasone CASTOR (RR): Daratumumab, Bortezomib and Dexamethasone Bellini (RR): venetoclax plus bortezomib and dexamethasone DREAMM 7 (RR): Belantamab Mafodotin, Bortezomib and Dexamethasone
carfilzomib	Kyprolis®	Proteasome inhibitors (PIs)	Amgen	IKEMA (RR): Isatuximab, Carfilzomib And Dexamethasone ATLAS (Maintenance): Carfilzomib, Lenalidomide, Dexamethasone Myeloma XI (ND): cyclophosphamide, dexamethasone plus lenalidomide with or without carfilzomib
ixazomib	Ninlaro®	Proteasome inhibitors (PIs)	Takeda	OPTIMUM (RR): Ixazomib, Lenalidomide TOURMALINE (RR): Ixazomib Plus Lenalidomide and Dexamethasone
Bb2121, Idecabtagene vicleucel	Abecma®	CAR T-cell therapy	BMS	KarMMa-3 (RR): Monotherapy
ciltacabtagene	Carvykti®	CAR T-cell therapy BCMA-directed	Janssen	CARTITUDE-4 (RR): Monotherapy
daratumumab	Darzalex®	Monoclonal antibody anti-CD38	Janssen	MajesTEC-3 : (RR): Teclistamab in Combination With Daratumumab Subcutaneously (SC) (Tec-Dara) MAIA (ND): daratumumab in combination with lenalidomide and dexamethasone DRAMMATIC (??): Lenalidomide, Daratumumab EQUATE (ND): daratumumab, bortezomib, lenalidomide and dexamethasone CASTOR : (RR): Daratumumab, Bortezomib and Dexamethasone POLLUX (RR): Daratumumab, Lenalidomide, and Dexamethasone MagnetisMM-5 (RR): Monotherapy or doublet therapy with daratumumab AURIGA (Maintenance): Daratumumab Plus Lenalidomide
isatuximab	Sarclisa®	Monoclonal antibody anti-CD38	Sanofi	IKEMA (RR): Isatuximab, Carfilzomib And Dexamethasone ICARIA-MM (RR): Isatuximab, Pomalidomide, and Dexamethasone
belantamab mafodotin-blmf	Blenrep® / Belamaf® (US)	Antibody-drug conjugates (BCMA)	GSK	DREAMM-3 (RR): Monotherapy DREAMM 7 (RR): Belantamab Mafodotin, Bortezomib and Dexamethasone DREAMM 8 (RR): Belantamab Mafodotin Plus Pomalidomide and Dexamethasone

Phase III Relapse/Refractory CAR-T: Regulatory Applications Accepted Across Three Regions Globally for Abecma for Earlier Use in Adults with Triple-Class Exposed Relapsed and/or Refractory Multiple Myeloma



Clinical trial mentioned/Sponsor

Headlines/Hot off the press



“Regulatory Applications Accepted Across Three Regions Globally for Abecma for Earlier Use in Adults with Triple-Class Exposed Relapsed and/or Refractory Multiple Myeloma”

“Bristol Myers Squibb and 2seventy bio, Inc. today announced that the U.S. Food and Drug Administration (FDA) has accepted the companies’ supplemental Biologics License Application (sBLA) for Abecma (idecabtagene vicleucel) with the KarMMA-3 study that investigated the treatment of adult patients with relapsed and refractory multiple myeloma who have received an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.” Click [here](#) to read the full article

“Leaked data shows stellar efficacy for J&J’s Carvykti”

“Johnson & Johnson was preparing to divulge the data from its eagerly-awaited CARTITUDE-4 trial of CAR-T therapy Carvykti later this year, but a leak of the data has given an early glimpse of what look like outstanding results.” Click [here](#) to read the full article

KarMMA-3
Ctrl + click to access the clinical trial : [NCT03651128](#)
“Efficacy and Safety Study of bb2121 Versus Standard Regimens in Subjects With Relapsed and Refractory Multiple Myeloma (RRMM) (KarMMA-3)”

Molecule

idecabtagene vicleucel

CARTITUDE-4
Ctrl + click to access clinical trial: [NCT04181827](#)
“A Study Comparing JNJ-68284528, a CAR-T Therapy Directed Against B-cell Maturation Antigen (BCMA), Versus Pomalidomide, Bortezomib and Dexamethasone (Pvd) or Daratumumab, Pomalidomide and Dexamethasone (DPd) in Participants With Relapsed and Lenalidomide-Refractory Multiple Myeloma”

Ciltacabtagene autoleucel



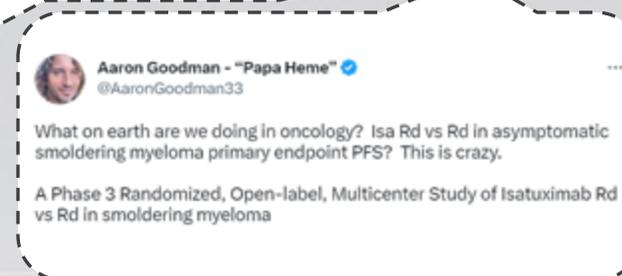
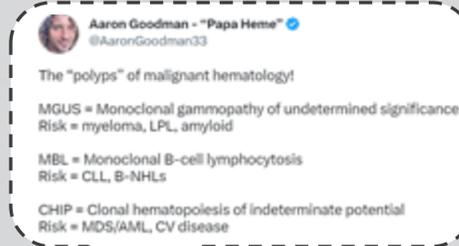
The posts receiving the most engagement during the period were mostly educational in nature.

DR Rajkumar shared his paper titled “Multiple myeloma with acute light chain cast nephropathy” on how to treat the aforementioned condition. Meanwhile, Dr Goodman offered an educational post on different cancer precursors.

Dr Goodman also offered his opinion on the [SAR650984](#) clinical trial. A study on isatuximab combination with lenalidomide and dexamethasone Versus len + dex in high-risk smoldering multiple m myeloma. Conversations that ensued focused on criticism regarding the trial design, doubt about its usefulness, general criticism towards pharma companies prioritizing profits over medical soundness, and more pointed criticism towards isatuximab as a “me-too” drug.

Most engagement

Most retweeted, liked and replied to (Ctrl + right click to access tweets)

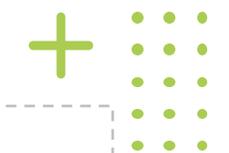


Top 5 influencers

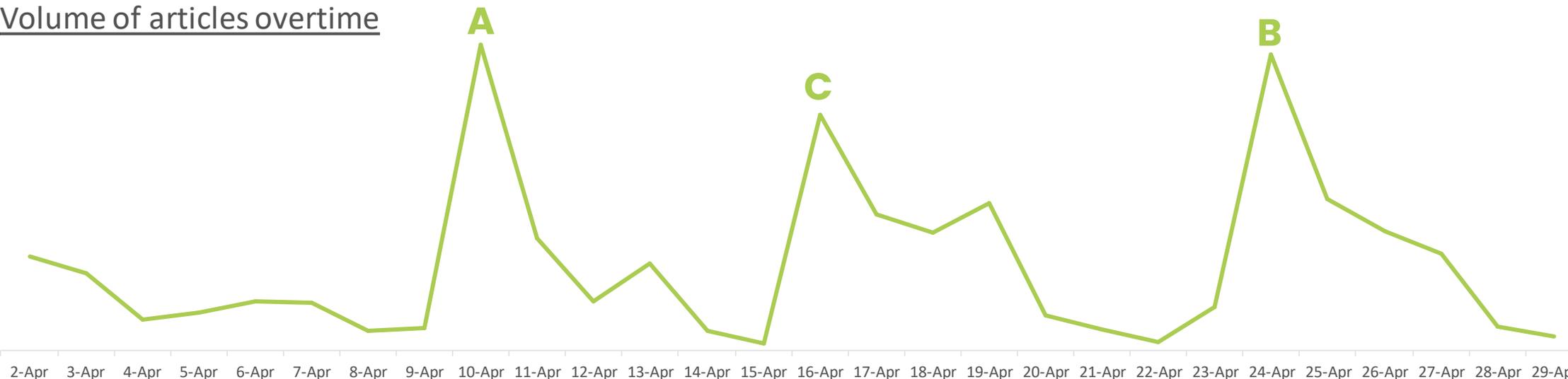
- **Vincent Rajkumar**
[@VincentRK](#)
76,1 K followers
- **Samer Al Hadidi**
[@HadidiSamer](#)
2,7 K followers
- **Saad Z. Usmani**
[@szusmani](#)
8,8 K followers
- **Noopur Raje**
[@NoopurRajeMD](#)
8,6 K followers
- **Al-Ola A Abdallah**
[@Abdallah81MD](#)
2,7 K followers



Media (press releases): volume and articles per peak



Volume of articles overtime



A Oncolyze Announces FDA **Orphan Drug Designation** for **OM-301** for the Treatment of Multiple Myeloma [Link](#)

Demonstration of Accurate **Screening of Gene Dependency** in Multiple Myeloma from **Aitia's Gemini Digital Twins** to be Presented at 2023 AACR Annual Meeting [Link](#)

K36 Therapeutics announces dosing of first patient in **KTX-1001 Phase 1 Clinical Trial for relapsed or refractory multiple myeloma** and addition of Mr. Michael Heffernan as Independent Board Director [Link](#)

B **ALX Oncology** Announces Clinical Trial Collaboration with Sanofi to Evaluate **Evorpaccept** in Combination with SARCLISA (**isatuximab-irfc**) in Patients with Multiple Myeloma [Link](#)

Prognosis of Multiple Myeloma **Has Improved** Since 2000 [Link](#)

Multiple myeloma patients in **Spain** face **regional disparities** [Link](#)

C **Regulatory Applications** Accepted Across Three Regions Globally for **Abecma** for Earlier Use in Adults with Triple-Class Exposed Relapsed and/or Refractory Multiple Myeloma [Link](#)

IU cancer center researcher leads first in-human **multiple myeloma study with 90.5 percent response rate** [Link](#)

BioLineRx Announces Publication in Nature Medicine of its **GENESIS Phase 3 Clinical Trial Data** Evaluating Motixafortide and G-CSF in Stem Cell Mobilization for Autologous Transplantation in Multiple Myeloma [Link](#)





Bispecific antibody

- IU cancer center researcher leads first in-human **multiple myeloma study with 90.5 percent response rate** [Link](#)

CAR T-cell therapy

- **Regulatory Applications** Accepted Across Three Regions Globally for **Abecma** for Earlier Use in Adults with Triple-Class Exposed Relapsed and/or Refractory Multiple Myeloma [Link](#)

CD47-Blocking Myeloid Checkpoint Inhibitor

- **ALX Oncology** Announces Clinical Trial Collaboration with Sanofi to Evaluate **Evorpcept** in Combination with SARCLISA (**isatuximab-irfc**) in Patients with Multiple Myeloma [Link](#)

CXCR4 chemokine receptor inhibitor

- **BioLineRx** Announces Publication in Nature Medicine of its **GENESIS Phase 3 Clinical Trial Data** Evaluating Motixafortide and G-CSF in Stem Cell Mobilization for Autologous Transplantation in Multiple Myeloma [Link](#)

Gene screening

- Demonstration of Accurate **Screening of Gene Dependency** in Multiple Myeloma from **Aitia's Gemini Digital Twins** to be Presented at 2023 AACR Annual Meeting [Link](#)

HDM2 fusion peptide

- Oncolyze Announces FDA **Orphan Drug Designation** for **OM-301** for the Treatment of Multiple Myeloma [Link](#)

Patient Life

- **Prognosis** of Multiple Myeloma **Has Improved** Since 2000 [Link](#)
- Multiple myeloma patients in **Spain** face **regional disparities** [Link](#)

Small molecule methyltransferase inhibitor

- **K36 Therapeutics** announces dosing of first patient in **KTX-1001 Phase 1 Clinical Trial for relapsed or refractory multiple myeloma** and addition of Mr. Michael Heffernan as Independent Board Director [Link](#)





Drug Market Watch

April 2023



“ Regulatory Applications Accepted Across **Three** Regions Globally for **Abecma** for Earlier Use in Adults with Triple-Class Exposed Relapsed and/or Refractory Multiple Myeloma [Link](#) ”

“ **Oncolyze** Announces **FDA Orphan Drug Designation** for **OM-301** for the Treatment of Multiple Myeloma [Link](#) ”

“ The FDA has granted **fast track designation** to the investigational allogenic CAR T-cell therapy product **CB-011** for the treatment of patients with relapsed or refractory multiple myeloma. [Link](#) ”

“ National Institute for Health and Care Excellence recommends **Darzalex® (daratumumab)** with bortezomib and dexamethasone for routine use on the NHS as treatment for multiple myeloma [Link](#) ”