









SMML newsletter

February 2023

Based on data from December 2022

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:

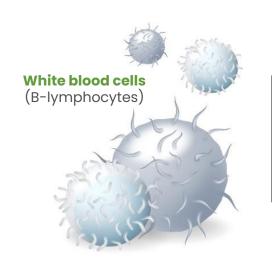
- Marketers
- **Business Analysts**
- But also HCPs who want to anticipate the future landscape of MM management



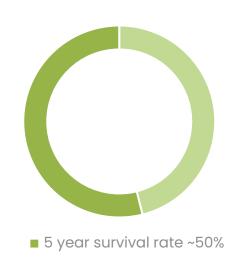
Introduction on Multiple Myeloma

What is Multiple Myeloma?











Read more on Multiple Myeloma:



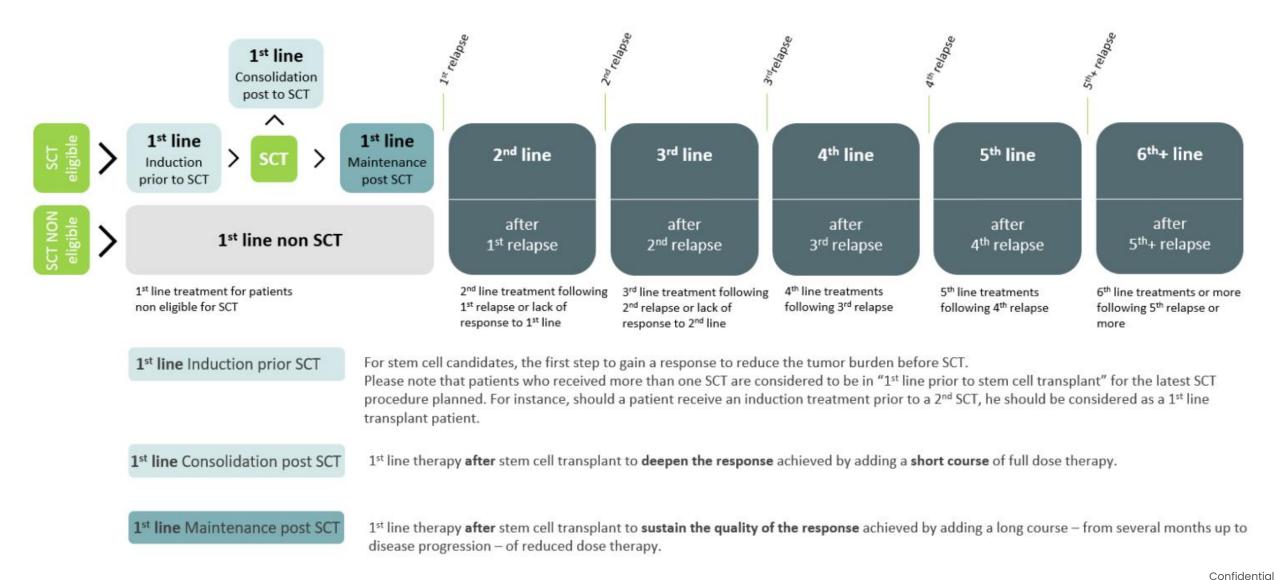
- → Professional version in English
- → Professional version in French



- → Consumer version in English
- → Consumer version in French

MM lines of therapy based on to the following definitions





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)	<u>Click here</u>
Pepaxti® / Pepaxto® (US)	melflufen	Oncopeptides AB	Peptide conjugated alkylator	17/08/2022	Triple class exposed / 3L+ / 4L+ / 5L+	<u>Click here</u>
Velcade®	bortezomib	Janssen	Proteasome inhibitors (PIs)	26/04/2004	1LSCT / 1LNSCT	<u>Click here</u>
Kyprolis®	carfilzomib	Amgen	Proteasome inhibitors (PIs)	19/11/2015	2L+ / 3L+	<u>Click here</u>
Ninlaro®	ixazomib	Takeda	Proteasome inhibitors (PIs)	21/11/2016	2L+	<u>Click here</u>
Farydak [®]	panobinostat	Novartis + (Secura Bio)	Histone deacetylase inhibitors (HDACis)	28/08/2015	2L+ Relapsed / Refractory	<u>Click here</u>
Darzalex®	daratumumab	Janssen	Monoclonal antibody against CD38 (Mabs)	20/05/2016	All lines	<u>Click here</u>
Empliciti [®]	elotuzumab	BMS + (AbbVie)	Monoclonal antibody against SLAMF7 (Mabs)	11/05/2016	2L+ / 3L+	<u>Click here</u>
Sarclisa®	isatuximab	Sanofi	Monoclonal antibody against CD38 (Mabs)	30/05/2020	2L+ / 3L+	<u>Click here</u>
Tecvayli®	teclistamab	Janssen	BITE	21/07/2022	2L+ / 3L+	<u>Click here</u>
Blenrep® / Belamaf® (US)	belantamab mafodotin-blmf	GSK	Antibody-drug conjugates (BCMA)	25/08/2020	2L+ (4L+ after P, IMiD and MAB (L5+ in Italy)	<u>Click here</u>
Nexpovio® / Xpovio® (US)	selinexor	Karyopharm Therapeutics	Nuclear export inhibitor (SINE)	26/03/2021	Penta-refractory (2xPI + 2xIMiDs + 1 Mab)	<u>Click here</u>
Venclyxto® / Venclexta® (US)	venetoclax	AbbVie	B-cell lymphoma 2 (BCL-2)	04/12/2016	2L+ (already used in CLL / AML treatments)	<u>Click here</u>
Abecma®	idecabtagene vicleucel	BMS	Cell-based gene therapy (CAR-T)	18/08/2021	Triple class exposed / 3L+ / 4L+ / 5L+	<u>Click here</u>
Carvykti [®]	ciltacabtagene autoleucel	Janssen	Cell-based gene therapy (CAR-T)	25/05/2022	L3 / L4+ / L5+	<u>Click here</u>
Aredia [®]	pamidronate	Novartis	Bisphosphonates for bone disease	31/10/1991	Supportive care / Long-term use (5+ years)	<u>Click here</u>
Zometa [®]	zoledronate	Novartis	Bisphosphonates for bone disease	20/03/2001	Supportive care / Long-term use (5+ years)	<u>Click here</u>
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	<u>Click here</u>

MM treatment history timeline 1958 1962 1984 1844 1947 1983 **IMiDs** Pls "Rhubarb & orange peel, Urethane Melphalan Autologous Vincristine Corticosteroids **IMS** strengthening plaster to the chest, + Adriamycin transplantation a pound of blood removed & leeches + Dexamethasone Mabs applied for maintenance therapy". **HDACi SINE BCMA** 2012 2010 2005 2002 2013 1999 **CAR-T**

bendamustine

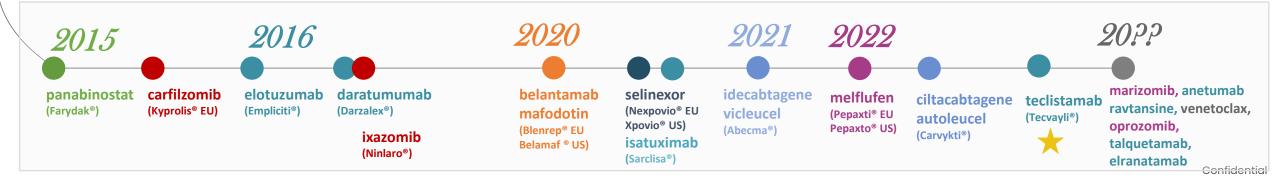
(Levact®)

pomalidomide

(Imnovid®/Pomalyst®)

carfilzomib

(Kyprolis® US)



lenalidomide

(Revlimid®)

bortezomib

(Velcade®)

thalidomide

MM studies at APLUSA







per wave per country per year

4,5k per wave

18k PATIENTS CHARTS per year (in EU5)



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



December 2022 (Focus on ASH 2022)





CONTENTS

News around clinical trials in phase II

- Phase II Line 1: quadruplet therapy
- Phase II Relapse/Refractory: Bispecific therapies
- Phase II Relapse/Refractory: CAR-T

02.

News around clinical trials in Phase III

- Phase III Line 1: Triplet **Therapy**
- Phase III Maintenance **Quadruplet therapy**
- Phase III Relapse/Refr actory Doublet Thera ру

03.

Themes of discussion: **HCPs**

- Focus on ASH 2022: generalities
- Focus on ASH 2022: Key clinical trial iSt **opMM**
- Focus on ASH 2022: bispecific antibodi es
- Focus on ASH 2022: **CART**
- Posts driving the m ost engagement

04.

News articles overtime

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





SCOPE



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



There were a total of **44K** mentions from patients recorded during the listening period from **December 1**st **2022** to **December 31**st **2022**.



A majority of mentions came from Twitter (56%), News (36%), Instagram (5%), Forums (1%), Blogs (1%), and Reddit (1%).

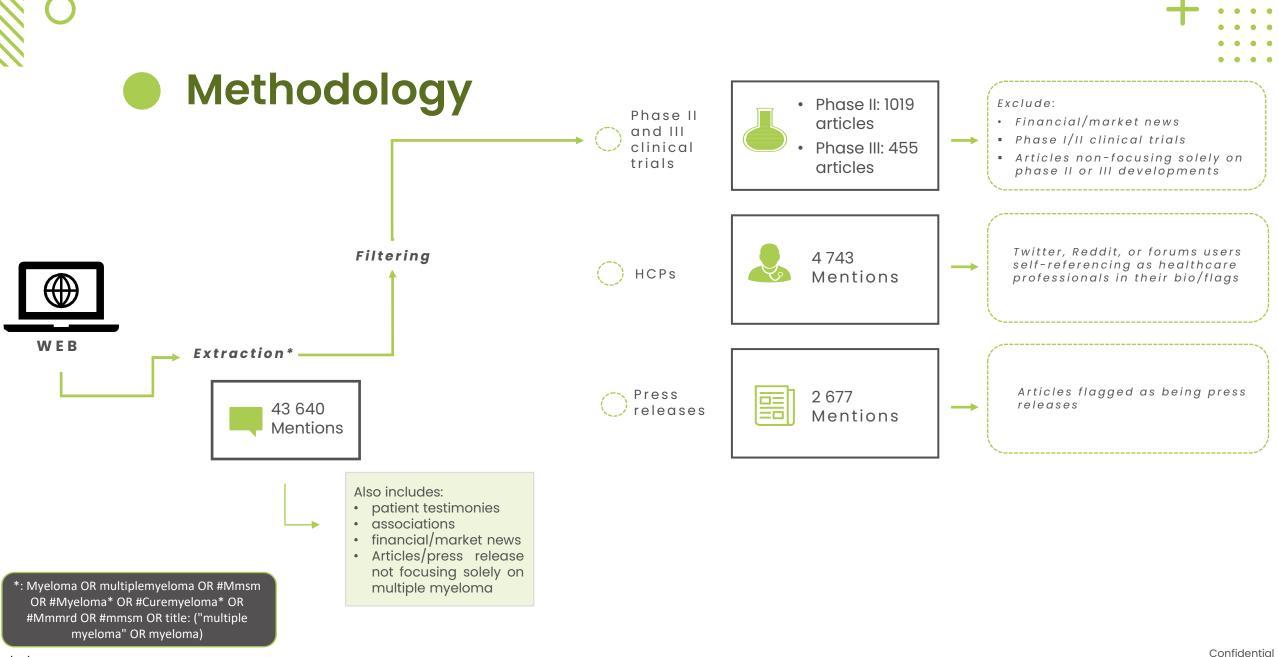


A total of 13K unique authors were identified.

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









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

CAR T-Cell Therapy Anti-BCMA

Bispecific Antibody anti-BCMA

Bispecific antibody T-cell redirecting

Bispecific Antibody anti-BCMA x Anti-CD3

C-CAR088

teclistamab

talquetamab

elranatamab (PF-06863135)

N/A

N/A

N/A

Tecvayli®

Molecule name	Commercial name	Class	Manufacturer	Trial names + link (ctrl + right click) / line of treatment / Combination being studied
lenalidomide	Revlimid®	immunomodulatory drugs (IMiDs)	BMS	<u>GRIFFIN</u> (ND): daratumumab, lenalidomide, bortezomib, and dexamethasone (D-RVd) <u>FORTE</u> (ND): carfilzomib, lenalidomide, daratumumab, dexamethasone <u>NCT02969837</u> (ND): elotuzumab, carfilzomib, lenalidomide, dexamethasone <u>MASTER</u> (???): dexamethasone, lenalidomide, daratumumab, carfilzomib
pomalidomide	Imnovid® / Pomalyst® (US)	immunomodulatory drugs (IMiDs)	BMS	NCT03590652 (RR): daratumumab, ixazomib, pomalidomide, dexamethasone ELOQUENT-3 (RR): elotuzumab plus pomalidomide, and dexamethasone
Bortezomib	Velcade [®]	Proteasome inhibitors	Takeda	<u>GRIFFIN</u> (ND): daratumumab, lenalidomide, bortezomib, and dexamethasone (D-RVd) <u>NCT03314181</u> (RR): Venetoclax, Daratumumab and Dexamethasone (With and Without Bortezomib)
carfilzomib	Kyprolis®	Proteasome inhibitor	Amgen	FORTE (ND): carfilzomib, lenalidomide, daratumumab, dexamethasone NCT02969837 (ND): elotuzumab, carfilzomib, lenalidomide, dexamethasone MASTER (???): dexamethasone, lenalidomide, daratumumab, carfilzomib Cardamon (???): cyclophosphamide, dexamethasone, carfilzomib

				Cardamon (???): cyclophosphamide, dexamethasone, carfilzomib
daratumumab	Darzalex®	Monoclonal antibody anti-CD38	Janssen	GRIFFIN (ND): daratumumab, lenalidomide, bortezomib, and dexamethasone (D-RVd) FORTE (ND): carfilzomib, lenalidomide, daratumumab, dexamethasone NCT03590652 (RR): daratumumab, ixazomib, pomalidomide, dexamethasone REBUILD (RR): Monotherapy NCT03314181 (RR): Venetoclax, Daratumumab and Dexamethasone (With and Without Bortezomib) MASTER (???): dexamethasone, lenalidomide, daratumumab, carfilzomib
elotuzumab	Empliciti®	Monoclonal antibody SLAMF7	BMS/AbbVie	ELOQUENT-3 (RR): elotuzumab plus pomalidomide, and dexamethasone

				FORTE (ND): carfilzomib, lenalidomide, daratumumab, dexamethasone NCT03590652 (RR): daratumumab, ixazomib, pomalidomide, dexamethasone REBUILD (RR): Monotherapy NCT03314181 (RR): Venetoclax, Daratumumab and Dexamethasone (With and Without Bortezomib) MASTER (???): dexamethasone, lenalidomide, daratumumab, carfilzomib
elotuzumab	Empliciti®	Monoclonal antibody SLAMF7	BMS/AbbVie	ELOQUENT-3 (RR): elotuzumab plus pomalidomide, and dexamethasone NCT02969837 (ND): elotuzumab, carfilzomib, lenalidomide, dexamethasone
isatuximab	Sarclisa®	Monoclonal antibody anti-CD38	Sanofi	NCT05123131 (ND): isatuximab, bortezomib, lenalidomide, dexamethasone NCT03590652 (RR): daratumumab, ixazomib, pomalidomide, dexamethasone
belantamab mafodotin, (GSK2857916)	Blenrep®	Antibody drug-conjugate (ADC)	GSK	DREAMM-2 (RR): Monotherapy

				MASTER (???): dexamethasone, lenalidomide, daratumumab, carfilzomib
elotuzumab	Empliciti [®]	Monoclonal antibody SLAMF7	BMS/AbbVie	ELOQUENT-3 (RR): elotuzumab plus pomalidomide, and dexamethasone NCT02969837 (ND): elotuzumab, carfilzomib, lenalidomide, dexamethasone
satuximab	Sarclisa [®]	Monoclonal antibody anti-CD38	Sanofi	NCT05123131 (ND): isatuximab, bortezomib, lenalidomide, dexamethasone NCT03590652 (RR): daratumumab, ixazomib, pomalidomide, dexamethasone
pelantamab mafodotin, (GSK2857916)	Blenrep [®]	Antibody drug-conjugate (ADC)	GSK	DREAMM-2 (RR): Monotherapy
Ciltacabtagene (cilta cel, JNJ 68284528)	Carvykti®	CAR T-Cell Therapy Anti-BCMA	Janssen	CARTITUDE (RR): Monotherapy CARTITUDE 2 (RR): Monotherapy

atuximab	Sarclisa®	Monoclonal antibody anti-CD38	Sanofi	NCT05123131 (ND): isatuximab, bortezomib, lenalidomide, dexamethasone NCT03590652 (RR): daratumumab, ixazomib, pomalidomide, dexamethasone
elantamab mafodotin, (GSK2857916)	Blenrep [®]	Antibody drug-conjugate (ADC)	GSK	<u>DREAMM-2</u> (RR): Monotherapy
ltacabtagene (cilta cel, JNJ 68284528)	Carvykti [®]	CAR T-Cell Therapy Anti-BCMA	Janssen	CARTITUDE (RR): Monotherapy CARTITUDE 2 (RR): Monotherapy
ecabtagene vicleucel (ide cel)	Abecma	CAR T-Cell Therapy Anti-BCMA	BMS	KarMMa-2 (RR): Monotherapy (one arm with lenalidomide)

Ciltacabtagene (cilta cel, JNJ 68284528)	Carvykti [®]	CAR T-Cell Therapy Anti-BCMA	Janssen	CARTITUDE (RR): Monotherapy CARTITUDE 2 (RR): Monotherapy
idecabtagene vicleucel (ide cel)	Abecma	CAR T-Cell Therapy Anti-BCMA	BMS	<u>KarMMa-2</u> (RR): Monotherapy (one arm with lenalidomide)
Zevorcabtagene autoleucel (zevor cel)	N/A	CAR T-Cell Therapy Anti-BCMA	CARsgen Therapeutics	LUMMICAR-2 (RR): Monotherapy

Janssen

Janssen

Pfizer

Cellular Biomedicine

NCT05521802 (RR): Monotherapy

MajesTEC-1: (RR): Monotherapy

MonumenTAL-1 (RR): Monotherapy

MagnetisMM-9 (RR): Monotherapy MagneticMM-2 (PR): Monotherany

<u>Phase II Line 1: Quadruplet Therapies</u>: Daratumumab regimen confers health-related quality of life benefit in multiple myeloma



Headlines/Hot off the press

Daratumumab regimen confers health-related quality of life benefit in multiple myeloma

"Adding daratumumab to bortezomib, lenalidomide and dexamethasone led to improved health-related quality of life for transplant-eligible patients with newly diagnosed multiple myeloma, study results showed." Click here to read the full article

Sponsor



GRIFFIN

Ctrl + click to access clinical trial:

"Study Comparing Daratumumab, Lenalidomide, Bortezomib, and Dexamethasone (D-RVd) Versus Lenalidomide, Bortezomib, and Dexamethasone (RVd) in Subjects With Newly Diagnosed Multiple Myeloma"

Combinations

daratumumab + lenalidomide + dexamethasone + bortezomib

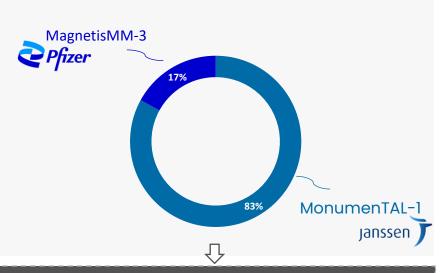




Phase II Relapse/Refractory Bispecific therapies: Antibody Treatment Makes Inroads Against **Multiple Myeloma**







MonumenTAL-1

Ctrl + click to access clinical trial:

MagnetisMM-3

Ctrl + click to access clinical trial: NCT04649359

Monotherapy in Participants With Multiple Myeloma Who Are Refractory to at Least

Headlines/Hot off the press

Multiple Myeloma

An experimental immunotherapy appears highly effective in attacking bone marrow cancer, with nearly three in four patients responding to the treatment, new clinical trial results show. Click here to read the full article

66 Janssen Submits Biologics License Application to 99 U.S. FDA for Talquetamab for the Treatment of **Patients with Relapsed or Refractory MM**

The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the submission of a Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) for talquetamab for the treatment of patients with relapsed or refractory multiple myeloma." Click here to read the full article

Molecules

Talquetamab

Elranatamab

Antibody Treatment Makes Inroads Against 99 66 Pfizer Presents Updated Favorable Elranatamab 99 Data from Pivotal Phase 2 MagnetisMM-3 Trial

"Data showed high objective response rate of 61% in RRMM patients with no prior BCMA-targeted treatment, with 84% probability of maintaining the response at nine months Results showed early and deep responses, and a manageable safety profile for elranatamab in heavily pretreated patients with advanced multiple myeloma" Click here to read the full article



"Study Of Elranatamab (PF-06863135) One PI, One IMiD and One Anti-CD38 mAb"

"The purpose of this study is to evaluate the efficacy of talquetamab in participants with

relapsed or refractory multiple myeloma at the

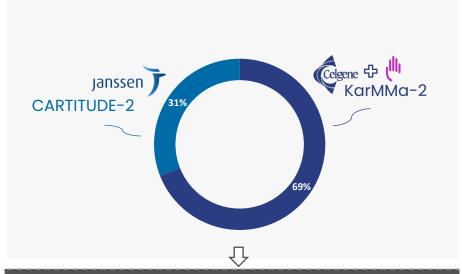
recommended Phase 2 dose(s) (RP2Ds) (Part 3)."



<u>Phase II Relapse/Refractory: CAR-T</u>: Bristol Myers Squibb Announces First Disclosures and New Data at ASH 2022



Clinical trial mentioned/Sponsor



Headlines/Hot off the press

66 Bristol Myers Squibb Announces First Disclosures 99
and New Data at ASH 2022, Demonstrating
Commitment to Raising Standards in Treatment
Through Broad Multiple Myeloma Portfolio

"Bristol Myers Squibb (NYSE: BMY) today announced the first disclosure of results and presentation of new research from its multiple myeloma portfolio across targets and molecular approaches at the 64 th American Society of Hematology (ASH) Annual Meeting and Exposition, underscoring the company's commitment to raising standards to transform multiple myeloma outcomes for every patient." Click here to read the full article

Cilta-Cel Shows Efficacy and Tolerability in Multiple Myeloma, Potentially Filling Unmet Need in Early-Line Therapy

"CAR-T cell therapy ciltacabtagene autoleucel has expanded options for adult patients with relapsed/refractory multiple myeloma after 4 or more lines of prior therapy in the United States, and has continued to display promising efficacy in patients with multiple myeloma following early relapse."

Click here to read the full article

KarMMA-2

Ctrl + click to access the clinical trial: NCT03601078

"An Efficacy and Safety Study of bb2121 in Subjects With Relapsed and Refractory Multiple Myeloma and in Subjects With High-Risk Multiple Myeloma (KarMMa-2)"

CARTITUDE-2

Ctrl + click to access clinical trial: NCTO4133636

"A Study of JNJ-68284528, a Chimeric Antigen Receptor T Cell (CAR-T) Therapy Directed Against B-cell Maturation Antigen (BCMA) in Participants With Multiple Myeloma"

Molecules

idecabtagene vicleucel

JNJ-68284528



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 Sarclisa® Monoclonal antibody anti-CD38 IKEMA (RR): Isatuximab, Carfilzomib And Dexamethasone isatuximab Sanofi ICARIA-MM (RR): Isatuximab, Pomalidomide, and Dexamethasone belantamab mafodotin-blmf Blenrep® / Belamaf® (US) **DREAMM-3** (RR): Monotherapy Antibody-drug conjugates (BCMA) **GSK** DREAMM 7 (RR): Belantamab Mafodotin, Bortezomib and Dexamethasone DREAMM 8 (RR): Belantamab Mafodotin Plus Pomalidomide and Dexamethasone <u>Phase III Line 1 Triplet Therapy</u>: Janssen Presents Efficacy and Subgroup Analyses from MAIA Study Showing Long-Term Results of DARZALEX® (daratumumab)-based Regimen in Newly Diagnosed, Transplant-Ineligible Multiple Myeloma



Headlines/Hot off the press

Janssen Presents Efficacy and Subgroup Analyses from MAIA Study Showing Long-Term Results of DARZALEX® (daratumumab)-based Regimen in Newly Diagnosed, Transplant-Ineligible Multiple Myeloma

"Updated analyses report on progression-free survival, minimal residual disease negativity, overall response and overall survival across patient types, regardless of age or cytogenetic risk" Click here to read the full article

Sponsor



MAIA

Ctrl + click to access clinical trial: NCT02252172

"Study Comparing Daratumumab, Lenalidomide, and Dexamethasone With Lenalidomide and Dexamethasone in Participants With Previously Untreated Multiple Myeloma"

Combinations

Lenalidomide **Daratumumab**

Dexamethasone



<u>Phase III Maintenance Quadruplet therapy</u>: How Long Should Myeloma Patients Continue Lenalidomide After AutoSCT?



Headlines/Hot off the press



How Long Should Myeloma Patients Continue Lenalidomide After **AutoSCT?**



"Data from a large phase III trial presented at the 2022 American Society of Hematologyopens in a new tab or window (ASH) annual meeting examined the relationship between minimal residual disease, progression-free survival, and overall survival in patients randomly assigned to lenalidomide maintenance or no maintenance at 3 months after autologous stem-cell transplant." Click here to read the full article

Sponsor

University of Leeds

Myeloma XI

Ctrl+ click to access clinical trial:

"The purpose of this study is to compare a standard chemotherapy regimen of cyclophosphamide, dexamethasone plus thalidomide with a newer regimen of cyclophosphamide, dexamethasone plus lenalidomide with or without carfilzomib."

Combinations

cyclophosphamide + lenalidomide

+ dexamethasone **±** carfilzomib





<u>Phase III Relapse/Refractory Doublet Therapy</u>: FDA Seeks to Withdraw Melphalan Flufenamide for Relapsed/Refractory Multiple Myeloma



Headlines/Hot off the press

FDA Seeks to Withdraw Melphalan Flufenamide for Relapsed/Refractory 55

Multiple Myeloma

"Oncopeptides AB announced December 7, 2022, that the FDA has asked the company to withdraw melphalan flufenamide (Pepaxto) from the US market. The company stopped marketing the peptide-drug conjugate in the United States as of October 22, 2021." Click here to read the full article

Oncopeptides presents new scientific data at the Annual American Society of Hematology Meeting ASH

"The clinical abstract evaluated patients with multiple myeloma who were refractory to prior alkylators in the phase 3 OCEAN study. Data shows that melflufen is a safe and effective therapy in patients who are alkylator refractory, regardless of whether they received a prior autologous stem cell transplant or not." Click here to read the full article

oncopeptides

Sponsor

OCEAN
Ctrl + click to access
clinical trial:

NCT03151811

"A Study of Melphalan Flufenamide (Melflufen)-Dex or Pomalidomide-dex for RRMM Patients Refractory to Lenalidomide"

Combinations

Melphalan Flufenamide

+ Dexamethasone



Focus on ASH 2022 HCPs' online conversations: the main topic of discussion for the period were centred around the ASH 2022 meeting (American Society of Hematology), that took place from December 10th to December 13th.

Encouraging results from trials (iStopMM, **GEM-CESAR** and **ASCENT**) focusing on multiple myeloma precursors SMM and MGUs were put forth.

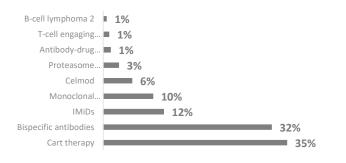
Apart from this, the spotlight was put on bispecific antobodies with talquetamab, elranatamab and cevostamab generating interest.

Volume of mentions

Ash 2021 3,754 mentions

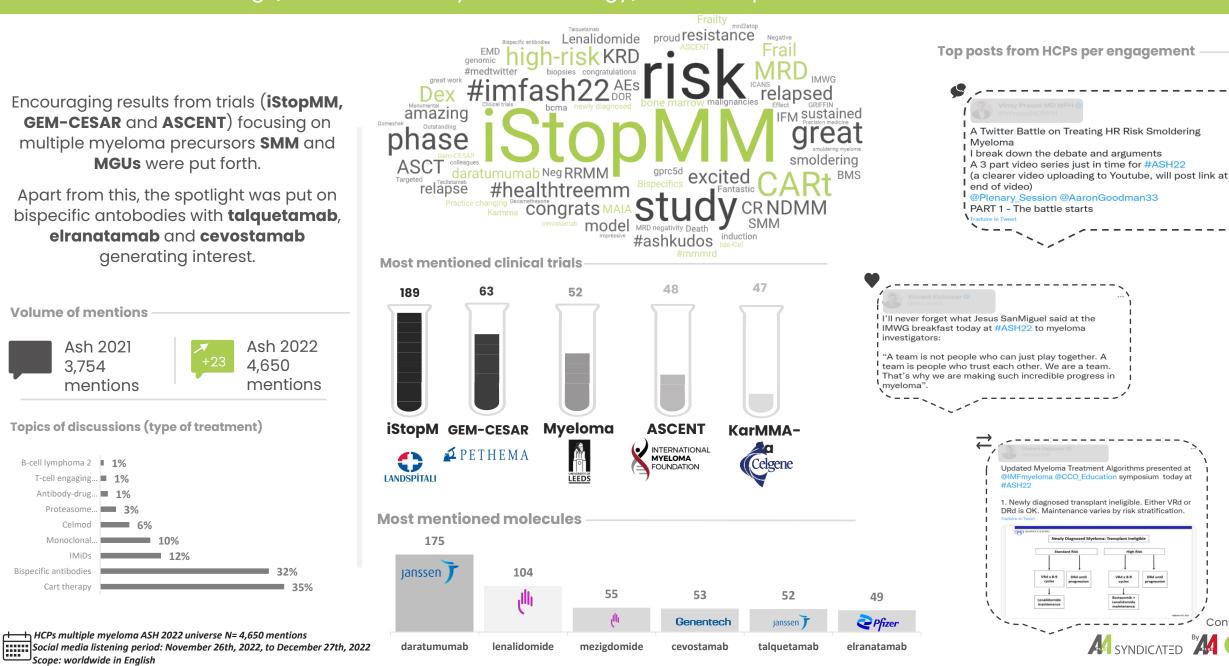
Ash 2022 4,650 mentions

Topics of discussions (type of treatment)



→ HCPs multiple myeloma ASH 2022 universe N= 4,650 mentions

Scope: worldwide in English



Focus on ASH 2022 HCPs' online conversations: Key clinical trial iStopMM

The iStopMM trial (Iceland Screen, Treats, or Prevents Multiple Myleoma), described as the largest scientific study conducted in Iceland, aim is to study the overall survival of individuals with MGUS receiving follow-up compared to those not receiving any follow-up within the study after 5 years of follow-up. Updates from this trial generated interest and enthusiasm from HCPs who deemed them practice-changing. The abstract "Predicting the Need for Upfront Bone Marrow" particularly stood out.



LANDSPÍTALI

Amongst the 10 iStopMM abstracts presented at ASH22, the following were the most mentioned:

"Predicting the Need for Upfront Bone Marrow Sampling in Individuals with MGUS: Derivation of a Multivariable Prediction Model" link

"Sars-Cov-2 Vaccinations Do Not Lead to Progression of Monoclonal Gammopathy of Undetermined Significance" link

"Autoimmune Diseases Are Not **Associated** with Monoclonal Gammopathy of Undetermined Significance" link

"Transient M-Proteins: Epidemiology, Causes, and the Impact of Mass Spectrometry" link

"Determining **Hemodilution** in Diagnostic Bone Marrow Samples in Multiple Myeloma and Its Precursors By Next-Generation Flow Cytometry" Link



#ASH22 a fabulous collection of abstracts and data from the @iStopMM team with practice changing data

En réponse à @ADesaiMD @HemOncFellows et 5 autres personnes

💴 and I don't agree on everything, but his list of practice changers at #ASH22 is on point!

Only real game changer in #MMsm was @iStopMM predictors of high BMPC% for MGUS, but tons of emerging therapies in myeloma we'll hopefully see more of next year!

@iStopMM presentation & USABLE ONLINE TOOL to help predict likelihood of a pt w monoclonal gammopathy actually having SMM (ie BMBx >10%)

before the BMBx is done....once fully validated, will

spare a lot pts an unpleasant invasive procedure



The single MOST important study presented at #ASH22 that can impact SO many patients. Please don't routinely order SPEP/light chains in patients with autoimmune diseases.

Such an honor to take a picture with @ingigerdursv by her incredible poster



According to Dr. Blin, our in-house expert, the most memorable iStopMM abstract touched upon the use of molecular biology for more precise diagnosis. Another abstract of interest was the use of mass spectrometry. Though providing a potential additional MRD methodology, Dr. Blin notes that this is an analytical tool difficult to implement and needs more research for MM. Ultimately, for our expert, those results show that one day MM treatment could evolve towards more personalized protocols in line with individual genomic signatures.

Dr. Blin shared with us that while overall interesting, results from iStopMM are not necessarily practice-changing, at least not in the short term.

mentioned

to least

mentioned

Focus on ASH 2022 HCPs' online conversations : bispecific antibodies developments in multiple myeloma; non-BCMA targeted bispecifics are highlighted, giving yet another set of potential tools to combat multiple myeloma



talquetamab

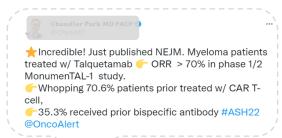
Results from the
Monumental-1 trial
showed that
Talquetamab, a novel
targeting the GPRC5D
antigen in Participants
With Relapsed or
Refractory Multiple
Myeloma
demonstrated an ORR
> 70% while being well
tolerated.



master presenter Ajai Chari presenting Talquetamab a bispecific antibody targeting GPRC5D. Amazing 74% ORR and even more remarkable low infection rates grade 3/4 at 17% and 12%. This is remarkable and may likely be the next bispecific and First GPRC5D available #ASH22 #MedIQ22ASH



ADC with other targets. Talquetamab is GPRC5DxCD3 targeted. Also showing great promise with toxicity as expected, but additional off-target AE of skin/hair/nail and dysgeusia. Management will be key. #ASH22 @IMFMyeloma #IMFASH22 #mmsm





cevostamab

Results from a **phase I**study showed that
Cevostomab, a FCRH5
bispecific antibodies in
combination with
Tocilizumab can
significantly reduce the risk
of developing TDB-induced
CRS without an apparent
impact on anti-myeloma
activity. Those results were
deemed encouraging by
HCPs for both cevostamab
and potentially bispecifics
as a class.



The block of IL-6 does not reduce efficacy of #Cevostamab. Median time to response was similar in Toci & nonToci groups.

Is this transferable to other Bispecifics? Could be a game changer.

#ASH22 @IMFMyeloma #IMFASH22 #mmsm



an ounce of prevention is worth a pound of cure #ASH22 Cevostamab making its way smoothly into the crowded bispecific myeloma space! @TheIACH @Mohty_EBMT



Encouraging results of pre-treatment tocilizumab with cevostamab (FcRH5DxCD3 BiTE @genentech) presented by Dr. Suzanne Trudel @pmcancercentre decreasing CRS rate from 90.9% to 38.7%!

rates of neutropenia, infection and G-CSF use, but did not affect efficacy #ASH22 #mmsm

Focus on ASH 2022 HCPs' online conversations : CART developments in multiple myeloma; while impactful developments around CART therapies were overall sparse, results from the FasTCAR and KarMMa-2a studies stood out

GC012F for newly diagnosed high risk MM. 69% extramedullary dz; Remarkable that CRS rate was so low (25%). Now we have to see how long this therapy lasts, but intriguing as we see other CAR T-cell approaches moving to the frontline setting in randomized designs. #ASH22 #mmsm



Dual BCMA/CD19 CAR in newly diagnosed high-risk #MultipleMyeloma show phenomenal responses. Small number and need to see long-term data, but impressive given the potential for long-term treatment-free remissions #ASH22 #mmsm

FastCAR

Results from a phase I trial studying a dual CART approach targeting BCMA and CD19 showed intriguing results in terms of ORR and MRD as well as faster CART manufacturing turnaround in transplant eligible newly diagnosed high risk patients.

Next, CART therapy, with focus on first line use with BCMA/CD19 product, with FasTCAR, reducing manufacturing time to days instead of weeks, more & better quality T-Cells.

#ASH22 @IMFMyeloma #IMFASH22 #mmsm



Results from FastCAR are from a very early phase I study done on 13 participants

ide-cel

Updates from KarMMa cohort 2a, a trial studying high-risk multiple myeloma patients with early relapse after frontline ASCT were deemed somewhat disappointing by some in terms of PFS and mDOR while others applauded the results in terms of ORR.



In KARMMA-2a, mPFS of less than 1 year is not what we like to see- more work to be done for this subset of

I do commend the authors too- but to be honest this is disappointing, and ide-cel failed to correct the natural history of this aggressive disease. Perhaps other products may do better for this population. #ASH22



Karmma-2a cohort of ide-cel in pts with early relapse in #mmsm. This is a tough group of patients - kudos to investigators for enrolling! PFS and DOR seem fairly similar to later lines. We need to do better for this population! #ash22



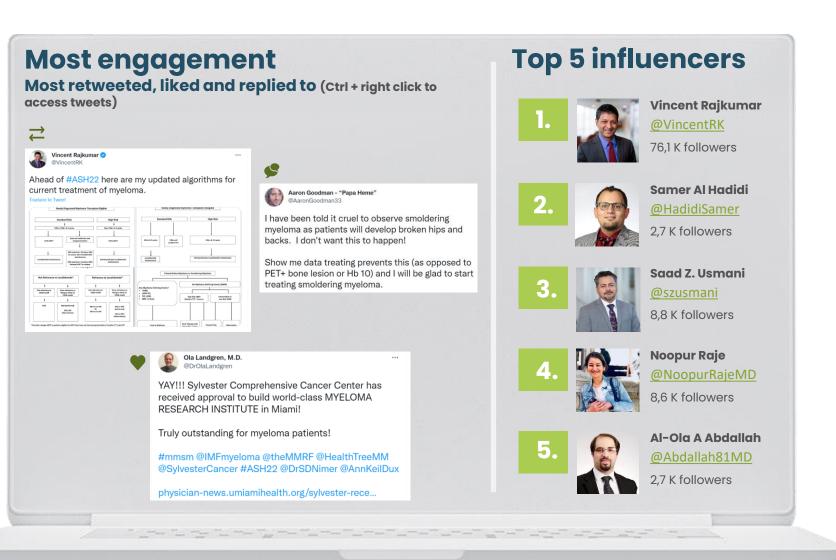
View from the expert

While some HCPs reacted online somewhat negatively to the results of the KarMMa 2a cohort, our in-house expert Dr. Blin has a more nuanced view. Some of the results presented actually offer an improvement upon what exists today, namely CRR (complete response rate) of 45,6% in KarMMa 2a versus around 20% for the existing therapy, DARA-KD. While other endpoints might not appear encouraging at first, this cohort concerns very difficult-to-treat patients that might still see benefits.



Dr Vincent Rajkumar is once again present with a post pertaining to a recap of the current treatment in multiple myeloma.

Other posts focused on the treatment of smoldering multiple myeloma and how to avoid side effects during treatment. This thread is in response to another Twitter conversation that ignited some controversies around the best course of treatment advisable. The most liked post from highlighted the announcement of a new multiple myeloma focused research institute.



Media (press releases): volume and articles per peak



- Janssen Presents New Data for Talquetamab, a First-in-Class GPRC5DxCD3 Bispecific Antibody, Suggesting Durable Responses in Patients with Heavily Pretreated Multiple Myeloma LINK
- Janssen Submits Biologics License Application to U.S. FDA for Talquetamab for the Treatment of Patients with Relapsed or Refractory Multiple Myeloma LINK
- Novel drug shows early promise in treating multiple myeloma LINK
- Janssen Presents Efficacy and Subgroup Analyses from MAIA Study Showing Long-Term Results of DARZALEX® (daratumumab)-based Regimen in Newly Diagnosed, Transplant-Ineligible Multiple Myeloma LINK

A (continued)

- Gracell Biotechnologies Presents Clinical Data for FastCAR-T GC012F for High Risk, Newly Diagnosed Multiple Myeloma Demonstrating 100% Overall Response Rate LINK
- Arcellx and Kite Announce Strategic Collaboration to Co-Develop and Co-Commercialize Late-Stage Clinical **CART-ddBCMA** in Multiple Myeloma LINK
- Arcellx Announces Continued Robust Long-Term Responses from its CART-ddBCMA Phase 1 Expansion Trial in Patients with Relapsed or Refractory Multiple Myeloma and Additional Pipeline Progress LINK

A (continued)

- Gilead to co-develop Arcellx's multiple myeloma drug <u>LINK</u>
- Janssen Presents First Data from MajesTEC-2 Trial of TECVAYLI™ (teclistamab-cqyv) in Combination with DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) and Lenalidomide in Relapsed or Refractory Multiple Myeloma LINK
- World-Renowned Myeloma Expert, Dr. Ivan Borrello, Joins TGH Cancer Institute to Lead Its Bone Marrow Transplant (BMT) and Cell Therapies Program LINK
- Pfizer Presents Updated Favorable **Elranatamab** Data from Pivotal Phase 2 MagnetisMM-3 Trial LINK



SYNDICATED A

Media (press releases): volume and articles per peak (continued)





- Circulating Tumor Cell detection by Menarini Group's CELLSEARCH® System leading to genomic profiling of myeloma cells shows potential for non-invasive management of Multiple Myeloma patients at early stages of disease LINK
- Immix Biopharma in-licenses NXC-201, BCMA-targeted Next-Generation CAR-T Therapy Demonstrating High Complete Response Rate in Heavily Pre-Treated Multiple Myeloma (71% Complete Responses) and AL Amyloidosis (100% Complete Responses) LINK

- ORIC Pharmaceuticals Announces Clinical Development Collaboration with Pfizer for ORIC-533 in Multiple Myeloma and Concurrent \$25 Million Equity Investment by Pfizer LINK
- U.S. FDA Approves Clinical Trial Application for IASO Bio's BCMA CAR-T CT103A for Relapsed/Refractory Multiple Myeloma LINK

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- Renal Impairment Linked to Worse Prognosis in IgD Multiple Myeloma LINK
- Ruxolitinib and methylprednisolone for treatment of patients with relapsed/refractory multiple myeloma LINK

Articles per theme



Antibody-cytokine fusion protein

Novel drug shows early promise in treating multiple myeloma LINK

Bispecific antibody

- Janssen Presents New Data for Talquetamab, a Firstin-Class GPRC5DxCD3 Bispecific Antibody, Suggesting Durable Responses in Patients with Heavily Pretreated Multiple Myeloma LINK
- Janssen Submits **Biologics License Application** to U.S. FDA for **Talquetamab** for the Treatment of Patients with Relapsed or Refractory Multiple Myeloma LINK
- Janssen Presents First Data from MajesTEC-2 Trial of TECVAYLI™ (teclistamab-cqyv) in Combination with DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) and Lenalidomide in Relapsed or Refractory Multiple Myeloma LINK
- Pfizer Presents Updated Favorable **Elranatamab** Data from Pivotal Phase 2 MagnetisMM-3 Trial LINK

CAR T-cell therapy

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HCPs

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Monoclonal antibody

Janssen Presents Efficacy and Subgroup Analyses from MAIA Study Showing Long-Term Results of DARZALEX® (daratumumab)-based Regimen in Newly Diagnosed, Transplant-Ineligible Multiple Myeloma LINK

New technologies

Circulating Tumor Cell detection by Menarini Group's CELLSEARCH® System leading to genomic profiling of myeloma cells shows potential for non-invasive management of Multiple Myeloma patients at early stages of disease LINK

Oral JAK1/2 inhibitor

Ruxolitinib and **methylprednisolone** for treatment of patients with relapsed/refractory multiple myeloma LINK

Small Molecule CD73 Inhibitor

ORIC Pharmaceuticals Announces Clinical Development Collaboration with Pfizer for ORIC-533 in Multiple Myeloma and Concurrent \$25 Million Equity Investment by Pfizer LINK

SYNDICATED