BEATING CANCER IS IN OUR BLOOD.

MULTIPLE MYELOMA

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Tisch Cancer Institute
Icahn School of Medicine at Mount Sinai
Director of Myeloma at The Blavatnik Family – Chelsea Medical Center at Mount Sinai
Saturday, November 1, 1845:

Dear Dr Jones,

The tube contains urine of very high specific gravity. When boiled it becomes slightly opaque. On the addition of nitric acid, it effervesces, assumes a reddish hue, and becomes quite clear; but as it cools, assumes the consistence and appearance which you see. Heat liquefies it. What is it?


WHAT IS MULTIPLE MYELOMA?

Multiple myeloma

Normal plasma cells

Antibodies

M proteins

Light chain

Heavy chains

Multiple myeloma cells

Bone

Bone marrow
MYELOMA IN MUMMIES

Ancient affliction. A high-resolution CT scan of the lumbar spine region of a 2150-year-old Egyptian mummy revealed small, round lesions.
Figure 2. Sarah Newbury, the first reported patient with multiple myeloma. (A) Bone destruction in the sternum. (B) The patient with fractured femurs and right humerus. (C) Bone destruction involving the femur. Adapted from Soilly with permission.

<table>
<thead>
<tr>
<th>Common Types of Cancer</th>
<th>Estimated New Cases 2022</th>
<th>Estimated Deaths 2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Breast Cancer (Female)</td>
<td>287,850</td>
<td>43,250</td>
</tr>
<tr>
<td>2. Prostate Cancer</td>
<td>268,490</td>
<td>34,500</td>
</tr>
<tr>
<td>3. Lung and Bronchus Cancer</td>
<td>236,740</td>
<td>130,180</td>
</tr>
<tr>
<td>4. Colorectal Cancer</td>
<td>151,030</td>
<td>52,580</td>
</tr>
<tr>
<td>5. Melanoma of the Skin</td>
<td>99,780</td>
<td>7,650</td>
</tr>
<tr>
<td>6. Bladder Cancer</td>
<td>81,180</td>
<td>17,100</td>
</tr>
<tr>
<td>7. Non-Hodgkin Lymphoma</td>
<td>80,470</td>
<td>20,250</td>
</tr>
<tr>
<td>8. Kidney and Renal Pelvis Cancer</td>
<td>79,000</td>
<td>13,920</td>
</tr>
<tr>
<td>9. Uterine Cancer</td>
<td>65,950</td>
<td>12,550</td>
</tr>
<tr>
<td>10. Pancreatic Cancer</td>
<td>62,210</td>
<td>49,830</td>
</tr>
<tr>
<td>11. Myeloma</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>14. Myeloma</td>
<td>34,470</td>
<td>12,640</td>
</tr>
</tbody>
</table>

Myeloma represents 1.8% of all new cancer cases in the U.S.
Estimated New Cases in 2022: 34,470
% of All New Cancer Cases: 1.8%

Estimated Deaths in 2022: 12,640
% of All Cancer Deaths: 2.1%

5-Year Relative Survival: 57.9%
(2012–2018)
Rate of New Cases per 100,000 Persons by Race/Ethnicity & Sex: Myeloma

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>MALE</th>
<th>FEMALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Races</td>
<td>8.8</td>
<td>5.9</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>8.1</td>
<td>5.0</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>17.0</td>
<td>12.9</td>
</tr>
<tr>
<td>Non-Hispanic Asian / Pacific Islander</td>
<td>5.1</td>
<td>3.2</td>
</tr>
<tr>
<td>Non-Hispanic American / Indian Alaska Native</td>
<td>9.1</td>
<td>6.1</td>
</tr>
<tr>
<td>Hispanic</td>
<td>8.1</td>
<td>5.9</td>
</tr>
</tbody>
</table>

SEER 22 2015–2019, Age-Adjusted

Percent of New Cases by Age Group: Myeloma

Myeloma is most frequently diagnosed among people aged 65–74.

Median Age At Diagnosis 69

SEER 22 2015–2019, All Races, Both Sexes
MYELOMA CELLS
NORMAL VS ABNORMAL PLASMA CELLS

Normal

Abnormal

Adapted from Multiple Myeloma Research Foundation.
Serum protein electrophoresis
Normal

Albumin
α zone proteins
β zone proteins
γ zone proteins

Antibodies

Lightest
Heaviest

IgG
IgA
IgM

Plasma cells

Normal

 alb α₁ α₂ β γ
Serum protein electrophoresis
Monoclonal gammopathy

Monoclonal protein

Treatment

Albumin
α zone proteins
β zone proteins

Monoclonal plasma cells

Lightest

Heaviest

Monoclonal gammopathy

IgG kappa M protein

BEATING CANCER IS IN OUR BLOOD.
Immunofixation to Determine Type of Monoclonal Protein

IgG kappa M protein

Lambda Light Chains

Kyle RA and Rajkumar SV. Cecil Textbook of Medicine, 22nd Edition, 2004
IMMUNOGLOBULIN

Heavy chains: IgG, IgA, IgM, IgD, IgE

Light chains are known as kappa (κ) or lambda (λ)

Most common isotype is IgGκ followed by IgGλ then IgAκ and IgAλ; rare cases of IgD and IgE
MEASURING THE MYELOMA PROTEIN

Intact Ig myeloma

Light chain myeloma

Oligosecretory myeloma: rare form of myeloma

Non-secretory myeloma: rare form of myeloma
**Underlying plasma cell proliferative disorder**

- M protein ≥3 g/dL (serum) or ≥500 mg/24 hrs (urine)
- Clonal plasma cells in BM ≥10%–60%
- No myeloma-defining events

**≥1 CRAB* feature**

- Clonal plasma cells in BM ≥60%
- Serum free light chain ratio ≥100
- >1 MRI focal lesion

**M protein ≥3 g/dL (serum) or ≥500 mg/24 hrs (urine)**

- Clonal plasma cells in BM ≥10%–60%
- No myeloma-defining events

**≥1 CRAB* feature**

- Clonal plasma cells in BM ≥60%
- Serum free light chain ratio ≥100
- >1 MRI focal lesion

---

**MGUS**

- M protein <3 g/dL
- Clonal plasma cells in BM <10%
- No myeloma-defining events

**Smoldering Myeloma**

- M protein ≥3 g/dL (serum) or ≥500 mg/24 hrs (urine)
- Clonal plasma cells in BM ≥10%–60%
- No myeloma-defining events

**Multiple Myeloma**

- Underlying plasma cell proliferative disorder
- AND ≥1 myeloma-defining events
- ≥1 CRAB* feature
- Clonal plasma cells in BM ≥60%
- Serum free light chain ratio ≥100
- >1 MRI focal lesion

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*R: Renal insufficiency (creatinine clearance <40 mL/min or serum creatinine >2 mg/dL)
A: Anemia (Hb <10 g/dL or 2 g/dL < normal)
B: Bone disease (≥1 lytic lesions on skeletal radiography, CT, or PET-CT)

Progression to Symptomatic Myeloma

Risk factors: higher M spike, higher plasma cell burden, type of M protein, abnormal free light-chain ratio, circulating plasma cells

Smoldering Multiple Myeloma

MGUS

Probability of Progression (%)

Years Since Diagnosis


# MYELOMA STAGING

## Table 4: The Durie and Salmon Staging System

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
<th>Measured Myeloma Cell Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage I</strong> (low cell mass)</td>
<td>All of the following:</td>
<td>600 billion*</td>
</tr>
<tr>
<td></td>
<td>- Hemoglobin value &gt;10g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Serum calcium value normal or &lt;10.5mg/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Bone x-ray, normal bone structure (scale 0), or solitary bone plasmacytoma only</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Low M-component production rates</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- IgG value &lt;5g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- IgA value &lt;3g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Urine light chain M-component on electrophoresis &lt;4g/24h</td>
<td></td>
</tr>
<tr>
<td><strong>Stage II</strong> (intermediate cell mass)</td>
<td>Fitting neither Stage I nor Stage III</td>
<td>600 to 1,200 billion*</td>
</tr>
<tr>
<td><strong>Stage III</strong> (high cell mass)</td>
<td>One or more of the following:</td>
<td>&gt;1,200 billion*</td>
</tr>
<tr>
<td></td>
<td>- Hemoglobin value &lt;8.5g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Serum calcium value &gt;12mg/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Advanced lytic bone lesions (scale 5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- High M-component production rates</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- IgG value &gt;7g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- IgA value &gt;5g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Bence Jones protein &gt;12g/24h</td>
<td></td>
</tr>
</tbody>
</table>

### Subclassification (either A or B)

- A: relatively normal renal function (serum creatinine value) <2.0 mg/dL
- B: abnormal renal function (serum creatinine value) >2.0 mg/dL

*Myeloma cells in whole body
mSMART 3.0: Classification of Active MM

**High-Risk**
- High Risk genetic Abnormalities \(^a,b\)
  - t(4;14)
  - t(14;16)
  - t(14;20)
  - Del 17p
  - p53 mutation
  - Gain 1q
- RISS Stage 3
- High Plasma Cell S-phase\(^c\)
- GEP: High risk signature
- Double Hit Myeloma: Any 2 high risk genetic abnormalities
- Triple Hit Myeloma: 3 or more high risk genetic abnormalities

**Standard-Risk\(^a\)**
- All others including:
  - Trisomies
  - t(11;14)\(^d\)
  - t(6;14)

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\(^a\)Trisomies may ameliorate
\(^b\) By FISH or equivalent method
\(^c\) Cut-offs vary
\(^d\) t(11;14) may be associated with plasma cell leukemia

A Controlled Trial of Urethane Treatment in Multiple Myeloma


Blood 1966; 27: 328-342
ALGORITHM FOR TREATMENT OF MM PER NCCN GUIDELINES AND PALUMBO ET AL.

Transplant ineligible

Transplant eligible

Induction

SCT

 +/- Maintenance

Relapsed/refractory MM

Eligibility determined by age, performance status, and comorbidities; exact criteria may vary by institution¹

Assess for response

Patients with response or stable disease after induction ± SCT may receive maintenance therapy until progression or intolerance²

Consider disease- and patient-related factors³

- Quality and duration of previous responses
- Aggressiveness of disease
- Age
- Preexisting toxicities
- Performance status
- Bone marrow reserve
- Renal function

² NCCN guidelines.
³
# CHOOSING THERAPIES FOR MYELOMA

## IMiDs
- Thalidomide
- Lenalidomide
- Pomalidomide

## Proteasome Inhibitors
- Bortezomib
- Carfilzomib
- Ixazomib

## Anthracyclines
- Doxil
- Doxorubicin
- Bendamustine

## Alkylators
- Melphalan
- Cytoxan
- Solumedrol

## Steroids
- Dexamethasone
- Prednisone
- Isatuximab

## Antibodies
- Elotuzumab
- Daratumumab
- Daratumumab

## SINE
- Selinexor

## ADC
- Belantamab

## CAR-T
- Ide-cel
- Teclistamab

## Bispecific Ab
- Cilta-cel
FACTORS IN SELECTING MM THERAPY

### PATIENT
- Age/frailty
- Performance status
- Lifestyle/pt preferences
- Drug metabolism
- Compliance/adherence
- Caregiver support
- Renal insufficiency
- Comorbidities
  - Neuropathy
  - Cardiac
  - Diabetes
  - Low blood counts

### DISEASE
- Burden
  - ISS/LDH
  - Rate of rise
  - Marrow burden
  - CRAB symptoms
  - Extramedullary – PCL, CNS
- Biology
  - Molecular
    - del[17p], t(4;14), t(14;16), ch 1 abnormalities
    - GEP

### TREATMENT
- Trial Availability
  - If Previously Treated
    - Depth/duration
    - Relapse > 60d vs Refractory
- Toxicity
  - Myelosuppresion
  - Neuropathy
  - VTE
  - Secondary cancers
- Administration route
  - Single or combination
- Cost and copays
- Access

MAIA: STUDY DESIGN
PATIENTS WERE ENROLLED FROM MARCH 2015 THROUGH JANUARY 2017

KEY ELIGIBILITY CRITERIA
- Transplant-ineligible newly diagnosed MM
- ECOG PS 0-2
- CrCl ≥30 mL/min

D-Rd
D: 16 mg/kg IV
QW Cycles 1-2, Q2W Cycles 3-6, then Q4W thereafter until PD
R: 25 mg PO
Days 1-21 until PD
d: 40 mg PO or IV
Days 1, 8, 15, 22 until PD

Rd
R: 25 mg PO Days 1-21 until PD
d: 40 mg PO
Days 1, 8, 15, 22 until PD
Cycles: 28 days

Primary end point:
- PFS

Secondary end points:
- OS
- PFS2
- ORR
- CR/sCR rate
- MRD (NGS; 10–5)

End-of-treatment visit
(30 days after last dose)

Long-term follow-up

MAIA is a multicentre, randomised, open-label, active-controlled, phase 3 study
MAIA: UPDATED 5-YEAR PFS DATA

**KEY ELIGIBILITY CRITERIA:**
- Transplant-eligible NDMM
- 18-70 years of age
- ECOG PS score 0-2
- CrCl ≥30 mL/min

**INDUCTION:**
Cycles 1-4

- **D-RVd**
  - D: 16 mg/kg IV Days 1, 8, 15
  - R: 25 mg PO Days 1-14
  - V: 1.3 mg/m² SC Days 1, 4, 8, 11
  - d: 20 mg PO Days 1, 2, 8, 9, 15, 16

**CONSOLIDATION:**
Cycles 5-6

- **D-RVd**
  - D: 16 mg/kg IV Day 1
  - R: 25 mg PO Days 1-14
  - V: 1.3 mg/m² SC Days 1, 4, 8, 11
  - d: 20 mg PO Days 1, 2, 8, 9, 15, 16

**MAINTENANCE:**
Cycles 7-32

- **D-R**
  - D: 16 mg/kg IV Day 1
  - R: 15 mg PO Days 1-21
  - Q4W or Q8W

**ENDPOINTS AND STATISTICAL ASSUMPTIONS**

**Primary endpoint:**
sCR rate (by end of consolidation);
1-sided alpha of 0.1
80% power to detect 15% improvement (50% vs 35%), N = 200

**Secondary endpoints:**
Rates of MRD negativity (NGS 10⁻⁴), ORR, ≥VGPR, CR

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*Presented By Jonathan Kaufman at ASH 2020*
Median follow-up: 38.6 months

Median PFS was not reached in either group

There is a positive trend toward improved PFS for D-RVd/DR versus RVd/R

The separation of the PFS curves begins beyond 1 year of maintenance and suggests a benefit of prolonged DR therapy

Laubach J, et al. ASH 2021

HR, hazard ratio.
VRD ± ASCT IN NDMM

PHASE III DETERMINATION TRIAL (IFM/DFCI 2009)

N = 700
- Pts ≤65 yrs of age
- Symptomatic, measurable NDMM

VRd 8 cycles
VRd 3 cycles
MEL200 ASCT†
VRd 2 cycles consolidation
Lenalidomide Maintenance**

PFS

Median PFS, Mos
VRd/ASCT 50
VRd 36

HR: 0.65 (95% CI: 0.53-0.80; \(P < .001\))

OS

4-Yr OS, %
VRd/ASCT 81
VRd 82

HR: 1.16 (95% CI: 0.80-1.68; \(P = .87\))

AUTOLOGOUS STEM CELL TRANSPLANT

Mobilization and leukapheresis of patient stem cells

Autologous stem cells

Cryopreservation of patient stem cells

-190°C Freezer

Thawing and infusion of patient stem cells

High-dose chemotherapy

Autologous stem cells
ALLOGENEIC STEM CELL TRANSPLANT

- High-dose chemotherapy
- +/- Total body irradiation
- HLA-matched donor stem cells
- Anti-rejection/anti-GVHD drugs
SYNGENEIC TRANSPLANTATION

# SEQUENCING STRATEGIES

<table>
<thead>
<tr>
<th>Relapse</th>
<th>Initial</th>
<th>Intermediate</th>
<th>Advanced</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 prior line</td>
<td>2-3 prior lines, or Double VR-refractory</td>
<td>&gt; 3 prior lines, or failed 2nd ASCT, or Triple (KVR)-refractory</td>
</tr>
</tbody>
</table>

**Prior Induction Regimen**
- PI or IMiD-based

**Prior Induction Regimen**
- Other

**Salvage if refractory**
- V-based (bortezomib-based)
  - VTd/VCD
  - VMP/VTP
- R-based (lenalidomide-based)
  - RD
- VR-based

**Salvage if refractory**
- V-refractory (relapse on V-based regimen)
  - Dara-Rd
  - KRd
  - Elo-Rd
- V-sensitive (relapse off V-based regimen)
  - Dara-Rd
  - KRd
  - Elo-Rd
  - Repeat VTD or VMP/VTP

**Salvage ASCT**
- Yes, if transplant-eligible & duration of response from 1st ASCT ≥ 18 months

**Abbreviations:**
- VTd: bortezomib-thalidomide-dexamethasone
- VCD: bortezomib-cyclophosphamide-dexamethasone
- VMP: bortezomib-melphalan-prednisolone
- VTP: bortezomib-thalidomide-prednisolone
- VRd: bortezomib-thalidomide-dexamethasone-rhIFN
- Rx Rd: bortezomib-rhIFN
- Rx Rd: lenalidomide-dexamethasone-rhIFN
- Rd: lenalidomide-dexamethasone
- R: lenalidomide
- V: bortezomib
- E: etoposide
- M: melphalan
- P: prednisone
- KG: lenalidomide plus bortezomib
- VCD: cyclophosphamide plus lenalidomide plus dexamethasone

**Clinical trials of novel agents**
- Selinexor (Ix)
- Venetoclax/Bortezomib-Venetoclax

**Clinical trials of immunotherapy**
- Allo-SCT
- BCMA CAR-T
- Anti-PD1

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First in Class, Oral Selective Inhibitor of Nuclear Export (SINE)

**Selinexor**
- Inhibits XPO1 through reversible covalent modification
- Currently FDA approved in combination with dexamethasone based on the STORM study
- Selinexor in combinations with bortezomib and dexamethasone was recently filed with FDA based on the BOSTON study
- Ongoing STOMP study looking into combinations of Selinexor with other anti-myeloma agents

Tai et al Leukemia 2014.
Schmidt et al Leukemia 2013.

**XPO1 in MM**
- Transports >200 proteins from the nucleus to cytoplasm
- Expression increased in MM vs normal PC/MGUS/SMM
- Correlates with shorter survival and increased bone disease

**FDA Approved 7/3/19**
STOMP: STUDY OVERVIEW & OBJECTIVES
SELINEXOR AND BACKBONE TREATMENTS OF MULTIPLE MYELOMA PATIENTS (STOMP): MULTI-CENTER, OPEN-LABEL, RANDOMIZED DOSE ESCALATION (PHASE 1) AND EXPANSION (PHASE 2) STUDY TO ASSESS THE MTD, EFFICACY, AND SAFETY OF SELINEXOR IN PATIENTS WITH RRMM

**Phase 1 (Dose Escalation) Objectives**

**Primary:** to determine the MTD for selinexor QW or BIW when combined with SOC MM therapies

**Secondary:** to determine the RP2D schedule for each arm independently


**XVd** Pomalidomide + Dexamethasone

**XVd** Bortezomib + Dexamethasone

**XKd** Ixazomib + Dexamethasone

**XNd** Carfilzomib + Dexamethasone

**XPVd** Pomalidomide + Bortezomib + Dexamethasone

**XPEd** Pomalidomide + Elotuzumab + Dexamethasone

**XRd** Lenalidomide + Dexamethasone

**XRd** RRMM and NDMM

**XPd** Ixazomib + Dexamethasone

**XPd** Daratumumab + Dexamethasone

**XNd** Carfilzomib + Dexamethasone

**XNd** Bortezomib + Dexamethasone

**XNd** Ixazomib + Dexamethasone

**XNd** Carfilzomib + Dexamethasone

**XNd** Bortezomib + Dexamethasone

**XNd** Ixazomib + Dexamethasone

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**XNd** Carfilzomib + Dexamethasone

**XNd** Bortezomib + Dexamethasone

**XNd** Ixazomib + Dexamethasone

**XNd** Carfilzomib + Dexamethasone

**XNd** Bortezomib + Dexamethasone
STARTING UP A BRAND NEW DAY  --- STING

IMMUNOTHERAPEUTIC TARGETS IN MULTIPLE MYELOMA

Antibody–Drug Conjugates (ADCs)
Belantamab mafodotin
CC-99712

CAR T-Cell Therapies
Idecabtagene vicleucel
Ciltacabtagene autoleucel
Orvacabtagene autoleucel
P-BCMA-101
bb21217
ALLO-715

Bispecific T-Cell Engagers
CC-93269
REGN5458
JNJ-64007957
PF-06863135

Figure from: Yu, B., Jiang, T. & Liu, D. J Hematol Oncol. 2020;13:125

BEATING CANCER IS IN OUR BLOOD.
## COMPARISON OF NEW MODALITIES

<table>
<thead>
<tr>
<th>Chimeric antigen receptor T cells (CAR-T)</th>
<th>Bispecific antibodies</th>
<th>Antibody-drug conjugates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pros</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unprecedented response rates including minimal residual disease (MRD) negativity in heavily pre-treated patients</td>
<td>Off the shelf</td>
<td>Off the shelf</td>
</tr>
<tr>
<td>One time intervention ; long chemo holiday resulting in median PFS ~1 year</td>
<td>Deep responses</td>
<td>Encouraging response rates</td>
</tr>
<tr>
<td><strong>Cons</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manufacturing time makes impractical for patients with aggressive/rapidly progressing disease</td>
<td>? Need for admissions with initial doses until cytokine release syndrome risk low</td>
<td>Ocular toxicity – will require close collaboration with ophthalmology and may negatively impact quality of life</td>
</tr>
<tr>
<td>Requires complex infrastructure – stem cell lab, nursing, ICU/ER training – thus restricted to accredited centers</td>
<td>Dosing/schedule to be determined</td>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Cytokine release syndrome- ? role in elderly/frail</td>
<td>Need for continuous treatment until progression</td>
<td>Need for continuous treatment until progression</td>
</tr>
<tr>
<td>Impact of bridging chemo on remission duration</td>
<td>Toxicities require further study – neuropathy, infections</td>
<td>Modest ORR and PFS in triple class/penta refractory</td>
</tr>
<tr>
<td>Cost given relapses are occurring even in MRD negative patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low white cells and platelets post CAR-T requiring ongoing/frequent monitoring and treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Management of CAR-T relapses challenging especially if soon after fludarabine/cyclophosphamide given impact on T cells</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BCMA (B-CELL MATURATION ANTIGEN)

- Receptor for BAFF and APRIL
- Expressed on mature B cell subsets, PC’s, and plasmacytoid DC’s
- Maintains plasma cell homeostasis
  - BCMA-/- mice have normal B cell #s, impaired PC survival

Belantamab mafodotin: a BCMA-directed antibody and microtubule inhibitor conjugate comprising 3 components

1. Humanized anti-BCMA IgG1 mAb that binds to BCMA-expressing MM cells
2. Protease-resistant maleimidocaproyl linker that joins MMAF to mAb and releases payload only in target cell
3. MMAF: microtubule-disrupting cytotoxic agent that leads to apoptosis of BCMA-expressing MM cells

Belantamab mafodotin binds to BCMA expressed on normal and malignant PCs

Belantamab mafodotin is internalized and MMAF is released after proteolytic cleavage from the mAb

MMAF disrupts the microtubule network intracellularly, resulting in cell cycle arrest and apoptosis
Belantamab mafodotin also induces tumor cell lysis via ADCC and ADCP

<table>
<thead>
<tr>
<th>STRUCTURE AND MANUFACTURING</th>
<th>CAR T cell</th>
<th>BsAb/antibody construct (e.g., BITE molecule)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ex vivo modified CAR T cell</td>
<td>Endogenous T cell</td>
</tr>
<tr>
<td></td>
<td>scFv targeting TAA (e.g., BCMA)</td>
<td>scFv targeting antigen on effector cell (e.g., CD3)</td>
</tr>
<tr>
<td></td>
<td>Hinge</td>
<td>Flexible linker</td>
</tr>
<tr>
<td></td>
<td>Transmembrane domain</td>
<td>scFv targeting TAA (e.g., BCMA)</td>
</tr>
<tr>
<td></td>
<td>Stimulatory/activation signaling domains (e.g., 4-1BB, CD28, CD3ζ)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Myeloma cell</td>
<td>Myeloma cell</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autologous T-cell collection</td>
<td>Viral vector carrying gene for CAR construct</td>
<td></td>
</tr>
<tr>
<td>T-cell transfection</td>
<td>CAR T-cell infusion</td>
<td></td>
</tr>
<tr>
<td>2-4 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAR T-cell infusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Off-the-shelf therapy allows for immediate treatment</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


BEATING CANCER IS IN OUR BLOOD.
Chimeric Antigen Receptor (CAR) T-cells are Genetically Engineered to Target Antigens on Cancer Cells

CARs: Chimeric Antigen Receptor engineered to be expressed on the surface of T-cells

Chimeric: an antibody single chain variable fragment (scFv) linked to T-cell signaling domain – CD3ζ

CARs permit recognition of specific antigen by the T cell independent of MHC and the signaling domain stimulate T-cell proliferation, cytolysis and cytokine secretion to eliminate the tumor cells.

CAR-T Timeline


1993 First-generation CAR (CD3ζ)
2003 2nd generation CAR (CD28-CD3ζ)
2004 2nd generation CAR (4-1BB-CD3ζ)
2007 First IND for CD19 CAR
2011 4th generation CAR (TRUCKs)
2014 First in-human BCMA CAR T therapy clinical trial (NCI)
2017 FDA approval of CD19 CAR T therapy (Kymriah) for ALL
2017 FDA approval of CD19 CAR T therapy (Liso-cel, Breyanzi) for NHL
2019 Cilta-cel (JNJ4528) granted Breakthrough-therapy designation award by FDA
2021 FDA approval of Ide-cel (bb2121) for myeloma??

Shank et al. Pharmacotherapy 2016

HOW CAR T-CELL THERAPY WORKS

- Viral DNA insertion
- Expression of CAR
- CAR enables T cell to recognize tumor cell antigen
- CAR T cells multiply and release cytokines
- Tumor cell apoptosis
CARTITUDE-1: Study Design

- Phase Ib/II trial conducted in the United States

  - Patients with R/R MM with measurable disease, ECOG PS 0-1; ≥3 prior therapies including PI, IMiD, and anti-CD38 therapy, or double refractory to PI and IMiD (N = 113)

  - Of 113 patients enrolled, 97 received cilta-cel; median administered dose: $0.71 \times 10^6$ (0.51-0.95 $\times 10^6$) CAR+ viable T-cells/kg

  - **Primary endpoint:** safety and RP2D (phase Ib), efficacy (phase II)

**CARTITUDE-1: PFS and OS by MRD Status**

- **PFS**
  - 2-yr PFS: 91.0% (95% CI: 67.1-97.8)
  - 2-yr PFS: 100%
  - 2-yr PFS: 60.5% (95% CI: 48.5-70.4)
  - Median PFS: NR (95% CI: 22.8 mo - NE)

- **OS**
  - 2-yr OS: 74.0% (95% CI: 61.9-82.7)
  - Median OS: NR (95% CI: 27.2 mo - NE)

**Patients at Risk, n**

- **Mo**
  - All patients: 97, 95, 85, 77, 74, 67, 63, 36, 19, 4, 1, 1, 0
  - MRD negativity ≥6 mo: 30, 30, 30, 30, 30, 30, 30, 30, 30, 17, 13, 3, 1, 0
  - MRD negativity ≥12 mo: 18, 18, 18, 18, 18, 18, 18, 18, 18, 2, 1, 1, 0

- **Mo**
  - All patients: 97, 96, 91, 88, 85, 81, 78, 63, 23, 8, 2, 1, 0
  - MRD negativity ≥6 mo: 30, 30, 30, 30, 30, 30, 30, 17, 13, 3, 1, 0
  - MRD negativity ≥12 mo: 18, 18, 18, 18, 18, 18, 18, 18, 18, 2, 1, 1, 0

**92% of 61 patients evaluable for MRD, were MRD negative (10^{-5})**

# List of Currently Ongoing Registered CAR-T Cell Clinical Trials

## Introduction

The table below provides an overview of ongoing clinical trials for CAR-T cell therapies. Each entry includes the trial's identifiers, designation, description, status, and location.

## Table

<table>
<thead>
<tr>
<th>Developer</th>
<th>Name (NCI)</th>
<th>Target antigen</th>
<th>Tools, technology, reservation, or other notes</th>
<th>Status</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beijing Hospital</td>
<td>MBB3112</td>
<td>CD30</td>
<td>Anti-CD30 CAR construct with a drug-like molecule containing both a CAMPATH antibody and a novel small molecule.;</td>
<td>Phase 1, recruiting</td>
<td>China</td>
</tr>
<tr>
<td>Shanghai Hospital</td>
<td>MBB3113</td>
<td>CD20</td>
<td>CD19-SH CAR, developed from a T-cell receptor engineered T-cell.;</td>
<td>Phase 1, recruiting</td>
<td>China</td>
</tr>
<tr>
<td>University of Oxford</td>
<td>MBB3114</td>
<td>CD30</td>
<td>Anti-CD30 CAR construct with a drug-like molecule containing both a CAMPATH antibody and a novel small molecule.;</td>
<td>Phase 1, recruiting</td>
<td>China</td>
</tr>
<tr>
<td>Shanghai Hospital</td>
<td>MBB3115</td>
<td>CD20</td>
<td>CD19-SH CAR, developed from a T-cell receptor engineered T-cell.;</td>
<td>Phase 1, recruiting</td>
<td>China</td>
</tr>
<tr>
<td>University of Oxford</td>
<td>MBB3116</td>
<td>CD30</td>
<td>Anti-CD30 CAR construct with a drug-like molecule containing both a CAMPATH antibody and a novel small molecule.;</td>
<td>Phase 1, recruiting</td>
<td>China</td>
</tr>
<tr>
<td>Shanghai Hospital</td>
<td>MBB3117</td>
<td>CD20</td>
<td>CD19-SH CAR, developed from a T-cell receptor engineered T-cell.;</td>
<td>Phase 1, recruiting</td>
<td>China</td>
</tr>
<tr>
<td>University of Oxford</td>
<td>MBB3118</td>
<td>CD30</td>
<td>Anti-CD30 CAR construct with a drug-like molecule containing both a CAMPATH antibody and a novel small molecule.;</td>
<td>Phase 1, recruiting</td>
<td>China</td>
</tr>
<tr>
<td>Shanghai Hospital</td>
<td>MBB3119</td>
<td>CD20</td>
<td>CD19-SH CAR, developed from a T-cell receptor engineered T-cell.;</td>
<td>Phase 1, recruiting</td>
<td>China</td>
</tr>
</tbody>
</table>

## Notes

- The table includes ongoing clinical trials for CAR-T cell therapies.
- Each entry provides the trial's identifiers, designation, description, status, and location.
- The trials are spread across various locations, including China, the United States, and the United Kingdom.

## Conclusion

The ongoing CAR-T cell clinical trials represent a significant advancement in the treatment of hematological malignancies. As research continues, these therapies promise to offer new hope for patients with refractory conditions.
# SAFETY AND EXPANSION OF MCARH109, A GPRC5D TARGETED CAR T CELL THERAPY IN OR REFRACTORY MULTIPLE MYELOMA

Mailankody, et al. ASH 2021: abstract 827

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>25 x10⁶ CAR+ T cells (n=3)</th>
<th>50 x10⁶ CAR+ T cells (n=3)</th>
<th>150 x10⁶ CAR+ T cells (n=3)</th>
<th>450 x10⁶ CAR+ T cells (n=3)</th>
<th>All Doses (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRS any grade</td>
<td>3 (100%)</td>
<td>3 (100%)</td>
<td>3 (100%)</td>
<td>2 (67%)</td>
<td>11 (92%)</td>
</tr>
<tr>
<td>Neurotoxicity any grade</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Nail changes (all grade 1)</td>
<td>1 (33%)</td>
<td>1 (33%)</td>
<td>1 (33%)</td>
<td>0 (0%)</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>MCARH109 expansion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median peak Expansion*, Vector copies/mL (range)</td>
<td>56,357 (44,670-1,661,354)</td>
<td>404,467 (162,947-770,785)</td>
<td>1,277,092 (157,749-3,560,000)</td>
<td>NA</td>
<td>404,467 (44,670-3,560,000)</td>
</tr>
<tr>
<td>Median time to peak expansion, weeks (range)</td>
<td>2.0 (2.0-2.1)</td>
<td>2.6 (1.9-3.9)</td>
<td>3.1 (2.1-4.1)</td>
<td>NA</td>
<td>2.1 (1.9-4.1)</td>
</tr>
</tbody>
</table>

* Peak expansion is assessed using quantitative polymerase chain reaction (qPCR) and is available only for the first 3 dose cohorts.

NA, Not yet available
BISPECIFIC CAR-T CELL THERAPY TARGETING BCMA AND CD38

Mei et al. J Hematol Oncol (2021) 14:161
BISPECIFIC T CELL ANTIBODIES IN MYELOMA: MECHANISM OF ACTION

Cytotoxic T-Cell

Anti-CD3 Antibody

Bispecific Antibody

Anti-BCMA Antibody

Myeloma Cell

CD3

BCMA
# Bispecific Antibodies - BCMAxCD3

<table>
<thead>
<tr>
<th>Bispecific Antibody</th>
<th>AMG-701</th>
<th>CC-93269</th>
<th>Elranatamab</th>
<th>REGN5458</th>
<th>Teclistamab</th>
<th>TNB-383B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>Weekly IV</td>
<td>Weekly IV</td>
<td>Weekly SC</td>
<td>Weekly IV</td>
<td>Weekly SC</td>
<td>IV q3w</td>
</tr>
<tr>
<td>Patients</td>
<td>N = 85</td>
<td>N = 19</td>
<td>N = 55</td>
<td>N = 73</td>
<td>N = 165</td>
<td>N = 118</td>
</tr>
<tr>
<td>Median prior lines</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Triple-class refractory</td>
<td>62%</td>
<td>IMiD/Pl/Dara 84%/90%/89%</td>
<td>50%; 22% prior BCMA-directed</td>
<td>19%</td>
<td>78%</td>
<td>61%</td>
</tr>
<tr>
<td>ORR @ therapeutic dose</td>
<td>26% all patients 10/12 (83%)</td>
<td>9/13 (69%)</td>
<td>22/37 (75%)</td>
<td>93/150 (62%)</td>
<td>60% in &gt; 40</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 6mg IV 1000 µg/kg SC</td>
<td></td>
<td>200-800 mg IV 1500ug/kg SC (RP2D)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of Response</td>
<td>17/21 (81%) ongoing at median 5.6 months</td>
<td>NR</td>
<td>NR</td>
<td>90% @ median 8 months</td>
<td>91% ≥ 6 mos</td>
<td>NR</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AEs, (All/(Gr 3+))</th>
<th>CRS</th>
<th>Infections</th>
<th>Neutropenia</th>
<th>Anemia</th>
<th>Thrombocytopenia</th>
<th>Deaths</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>64% (9%)</td>
<td>90% (5%)</td>
<td>87% (0%)</td>
<td>38% (0%)</td>
<td>72% (1%)</td>
<td>54% (3%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(17%)</td>
<td>NR (26%)</td>
<td>NR (5%)</td>
<td>NR (23%)</td>
<td>63% (35%)</td>
<td>32% (17%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>25%</td>
<td>NR (53%)</td>
<td>NR (21%)</td>
<td>21% (13%)</td>
<td>49% (35%)</td>
<td>27% (22%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>42%</td>
<td>NR (42%)</td>
<td>5 (7%)</td>
<td>32% (23%)</td>
<td>38% (22%)</td>
<td>25% (14%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>21%</td>
<td>NR (21%)</td>
<td>ISR 56% (0%)</td>
<td>21% (13%)</td>
<td>9, 7 COVID</td>
<td>22% (11%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 (5%)</td>
<td>1 (5%)</td>
<td>5 (7%)</td>
<td>5 (7%)</td>
<td>5 (7%)</td>
<td>6, 3 COVID</td>
<td></td>
</tr>
<tr>
<td>Neurotoxicity 8%</td>
<td>0%</td>
<td>Neurotoxicity 8%</td>
<td>0%</td>
<td>Neurotoxicity 8%</td>
<td>0%</td>
<td>Neurotoxicity 8%</td>
<td>0%</td>
</tr>
</tbody>
</table>

GPRC 5D EXPRESSION AND PROGNOSIS

G-protein–coupled receptor class 5 member D (GPRC5D) is a type-C 7-pass transmembrane receptor protein

- Orphan receptor - ligand and signaling mechanism unknown
- No known shed peptides or extracellular domain shedding (reduced risk for sink effect)

Predominantly expressed in cells with a plasma-cell phenotype, including the majority of malignant plasma cells from patients with MM

High GPRC5D expression associated with poor prognosis

GPRC mRNA expression

FC RECEPTOR-HOMOLOG 5 (FCRH5) PROTEIN & MRNA EXPRESSION

- Surface protein in immunoglobulin superfamily, closely related to Fc receptors
- Ligand(s) for FcRH5 are unknown, but implicated in proliferation and isotype expression in the development of antigen-primed B cells
- FcRH5 protein and mRNA over-expressed in malignant plasma cells

**FCRH5 protein expression by flow cytometry**

**FCRH5 mRNA expression in CD138+ plasma cells**

MGUS, monoclonal gammopathy of undetermined significance.

# NON-BCMA-TARGETED BISPECIFIC ANTIBODIES

<table>
<thead>
<tr>
<th>Bispecific Antibody</th>
<th>Anti-GPRC5d Talquetamab&lt;sup&gt;a&lt;/sup&gt; Phase 1 MonumenTAL-1 Study</th>
<th>Anti-GPRC5d Talquetamab + Daratumumab Phase 1b TRIMM 2 Study&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Anti-FcRH5 Cevostamab&lt;sup&gt;c&lt;/sup&gt; Phase 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>405 µg/kg SC QW (RP2D)</td>
<td>800 µg/kg SC QW</td>
<td>400 qwk &amp; 800 ug/kg q2wk</td>
</tr>
<tr>
<td>Patients</td>
<td>N = 30</td>
<td>N = 25</td>
<td>N = 29</td>
</tr>
<tr>
<td>Median prior lines</td>
<td>6</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Prior BCMA therapy</td>
<td>27%</td>
<td>16%</td>
<td>55%</td>
</tr>
<tr>
<td>Triple-class refractory</td>
<td>100%</td>
<td>92%</td>
<td>79%</td>
</tr>
<tr>
<td>Penta-drug refractory</td>
<td>80%</td>
<td>68%</td>
<td>66%</td>
</tr>
<tr>
<td>ORR at therapeutic dose</td>
<td>21/30 (70%)</td>
<td>14/21 (67%)</td>
<td>17/21 (81%)</td>
</tr>
<tr>
<td>AEs, (All/(Gr 3+))</td>
<td>77% (3%)</td>
<td>72% (0%)</td>
<td>55% (0%)</td>
</tr>
<tr>
<td>CRS</td>
<td></td>
<td></td>
<td>80% (2%)</td>
</tr>
<tr>
<td>Infections</td>
<td>33% (5%)</td>
<td></td>
<td>43% (19%)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>67% (60%)</td>
<td>44% (36%)</td>
<td>41% (31%)</td>
</tr>
<tr>
<td>Anemia</td>
<td>60% (27%)</td>
<td>36% (8%)</td>
<td>31% (21%)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>37% (23%)</td>
<td>20% (8%)</td>
<td>35% (21%)</td>
</tr>
<tr>
<td>Deaths</td>
<td>0%</td>
<td></td>
<td>% not reported</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>60% (N/A)</td>
<td>36% (N/A)</td>
<td>48% (N/A)</td>
</tr>
<tr>
<td>Other</td>
<td>Skin-related &amp; nail disorders 75%</td>
<td></td>
<td>Skin &amp; nail 65%</td>
</tr>
<tr>
<td></td>
<td>G3 rash 7.5%</td>
<td></td>
<td>G3 rash 10%</td>
</tr>
</tbody>
</table>

<sup>a</sup> Krishnan A et al. 2021 ASH. Abstract 158.  
<sup>b</sup> Chari et al. 2021 ASH. Abstract 161.  
<sup>c</sup> Trudel S et al. 2021 ASH. Abstract 157.
CAR T – BISPECIFIC ANTIBODY SEQUENCE: DOES IT MATTER?

- Both approaches have resulted in **durable responses and are tolerable** anecdotally
- Important unanswered question as products go into market
- More data needed to interpret role of **switch/sequencing of target antigen**

Van Oekelen, et al. IMW 2021
CEREBLON E3 LIGASE MODULATORS (CELMODS)

- Iberdomide (CC-220): novel small molecule inhibitor of cereblon E3 ligase – cereblon binding affinity 20* len and pom

IBERDOMIDE WITH DEXAMETHASONE IN TRIPLE CLASS REFRACTORY MYELOMA

All patients triple class-exposed:
• PIs 100%
• LEN 100%
• POM 100%
• Anti-CD38 mAbs 100%
• 97.2% triple-class refractory

Survival outcomes:
mDOR 7.0 (4.5–11.3) mos
mPFS 3.0 (2.8–3.7) mos
mOS 11.2 (9.0–NR) mos

<table>
<thead>
<tr>
<th>Response, n (%)</th>
<th>IBER + DEX (N = 107)</th>
<th>IBER + DEX post anti-BCMA therapy (N = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR(^a)</td>
<td>26 (26.2)</td>
<td>6 (25.0)</td>
</tr>
<tr>
<td>sCR</td>
<td>1 (0.9)</td>
<td>0</td>
</tr>
<tr>
<td>CR</td>
<td>0</td>
<td>1 (4.2)</td>
</tr>
<tr>
<td>VGPR</td>
<td>8 (7.5)</td>
<td>1 (4.2)</td>
</tr>
<tr>
<td>PR</td>
<td>19 (17.8)</td>
<td>4 (16.7)</td>
</tr>
<tr>
<td>MR</td>
<td>11 (10.3)</td>
<td>4 (16.7)</td>
</tr>
<tr>
<td>SD</td>
<td>46 (43.0)</td>
<td>8 (33.3)</td>
</tr>
<tr>
<td>PD</td>
<td>15 (14.0)</td>
<td>4 (16.7)</td>
</tr>
<tr>
<td>NE</td>
<td>7 (6.5)</td>
<td>2 (8.3)</td>
</tr>
</tbody>
</table>

Median DoR (95% CI), months
7.0 (4.5–11.3) NA

\(^a\)Defined as PR or better.

Lonial S et al. 2021 ASH. Abstract 162.
**VENETOCLAX**


MEK INHIBITOR “REPURPOSED” FOR MYELOMA

“Actionable” Genomic Alterations: occur in ~50% of patients

- KRAS and NRAS (40%)
- BRAF (8%)
- CDKN2C and CCND1 (18%)
- PI3K-AKT (5%)
- FGFR3 (5%)
- IGF1R and ALK (5%)
- MyD88 (3%)
- Others (11%)
- IDH1/2 (5%)


M-Spike (g/dL)

0.6
0.5
0.4
0.3
0.2
0.1
0
11/20/15 12/20/15

0.56
0.3
0.26
0.21
A PATH TO CURE!!!

A search on ClinicalTrials.gov for multiple myeloma resulted in 3404 studies. The search also included Myeloma, Plasma cell neoplasm, and Multi. See Search Details.

<table>
<thead>
<tr>
<th>Study Title</th>
<th>Conditions</th>
<th>Interventions</th>
<th>Locations</th>
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<td>The Aim is to Identify Recurrent Genomic Mutations and/or Predisposing Polymorphisms in Patients With Sporadic Cases of Multiple Myeloma</td>
<td>Multiple Myeloma</td>
<td>Genetic: DNA sequencing</td>
<td>Hospices Civil de Lyon Pierre Benite, France</td>
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<tr>
<td>A Head-to-head Comparative Study of 18F-PSMA-1007 PET/CT and 18F-FDG PET/CT Imaging in Multiple Myeloma</td>
<td>Multiple Myeloma</td>
<td>Drug: 18F-PSMA-1007</td>
<td>The First Affiliated Hospital of China Medical University Shenyang, Liaoning, China</td>
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<td>Multiple Myeloma (MM) Profile in Brazil: A Retrospective Observational Analysis</td>
<td>Multiple Myeloma</td>
<td>Drug: 18F-FDG</td>
<td>Centre de Hematologia e Oncologia (CEHON) Salvador, BA, Brazil</td>
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<td>Impact of Paramedical Consultations in Oncological Supportive Care in Outpatients With Multiple Myeloma</td>
<td>Multiple Myeloma</td>
<td>Other: Early oncological supportive care</td>
<td>Centre Henri Becquerel Rouen, France</td>
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<td>CAR-T Cells Therapy in Relapsed/Refractory Multiple Myeloma</td>
<td>Relapsed/Refractory Multiple Myeloma(MM)</td>
<td>Biological: CART therapy in Relapsed/Refractory multiple myeloma</td>
<td>Southern Medical University Zhuhai Hospital Guangdong, Guangdong, China</td>
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THANK YOU