Clinical trials are research studies of new treatments that involve patients. By testing new drugs or combinations of drugs, each study is designed to find better ways to prevent, detect, diagnose, or treat cancer, to improve the quality of life of the patient, and to answer scientific questions.

Many hospitals now take part in clinical trials, which are only begun after laboratory studies have outlined the potential safety of a new treatment or procedure, and it has been found to have the potential to work better than existing methods. Clinical trials vary greatly in size: from a single researcher in one hospital or clinic to an international multicenter study with several hundred participating researchers on several continents. The number of patients in a test can range from a few to several thousand.

Some relevant definitions:

- **Control group** – The arm of a randomized clinical trial that gets the standard treatment.
- **End Point** – What a clinical trial is trying to measure or find out; the goal of the trial. Typical end points include measurements of toxicity, response rate, and survival.
- **Experimental group** – The arm of a randomized trial that gets the new treatment.
- **Randomized clinical trial** – A research study in which subjects are randomly assigned to receive a particular treatment.
- **Phase 0** – A Phase 0 study is shorthand for a pilot study, which is small-scale preliminary study conducted in an attempt to predict an appropriate sample size and improve upon the study design prior to performance of a full-scale clinical trial.
- **Phase I trial** – A trial designed to determine the MTD (maximum tolerated dose) of a new drug or a new combination of drugs that has never been tried in humans. It is usually the first human testing of a new treatment, although in Phase I trials of combination therapies, the individual elements may already have been well tested. Patients in Phase I trials must have advanced cancer that is refractory to any standard treatment. In a typical Phase I trial, successive groups (“cohorts”) of 3 to 6 patients are given the treatment. The first cohort typically gets a very low dose, and the dose is raised in each subsequent cohort until a set number of patients experience DLT (dose limiting toxicity). The dose level used for the previous cohort is then taken to be the Maximum Tolerated Dose. This dose is then used in a Phase II trial.
- **Phase II trial** – A trial designed to determine the response rate of a new therapy that has already been tested in Phase I trials. Typically, 14 to 50 patients with one type of cancer are treated to see how many have a response. Patients are usually required to have advanced cancer that is refractory to any standard treatment, and in addition, they must have measurable disease. If results from a Phase II trial are promising enough, the treatment may then be tested in a Phase III trial. If the results are obviously much better than the standard treatment, then it may not be necessary to do a Phase III trial, and the treatment may become standard based on Phase II trial results.
- **Phase III trial** – A trial designed to compare two or more treatments for a given type and stage of cancer. The end point of a Phase III trial is usually survival or disease-free survival. Phase III trials are usually randomized, so patients don't choose which treatment they receive. A typical Phase III trial has 50 to thousands of patients. Some Phase III trials compare a new treatment that has had good results in Phase II trials with an older, well known, standard treatment. Other Phase III trials compare treatments that are already in common use. Some treatments in Phase III trials may be available outside the clinical trial setting.
- **FDA-approved** – even with approval from the Federal Drug Administration (FDA) for the indication of a drug, there is occasionally an identified need for additional safety surveillance and ongoing technical support. Furthermore, post FDA approval studies (also known as Phase IV trials) may be required by regulatory authorities or may be undertaken by the sponsoring company for competitive reasons (such as, finding a new market) or other reasons (such as, testing for interactions with other drugs, or on certain population groups who are unlikely to join a trial themselves). The safety surveillance is designed to detect any rare or long-term adverse effects over a much larger patient population and longer time period than was possible during the Phase I-III clinical trials.
For the most up-to-date information on clinical trials, please visit the Myeloma Matrix on our website myeloma.org

### FDA approved

<table>
<thead>
<tr>
<th>NAME (formal name/generic)</th>
<th>COMPANY/SPONSOR</th>
<th>INDICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adriamycin®, Rubex® doxorubicin</td>
<td>Pfizer, Bristol-Myers Squibb</td>
<td>Used as primary induction therapy in combination with Velcade and dexamethasone (PAD) or with vincristine and dexamethasone (VAD). May also be used with cyclophosphamide, vincristine, and dexamethasone (C-VAD) or with dexamethasone, thalidomide, cisplatin, and cyclophosphamide as salvage therapy (DT-PACE).</td>
</tr>
<tr>
<td>Alkeran® melphalan</td>
<td>Celgene Corporation</td>
<td>For transplant patients, used as high-dose therapy with stem cell rescue. For non-transplant patients, used as frontline therapy in combination with prednisone plus or minus another drug; may also be used as salvage therapy.</td>
</tr>
<tr>
<td>Aredia® pamidronate, pamidronic acid</td>
<td>Novartis</td>
<td>Administered monthly as an intravenous infusion lasting 2–4 hours for the prevention of bone disease in MM.</td>
</tr>
<tr>
<td>Cytoxan®, Neosar®, Procystin® cyclophosphamide</td>
<td>Cyclophosphamide Tablets (Roche Laboratories Inc - Boehringer Ingelheim), Cytoxan® (Bristol-Myers Squibb Co - Mead Johnson and Co), Neosar® (Pfizer - Pharmacia &amp; Upjohn)</td>
<td>Used in frontline treatment with Velcade and dexamethasone. Used in salvage therapy as monotherapy, with Velcade and dex, len and dex, and as part of DCP, DT-PACE, and C-VAD.</td>
</tr>
<tr>
<td>Decadron dexamethasone</td>
<td>off patient – many manufacturers</td>
<td>Used throughout treatment course of MM, both as monotherapy and in combination with other drugs.</td>
</tr>
<tr>
<td>DOXIL® doxorubicin liposome HCl injection</td>
<td>Janssen</td>
<td>In combination with bortezomib for patients who have not previously received bortezomib and have received at least one prior therapy.</td>
</tr>
<tr>
<td>Epispan, Etoposil®, Vepesid®, VP-16®, etoposide</td>
<td>off patient – many manufacturers</td>
<td>Used in salvage therapy for MM in combination with dexamethasone, cyclophosphamide, and cisplatin; in combination with dexamethasone, thalidomide, cisplatin, doxorubicin, and cyclophosphamide.</td>
</tr>
<tr>
<td>Farydak® panobinostat LBH589</td>
<td>Novartis</td>
<td>Approved for patients with MM who have received at least two prior standard therapies, including bortezomib and an immunomodulatory agent (IMiD).</td>
</tr>
<tr>
<td>KYPROLIS® carfilzomib</td>
<td>Onyx Pharmaceuticals / Amgen</td>
<td>1. For the treatment of patients with MM who have received at least two prior therapies, including bortezomib and an immunomodulatory agent, and have demonstrated disease progression on or within sixty days of the completion of the last therapy. 2. In combination with Revlimid and dexamethasone for the treatment of MM patients who have had at least one prior therapy.</td>
</tr>
<tr>
<td>Mozobil® plerixafor AMD 3100</td>
<td>Genzyme</td>
<td>Stem cell mobilizer used with G-CSF prior to transplant.</td>
</tr>
<tr>
<td>Plat® cisplatin, cisplatinum</td>
<td>Cadila Healthcare</td>
<td>Salvage therapy for MM used in combination with dexamethasone, cyclophosphamide, and etoposide (DCEP) and with dexamethasone, thalidomide, doxorubicin, cyclophosphamide, and etoposide (DT-PACE).</td>
</tr>
<tr>
<td>POMALYST® pomalidomide CC-4047</td>
<td>Celgene Corporation</td>
<td>Indicated for patients with MM who have received at least two prior therapies including lenalidomide and bortezomib and have demonstrated disease progression on or within 60 days of completion of last therapy.</td>
</tr>
<tr>
<td>Revlimid® lenalidomide CC-5913</td>
<td>Celgene Corporation</td>
<td>Numerous studies of Revlimid in various combinations or as a single agent.</td>
</tr>
<tr>
<td>Thalomid® thalidomide</td>
<td>Celgene Corporation</td>
<td>Indicated for the treatment of patients with newly diagnosed MM.</td>
</tr>
<tr>
<td>VELCADE® bortezomib PS-341</td>
<td>Millennium</td>
<td>Velcade is indicated for the treatment of patients with MM.</td>
</tr>
<tr>
<td>Zometa® zoledronate, zoledronic acid</td>
<td>Novartis</td>
<td>Given monthly as an IV infusion for the prevention of bone loss in MM. Also helps reduce serum calcium levels.</td>
</tr>
</tbody>
</table>

### Abbreviations used throughout this table:

- zoledronate, zoledronic acid
- PS-341
- VELCADE®
- CC-5013
- lenalidomide
- CC-4047
- pomalidomide
- cisplatin, cisplatinum
- plerixafor
- Mozobil®
- KYPROLIS®
- panobinostat
- LBH589
- DOXIL®
- dexamethasone
- Decadron
- cyclophosphamide
- Cytoxan®, Neosar®, Procytox®
- pamidronate, pamidronic acid
- Aredia®
- doxorubicin
- Adriamycin®, Rubex®
- MM
- Novartis
- Celgene Corporation
- Millennium
- Otsuka America Pharmaceutical
- Genentech Inc.
- Janssen Research & Development
- Bristol-Myers Squibb
- Amgen
- Vejle Hospital
- Myeloma Matrix
- Myeloma.org
- FDA approved
- for either autologous or allogeneic stem cell transplant.
- Multiple open trials using busulfan as part of the conditioning regimen in relapsed or refractory MM.
- Bevacizumab combined with lenalidomide and dexamethasone (BEV/REV/DEX) is active, no longer recruiting.
- AT9283 in patients with relapsed or refractory MM.
- Emphasis on the CD38 antibody daratumumab.
- Randomized, double-blind, multicenter study of denosumab compared with zoledronic acid (Zometa®) in the treatment of bone disease in subjects with newly diagnosed MM.
- Monoclonal antibodies for treatment of MM.
- Expanded Access Program for elotuzumab in combination with lenalidomide plus dexamethasone in patients with relapsed or refractory MM.
**INDICATION**

Beth Israel Deaconess Medical Center; For the most up-to-date information on clinical trials, please visit the

**SB - 497115-GR**

**eltrombopag**

**CT-011**

**pidilizumab**

**NOX-A12**

**olaptesed pegol**

**NK Cells**

**Natural Killer (NK) cells**

**LCL 161**

**filanesib**

**ARRAY-530**

**GlaxoSmithKline**

**Akt inhibitor given in combination with trametinib for the treatment of patients with rel/ref MM.**

**GSK214795**

**ibrutinib, Bruton’s tyrosine kinase inhibitor**

**PharmacyClics**

**Active, no longer recruiting:**

**iuemetstat**

**GRN163L**

**telomerase inhibitor GRN163L**

**ixazomib**

**MLN9708**

**Millennium**

**Active, no longer recruiting:**

**iL vaccine**

**keyhole limpet hemocyanin**

**U Penn; MD Anderson**

**1. Randomized trial of CD3/CD28 activated idiopathic KLH primed autologous lymphocytes in patients with MM undergoing autologous transplant.**

**2. Donor vaccinated lymphocyte infusion for patients with MM relapsing or failing to achieve a CR after allogeneic transplant.**

**LCL 161**

**Novartis**

**Oral IAP antagonist given either alone or in combination with cyclophosphamide in patients with rel/ref MM.**

**Natural Killer (NK) cells**

**University of Arkansas**

**1. Expanded NK cell therapy for high-risk MM patients who relapsed on TT2 or TT3.**

**2. Safety and in vivo persistence and expansion of autologous, ex vivo-expanded NK cells.**

**saptasedeg paliv**

**NOXION Pharma**

**Active, no longer recruiting:**

**Multi-center, open-label, uncontrolled trial evaluating the safety and efficacy of NOX II in combination with a background therapy of bortezomib and dexamethasone (VD) in previously treated patients with MM.**

**pidelizumab CT-011**

**CureTech Ltd.**

**Active, no longer recruiting:**

**To determine the safety and efficacy of the combination of the dendritic cell fusion vaccine and CT-011, a monoclonal antibody targeted to PD-1 (programmed death receptor 1).**

**Promacta**

**eltrombopag SB-497115-GR**

**GlaxoSmithKline**

**Active, no longer recruiting:**

**Eltrombopag for the treatment of thrombocytopenia in patients undergoing therapy for relapsed MM.**

**NAME (formal name/generic)**

**incyte Corporation**

**Study completed, with results:**

**Small molecule Janus kinase inhibitor for patients with rel/ref MM.**

**selenexor**

**Karyopharm Therapeutics, Inc.**

**Open-label single-arm study of selenexor + low-dose dexamethasone in patients with quadruple-refractory MM (STORM).**

**senolydig LDE225**

**SCI Development Innovations**

**Sonidipog plus bortezomib in patients with relapsed or rel/ref MM with a dose-finding lead-in.**

**isolatcept ACE-011**

**Acceleron / Celgene Corporation**

**Randomized study of isolatcept on bone mass and turnover in patients with MM.**

**STYVIANT® siluximab CNT3 328**

**Janssen Research & Development**

**Both trials active, no longer recruiting:**

**1. Open-label, single-arm study of the safety and efficacy of combination treatment with lenalidomide, bortezomib, dexamethasone, and siluximab in subjects with newly diagnosed, previously untreated MM.**

**2. Siluximab (Anti-IL-6 Monoclonal Antibody) in subjects with high-risk smoldering MM.**

**TAFINLAR® dabrafenib**

**GlaxoSmithKline**

**A phase II, open-label study in subjects with BRAF V600E mutated rare cancers with several histologies to investigate the clinical efficacy and safety of the combination therapy of dabrafenib and trametinib.**

**trametinib**

**GlaxoSmithKline**

**1. Trametinib in combination with Akt inhibitor GSK214795 in treating patients with rel/ref MM.**

**2. Phase II, open-label, non-randomized, multi-center study of oral dabrafenib in combination with oral trametinib in subjects with rare cancers with BRAF V600E positive mutations.**

**Trenda® bendamustine**

**Teva**

**• Many studies using bendamustine in combination with various other drugs for patients with rel/ref MM.**

**• Optimising renal outcome in MM renal failure with bortezomib, thalidomide, bendamustine, and dexamethasone.**

**• High-dose chemotherapy using BeAM for autologous transplant in MM.**

**Tricira*, Triglide* fenofibrate**

**Abbott and others (off patent)**

**Fenofibrate therapy in patients with smoldering or symptomatic MM.**

**Viraexct* nelfinavir SB-497115-GR**

**ViiV Healthcare**

**NFibvir as bortezomib-sensitizing drug in patients with proteasome inhibitor-nonresponsive MM.**

**ZDCOR® simvastatin**

**Pi initiated, U of Louisville, KY**

**Effect of simvastatin and zoleodronic acid on M-protein and/or free light chains when added to conventional chemotherapy for the treatment of MM patients.**

**PHASE III**

**ACP-196**

**Acerta Pharma**

**1. Proof-of-concept study of the combination of ACP-196, a novel Bruton tyrosine kinase inhibitor, and pembrolizumab in subjects with B-cell malignancies.**

**2. Study evaluating the safety, pharmacokinetics (PK), pharmacodynamics (PD), and efficacy of ACP-196 and ACP 319 in B-cell malignancies.**

**ACP-319**

**Acerta Pharma**

**1. ACP-196 in combination with ACP-319 in subjects with B-cell malignancies.**

**2. ACP-196 in combination with pembrolizumab for treatment of B-cell malignancies.**

**Actos* pioglitazone**

**Takeda**

**Third-line therapy of MM with lenalidomide in combination with pioglitazone, dexamethasone and metronomic low-dose chemotherapy with treosulfan.**

**Altor* everolimus RAD-001**

**Novartis**

**Both studies active, no longer recruiting:**

**1. Socalfam and everolimus in treating patients with relapsed or refractory lymphoma or MM.**

**2. Everolimus and bendamustine hydrochloride in treating patients with relapsed or refractory histiocytic cancer.**

**ALT-801**

**Altor BioScience Corporation**

**Active, no longer recruiting:**

**Study of a p53-specific, scTCR/IL-2 fusion protein in patients with relapsed or refractory MM.**
ALT-803
Altor BioScience Corporation
Modified IL-5 that recognizes, kills, and creates immune memory against MM cells.

BT062
Biostat Pharmaceuticals Corporation
1. Active, no longer recruiting: Study of safety, dose, and anti-tumor activity of BT062 for patients with relapsed and refractory MM.
2. BT062 in combination with lenalidomide/dexamethasone in patients with MM.

BYL719
Novartis
Active, no longer recruiting: Oral LGH447 in combination with oral BYL719 in patients with relapsed and refractory MM.

CC-233
Celgene Corporation
Active, no longer recruiting: Oral mTOR kinase inhibitor in open-label study for patients with solid tumors, NHL, and MM.

Chimeric antigen receptor-modified T cells
CART cells
Chinese PLA General Hospital
CD-138 antigen receptor-modified T cells in rel/ref MM.

Cometesi
cabozantinib
XL184
Exelixis, Inc.
Active, no longer recruiting: Cabozantinib (XL184) in patients with relapsed or refractory MM.

DKN-01
HealthCare Pharmaceuticals, Inc.
DKN-01 and Revlimid/dexamethasone in patients with rel/ref MM.

Donor lymphocyte infusion
DLI
MD Anderson Cancer Center & Bellicum Pharmaceuticals
DLI of T cells genetically modified with iCas9 suicide gene.

Eloctuzumab
Hu5C8
Bristol-Myers Squibb
Bortezomib, dexamethasone, and lenalidomide with or without elotuzumab in treating patients with newly diagnosed high-risk MM.

Evofosfamide
TH-302
Threshold Pharmaceuticals
Open-label study of TH-302 as monotherapy and in combination with bortezomib in subjects with rel/ref MM.

Filanesib
ARRY-310
Array BioPharma
Study not yet open as of 9-30-15: Monotherapy of filanesib in rel/ref MM patients.

Flavopiridol; alvocidib
HMR 1275, LB-8275
NCI
Flavopiridol administered as a 30-minute bolus followed by a 4-hour infusion in lymphomas and MM.

Folfyten
pallitaxelate
Afflux Therapeutics, Inc.
Novel antifolate agent pralatrexate in combination with the histone deacetylase inhibitor romidepsin for the treatment of patients with rel/ref lymphoid malignancies and MM.

HETERT vaccine + autologous T cells
University of Pennsylvania, University of Maryland
Active, no longer recruiting: Combination immunotherapy after ASCT for advanced MM to study HETERT vaccination followed by adoptive transfer of vaccine-primed autologous T cells.

Ibrutinib
Brentuximab vedotin/ibrutinib
PC-32765
Pharmacia
Currently recruiting: Study of ibrutinib in combination with rituximab (Kytril) in patients with rel/ref MM. Not yet recruiting: Study of brutinib in combination with ponatinib (Ponatinib) and dexamethasone in subjects with rel/ref MM.

Istodax
romidepsin (depsipeptide)
FRH1228, FR2228
Celgene Corporation, Janssen-Cilag
1. Romidepsin (depsipeptide) in combination with lenalidomide in adults with relapsed or refractory lymphomas and MM.
2. Lenalidomide and romidepsin for rel/ref Hodigkin lymphoma, mature T-cell lymphoma, and MM.
3. Pomalidomide, dexamethasone, and romidepsin for rel/ref MM.
4. Romidepsin and dexamethasone in rel/ref lymphoid malignancies.

Ixazomib
MLN9708
Millennium
Currently recruiting: Pomalidomide/dex with or without ixazomib in patients with refractory MM.

Not yet recruiting: Ixazomib in combination with len/dex in patients with newly diagnosed MM.
2. Bendamustine, ixazomib, dex in rel/ref MM.
3. Ixazomib, pomalidomide, clarithromycin, dex in treating patients with MM.

Keytruda
pembrolizumab
(formerly lambrolizumab)
MK-3475
Merck
1. Pembrolizumab in combination with pomalidomide and dexamethasome for the treatment of rel/ref MM.

LGH447
Novartis
Active, no longer recruiting: Safety and effectiveness of oral LGH447 and oral BYL719 in patients with rel/ref MM.

Luitos
ASP4847 (OIS-906)
Astellas Pharma
ASP4847 in combination with Velcade and dexamethasone in relapsed and refractory MM.

Marizomib
Ixazomib
(formal name/generic)
COMPANY/SPONSOR
INDICATION

Name  (formal name/generic)

Company/Sponsor

Indication

For the most up-to-date information on clinical trials, please visit the Myeloma Matrix on our website myeloma.org
### PHASE I

<table>
<thead>
<tr>
<th>Trial ID</th>
<th>Company/Sponsor</th>
<th>INDICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACP-196</td>
<td>Acerta Pharma</td>
<td>Open-label study of ACP-196 with and without dexamethasone in subjects who have had at least one therapy for MM that is progressing.</td>
</tr>
<tr>
<td>ACY-241</td>
<td>Acetylen Pharmaceuticals</td>
<td>Multi-center, single-arm, open-label dose escalation study to determine MTD and antitumor activity of oral ACY-241 as monotherapy and in combination with pom/dex in patients with rel/ref MM.</td>
</tr>
<tr>
<td>afuresertib</td>
<td>GSK2101083, PGB11525</td>
<td>1. Study in subjects with rel/ref MM to determine a dose of afuresertib in combination with carfilzomib (Part 1) and to investigate the safety, pharmacokinetics, and clinical activity of the combination of afuresertib with carfilzomib compared with carfilzomib alone (Part 2). 2. Study of afuresertib with bortezomib and dexamethasone in Japanese relapsed MM patients.</td>
</tr>
<tr>
<td>AG-120</td>
<td>Agios Pharmaceuticals, Inc.</td>
<td>Safety, pharmacokinetics, pharmacodynamics, and efficacy study of oral AG-120 for patients with advanced hematologic malignancies with an IDH1 mutation.</td>
</tr>
<tr>
<td>amrubin</td>
<td>Celgene Corporation</td>
<td>Active, no longer recruiting: Amrubin in combination with lenalidomide and weekly dexamethasone for the treatment of rel/ref MM.</td>
</tr>
<tr>
<td>Apidran®</td>
<td>PharmaMar, SA</td>
<td>Phthalimipropionaphosphonic acid (Apidran®) in combination with bortezomib and dexamethasone in patients with relapsed and/or refractory MM.</td>
</tr>
<tr>
<td>CAR T-Cell therapy</td>
<td>NCI</td>
<td>Study of engineered T cells targeted to the B-cell maturation antigen (BCMA) for patients who have had at least 3 prior regimens and have progressive or refractory hematological malignancies.</td>
</tr>
<tr>
<td>CB-5083</td>
<td>Clove Biosciences</td>
<td>Study of oral p7E3 inhibitor for patients with rel/ref MM who have at least two prior lines of therapy, including an immunomodulatory agent and a proteasome inhibitor.</td>
</tr>
<tr>
<td>CB-839</td>
<td>Calithera Biosciences</td>
<td>Safety and dosing study of a potent orally bioavailable glutaminase inhibitor for patients with advanced and/or treatment-refractory hematological malignancies.</td>
</tr>
</tbody>
</table>

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