



Managing Your Myeloma

Craig Emmitt Cole, MD

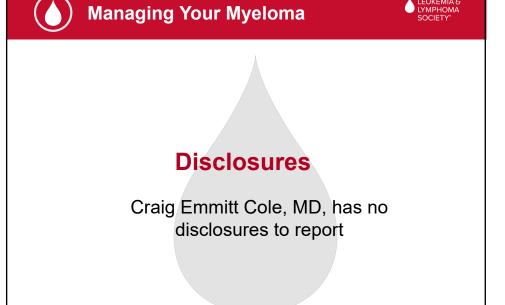
Assistant Professor of Internal Medicine

Multiple Myeloma and Plasma Cell Dyscrasia Program

Division of Hematology/Oncology

University of Michigan Medical School

Ann Arbor, MI



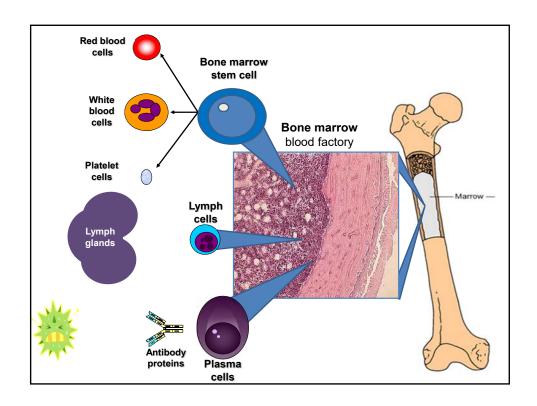


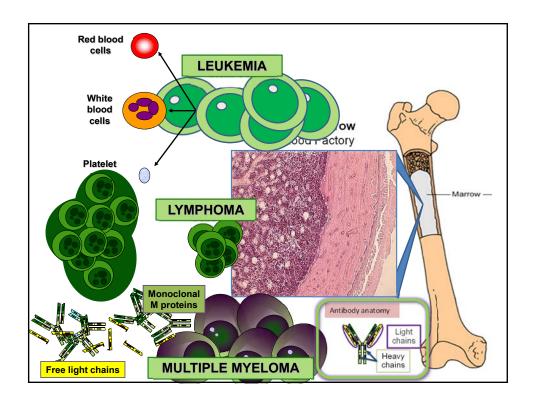
What Are We Going to Talk About?

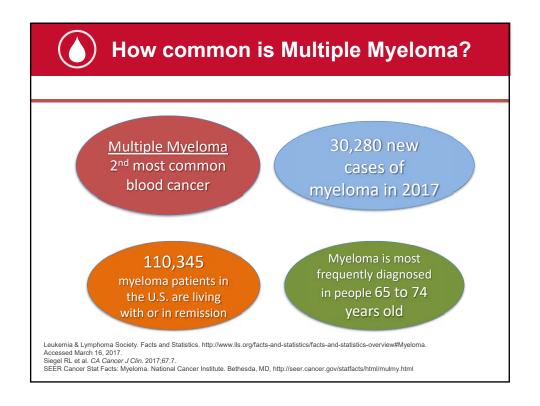
- How multiple myeloma is diagnosed
- Treatments for myeloma
- Advances in research and its impact on treatment
- Improving physician-patient communication

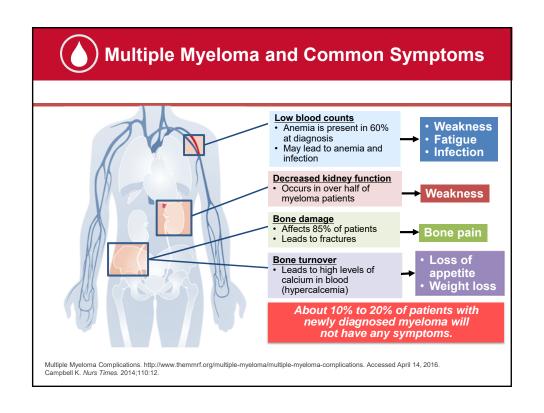


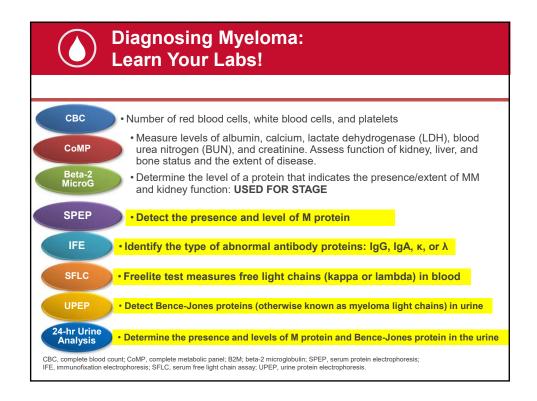
How Multiple Myeloma is Diagnosed

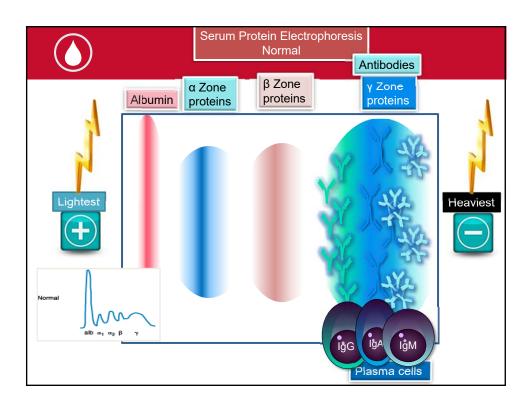


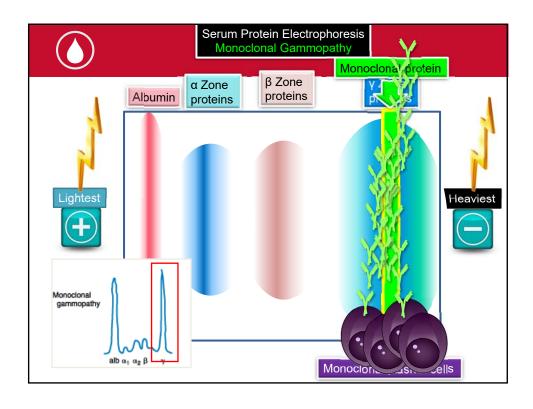


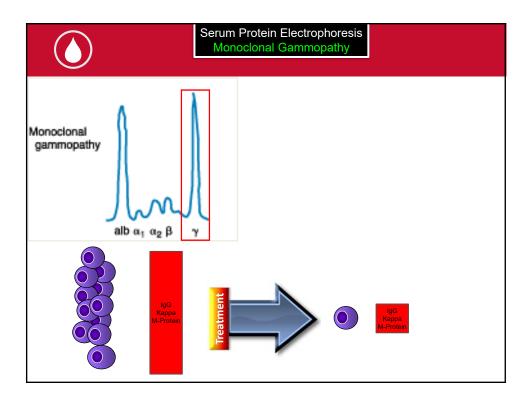


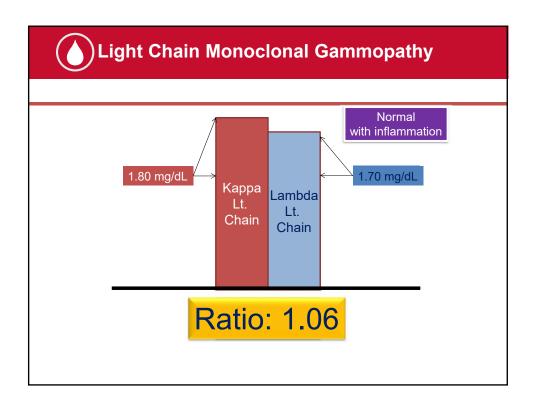


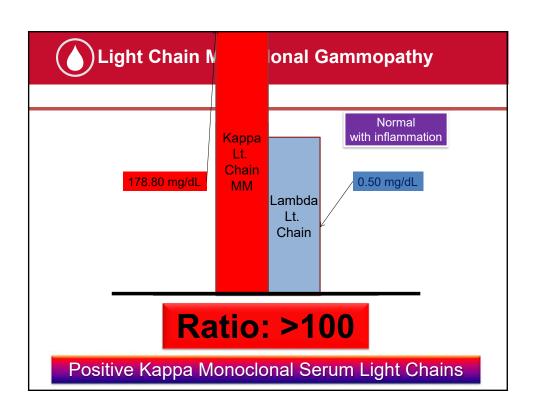


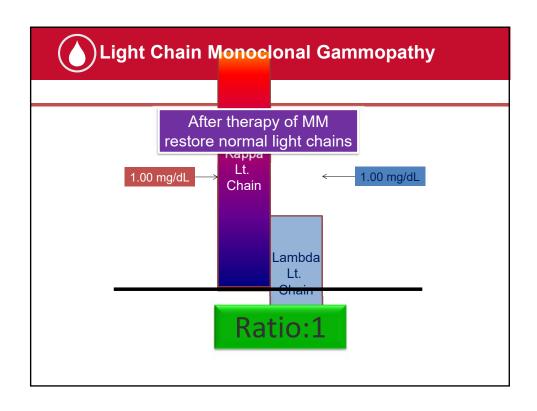


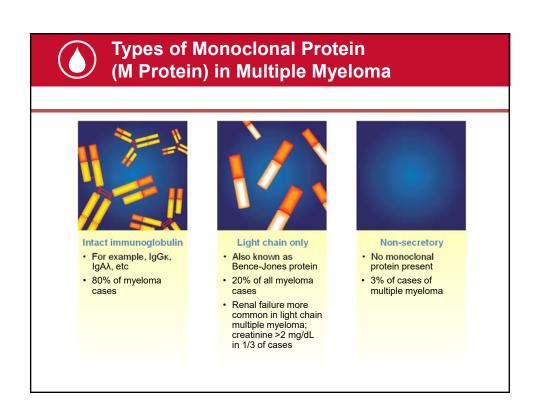














Diagnosis of Multiple Myeloma

- Conventional X-rays reveal punched-out lytic lesions, osteoporosis, or fractures in 75% of patients.
- PET/CT and MRI appears to be more sensitive (85%) than skeletal survey for the detection of small lytic bone lesions.
- Diagnosis is confirmed with bone marrow demonstrating greater than 10% involvement by malignant plasma cells.







Kyle RA, et al. Mayo Clin Proc. 2003; 78(1):21-33. Nanni C et al. European Journal of Nuclear Medicine and Molecular Imaging. 2006;33(5):525-31. Dimopoulos MA, et al. Leukemia. 2009



Know the Diagnosis Key Items That Define the Diagnosis

MGUS

M protein <3 g/dL

- Clonal plasma cells in BM <10%
- No myelomadefining events

1% risk of progression/year to multiple myeloma or related conditions

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

10% risk of progression/year to active myeloma

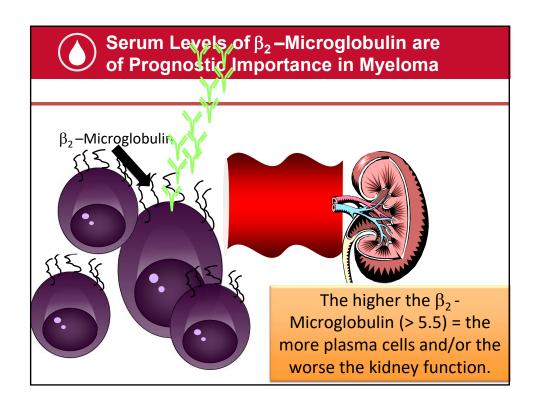
Multiple Myeloma

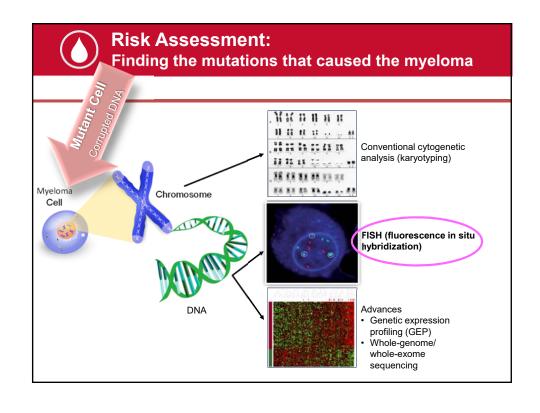
- Underlying plasma cell proliferative disorder
- AND ≥1 myelomadefining events
- ≥1 CRAB* feature
- Clonal plasma cells in BM ≥60%
- Serum free light chain ratio ≥100
- · >1 MRI focal lesion

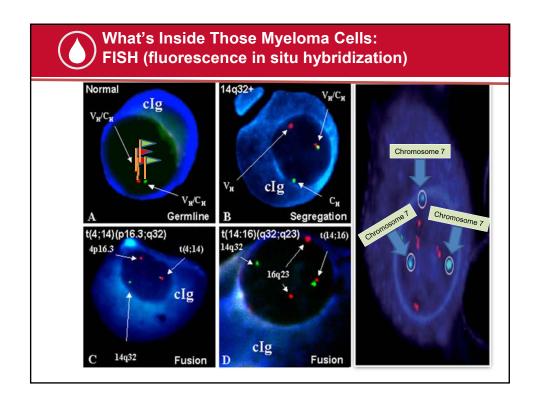
*C: Calcium elevation (>11 mg/dL)

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

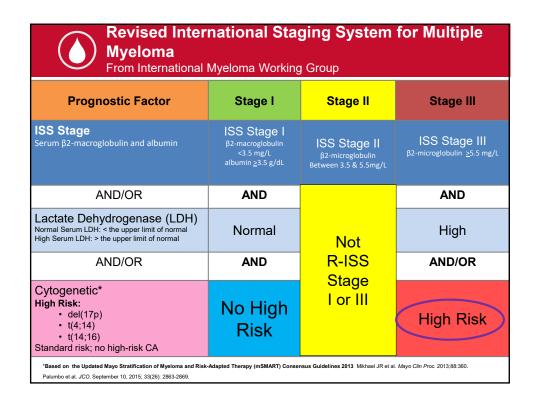
Rajkumar SV, et al. Lancet Oncol. 2014;15:e538.

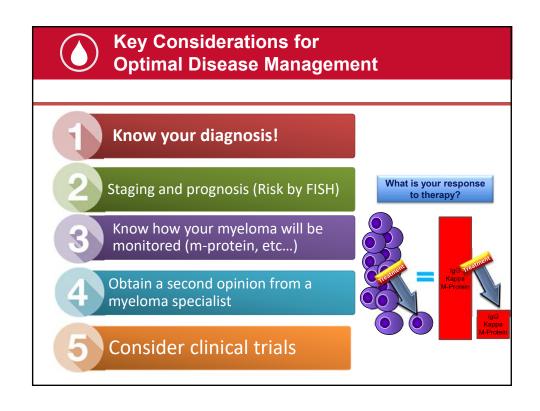




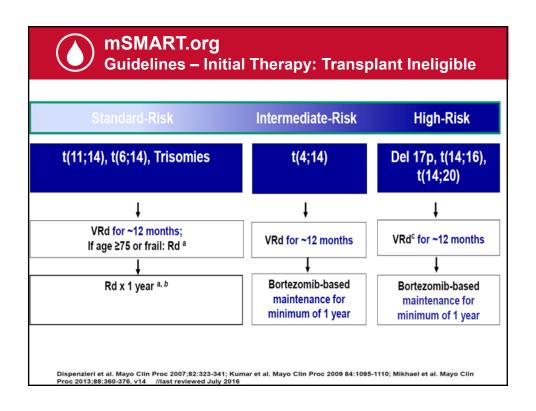


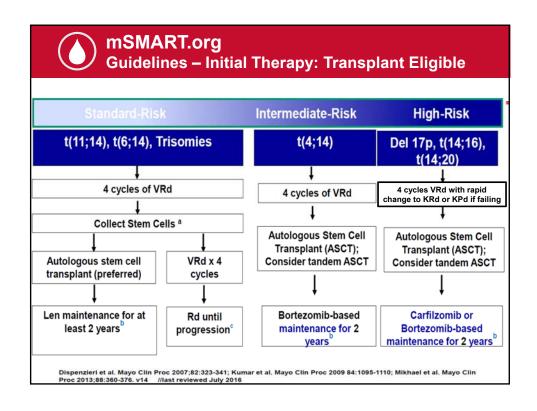
What Does FISH Tell Me About My Myeloma?				
	Risk Level* (Degree High Risk	of Aggressivenes Intermediate Risk	s) Standard Risk	
% Patients affected	20%	20%	60%	
Chromosome Analysis Results on Bone Marrow	 FISH: deletion 17th chromosome Translocation 14th and 16th Translocation 14th and 20th 	FISH: • translocation (4;14) • Extra copies chromosome1 Cytogenetic • deletion 13 or • Hypodiploid: any missing chromosomes	All others types including: • Hyperdiploid: More than 1 pair of chromosomes • Translocation (11;14) • Translocation (6;14) • Normal	



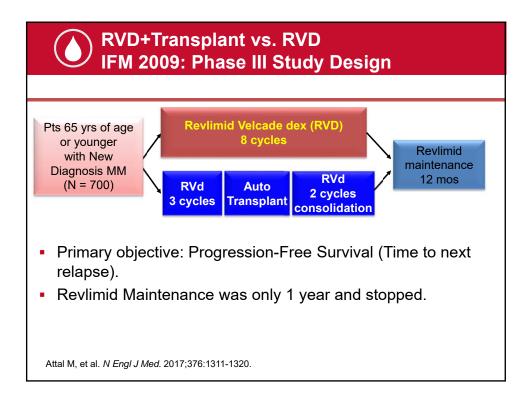


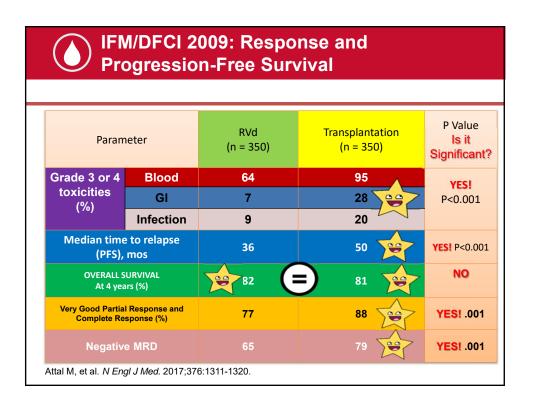
Tools of the Trade for Frontline Therapy Standard Drug Overview					
	-		1		
Class	Drug Name	Abbreviation	Administration		
IMiD	Revlimid (lenalidomide)	R or Rev	Oral		
immunomodulatory drug	Thalomid (thalidomide)	T or Thal			
Proteasome inhibitor	Velcade (bortezomib)	V or Vel or B	Intravenous (IV) or subcutaneous injection (under the skin)		
	Kyprolis (carfilzomib)	C or K or Car			
	Ninlaro (ixazomib)	N or I	Oral		
Character and	Cytoxan (cyclophosphamide)	С	Oral or intravenous		
Chemotherapy	Alkeran or Evomela (melphalan)	M or Mel			
	Decadron (dexamethasone)	Dex or D or d	Oral or intravenous		
Steroids	Prednisone	Р			
Steroids	Decadron (dexamethasone)	Dex or D or d	Oral or intrav		

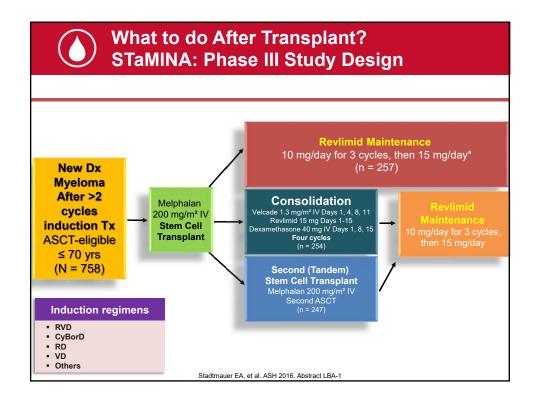










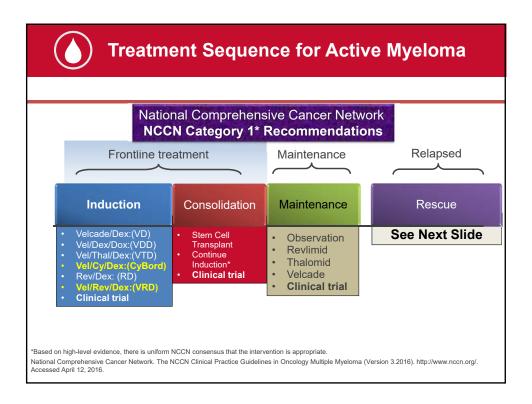


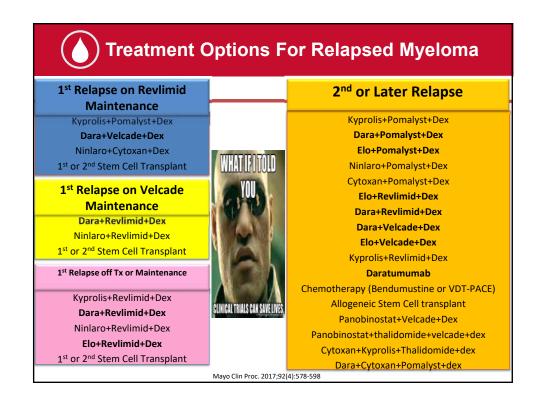


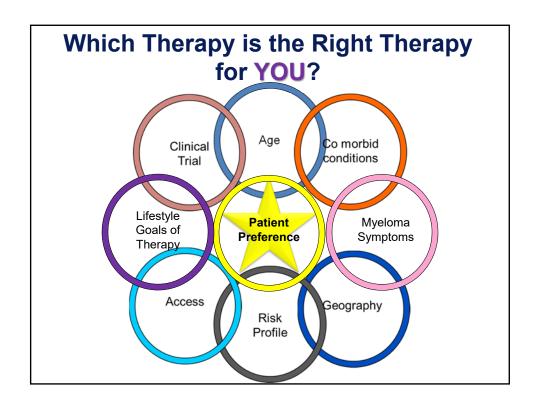
What to do After Transplant? STaMINA: Bottom Line for New MM patients

- Largest randomized comparison to date of therapeutic approaches after first ASCT in MM in US.
 - No difference in time to relapse (PFS) or Overall Survival in patients who have 2 transplants, consolidation therapy or just straight to maintenance after first BMT.
 - Straight to maintenance is the easiest!
 - No difference between arms for pts with highrisk disease.

Stadtmauer EA, et al. ASH 2016. Abstract LBA-1.

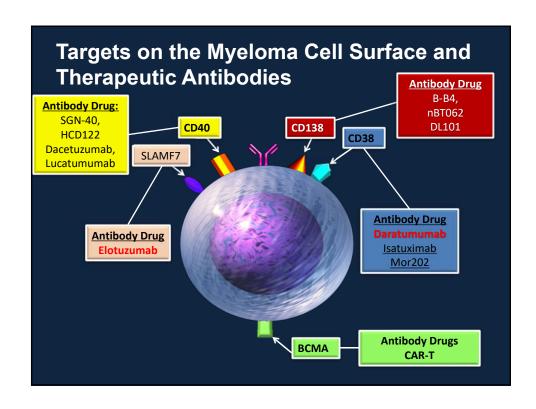


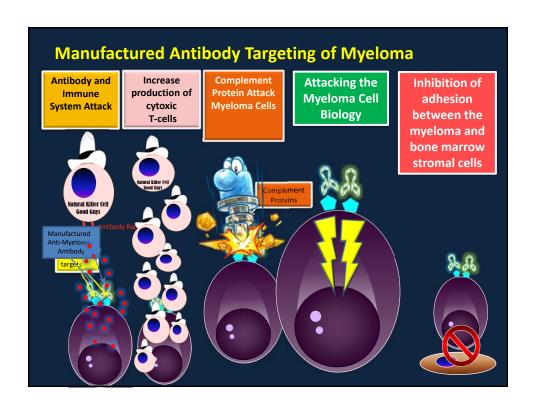






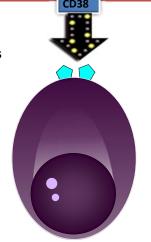
Advances in Myeloma Research and its Impact on Treatment

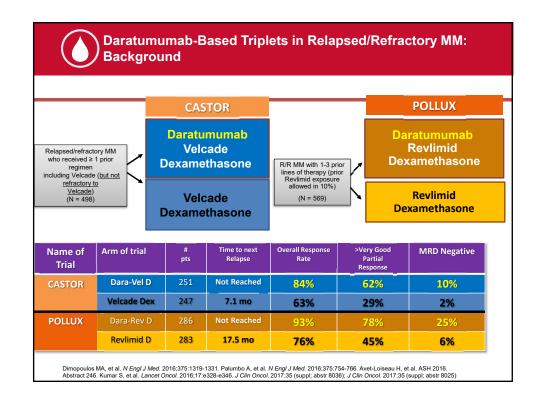






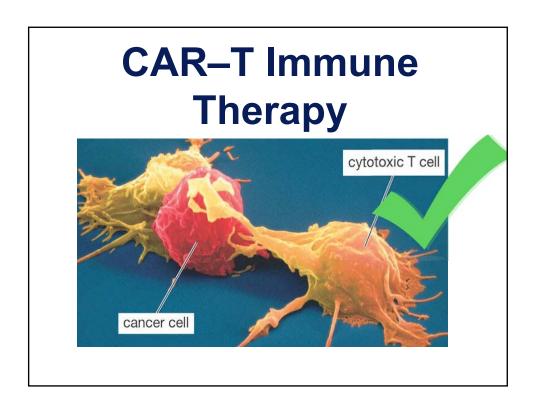
- Daratumumab is an IV human IgG manufactured antibody.
- It is a targeted immunotherapy that binds to the CD38 on MM cells.
- Daratumumab as a single agent has a 30% response rate in relapsed myeloma.
- 2 Phase III trials in early relapsed Myeloma.
 - Daratumumab + Revlimid/ dexamethasone (POLLOX).
 - Daratumumab + Velcade/ dexamethasone (CASTOR).

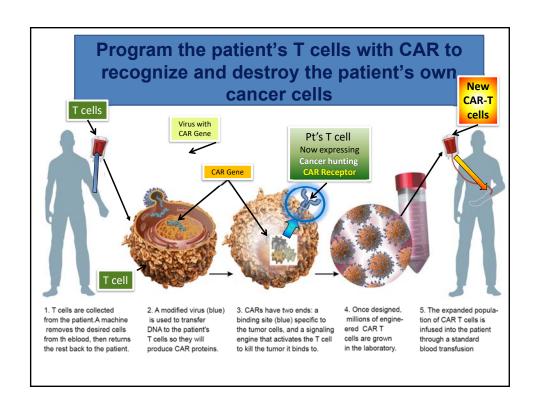


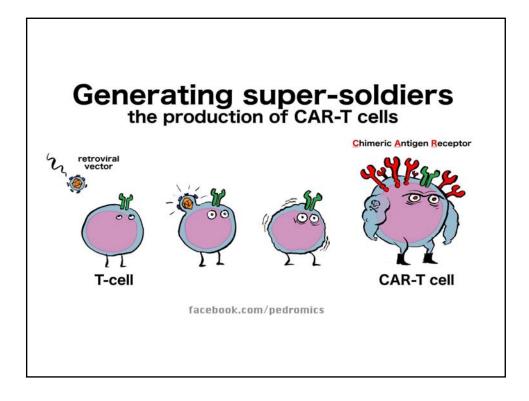


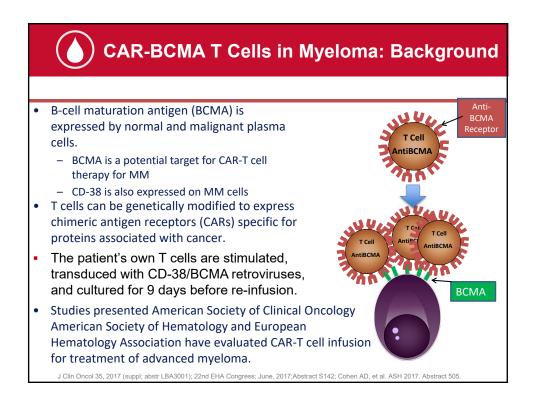
Performance of Daratumumab					
Regimen	Phase	Patient Population	Number of patients	Outcomes	Adverse Events
Daratumumab Revlimid Dexamethasone Vs. Rev/dex. POLLUX	III	569	RRMM (median of 1 prior regimens)	Dara + Rev/dex vs. Rev/Dex Response rate DRD: 93% vs Response rate RD: 76% ≥Complete Response (43% vs 19%) Time to relapse (PFS): DRD not reached	Low WBC, muscle spasms, diarrhea, fatigue, •• Infusion-related reactions: 56%
Daratumumab Pomalyst Dexamethasone (Chari et al, ASH 2015)	Ib	77	RRMM (median of 3.5 prior regimens)	Response rate: 59% PR: 28% VGPR: 23% CR: 8% Response rate of 57.5% in patients who failed Rev and Velcade	Neutropenia, anemia, fatigue, dyspnea, cough, nausea, diarrhea •• Infusion-related reactions: 61%
Daratumumab Velcade Dexamethasone Vs. Velcade/Dex.	111	498	RRMM (median of 2 prior regimens) not refractory to bortezomib	Dara+Velcade dex vs Vel/dex: Response rate DVD:84% vs Response rate Vd:63% ≥VGPR (62% vs 29% P<0.0001) ≥CR (19% vs 9% P= 0.0012)	Thrombocytopenia peripheral sensory neuropathy, diarrhea, and anemia •• Infusion-related reactions: 45%
Daratumumab Kyprolis,Revlimid Dex for New dx: (Jakubowiak et al) ASCO 2017	l	22	Newly diagnosed	100% Response rate 5% complete response, 86% ≥very good partial resp 6-month PFS rate was 100%.	Fatigue, Anemia Low platelets •• Infusion-related reactions: 21%; SERIOUS SIDE EFFECTS: 27%

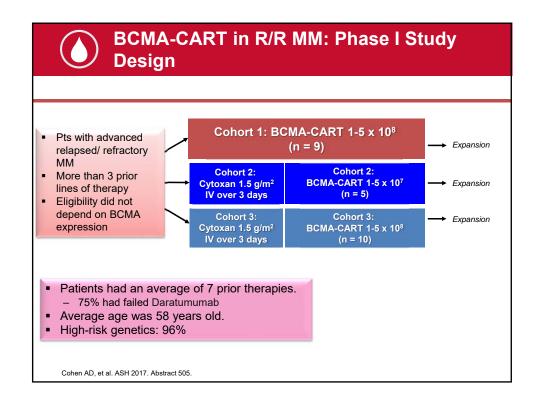
Regimen	Phase	Patient Population	Number of patients	Outcomes	Adverse Events
Elotuzumab + Revlimid+ Dexamethasone Vs. Rev Dex ELOQUENT-2	3	646 ERD:321 RD:325	RRMM 1 to 3 prior regimens	EloRD vs. RD Response rate: EloRD: 79% vs RD: 66% Median Duration of response: Elo RD:19.4 vs RD:14.9 months	Severe toxicities: Low lymphocytes, fatigue, pneumonia •• Infusion reaction in 10% of patients
Elotuzumab + Velcade + Dexamethasone Vs. Vel Dex (Palumbo et al, 2015)	2	152 Ebd:77 Bd: 75	RRMM 1 to 3 prior regimens	EloVD vs. VD Response rate: Elo VD: 65% vs VD: 63% Median Duration of response: EloVD:9.9 vs VD:6.8 months	Severe toxicities: Low platelets (9%), infections (23%) •• Infusion reaction in 5% of patients
Elotuzumab + Pomalyst + Dexamethasone (Jagannath et al, 2017)	2	53	RRMM 1 to 3 prior regimens	**Very Early Data after 3 cycles** 77% patients remain on treatment 9% discontinuation for disease progression	Most common: fatigue, infections, cough, anemia Severe Toxicities: Infections (13%), Pneumonia (9%)
Elotuzumab + Lenalidomide+ Bortezomib+ Dexamethasone (Laubach J, et al. ASCO 2017)	2	40	Newly diagnosed, MM	Response rate after 4 cycles: Overall: 97% >VGPR: 88% Median Duration of Response: Not Reached	Most common adverse effects: Infection (50%) fatigue, peripheral neuropathy, edema leukopenia

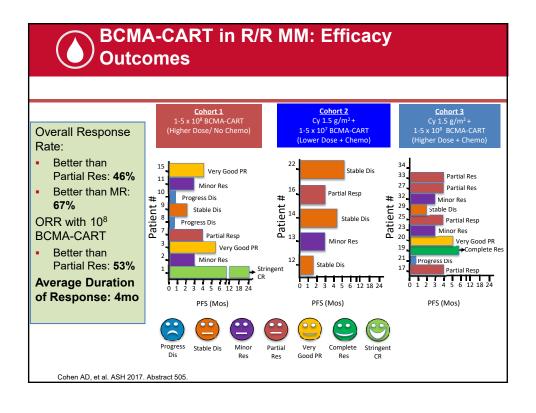














CAR-BCMA T Cells in Myeloma: Toxicities

- After CAR-BCMA T-cell infusion, patients may experience cytokine release syndrome (CRS)!
 - Fever
 - Low Blood pressure (hypotension)
 - High heart rate (tachycardia)
 - High creatinine kinase (muscle damage) and liver enzymes (liver damage)
 - Acute kidney damage
 - Shortness of breath
- All-grades CRS: 83%; Severe CRS: 33%!
- 1 death in cohort 1 pt: Fungal infection, MM progression, plasma cell leukemia.

Cohen AD, et al. ASH 2017. Abstract 505.



Improving Physician-Patient Communication



Steps to Make an Informed Treatment Decision

Diagnosis and Treatment

- Ask your doctor for your specific diagnosis and write it down.
 - Your specific diagnosis is important in determining treatment.
- Gather information about all your treatment options.
 - Ask your doctor to explain the treatment options.
 - Ask about clinical trials!
 - www.lls.org/treatment/types-oftreatment/clinical-trials
 - www.cancer.gov
 - Refer to Questions to Ask Your Healthcare Provider About Treatment Options when you meet with your doctor www.LLS.org/whattoask





Steps to Make an Informed Treatment Decision

Clinical Trial

Personal Medical Records

- Establish a file and keep it with you for reference
 - Specific diagnosis, Stage, cytogenetics (FISH).
 - Laboratory reports: keep track of your measurement of disease (protein level).
 - Radiology reports.
 - Current medications you are taking (including vitamin supplements).
 - Past and current treatments you have had for your myeloma.
 - Medical history.
 - Reactions/ side effects to medications.
 - Financial information on cost of treatment.
 - List of your healthcare providers and information/business cards.





Be an INFORMED and EMPOWERED Patient

- Ask your doctor...
 - What is the goal of treatment?
 - What are the options for my treatment?
 - What is the best therapy for ME!
- If you don't understand <u>ask again!</u>
- Ask yourself...
 - What are my personal goals for treatment?
 - Your goals are an important part of your treatment decision process.
 - Do I have the information I need to make an informed decision?

Take an active role in making treatment decisions for yourself



Choosing Your Healthcare Team

When choosing your healthcare team, it is helpful to:

- Feel that you can trust your doctor <u>open</u> <u>communication</u> is key!
- Feel that you are <u>respected and listened to</u> by your doctor, nurse, and other individuals on your team.
- Try to partner with a <u>hematologist-oncologist</u> affiliated with a *National Comprehensive Cancer Center* (designated by NCI) or a practice highly experienced in treating multiple myeloma.
- Seek a second opinion for diagnosis and/or treatment.
 - A second opinion with a myeloma specialist can help you understand your illness and decide what treatment is best.



Helpful Communication Tips

- Keep a list of questions to bring to your medical appointments.
 - Ask your doctor about a preferred method of ongoing communication (email? phone? office visits only, patient computer portal?).
 - Ask your doctor about clinical trials for which you may be eligible.
- Bring a friend or relative with you to appointments.
 - Take notes or audio record instructions to help you remember what the doctor says at a later date.
- Ask for help from your healthcare team in gathering information about your myeloma.
 - 88% MM patient experience registrants said it was at least somewhat important to get help with gathering information before their meetings with cancer specialists.
 - 83% said it was at least somewhat important to get help with a written list of questions.

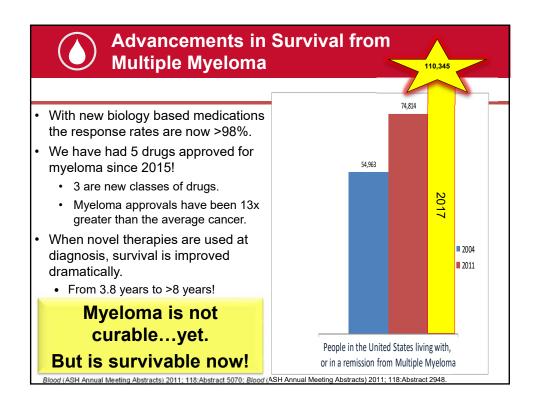
Multiple Myeloma Specialty Registry Report 2017; www.cancersupportcommunity.org/RegistryIndexReport2017.

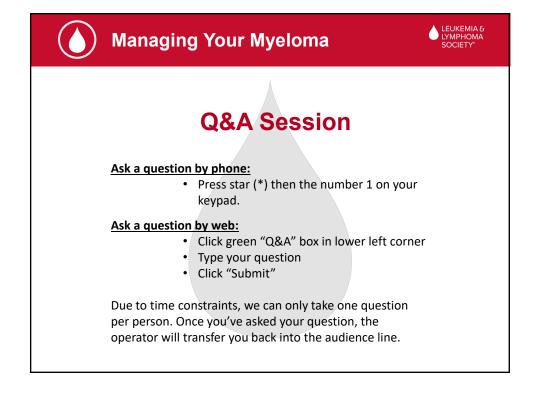


Helpful Communication Tips (continued)

- Describe specific symptoms or side effects you experience and how they impact your life.
 - 36% of MM patient experience registrants never, rarely, or sometimes report full extent of side effects and/or symptoms to health care team.
- Tell your healthcare team if you use any form of alternative treatment (such as vitamins or herbs) since these could interfere with cancer medications.
- Discuss with your healthcare team about the cost of myeloma care and opportunities for assistance.
 - 38% of respondents had not discussed costs with their health care team.
- Talk openly with your healthcare team about your goals for treatment over the course of your life!

 $Multiple\ Myeloma\ Specialty\ Registry\ Report\ 2017;\ www. cancer support community. or g/Registry\ Index Report\ 2017.$







The Leukemia & Lymphoma Society Offers:

 Information Resource Center: Information Specialists, who are master's level oncology professionals, are available to help cancer survivors navigate the best route from diagnosis through treatment, clinical trials and survivorship.

➤ EMAIL: infocenter@LLS.org

➤ TOLL-FREE PHONE: 1-800-955-4572

- Free Education Booklets:
 - > www.LLS.org/booklets
- Free Telephone/Web Programs:
 - >www.LLS.org/programs
- Live, weekly Online Chats, including 'Living with Myeloma' on Mondays:

> www.LLS.org/chat







The Leukemia & Lymphoma Society Offers:

- Support Resources: LLS Community, discussion boards, blogs, support groups, financial assistance and more: www.LLS.org/support
 - NEW LLS Podcast, The Bloodline with LLS! Listen in as experts and patients guide listeners in understanding diagnosis, treatment, and resources available to blood cancer patients: www.thebloodline.org
- Education Video: Free education videos about survivorship, treatment, disease updates and other topics: www.LLS.org/educationvideos
- Patti Robinson Kaufmann First Connection Program: Peer-to-peer program that matches newly diagnosed patients and their families: www.LLS.org/firstconnection
- Free Nutrition Consults: Telephone and email consultations with a Registered Dietitian: www.LLS.org/nutrition
- What to ask: Questions to ask your treatment team: www.LLS.org/whattoask
- For more information about myeloma: www.LLS.org/myeloma



