Impact of New Immune Therapies

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RESEARCH INITIATIVE
Signature Project of the International Myeloma Foundation

Three types of Myeloma Treatment

- **Chemotherapy**
- **Novel Therapy**
- **Immune Therapy**

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Introduction of New Treatments

FRONTLINE  RELAPSE

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Currently Available Anti-Myeloma Agents in 2023

Steroids	Conventional Chemo	ImIDs	Proteasome Inhibitors	Immunologic approaches	XPO inhibitor
Prednisone	Melphalan	Thalidomide	Bortezomib	Daratumumab (anti-CD38)	Selinexor
Dexamethasone	Cyclophosphamide	Lenalidomide	Carfilzomib	Isatuximab (anti-CD38)	
	Doxorubicin	Pomalidomide	Ixazomib	Elotuzumab (anti-CS1)	
	DCEP/D-PACE			Talquetamab anti-GPRC5d*CD3	
	METRO28			Teclistamab anti-BCMA*CD3	
	Carmustine			Elranatamab anti-BCMA*CD3	
	Bendamustine			idecabtagene vicleucel: anti-BCMA CART	
				ciltacabtagene autoleucel: anti-BCMA CART	

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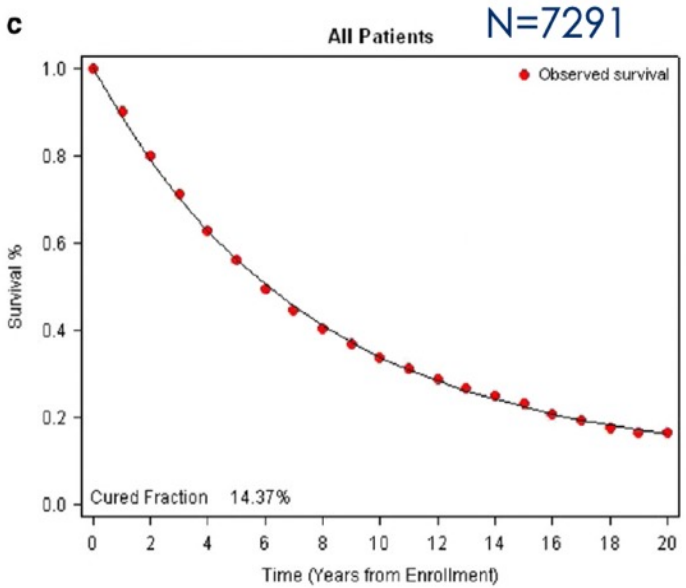
IMWG Research Project on Long-Term Survival in Newly Diagnosed Transplant-Eligible MM

Clinical predictors of long-term survival in newly diagnosed transplant eligible multiple myeloma — an IMWG Research Project

Saad Z. Usmani[1], Antje Hoering[2], Michele Cavo[3], Jesus San Miguel[4], Hartmut Goldschimdt[5], Roman Hajek[6], Ingemar Turesson[7], Juan Jose Lahuerta[8], Michel Attal[9], Bart Barlogie[10], Jae Hoon Lee[11], Shaji Kumar[12], Stig Lenhoff[13], Gareth Morgan[14], S. Vincent Rajkumar[15], Brian G. M. Durie[16] and Philippe Moreau[17]

Blood Cancer Journal 2018



Before Novel & Immune Therapies

14.37% @ 20 Years

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Study Results

- Detailed studies show residual microscopic disease
- Immune microenvironment remains seriously disturbed
- Very late relapses occur linked to **exhausted T cells and other immune abnormalities**

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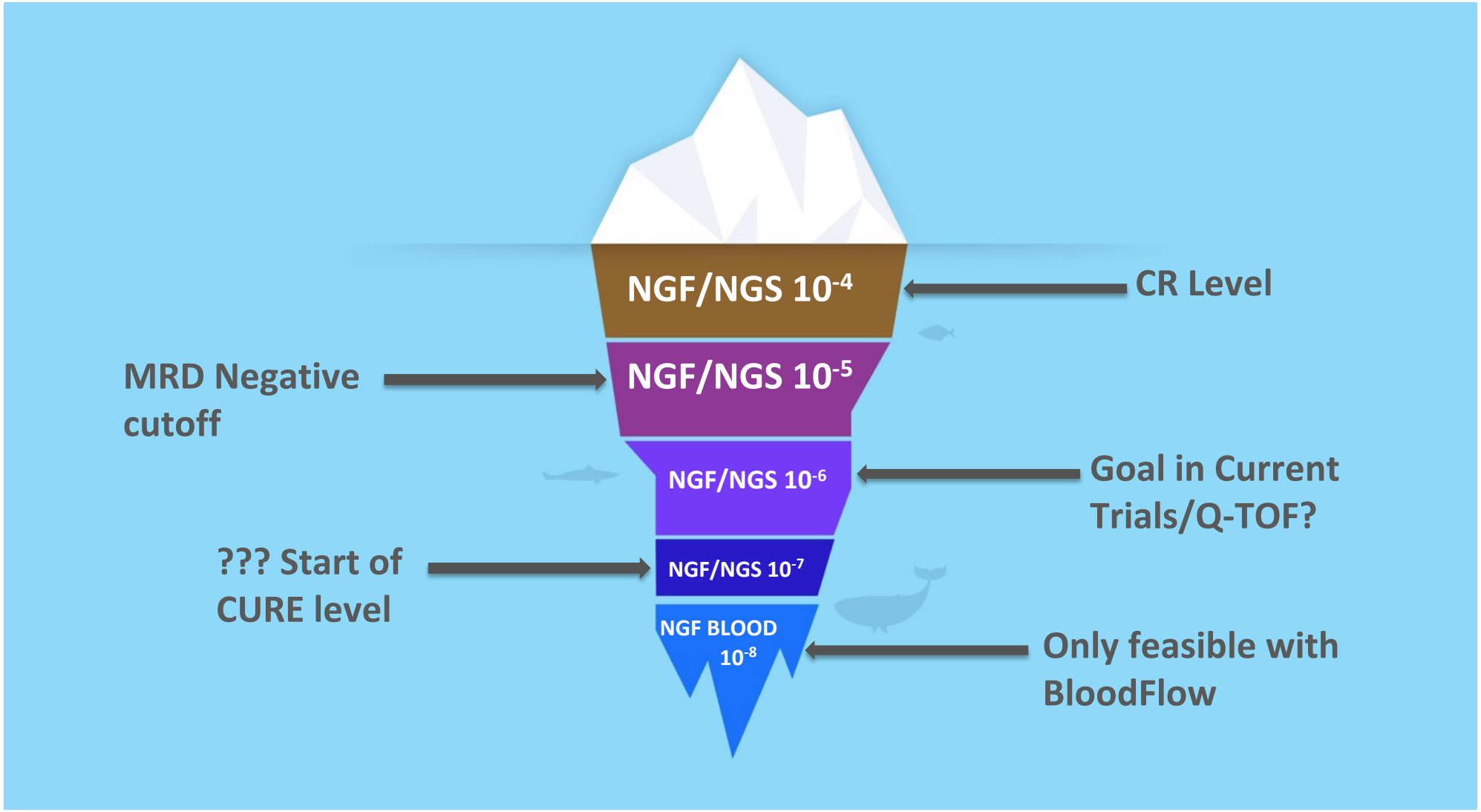
Getting to the Bottom of the Iceberg



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GEM-CESAR Trial

GEM-CESAR: 90 HR SMM patients

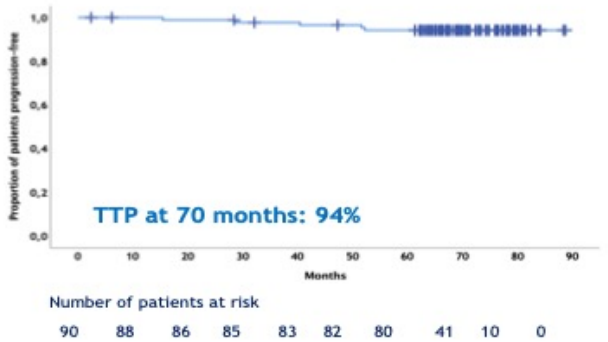
- Multicenter, open-label, phase II trial (June 2015-June 2017): Follow-up of 70.1 months

**High-risk was defined according to the Mayo and/or Spanish models*

	3 months after HDT-ASCT (n=82)	4 years post ASCT (n=58)
MRD-ve 10^{-5}	56/82→ 68.3%	28/58→ 48%
MRD-ve 10^{-6}	39/82→ 48%	25/58→ 43%

Evaluable patients include: Patients at risk with the Bone Marrow and MRD assessment performed as well as those patients who have discontinued earlier than the specific time point because of progressive or biochemical progressive disease (they qualify as MRD +ve)

TTP to active MM



- The lack of achievement of MRD-ve at the end of maintenance predicted both biochemical and clinical progression
- 92% of patients remain alive at 70 months
- Early rescue intervention planned in biochemical progressions to maintain to the patients MDE-free

Mateos MV ASH2022: oral presentation

ASCENT Trial

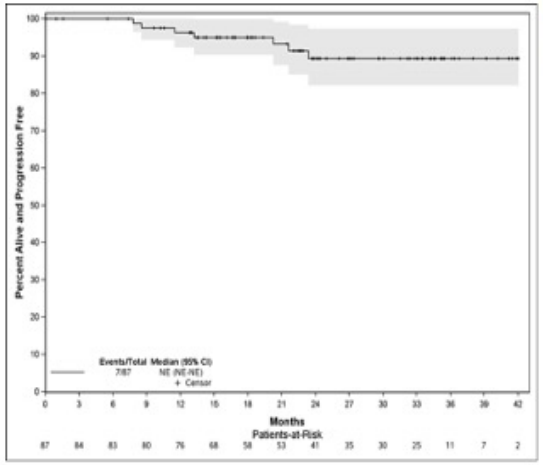
ASCENT trial: Curative approach in HR-SMM patients

INDUCTION
(4-week cycles for 6 cycles)
- Carfilzomib (36 mg/m² twice weekly or 56mg/m² weekly)
- Lenalidomide (25 mg daily for three weeks)
- Daratumumab (weekly for 8, every other week for 16 weeks)
- Dexamethasone 40 mg weekly

CONSOLIDATION
(4-week cycles for 6 cycles)
- Carfilzomib (36 mg/m² twice weekly or 56mg/m² weekly)
- Lenalidomide (25 mg daily for three weeks)
- Daratumumab (every 4 weeks)
- Dexamethasone 20 mg weekly

MAINTENANCE
(4-week cycles for 12 cycles)
- Lenalidomide (10 mg daily for 3 weeks)
- Daratumumab (q 8 weeks)

- 87 HRSMM patients according to the IMWG 2/20/20 model



ORR: 97% with 94% of VGPR or better

MRD-ve rate: 84%

- Three patients have progressed, median PFS for the cohort has not been reached; PFS rate (95%CI) at 3 years was 89.9% (82.3-98.3%)

Kumar S et al.. ASH 2022: oral presentation

How to Achieve Long-Term Survival

- **Start treatment as early as possible**
  - **HR SMM – 2/20/20 + circulating myeloma**
  - **EARLY ACTIVE MYELOMA**
- **Prioritize young, healthy, good risk for cure efforts**
- **When possible, also use triplets/max efforts in elderly**
- **Use maintenance as feasible/appropriate for control**

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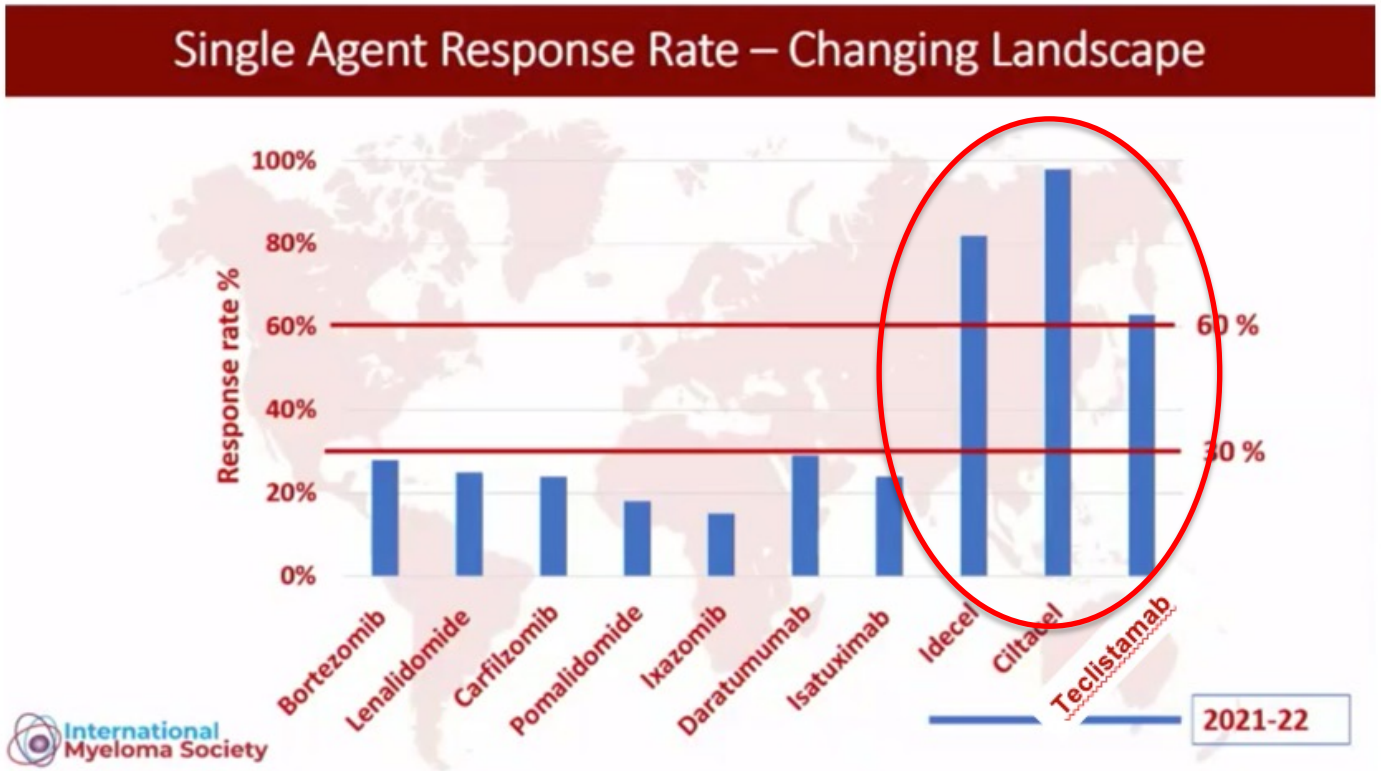
Immunotherapy

Amazing Success in Immunotherapy for MM



Munshi COMy 2023

Right patient, right treatment, right time

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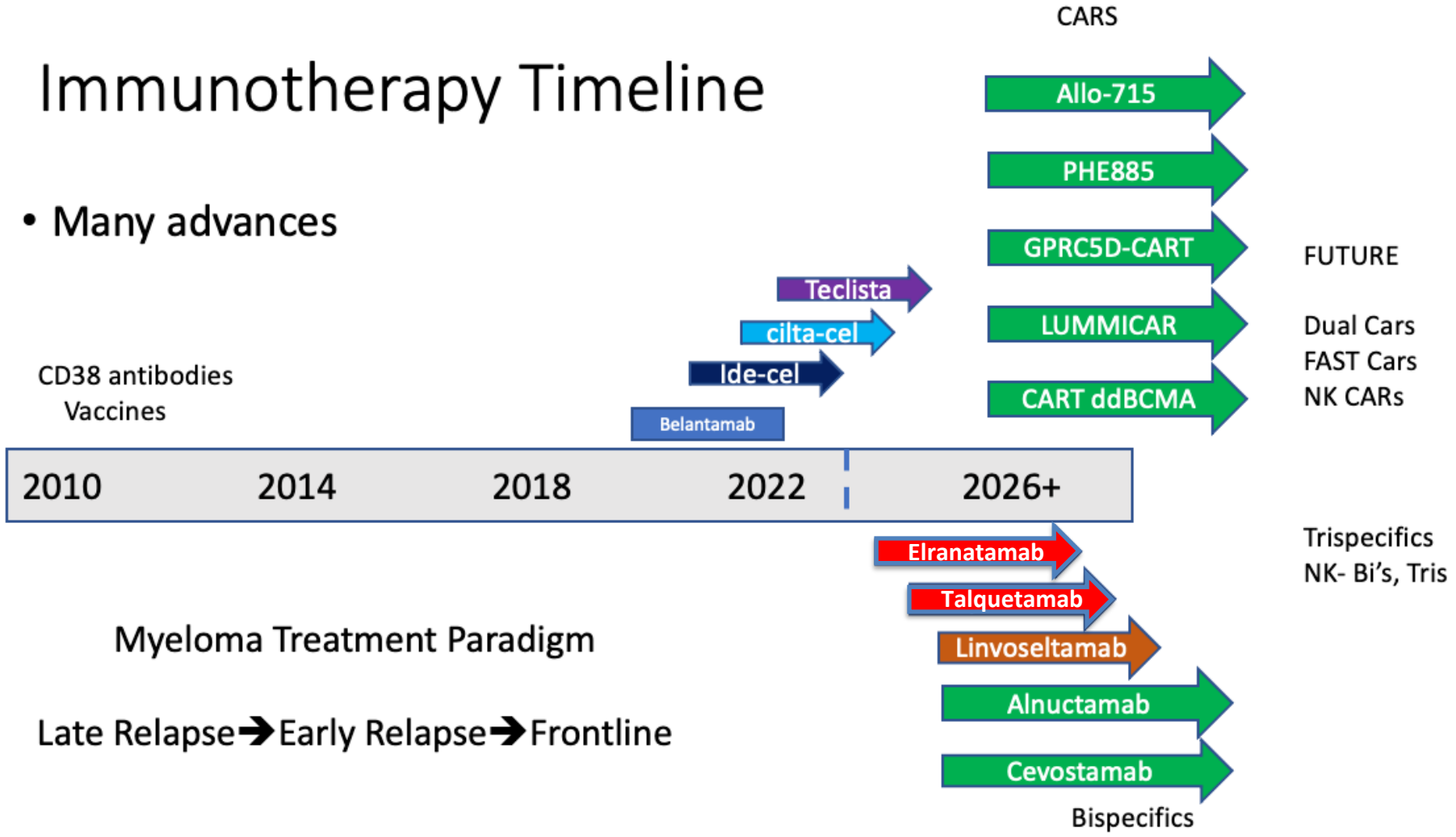
Immunotherapy Timeline



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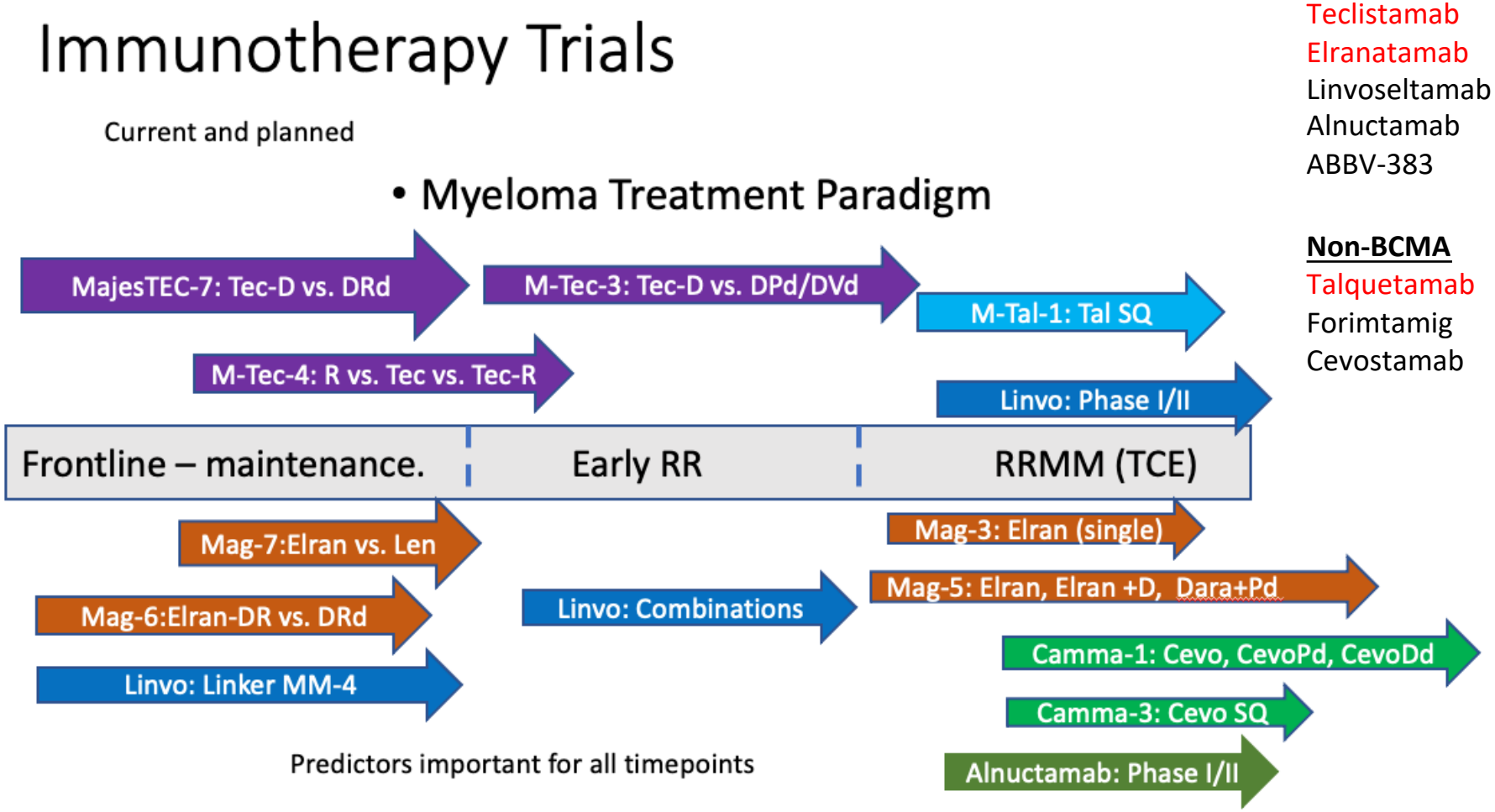
Immunotherapy Trials



BCMA
Teclistamab
Elranatamab
Linvoseltamab
Alnuctamab
ABBV-383

Non-BCMA
Talquetamab
Forimtamig
Cevostamab

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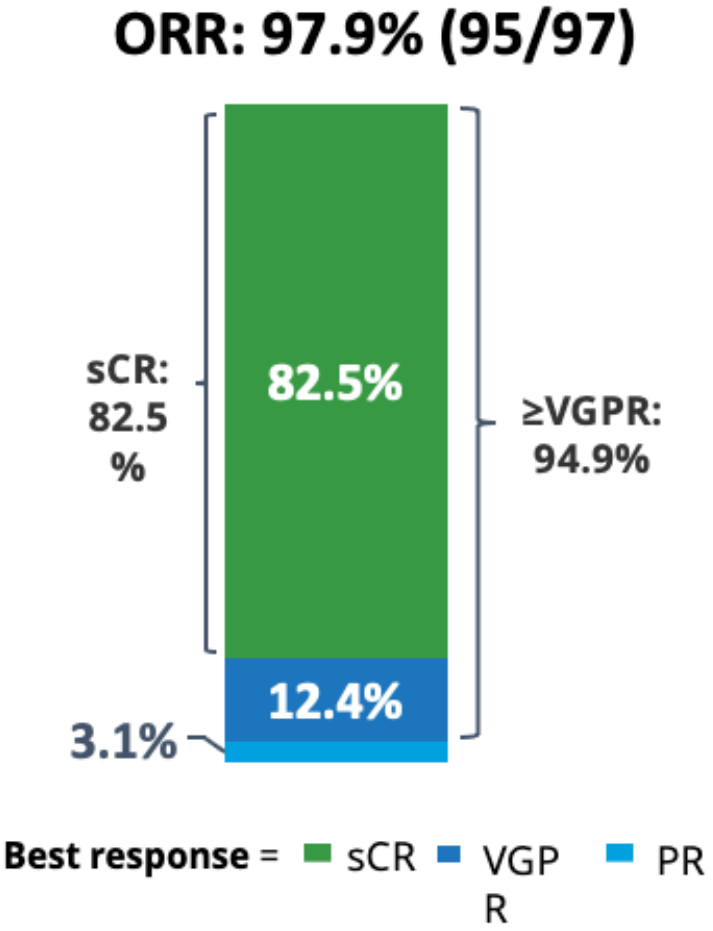
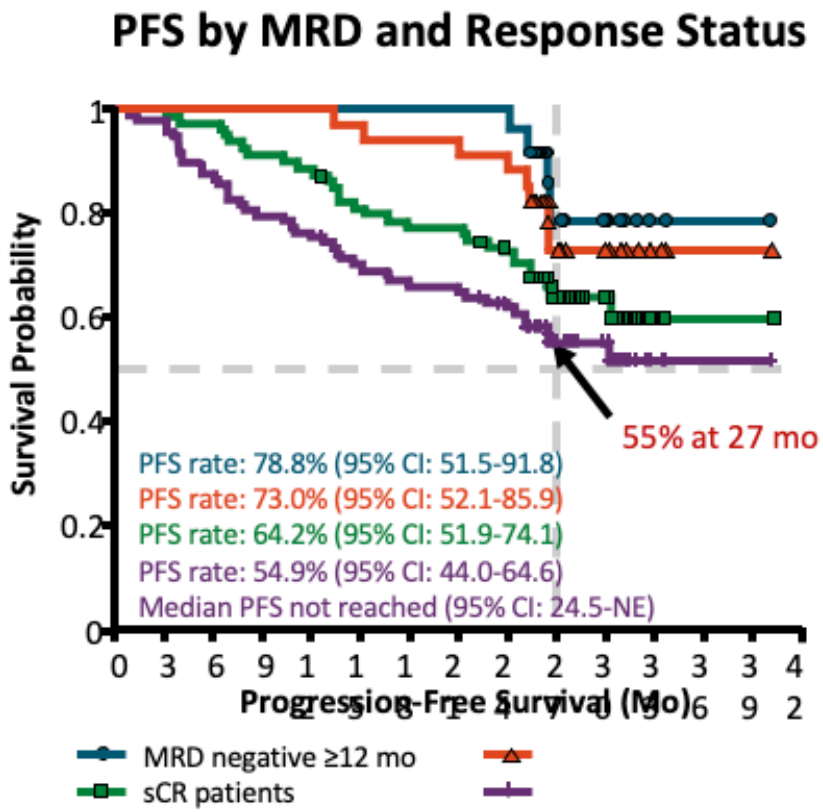
CARTITUDE-1: Cilta-Cel Outcomes





Usmani. ASCO 2022. Abstr 8028. Lin. EHA 2022. Abstr P961. Usmani. SOHO 2022. Abstr MM-181.

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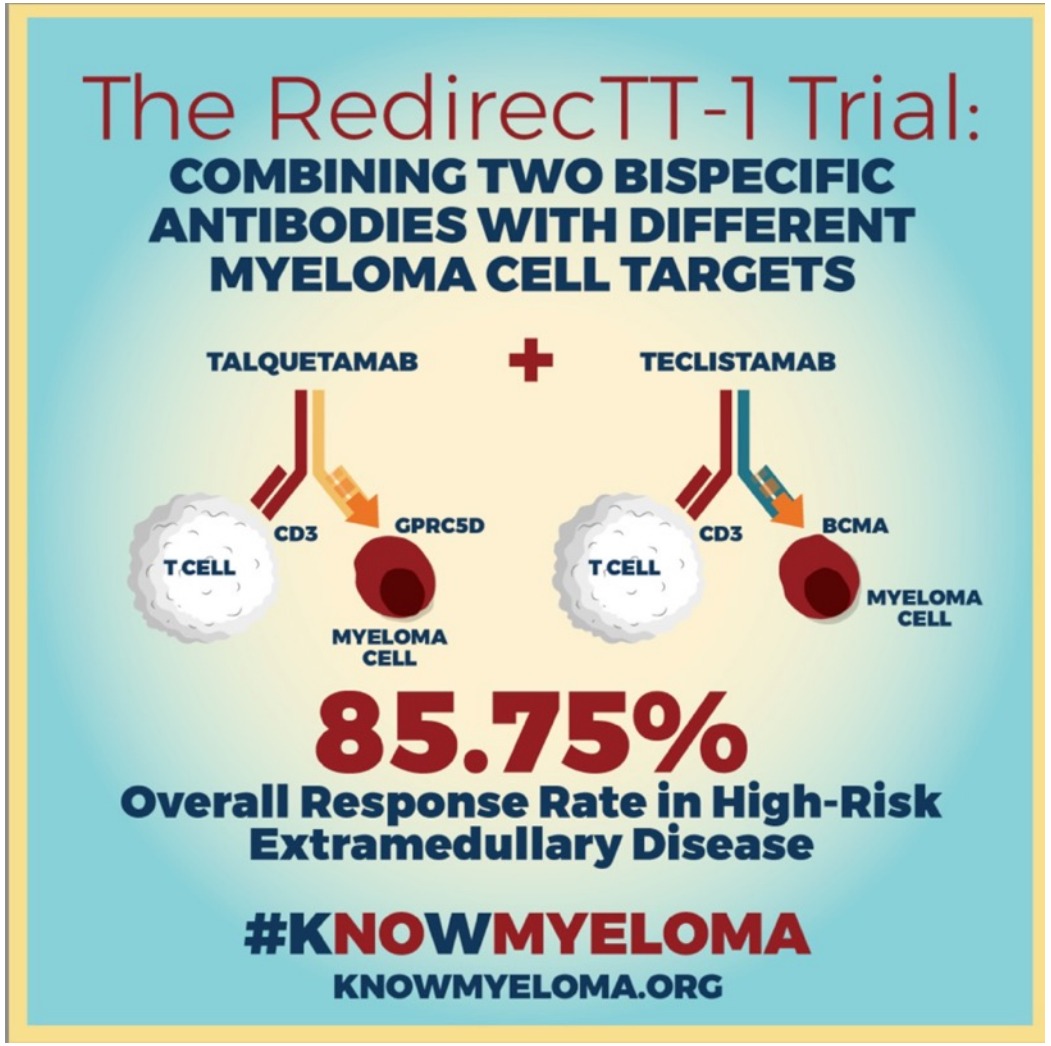
The RedirecTT-1 Trial



TT-1 Combination can be a GAME CHANGER.

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Issues to Consider

- EFFICACY
- SIDE EFFECTS (CRS / ICANS)
- ACCESS
- COSTS

Two Key New Projects

VIRTUAL TISSUE BANK

IMMUNE THERAPIES REGISTRY

Iceland playing a ROLE.

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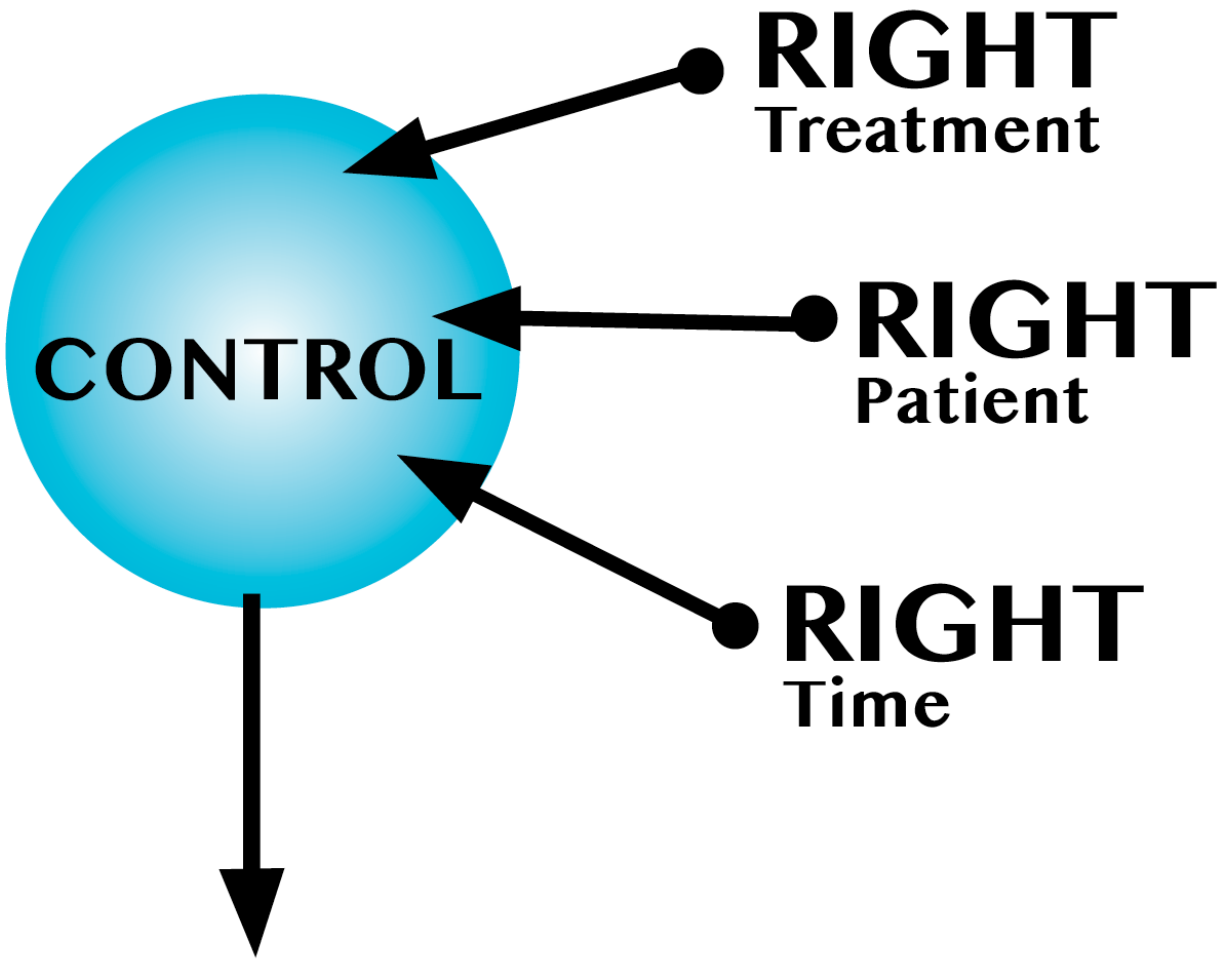
Two Key Tests Required

- **Mass Spectrometry: Maldi TOF/Q TOF**
  - EXENT®
- **NGF with commercial kit (Marrow and BloodFlow)**

Best Approach To Treatment



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Final Thoughts

- **USE BEST THERAPY AVAILABLE AS EARLY AS POSSIBLE FOR ALL PATIENTS**
  - **This will give maximum CONTROL and maybe CURE**

- **CONTROL DOES NOT MANDATE CONTINUOUS MAINTENANCE**
  - **REST off treatment and early re-treatment work well incorporating best new Rx**
  - **Introducing new immune therapies can be a GAME CHANGER**

- **IMPLEMENTATION OF NEW MONITORING TOOLS REQUIRED**
  - **Is patient negative for NGF (BloodFlow) at 10^{-8} Level?**
  - **Is patient negative with high sensitivity Q TOF Mass Spec?**
  - **What is the status of the immune system?**

The introduction of new testing and treatments in Iceland can lead the way in search for LONG-TERM SURVIVAL and POTENTIAL CURE!!!

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