Denver ASH Review

Updates on Multiple Myeloma

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Learning Objectives

1. Identify the benefits of **Daratumumab** in preventing or delaying progression to active multiple myeloma in patients with **high-risk smoldering multiple myeloma**.
2. Recognize the potential benefits of **urine-free IMWG response criteria** for reducing patient burden, simplifying logistics, and lowering operational costs.
3. Implement a steroid-sparing regimen, **Daratumumab/Lenalidomide**, to improve safety and enhance health-related quality of life in **frail patients with newly diagnosed multiple myeloma**.

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ASH24 – Multiple Myeloma

1. AQUILA: Dara vs Obs for hrSMM [773]
2. 24hr Urine Does Not Add Value [81]
3. IVIG ppx during Tec treatment [256]
4. IFM2017-03: DR vs Rd for Frail NDMM [774]
5. Talquetamab bridging for BCMA-CART [931]
6. IMMagine-1: Anito-cel (ddBCMA-CART) for RRMM [1031]

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#1 AQUILA: Dara vs Obs for hrSMM

Background

- iStopMM: Prevalence 0.5% in >40yo
- +20 different risk criteria: high-risk means 50% risk of progression at 2y
  - SMP >3 g/dL
  - IgA SMM
  - Immunoparesis of two uninvolved Ig
  - i/uFLCr between 8-100
  - BMPC between 50-60%
  - Mayo 2018/IMWG 20/2/20 criteria*
- Current practice:

  Low and Intermediate Risk: Observation

  High: Observation or Clinical trial
  - Rd (QuiRedex) or R (ECOG-E3A06) for 2y prevents end-organ damage, delays more intensive myeloma-directed therapy, and improves OS, but increases SPM and had a 20% treatment discontinuation.

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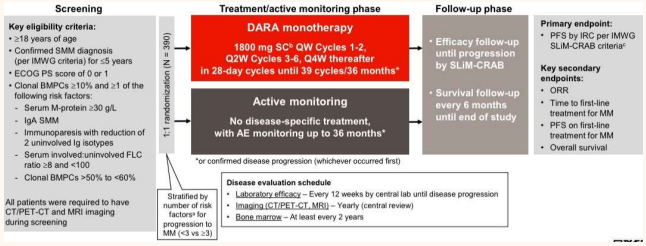
#1 AQUILA: Dara vs Obs for hrSMM

Study



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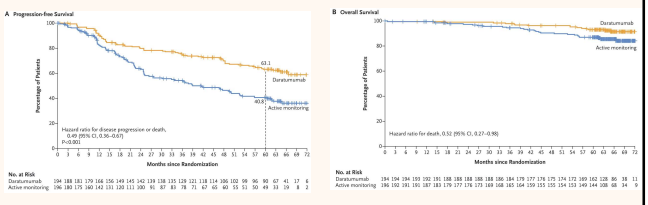
#1 AQUILA: Dara vs Obs for hrSMM

Results



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#1 AQUILA: Dara vs Obs for hrSMM

Results

	DARA (n = 194)	monitoring (n = 196)
PFS event, n (%)	67 (34.5)	99 (50.5)
Death without disease progression	5 (7.5)	5 (5.1)
Disease progression[a,b]	62 (92.5)	94 (94.9)
CRAB criteria[c]	12 (19.4)	34 (36.2)
Calcium elevation	0	2 (2.1)
Renal insufficiency[d]	0	0
Anemia	2 (3.2)	14 (14.9)
Bone disease	10 (16.1)	18 (19.1)
SLiM criteria[c]	50 (80.6)	65 (69.1)
Clonal BMPCs	5 (8.1)	16 (17.0)
Serum FLC	33 (53.2)	33 (35.1)
Focal lesion by MRI	12 (19.4)	16 (17.0)

	DARA (n = 194)	monitoring (n = 196)
Deaths, n (%)	15 (7.7)	26 (13.3)
Primary cause, n		
Disease progression	3	9
AE	2	4
Other*	10	13

*Deaths due to an event occurring after the AE reporting window (ie, events that happened after patient started subsequent therapy or >30 days after last dose) or deaths with unknown reason.

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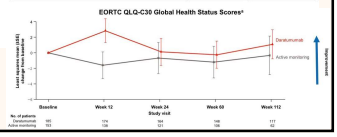
#1 AQUILA: Dara vs Obs for hrSMM

Results

Event, n (%)	DARA (n = 193)	Active monitoring (n = 196)
Median duration of AE reporting	35 months	26 months
Any grade TEAEs	187 (96.9)	162 (82.7)
Grade 3 or 4 TEAEs	78 (40.4)	59 (30.1)
Most common grade 3 or 4 TEAEs (≥5% in either group)		
Hypertension	11 (5.7)	9 (4.6)
Serious TEAEs	56 (29.0)	38 (19.4)
Most common serious TEAEs (≥2% in either group)		
Pneumonia	7 (3.6)	1 (0.5)
Grade 5 TEAEs[a]	2 (1.0)	4 (2.0)

Event, n (%)	DARA (n = 193)	Active monitoring (n = 196)
Treatment discontinuations due to a TEAE[b]	11 (5.7)	–
Dose modifications due to a TEAE[c]	90 (46.6)	–
COVID-19 TEAEs	17 (8.8)	10 (5.1)
Serious COVID-19 TEAEs	5 (2.6)	1 (0.5)
Deaths due to COVID-19	2 (1.0)	0



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#2 24hr Urine Does Not Add Value

Background

2016 IMWG Response Criteria:

Standard IMWG response criteria[1]	
Stringent complete response	Complete response as defined below plus normal FLC ratio[3] and absence of clonal cells in bone marrow biopsy by immunohistochemistry (κ/λ ratio ≤4:1 or ≥1:2 for κ and λ patients, respectively, after counting ≥100 plasma cells).[3]
Complete response	Negative immunofixation on the serum and urine and disappearance of any soft tissue plasmacytomas and <5% plasma cells in bone marrow aspirates.
Very good partial response	Serum and urine M-protein detectable by immunofixation but not on electrophoresis or ≥90% reduction in serum M-protein plus urine M-protein level <100 mg per 24 hours.
Partial response	≥50% reduction of serum M-protein plus reduction in 24-hour urinary M-protein by ≥90% or to <200 mg per 24 hours. If the serum and urine M-protein are unmeasurable, a ≥50% decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria. If serum and urine M-protein are unmeasurable, and serum free light assay is also unmeasurable, ≥50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma-cell percentage was ≥30%. In addition to these criteria, if present at baseline, a ≥50% reduction in the size (SPD)[4] of soft tissue plasmacytomas is also required.
Minimal response	≥25% but ≤49% reduction of serum M-protein and reduction in 24-hour urine M-protein by 50 to 89%. In addition to the above listed criteria, if present at baseline, a ≥50% reduction in the size (SPD)[4] of soft tissue plasmacytomas is also required.
Stable disease	Not recommended for use as an indicator of response; stability of disease is best described by providing the time-to-progression estimates. Not meeting criteria for complete response, very good partial response, partial response, minimal response, or progressive disease.

Progressive disease[4,5,6]	Any one or more of the following criteria:
	• Increase of 25% from lowest confirmed response value in one or more of the following criteria:
	  ▪ Serum M-protein (absolute increase must be ≥0.5 g/dL);
	  ▪ Serum M-protein increase ≥1 g/dL, if the lowest M component was ≥5 g/dL;
	  ▪ Urine M-protein (absolute increase must be ≥200 mg/24 hours);
	  ▪ In patients without measurable serum and urine M-protein levels, the difference between involved and uninvolved FLC levels (absolute increase must be >10 mg/dL);
	  ▪ In patients without measurable serum and urine M-protein levels and without measurable involved FLC levels, bone marrow plasma-cell percentage irrespective of baseline status (absolute increase must be ≥ 10%);
	• Appearance of a new lesion(s), ≥50% increase from nadir in SPD[4] of >1 lesion, or ≥50% increase in the longest diameter of a previous lesion >1 cm in short axis;
	• ≥50% increase in circulating plasma cells (minimum of 200 cells per microL) if this is the only measure of disease.

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#2 24h Urine Does Not Add Value

Background

- Secondary analysis in clinical trials:
  - IFM2009: sFLC is more prognostic than 24hUPEP
  - GEM2012: 24h UIFE is not needed for CR in terms of prognosis

- Real-world analysis (n=4591): only 28% of pts in US undergo 24h Urine testing at diagnosis

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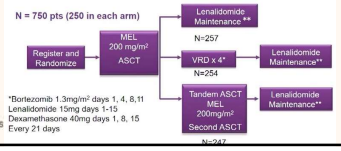
#2 24hr Urine Does Not Add Value

Study

	Traditional responses	Proposed urine-free responses
CR	• <5% BMPCs, no EMD, negative serum and urine IFE • (Also: normal FLC ratio for light-chain-only disease)	• <5% BMPCs, no EMD, negative serum and urine IFE • (Also: normal FLC ratio for light-chain-only disease)
VGPR	• M-protein detectable only by serum/urine IFE; or, ≥90% reduction in serum M-protein and urine M-protein < 100mg/24hrs • (Or: ≥90% reduction in Δ serum FLC in light-chain-only disease)	• M-protein detectable only by serum/urine IFE; or, ≥90% reduction in serum M-protein and urine M-protein <~~100mg/24hrs~~ • (Or: ≥90% reduction in Δ serum FLC in light-chain-only disease)
PR	• 50-89% reduction in serum M-protein; or, urine M-protein reduced by ≥90% or to <200mg/24hrs • (Or: 50-89% reduction in Δ serum FLC in light-chain-only disease) • (Or: ≥50% reduction in BMPCs & EMD for non-secretory disease)	• 50-89% reduction in serum M-protein; ~~or, urine M-protein reduced by ≥90% or to < 200mg/24hrs~~ • (Or: 50-89% reduction in Δ serum FLC in light-chain-only disease) • (Or: ≥50% reduction in BMPCs & EMD for non-secretory disease)

Secondary analysis of d+56 response from the BMT CTN 0702 (STaMINA)



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#2 24hr Urine Does Not Add Value

Results

- Of 758 randomized patients, 645 (85%)* were analyzed:
  - Median age 56 (interquartile range 50-61)
  - 41% female (*n* = 262), 17% Black (*n* = 109), 7% Hispanic (*n* = 42)
  - 26% with light-chain only disease (*n* = 166)
- Post-ASCT strategies (regardless of intended arm assignment):
  - 49% Lenalidomide alone (*n* = 315)
  - 28% Post-ASCT consolidation followed by lenalidomide (*n* = 178)
  - 24% Tandem ASCT followed by lenalidomide (*n* = 152)

High concordance with traditional assessmer

- Only **1.1% of 645 analyzed patients** (*n* = 7) had discordant responses between traditional and urine-free response criteria
- VGPR → urine-free CR (*n* = 2)
  - Met all other stringent CR criteria but still had positive urine paraprotein at Day +56 (faint UIFE+ in one case, UPEP 89 mg/24h in another)
- VGPR → urine-free PR (*n* = 1)
  - Negative serum paraprotein throughout, urine paraprotein had cleared, and BMPC not assessed; however, only 89% reduction in difference of serum FLC
- Non-evaluable → evaluable with urine-free criteria (*n* = 4)
  - Missing UPEP values no longer precluded achievement of VGPR (*n* = 3) or PR (*n* = 1) based on serum paraprotein reductions using urine-free criteria

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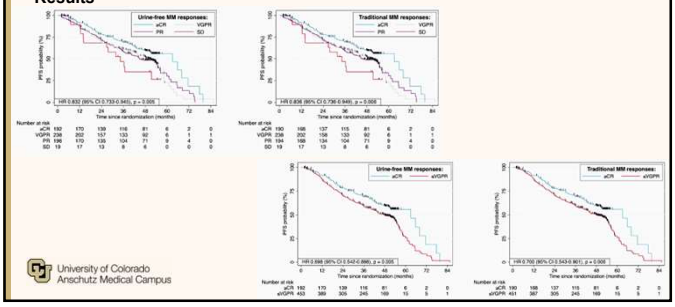
#2 24hr Urine Does Not Add Value

Results



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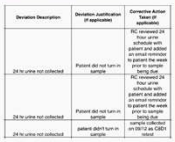
#2 24hr Urine Does Not Add Value

Conclusion

- Our results strongly support the planned de-emphasis of 24-hour urine requirements in future IMWG response criteria
- Our ideal state for urine assessments (outside of MGRS):
  - Removal from MM response criteria unless Bence-Jones proteinuria is the only marker of measurable disease
  - **Removal from refrigerators and emails about protocol deviations all over the world!**



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#3 IVIG ppx during Tec treatment

Background

- Teclistamab is approved for the treatment of pts with RRMM with 4PL and TCE.

- Infectious AEs are prevalent (all, grade 3/4):
  - Pneumonia: 18%, 13%
  - COVID-19: 18%, 12%

- Near universal hypogammaglobulinemia in responding pts

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#3 IVIG ppx during Tec treatment

Study

- Multicenter, retrospective study

- Consecutive pts with RRMM on Teclistamab
  - Primary IVIG prophylaxis = before a documented infection
  - Secondary IVIG prophylaxis = after a documented infection

- Endpoint: Infection-free, progression-free and overall survival

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#3 IVIG ppx during Tec treatment

Results

Characteristic	No primary IVIG prophylaxis (N = 133)[1]	Primary prophylaxis (N = 92)[1]	p-value[2]
bsAb type			<0.001
Investigational	51 (38%)	14 (15%)	
Teclistimab	82 (62%)	78 (85%)	
High risk disease	69 (63%)	38 (51%)	0.10
Presence of extramedullary disease[3]	57 (47%)	25 (28%)	0.006
Median number of prior lines of therapy	5 (2 - 12)	5 (2 - 12)	0.070
Triple-Class Refractory myeloma	123 (92%)	73 (79%)	0.004
Recipient of prior ASCT	88%	98%	0.024
Baseline median absolute neutrophil count, 10^3/uL	2.65 (0.30 - 66.98)	2.55 (0.10 - 12.20)	0.7
Baseline neutropenia	5 (3.8%)	2 (2.2%)	0.7
Baseline median absolute lymphocyte count, 10^3/uL	0.90 (0.01 - 4.82)	0.89 (0.01 - 5.00)	0.6
Baseline lymphopenia	73 (55%)	50 (54%)	>0.9
Use of prior BCMA-directed Therapy	27 (20%)	25 (27%)	0.2
Median number of doses of bsAb	7 (1 - 49)	19 (1 - 47)	<0.001
Rate of bsAb dosing/month	5 (1 - 30)	3 (1 - 30)	<0.001
Longest bsAb gap, days	14 (2 - 264)	21 (6 - 133)	0.003
Median duration of bsAb use months	2 (0 - 40.4)	6.8 (0 - 37.2)	<0.001
Incidence of CRS	72 (54%)	51 (55%)	0.8
Incidence of ICANS	12 (9.0%)	3 (3.3%)	0.089
Systemic steroids for CRS/ICANS	21 (16%)	17 (18%)	0.6
Use of Tocilizumab	41 (31%)	22 (24%)	0.3
Any IVIG administered	39 (29%)	92 (100%)	<0.001
Median time to first IVIG dose, if any	115 (11 - 493)	39 (0 - 359)	<0.001
Median follow up of survivors, months	11 (0 - 66)	9 (1 - 44)	0.10

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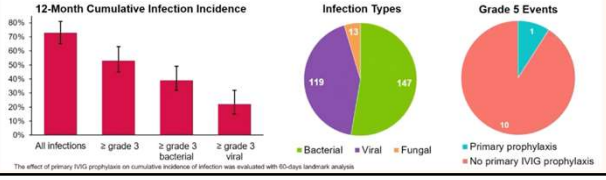
#3 IVIG ppx during Tec treatment

SPECTRUM OF INFECTIONS

- 288 infections in 136 patients (Median time to infection = 97 days from start of therapy)
- Most common: respiratory tract infections
- Majority of patients hospitalized inpatient for infectious complications (n = 175, 61%)
- 11 grade 5 infection events (CTCAE)



The effect of primary IVIG prophylaxis on cumulative incidence of infection was evaluated with 60-days landmark analysis

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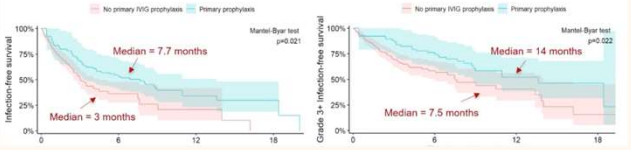
#3 IVIG ppx during Tec treatment

Results

PRIMARY IVIG PROPHYLAXIS IMPROVES INFECTION FREE SURVIVAL



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#3 IVIG ppx during Tec treatment

CONCLUSIONS

- Primary IVIG prophylaxis was associated with a statistically significant reduction in all-grade and ≥ grade 3 infection free survival
- Administration of tocilizumab for CRS was associated with an increased risk of all-grade, ≥3 grade infections, bacterial and viral infections
- Use of primary IVIG prophylaxis was independently associated with improved overall survival in patients treated with BCMA directed bispecific antibody therapy

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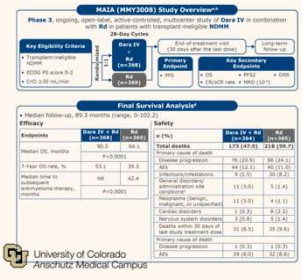
#4 IFM2017-03: DR vs Rd for Frail NDMM

Background



Parameter, n (%)	Frail (n=334)	
	D-Rd (n= 168)	Rd (n= 166)
Total number of patients with grade 3/4 TEAEs	159 (94.6)	146 (89.2)
Hematologic TEAEs		
Neutropenia	97 (57.7)	53 (32.1)
Lymphopenia	31 (18.5)	19 (11.6)
Leukopenia	22 (13.1)	9 (5.4)
Anemia	28 (16.7)	40 (24.1)
Thrombocytopenia	17 (10.1)	19 (11.4)
Nonhematologic TEAEs		
Infections	70 (41.7)	44 (27.7)
Pneumonia	33 (19.6)	17 (10.2)
Cataract	13 (7.7)	19 (11.4)
Pulmonary embolism	7 (4.2)	5 (3.0)
Hypokalemia	18 (10.7)	20 (12.0)
Hyperglycemia	12 (7.1)	6 (3.6)
Total number of patients with TEAE with an outcome of death	20 (11.9)	20 (12.0)

Abbreviations: D-Rd, DARZALEX + lenalidomide + dexamethasone.

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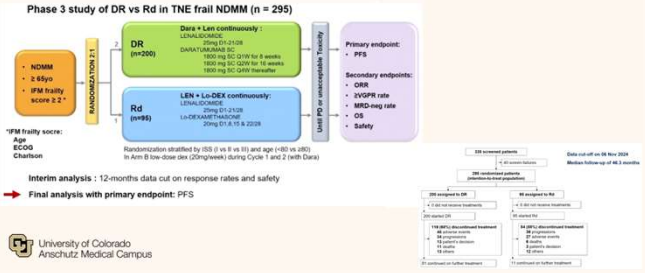
#4 IFM2017-03: DR vs Rd for Frail NDMM

Study



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#4 IFM2017-03: DR vs Rd for Frail NDMM

Results

Characteristics	DR group (N=200)	Rd group (N=95)
Median age (range) - yr	81 (68-92)	81 (68-90)
Age category – no. (%)		
65 to < 70 yr	2 (1%)	2 (2%)
70 to < 75 yr	30 (15%)	13 (14%)
75 to < 80 yr	49 (24%)	19 (20%)
≥ 80 yr	119 (60%)	61(64%)
Sex - no. (%)		
Female	102 (51%)	49 (52%)
Male	98 (49%)	46 (48%)
ECOG – no. (%)		
0	21 (10%)	9 (10%)
1	93 (46%)	48 (50%)
2	86 (44%)	38 (40%)
≥ 3	11 (6%)	3 (3%)
Charlson – no. (%)		
≤ 1	117 (58%)	57 (60%)
> 1	83 (42%)	38 (40%)
IFM frailty score – no. (%)		
≤ 1	0	0
2	58 (29%)	35 (37%)
3	80 (40%)	26 (28%)
4	46 (23%)	24 (25%)
5	16 (8%)	9 (9%)

Characteristics	DR group (N=200)	Rd group (N=95)
ISS disease stage – no. (%)		
I	33 (16%)	19 (20%)
II	103 (52%)	49 (52%)
III	64 (32%)	27 (28%)
NA	0	1
Type of measurable disease – no (%)		
IgG	115 (57%)	50 (53%)
IgA	36 (18%)	20 (21%)
PBJ only	6 (3%)	7 (7%)
SFLC only	26 (13%)	10 (11%)
Cytogenetics profile* – no (%)		
Standard risk	146 (84%)	56 (77%)
High risk	28 (16%)	17 (23%)
NA	26	22
del17p	16 (9%)	11 (14%)
t(4;14)	9 (5%)	5 (6%)
t(14;16)	5 (3%)	2 (3%)
Creatinine clearance – no. (%)		
< 30mL/min	1 (1%)	3 (3%)
30 to < 60mL/min	120 (59%)	50 (53%)
≥ 60 mL/min	79 (40%)	41 (44%)

* HR defined as del17p and/or t(4;14) and/or t(14;16)

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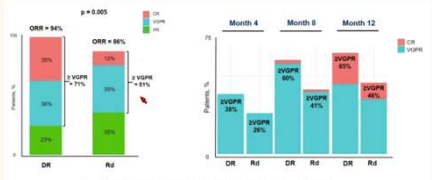
#4 IFM2017-03: DR vs Rd for Frail NDMM

Results



VGPR or better rate was significantly higher with DR
Deeper responses were obtained with DR at all time points, including at early time points

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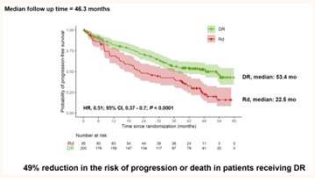
#4 IFM2017-03: DR vs Rd for Frail NDMM

Results



49% reduction in the risk of progression or death in patients receiving DR

48% reduction in the risk of death in patients receiving DR

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#4 IFM2017-03: DR vs Rd for Frail NDMM

Results

	DR group (n=200) Grade ≥ 3	Rd group (n=95) Grade ≥ 3
Median treatment duration	31.6 months	14.3 months
All grade ≥ 3 AEs, n (%)	178 (89%)	75 (79%)
All grade 5, n (%)	23 (12%)	12 (13%)
Hematologic, n (%)	123 (62%)	32 (34%)
neutropenia	110 (55%)	23 (24%)
anemia	24 (12%)	3 (3%)
thrombocytopenia	19 (10%)	5 (5%)
Non-hematologic AEs, n (%)	132 (66%)	68 (72%)
Infection, n (%)	38 (19%)	20 (21%)
pneumonia	11 (6%)	8 (8%)
Infection rate per patient-year	0.07	0.09

	DR group (n=200)	Rd group (n=95)
Treatment discontinuation due to AE, n (%)	60 (30%)	32 (34%)

No increased rates of infection or treatment discontinuation in patients receiving DR

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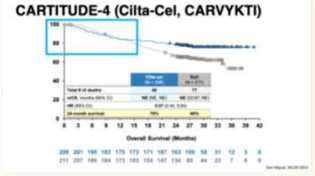
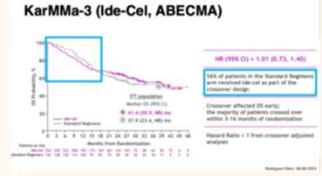
#5 Talquetamab bridging for BCMA-CART

Background

CARTITUDE-4 (Cilta-Cel, CARVYKTI)



KarMMa-3 (Ide-Cel, ABECMA)



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#5 Talquetamab bridging for BCMA-CART

Background

Maintaining disease control while awaiting CAR-T manufacturing is challenging

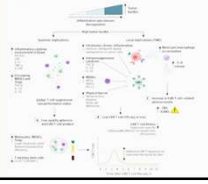
Clinical trials and Real World: **10-15%**
Do not receive CAR-T due to progression/death while awaiting manufacturing

Manufacturing time for CAR-T: **6-8 weeks**

75% of patients need bridging therapy

Increased disease burden prior to lymphodepletion is associated with
- decreased CAR-T efficacy,
- increased immune-mediated toxicity

High disease burden prior to CAR-T ↑ toxicity and ↓ efficacy



- **Low quality apheresis product**
- **Low CAR-T cell efficacy**
- **Increased CRS, ICANS, IEC/HS**

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#5 Talquetamab bridging for BCMA-CART

Study

Safety and feasibility of Talquetamab bridging prior to ide-cel and cilta-cel in the standard of care setting for relapsed and/or refractory multiple myeloma.

Primary outcomes:
Safety: CRS, ICANS, Talq related unique toxicities
Efficacy: Response to Talquetamab bridging, response to CAR-T therapy at different time points

Secondary outcomes:
Survival: Progression-free survival and overall survival
Infections, cytopenia and SPM

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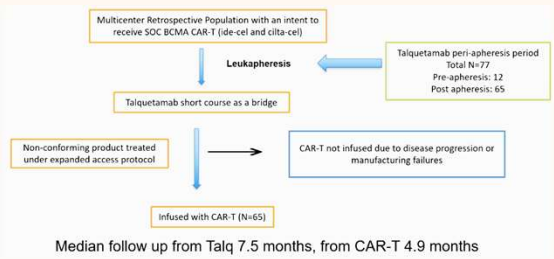
#5 Talquetamab bridging for BCMA-CART

Study



Median follow up from Talq 7.5 months, from CAR-T 4.9 months

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#5 Talquetamab bridging for BCMA-CART

Results

Characteristic	Overall (N=77)	No Subsequent CAR (N= 12)	Subsequent CAR (N=65)
Age, years	66 (58-73)	68 (64-72)	65 (58-73)
Male sex	43 (56)	7 (58)	36 (56)
Race, white	57 (74)	8 (67)	49 (75)
Extramedullary disease	33 (43)	4 (33)	29 (45)‖
High risk cytogenetics	35 (45)	3 (25)	32 (49)
Prior BCMA	10 (13)	5 (42)	5 (9)
ECOG ≥ 2	15 (19)	3 (16)	12 (21)

Characteristic	Overall (N=77)	No subsequent CAR (N=12)	Subsequent CAR (N=65)
Prior lines, median	5 (3-11)	5 (3-11)	5 (3-11)
Triple class refractory	56 (73)	13 (68)	43 (74)
Penta class refractory	28 (36)	5 (26)	23 (40)
Prior auto	58 (75)	8 (67)	50 (77)
CAR-T Ide-cel Cilta-cel	15 50	NA	15 50
Talq dose 0.8 Q2W 0.4 QW	59 (77) 18 (23)	10 (13) 2 (3)	50 (65) 15 (19)

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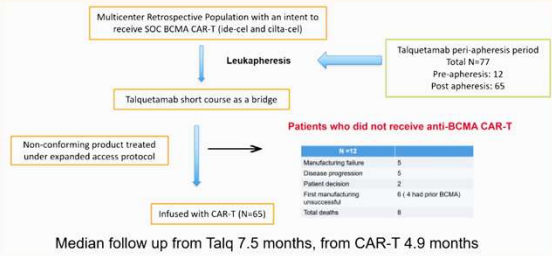

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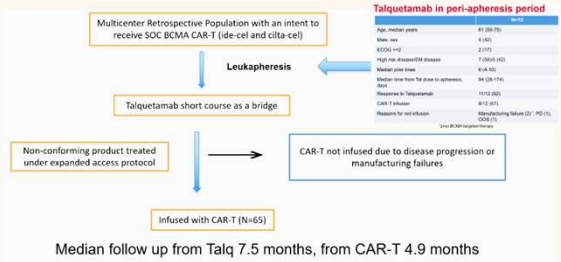
#5 Talquetamab bridging for BCMA-CART



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#5 Talquetamab bridging for BCMA-CART

Talquetamab in peri-apheresis period

	N=12
Age, median years	61 (50-75)
Male, sex	5 (42)
ECOG >=2	2 (17)
High risk disease/EM disease	7 (58)/5 (42)
Median prior lines	6 (4-10)
Median time from Tal dose to apheresis, days	94 (28-174)
Response to Talquetamab	11/12 (92)
CAR-T infusion	8/12 (67)
Reasons for not infusion	Manufacturing failure (2)*, PD (1), OOS (1)

*prior BCMA targeted therapy

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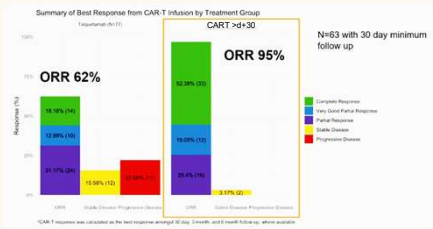
#5 Talquetamab bridging for BCMA-CART

Results



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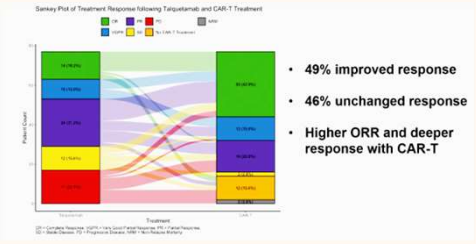
#5 Talquetamab bridging for BCMA-CART

Results



- 49% improved response
- 46% unchanged response
- Higher ORR and deeper response with CAR-T

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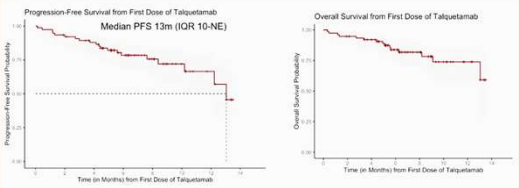
#5 Talquetamab bridging for BCMA-CART

Results



Median follow up time: from Talquetamab first dose 7.5 months (IQR 5.4-10.4)
Median follow up from CAR-T infusion 4.9 months (IQR 3.6- 6.9)

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#5 Talquetamab bridging for BCMA-CART

Results

Talquetamab Safety

	N=77	
	Any Grade	Grade 3/4
CRS	52 (68%)	0
ICANS	8 (10%)	2 (2.5%)
Skin toxicities	32 (42%)	0
Nail toxicities	19 (25%)	0
Oral toxicities	43 (56%)	1 (1.2%)
Weight loss	9 (12%)	2 (2.5%)

40/67 (60%) of patients observed complete resolution of Talq related toxicities

CAR-T safety

	N=65	
	All grades	Grade 3/4
CRS	47 (72%)	2 (3%)
ICANS	7 (10%)	1 (2%)
Delayed neurotoxicity	1 (1.5%) (CN VII palsy)	0
Infections	16 (27%)	6 (9%)
Second malignancies	1 (1.5%) (AML TP53 and DNMT3A)	NA
Severe cytopenia (day+60)	7 (10%)	7 (10%)

No cases of Guillain Barre syndrome and no Parkinsonian-like syndromes
35/59 (61%) showed complete resolution of Talq related toxicities

Total deaths overall: 16

Total deaths after CAR-T infusion: 8

Non relapse mortality after CAR-3 (2 sepsis/shock and 1 AML/MDS)

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#6 IMMagine-1: Anito-cel (ddBCMA-CART) for RRMM

Background

	Ide-cel	Cilta-cel	Teclistamab	Elranatamab	Talquetamab*
Target	BCMA	BCMA	BCMAxCD3	BCMAxCD3	GPRC5DxCD3
Median PL	6	6	5	5	5
Efficacy					
ORR (%)	**73**	**98**	**63**	**61**	**72**
≥CR (%)	33	83	39	35	32
PFS (months)	**9**	**35**	**11**	**17**	**14**
Safety					
CRS (%)	84	95	72	58	75
NTx (%)	18	22 (6)	15	3	11
Infections (%)	69	58	80	70	65

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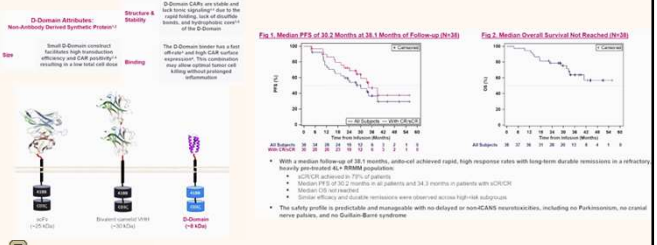
#6 IMMagine-1: Anito-cel (ddBCMA-CART) for RRMM

Background



- With a median follow-up of 38.1 months, anito-cel achieved rapid, high response rates with long-term durable remissions in a refractory, heavily pre-treated 4L+ RRMM population:
  - sCR/CR achieved in 79% of patients
  - Median PFS of 30.2 months in all patients and 34.3 months in patients with sCR/CR
  - Median OS not reached
  - Similar efficacy and durable remissions were observed across high-risk subgroups
- The safety profile is predictable and manageable with no delayed or non-ICANS neurotoxicities, including no Parkinsonism, no cranial nerve palsies, and no Guillain-Barré syndrome

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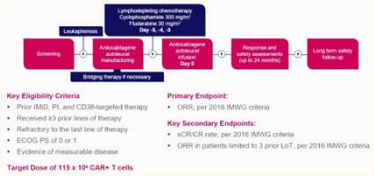
#6 IMMagine-1: Anito-cel (ddBCMA-CART) for RRMM

Study



Key Eligibility Criteria

- Prior IMiD, PI, and CD38-targeted therapy
- Received ≥3 prior lines of therapy
- Refractory to the last line of therapy
- ECOG PS of 0 or 1
- Evidence of measurable disease

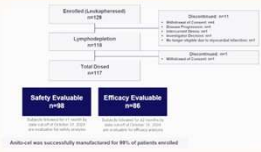
Target Dose of 115 x 10⁶ CAR+ T cells

Primary Endpoint:

- ORR, per 2016 IMWG criteria

Key Secondary Endpoints:

- sCR/CR rate, per 2016 IMWG criteria
- ORR in patients limited to 3 prior LoT, per 2016 IMWG criteria



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#6 IMMagine-1: Anito-cel (ddBCMA-CART) for RRMM

Results

Characteristics	Safety Evaluable (n=98)
Age (yrs): median (min – max)	65 (38 – 78)
Age ≥ 65	51 (52%)
Age ≥ 70	30 (31%)
Age ≥ 75	10 (10%)
Gender (male / female)	55 (56%) / 43 (44%)
Race	
White	79 (81%)
Black / African American	9 (9%)
Asian / Other	10 (10%)
ECOG PS 0 / 1	45 (46%) / 53 (54%)
Extramedullary disease*	16 (16%)
High-Risk Cytogenetics*	39 (40%)
Refractory to last line of therapy	98 (100%)
Triple refractory	85 (87%)
Penta refractory	41 (42%)
Prior Lines of Therapy: median (min – max)	4 (3 – 8)
3 Prior LoT	45 (46%)
Time since diagnosis (yrs): median (min-max)	7.2 (1 – 23)
Prior ASCT	73 (75%)
Bridging therapy	65 (66%)
Cilta-cel administration	8 (8%)

Efficacy Evaluable Patients (N=86)

- At a median follow-up of 9.5 months, ORR was 97% and sCR/CR rate was 62%
- 93.1% (n=54/58) of evaluable patients were MRD negative at minimum of 10^{-5} sensitivity

	Evaluable Patients	Months (min - max)
Median time to first response	86	1.0 (0.9 - 7.3)
Median time to MRD negativity of ≤10^{-5}	54	1.0 (0.9 - 6.4)

	PFS Rate (%) (95% CI)	OS Rate (%) (95% CI)
6-Month	93.3% (84.4%, 97.2%)	96.5% (89.6%, 98.9%)
12-Month	78.5% (63.5%, 87.9%)	96.5% (89.6%, 98.9%)

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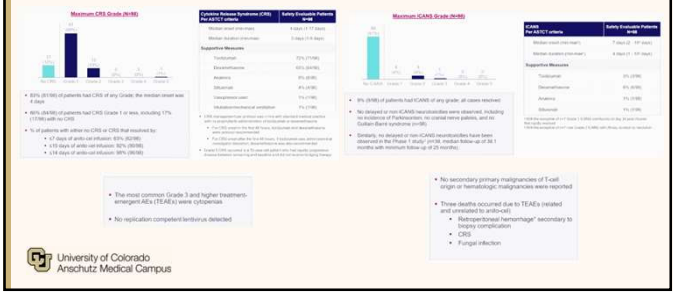
Results



- The most common Grade 3 and higher treatment-emergent AEs (TEAEs) were cytopenias
- No replication competent lentivirus detected

- No secondary primary malignancies of T-cell origin or hematologic malignancies were reported
- Three deaths occurred due to TEAEs (related and unrelated to anito-cel)
  - Retroperitoneal hemorrhage* secondary to biopsy complication
  - CRS
  - Fungal infection

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