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MEETING SUMMARY
ASCO AND EHA 2021, VIRTUAL MEETINGS
MULTIPLE MYELOMA

Dr. Hans Lee, MD

University of Texas, MD Anderson Cancer Center
Houston, TX, USA

HIGHLIGHTS FROM LYMPHOMA & MYELOMA CONNECT
JUNE 2021

CONFLICT OF INTEREST AND FUNDING

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Dr. Hans Lee has received financial support/sponsorship for research support or consultation from the following companies:

- Amgen, Bristol Myers Squibb, and Celgene, Genentech, GlaxoSmithKline, Immunitis, Janssen, Karyopharm, Oncopeptides, Regeneron, Sanofi and Takeda

OS RESULTS WITH DARATUMUMAB, LENALIDOMIDE, AND DEXAMETHASONE VERSUS LENALIDOMIDE AND DEXAMETHASONE IN TRANSPLANT-INELIGIBLE NDMM: PHASE 3 MAIA STUDY

Facon T, et al.

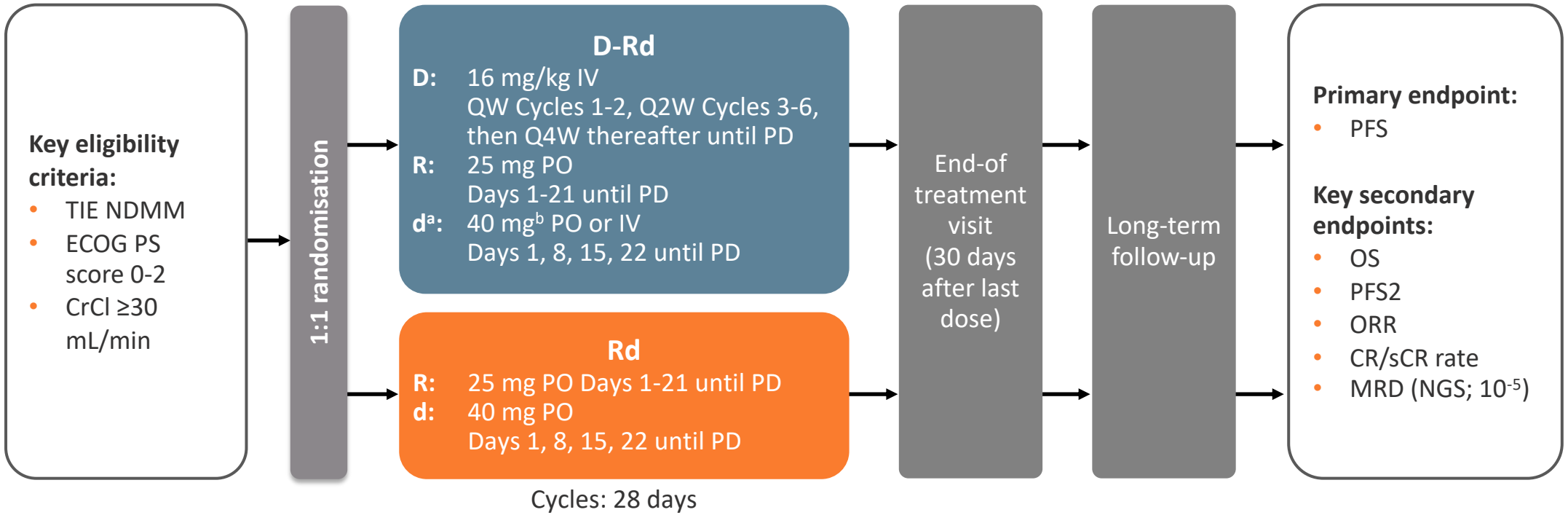
EHA 2021. Abstract #LB1901. Oral presentation

NDMM, newly diagnosed multiple myeloma; OS, overall survival

STUDY DESIGN

MAIA: A MULTICENTRE, RANDOMISED, OPEN-LABEL PHASE 3 STUDY

- **D-Rd versus Rd** alone in transplant-ineligible patients with **NDMM**



Cycles: 28 days

- >40% of patients in each arm was ≥75 years of age (median age 73-74 years)
- Updated results from a **prespecified interim OS analysis**, after a median follow-up of 56 months

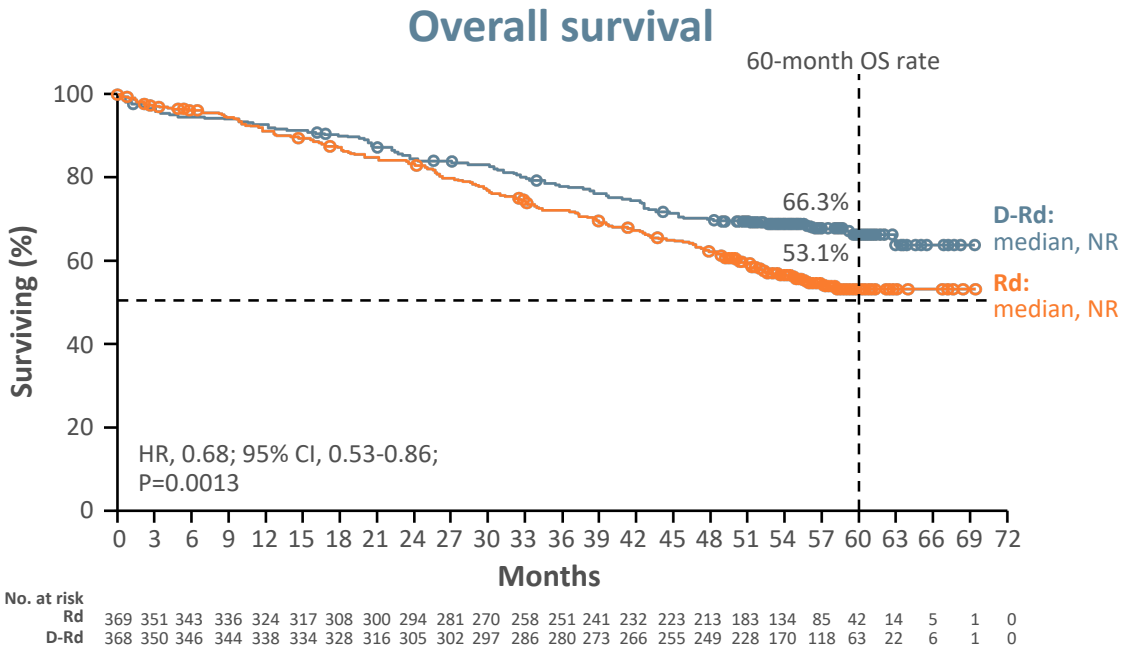
[a]On days when daratumumab is administered, dexamethasone will be administered to patients in the D-Rd arm and will serve as the treatment dose of steroid for that day, as well as the required pre-infusion medication; [b]For patients >75 years of age or with BMI <18.5 kg/m^2, dexamethasone was administered at a dose of 20 mg QW

BMI, body mass index; CR, complete response; CrCl, creatinine clearance; d, dexamethasone; D, daratumumab; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGS, next-generation sequencing; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PO, oral; QW, once weekly; Q2W, once every 2 weeks; Q4W, once every 4 weeks; R, lenalidomide; sCR, stringent CR; TIE, transplant-ineligible. Facon T, et al. EHA 2021. Abstract #LB1901. Oral presentation

RESULTS

Efficacy

- D-Rd induced **deeper responses** compared with Rd
  - After 56.2 months, ORR was 93% vs 82%
- D-Rd continued to show a **significant PFS benefit**, with median PFS not reached with D-Rd
  - After 60 months, the PFS rate was 52.5% vs 28.7%
- After 5 years of follow up, a **significant OS benefit** is seen, with median OS not reached with D-Rd
  - After 60 months, the OS rate was 66.3% vs 53.1%



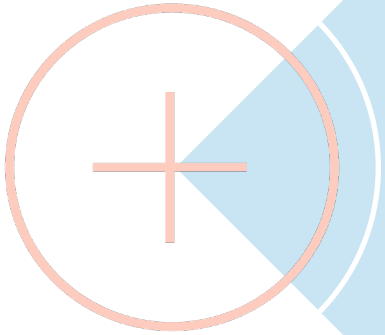
Safety

- Higher incidence of **neutropenia (54% grade 3/4) and pneumonia (19% grade 3/4)** in the D-Rd arm
  - No new safety concerns were identified with longer follow up

CI, confidence interval; D, daratumumab; d, dexamethasone; HR, hazard ratio; NR, not reached; OS, overall survival; ORR, overall response rate; PFS, progression-free survival; R, lenalidomide

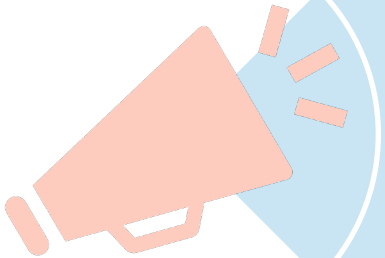
Facon T, et al. EHA 2021. Abstract #LB1901. Oral presentation

CLINICAL INTERPRETATION



Second study to show benefit

- After the **ALCYONE study** showed the benefit of adding daratumumab to VMP, **MAIA** is the second study to show **OS benefit with daratumumab** in a frontline regimen in NDMM



New standard of care

- **D-Rd is a new standard of care in newly diagnosed transplant ineligible MM**

MM, multiple myeloma; NDMM, newly diagnosed multiple myeloma; OS, overall survival; VMP, bortezomib, melphalan, and prednisone

Facon T, et al. EHA 2021. Abstract #LB1901. Oral presentation

CILTA-CEL, A BCMA-DIRECTED CAR-T THERAPY, IN R/R MM: UPDATED RESULTS FROM CARTITUDE-1

Usmani SZ, et al.
ASCO 2021. Abstract #8005. Oral presentation
EHA 2021. Abstract #EP964. Poster presentation

BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T-cell; cilta-cel, ciltacabtagene autoleucel; MM, multiple myeloma; R/R, relapsed/refractory

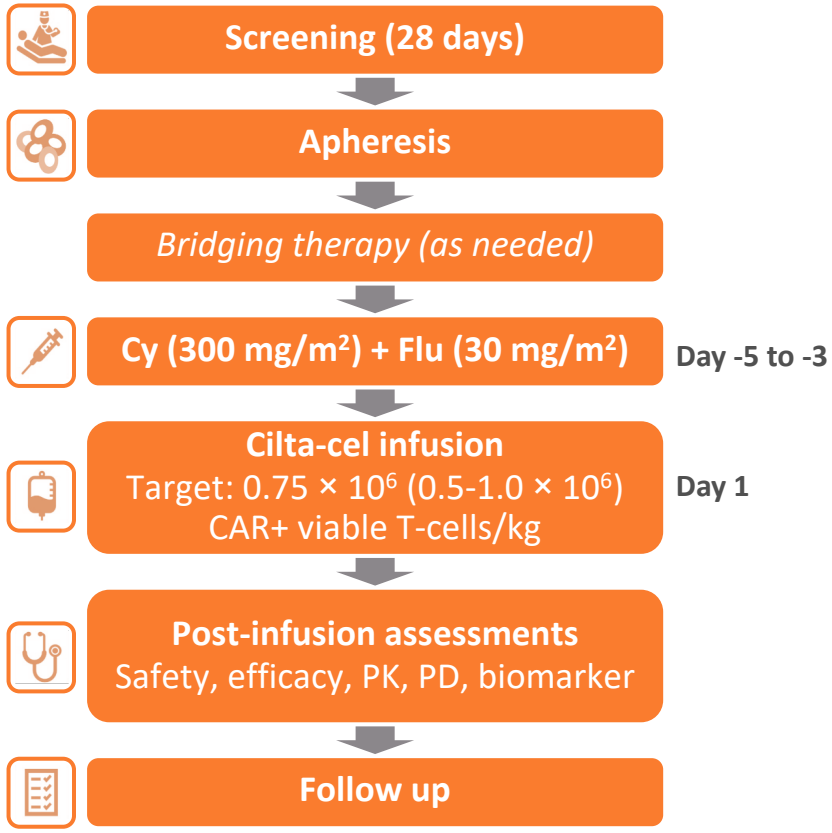
BACKGROUND AND STUDY DESIGN

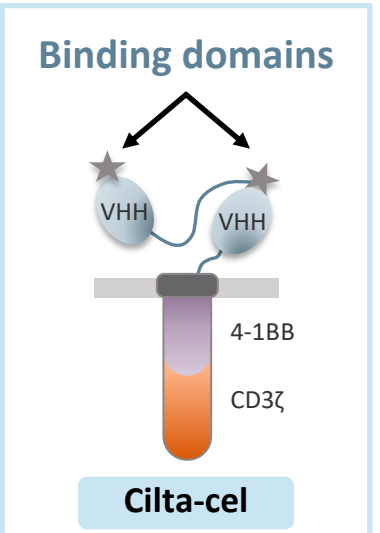
CARTITUDE-1: PHASE 1B/2 STUDY OF CILTA-CEL IN R/R MM

- Ciltacabtagene autoleucel (cilta-cel) is a **CAR-T cell therapy** with two BCMA-targeting single-domain antibodies

- **CARTITUDE-1 primary objectives:**
  - Phase 1b: safety and RP2D
  - Phase 2: efficacy
- Results after median **follow up of 18 months**

- **Heavily pre-treated patients (N=97)**
  - Median of 6 prior lines of therapy (range 3-18)
  - 88% was triple-class refractory (refractory to IMiD, proteasome inhibitor, anti-CD38 monoclonal antibody)





BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; Cy, cyclophosphamide; Flu, fludarabine; IMiD, immunomodulatory drug; MM, multiple myeloma; PD, pharmacodynamic; PK, pharmacokinetic; RP2D, recommended phase 2 dose; R/R, relapsed/refractory; VHH, variable heavy chain

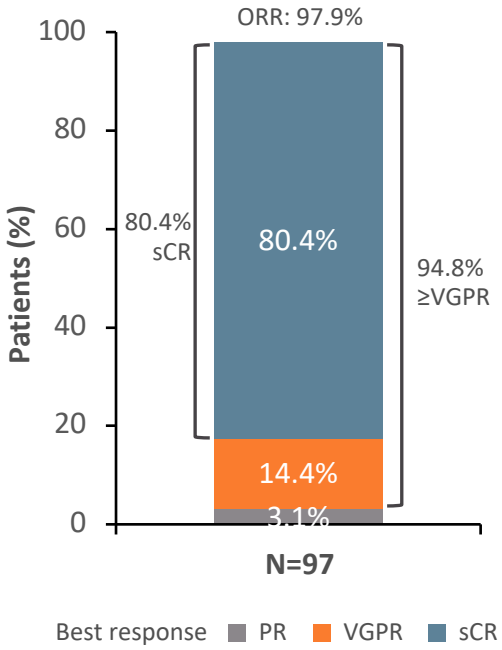
Usmani SZ, et al. ASCO 2021. Abstract #8005. Oral presentation; Usmani SZ, et al. J Clin Oncol. 2021;39(suppl 15):8005-8005

RESULTS

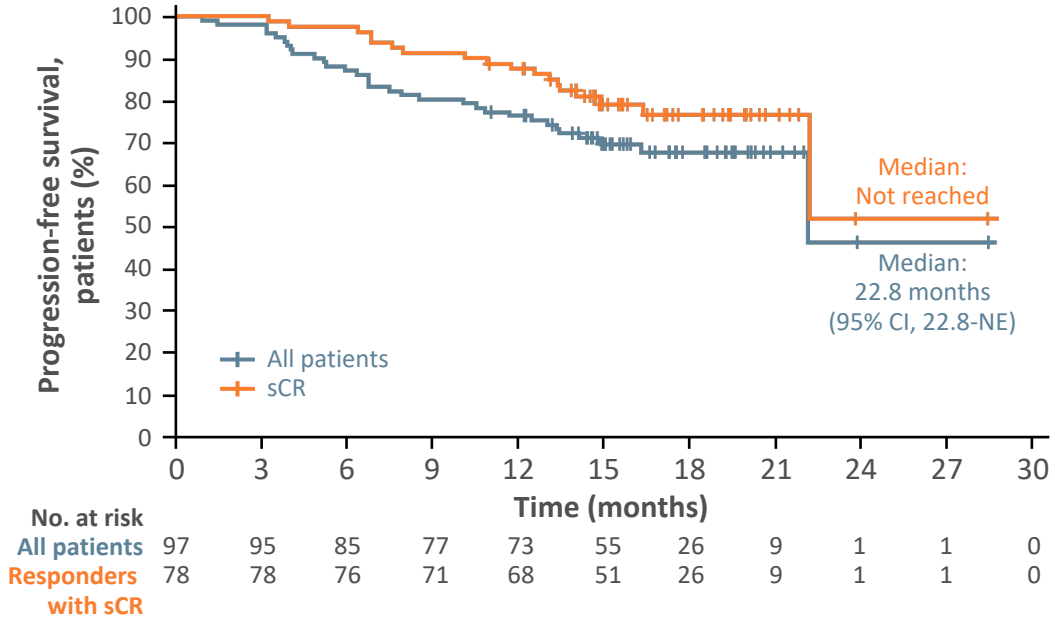
Efficacy

- Unprecedented ORR and depth of response
  - Median DoR 21.8 months
- 66% 18-month PFS
- 81% 18-month OS

Response



PFS



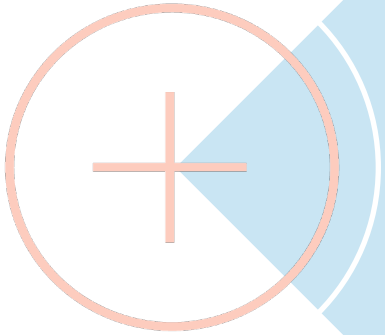
Safety

- CRS occurred in 95% of patients (almost all grade 1/2)
- Neurotoxicity occurred in 21% of patients (10% grade ≥3), including ICANS in 16.5% (2.1 grade ≥3)

CI, confidence interval; CRS, cytokine release syndrome; DoR, duration of response; ICANS, immune effector cell-associated neurotoxicity syndrome; NE, not estimable; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; VGPR, very good PR

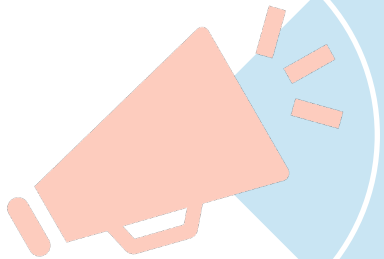
Usmani SZ, et al. ASCO 2021. Abstract #8005. Oral presentation; Usmani SZ, et al. J Clin Oncol. 2021;39(suppl 15):8005-8005

AUTHORS' CONCLUSIONS AND CLINICAL INTERPRETATION



A single infusion of cilta-cel yielded **early, deep, and durable responses** in heavily pretreated patients with MM

Cilta-cel had a **manageable safety profile** at the RP2D



These cilta-cel data on a longer follow-up time continue to be **very encouraging**

Cilta-cel is undergoing review by FDA and EMA for regulatory approval

Cilta-cel, ciltacabtagene autoleucel; EMA, European Medicines Agency; FDA, Food and Drug Administration; MM, multiple myeloma; RP2D, recommended phase 2 dose

Usmani SZ, et al. ASCO 2021. Abstract #8005. Oral presentation; Usmani SZ, et al. J Clin Oncol. 2021;39(suppl 15):8005-8005

IDE-CEL (BB2121), A BCMA-DIRECTED CAR-T CELL THERAPY, IN R/R MM: UPDATED KarMMA RESULTS

Anderson LD, et al.
ASCO 2021. Abstract #8016. Poster presentation

BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T-cell; ide-cel, idecabtagene vicleucel; MM, multiple myeloma; R/R, relapsed/refractory

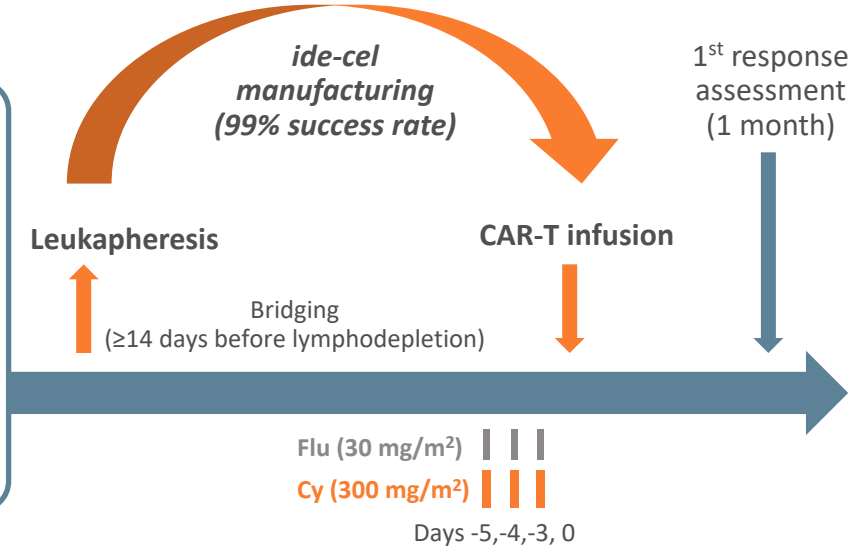
BACKGROUND AND STUDY DESIGN

KarMMa: PHASE 2 STUDY OF IDE-CEL IN R/R MM

- Idecabtagene vicleucel (ide-cel) is a BCMA-directed **CAR-T cell therapy approved by the FDA** for R/R MM after ≥4 lines of therapy, based on the KarMMa trial
- At ASCO 2021, updated results after approx. **25 months of follow up** were presented

- **Heavily pre-treated patients (N=128)**
  - Median of 6 prior lines of therapy (range 3-16)
  - 84% was triple-class refractory (refractory to IMiD, proteasome inhibitor, anti-CD38 monoclonal antibody)

- R/R MM
- ≥3 prior regimens with ≥2 consecutive cycles each (or best response of PD)
- Previously exposed to:
  - Immunomodulatory agent
  - Proteasome inhibitor
  - Anti-CD38 antibody
- Refractory to last prior therapy per IMWG



BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T-cell; Cy, cyclophosphamide; FDA, Food and Drug Administration; Flu, fludarabine; ide-cel, idecabtagene vicleucel; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MM, multiple myeloma; PD, progressive disease; R/R, relapsed/refractory

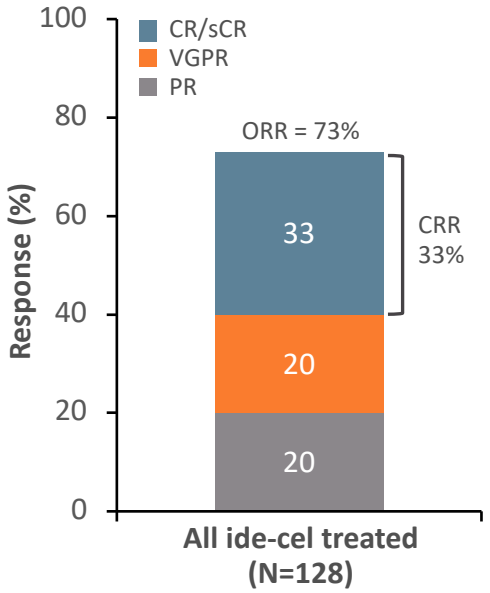
Anderson LD, et al. ASCO 2021. Abstract #8016. Poster presentation; Anderson LD, et al. J Clin Oncol. 2021;39(suppl 15):8016-8016

RESULTS

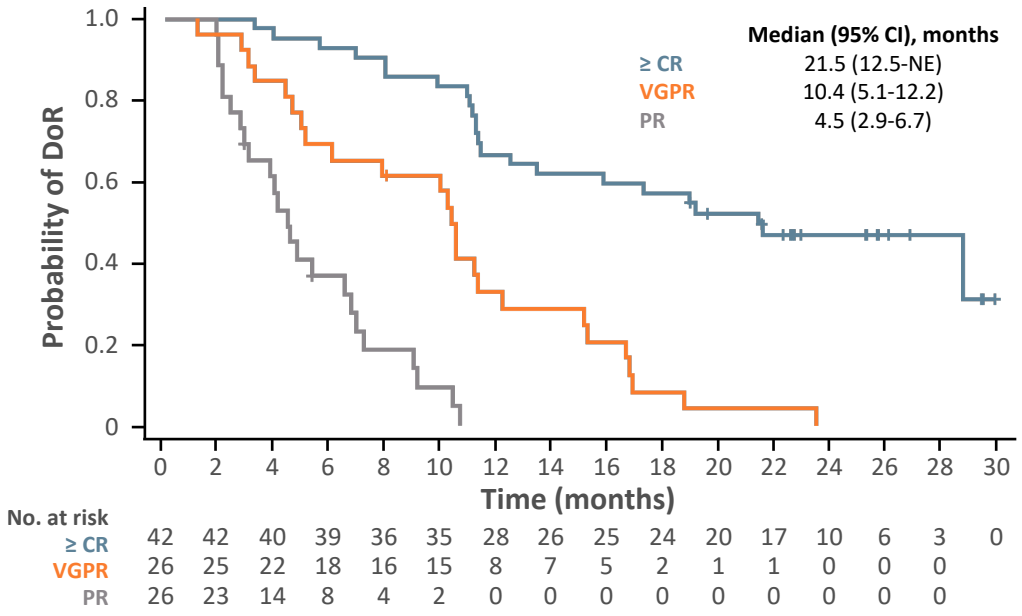
Efficacy

- Unprecedented ORR and depth of response
  - Median DoR 10.9 months
- Median PFS: 8.6 months
- Median OS: 24.8 months

Response



DoR



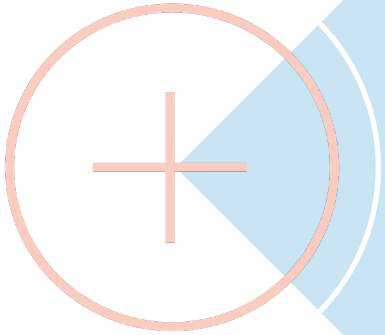
Safety

- CRS occurred in 84% of patients (78% grade 1/2) and neurotoxicity occurred in 18% of patients (4% grade 3)
- The safety profile remained consistent with longer follow up

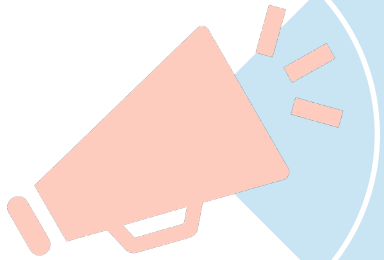
CI, confidence interval; CR, complete response; CRS, cytokine release syndrome; DoR, duration of response; NE, not estimable; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; VGPR, very good PR

Anderson LD, et al. ASCO 2021. Abstract #8016. Poster presentation; Anderson LD, et al. J Clin Oncol. 2021;39(suppl 15):8016-8016

CLINICAL INTERPRETATION



BCMA CAR-T cell therapy with both ide-cel and cilta-cel shows very high **ORR, DoR, and PFS** compared with historic drug approvals in similarly heavily pre-treated myeloma patients



Ide-cel was FDA approved in March 2021 and EMA review is ongoing

BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T-cell; cilta-cel, ciltacabtagene autoleucel; DoR, duration of response; EMA, European Medicines Agency; FDA, Food and Drug Administration; ide-cel, idecabtagene vicleucel; MM, multiple myeloma; ORR, overall response rate; PFS, progression-free survival; R/R, relapsed/refractory

Anderson LD, et al. ASCO 2021. Abstract #8016. Poster presentation; Anderson LD, et al. J Clin Oncol. 2021;39(suppl 15):8016-8016

SUBCUTANEOUS DARATUMUMAB + VCD IN PATIENTS WITH NEWLY DIAGNOSED AL AMYLOIDOSIS: UPDATED RESULTS FROM THE PHASE 3 ANDROMEDA STUDY

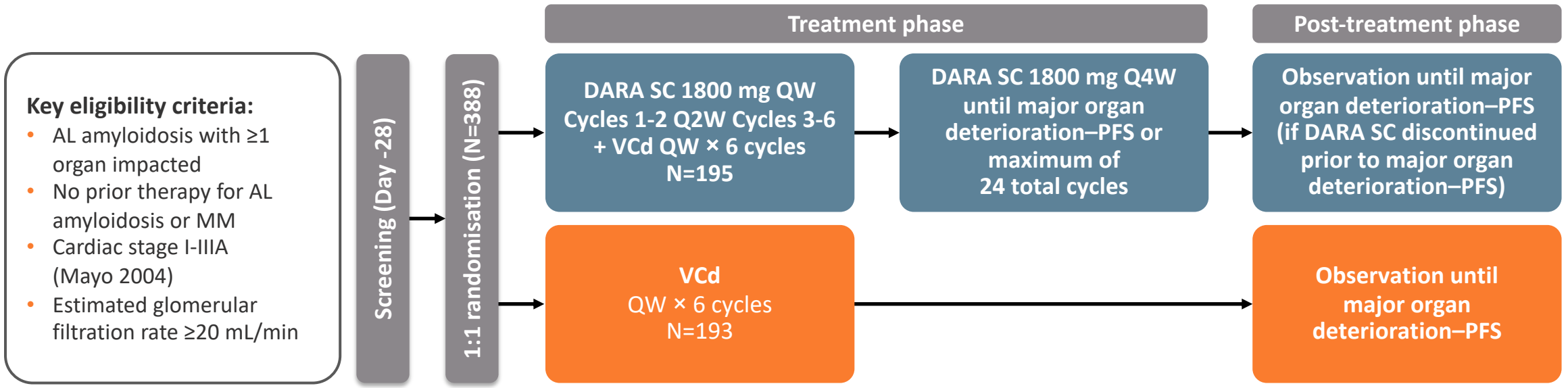
Kastritis E, et al. ASCO 2021. Abstract #8003. Oral presentation
Kastritis E, et al. EHA 2021. Abstract #S189. Oral presentation

AL, light chain; VCD, bortezomib, cyclophosphamide, and dexamethasone

BACKGROUND AND STUDY DESIGN

ANDROMEDA: PHASE 3 STUDY OF DARATUMUMAB +/- VCD IN AL AMYLOIDOSIS

- Primary results from ANDROMEDA were presented at EHA 2020, at 11.4 months median follow-up
  - Adding Dara to VCd led to significantly greater CR, VGPR rates, more rapid haematologic responses and improved organ responses at 6 months
  - Led **Dara-VCd** to become the **first FDA approved therapy for newly diagnosed AL amyloidosis**; in June 2021 it was **approved by EMA**
- At ASCO and EHA 2021, updated results after **20.3 months of follow up** were presented



AL, light chain; CR, complete response; Dara, daratumumab; FDA, Food and Drug Administration; Mayo 2004, Mayo 2004 cardiac staging system; MM, multiple myeloma; PFS, progression-free survival; QW, once weekly; Q2W, once every 2 weeks; Q4W, once every 4 weeks; SC, subcutaneous; VCd, bortezomib, cyclophosphamide, and dexamethasone; VGPR, very good partial response

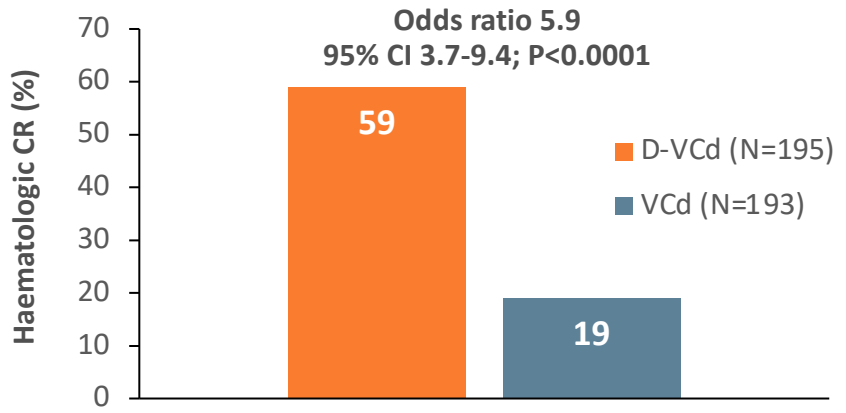
Kastritis E, et al. ASCO 2021. Abstract #8003. Oral presentation; Kastritis E, et al. J Clin Oncol. 2021;39(suppl 15):8003-8003; Kastritis E, et al. EHA 2021. Abstract #S189. Oral presentation; Kastritis E, et al. EHA 2020. Abstract #LB2604. Oral presentation

RESULTS

Efficacy

- Adding Dara to VCd **increased the haematologic CR rate** from 19% to 59%
  - Benefit seen across **all subgroups**, including patients with cardiac AL amyloidosis
- 12-month **cardiac and renal responses doubled** with Dara + VCd vs VCd
  - 12-month cardiac response: 57% vs 28%
  - 12-month renal response: 57% vs 27%

Hematologic CR at a median follow-up of 20.3 months



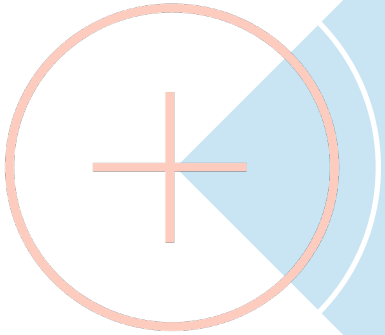
Safety

- The safety profile remained consistent with longer follow up
- In the Dara-VCd group from cycle 7 (Dara monotherapy) grade 3-4 TEAEs occurred in <5% of patients

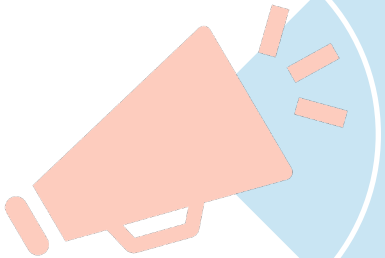
CI, confidence interval; CR, complete response; D, daratumumab; Dara, daratumumab; VCd, bortezomib, cyclophosphamide, and dexamethasone; TEAE, treatment-emergent adverse event

Kastritis E, et al. ASCO 2021. Abstract #8003. Oral presentation; Kastritis E, et al. J Clin Oncol. 2021;39(suppl 15):8003-8003; Kastritis E, et al. EHA 2021. Abstract #S189. Oral presentation

CLINICAL INTERPRETATION



Daratumumab + VCd is a **new standard of care** for newly diagnosed AL amyloidosis patients



In January 2021, SC datatumumab + VCd was **approved by FDA** for newly diagnosed AL amyloidosis

In June 2021 it was **approved by EMA**

AL, light chain; EMA, European Medicines Agency; FDA, Food and Drug Administration; SC, subcutaneous; VCd, bortezomib, cyclophosphamide, and dexamethasone

Kastritis E, et al. ASCO 2021. Abstract #8003. Oral presentation; Kastritis E, et al. J Clin Oncol. 2021;39(suppl 15):8003-8003; Kastritis E, et al. EHA 2021. Abstract #S189. Oral presentation

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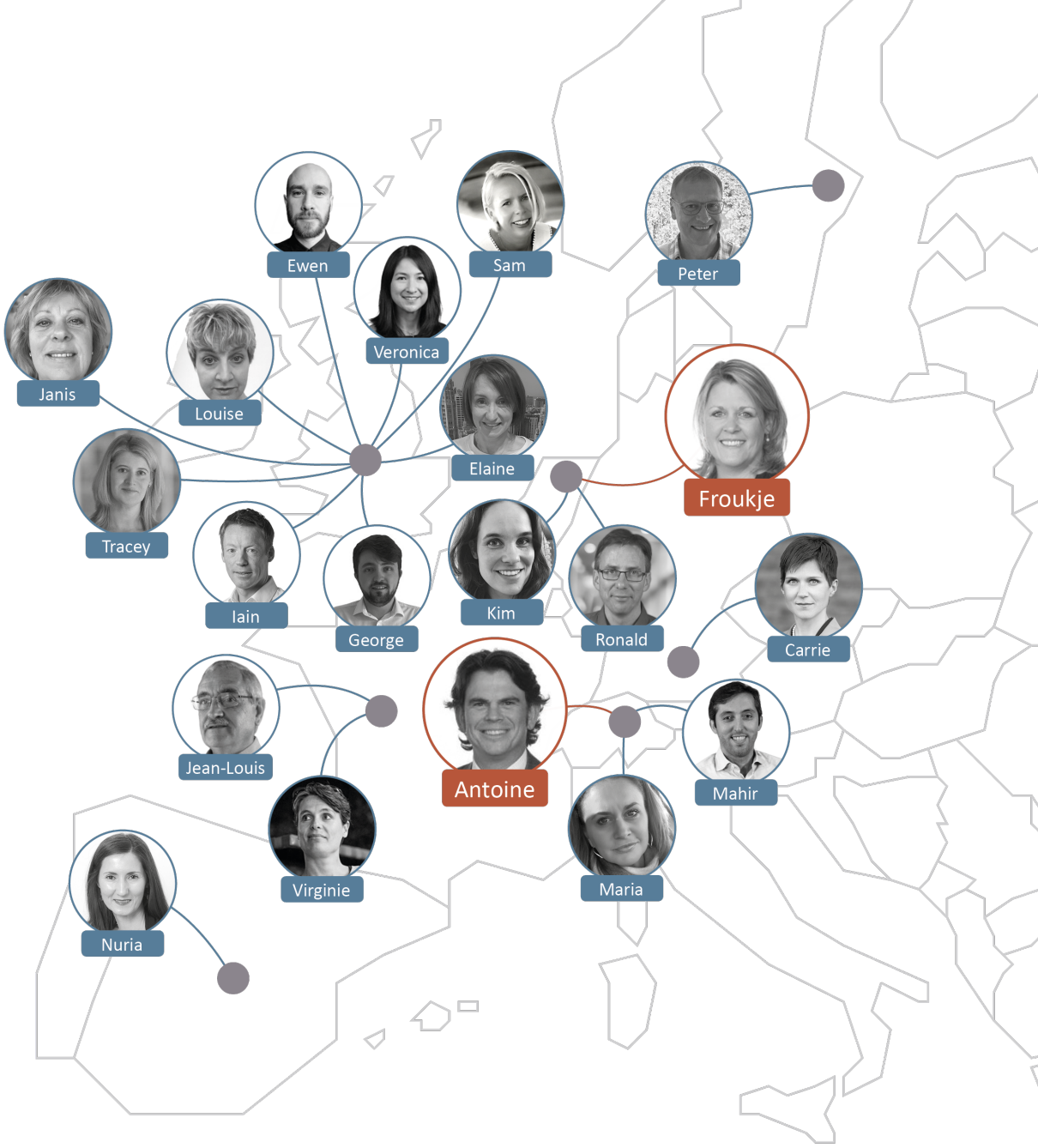

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