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MEETING SUMMARY
AUTUMN 2021 MEETINGS IN MULTIPLE MYELOMA
IMW | SOHO | SOHO ITALY

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HIGHLIGHTS FROM LYMPHOMA & MYELOMA CONNECT
NOVEMBER 2021

CONFLICT OF INTEREST AND FUNDING

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Dr. Claudio Cerchione has no conflicts of interest to declare.

NEWLY DIAGNOSED MULTIPLE MYELOMA

OS AND PFS BY TREATMENT DURATION WITH DARATUMUMAB + LENALIDOMIDE / DEXAMETHASONE IN TRANSPLANT-INELIGIBLE NDMM: PHASE 3 MAIA STUDY

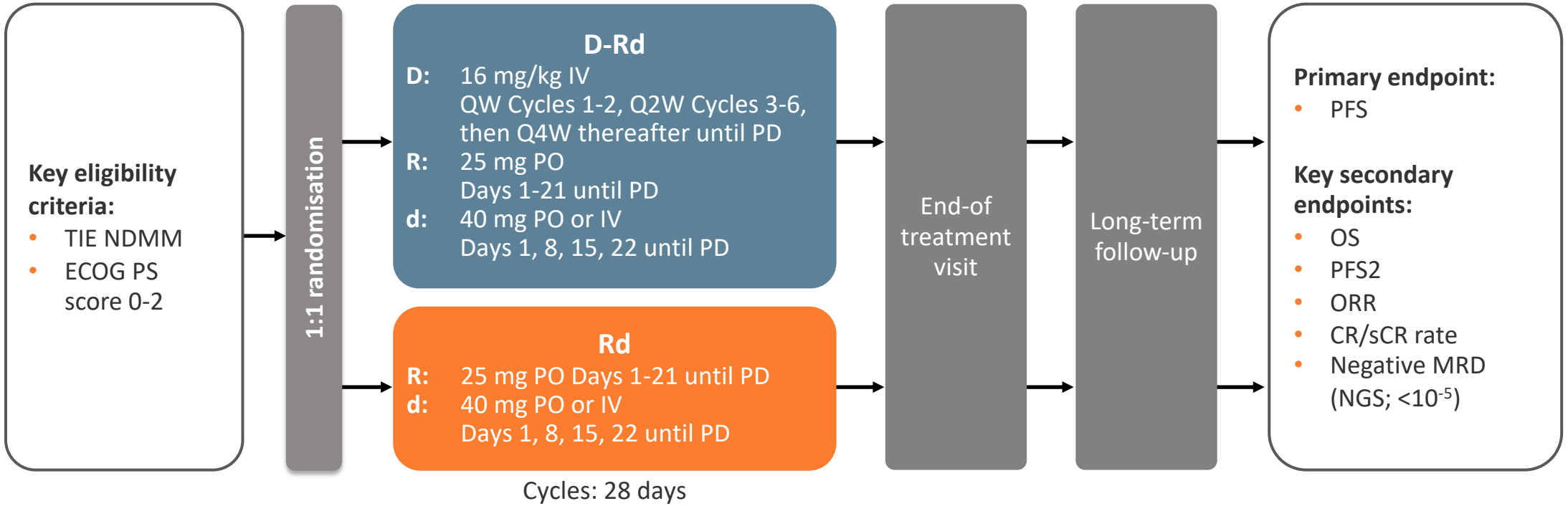
Moreau P, et al.
IMW 2021. Abstract #OAB-001. Oral presentation

NDMM, newly diagnosed multiple myeloma; OS, overall survival; PFS, progression-free 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

- Updated efficacy and safety data after **almost 5 years of median follow-up** from the prespecified interim OS analysis

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; PFS2, PFS on next line of therapy; PO, oral; QW, once weekly; Q2W, once every 2 weeks; Q4W, once every 4 weeks; R, lenalidomide; sCR, stringent CR; TIE, transplant-ineligible

Moreau P, et al. IMW 2021. Abstract #OAB-001; Clinicaltrials.gov NCT02252172

RESULTS

Efficacy

- At a 56.2-month median follow-up, a D-Rd vs Rd showed a **significant improvement in OS and clinically meaningful improvement in PFS**
- Adding D to Rd led to a **32% reduction in the risk of death**
  - Median OS was not reached in either arm (HR 0.68; 95% CI, 0.53-0.86; p=0.0013)
  - Estimated 5-year OS: 66.3% with D-Rd and 53.1% with Rd
- **Median PFS was not reached** with D-Rd vs 34.4 months with Rd (HR 0.53; 95% CI, 0.43-0.66; p=0.2480)
  - D-Rd showed a greater PFS benefit vs Rd among patients treated for ≥18 months than those treated for shorter durations

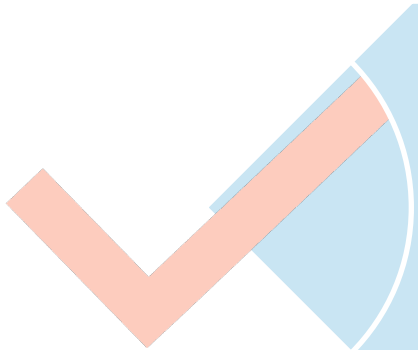
Safety

- **No new safety concerns** with longer follow-up
- Most common grade 3/4 treatment-emergent adverse event: **neutropenia** (D-Rd, 54.1%; Rd, 37.0%)

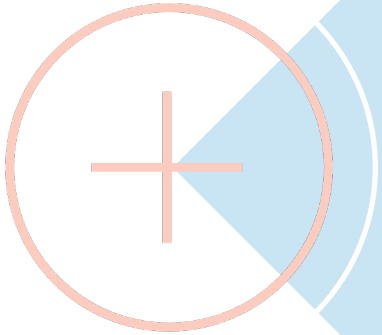
CI, confidence interval; D, daratumumab; d, dexamethasone; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; R, lenalidomide

Moreau P, et al. IMW 2021. Abstract #OAB-001

AUTHOR'S CONCLUSIONS AND CLINICAL INTERPRETATION



After ~5 years of follow-up, D-Rd vs Rd showed a **clinically meaningful PFS and significant OS improvement**



The favourable benefit-risk profile **supports the frontline use of D-Rd** in transplant-ineligible patients with NDMM

D, daratumumab; d, dexamethasone; NDMM, newly diagnosed multiple myeloma; OS, overall survival; PFS, progression-free survival; R, lenalidomide

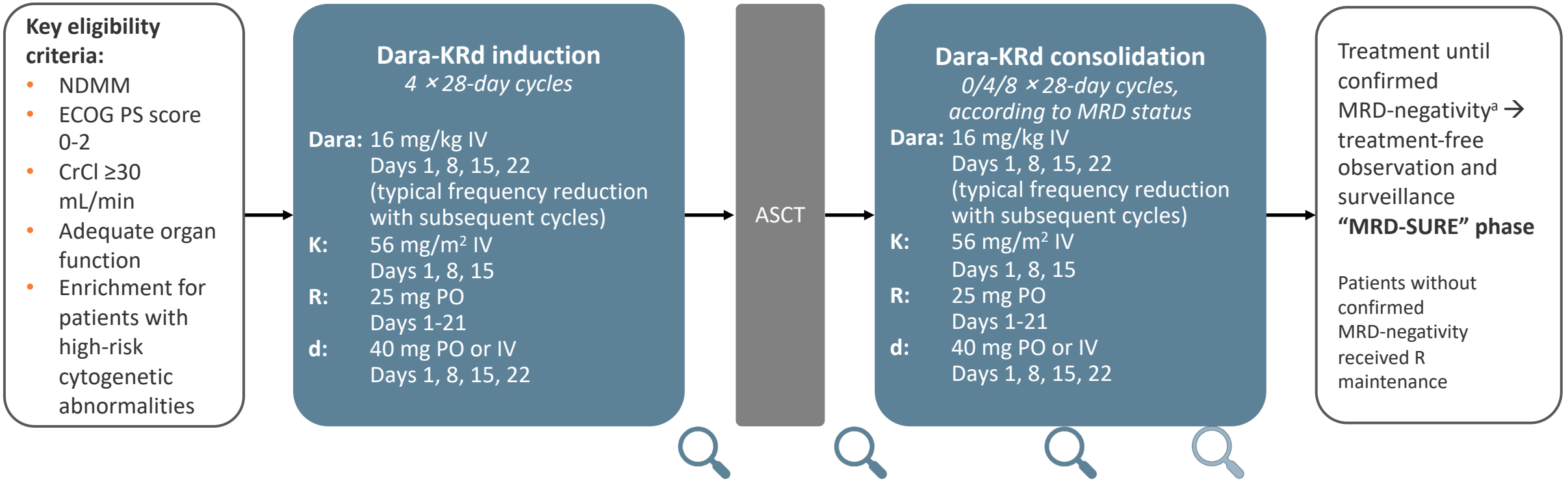
Moreau P, et al. IMW 2021. Abstract #OAB-001

DARA-KRD, ASCT AND MRD RESPONSE-ADAPTED TREATMENT DURATION AND CESSATION IN NDMM

Costa L, et al.
IMW 2021. Abstract #OAB-051. Oral presentation

ASCT, autologous transplantation; Dara-KRd, daratumumab, carfilzomib, lenalidomide, dexamethasone; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma

STUDY DESIGN



- MRD was evaluated by NGS at end of induction, post-ASCT, and during each 4-cycle block of Dara-KRd consolidation
- Primary endpoint: MRD negativity

[a]2 consecutive MRD $<10^{-5}$

ASCT, autologous transplantation; CrCl, creatinine clearance; d, dexamethasone; Dara, daratumumab; Dara-KRd, daratumumab, carfilzomib, lenalidomide, dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; K, carfilzomib; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGS, next-generation sequencing; PO, oral; R, lenalidomide

Costa L, et al. IMW 2021. Abstract #OAB-051

RESULTS

Efficacy

- 123 patients included
  - 37% had 1 and 20% had 2+ high-risk cytogenetic abnormalities
  - Median age was 60 years (36-79)
- Median follow-up was 25.1 months

%	Total	0 HRCA	1 HRCA	2+ HRCA
MRD negative	80	78	82	79
Post induction	38			
Post ASCT	65			
Post Dara-KRd consolidation	80			
Confirmed MRD negative, entered MRD-SURE	71			
MRD $<10^{-6}$	65	62	73	58

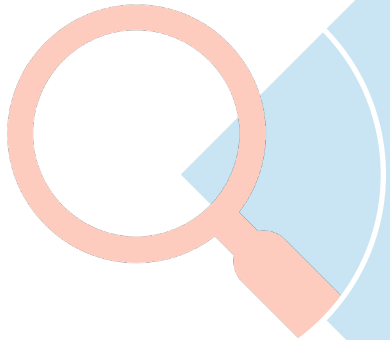
Safety

- Most common severe adverse events were **pneumonia** and **venous thromboembolism**

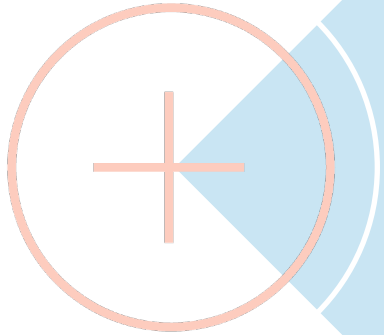
ASCT, autologous transplantation; Dara-KRd, daratumumab, carfilzomib, lenalidomide, dexamethasone; HRCA, high-risk cytogenetic abnormalities; MRD, minimal residual disease

Costa L, et al. IMW 2021. Abstract #OAB-051

AUTHOR'S CONCLUSIONS AND CLINICAL INTERPRETATION



Monoclonal antibody-based quadruplet therapy, ASCT and MRD response-adapted consolidation therapy leads to **high rate of MRD-negativity in NDMM**



For most patients with NDMM, **MRD-directed adaptive treatment** offers the prospect of confirmed deep responses and investigation of **MRD surveillance as an alternative to indefinite maintenance**

ASCT, autologous transplantation; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma

Costa L, et al. IMW 2021. Abstract #OAB-051

RELAPSED/REFRACTORY MULTIPLE MYELOMA

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

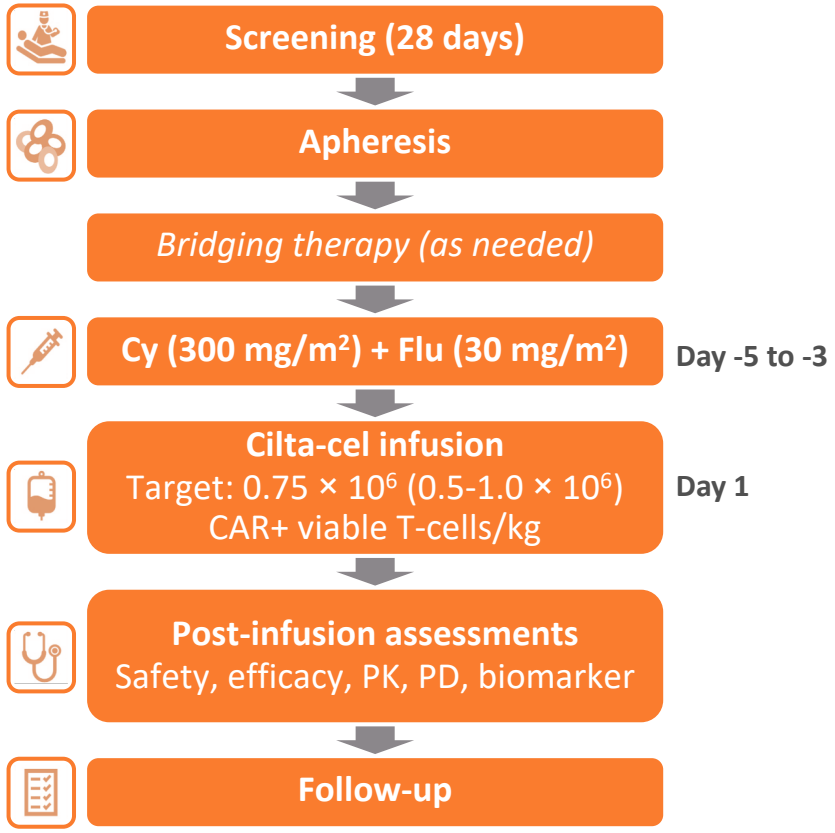
Jagannath S, et al.
IMW 2021. Abstract #OAB-024. Oral presentation

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

BACKGROUND AND STUDY DESIGN

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

- Ciltacabtagene autoleucel (cilta-cel) is a **CAR-T cell therapy** with two BCMA-targeting single-domain antibodies
  - Eligible patients received ≥3 prior regimens (or PI and IMiD refractory) and received an anti-CD38 antibody
- **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



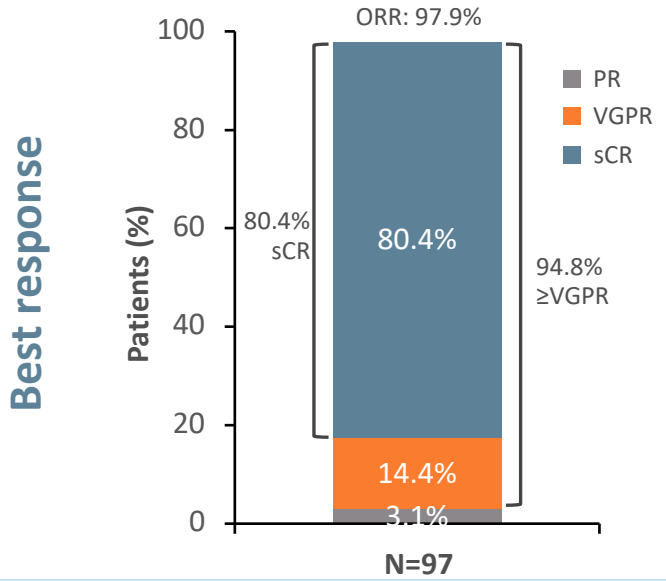
BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; Cy, cyclophosphamide; Flu, fludarabine; IMiD, immunomodulatory drug; MM, multiple myeloma; PD, pharmacodynamic; PI, proteasome inhibitor; PK, pharmacokinetic; RP2D, recommended phase 2 dose; RRMM, relapsed/refractory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

Jagannath S, et al. IMW 2021. Abstract #OAB-024; Clinicaltrials.gov NCT03548207

RESULTS

Efficacy

- **Response**
  - Median time to first response: 1 month (2.6 months to ≥CR)
  - Median duration of response: 21.8 months
- 91.8% of 61 evaluable patients were **MRD negative** at 10^{-5}
- **18-month PFS**: 66%
  - Median PFS was 22.8 months; not reached for patients with sCR
- **18-month OS**: 81%



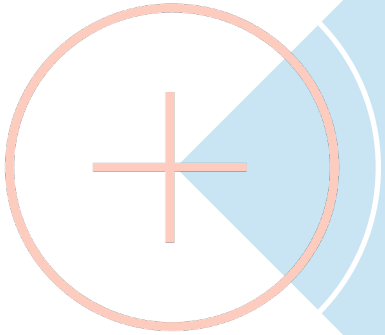
Safety

- Most common **grade 3/4 haematologic AEs**: neutropenia (95%), anaemia (68%), leukopenia (61%)
- 95% of patients had **CRS** (4% grade 3/4) and resolved in all but one (grade 5 CRS/haemophagocytic lymphohistiocytosis)
  - Median time to onset was 7 days and the median duration was 4 days
- **Neurotoxicity** occurred in 21% of patients (10% grade ≥3)
- 21 **deaths** on study; 10 due to disease progression, 6 treatment-related, 5 due to AEs unrelated to treatment

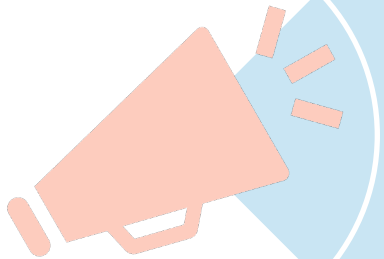
AE, adverse event; CR, complete response; CRS, cytokine release syndrome; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; VGPR, very good PR

Jagannath S, et al. IMW 2021. Abstract #OAB-024

AUTHOR'S CONCLUSIONS AND CLINICAL INTERPRETATION



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



Cilta-cel is being investigated in **earlier lines of therapy** and in **outpatient settings**

Cilta-cel, ciltacabtagene autoleucel; RRMM, relapsed/refractory multiple myeloma

Jagannath S, et al. IMW 2021. Abstract #OAB-024

IBER IN COMBINATION WITH DEX AND DARA, BORT, CFZ IN PATIENTS WITH RRMM

Lonial S, et al.
IMW 2021. Abstract #OAB-013. Oral presentation

BORT, bortezomib; CFZ, carfilzomib; DARA, daratumumab; DEX, dexamethasone; Iber, iberdomide; RRMM, relapsed/refractory multiple myeloma

STUDY DESIGN

CC-220-MM-001: PHASE 1/2 STUDY OF IberDd VS IberVd VS IberKd IN RRMM

- Study evaluating the **MTD, RP2D, safety, and preliminary efficacy** of the oral CELMoD Iber
- **Eligibility**
  - ≥2 (IberDd and IberKd cohorts) or ≥1 prior regimens (IberVd cohort), containing lenalidomide or pomalidomide, and a proteasome inhibitor
  - Progression ≤60 days from last therapy
- **Treatment**

IberDd cohort - 28-day cycles	IberKd cohort - 28-day cycles	IberVd cohort - 21-day cycles
• Escalating doses of Iber on Day 1-21 • Weekly DARA at Cycle 1-2; biweekly DARA at Cycle 3-6; DARA on Day 1 at Cycle ≥7 • Weekly DEX	• Escalating doses of Iber on Day 1-21 • Weekly CFZ • Weekly DEX	• Escalating doses of Iber on Day 1-14 • BORT twice a week for the first 2 weeks of Cycle 1-8, and weekly for the first 2 weeks of Cycle ≥9 • Weekly DEX

BORT, bortezomib; CELMoD, cereblon E3 ligase modulator; CFZ, carfilzomib; DARA, daratumumab; DEX, dexamethasone; Iber, iberdomide ; IberDd, iberdomide + daratumumab + dexamethasone; IberVd, iberdomide + bortezomib + dexamethasone; IberKd, iberdomide + carfilzomib + dexamethasone; MTD, maximum tolerated dose; RP2D, recommended phase 2 dose; RRMM, relapsed/refractory multiple myeloma

Lonial S, et al. IMW 2021. Abstract #OAB-013; Clinicaltrials.gov NCT02773030

RESULTS

	IberDd	IberVd	IberKd
Patients treated, n	43	25	9
Median age, years	67	64	61
Median time since diagnosis, years	7.4	7.1	6.7
Extramedullary plasmacytomas, n (%)	7 (16)	4 (16)	2 (22)
Median follow-up, months	4.17	4.86	5.03
Patients on treatment, n (%)	22 (51)	6 (24)	5 (56)
Median number of cycles received	4	6	5

Efficacy	IberDd	IberVd	IberKd
ORR, %	46	56	50
≥VGPR, %	24	28	38
Median time to response, weeks	4.1	3.6	4.1
Median DoR, weeks	NR	35.7	NR
RP2D of Iber	1.6	NE	NE

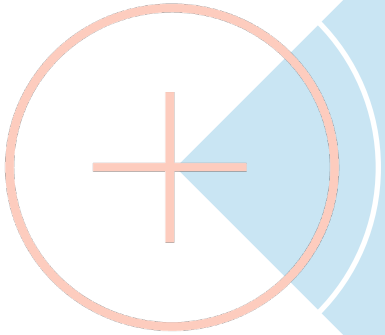
Haematological grade 3/4 TEAEs of interest

- IberDd: neutropenia (67%), leukopenia (23%), anaemia (21%), and febrile neutropenia (5%)
- IberVd: neutropenia (28%) and thrombocytopenia (24%)
- IberKd: lymphopenia (44%) and neutropenia (33%)
- Neutropenia was manageable with G-CSF

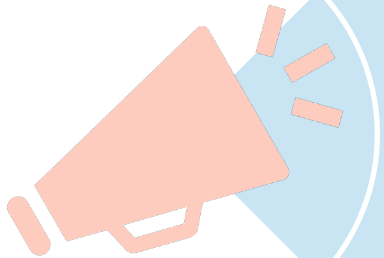
DoR, duration of response; G-CSF, granulocyte colony-stimulating factor; Iber, iberdomide; IberDd, iberdomide + daratumumab + dexamethasone; IberVd, iberdomide + bortezomib + dexamethasone; IberKd, iberdomide + carfilzomib + dexamethasone; NE, not evaluated; NR, not reached; ORR, overall response rate; RP2D, recommended phase 2 dose; TEAE, treatment-emergent adverse event; VGPR, very good partial response

Lonial S, et al. IMW 2021. Abstract #OAB-013

AUTHOR'S CONCLUSIONS AND CLINICAL INTERPRETATION



IberDd, IberVd, and IberKd showed a **tolerable safety profile and promising efficacy** in heavily pre-treated RRMM



These results **support further development** of Iber-based regimens in MM, including Phase 3 combination studies

Iber, iberdomide; IberDd, iberdomide + daratumumab + dexamethasone; IberVd, iberdomide + bortezomib + dexamethasone; IberKd, iberdomide + carfilzomib + dexamethasone; MM, multiple myeloma; RRMM, relapsed/refractory multiple myeloma

Lonial S, et al. IMW 2021. Abstract #OAB-013

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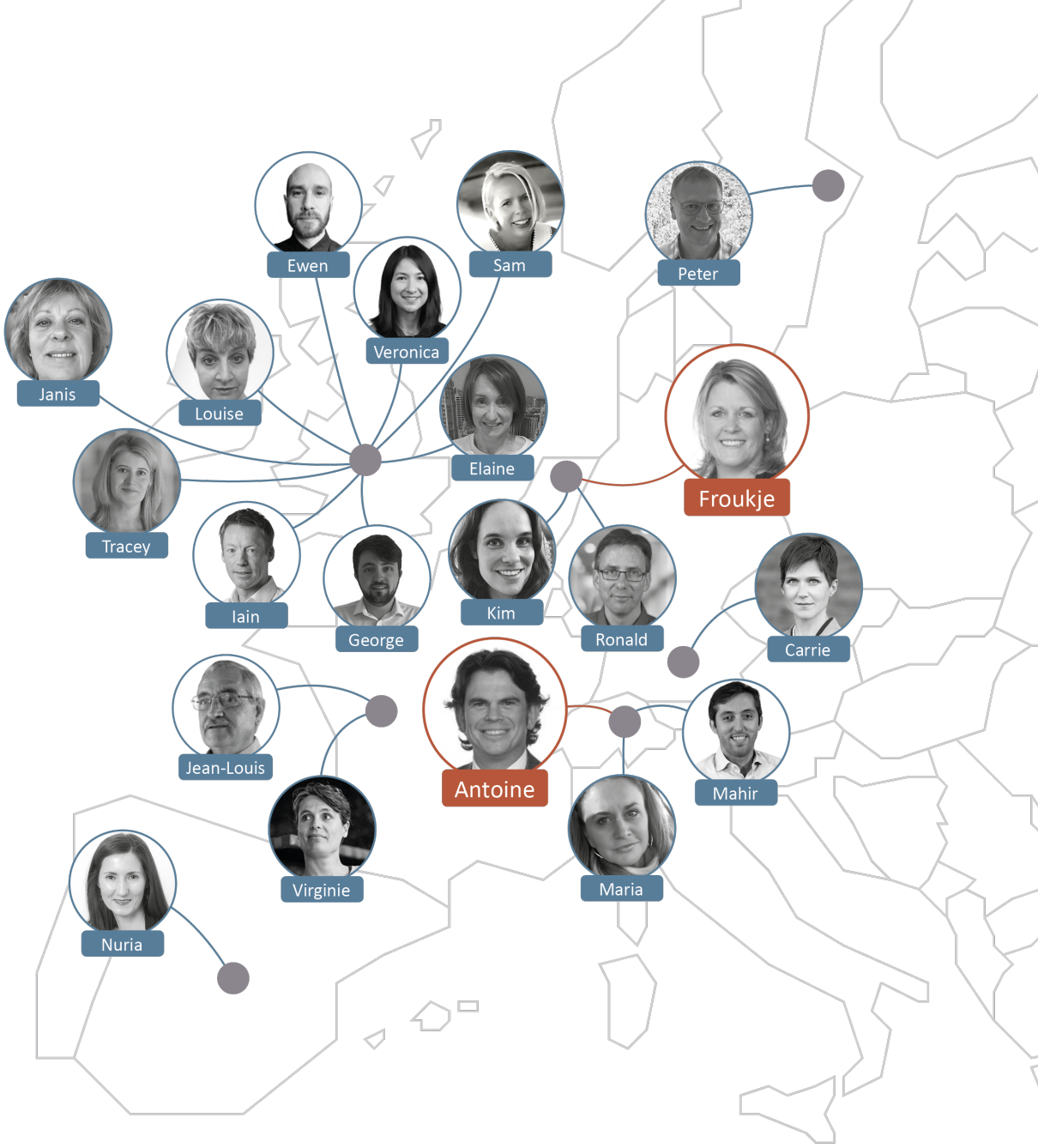

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