

**How can real-world evidence
guide the management of
elderly and frail patients with
multiple myeloma?**

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The value of real-world evidence in supporting clinical decision making

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Information lacking from randomized control trials

Use of therapies in excluded populations, such as those with:^{1,2}

- Advanced age
- Rare molecular alterations
- Low performance status
- High rate of comorbidities
- Low socioeconomic status
- Rural location or further from academic medical centres



The rate of clinical trial ineligibility is reported to be between 22 and 72% of real-world patients with MM³

Management of issues faced in the real world:²

- Compliance
- Rare or long-term AEs



A review of 81 cancer therapy trials found 90% scored poorly in reporting recurrent and late toxicities²

RWE studies can be used to bridge the **knowledge gap** and improve the **evidence** used in drug approvals¹

Real-world evidence on the treatment of elderly/frail patients with multiple myeloma

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First-line therapy for non-transplant candidates



NCCN guidelines

Preferred regimens for non-transplant candidates:¹

- Bortezomib/lenalidomide/dexamethasone (VRd)
- Daratumumab/lenalidomide/dexamethasone (DaraRd)



ESMO guidelines

Preferred regimens for elderly or non-transplant candidates:²

- Bortezomib/lenalidomide/dexamethasone (VRd)
- Daratumumab/lenalidomide/dexamethasone (DaraRd)
- Daratumumab/bortezomib/melphalan/prednisone (DaraVMP)

ESMO, European Society for Medical Oncology; NCCN, National Comprehensive Cancer Network.

1. NCCN Guidelines. Multiple Myeloma. Version 5.2022. Available at: www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf (accessed 5 April 2022);

2. Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309–22.

Examples of RWE in elderly/frail patients with MM

Patients with NDMM

Novel therapies

- First/second-line use of regimens containing **bortezomib, lenalidomide** or **thalidomide** improve outcomes in elderly patients with NDMM compared with their use in later lines¹⁻⁴
- **Ixazomib** triplet therapies are effective in fragile elderly patients⁵

Stem cell transplantation

- Patients ≥ 70 years can undergo transplant **safely** and achieve similar **disease control benefits** as those 60–69 years old⁶
- Transplant results in a survival benefit for older patients (≥ 66 years) with MM vs no transplant⁷



Treatment options

Patients with RRMM

PI-triplet or monoclonal antibody therapy

- **Ixazomib** triplet therapy is effective and well tolerated in elderly patients with RRMM⁸
- Longer TTNT for intermediate/frail patients with **ixazomib** or **bortezomib** compared with carfilzomib⁹
- More patients ≥ 75 years receive **ixazomib** or **bortezomib** triplets compared with carfilzomib or daratumumab triplets¹⁰

CAR T-cell therapy

- $<10\%$ of newly diagnosed older patients are expected to be eligible for CAR T-cell therapy¹¹

CAR, chimeric antigen receptor; MM, multiple myeloma; NDMM, newly diagnosed multiple myeloma; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma; RWE, real-world evidence; TTNT, time to next therapy.

1. Lee HC, et al. *Blood Cancer J.* 2021;11:134; 2. Remes K, et al. *PLoS One.* 2018;13:e0208507; 3. Bonomo L, et al. *Cancer Med.* 2016;5:500–5;
4. Liwing J, et al. *Br J Haematol.* 2014;164:684–93; 5. Bao L, et al. *Clin Lymphoma Myeloma Leuk.* 2021;21:S123; 6. Munshi PN, et al. *Blood.* 2019;134(Suppl. 1):782;
7. Winn AN, et al. *J Natl Cancer Inst.* 2015;107:djv139; 8. Hajek R et al. *Future Oncol.* 2021;17:2499–512; 9. Chari A, et al. *Expert Rev Hematol.* 2020;13:421–33;
10. Davies F, et al. *Ann Hematol.* 2021;100:2325–37; 11. Giri S, et al. *Blood.* 2021;138:4107.

Connect[®] MM registry: Observational study of patients with NDMM in the USA



Sub-analysis of treatment patterns and survival outcomes in elderly patients (≥ 75 years old) compared with younger patients

3,007 patients (median age of 67 years):

- Most patients < 75 years (43% < 65 years; 33% 65–74 years) and 24% were elderly (20% 75–84 years; 4% ≥ 85 years)
- Greater proportion in ≥ 85 -year group with a performance status ≥ 2 (20%) vs the younger < 65 -year group of patients (9%)
- Severe and moderate renal impairment more common in the ≥ 85 -year group

Fewer elderly patients received triplet therapies as first-line therapy (18–40%) vs younger patients (56–66%)

Common initial therapies in ≥ 85 -year group: Vd, Rd, RVd and dexamethasone

Adjusted outcomes found no notable changes in TTP, PFS or OS between age groups

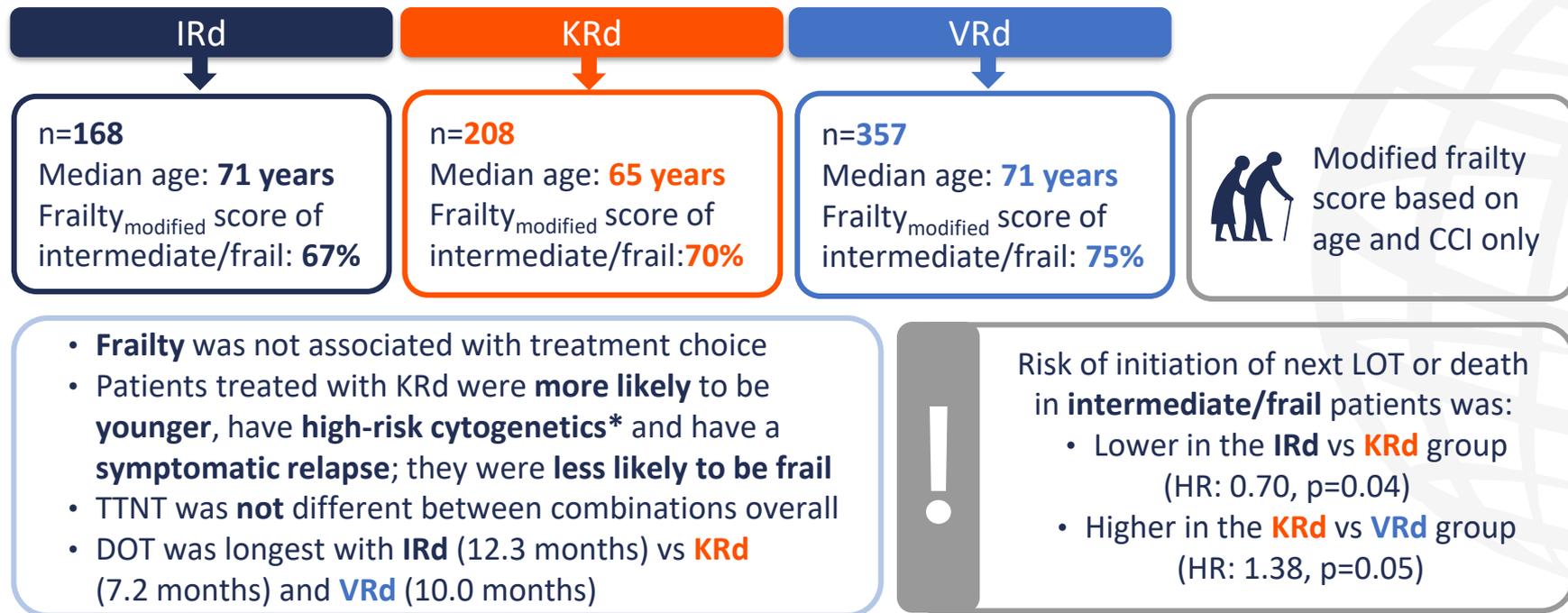


Findings support the use of novel agents and aggressive supportive care for elderly patients with NDMM to improve outcomes and reduce early mortality

MM, multiple myeloma; NDMM, newly diagnosed multiple myeloma; OS, overall survival; PFS, progression-free survival, Rd, lenalidomide-dexamethasone; RVd, lenalidomide-bortezomib-dexamethasone; TTP, time to progression; Vd, bortezomib-dexamethasone.

Lee HC, et al. *Blood Cancer J.* 2021;11:134.

Real-world comparison of PI triplet combinations in patients with RRMM in LOT ≥ 2



*Cytogenetic data were missing for the majority of patients.

CCI, Charlson Comorbidity Index; DOT, duration of therapy; HR, hazard ratio; IRd, ixazomib-lenalidomide-dexamethasone; KRd, carfilzomib-lenalidomide-dexamethasone; LOT, line of therapy; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma; TTNT, time to next therapy; VRd, bortezomib-lenalidomide-dexamethasone.

Chari A, et al. *Expert Rev Hematol*. 2020;13:421–33.

Managing elderly/frail patients with multiple myeloma in clinical practice

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Assessing frailty in patients with MM



Frailty is defined as increased vulnerability to stressors because of a multisystem reduction in reserve capacity that is associated with **poor response to treatment, increased toxicity and worse survival**¹

One-third of patients with MM are frail at the time of diagnosis¹

Frailty assessment tools in MM

IMWG Frailty Index²

- Age
- Katz Activity of Daily Living (ADL)
- Lawton Instrumental Activities of Daily Living (IADL)
- Charlson Comorbidity Index (CCI)

Incorporates assessment of comorbidities alongside daily functioning

Simplified IMWG Frailty Index^{3,4}

- Age
- Eastern Cooperative Oncology Group (EGOC) performance status
- Charlson Comorbidity Index (CCI)

Performance status is a surrogate for a patient's functional reserve

Others include:¹

- Revised Myeloma Comorbidity Index (R-MCI)
- Mayo risk score
- UK Myeloma Research Alliance Risk Profile (MRP)

IMWG, International Myeloma Working group; MM, multiple myeloma.

1. Möller MD, et al. *Curr Opin Oncol.* 2021;33:648; 2. Palumbo A, et al. *Blood.* 2015;125:2068–74; 3. Facon T, et al. *Leukemia.* 2020;34:224–33;

4. Bonello F, et al. *Cancers.* 2020;12:3106.