INTERIM RESULTS FROM THE CARO STUDY AND THE MYRIAM REGISTRY COMPARED WITH DATA FROM ACADEMIC INSTITUTION

IMPLEMENTATION OF THE REVISED MYELOMA COMORBIDITY INDEX (R-MCI) IN PATIENTS WITH MULTIPLE MYELOMA IN REAL WORLD

Engelhardt M[1,2]
Woerner SM[3]
Möller MD[1]
Vannier C[3]
Ihorst G[2]
Schuch A[3]
Duyster J[1,2]
Wäsch R[1,2]
Potthoff K[3]

1 Department of Medicine I Hematology and Oncology, Faculty of Medicine and Medical Center, University of Freiburg (UKF)

2 Comprehensive Cancer Center Freiburg (CCCF), Faculty of Medicine and Medical Center, University of Freiburg

3 iOMEDICO, Freiburg Im Breisgau, Germany

BACKGROUND

Risk-adapted treatment strategies to further improve outcome in multiple myeloma (MM) are crucial, especially for elderly patients. The R-MCI is a validated prognostic risk tool for MM patients developed at the University Clinic Freiburg (UKF)[1–5] based on 5 risk factors determined from multivariate analysis, being widely available in the clinics: impaired lung and kidney function, Karnofsky Performance Status, frailty, age and, if available, cytogenetics (**Figure 1**). Based on these risk factors and an easy-to-use webpage (www.myelomacomorbidityindex.org), patients can be classified into fit (R-MCI: 0-3), intermediate-fit (R-MCI: 4-6) or frail (R-MCI: 7-9) (**Figure 2**) with substantially different prognosis, PFS, OS, hematologic and non-hematologic side effects (SAEs) and treatment endurance. Whereas the R-MCI has been successfully performed and validated in a small multicenter validation in academic cohorts (other referral and university DSMM study group centers) in Germany[6],the external validation of the R-MCI in real world is missing, i.e., data on the feasibility of the R-MCI from secondary and primary sites. This was therefore performed in this analysis and compared to UKF data.

CONCLUSION

In real world, the R-MCI was adapted for lung function and frailty assessment to make it feasible for routine use. With these minor adjustments, the real world R-MCI risk group distribution was comparable with the R-MCI risk groups in the academic settings.

Next steps will be to correlate the R-MCI risk groups with treatment decision and outcome, plus learn which and why differences in primary, secondary and tertiary centers in terms of the R-MCI may exist. In the future, real world data on R-MCI may play a central part in trial design and risk-adapted treatment approaches in the elderly and/or impaired younger MM patients. Taken together, the real world data demonstrate that the R-MCI is of value also in real world settings and, thus, may be widely applicable in daily practice, e.g. for tailoring myeloma therapies.

Figure 1

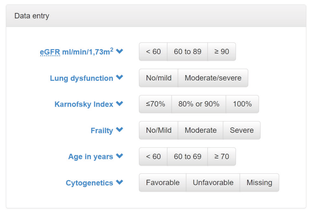

Figure 1. Factors of the revised myeloma comorbidity index (R-MCI).
The first five of the 6 factors are mandatory and should be available. Cytogenetics can be available. (https://www.myelomacomorbidityindex.org)

Figure 2

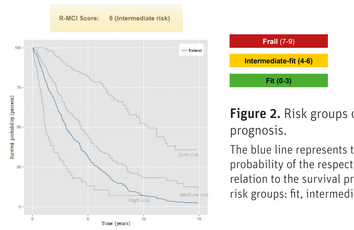

Figure 2. Risk groups of the R-MCI and prognosis.
The blue line represents the survival probability of the respective patient in relation to the survival probability of the 3 risk groups: fit, intermediate-fit and frail.

METHODS

The prospective, multicenter, non-interventional study CARO evaluates the combination of carfilzomib with a) lenalidomide / dexamethasone, b) dexamethasone or c) dexamethasone / daratumumab in patients with at least one prior therapy, and the registry MYRIAM collects longitudinal data on routine clinical care of primary and secondary myeloma treatment in hospitals and private practices in Germany (Sponsor: iOMEDICO).

Both studies collect parameters to calculate the R-MCI and, therefore can serve as external validation cohorts for the R-MCI. We here compared the frequency of R-MCI risk-groups from CARO and MYRIAM with historical UKF data (>1,000 patients), thus from a tertiary referral center. Descriptive statistics were used for the analysis.

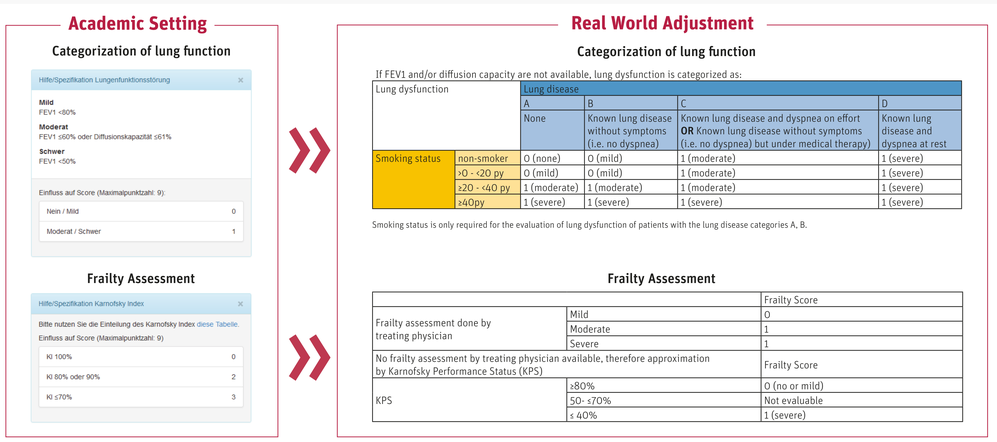

Table 1

Parameters	MYRIAM n=1,236	CARO n=312	UKF n=1,080
Age at inclusion (years), median (range)	72 (29-97)	74 (35-90)	72 (31–99)
Sex, n (%)			
Female	556 (45)	141 (45)	455 (42)
Male	680 (55)	171 (55)	625 (58)
Type of MM, n (%)			
IgG	713 (58)	173 (56)	604 (56)
IgA	227 (18)	69 (22)	204 (19)
κ- / λ- light chain only	263 (21)	63 (20)	202 (19)
Other	33 (3)	7 (2)	70 (6)
Cytogenetics*, n (%)			
Favorable	406 (33)	191 (61)	430 (40)
Unfavorable	308 (25)	52 (17)	316 (29)
Missing	522 (42)	69 (22)	334 (31)

*Cytogenetics: favorable = Hyperdiploidity, t(11;14), normal Karyotype, del(13q14); unfavorable = t(4;14), t(14;16), t(14;20), del(17p), Hypodiploidity, c-myc, Chromosome1-Aberrations. (www.myelomacomorbidityindex.org / Sonneveld et al. Blood 2016)

Table 1: Patient characteristics
Patient characteristics were comparable throughout all 3 cohorts for age, sex and myeloma paraprotein subtypes. Smaller, albeit expected differences were determinable in cytogenetics.

Table 2

	Academic Setting	Real world Setting
Lung Function	Pulmonary function test (FEV1)	Pre-existing lung disease +/- Medication +/- Smoking Status
Frailty	Timed up and go Instrumental activities of daily living (IADL) etc.	Simple estimation by treating physician: • KPS • Mobility assessment (walking into consultation room) • Performance regarding daily tasks • Overall fitness grade (1= very good – 6 = unsatisfactory)

Table 2: Lung function and frailty assessment in real world
Lung and frailty assessment was adapted for real world. With this adaption, it was possible to determine the R-MCI of real world patients more easily.

RESULTS

In CARO, 334 patients have been enrolled from 65 sites across Germany. Thereof, at database cut for this interim analysis, data of 312 (93%) patients were available for R-MCI assessment. In MYRIAM, at database cut for this interim analysis, 1,917 patients had been enrolled from 150 sites in Germany and for 1,236 (65%) patients the R-MCI could as yet be obtained (**Table 1**).

In order to implement the R-MCI in the real world setting, we did adapt two assessments to make its usage even more feasible: Firstly, the lung function was more easily defined as moderately or severely impaired and secondly, the frailty assessment according to Fried[7] as exemplified for both in **Table 2**. These two minor adjustments made it possible to use the R-MCI in real world settings even more swiftly.

Notably, the R-MCI results, as assessed from the webpage and exemplified in **Fig. 1 & 2,** revealed similar results in all 3 cohorts. In patients with evaluable R-MCI, the risk distribution in MYRIAM, CARO and UKF was similar with 31%, 31% and 27% of fit, 57%, 53% and 55% of intermediate-fit and 11%, 16% and 18% of frail patients, respectively (**Figure 3**).

Figure 3

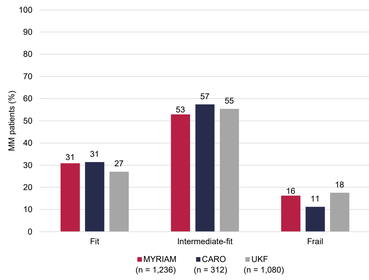

Figure 3. Distribution of R-MCI risk groups.
Distribution of R-MCI risk groups was similar throughout the 3 cohorts.

Abbreviations:
DSMM Deutsche Studiengruppe Multiples Myelom
eGFR estimated glomerular filtration rate
FEV1 Forced expiratory volume in 1 second
IADL Instrumental activities of daily living
KPS Karnofsky Performance Status
MM Multiple Myeloma
OS Overall survival
py pack years
PFS Progression-free survival
R-MCI Revised Myeloma Comorbidity Index
UKF University Clinic Freiburg

References
1. Engelhardt, M. et al. Geriatric assessment in multiple myeloma patients: validation of the International Myeloma Working Group (IMWG) score and comparison with other common comorbidity scores. Haematologica 101, 1110–1119 (2016).
2. Engelhardt, M. et al. A concise revised Myeloma Comorbidity Index as a valid prognostic instrument in a large cohort of 801 multiple myeloma patients. Haematologica 102, 910–921 (2017).
3. Gay, F. et al. From transplant to novel cellular therapies in multiple myeloma: European Myeloma Network guidelines and future perspectives. Haematologica 103, 197–211 (2018).
4. Kleber, M. et al. Comorbidity as a prognostic variable in multiple myeloma: comparative evaluation of common comorbidity scores and use of a novel MM–comorbidity score. Blood Cancer J. 1, e35 (2011).
5. Kleber, M. et al. Validation of the Freiburg Comorbidity Index in 466 Multiple Myeloma Patients and Combination With the International Staging System Are Highly Predictive for Outcome. Clin. Lymphoma Myeloma Leuk. 13, 541–551 (2013).
6. Dold, S. M. et al. Validation of the revised myeloma comorbidity index and other comorbidity scores in a multicenter German study group multiple myeloma trial. Haematologica 106, 875–880 (2021).
7. Fried, L. P. et al. Frailty in Older Adults: Evidence for a Phenotype. The Journals of Gerontology: Series A 56, M146–M157(2001)

Acknowledgements:
MYRIAM and CARO are designed, managed and analyzed by iOMEDICO and receive continuous financial support from AMGEN GmbH (CARO) and AMGEN GmbH, Bristol Myers Squibb GmbH & Co. KgaA, GSK Research and Development Limited, Janssen-Cilag GmbH and Oncopeptides AB (until May 2022) (MYRIAM). None of the funders had any role in study design, data collection and analysis, interpretation of results, decision to publish, or preparation of the abstract.

Conflicts of Interest:
The authors declare no conflicts of interest.

In cooperation with:

DGHO Jahrestagung 2022
7. October - 10. October, Vienna
Posternummer: P978