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Blood 142 (2023) 4733–4734

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Comparison of Lenalidomide Based Triplets (IRD, KRD and DRD) in Relapsed and Refractory Multiple Myeloma in Routine Practice

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Background: Treatment of relapsed and refractory multiple myeloma (RRMM) has become a chalenge with the introduction of combined lenalidomide-based triplets. The addition of proteasome inhibitors (PI) or monoclonal antibodies (MoAb) significantly improved the therapeutic outcomes of previous RD regimen (lenalidomide, dexamethasone). The clinical trials with RD triplets confirmed the outstanding synergistic effects of lenalidomide with PIs or MoAbs. However, the outcomes between individual regimens are not easily comparable as the trials used different cohorts of patients. Moreover, the clinical trials often overestimate the outcomes due to selection bias.
Aims: Our aim was to compare the outcomes of lenalidomide-based triplets in an unselected "real-world population".
Patients and methods: We performed a large registry based analysis of RRMM patients treated with daratumumab, lenalidomide and dexamethasone (DRD), carfilzomib, lenalidomide and dexamethasone (KRD), and ixazomib, lenalidomide and dexamethasone (IRD) from the Czech Registry of Monoclonal Gammopathies (RMG) treated within 1st-3rd relapse. We excluded patients treated in clinical trials as well as patients with follow-up shorter than 6 months. For the IRD combination we performed 2 separate analyses: from 2016-2018 (early IRD, e-IRD) and 2019 onwards (late IRD, l-IRD), as the first cohort was treated within a Named Patient Program and had no competitive RD triplet or clinical trial, whereas patients treated after 2019 were those who were generally not eligible for competing KRD or DRD regimens.
Altogether we assessed 224 patients with DRD regimen, 143 with KRD, 104 with e-IRD and 67 with l-IRD regimen.
Data were described by absolute and relative frequencies of categorical variables and median (min-max and 5 th-95 th percentile) for quantitative variables. Survival analysis for different endpoints - overall survival (OS), progression free survival (PFS), time to next treatment (TNT), and duration of therapy (DOT) - was conducted using the Kaplan-Meier method complemented by the 95% Greenwood confidence interval for estimates of probability survival. Statistical significance of differences in survival among subgroups was assessed using the log-rank test. All statistical tests were performed at a significance level of $\alpha = 0.05$ (all tests two-sided).

Results: There were slight but significant differences within the demographic data: Patients treated with DRD and KRD were younger than patients on both e-IRD and l-IRD (median 65.5 vs 64.4 vs 67.2 vs 69.9 years) and had better overal performance status (PS 0 or 1 in 87.9 vs 92.2 vs 83.5 vs 76.1%). They were also less pretreated (1 previous line in 73.2 vs 70.6 vs 62.5 vs 38.8%). Also, patients on DRD and KRD had slightly lower ISS stage versus e-IRD and l-IRD patients (ISS 1 in 48.4 vs 55.5 vs 42.2 vs 37.5%). Patients on KRD had slightly higher presence of extramedullary and/or paraskeletal disease (45.6% versus 32.5% and 35.0% vs 31.6% in DRD and e-IRD and l-IRD, respectively). The presence of high-risk cytogenetics was higher in KRD and l-IRD (42.7 vs 53.1%) than in the e-IRD and DRD group (32.3% and 24.6%).
The overal response rates (ORR) in DRD, KRD, e-IRD and l-IRD were following: 91.4% vs 89.6% vs 79.6% vs 70.8%. The rates of very good partial response or better (VGPR+) were 67.3% vs 62.3% vs 40.8% vs 25%.
Median PFS in DRD vs KRD vs e-IRD vs l-IRD was 23.64 vs 16.52 vs 19.97 vs 11.57 months. Due to short follow-up, the median OS was not assessable with an estimate around 40 months for all the cohorts.
The toxicity was similar to the data reported from clinical trials with no new safety alerts.
Conclusions: We conclude that lenalidomide based triplets (DRD, KRD and IRD) have significant efficacy in RRMM even in the routine clinical practice but as expected, they do not achieve the outcomes reported in clinical trials. DRD regimen seems to be the most efficient regimen even in "real-world" setting but the results are biased by the cohort heterogeneity. The outcome of a regimen in "real-world" depends significantly on other variables including competing regimens or clinical trials, and may have large individual differences as seen in the case of e-IRD (assessed at the time with no competing lenalidomide-based triplets) versus l-IRD (influenced by the choice between several effective modalities).
Supported by MH CZ - DRO (FNOL, 00098892).

Disclosures Spicka: *Sanofi:* Consultancy, Other: Received payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; Participation on a Data Safety Monitoring Board or Advisory Board; *Janssen-Cilag:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; Support for attending meetings and/or travel events; *Karyopharm:* Membership on an entity's Board of Directors or advisory committees; *Takeda:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; Support for attending meetings and/or travel events; *GSK:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Novartis:* Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; *Amgen:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; Support for attending meetings and/or travel events; *Celgene:* Consultancy, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; Support for attending meetings and/or travel events; *Bristol Myers Squibb:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; Support for attending meetings and/or travel events. **Radocha:** *GlaxoSmithKline:* Consultancy, Honoraria; *Amgen:* Consultancy, Honoraria; *Sanofi:* Consultancy, Honoraria, Other: Travel expenses; *Janssen:* Consultancy, Honoraria, Other: Travel expenses; *Bristol Myers Squibb:* Consultancy, Honoraria, Other: Travel expenses. **Hajek:** *Takeda:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Support for attending meetings and/or travel, Research Funding; *Novartis:* Consultancy, Research Funding; *Bristol Myers Squibb:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Celgene:* Consultancy, Honoraria, Other: Support for attending meetings and/or travel, Research Funding; *Amgen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Support for attending meetings and/or travel, Research Funding; *Janssen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Support for attending meetings and/or travel, Research Funding; *Sanofi:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Oncopeptides:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *GlaxoSmithKline:* Membership on an entity's Board of Directors or advisory committees; *AbbVie:* Consultancy; *PharmaMar:* Consultancy, Honoraria.

https://doi.org/10.1182/blood-2023-179299