soho2023
ELEVENTH ANNUAL MEETING

Multiple Myeloma Oligosecretory Relapse – A Cross Sectional Historical Cohort Study

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INTRODUCTION

- Presence of monoclonal antibodies in the serum and/or urine, secreted by malignant plasma cells is the hallmark of multiple myeloma (MM)
- Infrequently, monoclonal protein (M-protein) and involved free light chain (iFLC) are either **not detected** or are both **below the threshold for measurable disease**, termed **oligo-secretory MM**
- The incidence of oligo-secretory MM at presentation was found to be around 10%[1,2]
- **Data regarding the frequency and clinical phenotype of oligo-secretory relapse (OSR) are lacking**

AIM

To report the characteristics and outcomes of OSR.

METHODS

Definitions

Oligosecretory myeloma:

- M-protein<1 gr/dL &
- U-PEP <200 mg/24 hrs &
- iFLC< 10 mg/dL

Relapse in the absence of measurable disease in serum or urine, was defined by IMWG criteria[3]:

- new or increasing lesion(s)
- increase in bone marrow or circulating plasma cells (PCs)

Index OSR *defined as the 1st OSR that the patient experienced.*

Study population

The OSR Cohort - included all consecutive MM pts who had **measurable disease at diagnosis and developed an OSR** between January 2016 and July 2020, across two centers (Mayo Clinic Rochester, US and Tel Aviv Sourasky medical center, Israel)

The SR Cohort - for each patient (pt) with an OSR, we identified a pt with a secretory relapse (SR) in the dataset, matched by the relapse index number, calendar year of relapse, and medical center.

Analysis

We compared pt and disease characteristics at MM diagnosis and at relapse, therapy patterns, and outcomes between the OSR and SR groups.

RESULTS

905 patients with RRMM were identified, 57 (6.3%) had OSR; 40 at Mayo, 17 at TLVMC.

Patients & Disease Characteristics at Diagnosis

Variable	OSR (n=57)	SR (n=57)	P value
Age, median (IQR)	59.8 (53-65)	65.6 (56-69.5)	0.038
Male/Female, %	53/47	54/46	0.85
Heavy chain IgG/IgA/IgD, %	54/34/0	70/13/3.8	0.091
Light chain kappa/lambda, %	70/30	60/40	**<0.001**
M-protein, g/dL, median (IQR)	2.3 (1.25-3.7)	2.2 (0.35-4.05)	0.372
Involved Ig levels, mg/dL, median (IQR)	3240 (2525-4967)	2790 (1067-5050)	0.144
Involved LC, mg/dL, median (IQR)	13.83 (4.63-67.3)	133 (34.4-554)	**<0.001**
ISS (I/II/III), n (%)	44/25/31	29/29/42	0.35
FISH*: high risk/standard risk. N (%)	14 (26)	18 (34.6)	0.33
Bone marrow plasma cells, %	40 (25-65)	60 (30-80)	**0.02**
Renal failure, N (%)	6 (10.5)	16 (28)	**0.018**
Hypercalcemia, N (%)	10 (17.5)	14 (24.6)	0.358
Bone disease, %	44 (77.2)	43 (75.4)	0.826
Extramedullary disease, %	5 (8.8)	4 (7.1)	1

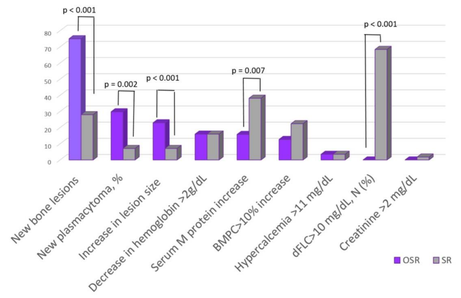
**high risk FISH - del17p, t(4;14), t(14;16); t(14;20), gain 1q*

Patient Characteristics at Index Relapse

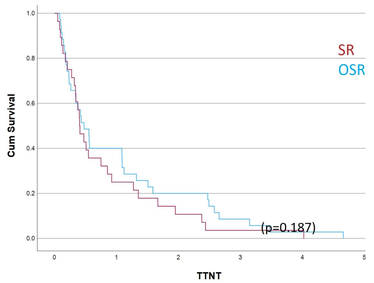
Most (66.6%) OSR occurred in early relapses (first (n=21) or second (n=17)).

	OSR	SR	P value
Serum creatinine, mg/dL, median (IQR)	0.93 (0.7-1.1)	1 (0.9-1.21)	**0.011**
PLT, median (IQR)	172 (127-232)	140 (114-198)	**0.025**
M-protein, g/dL, median (IQR)	0.2 (0-0.575)	0.5 (0-1.775)	**0.014**
Involved LC, mg/L, median (IQR)	2.5 (1.65-4.24)	19 (12.85-47.3)	**<0.001**
LDH, median (IQR)	330 (205-424)	271 (160-452)	0.532

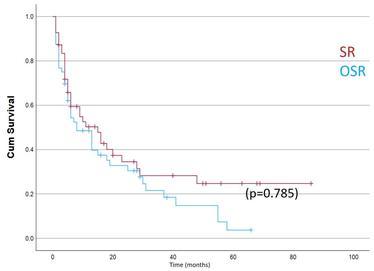
Criteria for Relapse: OSR vs. SR



Time to Next Treatment



Overall Survival



CONCLUSIONS

- OSR pts differed from SR patients starting at MM onset, with **younger age, lower iFLC** and **PC infiltration**, and **kappa predominance**
  → suggests an inherent biological difference associated with attenuation of immunoglobulin production at relapse
- OSR was characterized by worse bone disease and extra-medullary lesions; response assessments were frequently unavailable
  → probably due to the challenge of effective monitoring of disease response in the absence of laboratory biomarkers
- Improved monitoring strategies for OSR pts are warranted
- Awareness is warranted for OSR, in particular among patients with low PC infiltration and low iFLC at diagnosis

REFERENCES

1. Migkou et al. Clinical characteristics and outcomes of oligosecretory and non-secretory multiple myeloma. Ann Hematol. 2020.
2. Larson et al. Prevalence and monitoring of oligosecretory myeloma. N Engl J Med. 2012.
3. Kumar et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. The Lancet Oncology. 2016.

CONTACT INFORMATION

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