IS IT TIME TO FIGHT MULTI-REFRACTORINESS IN PATIENTS WITH FIRST RELAPSE IN MULTIPLE MYELOMA IN ITALY?

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BACKGROUND

First-line Multiple Myeloma (MM) therapy is rapidly evolving, more and more including anti-CD38 antibodies with lenalidomide (R) and/or proteasome inhibitors. So multi-refractoriness is increasing and depends on therapies approval time by national regulatory agencies, various therapies' time to progression as well as attrition rate, resulting in different multi-refractory pts burden in several countries.

PURPOSE/METHODS

The aim of this study is to recognize the current refractory MM pts burden and the future potential one, analysing our single tertiary centre MM population, defining a current and a near future refractoriness real-life scenario. We retrospectively analysed 476 patients, treated from 2010 to 2024, among whom we considered 324 relapsed pts.

RESULTS

Previous therapies at first relapse	No 324 (%)
Induction	
Standard	187 (58)
Clinical trial	137 (42)
ASCT	109 (34)
Maintenance	84
R	49 (59)
KR	6 (7)
Dara-R	1 (1)
Ixa	2 (2)
Dara	1 (1)
Others	25 (30)
Continuous therapy	169 (52)
Rd/R	159
Dara-Rd	6
Dara-VMP	4
Refractoriness	
Not-refractory	155 (48)
R-refractory	159 (49)
Dara-ref	6 (2)
Dara-R	4 (1)

From 2010 to 2024, we treated 476 patients among whom 324 relapsed and 152 did not. In the 324 relapsed pts median age was 71 years (range 30-93), 84 patients (25%) had PS ≥ 2, 110 patients (34%) were high-risk cytogenetic and 255 (79%) were intermediate-high risk R-ISS. Images on the left describe therapeutic patterns.

Splitting these 324 pts into 3 groups according to years of relapse we obtained:

- **first period:** 2010-2015, 117 pts
- **second period:** 2016-2021, 146 pts
- **third period:** 2022-2024, 61 pts.

Their refractory status spread as follows:

- 42 pts (36%) were **R-ref i**n the first period, 87 (60%) in the second and 30 (50%) in the third period;
- **dara-R-ref** was recognized in 6 (10%) pts only in the third period;
- **dara-ref** in none pts, 1 (1%) and 3 (5%) in the 3 periods, respectively (Figure below).

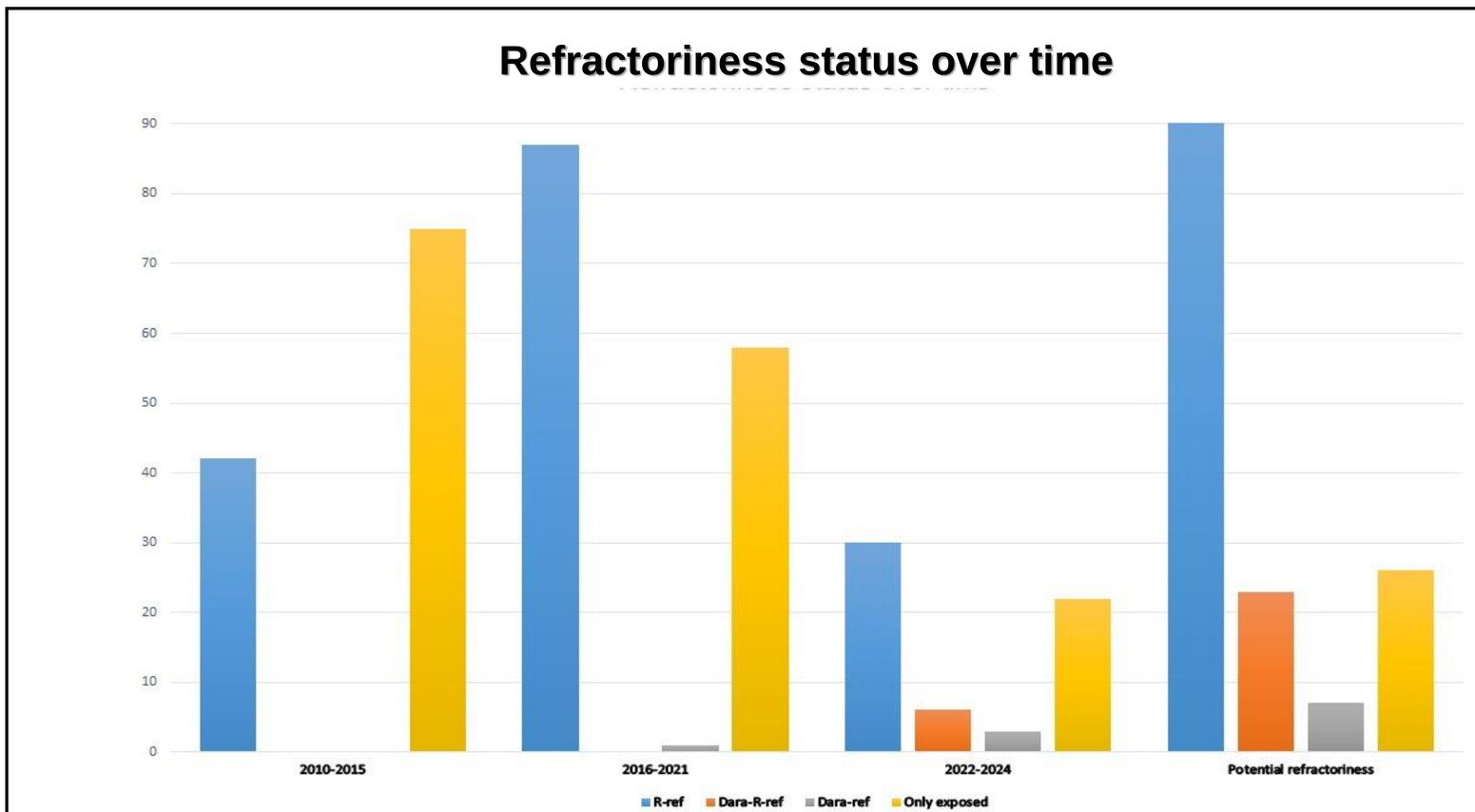
Second line therapy was detailed on the figure on the left. Out of these, 59 (63%) pts are receiving R-based treatment so they could become R-ref at first relapse, 23 (15%) dara-R becoming double-ref, 7 (5%) dara becoming dara-ref and 26 (17%) fixed therapy remaining only exposed.

Relapsed patients from LOT1 324

Relapsed patients from cont therapy = 169
Relapsed patients from fixed therapy= 155

Second line therapy = 244

Therapies	≤ 2015 (%) No Pts: 95	2016-2021 (%) No Pts: 100	2022-2025 (%) No Pts: 49
PI-based	51 (54)	30 (30)	6 (12)
IMiDs-based	40 (42)	28 (28)	9 (18)
PVD	0	3 (3)	5 (10)
Dara-based	0	27 (27)	13 (27)
DaraPd	0	1 (1)	2 (4)
DaraRd	0	22 (22)	9 (18)
DaraVd	0	4 (4)	2 (4)
Isa-based	0	0	10 (21)
Teclistamab	0	0	2 (4)
Other	4 (4)	12 (12)	4 (8)



CONCLUSIONS

Only exposed pts are decreasing over time, due to the major spread of continuous frontline therapies in MM landscape. However, the current highest burden of refractoriness at first relapse consisted of the R exposure/refractoriness. Considering available regimens, new therapies approval time and their time to progression, the challenging problem will continue to be R exposition/refractoriness rather than multi-refractoriness, that will be low for some years to come.

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