

# Isatuximab, pomalidomide, and dexamethasone as salvage therapy for patients with multiple myeloma: the Italian, multicenter, retrospective clinical experience with 270 cases outside of controlled clinical trials

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## SUPPLEMENTARY APPENDIX CONTENTS

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**CONFLICT OF INTERESTS:** No conflict

**Supplementary Tables**

**Supplementary Table 1. Comparison of characteristics at baseline between the cohorts of patients treated with IsaPd in a real-world setting and those enrolled in the ICARIA-MM clinical trial.**

|                                                  | <b>ICARIA-MM trial</b> | <b>Italian Real-World study</b> | <b>UK-Wide Real-World study</b> | <b>IMAGE Real-World study</b> |
|--------------------------------------------------|------------------------|---------------------------------|---------------------------------|-------------------------------|
| <b>Time of accrual</b>                           | Jan 2017/<br>Feb 2018  | Jan 2021/<br>Jun 2024           | Jan 2020/<br>May 2021           | Jul 2019/<br>Sep 2020         |
| <b>No of cases</b>                               | 154                    | 270                             | 107                             | 299                           |
| <b>Median follow-up (months)</b>                 | 52.4                   | 23.5                            | 12.1                            | 14.2                          |
| <b>Median age (years)</b>                        | 68                     | 69                              | 69                              | 70.2                          |
| range                                            | (60-74)                | (39-88)                         | (61-77)                         | (39.9-89.8)                   |
| ≥75 (%)                                          | 21                     | 24.1                            | NR                              | 28.2                          |
| <b>Creatinine Clearance (mL/min) (%)</b>         |                        |                                 |                                 |                               |
| <60                                              | 39                     | 29.3                            | 43                              | 36.6                          |
| <30                                              | --                     | 3.7                             | 7.5                             | 10.8                          |
| <b>Stage ISS, (%)</b>                            |                        |                                 |                                 |                               |
| III                                              | 22                     | 13.7                            | 32.9                            | 36.4                          |
| <b>Previous lines of therapy, median (range)</b> |                        |                                 |                                 |                               |
|                                                  | 3 (2-4)                | 2 (2-7)                         | 3 (3-3)                         | 2 (1-9)                       |
| <b>Prior daratumumab exposure (%)</b>            | --                     | 18.9                            | 4.7                             | 26.5                          |
| <b>Lenalidomide refractory (%)</b>               | 94                     | 98.5                            | 100*                            | 73.1                          |
| <b>FISH analysis (%)</b>                         |                        |                                 |                                 |                               |
| High Risk <sup>o</sup>                           | 33.1                   | 29.3                            | 14                              | 13.6                          |
| <b>ORR (%)</b>                                   | 63                     | 74.1                            | 66.4                            | 46.3                          |
| <b>median PFS (months)</b>                       | 11.1                   | 15.7                            | 10.9                            | 12.4                          |
| <b>median OS (months)</b>                        | 24.6                   | NR                              | 18.8                            | NR                            |
| <b>median TTNT (months)</b>                      | 15.5                   | 17.7                            | NA                              | 15.1                          |
| <b>Grade 3-4 adverse events (%)</b>              |                        |                                 |                                 |                               |
| Anemia                                           | 35                     | 13.7                            | 8.4                             | NA                            |
| Neutropenia                                      | 51                     | 56.3                            | 45.8                            | NA                            |
| Thrombocytopenia                                 | 13                     | 15.9                            | 14                              | NA                            |
| Infections                                       | 53                     | 47.8                            | 18.7                            | NA                            |
| Pneumonia                                        | 23                     | 26.7                            | NA                              | NA                            |
| Fatigue                                          | 4                      | 16.3                            | 0.9                             | NA                            |
| Gastrointestinal toxicity                        | 9                      | 6.3                             | NA                              | NA                            |

\*Lenalidomide exposed; \*High Risk= patients with the presence of either t(4;14), or t(14;16) or del(17p); NR= not reached; NA= not available

1 **Supplementary Table 2. Univariable and multivariable analyses for PFS (Panel 1) and OS (Panel 2).**

2

3 **PANEL 1**

|                                    |     | Univariable analysis |                  |                   | Multivariable analysis |              | 4  |
|------------------------------------|-----|----------------------|------------------|-------------------|------------------------|--------------|----|
|                                    | N   | PFS @ 24 months      | HR (%95 CI)      | P-value           | HR (%95 CI)            | P-value      | 5  |
| <b>Age, (years)</b>                |     |                      |                  |                   |                        |              | 6  |
| ≤70                                | 159 | 44.1                 |                  |                   |                        |              | 7  |
| >70                                | 111 | 31.3                 | 1.35 (0.98-1.85) | 0.064             |                        |              | 8  |
| <b>Gender</b>                      |     |                      |                  |                   |                        |              | 9  |
| Male                               | 147 | 39                   |                  |                   |                        |              | 10 |
| Female                             | 123 | 39.1                 | 1.16 (0.84-1.59) | 0.37              |                        |              | 11 |
| <b>Creatinine Clearance mL/min</b> |     |                      |                  |                   |                        |              | 12 |
| ≥60                                | 191 | 43                   |                  |                   |                        |              | 13 |
| <60                                | 79  | 28.7                 | 1.49 (1.07-2.09) | <b>0.019</b>      | 1.15 (0.79-1.68)       | 0.44         | 14 |
| <b>ISS</b>                         |     |                      |                  |                   |                        |              | 15 |
| I                                  | 131 | 48.6                 |                  |                   |                        |              | 16 |
| II                                 | 102 | 35.6                 | 1.57 (1.1-2.22)  | <b>0.011</b>      | 1.47 (1.03-2.12)       | <b>0.035</b> | 17 |
| III                                | 37  | 14.1                 | 3.14 (1.99-4.96) | <b>&lt;0.0001</b> | 2.44 (1.45-4.1)        | <b>0.001</b> | 18 |
| <b>LDH serum level</b>             |     |                      |                  |                   |                        |              | 19 |
| Normal                             | 222 | 42.5                 |                  |                   |                        |              | 20 |
| Elevated                           | 48  | 21.7                 | 1.84 (1.26-2.69) | <b>0.001</b>      | 1.51 (1.02-2.25)       | <b>0.04</b>  | 21 |
| <b>Previous lines of therapy</b>   |     |                      |                  |                   |                        |              | 22 |
| 2                                  | 172 | 40.4                 |                  |                   |                        |              | 23 |
| >2                                 | 98  | 36.1                 | 1.23 (0.90-1.7)  | 0.19              |                        |              | 24 |
| <b>Previous ASCT</b>               |     |                      |                  |                   |                        |              | 25 |
| No                                 | 107 | 36.7                 |                  |                   |                        |              | 26 |
| Yes                                | 163 | 40.5                 | 1.08 (0.78-1.48) | 0.63              |                        |              | 27 |
| <b>Previous daratumumab</b>        |     |                      |                  |                   |                        |              | 28 |
| No                                 | 219 | 42.9                 |                  |                   |                        |              | 29 |
| Yes                                | 51  | 16.3                 | 2.12 (1.43-3.13) | <b>&lt;0.0001</b> | 1.87 (1.26-2.79)       | <b>0.002</b> | 30 |
| <b>Disease status</b>              |     |                      |                  |                   |                        |              | 31 |
| Biochemical relapse                | 57  | 44.6                 |                  |                   |                        |              | 32 |
| Symptomatic relapse                | 141 | 38.7                 | 1.21 (0.78-1.85) | 0.39              |                        |              | 33 |
| Refractory to last treatment       | 72  | 33.8                 | 1.59 (0.98-2.54) | 0.06              |                        |              | 34 |

36

37

38

**PANEL 2**

|                                    |     | Univariable analysis |                  |                   | Multivariable analysis |              |
|------------------------------------|-----|----------------------|------------------|-------------------|------------------------|--------------|
|                                    | N   | OS @ 24 months       | HR (%95 CI)      | P-value           | HR (%95 CI)            | P-value      |
| <b>Age, (years)</b>                |     |                      |                  |                   |                        |              |
| ≤70                                | 159 | 66.9                 |                  |                   |                        |              |
| >70                                | 111 | 60.2                 | 1.42 (0.93-2.17) | 0.11              | -                      |              |
| <b>Gender</b>                      |     |                      |                  |                   |                        |              |
| Male                               | 147 | 62.2                 |                  |                   |                        |              |
| Female                             | 123 | 66.9                 | 0.95 (0.62-1.46) | 0.82              | -                      |              |
| <b>Creatinine Clearance mL/min</b> |     |                      |                  |                   |                        |              |
| ≥60                                | 191 | 70.1                 |                  |                   |                        |              |
| <60                                | 79  | 49.5                 | 2.05 (1.33-3.16) | <b>0.001</b>      | 1.52 (0.94-2.46)       | 0.088        |
| <b>ISS</b>                         |     |                      |                  |                   |                        |              |
| I                                  | 131 | 75.1                 |                  |                   |                        |              |
| II                                 | 102 | 60.8                 | 2.03 (1.24-3.33) | <b>0.005</b>      | 1.77 (1.06-2.95)       | <b>0.029</b> |
| III                                | 37  | 31.1                 | 3.63 (2.0-6.59)  | <b>&lt;0.0001</b> | 2.23 (1.13-4.4)        | <b>0.02</b>  |
| <b>LDH serum level</b>             |     |                      |                  |                   |                        |              |
| Normal                             | 222 | 68.9                 |                  |                   |                        |              |
| Elevated                           | 48  | 42.9                 | 2.44 (1.53-3.89) | <b>&lt;0.0001</b> | 2 (1.22-3.28)          | <b>0.006</b> |
| <b>Previous lines of therapy</b>   |     |                      |                  |                   |                        |              |
| 2                                  | 172 | 68.1                 |                  |                   |                        |              |
| >2                                 | 98  | 57.5                 | 1.59 (1.04-2.44) | <b>0.032</b>      | 1.26 (0.8-1.98)        | 0.31         |
| <b>Previous ASCT</b>               |     |                      |                  |                   |                        |              |
| No                                 | 107 | 66.2                 |                  |                   |                        |              |
| Yes                                | 163 | 62.7                 | 1.07 (0.69-1.65) | 0.77              | -                      |              |
| <b>Previous daratumumab</b>        |     |                      |                  |                   |                        |              |
| No                                 | 219 | 68.8                 |                  |                   |                        |              |
| Yes                                | 51  | 36.0                 | 2.05 (1.25-3.38) | <b>0.005</b>      | 1.6 (0.95-2.71)        | 0.079        |
| <b>Disease status</b>              |     |                      |                  |                   |                        |              |
| Biochemical relapse                | 57  | 73.8                 |                  |                   |                        |              |
| Symptomatic relapse                | 141 | 62.1                 | 1.48 (0.8-2.7)   | 0.21              | -                      |              |
| Refractory to last treatment       | 72  | 61                   | 1.9 (0.98-3.72)  | 0.06              | -                      |              |

**Supplementary Table 3. Salvage therapy regimens after IsaPd.**

| Salvage therapy regimen                    | No of cases (%)  |
|--------------------------------------------|------------------|
| <b>Ab drug-conjugates</b>                  | <b>38 (33.9)</b> |
| Belantamab                                 | 38 (33.9)        |
| <b>PI containing regimens</b>              | <b>27 (24.1)</b> |
| Kd                                         | 9 (8)            |
| KRd                                        | 1 (0.9)          |
| V-Ctx-d                                    | 4 (3.6)          |
| V-Benda-d                                  | 1 (0.9)          |
| VMP                                        | 1 (0.9)          |
| V-Caelyx-d                                 | 2 (1.8)          |
| Ixa-Rd                                     | 8 (7.1)          |
| Ixa-Ctx-d                                  | 1 (0.9)          |
| <b>XPO-1 inhibitor-containing regimens</b> | <b>9 (8)</b>     |
| Selinexor                                  | 1 (0.9)          |
| SVd                                        | 8 (7.1)          |
| <b>BsAbs</b>                               | <b>8 (7.1)</b>   |
| Teclistamab                                | 6 (5.4)          |
| Talquetamab                                | 1 (0.9)          |
| RO7425781                                  | 1 (0.9)          |
| <b>Anti-SLAMF-7 containing regimens</b>    | <b>1 (0.9)</b>   |
| EloPd                                      | 1 (0.9)          |
| <b>CAR T-cell therapy</b>                  | <b>1 (0.9)</b>   |
| Ciltacabtagene autoleucel                  | 1 (0.9)          |
| <b>Other therapies</b>                     | <b>28 (25)</b>   |
| Bendamustine                               | 1 (0.9)          |
| Ctx                                        | 20 (17.9)        |
| CHOP                                       | 2 (1.8)          |
| Melphalan                                  | 1 (0.9)          |
| Melflufen                                  | 2 (1.8)          |
| D-PACE                                     | 2 (1.8)          |

**Legend:** Ab=antibody; PI=proteasome inhibitor; Kd=carfilzomib, dexamethasone; KRd=carfilzomib, lenalidomide, dexamethasone; V-Ctx-d=bortezomib, cyclophosphamide, dexamethasone; V-benda-d=bortezomib, bendamustine, dexamethasone; VMP=bortezomib, melphalan, prednisone; V-Caelyx-d=bortezomib, caelyx, dexamethasone; IxaRd=ixazomib, lenalidomide, dexamethasone; Ixa-Ctx-d=ixazomib, cyclophosphamide, dexamethasone; XPO-1=exportin-1; SVd=selinexor, bortezomib, dexamethasone; EloPd=elotuzumab, pomalidomide, dexamethasone; Ctx=cyclophosphamide; CHOP=cyclophosphamide, doxorubicin, vincristine, prednisone; D-PACE=dexamethasone, cisplatin, doxorubicin, cyclophosphamide, etoposide.