

# Impact of prior therapy on the efficacy and safety of oral ixazomib-lenalidomide-dexamethasone vs. placebo-lenalidomide-dexamethasone in patients with relapsed/refractory multiple myeloma in TOURMALINE-MM1

María-Victoria Mateos,<sup>1</sup> Tamas Masszi,<sup>2</sup> Norbert Grzasko,<sup>3</sup> Markus Hansson,<sup>4</sup> Irwindeep Sandhu,<sup>5</sup> Ludek Pour,<sup>6</sup> Luísa Viterbo,<sup>7</sup> Sharon R. Jackson,<sup>8</sup> Anne-Marie Stoppa,<sup>9</sup> Peter Gimsing,<sup>10</sup> Mehdi Hamadani,<sup>11</sup> Gabriela Borsaru,<sup>12</sup> Deborah Berg,<sup>13</sup> Jianchang Lin,<sup>13</sup> Alessandra Di Bacco,<sup>13</sup> Helgi van de Velde,<sup>13</sup> Paul G. Richardson<sup>14</sup> and Philippe Moreau<sup>15</sup>

<sup>1</sup>Hospital Universitario de Salamanca, Instituto Biosanitario de Salamanca (IBSAL), Spain; <sup>2</sup>St. István, St. László Hospital, <sup>3</sup>rd Department of Internal Medicine, Semmelweis University, Budapest, Hungary; <sup>3</sup>Medical University of Lublin and St John's Cancer Center, Lublin, Poland; <sup>4</sup>Skåne University Hospital, Lund University, Sweden; <sup>5</sup>University of Alberta Edmonton, Canada; <sup>6</sup>University Hospital Brno, Czech Republic; <sup>7</sup>Instituto Português de Oncologia do Porto Francisco Gentil, Entidade Pública Empresarial (IPOPFG, EPE), Portugal; <sup>8</sup>Middlemore Hospital, Auckland, New Zealand; <sup>9</sup>Institut Paoli-Calmettes, Marseille, France; <sup>10</sup>University Hospital Rigshospitalet, Copenhagen, Denmark; <sup>11</sup>Medical College of Wisconsin, Milwaukee, WI, USA; <sup>12</sup>Spitalul Clinic Coltea, Bucharest, Romania; <sup>13</sup>Millennium Pharmaceuticals Inc., Cambridge, MA, a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, MA, USA; <sup>14</sup>Dana-Farber Cancer Institute, Boston, MA, USA and <sup>15</sup>University Hospital Hôtel Dieu, Nantes, France

©2017 Ferrata Storti Foundation. This is an open-access paper. doi:10.3324/haematol.2017.170118

Received: March 31, 2017.

Accepted: July 19, 2017.

Pre-published: July 27, 2017.

Correspondence: mvmateos@usal.es

---

**Supplementary Table S1. Common grade  $\geq 3$  AEs ( $\geq 5\%$  in any patient subgroup), according to number and type of prior therapies**

	<b>Overall population</b>	<b>PI-naïve</b>	<b>PI-exposed</b>	<b>Immuno-modulatory drug-naïve</b>	<b>Immuno-modulatory drug-exposed</b>	<b>1 prior therapy</b>	<b>2-3 prior therapies</b>
<b>Neutropenia*</b>							
Ixazomib-Rd	81/361 (23)	27/109 (25)	54/252 (21)	35/166 (21)	46/195 (24)	51/212 (24)	30/149 (20)
Placebo-Rd	85/359 (24)	23/109 (21)	62/250 (25)	36/158 (23)	49/201 (24)	49/211 (23)	36/148 (24)
<b>Thrombocytopenia†</b>							
Ixazomib-Rd	69/361 (19)	28/109 (26)	41/252 (16)	29/166 (17)	40/195 (21)	36/212 (17)	33/149 (22)
Placebo-Rd	32/359 (9)	8/109 (7)	24/250 (10)	16/158 (10)	16/201 (8)	18/211 (9)	14/148 (9)
<b>Anemia</b>							
Ixazomib-Rd	34/361 (9)	5/109 (5)	29/252 (12)	18/166 (11)	16/195 (8)	14/212 (7)	20/149 (13)
Placebo-Rd	48/359 (13)	10/109 (9)	38/250 (15)	21/158 (13)	27/201 (13)	18/211 (9)	30/148 (20)
<b>Leukopenia</b>							
Ixazomib-Rd	16/361 (4)	5/109 (5)	11/252 (4)	8/166 (5)	8/195 (4)	8/212 (4)	8/149 (5)
Placebo-Rd	6/359 (2)	4/109 (4)	2/250 (<1)	1/158 (<1)	5/201 (2)	2/211 (<1)	4/148 (3)
<b>Pneumonia</b>							
Ixazomib-Rd	29/361 (8)	4/109 (4)	25/252 (10)	16/166 (10)	13/195 (7)	17/212 (8)	12/149 (8)
Placebo-Rd	31/359 (9)	10/109 (9)	21/250 (8)	14/158 (9)	17/201 (8)	16/211 (8)	15/148 (10)
<b>Peripheral neuropathy‡</b>							
Ixazomib-Rd	9/361 (2)	3/109 (3)	6/252 (2)	2/166 (1)	7/195 (4)	5/212 (2)	4/149 (3)
Placebo-Rd	6/359 (2)	1/109 (<1)	5/250 (2)	5/158 (3)	1/201 (<1)	4/211 (2)	2/148 (1)

Diarrhea							
Ixazomib-Rd	23/361 (6)	6/109 (6)	17/252 (7)	11/166 (7)	12/195 (6)	9/212 (4)	14/149 (9)
Placebo-Rd	9/359 (3)	3/109 (3)	6/250 (2)	6/158 (4)	3/201 (1)	7/211 (3)	2/149 (1)
Rash <sup>§</sup>							
Ixazomib-Rd	9/361 (2)	7/109 (6)	2/252 (<1)	3/166 (2)	6/195 (3)	5/212 (2)	4/149 (3)
Placebo-Rd	6/359 (2)	1/109 (<1)	5/250 (2)	4/158 (3)	2/201 (<1)	5/211 (2)	1/148 (<1)

\*Data based upon standardized MedDRA query, including neutropenia and neutrophil count decreased.

†Data based upon standardized MedDRA query, including thrombocytopenia and platelet count decreased.

‡High-level term including peripheral neuropathy, peripheral sensory neuropathy, peripheral sensorimotor neuropathy, and peripheral motor neuropathy.

§High-level term including acute febrile neutrophilic dermatosis, acneiform dermatitis, allergic dermatitis, drug eruption, erythema multiforme, exfoliative rash, interstitial granulomatous dermatitis, pruritus, generalised pruritus, purpura, rash, erythematous rash, follicular rash, generalised rash, macular rash, maculo-papular rash, maculovesicular rash, morbilliform rash, papular rash, pruritic rash, pustular rash, vesicular rash, red man syndrome, Stevens-Johnson syndrome, Toxic epidermal necrolysis, urticaria, urticarial papular, and vasculitic rash.