

# Effect of Daratumumab on Pneumonia in Patients with Multiple Myeloma Using Population based Real-World Data



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## INTRODUCTION

- Infection due to both disease progression and subsequent treatment is one of the most common causes of premature death in patients with MM.
- Daratumumab improved patient outcomes but increased the risk of infectious complications, including pneumonia.
- The purpose of this study was to analyze the effect of daratumumab on pneumonia in a large population.

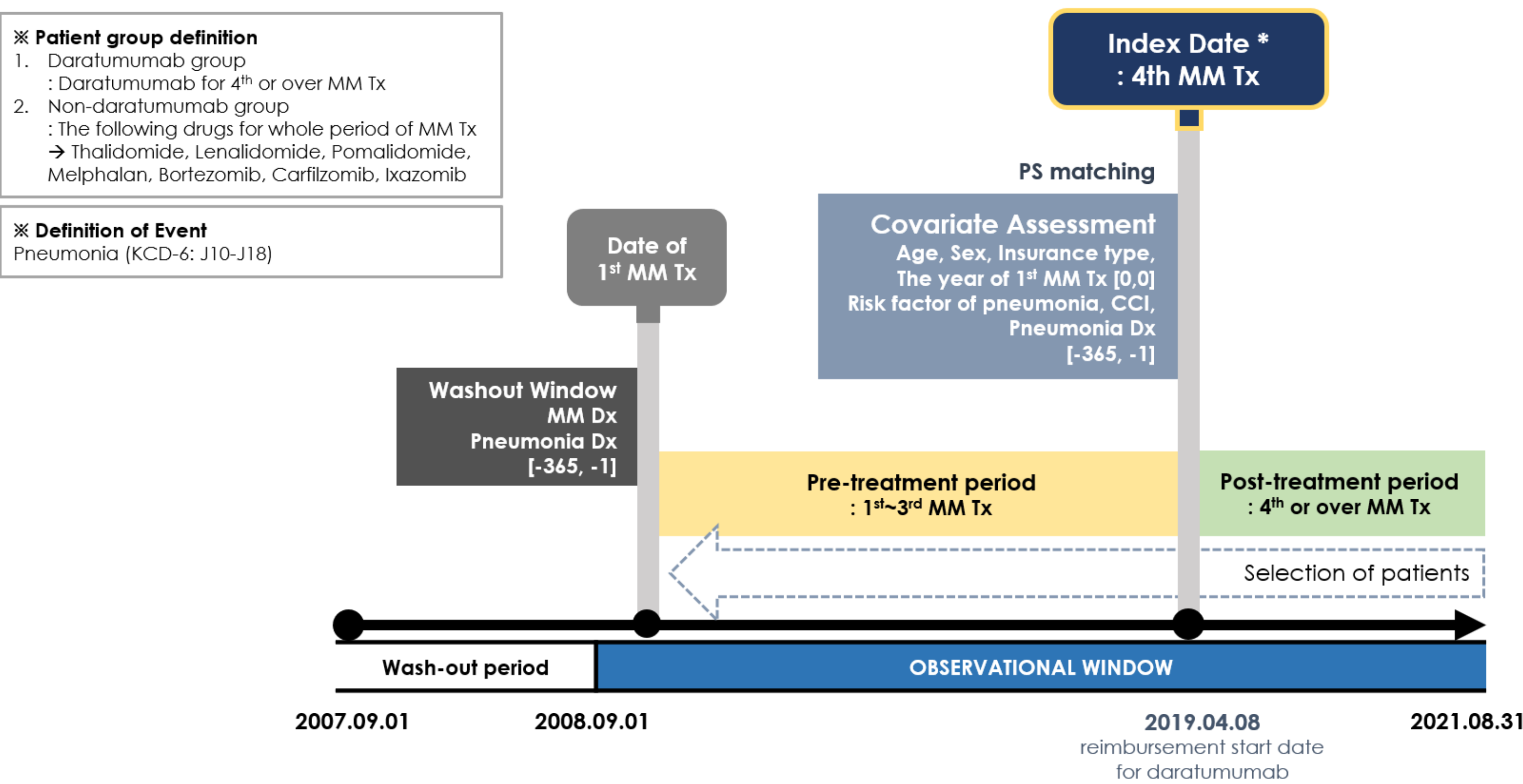
## METHODS

- Study design:** a retrospective observational study
- Data source:** Health Insurance Review and Assessment Service database
- Study population**

|                           |                                                                                                                                   |
|---------------------------|-----------------------------------------------------------------------------------------------------------------------------------|
| Inclusion Criteria        | – Adult patients who experienced MM from the first diagnosis to the fourth-line therapy from September 1, 2008 to August 31, 2021 |
| Exclusion Criteria        | – History of pneumonia within year prior to MM diagnosis<br>– Received Daratumumab from the 1st to the 3rd treatment              |
| Daratumumab group         | Non-Daratumumab group                                                                                                             |
| Daratumumab at least once | MM treatments other than daratumumab (7 drugs) <sup>†</sup>                                                                       |

† As of November 2022, four classes of MM treatments that are covered by insurance reimbursement in Korea

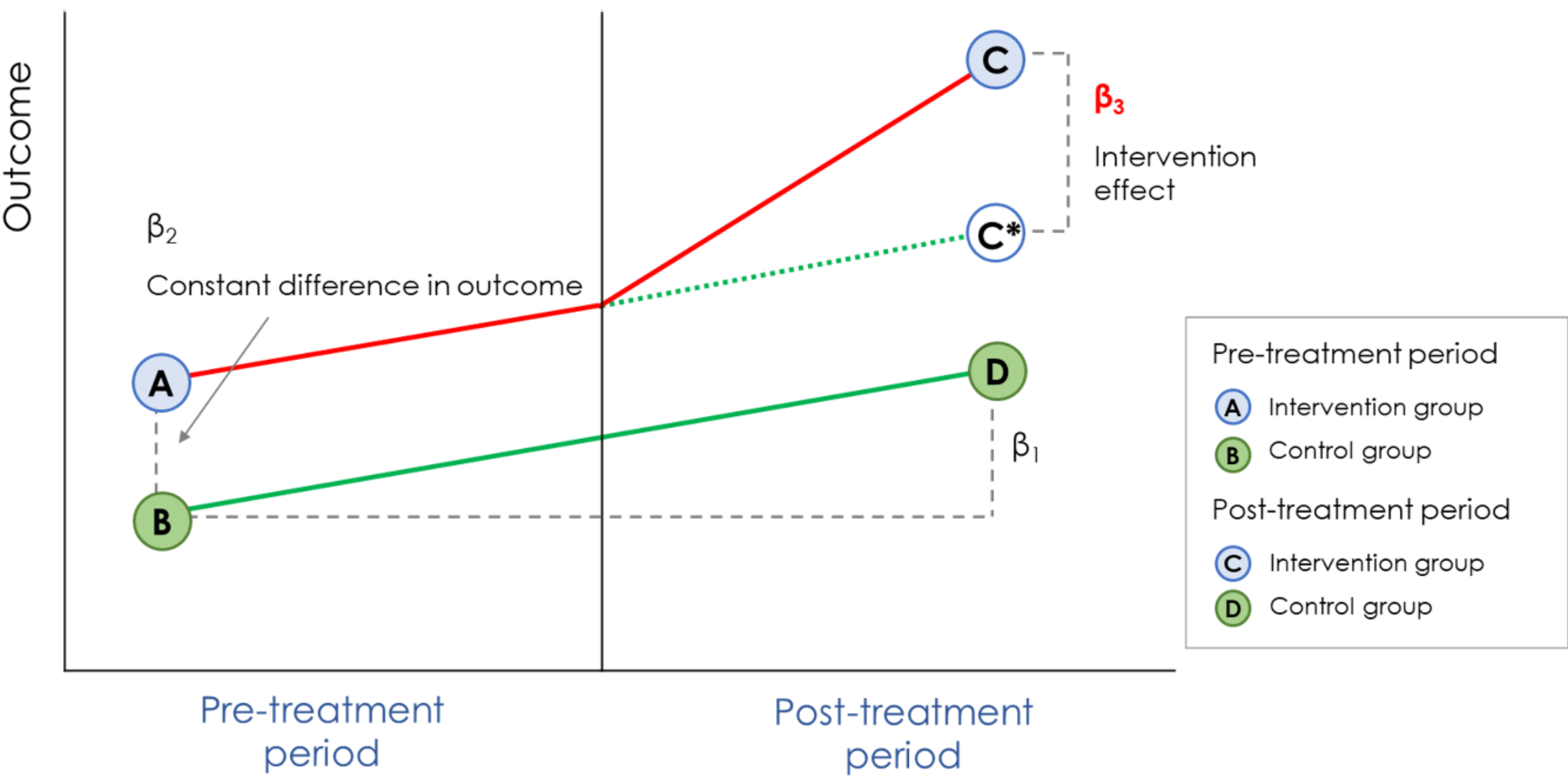
- Study scheme**



Abbreviation, MM, multiple myeloma; Dx, diagnosis; Tx, treatment.

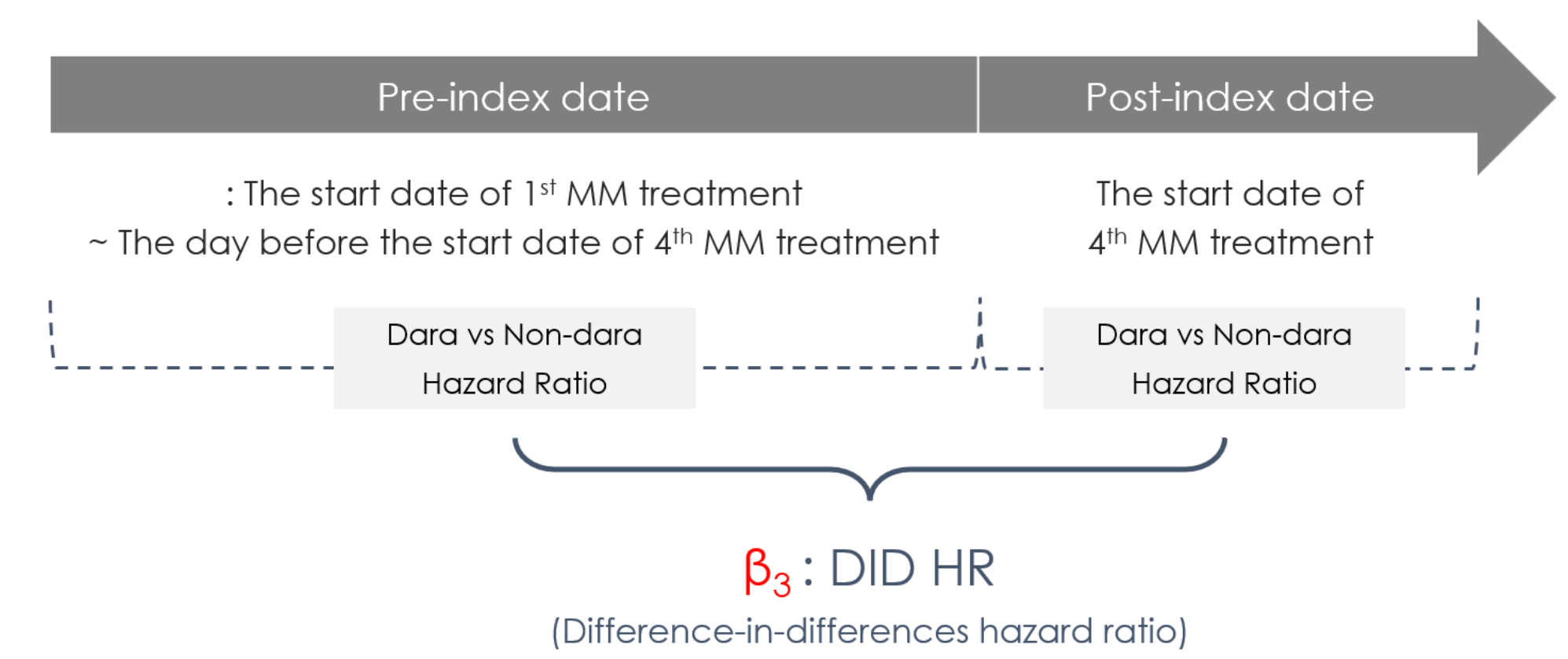
\*In Korea, daratumumab is reimbursed for patients with multiple myeloma who have received at least 3 prior treatments. And for patients with multiple myeloma, daratumumab is reimbursed for combination therapy at full patient responsibility.

- Study outcome**
  - Occurrence of pneumonia during the observational window
  - Diagnosis of pneumonia (ICD 10: J10-J18)
- Statistical analysis**
  - 1:1 Propensity score (PS) matching**
    - using logistic regression model selected based on C-statistics and the balance of matched groups (standardized mean difference)
  - Difference-in-Differences**
    - to control of unobserved confounding factors
    - parallel trend assumption was met



| Coefficient | Calculation | Interpretation                                 |
|-------------|-------------|------------------------------------------------|
| $\beta_0$   | B           | Baseline average                               |
| $\beta_1$   | D-B         | Time trend in control group                    |
| $\beta_2$   | A-B         | Difference between two groups pre-intervention |
| $\beta_3$   | (C-D)-(A-B) | Difference in changes over time                |

- Cox proportional hazard model**
  - covariates: the year of the first MM treatment (confounder with statistically significant difference between two groups after the PS matching)

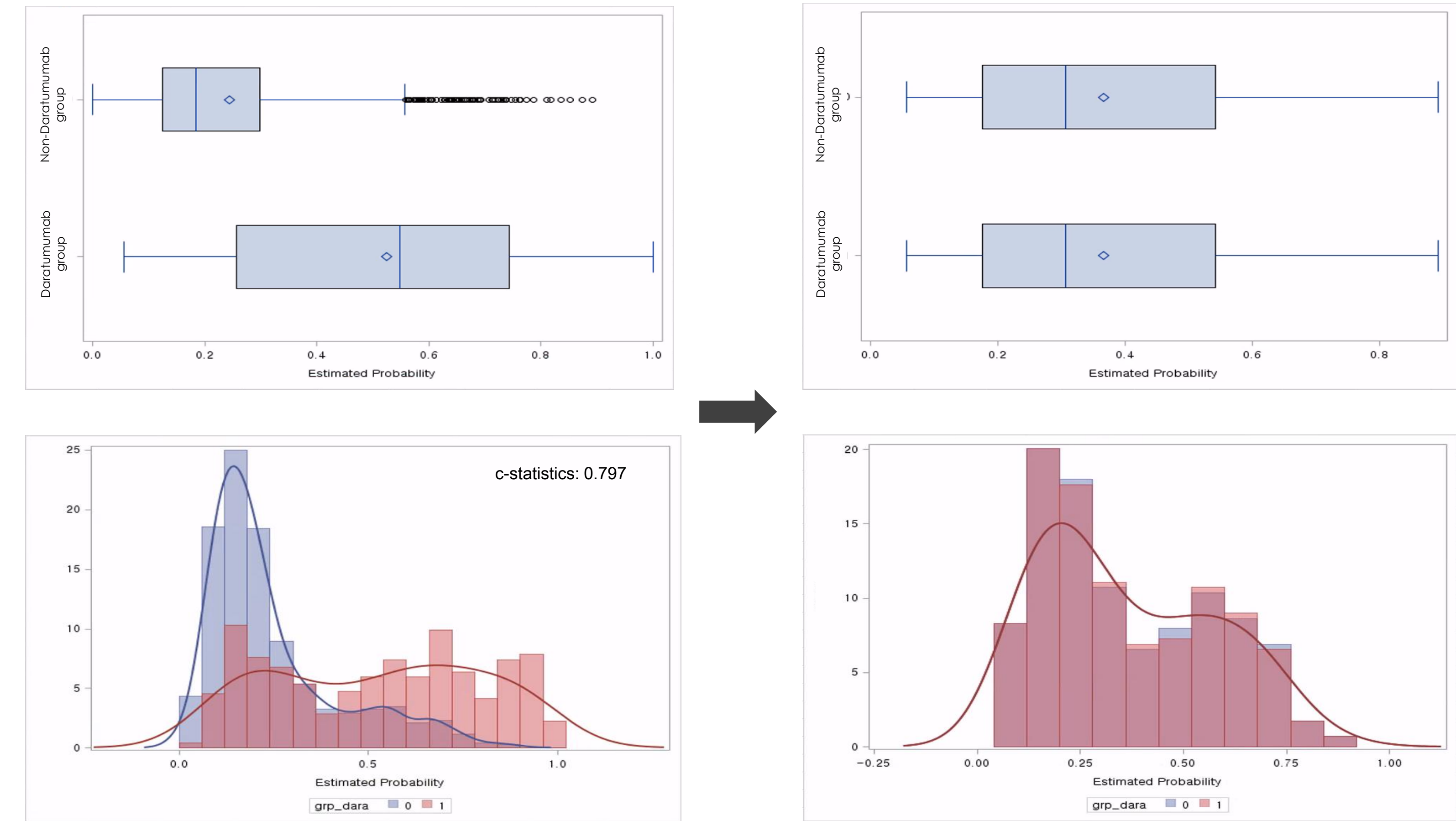


## ACKNOWLEDGEMENT

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## RESULTS

- Propensity score distributions of both groups before and after matching**



- Baseline characteristics before and after PS matching**
- By tracking each patient's treatment history, we identified 1,433 patients who were treated up to the fourth line.
  - Daratumumab group: 485 patients
  - Non-Daratumumab group: 948 patients
- After matching, 289 patients in the daratumumab-group and 289 patients in the non-daratumumab group were selected.

| Characteristics                 | Before propensity score matching |                    |          | After propensity score matching |                    |          |
|---------------------------------|----------------------------------|--------------------|----------|---------------------------------|--------------------|----------|
|                                 | Non-dara group (n=948)           | Dara group (n=485) | STD diff | Non-dara group (n=289)          | Dara group (n=289) | STD diff |
| Age (years),mean(SD)            | 62.47(9.14)                      | 65.62(10.02)       | 0.33     | 63.57(9.47)                     | 61.02(9.52)        | 0.05     |
| Male, %                         | 56.75                            | 50.10              | 0.04     | 51.90                           | 53.98              | -0.01    |
| Prior Treatment, %              |                                  |                    |          |                                 |                    |          |
| Bortezomib                      | 96.41                            | 94.02              | -0.11    | 94.46                           | 93.77              | -0.03    |
| Thalidomide                     | 77.43                            | 51.96              | 0.55     | 64.36                           | 61.59              | -0.06    |
| Lenalidomide                    | 44.20                            | 77.53              | 0.73     | 64.36                           | 65.40              | 0.02     |
| Melphalan                       | 90.08                            | 77.32              | -0.35    | 83.39                           | 85.81              | 0.04     |
| Carfilzomib                     | 12.55                            | 43.92              | 0.74     | 27.68                           | 27.34              | -0.01    |
| Pomalidomide                    | 6.33                             | 34.43              | 0.74     | 13.49                           | 13.84              | 0.01     |
| Ixazomib                        | 0.21                             | 0.62               | 0.06     | 0.69                            | 0.69               | 0        |
| H SCT                           | 71.52                            | 55.46              | -0.34    | 66.09                           | 64.36              | -0.04    |
| The year of 1st MM Treatment, % |                                  |                    |          |                                 |                    |          |
| 2008-2010                       | 14.56                            | 6.19               |          | 6.92                            | 10.03              |          |
| 2011-2013                       | 37.76                            | 18.56              |          | 30.45                           | 26.30              |          |
| 2014-2016                       | 38.61                            | 39.79              | 0.77     | 43.94                           | 43.94              | 0.13     |
| 2017-2020                       | 9.07                             | 35.46              |          | 18.69                           | 19.72              |          |
| Risk Factor, %                  |                                  |                    |          |                                 |                    |          |
| COPD                            | 6.01                             | 8.66               | 0.10     | 5.88                            | 6.57               | 0.03     |
| Asthma                          | 22.36                            | 17.53              | -0.12    | 19.38                           | 20.07              | 0.02     |
| Diabetes Mellitus               | 35.65                            | 35.88              | 0        | 34.60                           | 34.60              | 0        |
| Kidney disease                  | 10.23                            | 12.58              | 0.07     | 11.07                           | 11.07              | 0        |
| Stroke                          | 2.11                             | 2.06               | 0        | 1.38                            | 1.38               | 0        |
| CVD                             | 19.30                            | 23.09              | 0.09     | 19.03                           | 22.49              | 0.09     |
| Liver disease                   | 29.54                            | 34.23              | 0.10     | 30.45                           | 32.18              | 0.04     |
| Dementia†                       | 0                                | 0                  | 0        | 0                               | 0                  | 0        |
| History of pneumonia‡, %        | 32.17                            | 32.37              | 0        | 31.14                           | 30.80              | -0.01    |
| CCI, mean (SD)                  | 2.88(0.33)                       | 2.90(0.30)         | 0.07     | 2.89(0.31)                      | 2.89(0.32)         | -0.01    |

STD diff, standardized difference; MM, multiple myeloma; H SCT, hematopoietic stem cell transplantation; MM, multiple

Myeloma; COPD, Chronic obstructive pulmonary disease;

CVD, Cardiovascular disease; CCI, Charlson comorbidity index

†Since dementia was masked from the data set, its history could not be identified.

‡History of pneumonia was identified by diagnosis within 1-year prior to the index date.

- Difference-in-differences Cox Regression**

- Before PS matching**

|                              | Dara vs Non-dara, HR (95% CI) | DID HR (95% CI)*    | p-value |
|------------------------------|-------------------------------|---------------------|---------|
| Pre-index date <sup>†</sup>  | 1.051 (0.899-1.226)           | 1 [Reference]       | NA      |
| Post-index date <sup>‡</sup> | 1.027 (0.866-1.215)           | 1.023 (0.813-1.288) | 0.8437  |

\* Refers to ratio of non-daratumumab to daratumumab HR in pre-index date compared with non- daratumumab to daratumumab HR in post-index date. Ratios greater than 1 indicate more pneumonia events in post-index date.  
† From the start date of 1st MM treatment to the day before the 4th MM treatment.  
‡ From date of start of 4th MM treatment to date of death or censor or the last observation, whichever comes first.

- After PS matching**

|                              | Dara vs Non-dara, HR (95% CI) | DID HR (95% CI)*    | p-value |
|------------------------------|-------------------------------|---------------------|---------|
| Pre-index date <sup>†</sup>  | 1.019 (0.818-1.271)           | 1 [Reference]       | NA      |
| Post-index date <sup>‡</sup> | 1.097 (0.869-1.389)           | 0.929 (0.673-1.282) | 0.6534  |

\* Refers to ratio of non-daratumumab to daratumumab HR in pre-index date compared with non- daratumumab to daratumumab HR in post-index date. Ratios greater than 1 indicate more pneumonia events in post-index date.  
† From the start date of 1st MM treatment to the day before the 4th MM treatment.  
‡ From date of start of 4th MM treatment to date of death or censor or the last observation, whichever comes first.

## CONCLUSIONS

- Daratumumab remains nearly the sole option for MM patients at the 4th treatment stage or beyond who have experienced failure with prior therapies.
- According to the results of Difference-in-differences Cox regression, there was no statistically significant difference in the effect of Daratumumab on pneumonia compared to other MM treatments.

### [References]

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