

Moonho Kim¹, Yongchel Ahn¹, Heui-June Ahn¹, Ho-Suk Oh¹, Jae-Seok Song², Woong-Sub Park², Sang-Wook Yi²

¹Department of Hematology and Oncology, Gangneung Asan Hospital, University of Ulsan College of Medicine, Gangneung, Republic of Korea, ²Department of Preventive Medicine and Public Health, Catholic Kwandong University College of Medicine, Gangneung, Republic of Korea

BACKGROUND

- Febrile neutropenia (FN) and Chemotherapy-induced neutropenia (CIN) are common conditions involving dose reduction or delayed chemotherapy in patients with diffuse large B-cell lymphoma (DLBCL).
- Primary prophylaxis (PP) by long-acting granulocyte colony-stimulating factor (G-CSF), such as pegfilgrastim, was introduced and available in Korea in 2014.
- However, real-world data on the effects of PP by pegfilgrastim have been lacking in DLBCL patients with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) treatment.
- We aimed to investigate the effects of PP on FN-related hospitalization and death in DLBCL patients with R-CHOP.

OBJECTIVE OF THE STUDY

- To evaluate whether PP by pegfilgrastim is effective in DLBCL treatment, assessed by FN-related hospitalization, mortality, and length of hospital stay (LOS), using healthcare utilization data from the National Health Insurance Service (NHIS).

METHODS

Study population

- The study population included patients aged ≥ 18 years who were newly diagnosed with DLBCL and started receiving R-CHOP, a myelosuppressive chemotherapy, from January 2010 to December 2016 (n=11,491). This is a nationwide cohort of DLBCL patients with R-CHOP treatments. Individuals were followed-up until December 31, 2020, for survival using beneficiary eligibility data, and for FN-related hospitalization using healthcare utilization data
- The NHIS provides health insurance benefits for approximately 98% of the population in Korea. NHIS healthcare utilization database includes information on health services such as treatment details, prescriptions, and bills.

Study exposures (main independent variables)

- **PP exposure** group: patients from January 2014 to December 2015 for whom PP by pegfilgrastim was available
- **Non-exposure** group: patients from July 2011 to June 2013 (who were the control or reference group)

Sensitivity analysis variables

- We performed a sensitivity analysis from 2010 to 2016 by chronological year. In additional sensitivity analyses, patients from 2014 to 2016 were categorized into two groups: **PP use** and **non-use**, based on whether PP was given during the first cycle of R-CHOP.

Outcomes

- The primary endpoint: FN-related hospitalization.
- The secondary endpoint: the 1-year and 5-year mortality.
- The tertiary endpoint: LOS and medical costs incurred after the start of the first cycle of R-CHOP.

RESULTS

- Characteristics of R-CHOP treated DLBCL patients according to PP exposure (n=6616).

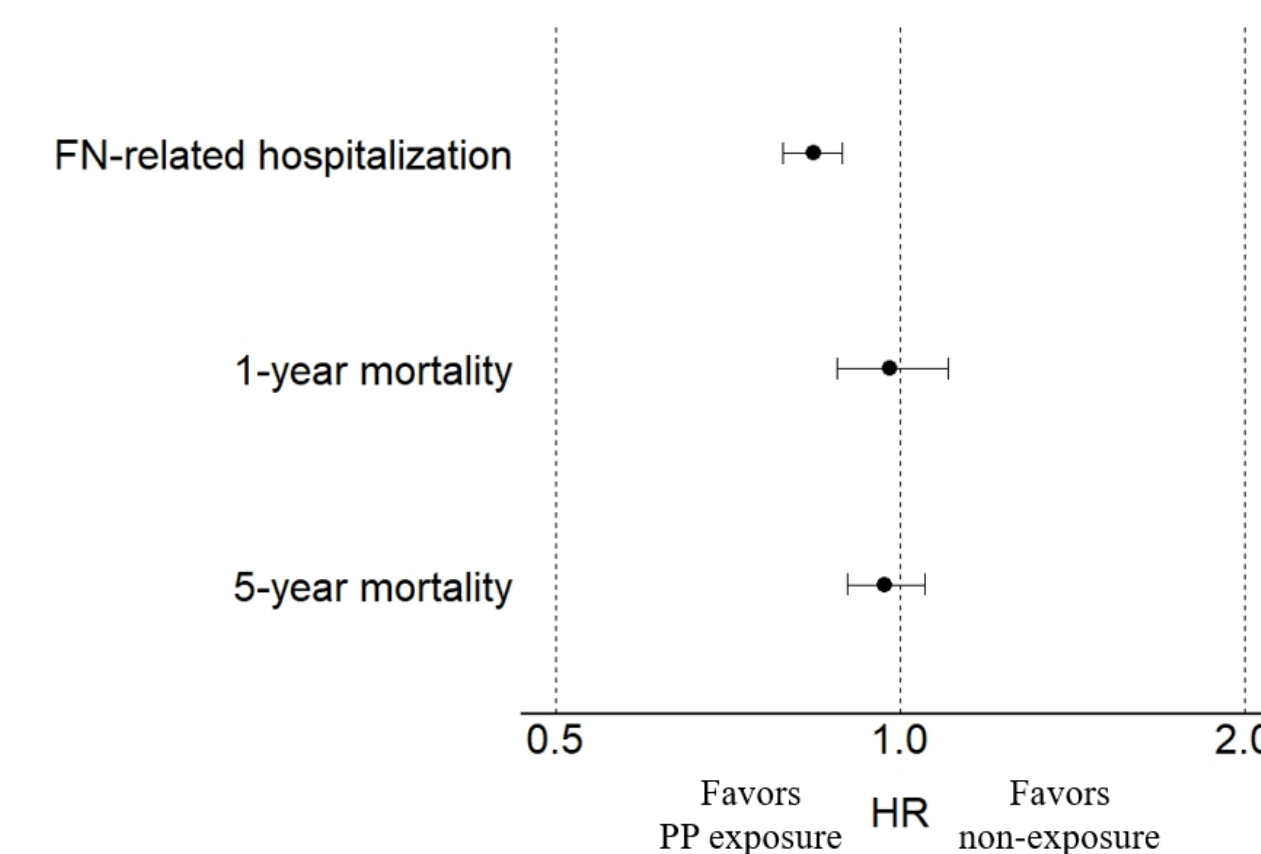
	Non-exposure (Patients from July 2011 to June 2013) (N=3017)	PP exposure (Patients from Jan. 2014 to Dec. 2015) (N=3599)	P-value
Age (mean \pm SD, years)	59.7 \pm 14.4	60.8 \pm 14.6	0.002
R-CHOP cycles (mean \pm SD)	4.9 \pm 1.9	4.9 \pm 1.8	0.162
No. of ER visits with antibiotics use (mean \pm SD, days)	0.0 \pm 0.2	0.0 \pm 0.2	0.721
Sex			0.360
Male	1676 (55.6%)	2053 (57.0%)	
Female	1341 (44.4%)	1546 (43.0%)	
Household income status			0.018
1Q(lowest income)	705 (23.4%)	773 (21.5%)	
2Q	498 (16.5%)	634 (17.6%)	
3Q	667 (22.1%)	819 (22.8%)	
4Q(highest income)	1147 (38.0%)	1373 (38.1%)	
No. of R-CHOP cycles			<0.001
1-2 cycles	448 (14.8%)	513 (14.3%)	
3-4 cycles	624 (20.7%)	610 (16.9%)	
5-6 cycles	1625 (53.9%)	2214 (61.5%)	
7-8 cycles	320 (10.6%)	262 (7.3%)	
Type of hospital treated*			0.952
Tertiary hospital	2377 (78.8%)	2840 (78.9%)	
Others	640 (21.2%)	759 (21.1%)	
No. of FN-related admissions			<0.001
0	1035 (34.3%)	1487 (41.3%)	
1	1085 (36.0%)	1234 (34.3%)	
2	489 (16.2%)	512 (14.2%)	
3	234 (7.8%)	213 (5.9%)	
≥ 4	174 (5.7%)	153 (4.3%)	

Values are presented as n (%), unless indicated.

R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; DLBCL, diffuse large B-cell lymphoma; SD, standard deviation; FN, febrile neutropenia; ER, emergency room; Q, quartile.

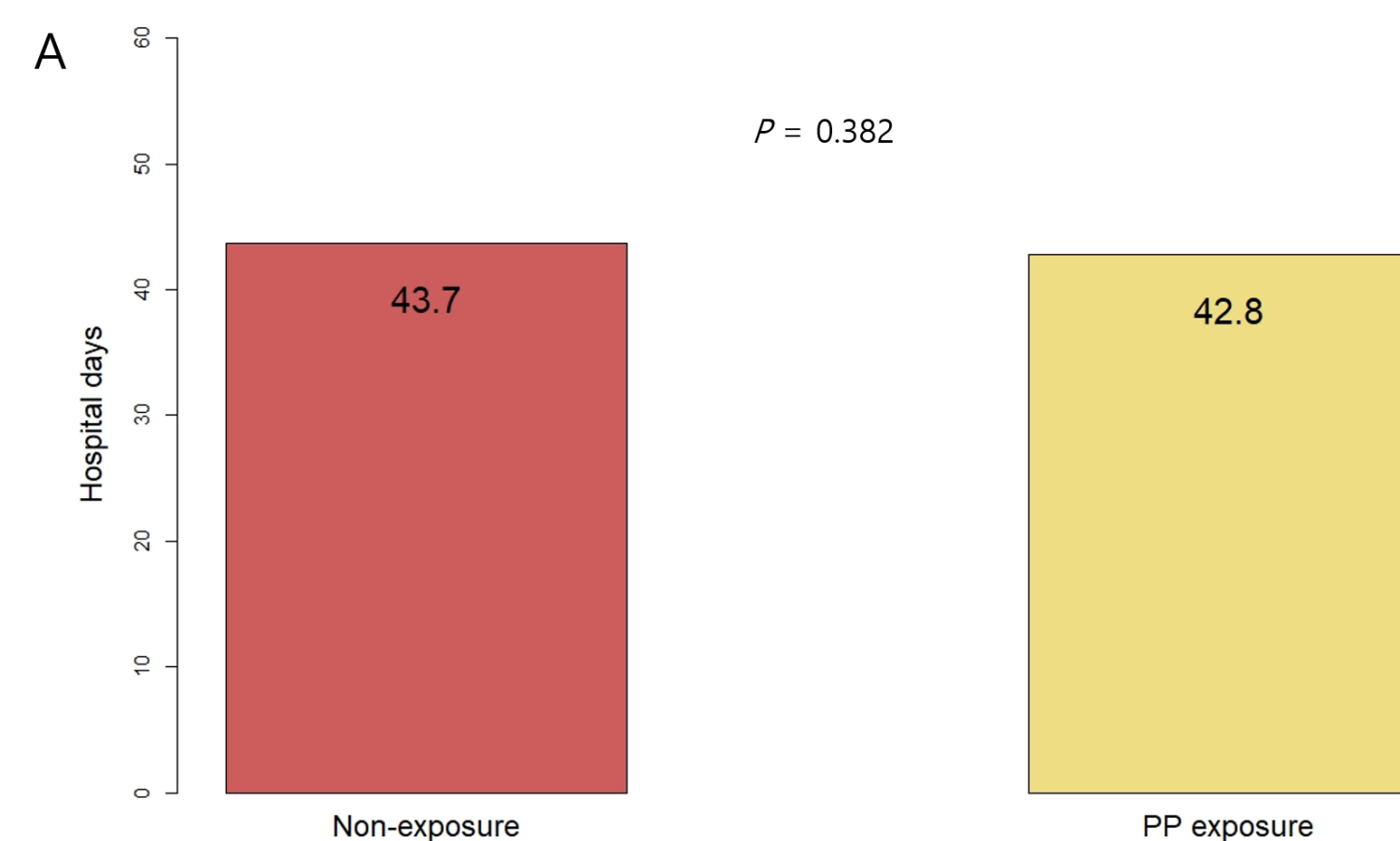
*Based on hospital wherein the first cycle of R-CHOP was received

- HRs* of FN-related hospitalization and overall survival associated with PP exposure (patients from Jan. 2014-Dec. 2015) compared to non-exposure (patients from July 2011-June 2013).

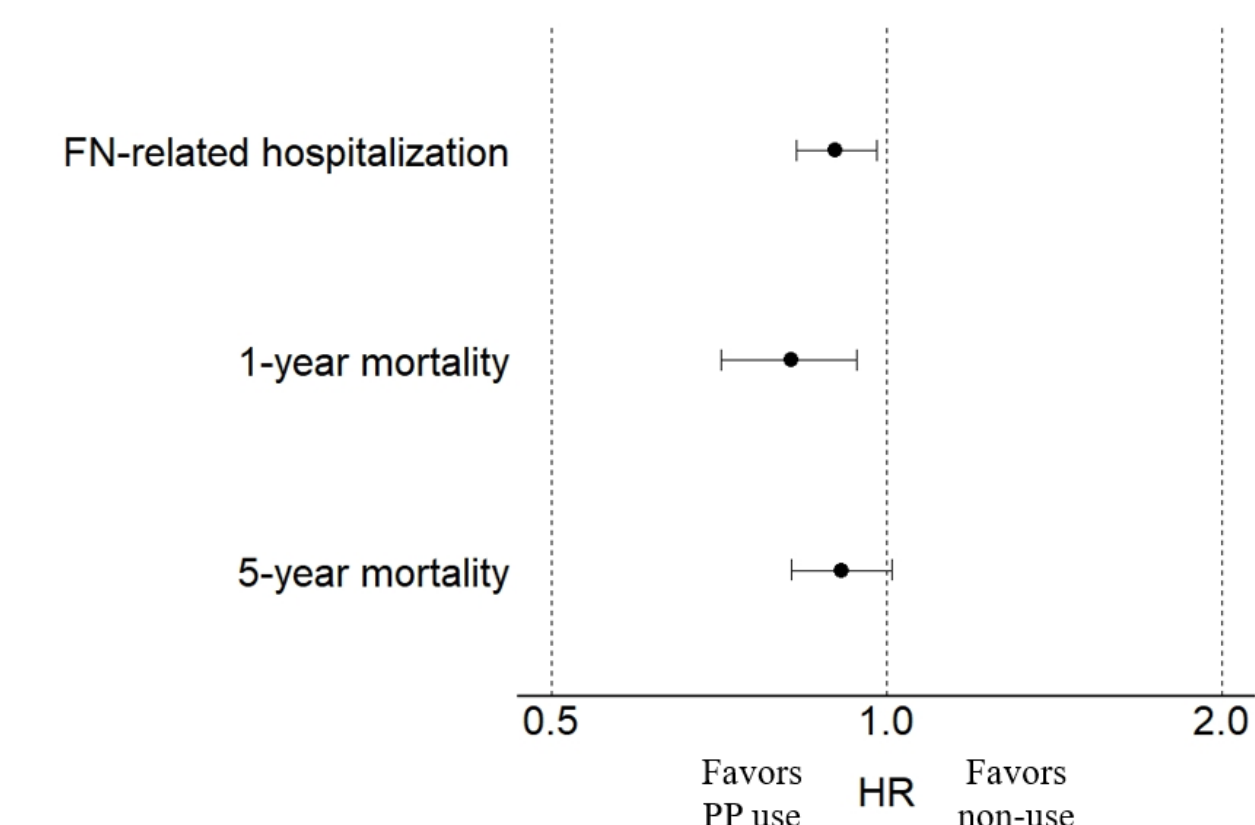


*Age, sex, household income status, and type of hospital were adjusted for.

- LOS and medical costs associated with PP exposure (Pts from Jan. 2014-Dec. 2015) compared to non-exposure (patients from July 2011-June 2013). KRW, Korean won (1150 KRW=1USD); PP, primary prophylaxis; Pts, patients. *P-values were calculated after adjustment for age, sex, household income status, and type of hospital.



- HRs* of FN-related hospitalization and overall survival associated with PP use compared to non-use among patients from 2014-2016 (n=5710).



Variables	Non-use		PP use	
	HR (95% CI)	P-value	HR (95% CI)	P-value
FN-related hospitalization	Age, sex adjusted		0.87 (0.80-0.94)	0.001
	Fully-adjusted*	reference	0.90 (0.83-0.98)	0.014
1-year mortality	Age, sex adjusted		0.79 (0.69-0.90)	0.001
	Fully-adjusted*	reference	0.82 (0.71-0.94)	0.006
5-year mortality	Age, sex adjusted		0.87 (0.79-0.96)	0.007
	Fully-adjusted*	reference	0.91 (0.82-1.01)	0.064

*Age, sex, household income status, and type of hospital were adjusted for.

CONCLUSION

- PP with long-acting G-CSF such as pegfilgrastim and its biosimilars lowered the risk of FN-related hospitalization in Korean DLBCL patients receiving R-CHOP. However, short- and long-term survival benefits associated with PP use were unclear.

- The authors declare no competing interests.
- This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (2021R1G1A101383912).