Effect of intravenous ferric carboxymaltose vs placebo among patients with acute isovolemic anemia following gastrectomy: the FAIRY randomized clinical trial

Young-Woo Kim, PhD [1,9]* Jae-Moon Bae, PhD [2]* Young-Kyu Park, PhD [3] Han-Kwang Yang, PhD [4] Wansik Yu, PhD [5] Jeong Hwan Yook, PhD [6] Sung Hoon Noh, PhD [7] Mira Han, MS[8] Keun Won Ryu, PhD [9] Tae Sung Sohn, PhD [2] Hyuk-Joon Lee, PhD [4] Oh Kyoung Kwon, PhD [5] Seung Yeob Ryu, PhD [3] Jun-Ho Lee, PhD [2] Sung Kim, PhD [2] Hong Man Yoon, MD [9] Bang Wool Eom, PhD [9] Min-Gew Choi, PhD [2] Beom Su Kim, PhD [6] Oh Jeong, PhD [3] Yun-Suhk Suh, PhD [4] Moon-Won Yoo, PhD [6] In Seob Lee, PhD [6] Mi Ran Jung, PhD [3] Ji Yeong An, PhD [2] Hyoung-Il Kim, PhD [7] Youngsook Kim, BS[9], Hannah Yang, BS[9] Byung-Ho Nam PhD [8] on behalf of the FAIRY study Group

[1]Department of Cancer Control and Population Health, Graduate School of Cancer Science and Policy, National Cancer Center

323 Ilsan-ro, Ilsandonggu, Goyang 10408, Republic of Korea;

[2]Center for Gastric Cancer, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-Ro Gangnam-gu. Seoul 06351, Republic of Korea;

[3]Department of Gastroenterologic Surgery, Chonnam National University Hwasun Hospital, 322 Seoyang-ro, Hwasun-eup, Hwasun-gun, Jeonnam 58128, Republic of Korea;

[4]Department of Surgery, Seoul National University College of Medicine, 101, Daehak-ro, Jongni-gu, Seoul 03080, Republic of Korea;

[5]Center for Gastric Cancer, Gastric Cancer Center, Kyungpook National University Medical

Center, 474 Hakjeongdong, Buk-gu, Daegu 702-210, Republic of Korea;

[6]Center for Gastric Cancer, Asan Medical Center, University of Ulsan College of Medicine, 88, Olympic-ro 43-Gil, Songpa-Gu, Seoul 05505, Republic of Korea;

[7]Department of Gastrointestinal Surgery, Yonsei University Health System, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Republic of Korea;

[8]Cancer Registration & Biostatistics Branch and Center for Clinical Trials, National Cancer Center, 323 Ilsan-ro, Goyang-si,10408, Republic of Korea

[9]Center for Gastric Cancer, Research Institute and Hospital, National Cancer Center, 323 Ilsan-ro, Goyang-si,10408, Republic of Korea;

Correspondence to: Young-Woo Kim, MD, PhD, FRCS

Department of Cancer Control and Population Health, Graduate School of Cancer Science and Policy, and Center for Gastric Cancer, Research Institute and Hospital, National Cancer Center

323 Ilsan-ro, Ilsandonggu, Goyang 10408, Republic of Korea

Tel: +82-10-8869-1635/+82-31-920-1635

Fax: +82-31-920-0696

E-mail:gskim@ncc.re.kr

14. Sample Size and Statistics

14.1. Sample size consideration

The sample size is based on a superiority design assuming an FCM response (per primary endpoint definition) of 75% by week 12 and a response of 60% in the control group.

For patients with intervention, the improvement is expected to be at least 15% higher (ie., 75% responders). This change would also be considered medically significant and warrant early intervention.

Using these estimates, 400 patients are required to have a 90% chance of detecting, as significant at the 5% level, an increase in the primary outcome measure from 60% in the control group to 75% in the experimental group.

Calculation based on the formula (Pocock): $n = f(\alpha, \beta) \times [p1 \times (100 - p1) + p2 \times (100 - p2)] / (p2 - p1)^2$ where p1 and p2 are the percent 'success' in the control and experimental group respectively and $f(\alpha, \beta) = [\Phi^{-1}(\alpha/2) + \Phi^{-1}(\beta)]^2$.

To account for potential patient drop-outs over the 12 week study period, the sample size is estimated at 450 patients (225 per group).

The parameters will be analyzed by a Pearson chi-square test or Fisher's exact test (patient age and gender, clinicopathologic data, and morbidity), and Student' t-test (Hb level before treatment and hospital days after treatment). The Z test will be used to determine whether or not a significant difference existed between two groups with respect to the slopes for changes in the Hb level during follow-up. (Pocock SJ. Clinical Trials: A Practical Approach. Wiley; 1983)

14.2. Analysis set

A. Efficacy Analysis Set

1) Intention to Treatment: That participants in the trials should be analysed in the groups to which they were randomized

2) Full analysis set (FAS): That participants who have results of at least one post baseline Hb value among the safety set

3) Per-Protocol set: The participants who fulfil the protocol in the terms of the eligibility, interventions, and outcome assessment.

B. **Safety Analysis Set**:

That participants in the trials should be analyzed in the groups to they were randomized and who took study medication