

Phase II Study of Trastuzumab Biosimilar (Herzuma®) plus Gedatolisib in Patients with HER-2 Positive Metastatic Breast Cancer

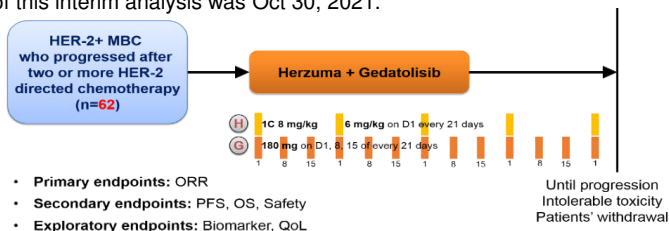
Who Progressed after 2 or more HER-2 directed Chemotherapy: KM-10A (KCSG BR 18-13) interim analysis

Ju Won Kim¹, Hee Kyung Ahn², Jong Gwon Choi³, Yee Soo Chae⁴, Gyeong-Won Lee⁵, KeonUk Park⁶, EUNMI LEE⁷, Sung Hoon Sim⁸, Jee Hyun Kim⁹, Yeon Hee Park¹⁰, Miso Kim¹¹, Jin Hyun Park¹², Jeong Eun Kim¹³, Han Jo Kim¹⁴, Mi Sun Ahn¹⁵, So Yeon Oh¹⁶, Min Hwan Kim¹⁷, Su-Jin Koh¹⁸, Kyoung Eun Lee¹⁹, Myoung Joo Kang²⁰, Jae Ho Byun²¹, Joo young Ha²², Jung Hye Kwon²³, Joo Young Jung²⁴, Su Ee Lee²⁵, Inhae Park²⁶, and Kyong Hwa Park¹

¹Korea University Anam Hospital ²Gachon University Gil Medical Center ³Konyang University Hospital ⁴Kyungpook National University Hospital ⁵Gyeongsang National University Hospital ⁶Keimyung University Dongsan Hospital ⁷Kosin University Gopel Hospital ⁸National Cancer Center ⁹Seoul National University Bundang Hospital ¹⁰Samsung Medical Center ¹¹Seoul National University Hospital ¹²Seoul Metropolitan Government-Seoul National University Boramae Medical Center ¹³Asan Medical Center ¹⁴SoonChunHyang University Hospital Cheonan ¹⁵Aju University Hospital ¹⁶Pusan National University Yangsan Hospital ¹⁷Severance Hospital ¹⁸Ulsan University Hospital ¹⁹Ewha Womans University Medical Center ²⁰Inje University Haeundae Paik Hospital ²¹The Catholic University of Korea, Incheon St. Mary's Hospital ²²Chung-Ang University Hospital ²³Kangdong Sacred Heart Hospital ²⁴Hallym University Dongtan Sacred Heart Hospital ²⁵Dong-A University Hospital ²⁶Korea University Guro Hospital

Background & Methods

- Development of resistance to HER-2 dual antibody and ADC is inevitable in patients with HER-2 positive metastatic breast cancer (MBC)
- PI3K-AKT-mTOR pathway aberration is known to be one of the resistance mechanisms.
- This phase 2 study evaluated safety and efficacy of Herzuma® (trastuzumab biosimilar) plus Gedatolisib (dual PI3K/mTORC inhibitor) in patients with HER-2 positive MBC who progressed after multiple lines of therapy.
- Key inclusion:** HER-2 positive MBC with known PIK3CA pathologic mutation or amplification whose disease progressed after more than two HER-2 directed therapy
- Treatment:** Herzuma® (8mg/kg IV for 1st cycle loading dose, and then 6mg/kg IV every 3 weeks) plus Gedatolisib (180mg on D1, 8, 15 of every 21 days).
- We evaluated efficacy of the combination treatment as interim analysis. The data cutoff of this interim analysis was Oct 30, 2021.



Results

Clinical characteristics of participants

Clinical characteristics	N=17
Age (median, years)	54.5
Menopausal status	
Pre-menopausal	2 (11.8%)
Menopausal	15 (88.2%)
Metastatic site: target or non-target lesion	
Breast	2 (12.5%)
Lymph node	7 (43.8%)
Bone	5 (83.3%)
Lung	12 (75.0%)
Liver	6 (37.5%)
Etc.	3 (18.8%)

Overall Response

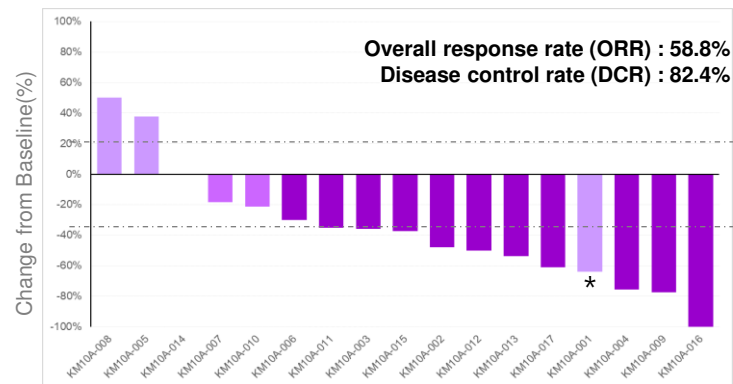


Figure 1. Best percentage change in size of target lesions. Three out of 17 participants confirmed as progressive disease (PD), 4 had stable disease (SD), and 10 showed partial response (PR). The asterisk indicates a patient whose target lesion decreased by 63% but a new leptomeningeal seeding occurred at confirmed to be PD.

Duration of Treatment

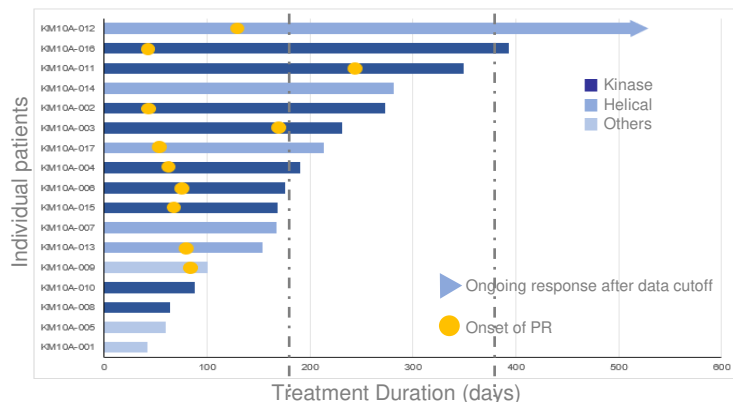


Figure 2. Swimmer plot of the treatment duration from the start of treatment to disease progression, as determined by local assessment. Median PFS was 5.9 months. At the time of the analysis, 1 patient had a continuing response. The dashed line shows the response at 6 months and 12 months.

Circulating Immune Cell Analysis

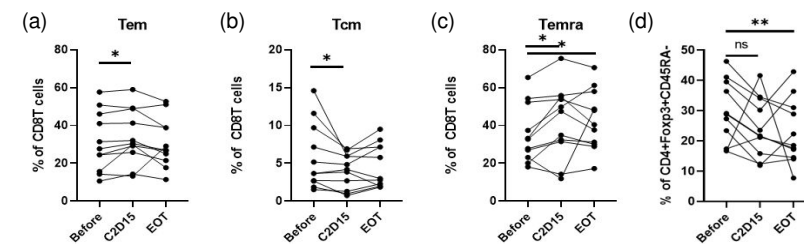


Figure 3. Distribution of memory CD8 T cell subsets and proliferation of memory Treg cells in patients. Graphs show the percentage of (a) CCR7⁺CD45RA⁻ effector memory (Tem), (b) CCR7⁺CD45RA⁻ central memory (Tcm), (c) CCR7⁺CD45RA⁻ effector memory RA (Temra) on CD8 T cells, and (d) the frequency of Ki67⁺ in CD45RA⁺ CD4⁺Foxp3⁺ cells.

cfDNA analysis

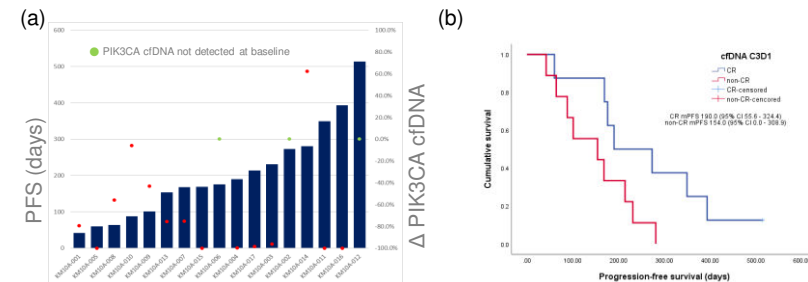


Figure 4. (a) Combined graph of PFS and delta PIK3CA cfDNA between baseline and C3D1. (b) Kaplan-Meier survival analysis of PFS. The patients were subgrouped according to whether their PIK3CA cfDNA was detected or not at C3D1. The patients who presented CR (not detected) showed longer PFS (p-value = 0.052).

Conclusion

In this phase 2 study, Trastuzumab biosimilar (Herzuma®) plus Gedatolisib presented 58.8% of response rate with manageable toxicity in patients with HER-2 positive MBC with PIK3CA aberration. A total of 62 patients will be enrolled to complete the trial.

Acknowledgement: this research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HI17C2206). cfDNA analysis was conducted using AlphaLiquid® by IMB Dx.