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PS16-03

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

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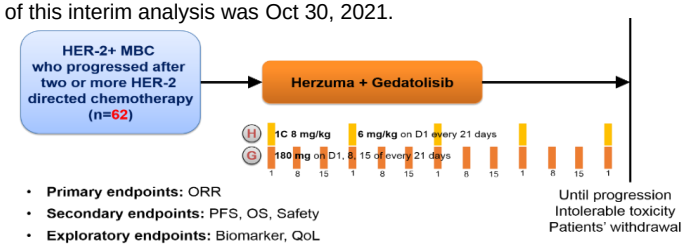
Background & Methods

- 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

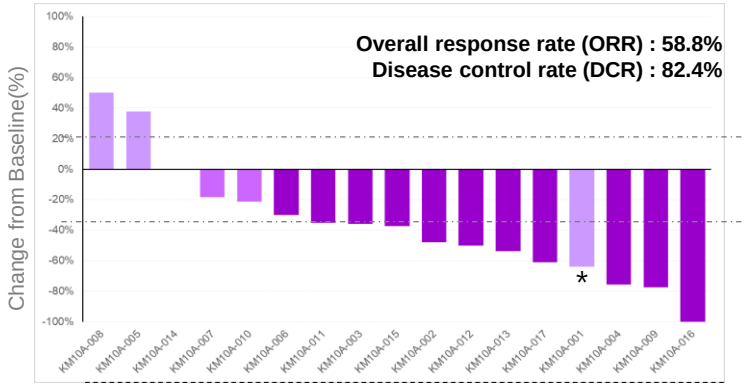


Figure 1. Best percentage change in size of target lesions. Three out of 17 participants confirmed as progressive disease(PD), 4 had stable disease(SD), and 10 showed partial response(PR). The asterisk indicate patient whose target lesion decreased by 63% but a new leptomeningeal seeding occurred at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

Duration of Treatment

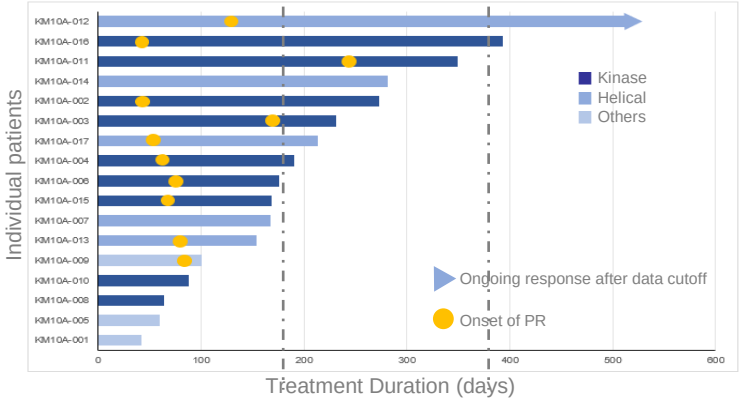


Figure 2. Swimmer plot of the treatment duration from the start of treatment to disease progression, as determined by local assessment. Median PFS was 5.9 months. At the time of the analysis, 1 patients had a continuing response. The dashed line show the response at 6 months and 12 months.

Circulating Immune Cell Analysis

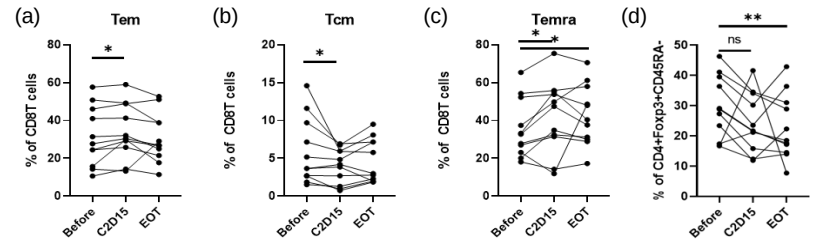


Figure 3. Distribution of memory CD8 T cell subsets and proliferation of memory Treg cells in patients. Graphs show the percentage of (a) CCR$^-$CD45RA$^-$ effector memory(Tem), (b) CCR7$^+$CD45RA$^-$ central memory(Tcm), (c) CCR$^-$CD45RA$^+$ effector memory RA(Temra) on CD8 T cells, and (d) the frequency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

cfDNA analysis

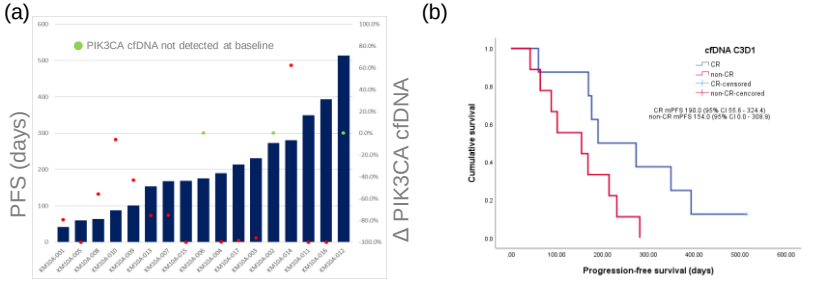


Figure 4. (a) Combined graph of PFS and delta PIK3CA cfDNA between baseline and C3D1. (b) Kaplan-Meier survival analysis of PFS. The patients were subgrouped according to whether their PIK3CA cfDNA were detected or not at C3D1. The patients who presented CR (not detected) showed longer PFS (p-value =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

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