

Human epidermal growth factor receptor 2 (HER2)-targeting [68Ga]Ga-ABY-025 PET predicts early metabolic response in breast cancer patients - Results from a Phase II study

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Background: [68Ga]Ga-ABY-025 PET was shown to reflect biopsy confirmed Human epidermal growth factor receptor 2 (HER2) status in metastatic breast cancer (MBC). This study aims to investigate how [68Ga]Ga-ABY-025 uptake corresponds to biopsy results and early treatment response in both primary breast cancer (PBC) and MBC.

Patients and Methods: Forty HER2-positive patients were included, 19 PBC and 21 MBC. [68Ga]Ga-ABY-025 PET/CT and [18F]F-FDG PET/CT were performed at baseline. A second [18F]F-FDG PET/CT was performed after two cycles of therapy to calculate metabolic response as reduction in tumor lesion glycolysis (delta-TLG). Up to five largest lesions (including the biopsied lesion) were followed in all three scans per patient. Standardized uptake values (SUV) from [68Ga]Ga-ABY-025 PET/CT were compared to biopsies HER2 status and delta-TLG by receiver operating characteristics analyses.

Results: Trial biopsies were HER2-positive in 31, negative in six, and borderline-positive in three patients. In multivariate analysis, global delta-TLG was positively associated with the number of previous treatments ($p < 0.0001$) and negatively with [68Ga]Ga-ABY 025 SUVmax ($p = 0.0005$), but not correlated with HER2 status ($p = 0.16$). [68Ga]Ga-ABY-025 PET SUVmax 6.0 cut-off predicted delta-TLG lower than -25% with 86% sensitivity and 67% specificity in soft tissue lesions (AUC=0.74, 95% CI 0.67 to 0.82, $p = 0.01$). Compared to HER2 status, this cut-off resulted in clinically relevant discordant findings in 12 of 40 patients. Delta-TLG was more pronounced in PBC (-71%, 95% CI -58% to -83%) than MBC (-27%, 95% CI -16% to -38%) ($p < 0.0001$), but [68Ga]Ga-ABY 025 uptake was similar in both with mean SUVmax of 9.8 (95% CI 6.3 to 13.3) and 13.9 (95% CI 10.5 to 17.2), respectively ($p = 0.10$).

Conclusion: [68Ga]Ga-ABY 025 PET predicted early metabolic response to HER2-targeted therapy in HER2-positive BC. Metabolic response was attenuated in recurrent disease. [68Ga]Ga-ABY 025 PET provided an estimate of HER2-receptor expression required to induce tumor metabolic remission by targeted therapies.