High Frequency of HER2-specific Immunity Observed in Patients (pts) with HER2+ Cancers Treated with Margetuximab (M), An Fc-enhanced Anti-HER2 Monoclonal Antibody (mAb)

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Abstract

T-cell repertoire responses were evaluated in 134 HER2+ patients treated with 3 mg/kg M in a phase 1 trial (NCT01148849) or 10–18 mg/kg Q3W (N = 32) in a phase 2 trial (NCT02674085). PBMC and plasma were collected at Day 1 (pre-treatment) or Day 50 (post-treatment), and were evaluated for changes in T-cell repertoire (TCR beta immunosequencing), antigen-specific T-cell and Ab responses. T-cell repertoire analyses revealed high frequency of HER2-specific immunity observed in patients treated with M, with at least 12 of 14 subjects showing increases in T-cell clonality, with an average of 138 expanded clones and an increase by 54% (p < 0.0001), with all subjects responding to ≥2 (median = 4) of the 6 Ag. A small 1.6-fold increase in Ab response to control Ag was noted. Subsets of HER2-specific T-cell and Ab responses were observed in patients with HER2+ breast cancers. The most frequent HER2-specific T-cell and Ab responses were observed in patients with high HER2 IHC expression, and may be associated with improved clinical outcome.

Methods

Pharmacokinetic (PK) and PK–PD data were generated with PBMC and plasma samples collected at Day 1 (pre-treatment) or Day 50 (post-treatment), and were evaluated for changes in T-cell repertoire (TCR beta immunosequencing), antigen-specific T-cell and Ab responses. T-cell repertoire analyses revealed high frequency of HER2-specific immunity observed in patients treated with M, with at least 12 of 14 subjects showing increases in T-cell clonality, with an average of 138 expanded clones and an increase by 54% (p < 0.0001), with all subjects responding to ≥2 (median = 4) of the 6 Ag. A small 1.6-fold increase in Ab response to control Ag was noted. Subsets of HER2-specific T-cell and Ab responses were observed in patients with HER2+ breast cancers. The most frequent HER2-specific T-cell and Ab responses were observed in patients with high HER2 IHC expression, and may be associated with improved clinical outcome.

Results

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Conclusions

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References