

POSTER PRESENTATION

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Serum immunoregulatory proteins as predictors of overall survival of metastatic melanoma patients treated with ipilimumab

Yoshinobu Koguchi^{1*}, Helena Hoen¹, Shelly Bambina¹, Michael Rynning², Richard Fuerstenberg², Zipei Feng¹, Bernard Fox¹, Carlo Bifulco^{1,3}, Brendan D Curti^{3,4}, Walter Urba¹, Christina Milburn⁵, Alan J Korman⁵, Keith S Bahjat^{1,3,6}

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Background

Treatment with ipilimumab improves overall survival (OS) in patients with metastatic melanoma. Because ipilimumab targets T lymphocytes and not the tumor itself, efficacy may be uniquely sensitive to immunomodulatory factors present at the time of treatment.

Methods

We analyzed serum from patients with metastatic melanoma (247 of 273, 90.4%) randomly assigned to receive ipilimumab or gp100 peptide vaccine (NCT00094653). We quantified candidate biomarkers at baseline and assessed the association of each with overall survival using univariate and multivariate analyses. Results were confirmed in an independent cohort of similar patients (48 of 52, 92.3%) treated with ipilimumab (NCT00495066).

Results

Univariate analysis of biomarkers identified chemokine (C-X-C motif) ligand 11 (CXCL11) and soluble MHC class I polypeptide-related chain A (sMICA) as potential predictive biomarkers for ipilimumab but not gp100 therapy for metastatic melanoma. After controlling for baseline covariates, elevated CXCL11 and sMICA were associated with poor OS in ipilimumab-treated patients (log₁₀ CXCL11: hazard ratio (HR), 1.88; 95% CI, 1.14 to 3.12; $P = 0.014$; and log₁₀ sMICA quadratic effect $P = 0.066$; sMICA (≥ 247 vs < 247): HR, 1.75; 95% CI, 1.02 to 3.01) but not in gp100-treated patients. Multivariate analysis of an independent ipilimumab-treated cohort

confirmed the association between log₁₀ CXCL11 and OS (HR, 3.18; 95% CI 1.13 to 8.95; $P = 0.029$), while sMICA was less strongly associated with OS (log₁₀ sMICA quadratic effect $P = 0.16$; sMICA (≥ 247 vs < 247): HR, 1.48; 95% CI, 0.67 to 3.27).

Conclusion

Low baseline CXCL11 and sMICA were associated with improved OS in patients with metastatic melanoma after ipilimumab treatment but not vaccine treatment. Thus, pretreatment CXCL11 and sMICA may represent predictors of survival benefit after ipilimumab treatment as well as therapeutic targets. Furthermore, their role in recruiting T regulatory cells (CXCL11) and inhibiting cytolytic effector cells (sMICA) suggests that combination therapies targeting these molecules may synergize with CTLA-4 blockade in patients.

Authors' details

¹Earle A. Chiles Research Institute, Portland, OR, USA. ²R&D Systems, Minneapolis, MN, USA. ³Providence Cancer Center, Portland, OR, USA. ⁴Providence Portland Medical Center, Portland, OR, USA. ⁵Bristol-Myers Squibb, Redwood City, CA, USA. ⁶Robert W. Franz Cancer Research Center, Portland, OR, USA.

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¹Earle A. Chiles Research Institute, Portland, OR, USA
Full list of author information is available at the end of the article