

Overall Survival Benefit with Sipuleucel-T by Baseline PSA: An Exploratory Analysis from the Phase 3 IMPACT Trial

Introduction and Objective: Sipuleucel-T is an autologous cellular immunotherapy approved for the treatment of asymptomatic or minimally symptomatic metastatic castrate-resistant prostate cancer. In the pivotal phase 3 IMPACT trial (NCT00065442), sipuleucel-T showed a 22.5% reduction in risk of death vs the control group (hazard ratio [HR]=0.775 [95% CI 0.614, 0.979]; $P=0.032$). A pre-specified subgroup analysis for baseline prognostic variables showed homogeneous treatment effects consistently favoring sipuleucel-T. In patients (pts) with baseline PSA below vs above the median, there was a trend toward greater treatment effect (HR=0.685 vs. 0.865). In this exploratory analysis, we further sub-divide baseline PSA into quartiles to evaluate potential treatment effect patterns.

Materials and Methods: The analysis included all randomized pts from the IMPACT trial (N=512). Pts were categorized by baseline PSA quartile, as well as by median for other baseline prognostic variables (i.e., ECOG, LDH, PAP, ALP in bone-only disease, and Hgb). Median overall survival (OS) was estimated using the Kaplan-Meier method. HR estimates were obtained from a Cox model.

Results: The HRs suggest a consistent treatment effect in all subsets, although there is inadequate power to show significant results within each quartile. There was a trend toward an increased magnitude of treatment benefit in pts with a lower baseline PSA. The median OS for sipuleucel-T vs control in the lowest quartile was 41.3 vs. 28.3 months (HR=0.51[95% CI 0.31, 0.85]). Results for other baseline prognostic variables also suggest a trend toward greater benefit in subjects with better prognostic features. However, results for baseline Hgb indicated an opposite trend.

Conclusions: Although not adequately powered for significance, the results of this analysis support a consistent OS benefit with sipuleucel-T across PSA quartiles. The greater magnitude of benefit in pts with lower baseline PSA suggests that pts with less advanced disease may benefit more from treatment with sipuleucel-T.

	Baseline PSA (ng/mL)			
	≤ 22.1 (n=128)	>22.1–50.1 (n=128)	>50.1–134.1 (n=128)	>134.1 (n=128)
Median OS, mos				
Sipuleucel-T	41.3	27.1	20.4	18.4
Control	28.3	20.1	15.0	15.6
Difference	13.0	7.1	5.4	2.8
HR (95% CI)	0.51 (0.31, 0.85)	0.74 (0.47, 1.17)	0.81 (0.52, 1.24)	0.84 (0.55, 1.29)