645

PROGNOSTIC SIGNIFICANCE OF THE QUANTIFICATION OF CIRCULATING TUMOR CELLS IN PATIENTS WITH METASTATIC HORMONO-SENSITIVE PROSTATE CANCER

Luis Resel, Carlos olivier, Luis San José, Isabel Galante, Marta Vidaurreta, Marisa Maestro, Eduardo Díaz-Rubio, Angel Silmi, Madrid, Spain*

INTRODUCTION AND OBJECTIVES: Analysis of the relationship between circulating tumor cells (CTC) levels with the clinical-pathologic parameters (PSA levels, Gleason score and TNM staging) in patients with metastatic hormone-sensitive prostate cancer (PC) and establish his prognostic value in the overall and progression-free survival.

METHODS: Prospective, three arms, study: 26 patients (p) with localized PC (Stage I–II)(LPC); 30p with metastatic PC (Stage IV) (MPC) and 30 healthy volunteers.

A single 7.5 ml sample of peripheral blood was taken, CTCs were isolated using and immunomagnetic method based on the CellSearch system (Veridex). CTCs were identified as nucleated cells negative for CD45 (leukocytes) and positive for cytokeratins. (8, 18 y 19).

RESULTS: The median of follow-up was 42.9 months (27.14–49.5). Patients with MPC had significantly higher CTC levels [m: 18.5 (1–126)] compared with the other two groups ($P < 0.001$). A significant positive correlation was demonstrated ($P < 0.001$) between CTC levels and all tumour burden markers: PSA (Rho = 0.55), T (Tau = 0.47), N (m N1: 18.5, m N0: 0.0) and M (Tau = 0.54) except Gleason score(Tau = 0.16).

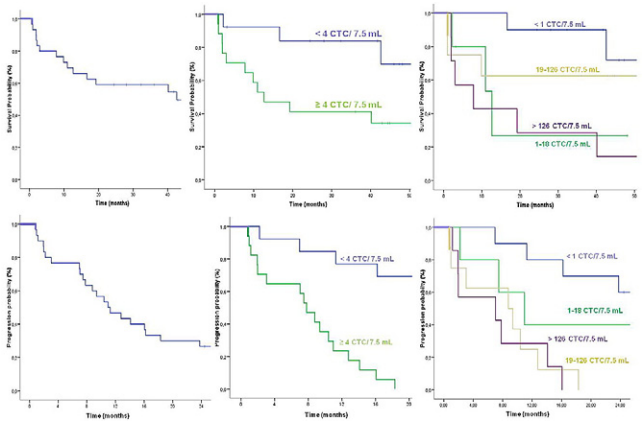
The overall survival to 6, 12 and 18 months was 80 %, 69 % and 62 % respectively. The progression-free survival to 6, 12 and 18 months was 76 %, 46 % and 33 % respectively.

A cutoff level ≥ 4 CTC (S: 90 %; E: 87.6 %) was chosen to distinguish patients with an unfavorable prognosis. These patients had a significantly shorten median overall and progression-free survival ($P < 0.001$). As the CTC levels were increasing, the overall survival and progression-free survival decreased.

The risk of mortality and progression for the patients with ≥ 4 CTC was 4.1 (IC 95 %: 1.1–14.6; P = 0.029) and 8.5 (IC 95 %: 2.6–26.9; $P < 0.001$) times higher.

Using a multivariate piecewise Cox regression mode, the level of ≥ 4 CTC was an independent predictor of PSA relapse(HR: 5,9; IC 95 %: 1,7-20,4; p <0,005).

CONCLUSIONS: The inmunomagnetic analysis allows us to quantify the CTC in peripheral blood and could provide a possibility for correctly staging and to estimate the prognostic value of the metastatic hormone-sensitive prostate cancer with the purpose of the early onset of new therapies.



Source of Funding: None

646

SAFETY OF LEUKAPHERESIS IN PROSTATE CANCER PATIENTS RECEIVING SIPULEUCEL-T

Robert Flanigan, Maywood, IL; Thomas Price, James Whitmore, Joan Holman, Seattle, WA*

INTRODUCTION AND OBJECTIVES: Sipuleucel-T is an autologous cellular immunotherapy designed to stimulate an immune response against prostate cancer. Infusion of sipuleucel-T consists of the patient's peripheral blood mononuclear cells (PBMCs) activated with a recombinant antigen consisting of prostatic acid phosphatase (PAP), linked to granulocyte-macrophage colony stimulating factor (GM-CSF). Here we describe the leukapheresis procedure required to collect the PBMCs.

METHODS: Eligibility criteria for three randomized, controlled studies included hemoglobin of ≥ 9g/dL, white blood cells (WBC) ≥ 2,000 cells/μL, and platelet count of ≥ 100,000 cells/μL. Patients were scheduled to undergo 3 leukapheresis procedures, 1 approximately every 2 weeks, then infusion of sipuleucel-T approximately 3 days post-leukapheresis. The leukapheresis procedure involved a 1.5 - 2 blood volume exchange lasting 3–4 hours during which a patient's PBMCs were removed.

RESULTS: 729 patients with asymptomatic or minimally symptomatic metastatic castrate-resistant prostate cancer had at least 1 leukapheresis procedure; 92% of sipuleucel-T patients received all 3 infusions. 55% had at least 1 adverse event (AE) ≥ 1 day of leukapheresis, mild/moderate in intensity in 92% of patients. The AEs reported in ≥ 5% of patients were symptoms of citrate toxicity and fatigue. Citrate, an anticoagulant used during leukapheresis, lowers ionized calcium. Toxicity involves paraesthesia around the mouth, in extremities, and, rarely, chills, cramps, and chest pressure. Citrate toxicity, paraesthesia/paraesthesia oral were reported for 33.5% of patients (all mild/moderate intensity). The serious adverse event (SAE) rate reported ≥ 1 day of leukapheresis was 3.3%; no single event reported ≥2 patients combined for both arms. Median values for WBC, absolute lymphocyte and monocyte counts at Weeks 6, 14, and 26 were within normal ranges. In the largest study (N=506, safety population), 23% of patients had a central venous catheter for leukapheresis; 34% received IV calcium as either prophylaxis or treatment of toxicity.

CONCLUSIONS: Leukapheresis is a required step in the manufacture of sipuleucel-T. AEs associated with citrate toxicity are common and managed with calcium administration. The majority of patients should be able to undergo the procedure without a central venous catheter.

Source of Funding: Dendreon