

102<sup>nd</sup> Annual American Association for Cancer Research (AACR) Meeting on April 2-6 in Orlando, Florida

Late-Breaking Research: Immunology - Exhibit Hall A4-C, Poster Section 40.

Monday, Apr 04, 2011, 8:00 AM -12:00 PM

***Low TCR diversity (divpenia®) is a new prognostic factor of overall survival in metastatic breast cancer.***

Manuarii MANUEL<sup>1,4</sup>, Olivier TREDAN<sup>2</sup>, Thomas BACHELOT<sup>2</sup>, Tioka RABEONY<sup>1</sup>, Sylvie CHABAUD<sup>3</sup>, Jean-François MOURET<sup>1</sup>, Audrey GRIVES<sup>1</sup>, Solène PEREZ<sup>1</sup>, Jean Yves BLAY<sup>4</sup>, Christophe CAUX<sup>4</sup>, Nicolas PASQUAL<sup>1</sup>, Christine MENETRIER-CAUX<sup>4</sup>.

<sup>1</sup> ImmunID, Rue des martyrs, CEA, Grenoble ; <sup>2</sup> Département de Médecine, Centre Léon Bérard, 28 rue Laennec 69373 Lyon Cedex 08 ; <sup>3</sup> Unité de Biostatistiques Centre Léon Bérard, 28 rue Laennec 69373 Lyon Cedex 08 ; <sup>4</sup> Equipe 11, CRCL UMR INSERM 1052 CNRS 5286, Cheney D, Centre Léon Bérard 28 rue Laennec 69373 Lyon Cedex 08

**Abstract Body:**

**Rationale**

Lymphopenia (<1000 Lymphocytes/ $\mu$ l) or CD4<sup>+</sup> T cell lymphopenia (<450/ $\mu$ l), detected before initiation of chemotherapy are predictive factors for toxicity and death in metastatic solid tumors (Borg *et al* 2004; Ray Coquard *et al* 2009).

The goal of the present study was to further identify the characteristics of the T cells in these lymphopenic patients. TCR diversity was investigated and tested as a predictive factor for overall survival (OS).

**Patients and methods**

The ImmunTraCkeR<sup>®</sup> assay (ImmunID, Grenoble, France), which analyzes, through semi quantitative multiplex PCR, the V-D-J combinatorial diversity of TCR-beta chain (TRB), was used to investigate the diversity of the T cell repertoire on cryopreserved blood samples from a prospective cohort of untreated metastatic breast cancer patients (SEMTOF study)(n=66). Univariate and multivariate analyses of several prognostic factors for OS were performed in this series as well as in a validation series.

**Results**

A severe T cell divpenia<sup>®</sup> (T cell diversity below 33%) (average diversity in healthy people is 70%) was associated with a median survival of 9 months vs. 24 months for the remaining patients (logrank p.value=0.0047). In a multivariate analysis, including haemoglobin level, polynuclear neutrophil count and liver metastasis, divpenia<sup>®</sup> was identified as an independent prognostic factor. The NDL<sup>®</sup> score (Number Diversity Lymphocytes representation) that combines lymphocytes count with TRB diversity, demonstrated that lympho-divpenia<sup>®</sup> (T cell diversity below 33% and lymphopenia at 1GIGA/L threshold) was associated with a poor prognosis in term of patients survival compared to patients with either a good cell count or good diversity or both good cell count and diversity (p.value=0.0202). The prognostic value of NDL<sup>®</sup> score was then evaluated on a prospective validation cohort of 33 patients (logrank p.value=0.002).

**Conclusion:**

Divpenia<sup>®</sup> and its combined parameter NDL<sup>®</sup> are predictive factors for survival in metastatic breast cancer patients. An open clinical study (LYMPHOS1) will investigate divpenia<sup>®</sup> and NDL<sup>®</sup> score in a larger prospective cohort of metastatic breast patients.

**Acknowledgments :**

Manuarii MANUEL is a CIFRE recipient. The presented results were generated through a Proof of Concept "LYMPHOS1" financially supported by CLARA.

**Contact:**

Isabelle Tanneau, Scientific Sales Manager – North America  
[itanneau@immunid.com](mailto:itanneau@immunid.com) - +33 (0) 438 785 770