P012

PATIENTS WITH CANCER AND PREEXISTING AUTOIMMUNE AND INFLAMMATORY DISEASES TREATED BY ANTI-PROGRAMMED DEATH 1 (PD-1) ANTIBODIES AT GUSTAVE ROUSSY CANCER CENTER

¹F-X Danlos*, ²M Najean, ³A-L Voisin, ⁴A Marabelle, ²M Texier, ⁵O Lambotte. ¹Laboratoire de Recherche Translationnelle en Immunothérapie (LRTI) – UMR1015; ²Département de biostatistique; ³Unité Fonctionnelle de Pharmacovigilance; ⁴DITEP – LRTI – UMR1015, Gustave Roussy, Villejuif; ⁵Service de Médecine Interne and Immunologie Clinique, CHU Bicêtre, Kremlin-Bicêtre, France

10.1136/annrhumdis-2018-EWRR2019.9

Career situation of first and presenting author Student for a master or a PhD.

Introduction Immune checkpoint inhibitors anti PD-1 are monoclonal antibodies used in cancers.¹ PD-1 ligand/PD-1 pathway antagonism between cancer cells and antitumoral cytotoxic CD8 T cells increase antitumoral immunity but is involved in autoimmune diseases (AID).

Objectives Evaluate tolerance and efficacy of anti PD-1 in AID patients.

Methods Patients had been included in REISAMIC registry (Registry of Severe Adverse Events of Immunomodulating Monoclonal Antibodies in Oncology) between June 1st, 2014, and December 31st, 2017. Patients were treated with anti-PD-1. Exclusion criteria were malignant hematologic disease, second advanced cancer or chronic viral infection. AID subtypes were defined for sensitivity analyses: diseases of clinical interest (DCI), prognostic interest (DPI) and vitiligo. One patient with pre-existing AID were matched on age, sex and cancer type with 3 patients without preexisting AID (controls). Analyses were adjusted for OMS status, corticosteroid, cerebral metastasis, LDH, albuminemia and neutrophil/lymphocyte ratio >3. End-points were grade ≥ 2 irAE free survival and overall survival (OS). Objective response rates (ORR) were described.

Results 641 patients were included in REISAMIC. Among them, 69 patients were excluded. 572 patients had been included: 63 with AID and 509 controls. Among AID patients, we observed 38% DCI, 38% DPI and 24% vitiligo. DCI were Sjögren syndrome (n=4), rheumatoid arthritis (n=4), polymyalgia rheumatica/giant cell arteritis (n=2) and others. DPI were psoriasis (n=11), thyroiditis (n=8) and others. We matched 55 AID patients with 165 controls. Cancer type, TNM or AJCC grade, age and sex were similar between AID patients and controls. Overall survival (HR 0,67, IC95% [0,42–1,08], p=0,098) and irAE free survival (HR 1,27, IC95% [0,84–1,90], p=0,25) were not different between AID patients and controls. After vitiligo exclusion in sensitivity analyses, irAE free survival was shorter for AID patients than controls (HR 1,69, IC05% [1- 2,87], p=0,05) and more for DCI patients only (HR 2,66, IC95% [1,01–7], p=0,049). ORR were 35,5% and 28,5% for AID patients and controls respectively.

Conclusions Preexisting AID should not be a contraindication for anti PD-1. We suspect that mechanisms involved in AID are important in irAE mechanism and antitumoral response. CD4 T cells and Th17 cells should be study in these situations.

REFERENCE

1. Ribas A, Wolchok JD. Cancer immunotherapy using checkpoint blockade. *Science* 2018 Mar 23;**359**(6382):1350–5.

Disclosure of Interest None declared.

P014/004 PHENOTYPIC HETEROGENEITY OF REGULATORY T CELLS IN RHEUMATOID ARTHRITIS

^{1,2}Y El Ahmadi*, ^{1,2}M Cren, ^{1,2,3}Y-M Pers, ¹E Dufourq-Lopez, ^{1,2,3}C Jorgensen, ³R Ferreira, ^{1,2}P Louis-Plence. ¹Inserm-Irmb; ²University of Montpellier; ³Lapeyronie University Hospital, Montpellier, France

10.1136/annrhumdis-2018-EWRR2019.10

Career situation of first and presenting author Student for a master or a PhD.

Introduction Rheumatoid arthritis (RA) is the most frequent chronic inflammatory rheumatism characterized by infiltration of many immune cells into the synovial tissue leading to cartilage and bone degradation over time. The working hypothesis of our team is to use immunomodulatory properties of regulatory T (Treg) cells to restore immune homeostasis in RA. These approaches are based on a better knowledge of the cell populations present in the inflamed tissue and in particular the sub-populations of Treg cells. Heterogeneity of Treg cells is well known however most Treg studies in RA have focused on CD25+FoxP3+ Treg cells in the peripheral blood of patients.

Objectives In this project using innovative approaches such as 18-colors cytometric analyses our project aims to better characterize the Treg subsets to unravel the heterogeneity of the Treg cell subsets in RA.

Methods The phenotypic analyses will be performed using 18-colors conjugated antibodies, analyzed on the LSR II, to allow the simultaneous characterization of CD25+FoxP3+ Tregs, Tr1 cells and CD8⁺ Tregs within the T lymphocytes. Activation status of the various subsets will be also investigated using various activation markers. The phenotypic characterization will be performed on the synovial fluid (SF) and peripheral blood (PB) from RA and Osteoarthritis patients used as controls.

Results The preliminary results showed that the frequency of CD25+FoxP3+ is higher in the SF compare with PB in both pathologies. Furthermore, the phenotype and activation status of CD25+FoxP3+ Treg cells is different between both fluids with an accumulation of effector activated CD25+FoxP3+ Treg cells in the SF. Interestingly, whereas Tr1 cells are barely detectable in the peripheral blood, the Tr1 subset seems to be enriched in the synovial fluid in both pathologies.

Conclusions This study confirm the presence of activated CD25+FoxP3+ Treg cells in the SF of RA and provide evidence for the presence of other Treg subsets in SF. A better characterization of the suppressive activity of the various Treg subsets need to be investigated and particularly in inflammatory conditions. A better understanding of the suppressive function of the various Treg subsets will thus provide identification of new therapeutic targets in RA patients.

Disclosure of Interest None declared.