Immuno-Oncology Group

CHECK'UP ELDERLY- Geriatric substudy

Analysis of relationship between geriatric profile and response to PD-1 or PD-L1 antagonists

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MINITRODUCTION

In this prospective multicentric national cohort study, we aim to address each of these areas of critical need by studying 2 parallel groups of patients receiving a PD-1 or PD-L1 antagonist treatment as part of their standard care for NSCLC or HNSCC. These 2 cancers have been chosen among all current indications in which a PD-1/PD-L1 antagonist is authorized in France for reasons of feasibility (availability of tumour specimens as well as sample size calculations based on docume objective response rates; ORR). Each indication will be analysed independently to develop and validate a signature which allows to identify patients with an objective response. A deep immune analysis of longitudinal tumour samples will be performed yielding insights into predictive biomarkers of response and mechanisms of initial or acquired resistance to therapy, including possible mechanistic differences between each of these tumour localisations and forms of therapy. A long-term follow-up of 5 years per patient will enable a full description of acute and chronic treatment-related toxicity in real-life conditions, and will provide the means to determine risk factors for treatment-related toxicity. This study will also allow the evaluation of the cost efficiency of treatment with PD-1 or PD-L1 antagonists in these indications.



In addition to the main analysis of CHECK'UP study, patients aged 70 and over will be invited to participate in a voluntary substudy developed in collaboration with the UNICANCER Oncogeriatrics Group (GERICO).

CHECK'UP ELDERLY - RATIONAL

In the last years, immune checkpoint inhibitors have become the new therapeutic option in many solid tumours including non-small cell lung cancer (NSCLC) urothelial carcinoma, renal carcinoma, cervix carcinoma, melanoma, head & neck squamous cell carcinoma (HNSCC), hepatocellular carcinoma, gastric carcinoma and tumours harbouring MSI ([1], [2], [3], [4]).

Compared to conventional cancer therapies, immunotherapy offers a better safety profile, with less than 10% of severe toxicities, and is therefore an attractive option in older patients [5]. However there is currently a lack of information available for clinicians concerning the use of immunotherapy in older patients. Most of the published data is based on subgroup analysis and lacks the genatric data needed to better characterize the population

The elderly population and the incidence of cancer therein is increasing. By 2050, it is estimated that 50% of all new cancer diagnoses in France will occur in patients over the age of 75 [6]. There is therefore a tremendous need for more data concerning the safety and efficacy of immunotherapy treatment in this population, and the development of evidence-based treatment strategies.

We propose to study in more detail the geriatric profile of patients aged 70 years and older, enrolled in the CHECK'UP study, in order to evaluate how this may affect their response to treatment with anti-PD1/PD-L1 inhibitors.

SUBSTUDY OBJECTIVES

Primary objective

The primary objective of the trial is to determine independently for each disease indication (NSCLC, HNSCC) the relationship between geriatric parameters and response to treatment with a PD-1 or PD-L1 antagonist for patients aged 70 years or older.

Secondary objectives

- To determine the relationship between geriatric parameters and treatment-related toxicity.
- To compare the response to treatment with PD-1 or PD-L1 antagonists between the older patients and their younger counterparts.
- To evaluate the evolution of quality of life (QOL) in individuals during the treatment period.

Exploratory objectives

 To explore specificity of aging (immunosenescence phenotype, microbiome modifications and auto antibodies modifications [consenting] patients]) and the link with response or toxicity to treatment with a PD-1 or PD-L1 antagonist.

SUBSTUDY DESIGN

The sub-study will recruit patients enrolled in the main CHECK'UP study who are aged 70 years or older, and who have provided additional specific informed consent to their participation. Due to the exploratory nature of this study, no formal sample size calculation will be performed. The exact number of enrolled patients will depend upon the demographics of the population enrolled in the main study and the willingness of eligible patient to consent to the additional assessments described below.

Geriatric parameters will be analysed at baseline and at specific time points during the treatment period to better characterize the population of patients aged 70 years or older and evaluate the relationship between geriatric parameters and response to PD-1/PD-L1 antagonists in terms of efficacy and safety.

M INCLUSION CRITERIA

Additional inclusion criteria to participate in CHECK'UP ELDERLY

- Participant in the main CHECK'UP study
- 2. Age ≥ 70 years old.
- 3. Specific written informed consent (signed and dated)

M GERIATRIC PARAMETERS TESTS

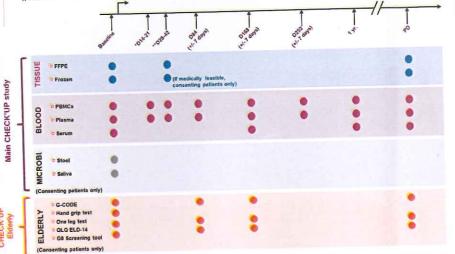
Following signature of the informed consent form, during the Screening period for the main study (max. 28 days prior to start of treatment), baseline geriatric parameters will be assessed using the following tools:

- The EORTC QLQ ELD-14 [7]
- The G8 screening tool [8]
- The hand grip test [9]
- The one-legged stance test
- The Geriatric Core Dataset* (G-Code)



The one-legged stance test

Additional assessment of geriatric parameters and quality of life will be performed during the treatment period, to coincide with the first two disease evaluation visits (main study) at intervals defined according to local standard practice (ideally at 84 and 168 days [±7 days] - see Protocol Section 6.1) using the QLQ ELD-14, one legged stance test, and TUG, ADL, and IADL examinations from the G Code.



"C2D1; "C3D1; EOS = End of Study; PD = Disease Progression; Tx = AntiPD-1 / AntiPD-L1 treatment

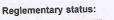
Collaborative groups:

UNICANCER H&N group.

UNICANCER Oncogeriatrics group (GERICO)

* The G-Code is a mini comprehensive geriatric assessment validated by national and international panels of oncologist and geriatrician experts [10], [11]. It includes 8 parameters measuring social support, functional status (activities of daily living [ADL], instrumental activities of daily living [IADL]), physical performance (Timed Up and Go test [TUG]), nutrition (10% weight loss from baseline weight); and BMI < 21 kg/m2

STUDY STATUS (AS OF JAN. 31, 2020)



Main CHECK'UP study

CPP: 12 Dec. 2017 ANSM: 27 Dec. 2017 First patient: Jun 2018

Amendement n° 3 - ANSM: 12 Dec. 2018 CPP: 15 Jan. 2019 Training of sites: Jun/Sept 2019

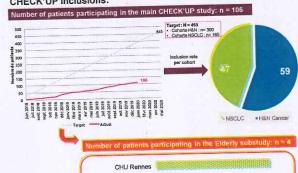
First patient: Jul. 2019

Sites participating: 21 sites participating / 19 open sites



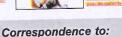


CHECK'UP inclusions:



Communications related CHECK'UP Elderly:





Cohorte NSCLC

Cohort H&N Cancer

References:

- [3]. Reck, 2016
- [7]. Wheelwright, 2013 [8]. Soubeyran, 2008
- [5]. Helissey. J Geriatr Oncol. 2016 [9]. Lauretani, 1985 [6]. INCa ©Les cancers en France en 2013 [10]. Martinez-Tapia, 2017 [11], Paillaud, 2018.

- The patients who accepted to participate in these trials & their families
- The investigators and their support staff
 Financial support from the ARC Foundation, the Unicancer's partner.