

## Complete remission with Immunotherapy in second-Line in metastatic lung cancer without targetable oncogenic addiction: About a case and revue of the literature

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### Abstract

Lung cancer is a public health problem in the world, in 2020: 2nd most common cancer after breast cancer. Smoking is the main risk factor constituting an essential axis of prevention. Non-small cell lung cancer is the most common histological component representing approximately 85%, currently 75% of patients have unfortunately become at advanced stages, the prognosis remains poor: incidence and expectation are close, but metastatic NSCLC has experienced a total renewal of the therapeutic arsenal. It is a model of precision medicine and also in particular a model for immunotherapy. We are recently faced with an expanded therapeutic arsenal posing a problem of choice. with a durable complete response with Atezolizumab.

**Keywords:** Metastatic Lung cancer; Chemotherapy PDL-1; Atezolizumab; Case

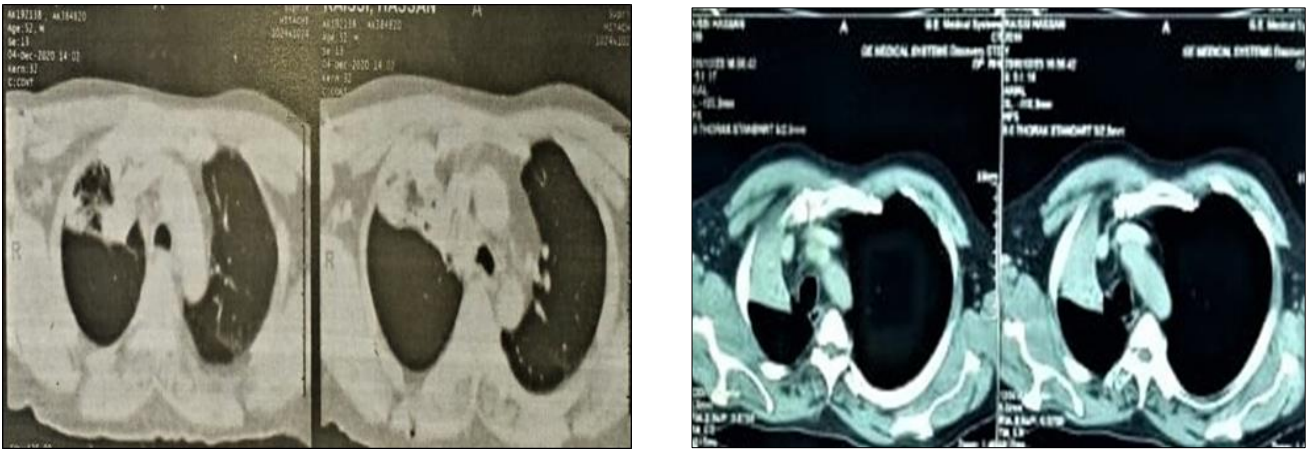
### 1. Introduction

Metastatic lung cancer is one of the greatest therapeutic challenges in oncology due to the modest benefit observed with chemotherapy initially. In recent years, significant therapeutic advances have been made thanks to a better understanding of molecular mechanisms. We present the case of a male patient diagnosed with metastatic lung cancer who had developed a complete response after treatment with atezolizumab.

### 2. Observation

This is a 54-year-old patient, chronic smoker, weaned 40 PA followed for a non-small cell bronchial adenocarcinoma objectified on CT-guided biopsy (TTF1 positive) initially classified as stage IIIB( Image 1) treated with neoadjuvant chemotherapy based on platinum three salts cures followed by concomitant radio-chemotherapy, 8 months after the end of the curative treatment, local and metastatic adrenal relapse with immunohistochemistry, absence of EGFR or ALK mutation, PDL status -1: 22%, having received d first a first-line chemotherapy based on Pemetrexed-carboplatin given the initially inaccessibility to immunotherapy.

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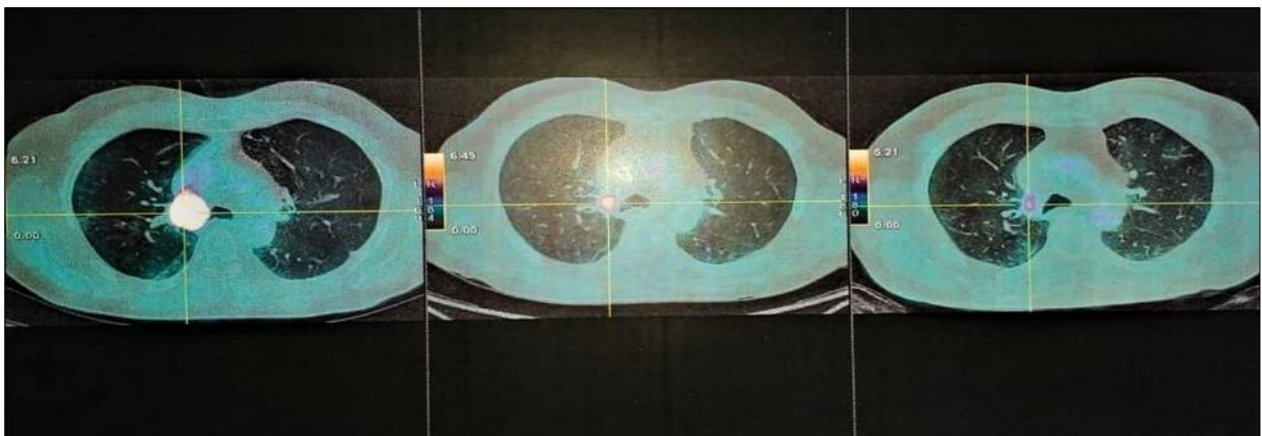


**Figure 1** Computed tomography of the thorax demonstrating tumor process mediastino-pulm right parahilar

After 03 courses of palliative chemotherapy radiological progression, the file was discussed in a multidisciplinary consultation meeting whose collegial decision was to start a systemic treatment based on immunotherapy given its availability after , patient was put on Atezolizumab in monotherapy in 2nd line for 3 months ( Image 2), with good overall tolerance in the assessment, no toxicities between cures, and radiologically partial response after 3 cures followed by a complete response after 06 cures ( Image 3),

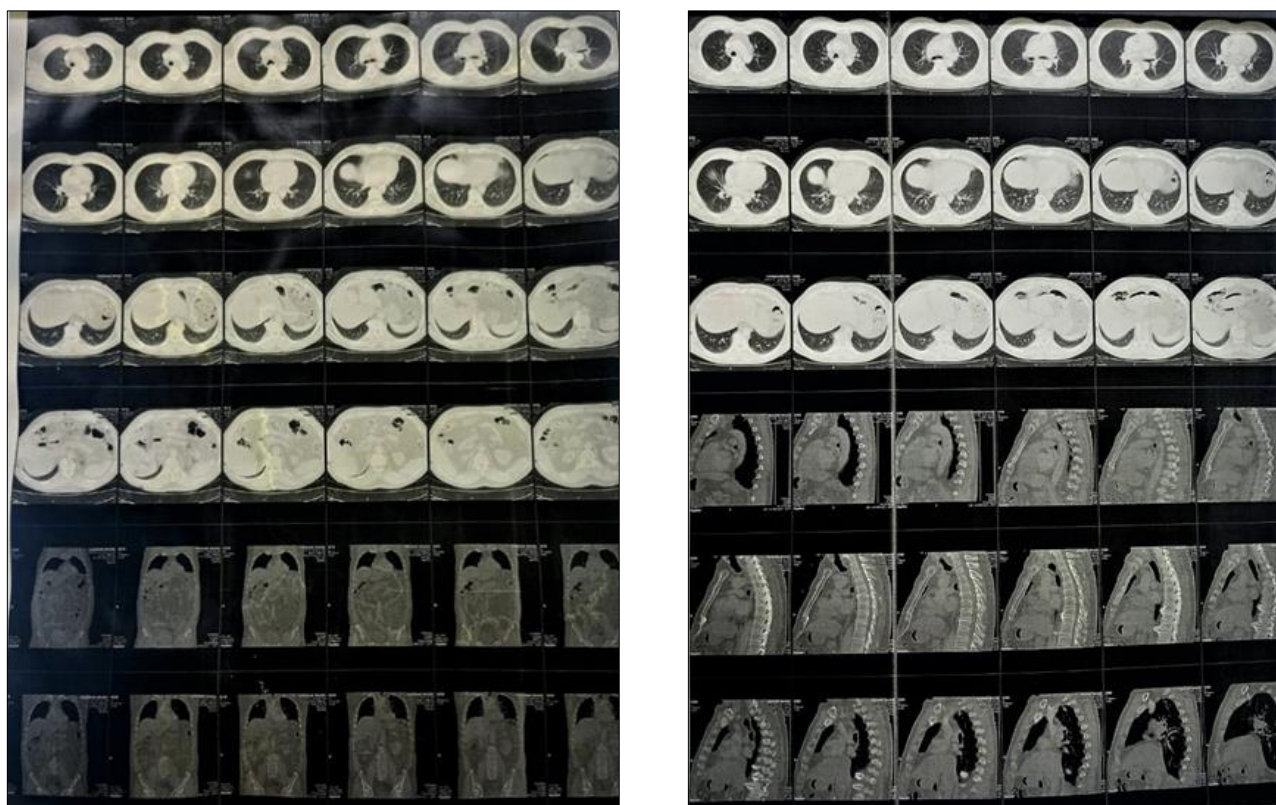


**Figure 2** Evaluation with Tepscan showing the partial response after three sessions of Atezolizumab



**Figure 3** Tepscan showing an complete response after 6 months of treatment

The last evaluation still in complete remission and in excellent general condition after 14 cures of Atezolizumab (Image 4),



**Figure 4** The last two CT evaluations objectivated a complete remission

### 3. Discussion

Worldwide, lung cancer is the leading cause of cancer death with an incidence of 2.3 million new cases (in 2020), increasing among women. In Morocco according to the large register of greater Casablanca (RGCC 2008 -2012) first cause of death by cancer in men, the third cause of death by cancer in women after breast cancer, the incidence is constantly increasing: Frequency 23%. Adenocarcinoma has become more common than squamous cell carcinoma, probably due to changes in toxic habits, particularly the composition of cigarettes. More than half of patients are diagnosed at advanced stages due to the indolent and asymptomatic nature of the disease. The question that opposes why this immunotherapy works in certain localizations and others not, the answer is in the publication Hedge et al: it is the presence of the concept of important inflammation in certain types of cancers the case of cancer non-small cell bronchial, kidney cancer and melanoma and other localization are weakly immune or so-called immune desert the case of cancer of prostate, and breast cancer with positive hormone receptors [1].

Regarding PDL-1 is a predictor of response in NSCLC and at the same time is a prognostic factor. The search for oncogenic drivers, in particular EGFR, ALK and ROS1, must be done systematically in parallel with the IHC PDL-1. Despite the success of clearly demonstrated first-line immune checkpoint inhibitors used either as monotherapy or in combination with chemotherapy or with targeted therapy, most patients with advanced NSCLC without oncogenic addiction accessible to these drugs will be confronted with a progression of the disease and therefore transition to a second line of therapy either by immunotherapy in monotherapy or palliative chemotherapy in the event of inaccessibility with Docetaxel for example compared initially in monotherapy with supportive care with a tolerance of 75 mg/m<sup>2</sup>, the results of which were in favor of prolonging survival [2] The idea in general of second-line immunotherapy is to replace palliative chemotherapy with Taxotere by immunotherapy, benefit clearly demonstrated with 4 pivotal studies with 3 molecules with almost the same design: Pembrolizumab in keynote 010, Nivolumab in checkmate 017/057 and Atezolizumab in the OAK trial[3.4] .This last study included patients regardless of histological type, regardless of PD-L1 status. An initial analysis of the data, carried out on the first 850 patients included (out of the 1,225 included in total), showed a significant improvement in overall survival in the group treated with atezolizumab, with a median of 13.8 versus 9.6 months (HR = 0.73; IC95: 11.8-15.7; p = 0.0003) with more benefit in case of PDL 1 expression a median overall survival was 15.7 months [5]. In terms of safety in the princeps trials, Nivolumab, Pembrolizumab and Atezolizumab presented a better safety profile than that of Docetaxel, as is the case with our patient, no toxicities were observed during treatment. Other biomarkers beyond PDL-1 currently being evaluated include the

example of the intestinal microbiota which is made up of billions of microorganisms, including many bacteria, which live permanently in the intestines, several works in progress including the goal is to diagnose quickly by specific tests or improvement of the intestinal flora, Lurienne et al demonstrate in their article the impact of the prescription of antibiotics on the response to immunotherapy in patients who have had recourse to antibiotic therapy in the month preceding the treatment leads to a reduction in the benefit of immunotherapy another explanation is that in patients who have had a lot of recourse to antibiotic therapy and corticosteroid therapy are immediately altered patients [6].

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#### **4. Conclusion**

The advent of immunotherapy to revolutionize the management of metastatic NSCLC in the face of the complexification of knowledge, the problem of therapeutic choice opposes, it is necessary to be demanding on the clinical benefit and the quality of life of the patient, Chemotherapy remains however a therapeutic option in the event of inaccessibility the prospect for the future is in the direction of improving the selection of patients (biomarker beyond PDL1) in view of the benefit of antiPDL-1/anti PD-1 currently demonstrated in second lines the same molecules tested in the first lines with spectacular results we find ourselves with a new desert of the second line [6].

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#### **Compliance with ethical standards**

##### *Acknowledgments*

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##### *Disclosure of conflict of interest*

The authors declare no conflict of interest.

##### *Statement of ethical approval*

The present research work does not contain any studies performed on animals/humans subjects by any of the authors.

##### *Statement of informed consent*

Informed consent was obtained from the patient.

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#### **References**

- [1] Hedge et al Immunity 52, January 14, 2020.
- [2] FA Shephred et al : Prospective randomized trial of docetaxel versus best supportive care in patients with non-small-cell lung cancer previously treated with platinum-based chemotherapy : 2000 May;18(10):2095-103.
- [3] Roy S Herbst et al Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial December 19, 2015.
- [4] Leora Horn et al Nivolumab Versus Docetaxel in Previously Treated Patients With Advanced Non-Small-Cell Lung Cancer: Two-Year Outcomes From Two Randomized 2017 Dec 10; 35(35):3924–3933.
- [5] Rittmeyer A et al Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial Lancet 2017;389:25
- [6] Lise leurienne et al : NSCLC Immunotherapy Efficacy and Antibiotic Use: A Systematic Review and Meta-Analysis July 2020, Pages 1147-1159.