Comparing overall survival outcomes of patients treated with immunotherapy ± chemotherapy, or chemotherapy ± radiation for non-small cell lung cancer (NSCLC)

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Introduction

Non-small cell lung cancer accounts for 85% of all lung cancer (Carbone 2015). Traditionally, non-small cell lung cancer has been treated with chemotherapy or surgery. Various immunotherapies such as CTLA-4 inhibitors were integrated into NSCLC treatment however chemotherapy remained first line treatment until around 2015 when PDL-1 immune checkpoint immunotherapy was introduced and for many patients became the standard first line treatment (*id*).

Non-small cell lung cancer has traditionally been referred to as a nonimmunogenic disease due to the lack of response of the immune system to it. One of the mechanisms through which the tumor cells develop immune resistance is through the PD-1 pathway (Carbone 2015). Through the upregulation of PD-1 receptor (which binds programmed death ligand PD-L1 and PD-L2), an inhibitory signal is given during the effector phase of the T cell response (*id*). This results in a decreased production of cytokines, specifically IL-2 as well as decreased cell proliferation and signals for cell survival; another effect of PD-1 and PD-L1 binding is the inhibition of the T-cell receptor, which results in a stop signal to occur altering the amount of time T cells contact the target cells and antigen presenting cells (*id)*. Through oncogenic signaling within the tumor cells themselves and resultant increased expression of PD-1 receptors, tumor cells gain a survival advantage (*id)*. Immunotherapies such as Nivolumab and pembrolizumab target PD-1 (Carbone 2015). PD-1 blockers allow for a boosted immune response against cancer cells, slowing tumor growth. PD-1 inhibitors Nivolumab and pembrolizumab were introduced in 2015 as second line therapy for NSCLC (*id)*.

A few research studies comparing outcome differences between patients receiving immunotherapy versus patients who did primarily chemotherapy as first line treatment indicate increased survival benefit, however, as immunotherapy is still relatively new, longer term survival benefit is continuing to be deliniated.
Current knowledge indicates that immunotherapy improves progression free survival compared to cytotoxic chemotherapy; in one study, 5 year survival rate was shown to increase by 25% in patients who had a high expression of PD-L1 (Arbour 2019).

Aims and Objectives

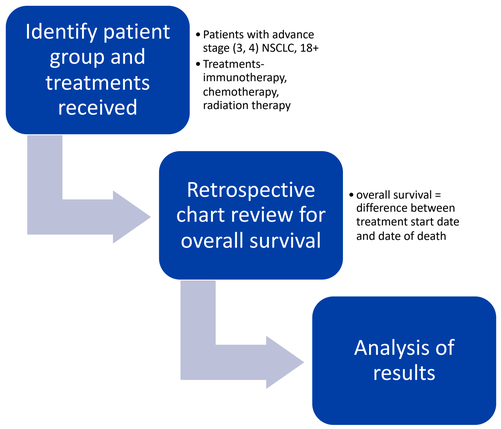
Identify and compare differences in survival between patient's given immunotherapy with or without chemotherapy/radiation versus chemotherapy with or without radiation at 3- and 5-years follow-up.

Methods

Retrospective chart review of patients with Non-Small Cell Lung Cancer NSCLC. The study will be using data from patients treated with non-small cell lung cancer through the Beaumont Health System between January 1, 2010 to December 31, 2018. A retrospective chart review is being done as the main purpose of the study is to determine 3 year-5 year outcomes following the initiation of immunotherapy for NSCLC and compare it the to the outcomes of patients who received chemotherapy (most patients prior to 2015). It is important to note that in some cases, patients may have been started on chemotherapy for a short period of time until treatment was decided upon and immunotherapy was initiated; these patients will be placed in the immunotherapy group as this was ultimately decided upon as the main course of treatment.

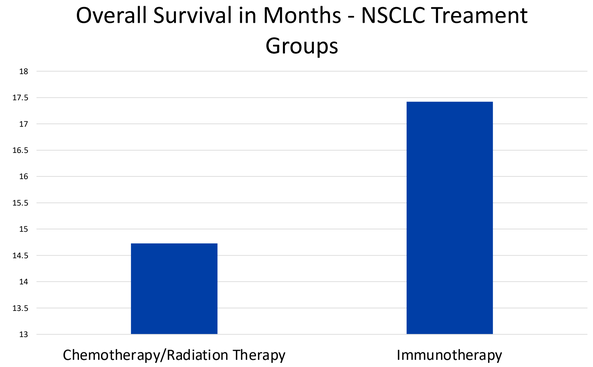
Inclusion criteria: patients on immunotherapy only, immunotherapy/chemotherapy combination, and chemotherapy only; advance stage (stages 3 and 4) NSCLC; age 18 or older.

Variables of interest:
Age of patient in years
Date of cancer diagnosis
Date of death
Time from diagnosis to death in months
Staging, T, N, M
Cancer Treatment (immunotherapy or immunotherapy/chemo, chemo or chemo/radiation only)



Results

Out of 173 patients analyzed, 86 were in the immunotherapy+chemotherapy group [Immunotherapy] while 87 were in the chemotherapy+radiation group. The immunotherapy ± chemotherapy group showed an increased overall survival [difference between treatment start date and date of death] with a mean of 17.42 months or 533.23 days compared to the chemotherapy ± radiation therapy group with a mean of 14.73 months or 448.53 days. P-value=0.22

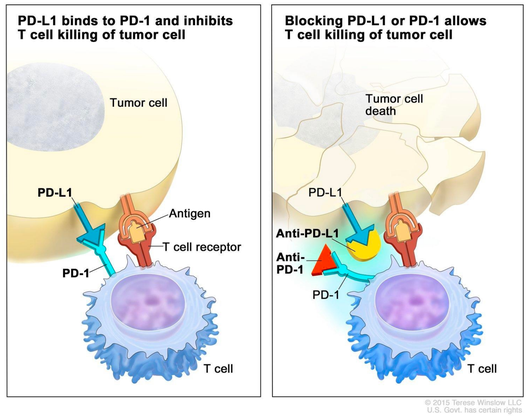


Conclusions

Based on the results of the study there was an improved overall survival group receiving immunotherapy for their NSCLC compared to chemotherapy for NSCLC however, the difference was not statistically significant with a p-value of 0.22. The results were however limited due to sample size. Statistically significant results were seen in randomized control trials that compared immune modulator therapy against PD1 receptors compared to traditional chemotherapy. A study found that there was a significantly higher survival rate when compared to platinum based chemotherapy agents (Ferrara 2021). In the immunotherapy group the median survival was 26.3 months vs 13.4 months for chemotherapy alone. It has also been shown that immunomodulatory therapy has been shown to improve progression free survival rates for patients, meaning the disease does not progress as rapidly when on immunomodulatory therapy (Reck 2016). When looking at mortality in this study the adverse outcomes were not evaluated. The Ferrara study additionally evaluated adverse outcomes using the CTCAE v 5.0 scale and found that patients on immunomodulatory therapy reported fever grade 3-5 adverse outcomes when compared to patients on chemotherapy alone.

Conclusions Cont.

In the immunomodulatory group the rate of grade 3-5 adverse outcomes occurred only 26.6% of the time whereas in the chemotherapy group it would occur 53.3% of the time (Reck 2016). In conclusion, the results of this study along with other evaluating the effectiveness of immunotherapy vs chemotherapy have shown an overall decrease in mortality along with fewer adverse health outcomes in patients receiving immunotherapy for treatment of their non small cell lung cancer.



References

Carbone DP, Ciernik IF, Kelley MJ, et al. Non-small-cell lung cancer: role of the immune system and potential for immunotherapy. J Thorac Oncol. 2015;10(7):974-984. doi:10.1097/JTO.0000000000000551.

Arbour KC, Riely GJ. Systemic therapy for locally advanced and metastatic non-small cell lung cancer. JAMA. 2019;322(8):764. doi:10.1001/jama.2019.11058.

Ferrara R, Imbimbo M, Malouf R, Paget-Bailly S, Calais F, Marchal C, Westeel V. Single or combined immune checkpoint inhibitors compared to first-line platinum-based chemotherapy with or without bevacizumab for people with advanced non-small cell lung cancer. Cochrane Database Syst Rev. 2021;4:CD013257. doi:10.1002/14651858.CD013257.pub3. Accessed May 1, 2023.

Reck M, Rodríguez-Abreu D, Robinson AG, et al. Pembrolizumab versus chemotherapy for PD-L1-positive non-small-cell lung cancer. N Engl J Med. 2016;375:1823-1833.

National Cancer Institute. (2023, April 14). Checkpoint Inhibitors to Treat Cancer. Retrieved May 9, 2023, from https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/checkpoint-inhibitors

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