Digital Approaches to Analyzing Evidence in Support of Personalized Oncology Guidelines

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BACKGROUND

Researchers know that cancer is not one disease, but many. One promising new therapeutic approach is immuno-oncology, which is a treatment modality that uses immunotherapies designed to target and harness patients' immune systems to kill tumor cells. Thirty years of research has demonstrated that the immune system recognizes tumors and immuno-surveillance can stop or control them from spreading. While immuno-oncology is still an evolving field, it has shown promising results in patients with metastatic melanoma, which have traditionally been treated with limited success using chemotherapy.

OBJECTIVES

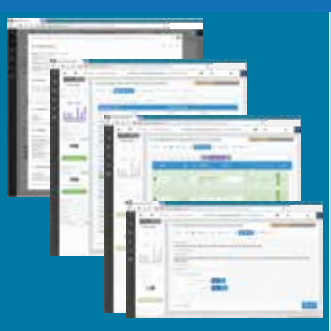
To demonstrate how a targeted systematic review including subgroup analyses can be used to inform personalized clinical practice guidelines by evaluating the efficacy of immunotherapy drugs for treating melanoma patients.

METHODS

We performed a systematic review of the literature for immunotherapy drugs for patients with any type of cancer. We conducted searches in PubMed and Embase for studies published from 2005 to March 2016. After removing duplicates, we identified 3,828 studies, which were then reviewed for inclusion and categorized in our library system (DOC Library) by cancer type and drug type. Studies addressing melanoma were identified and further reviewed for relevance. Ultimately, 26 randomized controlled trials that examined the use of immunotherapy drugs for patients with melanoma were extracted and digitized in our system (DOC Data).

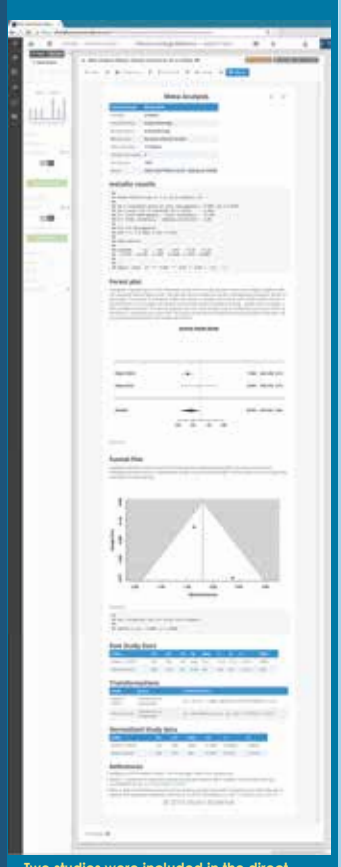
We used our Bayesian network meta-analysis tool to perform an indirect analysis and calculate odds ratios comparing overall survival for patients who received immunotherapy drugs in combination with chemotherapy to chemotherapy alone or immunotherapy alone.

Overall Survival IO vs IO+ Chemo vs Chemo



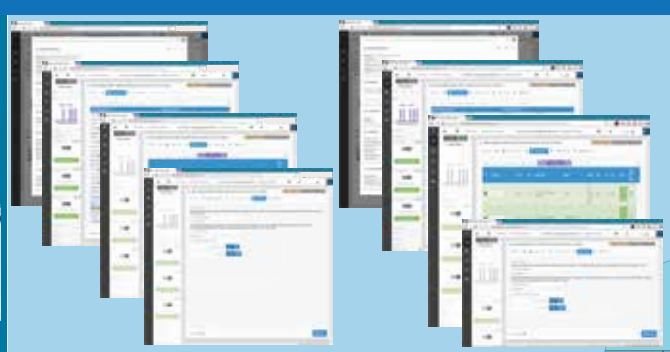
A direct meta-analysis was also performed using the generic inverse variance method to create a pooled estimate of the hazard ratios for overall survival for the immunotherapy and chemotherapy groups.

Overall Survival IO vs Chemo



Two studies were included in the direct meta-analysis comparing immunotherapy to chemotherapy. There was a statistically significant difference in risk of death in patients who received immunotherapy compared to patients who received chemotherapy (0.4977, 95% CI 0.27 - 0.92, p=0.0248).

There were 5 studies that reported on overall survival at one year for patients who received either an immunotherapy drug alone, in combination with chemotherapy, or chemotherapy alone. Based on the results from the network meta-analysis of the 5 studies, melanoma patients who received either an immunotherapy drug alone or an immunotherapy drug in combination with chemotherapy were more likely to be alive after one year of treatment compared to patients that received chemotherapy alone. Patients who received an immunotherapy drug were 2.1 times more likely to still be alive after one year compared to chemotherapy patients and patients that received combination therapy were 1.8 times more likely to be alive after one year of treatment than patients that received chemotherapy.



Subgroup analyses was performed using the hazard ratios of overall survival for melanoma patients with metastasis stages M0, M1a, or M1b, and stage M1c. The random effects model was used for the network and direct meta-analyses.

M0, M1a, M1b Overall Survival IO vs Chemo

Similar results favoring immunotherapy over chemotherapy were found in the 2 studies that reported on the M0, M1a, M1b subgroup (0.3703, 95% CI 0.17 - 0.79, p=0.0108.

M1c Overall Survival IO vs Chemo

A statistically significant difference was also found when the M1c subgroup was analyzed (0.4952, 95% CI 0.34 - 0.72, p=0.0003).

DISCUSSION

Doctor Evidence provides systematic review authors and guideline developers with a centralized system for cataloging studies identified in a systematic literature search, for storing data extracted from included studies and for analyzing data from digitized studies. The goal of this review was to demonstrate how the Doctor Evidence system can be used to synthesize evidence in a quickly evolving field of medicine such as immuno-oncology. As additional studies addressing immunotherapy for melanoma patients become available, they can be added to our digitized system and the saved analyses and subgroup analyses can be quickly updated. Since this project only included RCTs, there were a limited number of studies comparing overall survival for cancer patients receiving immunotherapy as a combination therapy with chemotherapy or immunotherapy alone to chemotherapy. This also extended to the subgroup analyses, the original plan was to examine overall survival for patients with specific biomarkers, however there were not enough studies examining this subgroup, so we were limited to examining metastasis stage instead. As this field continues to grow, hopefully future research will report on overall survival stratified by biomarkers so that additional subgroup analyses on biomarkers will be possible.

IMPLICATIONS FOR GUIDELINE DEVELOPERS/USERS

Using a digitized system such as Doctor Evidence allows guideline developers to quickly synthesize evidence from a systematic review to formulate recommendations that can be used in evidence-based clinical practice guidelines. This allows guideline developers to further dive into the data and perform analyses on specific population groups such as race, gender, age, and other patient characteristics, facilitating the development of more personalized guidelines.

DOCTOR EVIDENCE