

## Personalized multimodality therapy with immune checkpoint inhibitors, chemotherapy, and targeted treatment (ICTriplex) in advanced/refractory cancer.

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- **Abstract**

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**Background:**

Advanced/refractory malignancies are associated with poor prognosis and their treatment remains a major challenge. The combination of immune checkpoint inhibitors (ICI) and chemotherapy (CT) has been shown in some cancers to be superior to chemotherapy alone. In our treatment program (ICTriplex), targeted therapy (TT) was added to this combination for the treatment of these diseases, as these three approaches have convergent efficacy but divergent toxicity. Our initial data was previously reported in ASCO 2019 (abstract e14254) and ASCO 2020 (abstract e15150).

**Methods:**

Treatment was highly personalized and was tailored to the individual patient depending on diagnosis, prior therapy, and genomic profiling. Between April 2016 and January 2022, 41 patients with advanced malignancies were treated. The median age was 59 years (range 17-78). 24 patients were female. The Median Eastern Cooperative Oncology Group Performance Status was 2 (range 0-4). Tumor types included; lung (10), pancreas (7), colorectal (4), cholangiocarcinoma (3), breast (3), ovarian (2), Glioblastoma (2), cervical (2), sarcoma (2), melanoma (2), Hodgkin's (1), gallbladder (1), thymoma (1), and gastric (1). PDL-1 status was positive in 10, negative in 16 and unknown in 15. 32 patients received prior therapy. Of these, 9 received ICI, 14 received TT, and 31 received chemotherapy for a median of 2 regimens (range 1-11). In ICTriplex, the ICIs used were Pembrolizumab in 14, Nivolumab in 12, and Atezolizumab in 7. 8 patients received dual ICI with ipilimumab. Combination chemotherapy including platinum was used in 21 patients, taxanes in 17, and gemcitabine in 24. TT included 18 agents with erlotinib in 9 and bevacizumab in 8. Response was evaluated by both PET/CT and CT scans. A complete response was achieved when all metabolic activity had resolved.

**Results:**

A complete response (CR) was achieved in 19 patients (46.3%), and a partial response (PR) in 16 (39%), with a total response rate of 85.3%. All but 2 patients had response. Of the 10 patients with lung cancer, 7 had CR, and 3 of them had a duration of response of more than 30 months. Also, 3 of the complete responders with brain metastases achieved intracranial CR by MRI without radiation. 2 patients with pancreatic cancer had a response duration of more than 30 months. Regarding side effects, 2 patients died of pulmonary complications possibly due to treatment. There were no other unexpected side effects.

**Conclusions:**

ICTriplex therapy is highly effective in advanced/refractory cancer and therefore should be considered when standard therapy fails, as well as for patients for whom standard therapy is not available.