systemic anti-PD1 was able to significantly improve abscopal effect in 344SQR murine metastatic lung cancer model, most of the mice eventually died due to the growth of secondary tumors. Therefore, we intended to use HD-XRT plus NBTXR3 injection into primary tumors and low-dose (LD) radiation on secondary tumors plus dual-agent immunotherapy (IT) of anti-PD1 and anti-CTLA-4 to achieve complete control of both the primary and secondary tumors in mice.

Methods Five groups of 8 mice each were inoculated subcutaneously with $5 \times 104$ anti-PD1-resistant 344SQR cells in each hind leg, 3 days apart, to establish ‘primary’ (right) and ‘secondary’ (left) tumors. All mice in treatment groups received intraperitoneal anti-PD1 and anti-CTLA-4 on days 4, 7, 10, and 13, and continuing anti-PD1 treatment on days 20, 27, 34, 41, and 49 and 12Gy x3 (HD-XRT) to the primary tumors on days 7, 8, and 9. Primary tumors in groups 3 and 5 also received intratumoral NBTXR3 on day 6. Secondary tumors in groups 4 and 5 were also irradiated with 1Gy x2 (LD-XRT) on days 12 and 13. Experimental groups were designated as 1=Control, 2=HD+IT, 3=NBTXR3+HD+IT, 4=HD+LD+IT, and 5=NBTXR3+HD+LD+IT. The secondary tumors were analyzed by flow cytometry and Nanostring. On day 178, the survivor mice were rechallenged with $5 \times 104$ 344SQR cells on the right flank and the tumor growth was monitored for an additional 36 days.

Results All mice in all the groups except NBTXR3+HD+LD +IT died due to the growth of either the primary tumor or the secondary tumor by day 36. Both the primary and the secondary tumors in 4 mice of NBTXR3+HD+LD+IT group were completely eliminated. No tumor growth was observed in these mice after rechallenged with 344SQR cells. Flow cytometry data demonstrated that only the mice in the groups with NBTXR3 had significantly more CD8+ T cell infiltration in the secondary tumor collected on day 16 than the control. Both flow cytometry and Nanostring data showed that only the mice in NBTXR3+HD+LD+IT had a significantly higher CD8+/T-cell/Treg cell ratio than the control.

Conclusions The combination of NBTXR3 plus high and low dose radiation with immunotherapy effectively controlled the growth of both primary and secondary tumors, significantly extended the survival, generating long-term antimouse tumor memory. This combination therapy induced immune-mediated control of the secondary tumor at both genetic and cellular levels.

Acknowledgements This work was supported by Cancer Center Support (Core) Grant CA016672 to The University of Texas MD Anderson Cancer Center; the Goodwin family research fund; the family of M. Adnan Hamed and the Orr Family Foundation to MD Anderson Cancer Center’s Thoracic Radiation Oncology program; an MD Anderson Knowledge Gap award; Nanobiotix.

References


Abstracts

CARBOPLATIN, PACLITAXEL AND PEMBROLIZUMAB FOR THE FIRST LINE TREATMENT OF RECURRENT AND/OR METASTATIC HEAD AND NECK SQUAMOUS CELL CARCINOMA

Angelica Valadex*, Madeleine Welsh, Christine Kim, Angela Johns, Alain Alpazi, Hyunseok Kang, Hyunseok Kang. University of California, San Francisco, San Francisco, CA, USA

Background A recent phase III study (Keynote-048) demonstrated survival benefit of platinum, 5-FU and pembrolizumab in 1st line treatment of recurrent and/or metastatic head and neck squamous cell carcinoma (RM-HNSCC).1 However, administration of 5-FU has been a challenge for logistics and toxicities. As platinum, paclitaxel and pembrolizumab has been shown to be an effective and safe treatment for non-small cell lung cancer,2 we hypothesized that carboplatin, paclitaxel and pembrolizumab would be safe and effective for 1st line treatment of RM-HNSCC.

Methods We performed a retrospective study of RM-HNSCC patients who received carboplatin, paclitaxel and pembrolizumab for first line systemic therapy, treated between December 2015 and January 2020 at the University of California, San Francisco. Patients who received at least 1 cycle of treatment with pre-treatment and post-treatment images were included in the analyses. Response to the treatment was assessed using RECIST criteria version 1.1. We also estimated overall survival and progression free survival using Kaplan-Meier method.

Results Nine patients who received carboplatin, paclitaxel and pembrolizumab as first line systemic therapy for RM-HNSCC were identified. Two patients had HPV positive oropharyngeal SCC, the other patients unknown primary SCC in head and neck (2), oral cavity SCC (2), laryngeal SCC (1), hypopharyngeal SCC (1) and SCC of orbit (1). There were 1 complete response (CR, 11%), 6 partial responses (PR, 55%), 1 stable disease (SD, 11%) and 1 progressive disease (PD, 11%). Overall response rate (ORR) was 78%, and median progression free survival and median overall survival have not reached with median follow-ups of 6 months and 8 months, respectively. Two patients discontinued chemotherapy after 1 cycle for grade 4 acute kidney injury and grade 4 anaphylaxis, yet achieved CR and PR, respectively.

Conclusions The retrospective analysis suggests that first line carboplatin, paclitaxel and pembrolizumab for RM-HNSCC is an active regimen and can be considered in place of platinum, 5-FU and pembrolizumab, which merits further investigation.

Ethics Approval The study was approved by UCSF’s Institutional Review Board, approval number 19-29363.

REFERENCES


http://dx.doi.org/10.1136/jitc-2020-SITC2020.0201

IN VITRO AND IN VIVO COMBINATION THERAPY OF LOW MOLECULAR WEIGHT HEPARINS, CHEMOTHERAPY AND IMMUNOTHERAPY, INDUCE ANTITUMOR ACTIVITY IN PANCREATIC CANCER

1Michalis Karamouzis*, 1Michalis Karamouzis, 1Panagiotis Sarantis, 2Evangelos Koustas, 1Adriana Papadimitropoulou, 2Panatos Papakotoulas, 2Alexandros Bokas, 2Dimitrios Schizas, 2Alexandros Papalampos, 2Evangelos Filiekouras, 2Theodoros Liakakos, 1Athanasios Papavassiliou, 2Medical School of Athens, Athens, Greece; 2Medical School UOA, Athens, Greece; 2BRFAA, Athens, Greece; 2Thrigas Hospital, Thessaloniki, Greece

Background PDAC is recognized as a highly thrombogenic tumor; thus, low-molecular-weight heparin (LMWH) is routinely used for PDAC patients. Based on the combinatorial therapy approach to treating highly malignant and refractory cancers such as PDAC, we hypothesized that LMWHs could augment the effectiveness of immune checkpoint inhibitors and induce an efficient antitumoral activity.1

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0201

202