Abstracts

643 AUTOPSY REVIEW OF CHIMERIC-ANTIGEN RECEPTOR T CELL THERAPY: A SINGLE INSTITUTION EXPERIENCE

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Background Our institution has treated over 300 patients with chimeric antigen receptor (CAR) T-cell immunotherapy (CAR T-cell therapy) since 2013. Phase I and II trials were primarily based on heavily treated patients with B cell acute lymphoblastic leukemia (B-ALL), aggressive diffuse large B cell lymphoma (DLBCL), and multiple myeloma (MM) who had failed multiple lines of prior chemotherapy and/or hematopoietic stem cell transplantation (HSCT). In these relapsed and/or refractory patients, CAR-T therapy resulted in complete remission in 93% of B-ALL, 60% of DLBCL, and ~80% of MM. Our Pathology Group at Fred Hutch have reviewed and diagnosed in rare instances as in the patients summarized in this study. Infection, CRS with ICANS are the most common causes of death in our single institution study.

Methods A search for all autopsies conducted on patients treated with CAR T-cells. Three patients (Patients 1, 4, 9) had progression of disease that attributed to cause of death.

Conclusions CAR T-cell therapy is a highly effective treatment even for patients who have relapsed and/or refractory disease. Post-therapy complications range in severity and may be fatal in rare instances as in the patients summarized in this study. Infection, CRS with ICANS are the most common causes of death in our single institution study.

Ethics Approval The study was approved by Fred Hutchinson Cancer Research Center’s Institutional Review Board, approval number 1837

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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644 OCULAR ADVERSE EVENTS ASSOCIATED WITH PROGRAMMED DEATH-1 AND PROGRAMMED DEATH LIGAND-1 IMMUNOTHERAPY

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Background The programmed death-1 (PD-1) and programmed death ligand-1 (PD-L1) inhibitors are increasingly studied and are known to have unique inflammatory side effects due to non-specific immune system activation.1 While rare, PD-1/PD-L1 inhibitors can cause ocular toxicities, including inflammatory eye disease.2 However, these ocular adverse events are less well-studied.

Methods This was a retrospective review of two adverse event (AE) monitoring databases maintained by the National Cancer Institute’s Cancer Therapy Evaluation Program (CTEP), one of the largest public sponsors of clinical trials worldwide. One database (CTEP-AERS) is used for study sites to expeditiously report serious AEs for potential FDA review, while the other database (CDUS) is updated quarterly to reflect all the adverse events from the Phase 1 and Phase 2 trials in the CTEP network.

Results The two adverse event databases were queried for ocular adverse events up to May 19, 2020. A total of 331 adverse events from 259 patients were found. 73 patients (28%) were exposed to nivolumab, 117 patients (45%) were exposed to combination nivolumab and ipilimumab, 41 (16%) were exposed to pembrolizumab, 26 (10%) were exposed to atezolizumab, and 2 (0.8%) were exposed to durvalumab. 59 adverse events from 47 patients were reported by the study timelines, microbiology data, cytokine levels, other pathology biopsies, and pertinent laboratory values. Histologic tissues were reviewed.

Results Twelve autopsies were performed since 2013. Patient characteristics and causes of death are summarized in table 1. The most common cause of death was due to infectious causes (n=6). Two patients (Patients 10 and 11) had cardiovascular related deaths. Six patients (Patients 1, 2, 6, 7, 10, 12) suffered from CRS in their post-infusion course, four of whom (Patients 1, 2, 7, 10) had CRS directly attributed as the cause of death. CRS was further complicated by immune effector cell-associated neurotoxicity syndrome (ICANS) in 5 patients (Patients 1, 5, 6, 7, and 12). CRS with ICANS was the second most common cause of death in patients treated with CAR T-cells. Three patients (Patients 1, 4, 9) had progression of disease that attributed to cause of death.

Conclusions CAR T-cell therapy is a highly effective treatment even for patients who have relapsed and/or refractory disease. Post-therapy complications range in severity and may be fatal in rare instances as in the patients summarized in this study. Infection, CRS with ICANS are the most common causes of death in our single institution study.

Ethics Approval The study was approved by Fred Hutchinson Cancer Research Center’s Ethics Board, approval numbers 1837, 9364

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