CAR-T-cell-Related Encephalopathy Syndrome: High Rates of Neurotoxicity in Clinical Practice
Carlen Yuen1, Andrew Artz1, Deric Park1, Thomas Kelly2, Shasha Wu1, Anthony Reder1, Kourosh Rezania1, Betty Soliven1, Tao Xie1, James Mastrianni1, Satyajit Kosuri1, Peter Riedell1, Michael Bishop1
1University of Chicago, 2Univ Of Chicago Dept Of Neurology

Objective: To describe clinical features of Chimeric Antigen Receptor T cell (CAR-T-cell) Related Encephalopathy Syndrome (CRES) to better understand the clinical features to potentially permit instituting earlier treatment and supportive care.

Background: CRES is a known adverse event associated with CAR-T-cell therapy. Predictive modeling is essential for early identification and prevention of severe CRES.

Design/Methods: In this retrospective study, 26 patients with relapsed refractory diffuse large B cell lymphoma (DLBCL) who received commercial CAR-T cell therapy (25 axicabtagene ciloleucel [Yescarta®], 1 tisagenlecleucel [Kymriah®]) were assessed for CRES (CTCAE criteria), increased intracranial pressure (ICP), CSF abnormalities, CNS endothelial compromise, seizures and encephalopathy.

Results: Twenty-three patients developed CRES of any grade (I 43%, II 22%, III 17%, IV 17%). On average, CRES developed on Day 6 after CAR-T infusion (ranging from Day 1 to 13), resolving between 1 day to remaining unresolved. Death from disease progression occurred in 15%. Older age (average age 61 vs 52), male gender (65%), psychosis (9%), exclusive dysgraphia (22%), elevated OP (>20mmHg, 23%), and triphasic waves (25% of EEGs), were associated with severe (Grade III and IV) CRES. Tremulousness was the most common first sign of neurotoxicity (74%), followed by dysgraphia (61%), disorientation (48%), dyscalculia (48%), and dysnomia (30%).

Headache (74%) was noted in CRES of all grades. Of 13 who received lumbar punctures, 77% had lymphocytic pleocytosis and 85% had elevated protein. Of 12 patients who obtained EEG, findings of encephalopathy (75%), and Frontal Intermittent Rhythmic Delta Activity (17%) were noted. Of 13 who had brain MRI wwo, none showed enhancement. Abnormal average CARTOX-10 scores (Neelapu et al. 2017) were CRES Grade I 9.9, II 7.8, III 5.5, IV 4.9.

Conclusions: Off-protocol CAR-T for DLBCL results in a high frequency of CRES and heterogeneous presentations. Most patients recover. Additional studies on the value of baseline predictors are warranted.